MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Government

Immunisation Handbook 2020

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While the information and advice included in this publication are believed to be correct, no liability is accepted for any incorrect statement or advice. No person proposing to administer a vaccine to any other person should rely on the advice given in this publication without first exercising his or her professional judgement as to the appropriateness of administering that vaccine to another person.

Feedback

Comments on this book and suggestions for future editions are invited, to enhance the usefulness of future editions. These should be sent to the Manager Immunisation, Ministry of Health, at the address below.

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Foreword

With the publication of the *Immunisation Handbook 2020* (the *Handbook*), I would once again like to sincerely thank everyone involved in supporting, promoting or delivering immunisations to the people of New Zealand. This *Handbook* has been designed as a comprehensive source of information on immunisation, to support you in the work you do.

Since the July 2017 edition of the *Handbook*, there has been one subsequent online edition, the 2017 (2nd ed) which included PHARMAC's revised vaccine eligibility criteria for certain individuals at increased risk of the relevant vaccine-preventable diseases. On 1 July 2020, further changes were made to the online *Handbook* to include PHARMAC funding for the tetanus, diphtheria and pertussis vaccine to be given at ages 45 years and 65 years and also a change to the pneumococcal vaccination (PCV10) primary series with the 3-month dose no longer required.

This 2020 edition of the *Handbook* covers the 1 October 2020 schedule and updates the disease chapters affected by this schedule change. These changes include a new immunisation event at age 12 months with the pneumococcal vaccination booster and the first measles, mumps and rubella vaccinations given at this event followed by the second measles, mumps and rubella dose, varicella and *Haemophilus influenza* type b vaccinations given at age 15 months. As well as the schedule changes several chapters and appendices have been reviewed and updated.

Never in our generation has there been a greater need to have high immunisation coverage than in 2020 when New Zealand and the world are dealing with the COVID-19 pandemic. To quote the World Health Organization 'Immunisation is one of modern medicine's greatest success stories. Vaccination has greatly reduced the burden of infectious diseases. Only clean water, also considered to be a basic human right, performs better'.

At a population level, the effects of increasing immunisation coverage are clearly discernible, with fewer cases of vaccine-preventable diseases as coverage increases. In New Zealand, we have seen significant decline in hepatitis B, *Haemophilus influenzae* type b, genital warts and, in infants, pneumococcal and rotavirus diseases since the introduction of vaccines. Closing our immunisation equity gaps is essential for all scheduled vaccinations if we are to continue to maintain high immunisation coverage and to maintain our measles elimination status. In July 2020 the Ministry of Health launched a one-year measles vaccination campaign with a focus on our known measles vaccination gap in those aged 15 to 29 years.

I congratulate the health community on the past immunisation achievements and encourage your ongoing commitment to improving immunisation coverage and reducing vaccine-preventable diseases in New Zealand. Pharmacists can now also assist with achieving this goal and in 2020 it has been particularly pleasing to see the number of funded influenza vaccinations given by pharmacist vaccinators has more than doubled those given in previous years.

Immunisation is an important opportunity for health professionals to interact with people from all walks of life: mothers with newborns, school-age children and adults either working or retired. Your attitude and the conversations you have with people affect their attitudes toward immunisation and their engagement with the health care system in general. We hope this *Handbook* will support your interactions with your patients and their families/whānau.

In closing, I would like to thank the members of the Handbook Advisory Group who updated the *Handbook*. I trust this edition, like its predecessors, will prove a valuable resource for health professionals.

Ngā mihi.

Dr Ashley Bloomfield
Director-General of Health

The Immunisation Handbook Advisory Group

The Immunisation Handbook Advisory Group provided expert technical and medical advice for the *Immunisation Handbook 2020*. The Ministry of Health wishes to thank them for their time and commitment during the *Handbook* rewrite and ongoing updates. The Handbook Advisory Group members are as follows.

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New Zealand epidemiology data

Information on New Zealand epidemiology is sourced from data collated by the Institute of Environmental Science and Research (ESR), on behalf of the Ministry of Health, or from Analytical Services, Ministry of Health.

For the most up-to-date epidemiological data, see the ESR Public Health Surveillance (**surv.esr.cri.nz**) and Ministry of Health (**www.health.govt.nz/nz-health-statistics**) websites.

Commonly used abbreviations

Ad26-CV	adenovirus (Ad26) viral vector COVID-19 vaccine
AEFI	adverse event following immunisation
AFP	acute flaccid paralysis
AIDS	acquired immunodeficiency syndrome
AIR	Aotearoa Immunisation Register
AOM	acute otitis media
BCG	bacillus Calmette–Guérin vaccine
CARM	Centre for Adverse Reactions Monitoring
CDC	Centers for Disease Control and Prevention
ChAd-CV	adenovirus (ChAdOx1) viral vector COVID-19 vaccine
CHD	congenital heart disease
COVID-19	coronavirus disease 2019
CPR	cardiopulmonary resuscitation
CRS	congenital rubella syndrome
cVDPV	circulating vaccine-derived polio virus
CVWUS	COVID-19 vaccinators working under supervision
DHB	district health board
DNA	deoxyribonucleic acid
DT	diphtheria tetanus vaccine
DTaP	diphtheria, tetanus and acellular pertussis vaccine
DTaP-IPV	diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
DTaP-IPV-HepB/Hib	diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
DTwP	diphtheria, tetanus and whole-cell pertussis vaccine
DTwPH	diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b vaccine
ESR	Institute of Environmental Science and Research
GBS	Guillain–Barré syndrome
GP	general practitioner
GSK	GlaxoSmithKline (New Zealand)
HAV	hepatitis A virus
HBcAg	hepatitis B core antigen
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immunoglobulin

HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HepA	hepatitis A vaccine
HepB	hepatitis B vaccine
Hib	*Haemophilus influenzae* type b
Hib-PRP	*Haemophilus influenzae* type b polyribosylribitol phosphate vaccine
Hib-PRP-T	conjugated with tetanus toxoid
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSCT	haematopoietic stem cell transplant
ICD	International Classification of Diseases
IFNAR	interferon alpha receptor
IG	immunoglobulin
IgG	immunoglobulin G
IM	intramuscular
IMAC	Immunisation Advisory Centre
IMID	immune-mediated inflammatory disease
IPD	invasive pneumococcal disease
IPV	inactivated polio vaccine
ISRR	immunisation stress-related response
irAE	immunisation-related adverse events
ITP	idiopathic thrombocytopenic purpura (also known as immune thrombocytopenia)
IV	intravenous
IVIG	intravenous immunoglobulin
LAIV	live attenuated influenza vaccine
Medsafe	New Zealand Medicines and Medical Devices Safety Authority
4CMenB	Four-component recombinant meningococcal B vaccine
MenACWY (-D or -TT)	quadrivalent meningococcal conjugate vaccine (conjugated to diphtheria toxoid or tetanus toxoid)
MenC	meningococcal C conjugate vaccine
MeNZB	meningococcal B vaccine
MMR	measles, mumps and rubella vaccine
MMRV	measles, mumps, rubella and varicella vaccine
mRNA	messenger ribonucleic acid
mRNA-CV	messenger RNA COVID-19 vaccine
MSD	Merck Sharp & Dohme (New Zealand)
NHI	National Health Index
NIR	National Immunisation Register
NTHi	non-typeable Haemophilus influenzae

NZBS	New Zealand Blood Service
OPV	oral polio vaccine
PAV	provisional authorised vaccinator
PCR	polymerase chain reaction
PCV7	7-valent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
23PPV	23-valent pneumococcal polysaccharide vaccine
PFU	plaque-forming unit
PHARMAC	Pharmaceutical Management Agency
PMS	practice management system (also known as patient management system)
PPE	personal protective equipment
PRP	polyribosylribitol phosphate
PSNZ	Pharmaceutical Society of New Zealand
PTAC	Pharmacology and Therapeutics Advisory Committee
QIV	quadrivalent influenza vaccine
RIG	rabies immunoglobulin
RNA	ribonucleic acid
rCV	recombinant spike protein COVID-19 vaccine
RV1	rotavirus vaccine (monovalent)
RV5	rotavirus vaccine (pentavalent)
rZV	recombinant zoster vaccine
SARS-CoV-2	serious acute respiratory syndrome coronavirus 2
SBVS	school-based vaccination system
SC	subcutaneous
SCID	severe combined immune deficiency
STI	sexually transmitted infection
SUDI	sudden unexpected death in infancy
TB	tuberculosis
Td	adult tetanus and diphtheria vaccine (formerly ADT-Booster)
Tdap	adult tetanus, diphtheria and acellular pertussis vaccine
TIG	tetanus immunoglobulin
TIV	trivalent influenza vaccine
TTS	thrombosis with thrombocytopenia syndrome
UK	United Kingdom
US	United States of America
VAERS	vaccine adverse event reporting system (US)
VAPP	vaccine-associated paralytic poliomyelitis
VFC	vaccinator foundation course

VHW	vaccinating health workers
VLP	virus-like particle
VV	varicella vaccine
VZV	varicella zoster virus
WHO	World Health Organization
WHO EUL	World Health Organization emergency use listing
ZIG	zoster immunoglobulin
ZV	zoster vaccine

Glossary of vaccine brand names and abbreviations

Generic abbreviation	Vaccine trade name	Sponsor	Target antigens or disease
Schedule and funded vaccines			
BCG	BCG Vaccine SSI	Serum Institute India	tuberculosis (TB)
4CMenB	Bexsero	GSK	group B recombinant meningococcal vaccine
DTaP-IPV	Infanrix-IPV	GlaxoSmithKline (GSK)	diphtheria, tetanus, acellular pertussis, inactivated poliovirus
DTaP-IPV-HepB/Hib	Infanrix-Hexa	GSK	diphtheria, tetanus, acellular pertussis, inactivated poliovirus, hepatitis B and *Haemophilus influenzae* type b
HepA	Havrix	GSK	hepatitis A
HepB	Engerix-B	GSK	hepatitis B
Hib-PRP-T	Hiberix	GSK	*Haemophilus influenzae* type b conjugated with tetanus toxoid
HPV9	Gardasil 9	MSD	human papillomavirus (9-valent)
IPV	IPOL	sanofi-aventis	inactivated poliovirus
QIV	Afluria Quad	Seqirus	influenza – quadrivalent
MenC	NeisVac-C	Pfizer	meningococcal group C conjugate
MenACWY-D	Menactra	sanofi-aventis	quadrivalent meningococcal vaccine conjugated with diphtheria toxoid
MMR	Priorix	GSK	measles, mumps, rubella
mRNA-CV	Comirnaty	Pfizer/BioNTech	COVID-19
PCV10	Synflorix	GSK	pneumococcal conjugate vaccine (10-valent)
PCV13	Prevenar 13	Pfizer	pneumococcal conjugate vaccine (13-valent)
23PPV	Pneumovax 23	Merck Sharp and Dohme (MSD)	pneumococcal polysaccharide vaccine (23-valent)
rCV	Nuvaxovid	Biocelect (for Novavax)	COVID-19
RV1	Rotarix	GSK	rotavirus

Generic abbreviation	Vaccine trade name	Sponsor	Target antigens or disease
rZV	Shingrix	GSK	zoster (shingles; varicella-zoster virus)
Tdap	Boostrix	GSK	tetanus, diphtheria and acellular pertussis
Tdap-IPV	Boostrix IPV	GSK	tetanus, diphtheria, acellular pertussis and inactivated poliovirus
VV	Varivax	MSD	varicella (chickenpox; varicella-zoster virus)
Other available vaccines (excluding travel vaccines)			
HepA	Avaxim	sanofi-aventis	hepatitis A
HepA-typhoid	Vivaxim	sanofi-aventis	hepatitis A and *Salmonella typhi*
HepB-HepA	Twinrix / Twinrix Junior	GSK	hepatitis A and B
MenACWY-T	Nimenrix	Pfizer	quadrivalent meningococcal vaccine conjugated with tetanus toxoid
MMR	M-M-R-II	MSD	measles mumps rubella
Tdap	Adacel	sanofi-aventis	tetanus, diphtheria and acellular pertussis
Tdap-IPV	Adacel-Polio	sanofi-aventis	tetanus, diphtheria, acellular pertussis and inactivated poliovirus
VV	Varilrix	GSK	varicella (varicella-zoster virus)

Introduction

The purpose of the *Immunisation Handbook 2020* (the *Handbook*) is to provide clinical guidelines for health professionals on the safest and most effective use of vaccines in their practice. These guidelines are based on the best scientific evidence available at the time of publication, from published and unpublished literature.

> The information contained within the *Handbook* was correct at the time of publication. This edition of the *Handbook* will remain current unless amended electronically via the Ministry of Health website (**www.health.govt.nz/publication/immunisation-handbook-2020**) until the next edition or update is published.

Changes to the *Handbook* since 2020

All chapters have been updated and revised since the 2017 edition (2nd edition, 2018). The following changes have been made.

- Changes have been made to the anaphylaxis and emergency management section (section 2.3.3) in chapter 2 'Processes for safe immunisation' and Appendix A4.4 'Resuscitation requirements for all authorised vaccinators and pharmacy vaccinators'.
- Chapter 4 'Immunisation for special groups' has been rearranged and updated. Tables 4.4–4.7 and 4.9 have been updated. Table 4.3 for vaccination of children diagnosed with a condition requiring immunosuppression and updated recommendations for use of meningococcal vaccines have been added.
- Chapter 5 'Coronavirus disease (COVID-19)' has been added and continues to be updated.
- With the introduction of the 12-month immunisation event, the measles, mumps, rubella and pneumococcal chapters have been updated accordingly.
- Chapter 16 'Pneumococcal disease' has also been updated, to reflect the two-dose primary series of PCV10 and earlier booster at 12 months.
- Chapter 13 'Meningococcal disease' has been updated to include recommendations on the use of the recombinant group B meningococcal vaccine, 4CMenB (Bexsero).
- Following discontinuation of Td vaccine (ADT-Booster), the tetanus and diphtheria chapters have been updated to include recommendations on Tdap for adults.
- MMR and varicella vaccines are recommended to be administered either intramuscularly or subcutaneously as indicated (see section 2.2.3).

- Changes have been made to the following vaccine abbreviations – Hib-PRP, MenACWY, MenC (see Commonly used abbreviations table).
- Changes to authorisation of vaccinators for fully authorised vaccinators, pharmacist vaccinators and supervised vaccinating health workers (VHW) (Appendix 4).
- Chapter 23. Inclusion of recombinant zoster vaccine (rZV) and discontinuation of live zoster vaccine.

The National Immunisation Schedule

The National Immunisation Schedule (the Schedule) is the series of publicly funded vaccines available in New Zealand (see Table 1). Some vaccines are also offered as part of an extended immunisation programme for targeted special groups in response to a recognised need (see Table 2). See also section 2.1.7 for a summary of the primary immunisation requirements for adults (funded) and other funded and unfunded recommendations for this age group.

On 1 July 2012, the management and purchasing of vaccines transferred from the Ministry of Health to PHARMAC. All publicly funded vaccines are now listed on PHARMAC's Pharmaceutical Schedule (see **pharmac.govt.nz**), and the district health boards (DHBs) are responsible for funding these once PHARMAC has listed them.

PHARMAC considers medicine and vaccine funding applications from pharmaceutical suppliers, health professionals, consumer groups and patients. Usually, manufacturers/ suppliers decide whether to make an application for funding. Normally this will follow registration and approval of the medicine or vaccine by Medsafe. PHARMAC will generally only consider an application for a medicine or vaccine to be funded once it has been registered and approved by Medsafe.

Following a vaccine funding application, PHARMAC will assess the vaccine, seek clinical input (for vaccines this may be from the immunisation subcommittee of the Pharmacology and Therapeutics Advisory Committee [PTAC] or from PTAC itself), and conduct an economic analysis. The recommendations from the immunisation subcommittee are then considered by PTAC, which will provide advice to PHARMAC. PHARMAC then decides what priority the application has for funding and consults with the Ministry of Health on capacity and implementation issues that may be associated with introducing a new vaccine. Depending on the outcome of that process, PHARMAC may then negotiate with the supplier. If an agreement is reached, PHARMAC will consult with the health sector on a funding proposal.

The Ministry of Health remains responsible for and manages the National Immunisation Programme, which:

- aims to prevent disease through vaccination and to achieve coverage that prevents outbreaks and epidemics
- is accountable for achieving the Immunisation Coverage targets
- monitors disease burden and those at risk

- provides guidance to the sector on immunisation, cold chain and resources
- ensures immunisation providers deliver services that meet the needs of their population
- implements the National Immunisation Schedule
- delivers trusted and effective vaccine programmes
- provides immunisation resources, including the *Immunisation Handbook*
- improves information and data systems
- manages the National Immunisation Register (NIR) and the Aotearoa Immunisation Register (AIR) (see section 2.3.5).

The Ministry of Health works with PHARMAC to ensure there is a strong link between vaccine purchasing decisions and the management and implementation of the National Immunisation Programme.

> Although funding decisions will be communicated to the sector, vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (see **pharmac.govt.nz**) for changes to funding decisions, and the *Handbook* (available at **www.health.govt.nz/publication/immunisation-handbook-2020**) for the latest immunisation information.

Changes to the National Immunisation Schedule since 2020

Table 1 shows the 2020 National Immunisation Schedule, and Table 2 shows the vaccines funded for special groups at higher risk of some diseases.

Changes to vaccine funding in since 2020 are as follows:

- From 2020, the quadrivalent inactivated influenza vaccine (Afluria Quad; see chapter 11 'Influenza') will be the Schedule vaccine for eligible individuals, including pregnant women and adults aged 65 years and older.
- An immunisation event has been introduced at age 12 months. This enables two doses of MMR to be given in the second year of life, replacing the MMR dose that was previously given at age 4 years.
- PCV10 (Synflorix) will now be given at age 6 weeks, 5 months and 12 months (ie, 2+1 schedule, omitting the 3 months dose and bringing the booster dose in the second year of life from 15 months to 12 months). The extended immunisation programme for targeted special groups (using PCV13 and 23PPV) remains unchanged, except that eligibility has been extended to children aged 5–18 years who had received at least two (rather than four) doses of PCV10.
- DTaP-IPV (Infanrix-IPV) will continue to be given age 4 years.

- mRNA-CV (30 µg) is available for all adolescents and adults aged from 12 years, and a paediatric formulation (10 µg) is available for children aged 5 to 11 years, and rCV is now available from the age of 12 years (primary course only for 12–17 years) in New Zealand as part of the COVID-19 pandemic response. Booster doses of mRNA-CV are available from age 16 years at least three calendar months after completion of primary course. Booster doses of rCV are available from the age 18 years given at least six months after completion of primary course.
- Tdap (Boostrix) replaced Td at the 45-year and 65-year events and for tetanus-prone wounds.

Table 1: National Immunisation Schedule, commencing 1 October 2020 (revised 1 August 2022)

Antigen(s)	DTaP-IPV-HepB/Hib	PCV10	RV1	MMR	Hib-PRP-T	VV	DTaP-IPV	Tdap	HPV9	Influenza	rZV
Brand	Infanrix-hexa	Synflorix	Rotarix	Priorix	Hiberix	Varivax	Infanrix-IPV	Boostrix	Gardasil9	Afluria Quad	Shingrix
Manufacturer	GSK	GSK	GSK	GSK	GSK	GSK	GSK	GSK	Seqirus/MSD	Seqirus	GSK
Pregnancy								●[a]		●	
6 weeks	●	●	●								
3 months	●		●								
5 months	●	●									
12 months		●		●							
15 months				●	●	●[b]					
4 years							●				
11 or 12 years[c]								●	● 2 doses[c]		
45 years								●[d]			
65 years								●		● annually	● 2 doses

a. Tdap is for women during every pregnancy, from 16 weeks' gestation, preferably in the second trimester.

b. VV is funded for children born on or after 1 April 2016.

c. HPV is funded for individuals aged 26 years and under: 2 doses are recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose; 3 doses are recommended for those aged 9–26 years with certain medical conditions, plus an additional dose post-chemotherapy.

d. Funded only for adults who have not received 4 previous doses of tetanus vaccine.

Everyone aged 5 years and older is recommended and funded two doses of COVID-19 vaccine (mRNA-CV, Comirnaty). See section 5.4.2 for an alternative vaccine. A booster dose is recommended at least three calendar months after primary series for those aged 18 years and over or at least six months after primary series if aged 16–17 years.

Changes to extended immunisation programme for special groups

Vaccines funded for special groups are described in Table 2 below. Changes to existing programmes since 2020 are as follows.

1. Tdap vaccine funding for pregnant women was extended in 2019, it is now recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester. (Funded when given any time in the second or third trimester.)
2. A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than 3 days, who had not been exposed to maternal vaccination at least 14 days prior to birth.
3. A single dose of Meningococcal ACWY (MenACWY-D) is funded for individuals aged between 13 and 25 years entering or in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, or prisons.
4. Meningococcal B vaccine (4CMenB), MenACWY-D and meningococcal C vaccine (MenC) are funded for certain special groups at increased risk of meningococcal disease, including those who have previously had meningococcal disease of any group.
5. In addition to two primary doses and a booster dose routinely recommended from age 16 years, a third primary dose of mRNA-CV (30 µg or 10 µg, as age appropriate) given at least eight weeks after first two primary doses is recommended for certain individuals aged from 5 years who are severely immunocompromised (or where indicated, rCV from age 18 years). Those aged from 16 years are also eligible for a second booster dose, given at least six months after fourth dose (first booster). Other groups with increased risk of severe breakthrough COVID-19 are also eligible to a second booster dose.

Table 2: Extended immunisation programme for special groups – vaccines funded in addition to the routine schedule

Note: Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (**pharmac.govt.nz**) for changes to funding decisions for special groups. See also chapter 4 'Immunisation of special groups'.

Vaccine	Individuals eligible for funded vaccine
Haemophilus influenzae type b (Hib-PRP-T) (chapter 7)	For (re)vaccination of patients who are: • post-haematopoietic stem cell transplant (HSCT) or chemotherapy • pre- or post-splenectomy or with functional asplenia • pre- or post-solid organ transplant • pre- or post-cochlear implants • undergoing renal dialysis and other severely immunosuppressive regimens For use in testing for primary immune deficiency[a]
Hepatitis A (HepA) (chapter 8)	Transplant patients Children with chronic liver disease Close contacts of hepatitis A cases
Hepatitis B (HepB) (chapter 9)	Household or sexual contacts of patients with acute or chronic hepatitis B virus (HBV) infection Babies of mothers with chronic HBV infection need both hepatitis B vaccine (HepB) and hepatitis B immunoglobulin (HBIG) at birth Children aged under 18 years who have not achieved positive serology and who require additional vaccination HIV-positive patients Hepatitis C-positive patients Following non-consensual sexual intercourse Prior to any planned immunosuppression[b] Patients following immunosuppression[b] Solid organ transplant patients, including liver or kidney transplant Post-HSCT patients Following needle-stick injury Dialysis patients
Human papillomavirus (HPV) (chapter 10)	People aged 9 to 26 years inclusive who are: • confirmed with HIV infection • transplant (including stem cell) patients • post-chemotherapy

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Annual influenza vaccine (chapter 11)	Patients aged 6 months to <65 years who: • have any of the following cardiovascular diseases: – ischaemic heart disease – congestive heart failure – rheumatic heart disease – congenital heart disease – cerebrovascular disease • have either of the following chronic respiratory diseases: – asthma, if on a regular preventative therapy – other chronic respiratory disease with impaired lung function • have diabetes • have chronic renal disease • have any cancer, excluding basal and squamous skin cancers if not invasive • have any of the following other conditions: – autoimmune disease – immune suppression or immune deficiency – HIV – transplant recipients – neuromuscular and central nervous system diseases/disorders – haemoglobinopathies – are children on long-term aspirin – have a cochlear implant – errors of metabolism at risk of major metabolic decompensation – pre- and post-splenectomy – Down syndrome • are pregnant • are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness, including children age under 5 who were hospitalised with measles • are patients who are compulsorily detained long-term in a forensic unit within a DHB hospital[c] • all children aged 3–12 years[d]
Measles, mumps and rubella (MMR) (chapters 12, 14 and 19)	(Re)vaccination of patients prior to planned or following immunosuppression[b]

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Meningococcal C conjugate vaccine (MenC), quadrivalent meningococcal conjugate vaccine (MenACWY-D) and meningococcal B vaccine (4CMenB) (chapter 13)	• Pre- and post-splenectomy or with functional or anatomical asplenia • HIV • Complement deficiency (acquired or inherited) • Pre- or post-solid organ transplant • Close contacts of meningococcal case • HSCT (bone marrow transplant) patients • Prior to any planned immunosuppression[b] • Following immunosuppression[b] • Individuals who have had previous meningococcal disease (any group) MenACWY-D (Menactra) only: • Individuals aged between 13 and 25 years entering or in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, or prisons.
Pertussis-containing vaccines (chapter 15)	Pregnant women – recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester. (Funded when given any time in second or third trimester) Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than 3 days, who had not been exposed to maternal vaccination at least 14 days prior to birth (Re)vaccination of patients who are: • post-HSCT or chemotherapy • pre- or post-splenectomy • pre- or post-solid organ transplant • undergoing renal dialysis or other severely immunosuppressive regimens

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (23PPV) (chapter 16)	For (re)vaccination of high-risk children, PCV13 for patients aged under 5 years and 23PPV for patients aged under 18 years: • prior to planned or on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response) • with primary immune deficiencies • with HIV infection • with renal failure or nephrotic syndrome • who are immune-suppressed following organ transplantation (including HSCT) • with cochlear implants or intracranial shunts • with cerebrospinal fluid leak • receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater • with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy) • preterm infants, born before 28 weeks' gestation • with cardiac disease, with cyanosis or failure • with diabetes • with Down syndrome • who are pre- or post-splenectomy, or with functional asplenia PCV13 and 23PPV for (re)vaccination of patients aged 5 years and older: – with HIV – pre- or post-HSCT[d] or chemotherapy[e] – pre- or post-splenectomy or with functional asplenia – pre- or post-solid organ transplant – undergoing renal dialysis – with complement deficiency (acquired or inherited) – with cochlear implants with primary immune deficiency PCV13 and 23PPV for use in testing for primary immune deficiency.[a]
Inactivated polio vaccine (IPV) (chapter 17)	(Re)vaccination of patients prior to planned or following immunosuppression[b]
Tetanus, diphtheria and pertussis (Tdap) (chapter 20)	(Re)vaccination of patients prior to planned or following immunosuppression[b] Boosting of patients with tetanus-prone wounds For use in testing for primary immune deficiency[a]
Bacillus Calmette–Guérin (BCG) (chapter 21)	For infants at increased risk of tuberculosis (TB): • living in a house or family with a person with current or past history of TB; or • having one or more household members or carers who within the last 5 years lived in a country with a rate of TB ≥40 per 100,000 for 6 months or longer; or • who, during their first 5 years, will be living 3 months or longer in a country with a rate of TB ≥40 per 100,000

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Varicella vaccine (VV) (chapter 22)	Non-immune patients: • with chronic liver disease who may in future be candidates for transplantation • with deteriorating renal function before transplantation • prior to solid organ transplant • prior to any planned immunosuppression[b] • for post-exposure prophylaxis of immune-competent hospital in-patients Patients at least 2 years after bone marrow transplantation, on advice of their specialist Patients at least 6 months after completion of chemotherapy, on advice of their specialist HIV-positive patients with mild or moderate immunosuppression who are non-immune to varicella, on advice of their HIV specialist Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household contacts of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella

a. Upon the recommendation of an internal medicine physician or paediatrician.

b. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

c. This is a Pharmaceutical Schedule Section H – Hospital Medicines List funding restriction.

d. For 2022 season, from 1 July until 31 December 2022.

e. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

Eligibility for publicly funded vaccines

Only vaccines given according to the Schedule are available free of charge, unless there is a specific funded programme in response to a recognised need (see Table 2). The immunisation benefit is paid by DHBs to providers for the administration of:

- all childhood Schedule vaccines
- influenza vaccine to eligible children and adults (ie, those at higher risk of disease)
- rZV to individuals aged 65 years
- tetanus-diphtheria-pertussis (Tdap) boosters given at ages 45 and 65 years (now funded)
- hepatitis A, hepatitis B, Hib-PRP-T, human papillomavirus (HPV), inactivated polio vaccine (IPV), MMR, meningococcal conjugate, pertussis, pneumococcal conjugate and/or polysaccharide, and varicella vaccines only, for eligible children and adults

(ie, at higher risk of disease) as part of an extended immunisation programme for special groups.

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded (ie, free or subsidised) health and disability services.

Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines. All children are also eligible for Well Child Tamariki Ora services.

Non-residents who were aged under 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

Further information on eligibility can be found on the Ministry of Health website (**www.health.govt.nz/eligibility**).

As part of the COVID-19 pandemic response the preferred vaccine, mRNA-CV, is available for all children aged from 5 years and adults in New Zealand, regardless of eligibility for publicly funded health and disability services. An additional vaccine, rCV, is also available for individuals aged 12 years or over, if indicated or for personal choice. Access to these vaccines will be granted through a defined Ministry of Health vaccine rollout plan (see **www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines**).

Notifiable diseases

All diseases preventable by vaccines on the Schedule (or as part of a targeted programme) are notifiable, except for HPV, seasonal influenza, rotavirus, varicella and herpes zoster.

Note: Rotavirus infections presenting as gastroenteritis are notifiable as acute gastroenteritis.

> It is a legal requirement (under the Health Act 1956) that health professionals notify their local Medical Officer of Health of any notifiable disease they suspect or diagnose so that appropriate action (eg, public health prevention and control activities) can be undertaken.

Notification processes, and the diseases to which they relate, have been updated in the Health Act and supporting Health (Infectious and Notifiable Diseases) Regulations 2016. See the Ministry of Health's 2017 document *Guidance on Infectious Disease Management under the Health Act 1956* (available at

www.health.govt.nz/publication/guidance-infectious-disease-management-under-health-act-1956) for an explanation, as well as the processes and forms for notifiable diseases.

The case definitions used by the medical officer of health to classify the notified case for surveillance purposes (and to assist in identifying appropriate prevention and control activities) and the laboratory tests required to confirm the diagnosis can be found in the *Communicable Disease Control Manual*. For the most up-to-date information, refer to the online version (available at **www.health.govt.nz/publication/communicable-disease-control-manual-2012**).

1 General immunisation principles

It is not necessary to have an in-depth knowledge of the immune system to understand the first principles of vaccinology. The immune system is an extremely complex inter-connected system, but understanding certain aspects involved in the process of inducing specific immunity through vaccination inform vaccination practice.

As protective immunity develops over time, the timing of vaccine doses, along with a basic understanding of the different types of vaccines, becomes important.

1.1 Immunity and immunisation

Immunity is the biological state of being able to resist disease or a toxin: the primary objective of vaccination is to induce an immunological memory against specific diseases, so that if exposure to a disease-causing pathogen occurs, the immune response will neutralise the infection or toxins it releases before disease can occur.

1.1.1 Immune recognition

One of the primary ways in which the immune system achieves elimination of pathogens and other unwanted foreign material is being able to distinguish 'self' from 'non-self'. Each cell in the body is equipped with a type of molecule that identifies the individual from any other, much like a 3D barcode. Pathogens not only lack the individual's 'self' marker, they also contain 'virulence factors' that alert the immune system to danger.

Antigens (*anti*body *gen*erators) are the drivers of the specific immune response. Antigens are molecular shapes, such as part of a protein or glycoprotein, that the immune system recognises as foreign and can trigger an adaptive immune response. While some vaccines contain the entire weakened or attenuated organism (live viral vaccines like measles, mumps and rubella vaccines), increasingly, newer vaccines contain purified or recombinant protein antigens (as in acellular pertussis, HPV or pneumococcal vaccines).

The first process that occurs when a foreign antigen, such as a vaccine antigen, is introduced to the body is the recognition that the antigen is non-self by triggering an inflammatory response. The antigen is taken up at the local site (such as the injection site) by specialist phagocytic cells called antigen-presenting cells – macrophages and dendritic cells. Once inside the antigen-presenting cells, the foreign protein (or microbe) is dismantled into tiny fragments that are displayed on cell surface alongside a 'self' molecule. These antigen-presenting cells carry the antigen to through the lymph to the local lymph node where the adaptive immune response is initiated.

1.1.2 Induction of the adaptive immune response

The response that occurs the first time an antigen is 'seen' by the immune system is called the primary immune response.

The adaptive immune responses occur in lymphoid tissue, primarily in the spleen and in the 500–600 lymph nodes distributed throughout the body.

The adaptive immune response to most vaccines occurs at the draining lymph node proximal to the site of injection. The spleen and lymph nodes are densely populated with important effector lymphocytes of the immune response: T-cells and B-cells. In the lymph node, the vaccine antigen is presented to the specific T-cells and B-cells.

Among the trillions of specific T and B lymphocytes (there are ~10^{16} possibilities), there usually exists a match for the antigen. Cells that recognise the antigen are activated through communication with the antigen presenting cell and the primary immune response can be initiated. This process and the response matures over a period of four to six weeks.

An early outcome of the interaction between these antigen-presenting cells and T and B lymphocytes is the production of antibody-producing B-cells. Antibody can be measured in the blood as soon as 4–7 days after this interaction, but is usually more effectively measured weeks to months later. Initially, this is low in quantity and of low affinity for the antigen (it binds weakly to the antigen), and primarily consists of the antibody subtype immunoglobulin M (IgM), often referred to as 'early antibody'. It peaks at around 10 days then declines relatively quickly (see Figure 1.1).

For most vaccine-preventable diseases this process is too slow following infection, and disease occurs before an effective immune response can be mounted. Injecting a part or a weakened version of the pathogen in the form of a vaccine, readies the immune system so that it can mount a more rapid and effective response when the wild disease is encountered.

1.1.3 Development of immune memory and the secondary response

The response that occurs the second time an antigen is 'seen' by the immune system is called the secondary immune response.

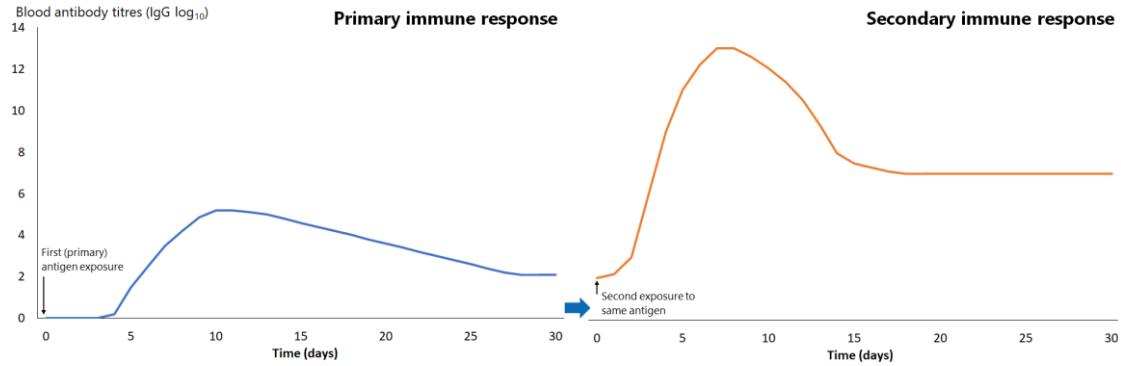
During the primary immune response, over a period of around two months, cells that are less specific for the specific antigen are deleted, and those that are highly specific are retained and multiply within the lymph node. Antibody production also switches from IgM to more specific IgG or IgA subtypes. During this time immunological memory cells also develop, but it takes around four months, after the initial antigen is cleared, to fully form immune memory.

The next time the same antigen is introduced, either as a pathogen component or as a further dose of vaccine, the immunological memory cells that recognise it will be activated and begin to proliferate. Highly specific antibody (primarily of the IgG subtype, but also IgA) is rapidly produced in large amounts. The lag phase is much shorter than the primary immune response (see Figure 1.1), at just 1–4 days; the antibody level peaks very quickly and lasts much longer.

The immune system has been readied by the vaccine; if the actual disease pathogen enters the body, then it is recognised promptly and neutralised by the immune system preventing it from causing disease.

Figure 1.1: Comparison of primary and secondary immune responses to protein-containing vaccines

Secondary responses are faster (peaking at day 7) than the primary immune response and the antibody titres are higher, more prolonged and of higher neutralising capacity.

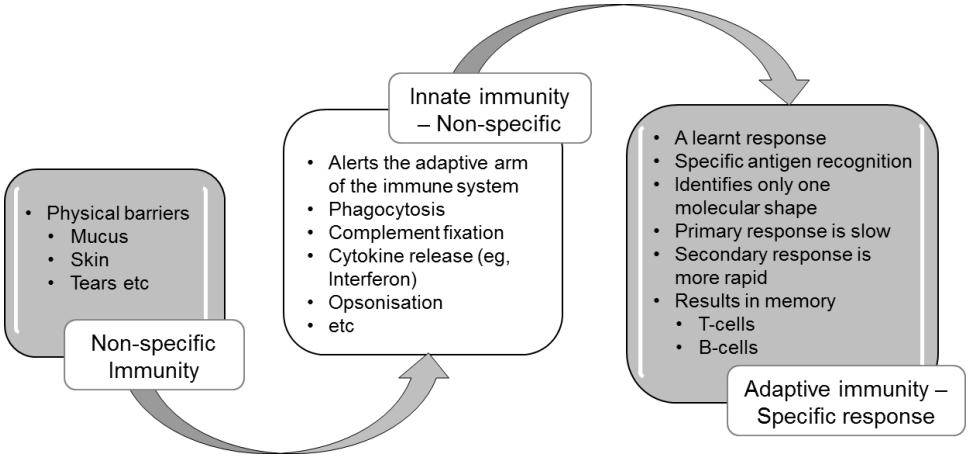


Innate immunity

Most infectious microbes (also known as micro-organisms) are prevented from entering the body by barriers such as skin, mucosa, cilia and a range of anti-microbial enzymes. Any microbes that breach these surface barriers are then attacked by other components of the innate immune system, such as polymorphonuclear leucocytes (neutrophils), macrophages and complement.

This innate immune response is a pre-programmed non-specific response that does not involve learnt or adaptive mechanisms. The cells and proteins of the innate immune system can recognise common microbial markers or virulence factors and can kill microbes without the need for prior exposure. The chemical messages (cytokines) and cells of the innate immune system also interact with the cells of the adaptive immune system (eg, lymphocytes) to induce a cascade of events that leads to adaptive, antigen-specific immunity and immune memory, as summarised in Figure 1.2.

Figure 1.2: Summary of non-specific innate and adaptive (specific) immunity



1.1.4 Acquisition of adaptive immunity

Specific immunity can be actively produced by directly responding to an antigen. This is termed adaptive or learnt immunity, in which the immune system learns to respond to specific antigens. Passive immunity is provided by transferring antibody from an immune person to temporarily protect another.

Naturally acquired immunity

Naturally acquired immunity occurs either actively by experiencing the infection or passively through the transfer of maternal antibodies from mother to fetus or infant (transplacentally or in breastmilk).

Artificially acquired immunity

'Artificially' acquired immunity occurs either actively through vaccination or passively through administration of immunoglobulin (IG) (see Appendix 6).

While actively acquired immunity lasts from years to life, passively acquired immunity lasts from weeks to months as the transferred antibodies decay and are not renewed.

1.1.5 Maternally derived immunity

The passive transfer of antibody from mother to fetus provides an opportunity to provide protection to the neonate against several diseases before they are old enough to be vaccinated themselves. Maternal vaccination boosts the immunity of the mother, inducing high levels of maternal antibody. This antibody is actively transported across the placenta to concentrate at protective levels by birth (in term infants).

Important diseases that maternal vaccination is effective at preventing include neonatal tetanus, influenza and pertussis in the infant for the first weeks or months of life (see section 4.1 and the relevant disease chapters).

1.1.6 Summary

- Successful immune responses occur following the recognition of, and appropriate response to, a foreign antigen.
- Specialised but non-specific cells, called antigen-presenting cells, take up, transport and present the vaccine antigen to antigen-specific T-cells and B-cells within the lymph nodes and spleen.
- The first wave of antibodies produced are short lived and of low affinity.
- Immune memory takes at least four months to fully develop, but the antibody and memory cells that arise are of high affinity.
- Immune memory can be boosted. This is called a secondary immune response.
- Adaptive immunity is learnt and acquired actively through disease or vaccination.
- Passive immunity is acquired through maternal transfer and administration of IG.
- Maternal vaccination offers passive protection to infants for the first weeks or months of life.

1.2 From personal protection to community (herd) immunity

By protecting individuals, vaccination can also protect the wider community. This herd immunity occurs when the vaccine coverage is high, meaning an infectious case is unlikely to encounter susceptible contacts, so transmission stops.

The whole population benefits when a vaccine prevents carriage and transmission of a human-only pathogen, such as polio virus, measles virus or *Streptococcus pneumoniae*, and circulation of these pathogens can be reduced and even eliminated. This phenomenon, called herd or community immunity, can prevent infections spreading and therefore protect vulnerable members of the population, such as the very young, the very old, or those with underlying conditions that increase their risk from infectious diseases (ie, the immunocompromised). These individuals may not themselves be able to receive some vaccines (eg, live vaccines) or may not mount a sufficiently effective immune response to other vaccines.

The population benefits depend on the disease itself, the nature of the vaccine and the proportion or target group of the population needed to be immunised to prevent the disease from spreading. A recent example of herd immunity in New Zealand is the significant reduction in rotavirus hospital discharge rates in children aged under 5 years following the July 2014 introduction of rotavirus vaccine for infants (see section 18.3.2).

1.2.1 Reproduction number and herd immunity threshold

A measure of the infectiousness of a disease is the basic reproduction number (R_0). This is the number of secondary cases generated by a typical infectious individual when the rest of the population is susceptible. In other words, R_0 describes the spreading potential of an infection in a population.[1] Measles is one of the most infectious diseases, with an R_0 of 12–18 (Table 1.1). In other words, one person with measles is likely to infect up to 18 other susceptible people. Pertussis is similarly infectious.

If a significant proportion of the population are immune, then the chain of disease transmission is likely to be disrupted. The herd immunity threshold (H) is the proportion of immune individuals in a population that must be exceeded to prevent disease transmission. For example, to prevent measles or pertussis transmission, 92–94 percent of the population must be immune (Table 1.1).

R_0 must remain above 1 for an infection to continue to exist. Once R_0 drops below 1 (such as in the presence of an effective vaccination programme), the disease can be eliminated. The greater the proportion of the population that is immune to the infection, the lower the R_0 will be. For example, data[2] indicates that a quadrivalent HPV vaccine programme with 70 percent coverage in young women may lead to the near disappearance of genital warts from the heterosexual population because the R_0 for HPV types 6 and 11 (causing genital warts) falls to below 1 (see 'Herd immunity and population impact' in section 10.4.2).

Table 1.1: Approximate basic reproduction numbers (in developed countries) and implied crude herd immunity thresholds[a] for common vaccine-preventable diseases[b]

Infection	Basic reproduction number (R_0)	Crude herd immunity threshold, H (%)
Diphtheria	6–7	83–85
Influenza[c]	1.4–4	30–75
Measles	12–18	92–94
Mumps	4–7	75–86
Pertussis	5–17	80–94
Polio[d]	2–20	50–95
Rubella	6–7	83–85
Varicella	8–10	Not defined

Notes

a. The herd immunity threshold (H) is calculated as $1-1/R_0$.

b. The values given in this table are approximate: they do not properly reflect the range and diversity among populations, nor do they reflect the full immunological complexity underlying the epidemiology and persistence of these infections.

c. The R_0 of influenza viruses varies among subtypes.

d. This is complicated by uncertainties over immunity to infection and variation related to hygiene standards.

Adapted from: Fine P, Mulholland K, Scott J, et al. 2018. Community Protection. In: Plotkin S, Orenstein W, Offit P, et al (eds). *Plotkin's Vaccines (7th edition)*. Philadelphia, US: Elsevier. Table 77.2.

1.2.2 Summary

- Not only do vaccines provide individual protection, but for many of the diseases we vaccinate against, there is also a population effect called herd/community immunity.
- Some diseases are extremely infectious and require a very high proportion of the community to be immune to prevent transmission (particularly measles and pertussis).

1.3 The importance of immunisation coverage

High immunisation coverage means more individuals are protected; it is also vital for achieving herd immunity. High coverage reduces the spread of disease to those who have not been vaccinated for medical reasons (eg, children with leukaemia while receiving treatment) or because of age (eg, infants who are too young to respond to some vaccines). High coverage also reduces the spread of disease to those who may not mount an effective immune response to vaccines because of an underlying condition (eg, those on immunosuppressive regimes).

The World Health Organization (WHO) and the New Zealand government target for immunisation coverage (since 2017/18) is for at least 95 percent of children to be fully vaccinated by age 2 years. The New Zealand target includes a marker for on-time immunisation of 95 percent by age 8 months, as well as at ages 2 years and 5 years.

This target is based on the need for:

- on-time immunisation coverage, particularly three doses of pertussis-containing vaccine for infants in the primary series and the first dose of measles vaccine at age 12 months
- achieving high herd immunity, particularly to prevent measles transmission.

For the three months ending 31 March 2020, 91 percent of New Zealand children were fully immunised by age 8 months and 92 percent were fully immunised by age 2 years. Up-to-date national and DHB immunisation coverage data is available at the Ministry of Health website (**www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-coverage/national-and-dhb-immunisation-data**).

1.4 Classification of vaccines

There are two broad categories of vaccine type: live attenuated (weakened) and non-live, which includes inactivated or whole killed, subunit and nucleic acid vaccines. Examples of the different types of vaccines are summarised in Table 1.2.

Table 1.2: Classification of vaccines, with examples

Live attenuated	Non-live			
	Inactivated or whole killed	**Subunit**	**Nucleic acid**	**Non-replicating viral vector**
Measles Mumps Rubella Varicella Rotavirus Tuberculosis (BCG) Zoster	Poliomyelitis (IPV) Hepatitis A Some influenza vaccines	Toxoid: • diphtheria • tetanus Polysaccharide: • pneumococcal (23-valent) Conjugate: • pneumococcal (10- and 13-valent) • *Haemophilus influenzae* type b • meningococcal C and ACWY Recombinant: • COVID-19 (rCV) • hepatitis B • human papillomavirus • meningococcal B • zoster (rZV) Other subunit: • pertussis, acellular • influenza	COVID-19 (mRNA-CV)	COVID-19 (Ad26-CV and ChAd-CV)

Note: Travel vaccines have been omitted from the above table.

1.4.1 Live attenuated vaccines

Live vaccines contain pathogens, usually viruses, which have been weakened (attenuated) so that they are able to replicate enough to induce an immune response but not cause disease. Immunity from live vaccines is usually very long-lived. The live vaccines on the National Immunisation Schedule are MMR, varicella, rotavirus and herpes zoster vaccines.

1.4.2 Non-live vaccines: Whole killed and inactivated vaccines

Killed vaccines contain whole bacteria that have been killed. The whole-cell pertussis vaccine is an example of a killed vaccine. There are no killed vaccines on the Schedule.

Inactivated vaccines contain viruses that have been inactivated in some way, such as splitting, so they are unable to replicate or cause disease. Examples of inactivated vaccines are influenza, hepatitis A and polio vaccines.

1.4.3 Non-live vaccines: Subunit vaccines

Subunit vaccines contain microbial fragments or particles that can induce an immune response which protects against disease. These are produced using a range of methods including recombinant engineering, detoxification processes and splitting and purification.

Toxoid vaccines

In some bacterial infections (eg, diphtheria and tetanus), the clinical manifestations of disease are caused not by the bacteria themselves but by the toxins they secrete. Toxoid vaccines are produced by harvesting a toxin and altering it chemically (usually with formaldehyde) to convert the toxin to a toxoid. The toxoid is then purified. Toxoid vaccines induce antibodies that neutralise the harmful exotoxins released from these bacteria.

Recombinant vaccines

Recombinant vaccines, such as those used against COVID-19 (rCV), hepatitis B virus (HBV) and human papillomavirus (HPV), are made using a gene from the (disease-causing) pathogen. The gene is inserted into a cell system capable of producing large amounts of the protein of interest. The protein produced can generate a protective immune response. For example, the gene for the hepatitis B surface antigen (HBsAg) is inserted into yeast cells, which replicate and produce large amounts of HBsAg. This antigen is purified and used to make vaccine. The advantage of this approach is that it results is a very pure vaccine that is efficient to produce.

Polysaccharide and conjugate vaccines

Polysaccharides are strings of sugars. Some bacteria, such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, have large amounts of polysaccharide on their surface, which encapsulate the bacteria. The polysaccharide capsules protect the bacteria from the host's immune system and can make the bacteria more virulent. Historically, it has been difficult to stimulate an effective immune response to these polysaccharide capsules using vaccines, particularly in children aged under 2 years.

First-generation capsular polysaccharide vaccines contained antigens isolated from the different polysaccharide capsules (eg, 23PPV, see chapter 16). Polysaccharide vaccines

are poorly immunogenic, and they only induce a primary immune response. They produce low affinity antibodies (which do not bind well to the antigen) and, because they do not elicit T-cell responses, immune memory is not strong. Multiple priming doses (even a single dose) can cause hyporesponsiveness in both children and adults to further doses. There is also concern that repeated doses could result in 'clonal deletion' where the specific B-cell pool becomes depleted due to successive primary responses.

Polysaccharide conjugate vaccines (eg, Hib-PRP, PCV13 and MenACWY) contain carrier proteins that are chemically attached to the polysaccharide antigens. Attaching relatively non-immunogenic polysaccharides to the highly immunogenic carrier proteins results in activation of a T-cell response; in this way, conjugate vaccines induce both high-affinity antibodies against the polysaccharide antigens, and immune memory, and can be used in infants.

Examples of carrier proteins and vaccines that use them are:

- tetanus toxoid, used in *Haemophilus influenzae* type B vaccine (Hib-PRP-T; Hiberix)
- a non-toxic recombinant variant of diphtheria toxin (CRM197), used in the 13-valent pneumococcal conjugate vaccine (PCV13; Prevenar 13)
- diphtheria toxoid (D), used in the quadrivalent meningococcal conjugate vaccine (MenACWY-D; Menactra).

These conjugate vaccines are limited by the number of polysaccharides that can be covalently linked to the carrier molecule, so there is still a role for polysaccharide vaccines to broaden the number of serotypes recognised. For example, PCV13 has 13 serotypes, compared to 23PPV with 23 serotypes. Polysaccharide vaccines are expected to be phased out eventually with improvements to conjugate vaccine technology and other vaccine technologies.

Principles and implications for using polysaccharide and conjugate vaccines

- Because of their improved immune response, where possible use polysaccharide-protein conjugate vaccines in preference to polysaccharide-only vaccines.
- To ensure broad protection against disease, use a conjugate vaccine to prime the immune system before using the polysaccharide vaccine to increase the number of serotypes recognised. For example, high-risk children are primed with PCV13 then boosted with 23PPV (see section 16.5.2).
- To avoid or minimise hyporesponsiveness, individuals should have a maximum of three lifetime doses of polysaccharide vaccine.
- Children aged under 2 years should not receive polysaccharide vaccines as they are likely to be ineffective in young children.

1.4.4 Non-live vaccines: Nucleic acid vaccines

Recent developments in vaccine technology have allowed the use of messenger ribonucleic acid (mRNA) to deliver the genetic code to our dendritic cells make specific viral proteins. Since mRNA is easily destroyed by ubiquitous ribonuclease enzymes, it is protected inside a lipid nanoparticle that also facilitates uptake by the dendritic cells. Inside the dendritic cell, ribosomes and vaccine mRNA generate the viral protein which is then presented to the T and B cells in the lymph nodes. For example, the mRNA COVID-19 vaccine (mRNA-CV) provides the instructions to make the SARS-CoV-2 virus spike protein and induces an effective humoral and cellular immune responses against this virus.

1.4.5 Non-live vaccines: Non-replicating viral vector vaccines

Another recent development in vaccine design is the use of adenoviruses as a vector to deliver the instructions to human cells to make antigens. The adenovirus is genetically modified to be unable to replicate (non-replicating or replication deficient), and as such are non-live vaccines, but can deliver its double-stranded DNA into the cell's nucleus as would normally occur during an adenovirus infection. The viral DNA contains a transgene, a portion that codes for the target antigen protein. Only this portion of the viral DNA can be expressed, thus preventing the vector from reproducing. The presence of the adenovirus triggers an immune response killing the infected cell and thereby releasing the new protein (antigen) to activate a specific immune response. For example, ChAdOx1 vector COVID-19 vaccine (ChAd-CV) uses a chimpanzee adenovirus and the Ad26 vector COVID-19 vaccine (Ad26-CV) uses a human adenovirus (Ad26) to produce SARS-CoV-2 spike proteins.

1.4.6 Summary

- Vaccines introduce antigens to the immune system in the form of live and non-live vaccines.
- Non-live vaccines include killed/inactivated, subunit or nucleic acid vaccines.
- Polysaccharide vaccines do not induce immune memory and have been associated with hyporesponsiveness to later doses. Polysaccharide conjugate vaccines overcome these problems.
- Nucleic acid vaccines and viral vector vaccines provide the instructions for our own cells to make the target antigen.

1.5 Vaccine ingredients

In addition to the antigen, a vaccine may contain a range of other substances; for example, an immune enhancer (adjuvant) and/or a preservative. Traces of residual components from the manufacturing process may also be present in the vaccine. For further information on vaccine content, see chapter 3 and the vaccine sections within the disease chapters of this *Handbook*.

1.5.1 Adjuvants

Adjuvants are substances that enhance the immune response to an antigen through a range of mechanisms, including improving the delivery of the antigen to the innate immune system and to the lymphoid organs. Use of adjuvants also means that less antigen, which can be difficult to produce, is needed (this is called antigen sparing).

Adjuvants licensed for human use include aluminium salts (eg, aluminium hydroxide and aluminium phosphate), oil-in-water emulsions (MF59, Seqirus; AS03, GSK), saponin-based liposomal suspension (AS01$_B$, GSK; Matrix-M, Novavax) and a bacterial endotoxin (AS04, GSK). Most non-live vaccines require an adjuvant, and most vaccines still use aluminium adjuvants. The amount of aluminium contained in a vaccine is very small compared with that present in our daily intake from food and water, including breastmilk.

1.5.2 Preservatives

Preservatives prevent the contamination of vaccines, particularly in multi-dose vials. 2-phenoxyethanol is an example of a preservative used in some vaccines. It is also used in many cosmetics and baby care products. Many vaccines do not contain a preservative. Mercury-based preservatives (thiomersal/thimerosal) are not used in vaccines on the New Zealand National Immunisation Schedule, and multi-dose vials are not used for Schedule vaccinations.

1.5.3 Stabilisers

Stabilisers protect the vaccine from adverse conditions (such as exposure to heat), inhibit chemical reactions and prevent components from separating. Examples include sucrose, lactose, albumin, gelatin, glycine and monosodium glutamate (MSG).

1.5.4 Surfactants/emulsifiers

These are wetting agents that alter the surface tension of a liquid, like a detergent does. Surfactants assist particles to remain suspended in liquid, preventing settling and clumping. One commonly used surfactant is polysorbate 80, made from sorbitol (sugar alcohol) and oleic acid (an omega fatty acid). It is also commonly used in foods such as ice-cream.

1.5.5 Residuals

Residuals are traces of substances that remain in the vaccine as an inevitable consequence of the manufacturing process. Regulatory bodies vary as to which trace substances must be specified. Residuals may include virus-inactivating agents (such as formaldehyde), antibiotics and other substances used in the manufacturing process, such as ovalbumin (an egg protein) and gelatin.

1.6 Safety monitoring of vaccines in New Zealand

1.6.1 The approval of vaccines for use in New Zealand

Vaccines, like all medicines, have benefits and risks of harm. Before a medicine or vaccine is approved for use, it must be tested in a series of clinical trials to determine its immunogenicity, efficacy and safety profile. The data from these trials is assessed and scrutinised by regulatory authorities, such as Medsafe in New Zealand, the European Medicines Agency and the Food and Drug Administration in the US, before the medicine or vaccine is approved for use.

Known information about each medicine and vaccine is published for health professionals in a manufacturer's data sheet, available on the Medsafe website (**medsafe.govt.nz**). Consumer medicine information is usually also published.

Once the vaccine is used widely (ie, outside of the clinical trials), more information is collected on its safety profile and effectiveness. Some adverse reactions are rare and may not be seen until a very large number (thousands or even millions) of people have received the medicine or vaccine. This is one of the reasons why it is important to monitor all medicines and vaccines after they have been approved (registered). Note that some vaccines that are approved for use by Medsafe may not have been made available for distribution by the manufacturer or supplier.

Most countries (including New Zealand) have a safety monitoring system, which includes a voluntary spontaneous reporting scheme, to help identify any possible safety concerns. These reporting systems feed into the WHO Collaborating Centre for International Drug Monitoring, called the Uppsala Monitoring Centre in Sweden. This means that international data, often covering millions of doses, is available for Medsafe, which is the medicines regulator responsible for monitoring information to ensure that approved vaccines remain acceptably safe for use in New Zealand. Vaccine safety is never reviewed in isolation from the expected benefits of the vaccine; it is always looked at in terms of the risk–benefit balance.

In addition, the WHO plays an important role in monitoring vaccine safety through its Strategic Advisory Group of Experts on Immunization and the Global Advisory Committee on Vaccine Safety.

1.6.2 The New Zealand spontaneous reporting scheme

Two terms are used to describe spontaneous reports in the context of vaccination. *Adverse events* are undesirable events experienced by a person, which may or may not be causally associated with the vaccine. *Adverse reactions* are undesirable effects resulting from medicines or vaccines (ie, they are causally associated).

Spontaneous reports are case reports of adverse events that people have experienced while or after taking a medicine or having a vaccine. Medsafe contracts the collection, review and analysis of this information to the New Zealand Pharmacovigilance Centre at the University of Otago in Dunedin.

Health care professionals and consumers are encouraged to report adverse events following immunisation (AEFIs) to the Centre for Adverse Reactions Monitoring (CARM), which is part of the New Zealand Pharmacovigilance Centre. Pharmaceutical companies also submit adverse event reports.

Further information about suspected adverse reactions (and events following immunisation) reported in New Zealand can be found in the *Suspected Medicine Adverse Reaction Search* on the Medsafe website (**www.medsafe.govt.nz/safety/safety-monitoring.asp**). See below for details about how to report to CARM and what information should be reported.

1.6.3 AEFI reporting process – notifying CARM

When obtaining consent for immunisation, vaccinators should also seek consent to report any adverse events that may occur, because AEFI reporting is considered part of immunisation programme quality control monitoring and public safety.

How to report to CARM

Adverse events may be reported to CARM through:

- the electronic adverse reaction reporting tool available in practice management software programmes
- online reporting at **https://nzphvc.otago.ac.nz/report/**
- using the iPhone/iPad iOS ADR reporting application (available at **https://nzphvc.otago.ac.nz/app**)
- downloading and printing a reporting form (**https://nzphvc.otago.ac.nz/reporting**), then mailing or email the completed form to the address below
- completing a Freepost Yellow Card – available from CARM, or found in the *MIMS New Ethicals* and inside the back cover of some editions of *Prescriber Update*
- by telephone, email or fax (see below). Outside office hours, a telephone-answering machine will take messages.

Send reporting forms to:

Freepost 112002
The Medical Assessor
Centre for Adverse Reactions Monitoring
University of Otago Medical School
PO Box 913
Dunedin 9710

Telephone: (03) 479 7247
Fax: (03) 479 7150
Email: **carmnz@otago.ac.nz**
Website: **nzphvc.otago.ac.nz/reporting**/

In terms of guidance, the sort of information the reporting form generally requires is a patient identifier (gender, age, initial), a medicine, a reaction and the reporter's contact details.

This information can also be accessed from the Medsafe website (revised 7 November 2019; **www.medsafe.govt.nz/safety/report-a-problem.asp**).

What should be reported?

Health professionals/vaccinators should report:

- all serious suspected AEFI and other reactions of clinical concern to established vaccines, such as those described in Table 1.3 below. The AEFIs should be reported regardless of whether they consider the event to have been caused by the vaccination, and they should still be reported even if the effect is well recognised
- all suspected adverse reactions (including minor reactions) to newly introduced vaccines, or those being used for new indications or being delivered by a different route.

Individuals or parents/guardians should be encouraged to notify vaccinators of any AEFI that they consider may have been caused by the vaccination. Alternatively, individuals or parents/guardians may wish to notify CARM themselves, or they can contact their general practice or the Immunisation Advisory Centre (IMAC) on 0800 IMMUNE/0800 466 863 to help with notification.

If in doubt, report it.

Table 1.3: Examples of AEFIs to be reported

Timeframe	Event
All vaccines	
Within 24 hours of vaccination	Anaphylactic reaction (acute hypersensitivity reaction) Anaphylaxis Persistent inconsolable screaming (more than 3 hours) Hypotonic-hyporesponsive episode Fever >40°C
Within 5 days of vaccination	Severe local reaction Sepsis Injection-site abscess
Within 12 days of vaccination	Seizures, including febrile seizures Encephalopathy
Within 3 months of vaccination	Acute flaccid paralysis* (AFP), including Guillain–Barré syndrome (GBS) Brachial neuritis (can occur around 2–28 days after tetanus-containing vaccine) Thrombocytopenia (can occur around 15–35 days after MMR)
Between 1 and 12 months after BCG vaccination	Lymphadenitis Disseminated BCG infection Osteitis/osteomyelitis
No time limit	Intussusception after rotavirus vaccine Any death, hospitalisation or other severe or unusual events of clinical concern that are thought by health professionals or the public to possibly be related to vaccination
Newly introduced vaccines, or those with new indications or being delivered by a different route	
No time limit	All suspected adverse reactions

* AFP in children is also monitored by the New Zealand Paediatric Surveillance Unit as part of polio eradication surveillance (see chapter 17).

Seriousness of AEFIs

Reports of suspected adverse reactions or AEFIs can be categorised as serious or non-serious. This categorisation system is a tool used to try and prioritise safety concerns. It is not a reflection of the importance of the events to the consumer or their health care professional. Because a report is defined as serious based on what is reported, it is possible to have both serious and non-serious cases reporting the same type of event; for example, headache.

International convention defines the seriousness of reports based on the outcome or nature of the reported event as documented in the report, *irrespective of whether there is any association to the medicine or vaccine*.

Serious events are based on the following international criteria:

- hospitalisation (or prolonged hospitalisation) of the patient
- life-threatening event
- persisting disability of the patient
- intervention required to prevent permanent impairment
- congenital anomaly
- death of the patient.

CARM assessment of causality

The WHO recommends that individual reports of adverse reactions to vaccines are assessed for causality. This assessment is a tool used to help detect new safety concerns; it is not a determination of whether a vaccine caused an adverse reaction.

The person reporting the event will receive a letter of response from CARM commenting on the adverse effect, the causal relationship and the number of other similar events, and advice about future use of the vaccine in the individual. Also, where applicable, CARM will provide a validated AEFI code to the NIR or the AIR (dependent on the system rollout for AIR, which is the replacement system for the NIR).

The information provided by CARM:

- needs to be communicated to the individual and parent/guardian (if applicable)
- must be entered in the medical notes
- will help to identify those individuals who should receive follow-up vaccination in a controlled environment, such as a hospital.

1.6.4 What does Medsafe do with this information?

Medsafe and CARM analyse spontaneous reports in conjunction with other information to determine whether there are any new potential safety signals. Medsafe seeks the advice of independent experts through the Medicines Adverse Reactions Committee or may form working groups of experts to provide advice. Medsafe works closely with other regulatory authorities from around the world.

Medsafe undertakes a risk–benefit assessment of safety signals to decide if action is required. Further information on risk–benefit assessment is provided on the Medsafe website (**www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medsafe-Evaluation-Process.asp**).

Most safety signals are not supported by any additional information, and no action is taken, although Medsafe may continue to monitor the issue closely. A small number of possible safety signals are confirmed as real. In these cases, Medsafe has several regulatory actions it can take, including withdrawing the product.

In New Zealand, it is less likely that any rare new side-effects to vaccines will be detected because of the small number of people immunised compared to other countries. Therefore, Medsafe uses international data available from the WHO, other regulators and pharmaceutical companies to help assess any reports of rare events following immunisation and to determine if they may be new events linked to immunisation.

1.6.5 Advantages and limitations of spontaneous reports

Spontaneous reports have been shown to be a very simple way of identifying potential or possible safety signals with medicines, and over 90 countries have a spontaneous reporting system. They can be used to monitor the safety of medicines in real-life use over the lifetime of the medicine, and for all types of people.

The limitations of using spontaneous reports include under-reporting, a lack of reliable information on the extent of use of the medicine and wide variations in the clinical details provided about the event and the history of the patient. Spontaneous reports are heavily subject to reporting bias, such as media or other attention on an issue. They are also not very effective at detecting adverse reactions that occur a long time after starting the medicine.

For these reasons, such reports are only used to identify safety signals. These signals require further formal epidemiological study before they can be validated or discounted. Information obtained from spontaneous reports needs to be interpreted with caution.

Understanding vaccine safety and spontaneous reporting

Spontaneous report patterns can be variable, and they depend on many factors. Summaries of reported events following immunisation *are not* lists of known or proven adverse reactions to vaccines. They cannot be used to determine the frequency of adverse reactions to vaccines in the whole population, and they cannot be used to directly compare the relative safety of vaccines. They must not be interpreted and used as such.

Health care professionals and consumers are encouraged to report any suspicions that an event they have experienced may have been caused by vaccination. Therefore, reports sent to CARM may be:

- real adverse reactions to the vaccine
- anxiety or nervousness about needles or the process of vaccination
- coincidental events that would have occurred anyway.

With any vaccine, the adverse events that are generally reported include:

- injection-site reactions
- well-recognised events, such as headaches, dizziness, muscle aches, mild fever and tiredness
- mild allergic reactions, such as mild rashes and itching
- rare but serious allergic reactions, called anaphylaxis, which can occur in response to any medicine or vaccine and some foods – health care professionals giving vaccines are trained to recognise the symptoms of serious allergic reactions and promptly treat them
- immunisation stress-related responses due to fear or anticipation of the needle injection (eg, fainting or hyperventilation)
- coincidental medical conditions
- new adverse events (ie, those not already listed in the prescribing information [data sheet]).

There will always be a few coincidental events reported because vaccines are given to large sections of the population. In some cases, vaccines are specifically targeted at people with underlying medical conditions (eg, the influenza vaccine). The challenge is to be able to distinguish these coincidental 'background' events from those that may have been caused by the vaccine. There are a range of research methods for assessing the risk of an event after a vaccine compared with the risk with no vaccine exposure.

The time between immunisation and an event can be important in determining whether the event was coincidental. Most reactions to vaccines occur within a very short time of immunisation, usually within days.

Another important approach taken when assessing vaccine safety is comparing the number of reports for a specific event with the expected background rate for that event. When doing this, it is important to ensure that definite diagnoses of the events reported were made and to adjust the background rate for any differences in population groups and seasonal variations.[3]

References

1. Fine P, Mulholland K, Scott J, et al. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, et al. (eds). Elsevier: Philadelphia, US.
2. Read TR, Hocking JS, Chen MY, et al. The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections*, 2011. 87(7): p. 544-7.
3. Sexton K, McNicholas A, Galloway Y, et al. Henoch-Schönlein purpura and meningococcal B vaccination. *Archives of Disease in Childhood*, 2009. 94(3): p. 224-6.

2 Processes for safe immunisation

This chapter provides information about:

- Pre-vaccination: cold chain management, informed consent, pre-vaccination screening, contraindications, spacing of doses, catch-up, and adult vaccination (section 2.1)
- Vaccine administration: preparation, route, vaccination techniques by age, and multiple injections (section 2.2)
- Post-vaccination: post-vaccination advice, pain and fever recommendations, anaphylaxis and emergency management, and documentation and insurance (section 2.3).

Who can administer a vaccine?

Vaccines can be administered by:

- a nurse practitioner
- a medical practitioner
- a registered midwife
- a designated prescriber (which includes a registered nurse fulfilling the designated prescriber criteria)
- a person authorised to administer the medicine in accordance with a prescription or a standing order
- a registered pharmacist and a registered intern pharmacist (who has completed approved training on vaccinations)
- a person who is authorised by either the Director-General of Health or a Medical Officer of Health under Regulation 44A or 44AB of the Medicines Regulations 1984 (see A3.6)
- a person authorised as a COVID-19 vaccinator (working under supervision) and vaccinating health worker by either the Director-General of Health or the national Medical Officer of Health under Regulation 44AB of the Medicines Regulations 1984 (see A3.6).

The vaccines a person may administer will vary depending on the lawful basis upon which they can administer a vaccine or vaccines (see A3.6).

2.1 Pre-vaccination

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' apply to the delivery of all Schedule vaccines and those not on the Schedule. See Appendix 3.

The vaccinator is responsible for ensuring all the vaccines they are handling and administering have been stored at the recommended temperature range of +2°C to +8°C at all times (see section 2.1.1 '**Cold chain management**' below and *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Information on vaccine presentation, preparation and disposal can be found in Appendix 7.

Vaccinators are expected to know and observe standard occupational health and safety guidelines to minimise the risk of spreading infection and needle-stick injury (see Appendix 7).

All vaccinations on the New Zealand National Immunisation Schedule are given parenterally (by injection) except for the rotavirus vaccine which is given non-parenterally (orally). For non-parenteral vaccine administration, follow the manufacturer's instructions.

2.1.1 Cold chain management

All vaccines must always be stored and/or transported within the recommended temperature range of +2°C to +8°C. See the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* for detailed vaccine storage, transportation and destruction information (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

The 'cold chain' is defined as 'the system of transporting and storing vaccines within the recommended temperature range of +2°C to +8°C from the place of manufacture to the point of vaccine administration (the individual)'. The integrity of the cold chain is dependent not only on the equipment used for storage, transportation and monitoring but also on the people involved and the processes/practices they undertake.

Table 2.1: Key points for cold chain management

All vaccinators are responsible for ensuring the vaccines they administer have been stored correctly.
All immunisation providers storing vaccines must use a pharmaceutical refrigerator.
The pharmaceutical refrigerator minimum and maximum temperatures must be monitored and recorded at the same time each working day.
All immunisation providers must monitor the refrigerator with an electronic temperature recording device (eg, a data logger) that records and downloads data on a weekly basis. This should be compared with the daily minimum/maximum recordings.
All immunisation providers who store vaccines and/or offer immunisation services must achieve Cold Chain Accreditation.
Each immunisation provider must have a written cold chain management policy in place and ensure their policy is reviewed and updated annually. Each vaccinator is responsible to ensure they are able to access this policy, as it will contain important practice information on vaccine storage.

If the vaccine refrigerator temperature goes outside the recommended +2°C to +8°C range
• Label the vaccines 'not for use'.
  – If the refrigerator is currently running within the +2°C to +8°C range, leave the labelled vaccines in your refrigerator.
  – If the refrigerator is not within the +2°C to +8°C range, look for obvious reversible causes (door open, power interruption). If no cause found, pack your labelled vaccines into a chilly bin, with a temperature monitoring device and consider transporting to your back-up provider (details for this are in your cold chain policy).
• Download the data logger and check for inconsistencies or temperature fluctuations; note any temperature fluctuations outside the +2°C to +8°C range, and the time-period
• Breeches of less than 30 minutes, under 12°C with a known cause can be documented but you do not need to report to local immunisation coordinator. If the cause is unknown, or multiple events occur on the same day, seek advice.
• Contact your local immunisation coordinator for advice and further actions.
• Document the steps and actions you have taken.

2.1.2 Informed consent

What is informed consent?

Informed consent is a fundamental concept in the provision of health care services, including immunisation. It is based on ethical obligations that are supported by legal provisions (eg, the Health and Disability Commissioner Act 1994, Code of Health and Disability Services Consumers' Rights 1996, Health Information Privacy Code 1994, Privacy Act 1993 and Privacy Amendment Act 2013).

Providing meaningful information to enable an informed choice and to seek informed consent is a duty that all health and disability providers must meet to uphold the rights of health and disability consumers. Informed consent includes the right to be honestly and openly informed about one's personal health matters. The right to agree to treatment carries with it the right to refuse and withdraw from treatment.

Informed consent is also an external expression of a health care provider's pivotal ethical duty to uphold and enhance their patient's autonomy by respecting the patient's personhood in every aspect of their relationship with that individual.

The informed consent process

Informed consent is a process whereby the individual or parent/guardian are appropriately informed in an environment and manner that are meaningful. Having been well informed, they are willing and able to agree to what is being suggested without coercion.

Regardless of age, an individual and/or their parent/guardian must be able to understand:

- that they have a choice
- why they are being offered the treatment/procedure
- what is involved in what they are being offered
- the probable benefits, risks, side-effects, failure rates and alternatives, and the risks and benefits of not receiving the treatment or procedure.

To make an informed choice and give informed consent for vaccination, the individual or parent/guardian needs to understand the benefits and risks of vaccination, including those to the child and community.

Consent for patients who are incompetent (individuals who do not have the capacity to consent) may be given by:

- a welfare guardian appointed under the Protection of Personal and Property Rights Act 1988
- an attorney under an activated enduring power of attorney in respect of care and welfare.

If there is no welfare guardian or attorney under an enduring power of attorney, treatment may be provided under Right 7(4) of the Code of Health and Disability Services Consumers' Rights if:

- the treatment is in the best interests of the patient; and
- attempts have been made to find out what the patient would have wanted if s/he were competent; or
- if it is not possible to find out what the patient would have wanted, the views of people interested in the patient's welfare have been considered.

The essential elements of the informed consent process are effective communication, full information and freely given competent consent. The specific rights in the Code of Health and Disability Services Consumers' Rights that represent these three elements are:

- Right 5: Right to effective communication
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent.[1]

For example, section 7(1) of the Code states that 'services may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of the Code provides otherwise.' Information on the Code of Health and Disability Services Consumers' Rights can be found on the Health and Disability Commissioner's website (**hdc.org.nz**).

Health professionals have legal obligations to obtain informed consent prior to a procedure and prior to data collection (eg, data collected for the NIR or the AIR, depending on the system rollout for AIR, which is the replacement system for the NIR). Unless there are specific legal exceptions to the need for consent, the health professional who acts without consent potentially faces the prospect of a civil claim for exemplary damages, criminal prosecution for assault (sections 190 and 196 of the Crimes Act 1961), complaints to the Health and Disability Commissioner and professional disciplining.

Ensuring that an individual has made an informed choice regarding treatment options has been included in the Health Practitioners Competence Assurance Act 2003. This Act ensures that health practitioners are, and remain, competent and safe to practise. For example, the Nursing Council of New Zealand competencies for the Registered Nurse Scope of Practice, Competency 2.4, 'ensures the client has adequate explanation of the effects, consequences and alternatives of proposed treatment options' (see the Nursing Council of New Zealand website, **nursingcouncil.org.nz**).

Privacy and control over personal information

The right to authorise, or to exert some control over, the collection and disclosure of personal information about oneself is a right closely allied to that of consent to treatment and is also relevant to personal integrity and autonomy. The Health Information Privacy Code 1994 gives people the right to access, and seek correction of, health information about them (Rules 6 and 7). It also requires health agencies collecting identifiable information to be open about how and for what purpose that information will be stored, and who will be able to see it (Rule 3).

Parents and guardians have a similar right of access to information about their children under section 22F of the Health Act 1956. This right is limited in that access requests can be refused if providing the information would be contrary to the interests or wishes of the child.

Further information about privacy and health information can be found on the Privacy Commissioner's website (**privacy.org.nz**), or by calling the privacy enquiries line: 0800 803 909.

Immunisation consent in primary care

Parents should be prepared during the antenatal period for the choice they will have to make about their child's vaccination. During the third trimester of pregnancy, the lead maternity carer must provide Ministry of Health information on immunisation and the NIR or the AIR (dependent on the system rollout for AIR). This is a requirement under

clause DA21(c) of the Primary Maternity Services Notice 2007, pursuant to section 88 of the New Zealand Public Health and Disability Act 2000.

Vaccine hesitancy

> Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It includes factors such as complacency, convenience and confidence.
>
> WHO: Addressing Vaccine Hesitancy

Effective communication and active listening are key components of the informed consent process, especially when health care providers are working with vaccine-hesitant individuals/parents/guardians. In this situation, providers should:

- be willing to initiate the conversation, and avoid leaving it to others
- tailor content to the needs of the individual
- ensure respect and acknowledgement of concerns
- use plain language, open-ended questions and active listening
- avoid medical jargon, or ensure it is explained
- offer resources
- finish with an effective immunisation recommendation.

Information for parents, guardians and health care providers

Health care providers must offer information without individuals or parents/guardians having to ask for it. The depth of information offered or required may differ, but it should at least ensure that the individual or parent/guardian understands what the vaccine is for and the possible side-effects, as well as information about the vaccination programme, the NIR or the AIR (dependent on the system rollout for AIR) and the risks of not being vaccinated (see chapter 3).

Every effort should be made to ensure that the need for information is met, including extra discussion time, use of an interpreter and alternative-language pamphlets. Ministry of Health immunisation pamphlets are produced in several languages, and are available from the local authorised provider or can be ordered, viewed and/or downloaded from the HealthEd website (**healthed.govt.nz**).

Issues to discuss with individuals or parents/guardians about immunisation include:

- the vaccine-preventable diseases
- the vaccines used on the Schedule (ie, the funded vaccines that are available)
- how vaccines work, known risks and adverse events, and what the vaccine is made of, in case of known allergies
- the collection of immunisation information on the NIR or the AIR (dependent on the system rollout for AIR) from birth, or as part of a targeted immunisation programme

(eg, the information that will be collected, who will have access to it and how it will be used; see section 2.3.5 for more information on the NIR or the AIR)

- the choice to vaccinate.

Informed consent is required for each immunisation episode or dose. Presentation for an immunisation event should not be interpreted as implying consent. Individuals and parents/guardians have the right to change their mind at any time. Where consent is obtained formally but not in writing, the provider should document what was discussed, and that consent was obtained and by whom.

Ministry of Health information

Ministry of Health immunisation information is available for parents and guardians on the Ministry of Health's website (**www.health.govt.nz/immunisation**). Parents and guardians may also order, view or download Ministry of Health immunisation information from the HealthEd website (**healthed.govt.nz**) or from the local authorised resource provider, including:

- Immunise Your Child on Time (leaflet, available in English [HE1327] and other languages)
- Childhood Immunisation (health education booklet [HE1323]).

Further immunisation consent information for health care providers is also available in Appendix 3 'Immunisation standards for vaccinators and guidelines for organisations offering immunisation services'. Responses to commonly asked questions and suggestions for addressing myths and concerns are available in chapter 3.

Other information sources

- Sharing Knowledge About Immunisation (SKAI) is an Australian suite of online resources and tools to support vaccination communication designed to aid conversations about childhood immunisation for parents and health care providers (www.ncirs.org.au/our-work/sharing-knowledge-about-immunisation).
- Offit PA, Moser C. 2011. *Vaccines and Your Child – Separating fact from fiction*. New York, NY: Columbia University Press.
- Vaccine manufacturers' data sheets, available on the Medsafe website (**medsafe.govt.nz**). Consumer and health care provider versions are available.
- Other recommended immunisation-related websites (see Appendix 8).

Alternatively, contact:

- the Immunisation Advisory Centre on freephone 0800 IMMUNE/0800 466 863, or see the IMAC website (**immune.org.nz**)
- your local immunisation coordinator (a list and contact details are available at (**immune.org.nz**).

Immunisation consent in other settings (eg, schools)

In mass immunisation campaigns, such as those undertaken at schools, the consent requirements are different from those that apply to the vaccination of individuals in primary care. The parent/guardian may not be with the child on the day of immunisation, so immunisation should proceed only after the parent/guardian has had the opportunity to read the immunisation information and discuss any areas of concern. Consent forms are provided for immunisations given in schools by public health nurses and may also be used in mass vaccination settings. For children aged under 16 years who are being immunised at school, written consent must be obtained from the parent/guardian. Individuals who are aged 16 years or older may self-consent.

Consent and children

Under the Code of Rights, every consumer, including a child, has the right to the information they need to make an informed choice or to give informed consent. The law relating to the ability of children to consent to medical treatment is complex. There is no defined age at which all children can consent to all health and disability services. The presumption that parental consent is necessary to give health care to those aged under 16 years is inconsistent with common law developments and the Code of Rights.

The Code of Rights makes a presumption of competence (to give consent) in relation to children, although New Zealand is unusual in this respect (ie, the obligations regarding consent of minors are greater in New Zealand than in many other jurisdictions).

A child aged under 16 years has the right to give consent for minor treatment, including immunisation, providing he or she understands fully the benefits and risks involved. In 2002 the Health and Disability Commissioner provided an opinion of a child's consent to a vaccine, whereby the Commissioner was satisfied that a 14-year-old was competent to give informed consent for an immunisation event due to an injury where a tetanus toxoid vaccine would be commonly given. More details of this opinion can be found on the Health and Disability Commissioner's website (**hdc.org.nz/** – Case: 01HDC02915).

Further information on informed consent can be found on the Health and Disability Commissioner's website (**hdc.org.nz**).

2.1.3 Pre-vaccination screening

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccine recipient (child or adult) has a condition or circumstance which may influence whether a vaccine is given, deferred or contraindicated. Table 2.2 below provides a checklist of conditions or circumstances to screen for, along with the appropriate action to take and a rationale.

The vaccinator will also need to determine which vaccines are due, assess the vaccine recipient's overall current vaccination status and address parental concerns. The vaccinator also needs to advise the individual/parent/guardian they will need to remain for 20 minutes post-vaccination.

Table 2.2: Pre-vaccination screening and actions to take

Condition* or circumstance	Action	Rationale
Is unwell today: • fever >38°C • acute systemic illness	Defer all vaccines until afebrile. Note: Children with minor illnesses (without acute symptoms/signs) should be vaccinated.	To avoid an adverse event in an already unwell child, or to avoid attributing symptoms to vaccination.
Is a preterm infant and had apnoea following immunisation in hospital (at 6-week and/or 3-month event)	Re-admission for the next infant immunisation and respiratory monitoring for 48 to 72 hours may be warranted,[2] but do not avoid or delay immunisation. Babies born <28 weeks' gestation and other preterm babies who develop chronic lung disease will require PCV13 plus 23PPV at 2 years (see section 4.2.2).	There is a potential risk of apnoea in infants born before 28 weeks' gestation. Preterm infants may be at increased risk of vaccine-preventable diseases (eg, invasive pneumococcal disease).
Previously had a severe reaction to any vaccine	Careful consideration will be needed depending on the nature of the reaction. If in doubt about the safety of future doses, seek specialist advice.	Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.
Anaphylaxis to vaccine components (eg, gelatin, neomycin)	Refer to the relevant vaccine data sheet (**www.medsafe.govt.nz**) for the components. If an individual has had anaphylaxis to any component contained in a vaccine, seek specialist advice. Note: Egg allergy, including anaphylactic egg allergy, is not a contraindication to MMR or influenza vaccination (see sections 11.6.3 and 12.6.3).	Vaccinators need to be aware of the possibility that allergic reactions, including anaphylaxis, may occur after any vaccination without any apparent risk factors (see section 2.3.3). Delayed hypersensitivity to a prior vaccine dose or a component of a vaccine is not a contraindication to further doses, but it is important to distinguish this from anaphylaxis.
Appropriate spacing between doses of the same vaccine (when was the last vaccination, and what was it?)	See section 2.1.5 and check the relevant disease chapters and catch-up schedules. (See below for live parenteral vaccines.)	The general rule is for a minimum of 4 weeks between doses of a primary series and 4 months between the priming dose(s) and the booster.

Continued overleaf

Condition* or circumstance	Action	Rationale
Had a live parenteral vaccine within the last 4 weeks – if in doubt, check the individual's immunisation status on the NIR (if applicable) or the AIR (dependent on the system rollout for AIR)	Delay further live attenuated parenteral vaccines to 4 weeks. Note that this does not apply to rotavirus vaccine, which is an oral vaccine.	The antibody response to the first dose may interfere with the response to the second. They may be given on the same day.
Had an injection of immunoglobulin or a blood transfusion within the last year and is now due for a live vaccine	Check which product the person received and the interval since administration. See Table A6.1. Delay vaccination if necessary.	Live virus vaccines should be given at least 3 weeks before or deferred. The interval will be determined by the blood product and dose received.
Has a disease that lowers immunity, is receiving treatment that lowers immunity or is an infant of a mother who received immunosuppressive therapy during pregnancy	See chapter 4 'Immunisation of special groups'. In some cases, specialist advice may need to be sought before vaccination. Note: Persons living with someone with lowered immunity should be fully vaccinated, including with live viral vaccines (see section 4.3.1).	The safety and effectiveness of the vaccine may be suboptimal in persons who are immunocompromised. Live attenuated vaccines may be contraindicated.
Is planning a pregnancy	See section 4.1.1 'Women planning pregnancy'. Ensure women and household members have received all vaccines recommended for their age group. Women should know if they are immune to measles (section 12.8.3), rubella (section 19.5.3) and varicella (section 22.5.4). Advise women not to become pregnant within 4 weeks of receiving live viral vaccines.	Vaccinating before pregnancy may prevent maternal illness, which could affect the infant, and may confer passive immunity to the newborn.
Is pregnant	See sections 4.1.2 'During pregnancy' and 4.1.3 'Breastfeeding and post-partum'. Influenza and Tdap vaccines are recommended.	Vaccinating (with inactivated or subunit vaccines) during pregnancy may prevent maternal illness, which could affect the infant, and confers passive immunity to the newborn.
	Live vaccines should be avoided until after the delivery.	Deferring administration of live vaccines until after delivery is a precautionary safety measure. Studies of women who inadvertently received a live vaccine during pregnancy and their infants have not identified any adverse effects.

Continued overleaf

Condition* or circumstance	Action	Rationale
Unstable neurological condition (for pertussis-containing vaccines only)	Seek specialist advice.	Vaccination is recommended for children with unstable neurological conditions as they may be at high risk of severe pertussis complications. Individual cases should be discussed with a specialist.
Thrombocytopenia or bleeding disorders	Administer intramuscular vaccines with caution: • use a 23-gauge or smaller needle and apply firm pressure to the injection site (without rubbing) for at least 10 minutes. (see section 2.2.3).	A haematoma may occur following intramuscular administration. In some cases, subcutaneous is preferred where datasheet allows. Seek specialist advice as appropriate.
Individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months.	Contraindication for live vaccines.	There is a theoretical risk that vaccines may trigger an autoimmune response in these individuals. See the 'Immune checkpoint inhibitor (immunostimulant) therapy' discussion in section 4.3.2.
History of Guillain–Barré syndrome (GBS)	The risks and benefits of withholding vaccination should be considered on an individual basis.	Consider the risk of recurrent GBS following influenza infection.

* See chapter 4 for more information about pregnancy and lactation and for information about infants with special immunisation considerations, immune-deficient and immunosuppressed individuals, immigrants and refugees, travel, and occupational and other risk factors.

Adapted from: Australian Technical Advisory Group on Immunisation (ATAGI). 2018. *Australian Immunisation Handbook* Canberra: Australian Government Department of Health URL: **https://immunisationhandbook.health.gov.au** (accessed 30 June 2020).

2.1.4 Contraindications

No individual should be denied vaccination without serious consideration of the consequences, both for the individual and for the community. Where there is any doubt, seek advice from the individual's general practitioner (GP), a public health medicine specialist, medical officer of health, consultant paediatrician or IMAC.

Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine. (Note that egg-related anaphylaxis and influenza vaccine or MMR are exceptions.)
For more detail on anaphylaxis, see section 2.3.3.

Live viral vaccines should not be given to pregnant women, nor, in general, to immunosuppressed individuals and those treated within the last 6 months with immune checkpoint inhibitors (see chapter 4).

See the relevant disease chapter section for more specific vaccine contraindications.

Conditions that are not contraindications to immunisation

The conditions in Table 2.3 are not contraindications to the immunisation of children and adults (see also section 3.1).

Table 2.3: Conditions that are not contraindications to immunisation

Individuals with these conditions should be vaccinated with all the recommended vaccines.

Mildly unwell, with a temperature ≤38°C
Asthma, hay fever, eczema, 'snuffles', allergy to house dust
Receiving treatment with antibiotics or locally acting steroids
A breastfeeding mother or a breastfed child
Neonatal jaundice
Low weight in an otherwise healthy child
The child being over the usual age for immunisation – use age-appropriate vaccines, as per the catch-up schedules in Appendix 2 (the exception is rotavirus vaccine: see section 18.5.2)
A previous hypotonic-hyporesponsive episode (see section 2.3.3)
Clinical history of pertussis, measles, mumps or rubella infection – clinical history without laboratory confirmation cannot be taken as proof of immunity (even when an individual is proven to be immune to one or two of either measles, mumps or rubella, there is still the need for immunisation against the other/s: see relevant chapters)
Prematurity, but an otherwise well infant – it is particularly important to immunise these children, who are at higher risk of severe illness if infected; immunisation is recommended at the usual chronological age (see 'Preterm and low birthweight infants' in section 4.2.2)
Stable neurological conditions, such as cerebral palsy or Down syndrome
Contact with an infectious disease
Egg allergy, including anaphylaxis, is not a contraindication to MMR (see section 12.6.3) or influenza vaccine (see section 11.6.3)
Family history of vaccine reactions
Family history of seizures
Family history of sudden unexpected death in infancy (SUDI)
Child's mother or household member is pregnant or immunocompromised

2.1.5 Spacing of doses

In general, follow the recommendations in the manufacturers' data sheets.

Principles for spacing of doses of the same vaccine

The immune response to a series of vaccines depends on the time interval between doses. The general rule is for a minimum of four weeks between doses of a primary series; however, the immune response may be better with longer intervals. A repeat dose of the same vaccine given less than four weeks after the previous dose may result in a reduced immune response. Specific recommendations for a rapid schedule by the manufacturer may apply for some vaccines.

Generally, a minimum interval of four to six months between priming dose(s) and the booster dose allows affinity maturation of memory B cells, and thus higher secondary responses (see section 1.1).

It is not necessary to repeat a prior dose if the time elapsed between doses is more than the recommended interval.

Spacing of different vaccines

Two or more parenterally administered live vaccines may be given at the same visit; for example, MMR and VV. However, when given at different visits, a minimum interval of four weeks is recommended. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine.

Note that no interval is required between administration of Bacillus Calmette–Guérin (BCG) and rotavirus vaccines.

Unless there is a specific recommendation against it, a subunit vaccine can be administered either simultaneously or at any time before or after a different subunit or live vaccine.

Concurrent administration of vaccines

Changing the timing of visits or increasing the number of visits to avoid multiple injections delays protection against potentially serious diseases and may also lead to incomplete immunisation. Best practice is to follow the Schedule.

> Where different injectable vaccines are given on the same day, they must be administered in separate syringes, at different sites.

2.1.6 Catch-up programmes for unimmunised or partially immunised children

The objective of a catch-up programme is to complete a course of vaccinations that provides adequate protection. Catch-up programmes should be based on documented evidence of previous vaccination (eg, the child's *Well Child Tamariki Ora My Health Book*, NIR or AIR, depending on system rollout for AIR, or overseas immunisation records).

When children have missed vaccine doses, it is important to bring them up to date as quickly as possible. Where more than one vaccine is overdue, it is preferable to give as many as possible at the first visit. For children aged 12 months and older, MMR is the priority.

See Appendix 2 for determining catch-up requirements and planning a catch-up programme.

If the vaccinator is uncertain about how to plan a catch-up programme, they should contact the local immunisation coordinator, IMAC, medical officer of health or public health service.

Once catch-up is achieved, vaccination for the child should continue as per the Schedule.

Vaccination of children with inadequate vaccination records

It is recommended that children *without a documented history of vaccination* have a full course of vaccinations appropriate for their age. It is preferable, and safe, for the individual to receive an unnecessary dose rather than to miss out a required dose(s) and not be fully protected.

2.1.7 Adult vaccination (aged 18 years and older)

Whenever adults are seen in general practice or by immunisation providers, there is an opportunity to ensure they have been adequately protected against the following diseases and have received at least a primary immunisation course as described in Table 2.4. If the requisite number of doses has not been received, catch-up vaccination is recommended and funded (see Appendix 2).

Women of childbearing age should know whether or not they are immune to measles (see chapter 12), rubella (see chapter 19) and varicella (see chapter 22).

Refer to the PHARMAC schedule for further details on vaccines funded for adults (available at **pharmac.govt.nz**).

Table 2.4: Funded immunisation for adults

Vaccine	Number of vaccine doses
Tdap	3 doses[a]
Poliomyelitis (IPV)	3 doses
Measles, mumps, rubella	2 doses
HPV (aged 26 years and under)	3 doses[b]
Influenza	1 dose annually (for eligible groups)
COVID-19 (mRNA-CV)	2 doses[c] plus booster doses
rZV (at age 65 years)	2 doses

a. Although pertussis protection is included in the Tdap vaccine as part of protection against Tetanus and diphtheria, if a patient is missing this antigen only but is otherwise fully vaccinated, no further vaccines are required unless the patient is pregnant.

b. Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 27 years when they complete it.

c. Includes all adults, regardless of eligibility to health and disability services. One other COVID-19 vaccine is available (see section 5.4.2).

See Table 2.5 for additional adult vaccination recommendations, including vaccinations recommended for special groups (funded vaccines are in the shaded boxes). See also chapter 4 'Immunisation of special groups' for information about immunisation during pregnancy and lactation (section 4.1), of immunocompromised individuals (section 4.3), of immigrants and refugees (section 4.7), for those with occupational-related vaccination (section 4.8) and for travel (section 4.9).

Table 2.5: Adult (≥18 years) vaccination recommendations, excluding travel requirements

Vaccine	Recommended and funded	Recommended but not funded
COVID-19 (chapter 5)	All adults A third primary dose for severely immunocompromised Second booster doses available for certain groups	
Hib-PRP-T (chapters 4 and 7)	(Re)vaccination of patients post-haematopoietic stem cell transplant (HSCT) or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant, pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens	
Hepatitis A (chapter 8)	Transplant patients Close contacts of hepatitis A cases[a]	Patients with chronic hepatitis B or C infection; men who have sex with men; adults at occupational risk

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
Hepatitis B (chapter 9)	Household or sexual contacts of patients with acute or chronic HBV infection HIV-positive patients Hepatitis C-positive patients Following non-consensual sexual intercourse Prior to or following immunosuppression[b] Solid organ transplant patients Post-HSCT patients Following needle-stick injury Dialysis patients Liver or kidney transplant patients	Non-immune adults at risk including occupational or other risk factors
HPV (chapter 10)	All individuals aged 9–26 years[c,d] Individuals aged 18–26 years who are:[c,d] • confirmed with HIV infection • transplant (including stem cell) patients • an additional dose post-chemotherapy	Adults ≥27 years:[c,d,e] • who have had little previous exposure to HPV and are now likely to be exposed • who are men who have sex with men • with HIV
Annual influenza vaccine (chapter 11)	Pregnant women and people Individuals aged 65 years and older Individuals aged from 55 years of Māori and Pacific ethnicity Individuals aged under 65 years with eligible conditions See **influenza.org.nz**	Close contacts of elderly adults and other high-risk groups All other adults
MMR (chapters 12, 14 and 19)	Any individual susceptible to any one of these three diseases (Re)vaccination prior to planned or following immunosuppression[b]	
MenACWY-D and 4CMenB (chapters 4 and 13)	For patients who are pre- or post-splenectomy or with functional asplenia; with HIV; with complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited); who are pre- or post-solid organ transplant Close contacts of meningococcal cases[a] Patients who have had previous meningococcal disease (any group) HSCT (bone marrow transplant) patients Patients prior to planned and following immunosuppression[b] MenACWY only: Adolescents and young adults aged 13–25 years inclusively who will be living or are currently living in a boarding school hostel or university hall of residence, military barracks or prison	Laboratory workers handling bacterial cultures Health care professionals in very close contact with cases

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
Pertussis-containing vaccine (chapters 4 and 15)	Tdap is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis Tdap for (re)vaccination of patients who are post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens	Tdap if in contact with infants aged under 12 months
PCV13 and 23PPV (chapters 4 and 16)	(Re)vaccination of patients with HIV; pre- or post-HSCT[f] or chemotherapy;[f] pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant; renal dialysis; complement deficiency (acquired or inherited); cochlear implants; primary immune deficiency	PCV13 followed by 23PPV for those with certain conditions PCV13 followed by 23PPV for those aged 65 years or older
IPV (chapter 17)	Any unvaccinated or partially vaccinated individual (Re)vaccination prior to planned or following immunosuppression[b]	Travellers to certain high-risk countries
Tdap (chapters 5 and 20)	Tdap for susceptible individuals (including following immunosuppression); boosters[g] at 45 (if had less than 4 previous doses of tetanus vaccine) plus 65 years; boosting of patients with tetanus-prone wounds	
Varicella (chapter 22)	Non-immune patients: • with chronic liver disease who may need a transplant in the future • with deteriorating renal function before transplantation • prior to solid organ transplant • prior to any planned immunosuppression[b] • for post-exposure prophylaxis of immune-competent hospital in-patients Patients at least 2 years after bone marrow transplant[h] Patients at least 6 months after completion of chemotherapy[h] HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression[h] Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella	Susceptible adults

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
Varicella *continued*	Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella	
rZV (chapter 23)	2 doses of rZV are funded for individuals at age 65 years	rZV may be considered, but is not funded, for individuals aged from 50[i] years who are: • at increased risk of shingles and who may benefit from being vaccinated earlier than the routine schedule • for those aged over 66 years

a. Only 1 dose of vaccine is funded for close contacts.

b. Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

c. Individuals who started with HPV4 may complete their remaining doses with HPV9.

d. Individuals who were <27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are ≥27 years when they complete it.

e. HPV9 vaccine is registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

f. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

g. The administration charge for the Td booster is not funded, although the vaccine is free.

h. On the advice of their specialist.

i. Available for use for certain medical conditions from age 18 years.

2.2 Vaccine administration

2.2.1 Minimising pain and distress at the time of vaccination

The WHO key recommendations for minimising pain and distress at the time of vaccination are:[3, 4]

- do not aspirate (draw back) when giving vaccines
- administer vaccines from the least to the most painful for all ages
- breastfeed before and during vaccine injection
- position (hold the infant/young child, individuals aged 3 years and older should sit up, parental presence)

- for infants, give oral rotavirus vaccine before injections (the vaccine contains sucrose that can reduce pain)
- use calming and supportive words at the time of vaccination; avoid language that increases anxiety
- provide appropriate distractions
- consider using topical anaesthetics (only if the cost is acceptable to the family).

See also section 2.3.2 and the IMAC factsheets *Mitigating Vaccination Pain and Distress* and *Fear of Needles and Needle Phobia* (available at **immune.org.nz/resources/written-resources**).

2.2.2 Preparing for vaccine administration

Key points for administering injectable vaccines

Vaccines should not be mixed in the same syringe, unless the prescribing information sheet specifically states it is permitted or essential (eg, DTaP-IPV-HepB/Hib).

Careful use of a longer needle will cause less damage than a short needle.

To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle.

Correct vaccine administration is important, and vaccinators have a responsibility to see that vaccines are given:

- in the optimal site as recommended in Handbook
- using the appropriate needle size for vaccine effectiveness and patient safety.

The use of alternative sites will be based on professional judgement, including knowledge of the potential risks at each site and recommendations in the manufacturer's data sheet.

The guidelines in Table 2.6 will help to make the experience less distressing for the individual, parent/guardian and/or whānau, and vaccinator.

Table 2.6: Guidelines for vaccine administration

Preparation	Immunisation event
Vaccinate in a private and appropriate setting.	Draw up injections out of sight, if possible. Medical equipment is commonplace to vaccinators, but it may heighten the anxiety of some individuals.
Prepare the area/room layout to suit the vaccinator and vaccination event.	Ensure the individual or parent/guardian has had the opportunity to discuss any concerns and has given informed consent.
Be familiar with the vaccines (eg, their correct preparation, administration and the potential for adverse events).	Be prepared to include other family members and whānau in the discussion; explain to older children accompanying infants why the injections are being given and what will happen.
Be aware of the individual's immunisation history (eg, submit a status query to the NIR or AIR, depending on the system rollout of AIR, if the history is unknown).	Give the appropriate immunisations due and advise when the next immunisation event is due.
Ensure there are age-appropriate distractions available.	For breastfed babies, suggest that the mother breastfeeds baby before, during and after immunisation. For children, sit them upright and talk quietly to them before and during immunisation. Make eye contact and explain what is going to happen. Even when a child is unable to understand the words, an unhurried, quiet approach has a calming effect and reassures the parent/guardian. See also section 2.3.2.
Ensure the relevant immunisation health education resources are available.	Give written and verbal advice to the individual and parent/guardian. The advice should cover what may be expected after immunisation, and what to do in the event of an adverse event, along with advice on when to notify the vaccinator.

Removal of air bubbles

Advice for removal of air in the syringe before vaccine administration is dependent on the vaccine presentation. For guidelines see Table 2.7.

Table 2.7: Guidelines for management of air bubbles in a vaccine syringe

Vaccine presentation	Management of air bubbles
Vaccines supplied in a prefilled syringe with a fixed needle	Do not expel the air
Vaccines supplied in a prefilled syringe without a fixed needle (eg, Gardasil 9)	Add an appropriate administration needle Do not expel the air
Vaccines supplied diluted in a vial	Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle Do not expel the air contained in the new needle
Vaccines supplied as diluent and powder/pellet requiring reconstitution[a]	Reconstitute the vaccine correctly Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle[a] Do not expel the air contained in the new needle

a. See section 5.4.5 for administration procedures of COVID-19 vaccines.

Skin preparation

Skin preparation or cleansing when the injection site is clean is not necessary. However, if an alcohol swab is used, it must be allowed to dry for at least two minutes, otherwise alcohol may be tracked into the muscle, causing local irritation. Alcohol may also inactivate a live attenuated vaccine such as MMR.

A dirty injection site may be washed with soap and water and thoroughly dried before the immunisation event.

Special considerations for COVID-19

In patients who have tested positive for COVID-19 (or SARS-CoV2 virus), COVID-19 vaccination is recommended to be continued from three calendar months after recovery from acute illness, or three calendar months from the first confirmed positive test if asymptomatic. This applies to any dose of the primary course or booster doses (see section 5.5.7). For all other vaccines, commence vaccination as soon as the individual is no longer acutely unwell and when cleared to leave isolation.

2.2.3 Route of administration

Most Schedule vaccines are administered by intramuscular injection. The exceptions are IPV (IPOL; subcutaneously), BCG (intradermally) and rotavirus (oral). Live vaccines have previously been given via SC route and data sheets may still show this as an option, which can be helpful for those with bleeding disorders (see below).

Needle angle, gauge and length

Intramuscular injections should be administered at a 90-degree angle to the skin plane. The needle length used will be determined by the size of the limb and muscle bulk, whether the tissue is bunched or stretched and the vaccinator's professional judgement. BCG vaccine (which can only be administered by authorised vaccinators with BCG endorsement) is given by intradermal injection. See Table 2.8.

Table 2.8: Needle gauge and length, by site and age

Age	Site	Needle gauge and length	Rationale
Intramuscular (IM) injection			
Birth	Vastus lateralis	23–25 G × 16 mm	
6 weeks	Vastus lateralis	23–25 G × 16 or 25 mm	Choice of needle length will be based on the vaccinator's professional judgement.
3–11 months	Vastus lateralis	23–25 G × 25 mm	A 25 mm needle will ensure deep IM vaccine deposition.
12 months to 3 years	Deltoid or	23–25 G × 16 mm	The vastus lateralis site may be the preferred option in young children if deltoid muscle bulk is small or multiple injections are necessary.
	Vastus lateralis	23–25 G × 25 mm	
3–7 years	Deltoid	23–25 G × 16 mm	A 16 mm needle should be sufficient to effect deep IM deposition in the deltoid in most children.
	Vastus lateralis[a]	21–22 G × 25 mm	
Older children (7 years and older), adolescents and adults	Deltoid	23–25 G × 16 mm, or 23–25 G × 25 mm, or 21–22 G × 38 mm	Most adolescents and adults will require a 25 mm needle to effect deep IM deposition.
	Vastus lateralis[a]	21–22 G × 38 mm	
Very large or obese person	Deltoid	21-22 G x 38 mm	Use clinical judgment to ensure needle length is appropriate to reach muscle.[4, 5]
Subcutaneous injection			
Subcutaneous injection	Deltoid region of the upper arm	25–26 G × 16 mm	An insertion angle of 45 degrees is recommended. The needle should never be longer than 16 mm or inadvertent IM administration could result.

Continued overleaf

Age	Site	Needle gauge and length	Rationale
Intradermal injection: BCG vaccine – for authorised vaccinators with BCG endorsement			
Intradermal injection	Slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The arm should be gently but firmly supported.	Drawing-up: Tuberculin syringe (attach a drawing-up needle), or a single-use insulin syringe with a needle attached	
		Administering: If using a tuberculin syringe, change the needle to a sterile 26 G × 13 or 16 mm needle (no needle change required if using an insulin syringe)	The syringe should be held with the bevel uppermost, parallel with the skin of the arm. The bevel should be fully inserted but visible under the skin. Inject the vaccine slowly and gradually to form a white 'bleb' or wheal, then gradually withdraw the needle.

a. Consideration may be given to the vastus lateralis as an alternative vaccination site, providing it is not contraindicated by the manufacturer's data sheet.

Intramuscular injection sites

Injectable vaccines should be administered in healthy, well-developed muscle, in a site as free as possible from the risk of local, neural, vascular and tissue injury. Incorrectly administered vaccines (incorrect sites and poor administration techniques) contribute to vaccine failure, injection-site nodules or sterile abscesses, and increased local reactions.

> Careful use of a longer needle will cause less damage than a shorter needle.

The recommended sites for intramuscular (IM) vaccines (based on proven uptake and safety data) are:

- the vastus lateralis muscle on the anterolateral thigh for infants aged under 12 months – the vastus lateralis muscle is large, thick and well developed in infants, wrapping slightly onto the anterior thigh
- either the vastus lateralis or deltoid site for children aged 12 months to 3 years (see below)
- the deltoid muscle for older children, adolescents and adults.

The deltoid muscle is not routinely used in infants and young children aged under 12 months, due to the potential for deltoid or radial nerve injury. However, when there is no access to the vastus lateralis (eg, the infant is in a spica cast), the deltoid muscle is used to administer intramuscular vaccines.

The buttock should not be used for the administration of vaccines in infants or young children, because the buttock region is mostly subcutaneous fat until the child has been walking for at least 9 to 12 months. Use of the buttock is not recommended for adult vaccinations either, because the buttock subcutaneous layer can vary from 1 to 9 cm and IM deposition may not occur.

With older children and adults, consideration may be given to using the vastus lateralis as an alternative site to the deltoid.

Subcutaneous injection sites

A subcutaneous (SC) injection should be given into healthy tissue that is away from bony prominences and free of large blood vessels or nerves. The recommended site for subcutaneous vaccine administration is the upper arm (overlying the deltoid muscle).

The principles for locating the upper arm site for an SC injection are the same as for an IM injection. *However, needle length is more critical than angle of insertion for subcutaneous injections*. An insertion angle of 45 degrees is recommended, and the needle should never be longer than 16 mm, or inadvertent IM administration could result. The thigh may be used for SC vaccination unless contraindicated by the manufacturer's data sheet. For patients with thrombocytopenia and bleeding disorders, the risk of haematoma may be reduced when given via SC route. See below for further details.

Intramuscular versus subcutaneous administration

The Ministry of Health recommends that parenteral live vaccines on the Schedule (MMR, varicella and zoster vaccines) be administered via intramuscular (IM) route, unless the patient is on an anticoagulant or has a bleeding disorder, in which case the preferred route is subcutaneous (SC) where the data sheet allows (see below). Historically, live vaccines have been given subcutaneously following on from their original licensure trials. Further research has now established immunogenicity and safety when these vaccines are administered by the IM route.[6] There is evidence that injections given intramuscularly, rather than deep subcutaneously, are less likely to cause local reactions.[8, 9, 10] There are no immunogenicity concerns when MMR, varicella and zoster vaccines are given either SC or IM. BCG is required to be given intradermally.

Thrombocytopenia, anticoagulant therapy and bleeding disorders

For patients with thrombocytopenia and bleeding disorders, the risk of haematoma may be reduced when given via SC route, where data sheet allows this option.

- Vaccines can be administered to people on anticoagulants, dabigatran (Pradaxa), enoxaparin (Clexane), heparin, ticagrelor (Brilinta) and warfarin. Subcutaneous route is preferred option where data allows, to reduce risk of haematoma. For vaccines that do not have the SC option administer IM. After vaccination, apply firm pressure over the injection site without rubbing for 10 minutes to reduce the risk of bruising.
- For patients with haemophilia receiving clotting factor replacement or a similar therapy, vaccinations should be given as soon as possible after receiving the medicine and vaccines should be given in the same way as for those on anticoagulants. Specialist advice is recommended.

Intradermal injections

The intradermal injection technique for BCG vaccine (see section 2.2.4) requires special training, and should only be performed by an authorised vaccinator with BCG endorsement (see A3.6).

Oral vaccine administration

The rotavirus vaccine is administered orally. Administer the entire contents of the oral applicator into the infant's mouth, towards the inner cheek (see section A7.2.4). **Do not inject oral vaccines.**

For specific oral vaccine administration instructions, refer to the vaccine data sheet (available on the Medsafe website at **medsafe.govt.nz**).

2.2.4 Infant vaccination

Infants aged under 6 months do not need to be grasped or restrained as firmly as toddlers or older children. At this age, excessive restraint increases their fear as well as muscle tautness. The recommended positioning for an infant is in a cuddle hold with parent/guardian, breastfeeding as appropriate. The cuddle position offers better psychological support and comfort for both the infant and the parent/guardian,[3] and the parent/guardian should be offered this position as a first choice (Figure 2.1).

If the parent/guardian is helping to hold the infant or child, ensure they understand what is expected of them and what will take place. Most vaccinators choose to quickly administer all the injections due and soothe the infant or child afterwards (see section 2.3.2 for soothing measures).

Figure 2.1: The cuddle position for infants

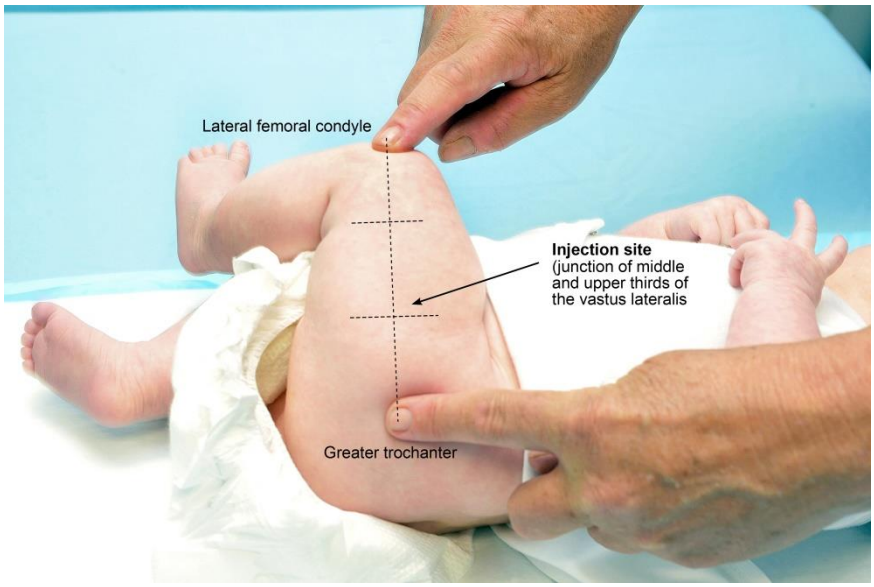
Vastus lateralis

To locate the injection site, undo the nappy, gently adduct the flexed knee and (see Figure 2.2):

1. find the greater trochanter
2. find the lateral femoral condyle
3. section the thigh into thirds and run an imaginary line between the centres of the two markers (look for the dimple along the lower portion of the fascia lata).

The injection site is at the junction of the upper and middle thirds and slightly anterior to (above) the imaginary line, in the bulkiest part of the muscle.

Figure 2.2: The infant lateral thigh injection site

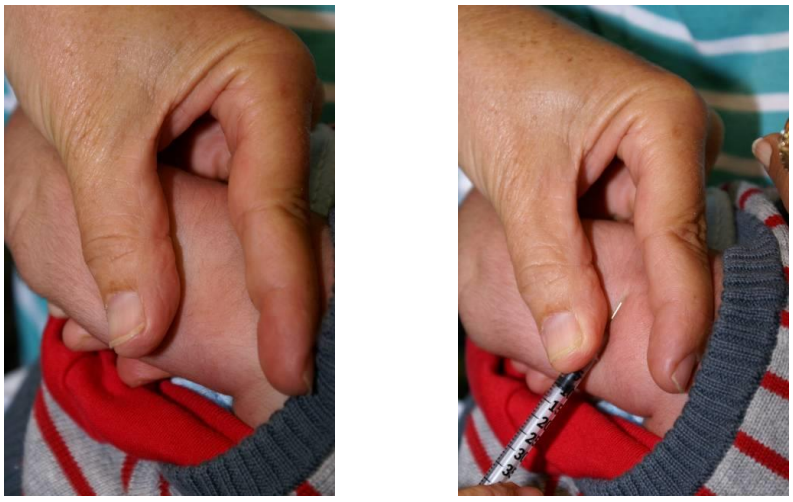


The needle should be directed at a 90-degree angle to the skin surface and inserted slightly anterior to (above) the junction of the upper and middle thirds. Inject the vaccine at a controlled rate. To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle. Do not massage or rub the injection site afterwards. However, infants with a bleeding disorder may require firm pressure over the injection site without rubbing for at least 10 minutes.

BCG vaccine (administered by authorised vaccinators with BCG endorsement)

The reconstituted BCG vaccine is given by intradermal injection slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The infant's arm should be gently but firmly supported (see Figure 2.3(a)). The syringe should be held with the needle bevel uppermost, parallel with the skin of the arm (see Figure 2.3(b)).

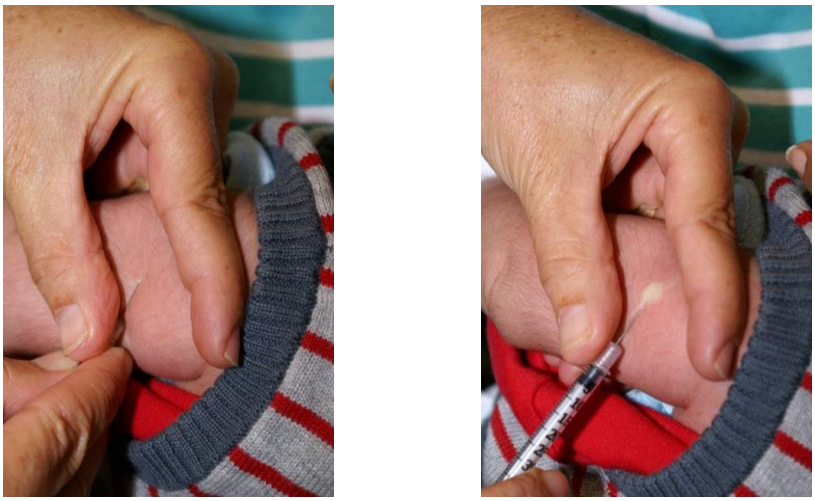
Figure 2.3: The infant BCG vaccination site, and how to support the infant's arm and hold the syringe



(a) (b)

Inject the vaccine slowly (see Figure 2.4(a)), then gradually withdraw the needle. The injection is given slowly to avoid leakage around the needle or vaccine being squirted. Safety glasses should be used to protect the eyes of those involved. If BCG vaccine is accidentally squirted into the eyes, wash them immediately with water. Following BCG vaccination a white weal should appear (see Figure 2.4(b)), which should subside in approximately 30 minutes. The vaccination site requires no swabbing or dressing.

Figure 2.4: The BCG vaccine being slowly injected, and a white weal appearing as the needle is gradually withdrawn



(a) (b)

2.2.5 Young child vaccination (vastus lateralis or deltoid)

The choice between the two sites for IM injections from 12 months of age will be based on the vaccinator's professional judgement, taking in account knowledge of the child and ease of restraint. Some vaccinators consider the vastus lateralis preferable for young children when the deltoid muscle bulk is small and because of the superficiality of the radial nerve. Discuss the options with the parent/guardian when making your decision. (See also 'The 12- and 15-month immunisation events' in section 2.2.7.)

The easiest and safest way to position and restrain a young child for a lateral thigh and/or deltoid injection is to sit the child sideways on their parent's or guardian's lap. The parent's/guardian's hand restrains the child's outer arm and the child's legs are either restrained between the parent's/guardian's legs or by placing a hand on the child's outer knee or lower leg. Alternatively, the child may face their parent/guardian while straddling the parent's/guardian's legs (see Figure 2.5 and Figure 2.6).

Figure 2.5: Cuddle positions for vastus lateralis or deltoid injections in children

(a)

(b)

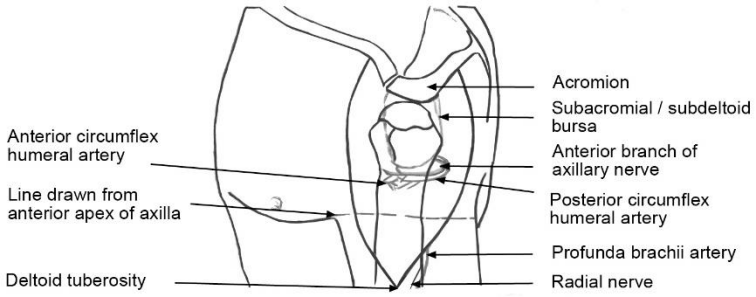
Figure 2.6: The straddle position for vastus lateralis or deltoid injections in children

In the straddle position, both the deltoid and vastus lateralis muscle are likely to be more tense or taut, and the injection may therefore be more painful.

2.2.6 Older child, adolescent and adult vaccination (deltoid)

The deltoid muscle is located in the lateral aspect of the upper arm. The entire deltoid muscle must be exposed to avoid the risk of radial nerve injury (an injection at the junction of the middle and upper thirds of the lateral aspect of the upper arm may damage the nerve) (see Figure 2.7).

Figure 2.7: Surface landmarks and structures potentially damaged by intramuscular injection in the upper limb



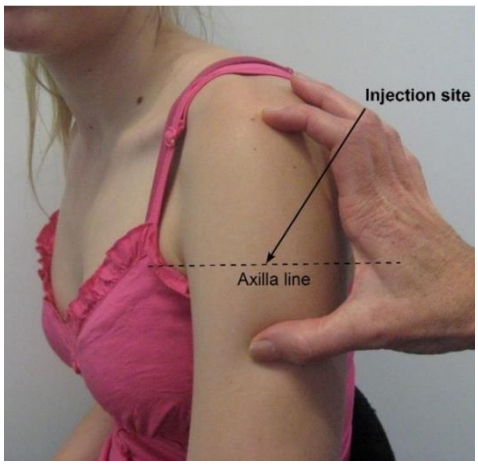
Reproduced with permission: Cook IF. 2011. An evidence-based protocol for the prevention of upper arm injury related to vaccine administration (UAIRVA). *Human Vaccines* 7(8): 845–8.

The volume injected into the deltoid should not exceed 0.5 mL in children and 1.0 mL in adults.

The vaccine recipient should be seated with their arm removed from the garment sleeve and hanging relaxed at their side. The vaccinator places their index finger on the vaccine recipient's acromion process (the highest point on the shoulder) and their thumb on the vaccine recipient's deltoid tuberosity (the lower deltoid attachment point).[7]

The injection site is at the axilla line, between these anatomical landmarks. The vaccine should be deposited at the bulkiest part of the muscle (Figure 2.8).

Figure 2.8: How to locate the deltoid site



2.2.7 Multiple injections at the same visit

A well-prepared and confident vaccinator will reassure the parent/guardian or whānau that giving concurrent vaccines is a safe and appropriate practice, avoiding multiple visits.

When more than one vaccine is scheduled at the same visit, it is recommended that vaccinators give all the scheduled vaccines at that visit. This particularly applies to the 15-month event (see below), when three vaccines are scheduled.

Multiple vaccines should not be mixed in a single syringe unless specifically licensed and labelled for administration in one syringe. A different needle and syringe should be used for each injection.

The 12-month and 15-month immunisation events

MMR1 and PCV are the vaccines are scheduled at the 12-month immunisation event. It is preferable to give these injections in the vastus lateralis.

Should parents request extra non-funded vaccines, such as 4CMenB (Bexsero), MenACWY-T (Nimenrix) or extra dose of VV. These vaccines can be given in the deltoid. To give two injections in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.9). The injection sites should be on the long axis of the thigh and *separated by at least 2 cm* so that potential localised reactions will not overlap.

MMR2, varicella and Hib-PRP-T vaccines are scheduled at the 15-month event. When giving these vaccines, it is preferable to give one in each vastus lateralis and the third in the deltoid.

The recommended vaccine administration sequence and location is:

1. Hib-PRP-T: IM in left leg (vastus lateralis)
2. Varicella: IM in left arm (deltoid)
3. MMR: IM in right leg (vastus lateralis).

If parents/guardians request to split the vaccines given at the 15-month event, then providers are advised to give MMR and VV at the first visit, followed by Hib-PRP-T at the second visit.

Note: there is a risk that the patient may not return for the second visit when the 15-month vaccines are split.

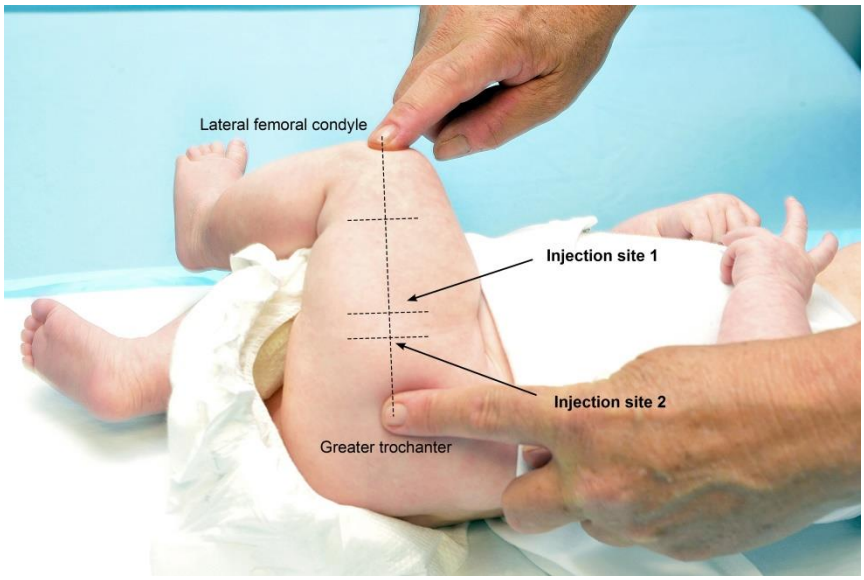
If MMR and VV are not given at the same visit (concurrently), then there should be an interval of at least four weeks between them. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine (see section 2.1.5).

Multiple injections in the same muscle

When two injections are to be given in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.9). The injection sites should be on the long axis of the thigh and *separated by at least 2 cm* so that localised reactions will not overlap.

If multiple injections in the deltoid are required, the sites should be separated by at least 2 cm.[8]

Figure 2.9: Suggested sites for multiple injections in the lateral thigh



2.3 Post-vaccination

2.3.1 Post-vaccination advice

Post-vaccination advice should be given both verbally and in writing. The advice should cover:

- which vaccines have been given and the injection sites, and whether the injections were IM or SC
- potential vaccine responses following immunisation (see Table 2.9) and what to do if these occur (eg, measures for relieving fever, when to seek medical advice)
- when the individual or parent/guardian should contact the vaccinator if they are worried or concerned
- contact phone numbers (including after-hours phone numbers).

Table 2.9: Potential vaccine responses

Vaccine	Potential vaccine responses
DTaP- or Tdap-containing vaccine	Localised pain, redness and swelling at injection site Mild fever Being grizzly and unsettled Loss of appetite, vomiting, and/or diarrhoea Drowsiness Extensive limb swelling after multiple doses of a DTaP-containing vaccine
Hib-PRP	Localised pain, redness and swelling at the injection site Mild fever Being grizzly and unsettled
Hepatitis B	Very occasionally pain and redness at the injection site Nausea or diarrhoea
HPV	Fainting, especially in adolescents – this is an injection reaction, not a reaction to the vaccine Localised discomfort, pain, redness and swelling at the injection site Mild fever Headache
Influenza	Localised pain, redness and swelling at injection site Headache Fever
MMR	Measles component: Fever which lasts 1–2 days; rash (not infectious) 6–12 days after immunisation Mumps component: Parotid and/or submaxillary swelling 10–14 days after immunisation Rubella component: Mild rash, fever, lymphadenopathy, joint pain 1–3 weeks after immunisation
Pneumococcal	Localised pain, redness and swelling at injection site Mild fever Irritability, sleep changes Loss of appetite
Rotavirus	Diarrhoea and or vomiting may occur after the first dose Mild abdominal pain
Varicella	Localised pain, redness and swelling at injection site Mild fever Mild rash, possibly at the injection site (2–5 lesions, appearing 5–26 days after immunisation)

2.3.2 Recommendations for fever and pain management

The use of paracetamol (or ibuprofen) around the time of immunisation in anticipation of immunisation-related fever or localised pain occurring is not generally recommended. However, use of these medicines is recommended if the child is distressed due to discomfort following immunisation. Antipyretic use may lower the immune response to some vaccines.[9] Although, there is no evidence that this results in less protection against disease.

Health care providers are encouraged to discuss with parents the possible immunisation responses and non-pharmaceutical management of fever or pain, as well as the role of medicines.

Fever

General fever-relieving measures include:

- giving extra fluids to drink (eg, more breastfeeds or water)
- reducing clothing if the baby is hot.

While a high fever alone does not need treatment, analgesics (paracetamol or ibuprofen) may be used for distress or pain in a febrile child.

It is recommended that infants and children under two years receiving 4CMenB (Bexsero) meningococcal vaccine be given three doses of paracetamol (or ibuprofen) prophylactically to reduce fever (see section 13.4.4).

Pain management and soothing measures

For breastfeeding infants, breastfeeding before, during and after the injection can provide comfort and pain relief.[3, 14]

Give the rotavirus vaccine 1–2 minutes before other immunisations; rotavirus vaccines contain sucrose that has been shown to reduce pain.[3, 14] The infant can then be breastfed (where possible) or held comfortably while the other immunisations are given.

For infants aged under 6 months, the 5 Ss (swaddling, side/stomach position, shushing, swinging and sucking) have been found to be effective for soothing and reducing pain after immunisations.[10]

Using age-appropriate distraction has been shown to reduce pain and distress.[3, 14] Examples include showing an interesting or musical toy to an infant, or encouraging an older child to blow using a windmill toy or bubbles. Electronic games/phone games can be useful for older children and teenagers. Do not rub the injection site after the injection, as it increases the risk of vaccine reactogenicity.

For infants and children, the use of a topical anaesthetic cream or patch has been found to be effective for immunisation pain management.[3, 14] Parents/guardians and those administering the vaccine should check the manufacturers' recommendations before using topical anaesthetics. The correct dose for infants needs to be followed particularly carefully due to risk of methaemoglobinaemia. Topical anaesthetics may have a role in managing immunisation pain and anxiety, particularly for children who have had previous multiple medical interventions or needle phobias.

Following immunisation, if an infant or child is distressed by pain or swelling at the injection site, placing a cold, wet cloth on the area may help relieve the discomfort. Antipyretic analgesics (paracetamol or ibuprofen) may be used if the above measure does not relieve the child's distress.

2.3.3 Anaphylaxis and emergency management

> All vaccinators must be able to distinguish anaphylaxis from fainting, anxiety, immunisation stress-related responses (ISRR), breath-holding spells and seizures.

Anaphylaxis is a very rare,[11] unexpected and potentially fatal allergic reaction. It develops over several minutes and usually involves multiple body systems. Unconsciousness is rarely the sole manifestation and only occurs as a late event in severe cases. A strong central pulse (eg, carotid) is maintained during a faint (vasovagal syncope), but not in anaphylaxis.

In general, the more severe the reaction, the more rapid the onset. Most life-threatening adverse events begin within 10 minutes of vaccination. The intensity usually peaks at around one hour after onset. Symptoms limited to only one system can occur, leading to delay in diagnosis. Biphasic reactions, where symptoms recur 8 to 12 hours after onset of the original attack, and prolonged attacks lasting up to 48 hours have been described. All patients with anaphylaxis should be hospitalised.

Signs of anaphylaxis

Anaphylaxis is a severe adverse event of rapid onset, characterised by circulatory collapse. In its less severe (and more common) form, the early signs are generalised erythema and urticaria with upper and/or lower respiratory tract obstruction. In more severe cases, limpness, pallor, loss of consciousness and hypotension become evident, in addition to the early signs. Vaccinators should be able to recognise all the signs and symptoms of anaphylaxis given in Table 2.10.

Table 2.10: Signs and symptoms of anaphylaxis

	Signs and symptoms	Severity
Early warning signs (usually within a few minutes)	Dizziness, perineal burning, warmth, pruritus, flushing, urticaria, nasal congestion, sneezing, lacrimation, angioedema	Mild to moderate
	Angioedema, hoarseness (laryngeal oedema), dyspnoea, abdominal pain, vomiting, substernal pressure	Moderate to severe
Life-threatening symptoms (usually from soon after the injection to within 20 minutes after)	Bronchospasm, stridor, collapse, hypotension, dysrhythmias	Severe

There is no place for conservative management of anaphylaxis. Early administration of adrenaline is essential (for more details, see Table 2.12).

Misdiagnosis of faints and other common causes of collapse as anaphylaxis may lead to inappropriate use of adrenaline. Misdiagnosis as a faint could also lead to a delay in the administration of adrenaline.

Vaccinators should therefore be able to distinguish anaphylaxis from fainting (vasovagal syncope), anxiety and breath-holding spells (see Table 2.11). Infants and babies rarely faint. Sudden loss of consciousness, limpness, pallor and vomiting (signs of severe anaphylaxis in children) should be presumed to be an anaphylactic reaction.

In adults and older children, the most common adverse event is a syncopal episode (fainting), either immediately or soon after vaccination. During fainting the individual suddenly becomes pale, loses consciousness and if sitting or standing will slump to the ground. Recovery of consciousness occurs within a minute or two. Fainting is sometimes accompanied by brief clonic seizure activity, but this generally requires no specific treatment or investigation if it is a single isolated event.

Immunisation stress-related response

Immunisation stress-related responses (ISRR) is a term used to cover a spectrum of responses to stress generated by immunisations.[12] These responses vary from fainting and hyperventilation through to dissociative neurological symptoms, which include non-epileptic seizures. They usually occur in individuals but have also been identified in clusters; this is often referred to as mass psychogenic illness. These stress responses are complex and involve both physiological and psychological factors. For more information see the WHO manual for health professionals, available from **www.who.int/publications/i/item/9789241515948**.

Table 2.11: Distinguishing anaphylaxis from a faint (vasovagal reaction)

	Faint	Anaphylaxis
Onset	Usually before, at the time, or soon after the injection	Soon after the injection, but there may be a delay of up to 30 minutes
System		
Skin	Pale, sweaty, cold and clammy	Red, raised and itchy rash; swollen eyes and face; generalised rash
Respiratory	Normal to deep breaths	Noisy breathing due to airways obstruction (wheeze or stridor); respiratory arrest
Cardiovascular	Bradycardia; transient hypotension	Tachycardia; hypotension; dysrhythmias; circulatory arrest
Gastrointestinal	Nausea/vomiting	Abdominal cramps
Neurological	Transient loss of consciousness; good response once supine/flat	Loss of consciousness; little response once supine/flat

Distinguishing a hypotonic-hyporesponsive episode from anaphylaxis

A hypotonic-hyporesponsive episode is a shock-like state defined by the sudden onset of limpness (muscle hypotonia) and decreased responsiveness, with pallor or cyanosis in infants and children aged under 2 years after immunisation.

A hypotonic-hyporesponsive episode can occur from 1 hour to 48 hours after immunisation, typically lasts less than 30 minutes, and resolves spontaneously.[13]

A hypotonic-hyporesponsive episode is a recognised serious reaction to immunisation and should be reported to CARM (see section 1.6.3).

Avoidance of anaphylaxis

Before immunisation:

- ensure there are no known contraindications to immunisation
- if in doubt about administering the vaccine, consult the individual's GP or a paediatrician.

> Individuals should remain under observation for 20 minutes following vaccination in case they experience an immediate adverse event requiring treatment. This observation period may vary for some vaccines and age groups.

Emergency equipment

Vaccinators, providers and quality managers are responsible for:

- ensuring emergency procedures are known by all staff
- practising emergency procedures regularly
- having an emergency kit (see Table 2.12) and adrenaline in every room where vaccinations/medications are given
- checking emergency kits regularly
- not giving vaccines when working alone.

Remember, events happen without warning. Appropriate emergency equipment must be immediately at hand whenever immunisations are given, and all vaccinators must be familiar with the practical steps necessary to save lives following an anaphylactic reaction (see Table 2.12 and Table 2.13).

Table 2.12: Emergency equipment

An emergency kit should contain: • adrenaline* 1:1,000 (at least 3 ampoules) and dosage chart • syringes: 1.0 mL (a minimum of 3; tuberculin not insulin, as the insulin needle is too short for IM injection) • needles: a range of needle lengths and gauges, including 23 or 25 G × 25 mm, 22 G × 38 mm Auto-injectors for self-administration of adrenaline should not be used as a substitute for a proper anaphylaxis pack. However, if an adrenaline auto-injector is the only available adrenaline preparation when treating anaphylaxis, health care providers should use it.
Other emergency equipment required It is also necessary to have on hand: • adult and paediatric bag valve mask resuscitator (eg, Ambu bag) • access to a telephone.

* The expiry date of the adrenaline and other medicines should be written on the outside of the emergency kit, and the kit should be checked every 4 weeks. Adrenaline is heat and light sensitive and should be stored appropriately. Adrenaline that has a brown tinge must be discarded.

The emergency kit may need to have additional equipment for non-clinical settings (see A3.6).

Hydrocortisone injection is used only under the direction of a medical practitioner (see the Practitioner's Supply Order, list available at **pharmac.govt.nz/pharmaceutical-schedule/community-section-b/practitioners-supply-order-pso-previously-the-mpso-list/**.

Emergency management

An IM injection of 1:1,000 adrenaline is the mainstay of the treatment of anaphylaxis, and adrenaline should be universally available when vaccinating. A tuberculin syringe should be used to ensure the accuracy of measurement when drawing up small doses.

In an emergency, there is no absolute contraindication to the use of adrenaline. It is, however, a very potent agent, and if used when anaphylaxis has not occurred or in excessive doses, adrenaline can cause dysrhythmias, severe hypertension and left ventricular failure. Tissue necrosis can occur if the same injection site is used repeatedly.

Intravenous adrenaline should be administered by a medical practitioner with extreme caution, in small boluses and under careful monitoring, and it is not appropriate as the first line of treatment of anaphylaxis.

Table 2.13: Initial anaphylaxis response/management

CALL FOR HELP – send for professional assistance (ambulance, doctor).
Never leave the individual alone.

ASSESS FOR ANAPHYLAXIS (see Table 2.10 for full details)

Airway and breathing
Noisy breathing due to airways obstruction; or respiratory arrest

Circulation/shock
Tachycardia; hypotension; dysrhythmias; circulatory arrest

Skin changes
Red, raised and itchy rash; swollen eyes and face; generalised rash

If cardiac arrest – commence age-appropriate CPR and life support measures

LAY THE PATIENT DOWN (do not allow them to stand)
If they have breathing difficulties, elevate the head and chest.

ADMINISTER ADRENALINE by deep IM injection into outer thigh

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 ml.

For those under 10 kg or if weight is not known, use the following guidelines:

Age	Dose
under 2 years	0.1 mL
2–4 years	0.2 mL
5–11 years	0.3 mL
12 years and over	0.5 mL
Adult	0.5 mL

You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15-minute intervals, while waiting for assistance.

ADMINISTER OXYGEN, if available, at high flow rates when there is respiratory distress, stridor or wheeze.

IF HYPOTENSIVE, ELEVATE LEGS.

RECORD VITAL SIGNS every 5–10 minutes. All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

ADMIT TO HOSPITAL – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

Note: Only medical practitioners should administer IV adrenaline.

In the unlikely event of a cardiac or respiratory arrest following anaphylaxis, assess respiration without putting your face close to the patient's face, don PPE as soon as it is available and ventilate via a bag valve mask.

Ongoing management in hospital or by a medical practitioner

Individuals who experience vaccine-related anaphylaxis should be admitted to hospital. If the individual is in an unstable or deteriorating condition, and is not being transported by ambulance, they must be accompanied by the attending health professional so that treatment can be continued during transfer.

Hydrocortisone may be used as adjunctive medication. Nebulised salbutamol is helpful for bronchospasm. For further information, refer to the product data sheet.

Additional drugs that may be administered under the direction of a medical practitioner include:

- nebulised adrenaline: for laryngeal oedema
- bronchodilators: salbutamol 5 mg nebulised, to help reverse bronchospasm
- corticosteroids: prednisone 2 mg/kg (up to 40 mg) orally, or hydrocortisone 4 mg/kg IV, to help resolve tissue swelling (prednisolone syrup may be more appropriate for young children and infants).

Observation for a period of up to 24 hours after stabilisation of the individual's condition is recommended due to the risk of late deterioration from delayed and biphasic reactions.

All anaphylaxis reactions should be reported to CARM (see section 1.6.3).

2.3.4 Documentation and insurance

Accurate documentation, including information on the National Immunisation Register (NIR) and the Aotearoa Immunisation Register (AIR), COVID-19 immunisation register (CIR), School-Based Vaccination System (SBVS) and practice management system (PMS), is essential. If the vaccinator has not kept accurate clinical records, it is difficult to prove what action/care was or was not taken/delivered if the patient notes are subject to legal scrutiny.

In addition to the information recorded on the NIR or AIR (see section 2.3.5), CIR, SBVS or PMS, information that should be collected in the patient's clinical notes includes:

- confirmation that informed consent was given
- confirmation that the individual was observed for the recommended time and no adverse events occurred during the observation period (if an adverse event does occur, it is essential to document the action and treatment given and inform CARM – see section 1.6.3).

The vaccinator should also complete the relevant sections in the *Well Child Tamariki Ora My Health Book* and, where applicable, the child's immunisation certificate (see Appendix 5), the Ministry of Health payment claim form (where applicable), and an NIR notification form if the vaccinator is not using a computerised PMS or the AIR (dependent on the system rollout for the AIR).

Indemnity insurance

All vaccinators should carry indemnity insurance. Most employers have indemnity cover, but vaccinators do not have an automatic right to claim under that cover. Indemnity insurance should cover vaccinators/health professionals for disciplinary proceedings, coroners' inquiries, and claims of negligence or error that may lead to injury, death or damage.

2.3.5 The National Immunisation Register and the Aotearoa Immunisation Register

The NIR is a computerised information system that has been collecting immunisation information on New Zealand children since 2005 and has been collecting some adult immunisation information since 2014. The purpose of the NIR is to facilitate immunisation delivery and provide an accurate record of an individual's immunisation history.

The Aotearoa Immunisation Register (AIR) is an information system that will replace the National Immunisation Register (NIR). The AIR will be available from 1 April 2022 but will have a phased roll out. This means that both the NIR and the AIR will be used concurrently. In time, the AIR will supersede the NIR. The NIR (or AIR) also:

- provides a more accurate record of immunisation coverage rates regionally and nationally – this information assists with better programme planning to improve coverage rates and identify areas with lower immunisation rates
- collects information about the Schedule, and some targeted programmes (eg, Tdap during pregnancy, BCG vaccine)
- collects information about influenza immunisations and high-risk adolescent and adult immunisations (since July 2014)
- enables health professionals to identify quickly and easily which vaccines an individual has received (especially if they have moved areas or changed health care providers) and any that are due or may have been missed
- enables individuals to have an accurate, up-to-date record of their immunisation history.

2.3.6 Managing the information on the National Immunisation Register or the Aotearoa Immunisation Register

The information held on the NIR and AIR (collection, holding, use and disclosure) is governed by the Health Information Privacy Code 1994 and section 22F of the Health Act 1956 (see section 2.1.2).

The NIR's privacy policy can be found on the Ministry of Health website (**www.health.govt.nz/nir**). The policy sets out the framework for data collection, storage, use and disclosure of health information held about identifiable individuals on the NIR.

Individuals or their parents/guardians may choose at any time not to have any health information collected on the register (ie, they can opt out of the further collection of immunisation data, recorded as an 'opt-off'). However, the NIR or AIR (dependent on the system rollout for the AIR) will retain the individual's National Health Index (NHI) number, date of birth, DHB they are resident in, date they opted out and any immunisation information recorded before they opted out. The reason for retaining this information is to provide an accurate denominator for immunisation coverage calculations, and to prevent inappropriate recall and referral.

An individual's immunisation information will be retained on the NIR or AIR (dependent on the system rollout for the AIR) for their whole life, plus a period of 10 years after their death.

Only authorised users have access to the information held on the NIR or AIR (dependent on the system rollout for the AIR). Such a person is authorised to use and disclose NIR / AIR information in accordance with their function. Penalties for unauthorised disclosure of information could include the revocation of authorised user privileges, complaints to the Privacy Commissioner, civil proceedings, professional sanctions and disciplinary action, up to and including termination of employment.

Information collected on the NIR / AIR includes:

- date of vaccination
- individual's name
- individual's NHI number
- individual's date of birth
- secondary contact details
- parent/guardian details for children aged under 18 years
- vaccine type and number in the series
- batch number and expiry date
- injection site, injection route and needle length used
- provider name
- vaccinator's name and title
- recall date (when applicable)

- adverse event data, once verified by CARM.

More information about privacy and informed consent can be found in section 2.1.2 and Appendix 3. Further information about the NIR and the AIR can be found on the Ministry of Health website (**www.health.govt.nz/nir**).

The SBVS

The SBVS collects and manages the data for school immunisation programmes (eg, where public health nurses deliver the school year 7 and year 8 immunisation programmes). The information collected on the SBVS for the school immunisation programmes is then transferred to the NIR or AIR (dependent on the system rollout for the AIR).

Not all DHBs use the SBVS software for managing their school-based programmes; however, all DHBs are required to record school-based vaccination events on the NIR or AIR (dependent on the system rollout for the AIR) regardless of whether they use the SBVS or a PMS, or direct enter on to the NIR.

COVID-19 immunisation register

As part of the COVID-19 immunisation programme, a COVID-19 immunisation register (CIR) has been specifically designed. The CIR will be integrated with the Aotearoa Immunisation Register (AIR) that will ultimately replace the NIR.

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3 Vaccination questions and addressing concerns

3.1 Some commonly asked questions

3.1.1 Vaccine scheduling

Which vaccines can be administered at the same visit?

There are no known contraindications to administering registered vaccines at the same visit, provided they are administered in separate syringes at separate sites. If two or more parenterally or intranasally administered *live* vaccines are not given at the same visit, then a minimum interval of four weeks is recommended. The rationale is based on limited data where VV has been given within four weeks of measles-containing vaccine and breakthrough varicella disease (chickenpox) has occurred. Any time interval is acceptable between administering live oral vaccines (eg, rotavirus) and live parenteral vaccines (BCG), live and inactive vaccines, or two inactive vaccines.

What steps are required if the Schedule is interrupted or varied?

Generally, there is no need to repeat prior doses; simply continue the Schedule as if no interruption has occurred (see Appendix 2). Special circumstances where the above does not apply are as follows:

- HepB given at birth to babies born to HBsAg-positive mothers – this dose does not count as part of a catch-up
- the two-dose course of rotavirus vaccine (RV1; Rotarix) should be started before age 15 weeks (ie, the latest is 14 weeks and 6 days) and completed by age 25 weeks (ie, the latest is 24 weeks and 6 days); if an infant reaches age 25 weeks without receiving the second dose, the first dose already given may offer them some protection against disease
- MMR given prior to age 12 months – infants who receive MMR prior to age 12 months still require two further MMR doses beyond age 12 months (scheduled at ages 12 months and 15 months)

- conjugate vaccine schedule requirements, which are age dependent (eg, children over 12 months of age do not require a full primary course of Hib-PRP or PCV vaccine, but do require one or two doses in the second year of life; see Appendix 2)
- when reconciling overseas schedules and the New Zealand Schedule – immigrant children who have commenced vaccine courses (eg, MenACWY, 4CMenB, PCV13) are not funded to complete these vaccine courses once in New Zealand unless they meet the high-risk criteria for these vaccines; however, if the parent or guardian wishes to purchase the vaccines to complete the course, they may do so.

Remember that children who miss one vaccine dose may do so again, so optimising a catch-up schedule is important.

How should the rest of the Schedule be handled when an adverse event has occurred following immunisation?

Proceeding with the Schedule after an AEFI depends on the nature of the event and the likelihood that the vaccine caused it. Most prior adverse events are not contraindications to receiving further immunisations. The only absolute contraindication to receiving a vaccine is anaphylaxis to a prior dose or an ingredient in the vaccine. However, immunocompromise can be a contraindication to receiving live vaccines (see section 4.3).

Adverse events should be reported to CARM (**nzphvc.otago.ac.nz/reporting**). See section 1.6.3 'AEFI reporting process – notifying CARM'.

Consult the AEFI section in each of the *Handbook* chapters, and seek specialist advice (eg, from the local medical officer of health, the Ministry of Health or IMAC). Other vaccines not related to the AEFI can usually be administered as per the Schedule.

3.1.2 Babies and children

What if a baby had a difficult birth or was premature?

Preterm and/or low birthweight infants should receive vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval), including rotavirus vaccination. These babies may be at higher risk of some of these diseases, so vaccinating them on time is particularly important. Infants with serious congenital conditions should generally receive Schedule vaccines at the usual chronological age. However, if the infant is still in hospital or has recently been discharged, please seek the advice of the treating specialist (see also section 4.2.2).

Rotavirus vaccine should be given on time to hospitalised infants, including those in neonatal units. When standard infection control precautions are maintained, the risk of rotavirus vaccine virus transmission will be minimal.[1, 2, 3] (See also sections 4.2.4, 4.3, 4.4, 4.5 and chapter 18.)

What special vaccines are offered to newborn babies?

Babies born to HBsAg-positive mothers should receive:

- 100–110 IU hepatitis B immunoglobulin (HBIG) neonatal, at or as close as possible to birth
- a birth dose of HepB (Engerix-B, 20 µg or paediatric formulation, Engerix-B 10 µg, if available), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice. These babies should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see section 9.5.2).

A baby at higher risk of TB is offered a BCG immunisation soon after birth (see section 21.5 for neonatal BCG eligibility and the timing of neonatal BCG). The lead maternity carer will discuss the need for the vaccine with the mother prior to her baby's birth and vaccination will be conducted at designated BCG clinics within each district health board.

What are the special requirements of immigrant children?

Immigrant children should be immunised according to the New Zealand Schedule with *due account taken of documented prior vaccine administration* and the eligibility criteria defined in the *Health and Disability Services Eligibility Direction 2011*, available on the Ministry of Health website at **health.govt.nz/eligibility** (see also section 4.7).

All children aged under 18 years are eligible to receive Schedule vaccines and Well Child Tamariki Ora services regardless of their immigration and citizenship status, and providers can claim the immunisation benefit for administering the vaccines.

If a refugee or immigrant has no valid documentation of vaccination, an age-appropriate catch-up programme is recommended. Only clearly documented doses should be considered as given. If there is no documented vaccination history, plan the catch-up schedule assuming the vaccines have not been given (see Appendix 2). The immunisation status of all immigrant children should be checked when they register with a primary health care provider.

Is it possible to boost a child's immune system by other means?

Eating a healthy diet, getting adequate sleep and exercise, having a smoke-free environment and minimising high levels of stress will help keep the child's immune system healthy. However, none of the above confers the disease-specific immunity that vaccination provides (see also section 3.2.4). All children get infections (eg, common colds); this does not mean the immune system is not working.

3.1.3 Allergies and illnesses

What if the child is unwell on the day of immunisation?

Minor illness or being in the recovery phase of an illness is not a reason to postpone immunisation. Babies and children with a significant acute illness and a temperature >38°C should have immunisation postponed until they are better. This is not because they are at particular risk of vaccine reactions, but because complications of the acute illness may be misinterpreted as a complication of the immunisation, or an AEFI may complicate the clinical picture of the acute illness. (See section 2.1.4 'Contraindications' and the contraindications sections in the disease chapters.) If immunisation is postponed, it is important to ensure the child is placed on the recall for the immunisation later.

What if the child is due to have an operation (elective surgery)?

There is no evidence that anaesthetic impairs the immune response to a vaccine or increases the risk of AEFI.

Vaccination with inactive vaccines is preferably avoided for 48 hours prior to an anaesthetic in case post-vaccination symptoms such as fever interfere with preparation for surgery; similarly, live vaccines may induce fever 6–12 days after vaccination. There is no reason to delay surgery following vaccination with a live vaccine if the child is well at the time of immediate pre-operative assessment. There is no reason to delay vaccination after surgery once the child is well and has recovered from the procedure. See the Association of Paediatric Anaesthetists of Great Britain and Ireland Immunisation guideline (**apagbi.org.uk/guidelines**).

Ideally, individuals scheduled for splenectomy should be immunised at least two weeks before the operation. Pneumococcal, meningococcal, Hib, influenza and varicella vaccines are recommended for these individuals pre- or post-splenectomy (see section 4.3.4 and the relevant disease chapters). Note: If the surgery is an emergency, then the immunisation programme should commence seven days post-splenectomy.

Can immunisations be given during an operation?

Vaccination can be administered while a child is under anaesthesia.[1]

What if the child has a chronic disease?

Children with chronic diseases should be immunised in the normal way, especially as they may be more at risk from the severe effects of vaccine-preventable diseases. However, if the illness or its treatment results in impaired immunity, immunisation with live vaccines should be considered carefully (see section 4.3), and the child's GP or paediatrician should be consulted before immunisation.

What if the child has had seizures?

A diagnosed neurological condition is not a contraindication to any vaccine on the Schedule. A history of well-controlled seizures in the vaccine recipient or a family history of seizures (febrile or afebrile) or other neurologic disorder is not a contraindication to vaccination against pertussis.[2]

Vaccination for children with an unstable neurological disorder (eg, poorly controlled epilepsy or deteriorating neurological state) has previously been considered a precaution for pertussis vaccination, but as these children may be high risk of severe pertussis complications, vaccination is recommended. Individual cases should be discussed with the specialist.[2]

A febrile reaction may occur after any vaccine and result in a febrile seizure in a susceptible child. Vaccine-related febrile seizures are rare, although the risk is higher following administration of certain vaccines, such as influenza vaccine (section 11.7), MMR (section 12.7) and meningococcal B vaccine (4CMenB, Bexsero; see section 13.7.3). These seizures, although frightening for a parent, are almost always benign with no associated sequelae.

What if the child is allergic?

Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute contraindication. See the contraindications and precautions section in each disease chapter. Children with asthma, eczema, hay fever and other allergies should be immunised in the usual way. Studies have shown that immunised children have slightly lower rates of atopic diseases.[6, 7]

Can children be immunised if they are known to develop a rash with antibiotics?

Children can be immunised if they are known to develop a rash with antibiotics. Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute contraindication to vaccination. A rash alone is not anaphylaxis.

Can all children receive all the vaccines?

A child cannot receive a vaccine if they have had anaphylaxis to a prior dose of a vaccine or to an ingredient in the vaccine. A child may have an underlying condition that is a contraindication to some vaccines; for example, children with illnesses or treatments that cause immunocompromise may be unable to receive live attenuated vaccines (see chapter 4 for special groups, chapters 12, 14 and 19 for MMR and chapter 22 for varicella).

3.1.4 Parents, guardians and contacts

What if the child's mother or guardian is pregnant or breastfeeding?

These are not contraindications to giving any of the Schedule vaccines to a child, including live vaccines, such as MMR. In addition, consideration should be given to the risks for the mother or guardian and baby from diseases such as pertussis, which can be life-threatening in infants.

Pregnancy provides an important opportunity to ensure the infant's siblings have received age-appropriate immunisation.

Pertussis (as Tdap) and influenza vaccines are recommended and funded for pregnant women (see section 4.1).

Are the viruses in live vaccines, such as MMR and varicella, transmissible?

These are highly attenuated (weakened) viruses designed specifically to induce an immune response without causing disease. There have been no recorded cases of measles, mumps or rubella disease in individuals who were in contact with a vaccine recipient. Vaccine-strain varicella transmission to contacts is rare (documented in only 9 immunised people, resulting in 11 secondary cases), and the documented risk of transmission exists only if the immunised person develops a rash[3] (see chapters 12, 14 and 19 for MMR and chapter 22 for varicella).

3.2 Addressing myths and concerns about immunisation

Myths about immunisation have existed since the first use of smallpox vaccine over 200 years ago and have resulted in loss of confidence in immunisation programmes. Misconceptions about vaccines contribute to vaccine hesitancy, which is an issue of global concern. This section provides information to assist providers with addressing concerns about immunisation.

3.2.1 Background

Concerns about immunisation should be taken seriously and responded to appropriately, providing as much information as possible. Individuals have the right to make informed decisions for themselves and those in their care, and to accept responsibility for their decisions. It is important to respect this right.

Many individuals and groups actively campaign against immunisation in New Zealand and globally. Their reasons for doing so may include personal experience, such as an adverse event they have attributed to immunisation, philosophical beliefs, conspiratorial beliefs or dissatisfaction with inadequate or superficial responses from health professionals or other authorities, who can seem at times to be dismissive of people's concerns. It is important for all health professionals to be able to provide accurate information about the benefits and risks of immunisation and to respond with as much information as possible to parent/guardian concerns or refer people appropriately.

It is not always possible to change people's position by way of scientific argument or presentation of evidence. Anti-immunisation arguments are almost exclusively based on fallacies of fact or logic, or on historical information that is no longer applicable in the current context. Often these arguments can be challenging for the health professional, particularly if the professional is unfamiliar with the argument and when they are complicated by logical flaws.

In any discussion, it may help to acknowledge that science does not always have all the answers, but that it provides a tool with which to answer questions and evaluate the evidence. It is important to point out that an event that follows immunisation is not necessarily caused by the immunisation. Finally, it is always helpful to inform parents/guardians about additional sources of reliable information (see section 2.1.2 on informed consent and section 1.6 on the safety monitoring of vaccines in New Zealand).

3.2.2 Understanding anti-immunisation

People tend to take on board information that supports their belief system and to ignore information that does not. The internet makes it very easy to access material that is appealing. Most people usually make logical decisions based on their perception of risk. Therefore, when a person has the perception that the risk of disease is real and that vaccines are reasonably safe and work, they are more likely to vaccinate. People are unlikely to vaccinate if they perceive that there is little risk of disease and that vaccines are not safe and do not work.[4]

3.2.3 Addressing concerns

If a parent is concerned about immunising their child, determining their concerns and addressing them can be helpful. Most often these concerns are around vaccine safety. As a health professional, you should challenge poor information, in a respectful way.

There are steps you can take when addressing a parent's or an individual's concerns (as detailed on the Canadian Paediatric Society website at **www.cps.ca/documents/position/working-with-vaccine-hesitant-parents**).[5] These include the following:

1. Understand the key role that sound advice from a health professional can play in parental decision making.
2. Use presumptive and motivational interviewing techniques to understand specific vaccine concerns.
3. Use clear and simple language to present evidence of disease risks and vaccine benefits, fairly and accurately.
4. Address injection pain head on.
5. Explain that community (herd) immunity does not guarantee personal protection.

For further information to help to address concerns, see also resources on the IMAC website (immune.org.nz), and other websites, such as the Centers for Disease Control and Prevention (CDC), the Immunization Action Coalition, Sharing Knowledge about Immunisation (SKAI) and the National Centre for Immunisation Research and Surveillance (see Appendix 8).

3.2.4 Debunking a myth

Debunking myths can be very challenging and can also backfire. When you are addressing a myth, there are three important points to remember.[6]

1. Try not to repeat the myth. Focus on the core facts.

This is because people cannot remember if what they hear was a myth or a fact later. Debunking can serve to strengthen the myth in people's minds as either familiar or a threat to their world view. Begin with the core facts; if it is easy to do in a few clear words, state what is true first.

2. Precede a myth with a warning.

Let them know that 'this is untrue' because you often cannot avoid mentioning the myth. Warn beforehand that a myth is coming and mention it once only directly prior to the correction.

3. Explain the fallacy – include an alternative explanation that accounts for how the myth misleads.

Explain why the misinformation is wrong. Do not leave a void but rather replace the myth with accurate information. You can highlight the problems with cherry picking, conspiracy theories and fake experts. If you have them, graphics can be extremely helpful, such as pictures of vaccine-preventable diseases or even a graph showing the impact of vaccination – if you feel it is appropriate.

4. State the core facts again.

Restate the fact again so that the core fact is the last thing the person processes.

Facts and myths about immunisation

Core fact: Measles and rubella have been eliminated in some countries. The WHO has set targets for global eradication.

Myth: MMR causes autism.

Explanation: There is no evidence that the MMR causes autism.[7, 8]

In 1998 a British physician announced he had found an association between the receipt of MMR and the development of a new disorder that included autism in a study of 12 children. No subsequent studies following his study have been able to reproduce his results.

In 2004 *The Lancet* retracted the original 1998 study from the scientific literature on the grounds that it was the product of dishonest and irresponsible research and the British authorities revoked the doctor's licence to practise medicine.[9] In 2008 a press investigation revealed that the doctor had falsified patient data and relied on laboratory reports that he had been warned were incorrect. Multiple studies have exonerated MMR vaccination.

Core fact: The incidence of allergic diseases has been increasing. It is thought that lack of exposure to microbes may play a role.

Myth: Vaccines cause allergic diseases.

Explanation: Extensive research shows that, if anything, vaccines may have a protective effect against allergic disease.

Many studies have explored this issue. A few have shown a positive association, but the majority show no association or a negative association. The international scientific community generally accepts that vaccines do not lead to allergies and in fact have a small protective effect against the development of allergy.[6, 10, 11]

The 2012 Institute of Medicine review of adverse events rejected any causal relationship between inactivated influenza vaccine and asthma exacerbation or reactive airway disease episodes in children and adults.[8]

Core fact: On-time vaccination is associated with a reduced risk of hospitalisation for diseases such as pertussis and pneumococcal disease in children under 1 year of age.

Myth: Vaccines cause cot death.

Explanation: Vaccines may reduce the risk for cot death.

Sudden unexpected death in infancy (SUDI), also known as cot death, usually occurs in children aged under 12 months and is most common around age 3 months, when many immunisations are given. SUDI may occur by chance within a day or so of immunisation.[12] There is no evidence that vaccination causes SUDI. Despite solid evidence against a link, the claims continue to be made.

Many studies have conclusively shown that SUDI is not caused by immunisation.[12] Some studies, including the New Zealand Cot Death Study, found a lower rate of SUDI in immunised children.[13] This is consistent with a Scandinavian study, which found that some cases of SUDI were probably caused by undiagnosed pertussis.[14] A large case-control study showed no increased risk of SUDI associated with immunisation,[15] and a meta-analysis of nine case-control studies further suggested that immunisation is protective against SUDI.[16] Consistent findings from several studies using a range of methods invalidate claims that associate vaccination with SUDI or cot death.[17]

Core fact: At birth, an infant is exposed to thousands of microbes.

Myth: Vaccines 'overload' or 'overwhelm' the infant immune system.

Explanation: It is estimated that the infant immune system could respond to over 10,000 vaccines all at once.

There is no evidence of immune system 'overload', either theoretical or actual. The immune system can deal with an extraordinarily large number of different antigens at any one time.

Every day we all encounter viruses, bacteria and other agents to which the immune system responds. Any demands placed on the immune system by vaccines are minuscule compared to its ability to respond.

Vaccines have very few antigens in them. The number of immunogenic proteins and polysaccharides in modern vaccines has decreased dramatically compared with early vaccines because of advances in vaccine technology. For example, early whole-cell pertussis vaccines contained around 3,000 immunogenic proteins, compared with two to five in the modern acellular pertussis vaccines. In spite of an increase in the number of vaccines on the Schedule, an infant now receives far fewer immunogenic proteins and polysaccharides than with earlier vaccines.[18] There are considerably more antigens in the organisms that cause disease than in the vaccines.

Explanation: Delaying immunisation for fear that an infant is too young leaves the infant vulnerable to disease, particularly pertussis and pneumococcal diseases. Infants delayed for their pertussis vaccinations are 4–6 times more likely to be hospitalised with the disease.[19] On-time vaccination is important.

Core fact: Vaccines induce immunity through natural processes.

Myth: It is better to get 'natural immunity' than get vaccinated.

Explanation: There is no evidence that experiencing vaccine-preventable diseases has any benefit on health; on the contrary, these diseases are serious and sometimes fatal. Vaccinated people have fewer diseases than unvaccinated people. Some vaccines induce better protection than that resulting from natural disease. Examples are tetanus, HepB and HPV, and protein conjugate polysaccharide vaccines administered to children aged under 2 years (Hib-PRP and PCV).

Core fact: The scientific evidence shows there is no association between HPV vaccines and autoimmune conditions.

Myth: HPV vaccines cause autoimmune conditions.

Explanation: Several large cohort studies have been conducted to investigate the link between HPV vaccine and autoimmune conditions.[20, 21, 22, 23, 24] No association has been found in these studies.

Core fact: The quadrivalent human papillomavirus vaccine has reduced cervical disease in countries using the vaccine, and Australia has almost eliminated genital warts.

Myth: HPV vaccines cause postural orthostatic tachycardia syndrome (POTS), complex regional pain syndrome (CRPS) and chronic fatigue syndrome (CFS).

Explanation: There is no scientific evidence that links POTS, CRPS or CFS with HPV vaccination.

POTS is a condition in which tachycardia occurs when a patient moves from a supine position to upright. The condition is associated with a collection of other symptoms, which include palpitations, light-headedness, weakness, blurred vision, headache, extreme fatigue, nausea, syncope and sleep disturbance. Up to 50 percent of people with POTS have an antecedent viral illness and 25 percent have a family history of similar complaints. There is an overlap between POTS and CFS.[25]

CRPS describes a variety of disorders characterised by pain that is disproportional to the inciting event. In children and adolescents, it often presents as a painful mottled swollen limb with allodynia and hyperalgesia. Girls are six times more likely to be affected than boys and the peak age of onset is at age 12–13 years. Often minor trauma is the inciting event, but around one-third of people with CRPS are unable to recall an inciting injury or trauma.[26]

CFS is a disorder characterised by extreme fatigue that cannot be explained by an underlying medical condition. The causes are unknown, but it has been linked to infection with Epstein–Barr virus and human herpesvirus 6.

Cases of these disorders have been reported in association with HPV vaccination, particularly in the media, and social media. The variable time between vaccination and onset of symptoms, lack of consistent symptoms and a reporting rate that remains below the expected rate for these syndromes all point to HPV vaccine not being the cause of these conditions.[27]

Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.[28, 29, 30] The WHO's Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.[31] The main challenge with HPV vaccine is communicating its excellent safety profile.[32]

Core fact: Everything is made of chemicals and any chemical can be toxic, even water.

Myth: Vaccines contain toxic chemicals, viruses and cells.

Explanation: Vaccine ingredients are not toxic in the amounts present in a vaccine. It is the dose that differentiates a poison from a harmless substance, essential substance or a medicine.

Most of the ingredients in vaccines are present already in our bodies and we consume them in some way every day. For example, aluminium is the most common metallic element on earth, and the body makes and uses formaldehyde for synthesising deoxyribonucleic acid (DNA).

- There is approximately 60 times more formaldehyde in a pear than a vaccine.
- Polysorbate 80 is used in many foods, including ice cream.
- Vaccines do not contain extraneous cells or viruses.
- Aluminium compounds administered via vaccination do not contribute significantly to the general aluminium exposure and do not raise human serum aluminium levels.[33] Based on 80 years of experience, the use of aluminium adjuvants in vaccines has proven to be extremely safe and effective.[34, 35]

For more information, see the IMAC factsheet *Vaccine Ingredients* (available at **immune.org.nz/resources/written-resources**).

Core fact: With the exception of safe water, no other intervention, not even antibiotics, has had such a major effect on mortality reduction and population growth. – S Plotkin[36]

Myth: Vaccination has played little role in controlling disease.

Explanation: Vaccine programmes have controlled or eliminated polio, tetanus, diphtheria, pertussis, *Haemophilus influenzae* type b, hepatitis B, pneumococcal disease, meningococcal disease, rotavirus, human papillomavirus, varicella, hepatitis, yellow fever, measles, mumps, rubella and others, in populations where vaccines have been used.

Improvements in living conditions and medical care have reduced the chances of dying from infectious disease, but without immunisation most people will still acquire vaccine-preventable infections. For example, measles, which spreads through the air, is largely unaffected by improvements in living conditions other than reduced overcrowding. Indigenous cases of measles, mumps and rubella were eliminated from Finland over a 12-year period using a two-dose MMR vaccination schedule given between 14 and 16 months and at age 6 years.[37] In September 2016, the Region of the Americas was the first WHO region to be declared free of measles and rubella. Endemic measles and rubella were declared eliminated in New Zealand in 2017.

Core fact: No vaccine is 100 percent effective and some immunised children will get the disease.

Myth: Vaccines do not work, as most cases of disease are in immunised children.

Explanation: As immunisation coverage increases, the proportion of cases that occur in children who have been immunised compared with those who are unimmunised increases. There is a mathematical relationship between vaccine effectiveness, immunisation coverage and the proportion of cases that are immunised.

To see this clearly, imagine a group of 100 children. If 90 percent of children are given a vaccine with 90 percent efficacy, then:

- 81 of the 100 children will be immune
- 10 children will be susceptible because of not having the vaccine, and another 9 because of vaccine failure.

This means that in the situation of exposure to the infection in a community, we expect that nearly half the cases of disease will be in immunised children, even though only 10 percent of immunised children were susceptible.

Of course, if all 100 children had been vaccinated only 10 would be susceptible to disease. As vaccine uptake rises, the proportion of cases of disease that occur in vaccinated people increases dramatically, but the absolute number of cases of disease falls to very low levels. Failing to provide the denominators (how many vaccinated and how many unvaccinated) can lead to misunderstanding.

For pertussis, where the protection following immunisation lasts only four to six years, immunised children can be infected but the resultant illness is usually milder, with fewer serious consequences and at an older age than if they had not received vaccine. The disease is most severe in infants, but adolescents and adults contribute to the carriage and spread of the disease (see sections 15.2 and 15.3).

For further details on the effectiveness of vaccines, see the 'Written resources' section of the IMAC website (**immune.org.nz/resources/written-resources**).

3.3 Addressing immunisation issues in a constantly changing environment

In recent years, the internet has exploded with a variety of forums that disseminate anti-immunisation material effectively. It is no longer practical to prepare official rebuttals to each new article. Fortunately, the internet also facilitates the rapid communication of scientific commentary on new misinformation as they appear. There are several scientists who regularly address immunisation myths in the form of regular blogs. In addition, some organisations provide position statements and discussion forums. While the format is often colloquial, the writers are respected scientists who volunteer commentary against the abuse of science and evidence-based medicine.

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4 Immunisation of special groups

This chapter discusses the special immunisation requirements of individuals at risk of vaccine-preventable diseases due to certain conditions or underlying disease, or through their occupation or other risk factors. The topics covered are:

- pregnancy and lactation (section 4.1)
- infants with special immunisation considerations from birth (section 4.2)
- immunocompromised individuals (section 4.3)
- chronic kidney disease (section 4.4)
- chronic liver disease (section 4.5)
- other special groups (section 4.6)
- immigrants and refugees (section 4.7)
- occupation-related vaccinations (section 4.8)
- travel (section 4.9).

Note: Vaccinators are advised to check the Pharmaceutical Schedule and any online updates (available at **pharmac.govt.nz/**) for changes to funding decisions for special groups.

4.1 Pregnancy and lactation

4.1.1 Women planning pregnancy

Women who are planning pregnancy should know whether they are immune to measles, rubella and varicella (see sections 12.8.3, 19.5.3 and 22.5.4).

Measles, mumps and rubella vaccine

Two doses of MMR are recommended and funded for eligible women who do not have documented evidence of immunity to measles, mumps and rubella (see section 12.8.3 for evidence). Pregnancy should be avoided for four weeks after vaccination (see section 19.6.1).

Varicella vaccine

Two doses of VV are recommended but not funded for adults who are susceptible to varicella (see section 22.5). VV should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after vaccination (see section 22.5.4).

4.1.2 During pregnancy

There are no safety concerns around giving non-live vaccines in pregnancy, including subunit vaccines and COVID-19 mRNA vaccine.[1, 2] Live vaccines should not be administered to a pregnant woman because of the theoretical possibility of fetal harm. Seek specialist advice in circumstances where the risk of exposure to an infection outweighs any potential risk of the fetus from immunisation.

Although MMR should not be given to women who are pregnant, in follow-up studies of women who inadvertently received MMR during pregnancy, there was no evidence that MMR is teratogenic or harmful to the mother, her fetus or her newborn.[3] Inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy.[3] See the relevant disease chapters, particularly measles (section 12.8.2), rubella (section 19.8.3) and varicella (section 22.8.6), for recommendations on managing exposure to diseases during pregnancy.

COVID-19 vaccine

Women/people who are pregnant are encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy (see sections 5.2.3, 5.5.4 and 5.5.10) and to discuss questions or concerns with their health professional. People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

Influenza vaccine

The quadrivalent influenza vaccine is recommended and funded for pregnant women and should be offered to women at any stage of pregnancy, as soon as the annual influenza vaccine becomes available (see section 11.5). Both the pregnant woman and her fetus are at increased risk of influenza complications;[4, 5] influenza vaccination is therefore recommended during pregnancy to reduce this risk.[6]

Maternal influenza vaccination also offers protection to the neonate through maternal antibody transfer.[3, 4] Influenza vaccines are not registered for infants aged under 6 months; therefore vaccination during pregnancy helps protect newborns and infants who are too young to be vaccinated.[4, 5] Maternal influenza vaccination is significantly associated with reduced risk of influenza virus infection[5] and hospitalisation for an influenza-like illness in infants up to 6 months of age.[5, 7]

There is no evidence that influenza vaccine prepared from a virus subunit causes harm to the fetus or neonate.[8, 9, 10]

Pertussis vaccine (Tdap)

Pertussis is a severe infection in infants too young to have been fully immunised. The tetanus, diphtheria and pertussis vaccine (Tdap) is recommended and funded to be given from 16 weeks' gestation in every pregnancy, preferably in the second trimester, to protect both the mother and her infant from pertussis (see section 15.5).[11, 12, 13] Postpartum maternal Tdap vaccination can reduce the risk of a mother infecting her baby but does not have the added benefit of providing passive antibodies.

See section 15.5 for information about maternal pertussis vaccine effectiveness and safety.

Close contacts

Confirmation of pregnancy should act as a trigger to review the pertussis vaccination status of all the pregnant woman's close contacts. This includes making sure siblings have received the usual Schedule vaccines and offering Tdap to adults, although this is only currently funded for certain special groups.

4.1.3 Breastfeeding and post-partum

> All vaccines on the National Immunisation Schedule and those recommended for special groups are safe for breastfeeding women.

Measles, mumps and rubella vaccine

Up to two doses of MMR are recommended and funded **after delivery** for eligible women who do not have documented evidence of immunity to measles, mumps and rubella. Breastfeeding is not a contraindication to MMR (see section 12.8.3).

Pertussis vaccine (Tdap)

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to birth.

A single dose of Tdap is also recommended but not funded for all new mothers who did not receive a Tdap vaccination during pregnancy.

Varicella vaccine

VV is recommended but not funded for all susceptible adults. Pregnant women who are non-immune can be offered VV **after delivery**.

If the mother is susceptible to varicella, VV for the mother is recommended and funded after delivery if the baby or other household members are immunocompromised (see section 22.5).

4.2 Infants with special immunisation considerations from birth

Further details are given in section 4.3 for infants born with primary immunodeficiency, including Down syndrome (section 4.3.3), secondary immunodeficiency (section 4.3.4), functional asplenia (section 4.3.12) and HIV (section 4.3.13).

4.2.1 Infants born to mothers with positive or unknown hepatitis B (HBsAg) status

Infants born to mothers who are known to be HBsAg-positive require hepatitis B vaccine (HepB) plus hepatitis B immunoglobulin (HBIG) to be given at or as soon as possible after birth; to continue vaccination as per the Schedule at 6 weeks, 3 and 5 months; and to undergo serological testing for hepatitis B antigen and antibodies (HBsAg and anti-HBs) at 9 months of age.

Infants of mothers whose HBsAg status is unknown at the time of delivery require HepB at birth while waiting for the results of urgent HBsAg testing on the mother (see section 9.5.2). If mother is found to be HBsAg positive, HBIG will also be required.

4.2.2 Preterm and/or low birthweight infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm and/or low birthweight infants. There is a potential risk of apnoea in preterm infants with respiratory immaturity. Apnoea monitoring should be considered after the first vaccination event.[12] For infants who experience apnoea after their first vaccination event, apnoea monitoring should be considered for 48–72 hours after subsequent vaccination events, but avoiding or delaying vaccination is not recommended.[14]

Hepatitis B vaccine

All preterm and low birthweight infants born to HBsAg-positive mothers should be managed the same way as term infants and receive HepB and HBIG to be given at or as soon as possible after birth (see section 9.5.2). These infants should continue vaccination as per the usual Schedule, starting at age 6 weeks.

Rotavirus vaccine

If an infant is in hospital at 6 weeks old, the Schedule vaccines, including rotavirus vaccine, should be given in hospital. Standard infection control precautions should be maintained. Administration of rotavirus vaccine to medically stable, hospitalised infants at 6 weeks of age has been shown to be well-tolerated. No increase in nosocomial rotavirus transmission has been observed within neonatal intensive care units.[15, 16, 17] Rotavirus vaccine can be given to preterm infants who are receiving corticosteroids. For immunocompromised infants or mothers, also see section 4.3.3 and section 4.3.6.

Pneumococcal vaccines

Infants born before 28 weeks' gestation are eligible for pneumococcal vaccination as part of an extended immunisation programme for high-risk groups (see section 16.5.2).

Infants born at 28 weeks' gestation or later, who do not have a condition eligible for extended pneumococcal immunisation, should receive PCV10 (Synflorix) as per the Schedule at ages 6 weeks, 5 months and 12 months.

Influenza vaccine

Preterm and/or low birth weight infants with an eligible condition are recommended to receive an annual funded influenza vaccination from 6 months of age (see Table 11.2).

Influenza vaccination is recommended (but not funded) for close contacts of preterm infants, including children from age 6 months (see section 11.5.4).

Pertussis vaccine (Tdap)

It is essential that siblings of preterm infants are up to date with Schedule vaccinations, to reduce the risk of pertussis transmission to the infant (see section 15.5). Adolescents should have received Tdap in year 7 or at age 11 years as part of the Schedule. Pertussis-containing vaccine is funded for primary and catch-up vaccination of all children aged under 18 years (see Appendix 2 for catch-up schedules).

A single dose of Tdap is recommended and funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mother did not receive maternal Tdap vaccination at least 14 days before the baby's birth.

Regardless of maternal vaccination history, it is recommended that all caregivers of infants born at less than 32 weeks' gestation receive a single dose of Tdap (not funded). This is because by 28–32 weeks' gestation the level of transplacental maternal antibodies in the infant is only half of the maternal circulating level, compared with higher than maternal levels by term.[11, 18, 19]

4.2.3 Infants with congenital heart disease

Congenital heart disease (CHD) may occur alone (eg, a single ventricle defect or shunt dependent lesion), or with other congenital defects (eg, immunodeficiency, endocrine dysfunction and facial abnormalities in DiGeorge syndrome or asplenia in heterotaxy syndrome).

Vaccination of infants with congenital heart disease

Infants with CHD and who are immunocompetent can receive vaccination as per the Schedule including rotavirus and varicella vaccines. For infants with CHD who were also born preterm or with a low birthweight, see also section 4.2.2.

Infants with a complex single ventricle defect or shunt dependent lesion who have undergone the Norwood procedure may have an increased risk of systemic decompensation. There is limited evidence linking the onset of decompensation to vaccination. As a precautionary measure, these infants may require hospital admission for observation or close parental monitoring at home for 48–72 hours after vaccination events. Discuss monitoring requirements with the infant's specialist prior to vaccination.[20]

Timing of vaccination may be affected when cardiac surgery is scheduled to avoid adding extra stress on these infants during this time. Vaccines should be administered at least one week before planned cardiac surgery. After cardiac surgery, administration of subunit vaccines should be delayed by 4–6 weeks for those at risk of systemic decompensation (eg, after a Norwood procedure).

For further information see Starship guidelines available from **www.starship.org.nz/guidelines/immunisations-and-cardiac-infants/**

Live vaccines – caution

If an infant has received blood products (eg, bypass or blood transfusion during surgery), delay administration of live vaccine is until seven months post-surgery.[20] This does not apply to administration of rotavirus vaccine.

See Table A6.1 in Appendix 6 for suggested intervals between administration of blood products and MMR or VV.

If no blood products have been given, the usual 4–6 weeks post-operative interval is recommended for those at risk of systemic decompensation, as above.

Some cardiac defects can be associated with immune deficiency, eg Di George syndrome. Most such patients can safely be given live viral vaccines when due – after assessment of immune function (see section 4.3.3). Seek specialist advice.

Pneumococcal vaccine

Children who have cardiac disease with cyanosis or failure, chronic pulmonary disease, Down syndrome, functional asplenia, immunodeficiency, or renal failure are eligible for extended pneumococcal immunisations as high-risk groups (see section 16.5.2).

Influenza vaccine

Infants and children with CHD, with or without cyanosis or failure, and children on long-term aspirin are eligible to receive funded annual influenza vaccination from 6 months of age (see Table 11.2).

Influenza vaccination is recommended (but not funded) for close contacts of infants and children with CHD, including children (see section 11.5.4).

Pertussis vaccination

It is essential that siblings and other close household contacts of infants with CHD are up to date with Schedule vaccinations, to reduce the risk of pertussis transmission to the infant (see section 15.5). Ensure catch-up vaccination of all children aged under 18 years (see Appendix 2 for catch-up schedules).

Varicella vaccine

Children on long-term aspirin can receive varicella vaccination as per the Schedule. There has been no reported association between varicella vaccination and the onset of Reye's syndrome in children on long-term aspirin to prevent thrombosis. The use of aspirin during natural chickenpox infection has been associated with Reye's syndrome.[20]

4.2.4 Infants with immunocompromise, including primary immunodeficiencies from birth

Seek guidance on immunisation of infants with severe primary immunodeficiencies (see section 4.3.3). Often these infants are unable to mount adequate responses to vaccines. Note: Rotavirus vaccine is contraindicated in any infant with possible severe combined immune deficiencies (SCID) due to the risk of chronic diarrhoea and prolonged viral shedding.[21, 22]

Some infants with congenital liver or kidney conditions are likely to need transplantation. An accelerated immunisation schedule for these infants in provided in Table 4.4. Extra immunisations may be warranted for other chronic kidney and chronic liver conditions (see sections 4.4 and 4.5). Infants with biliary atresia may have polysplenia (functional hyposplenia; see section 4.3.12).

Infants of mothers who have received immunomodulatory biologic agents (also known as biologic response modifiers) during pregnancy also may have a reduced response to the primary series vaccinations (section 4.3.6).

4.3 Immunocompromised individuals

The nature and degree of immunocompromise determines an individual's immune response and which vaccines are recommended and can be safely administered. Individuals who are immunodeficient or immunosuppressed due to a disease and/or treatment may have an increased risk from infectious diseases. These individuals should be vaccinated as a matter of priority, however, it should be recognised that they have a suboptimal response.

Children aged under 18 years, and adults aged 18 years or older who are eligible to receive publicly funded health and disability services in New Zealand, are eligible to receive the usual Schedule vaccines and additional funded vaccines when they meet the eligibility criteria for special groups.

Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (**pharmac.govt.nz/**) for changes to funding decisions for special groups.

> It is important to ensure that the household contacts of these individuals are immune to vaccine-preventable diseases whenever possible.

The following definitions are used in this *Handbook*:

- **Immunocompetent** – a broad term referring to normal immune system function.
- **Immunocompromise** – a broad term referring to altered immune system function. The individual's ability to mount an immune response may be reduced or increased because of a disease, treatment or genetic disorder.
- **Immunomodulation** – changes in immune system function in response to medication, cancer chemotherapy or immunotherapy treatments.
- **Immunostimulant** – a substance able to stimulate or increase an immune response.
- **Immunosuppression** – a reduced ability to mount an immune response caused by medication, cancer chemotherapy or immunotherapy treatment.
- **Immunodeficiency** – a reduced ability to mount an immune response and fight off infection. Immunodeficiency conditions are classified as primary and secondary, dependent on the cause.

4.3.1 Vaccination of close contacts of immunocompromised individuals

> Immunocompetent siblings, household and other close contacts of immunocompromised individuals are recommended to receive all the Schedule vaccines at the recommended ages.

All Schedule vaccines can be given to close contacts of immunocompromised individuals. It is important to ensure that close contacts are immune for the added protection of the immunocompromised individual.

Rotavirus vaccine

Rotavirus vaccine can be given to infants who are in close contact with an immunocompromised individual. The evidence shows that transmission of the rotavirus vaccine virus to contacts is low, and no cases were symptomatic.[15, 16, 17]

Measles, mumps and rubella vaccine

MMR can be given to children and eligible adults who are in close contact with an immunocompromised individual. MMR vaccine viruses are considered non-transmissible; there is no evidence of the current MMR vaccine viruses being transmitted from vaccine recipient to a close contact.[23, 24] See section 12.5 for information about eligibility and the recommended MMR vaccination schedule.

Varicella vaccine and zoster vaccine

Age-appropriate varicella (VV) or zoster (ZV) vaccine can be given to close contacts of an immunocompromised individual. Transfer of vaccine virus to an immunocompromised person is rare and only possible if the vaccinated person develops a varicella- or zoster-like rash. In this situation, the rash should be covered and close contact with the person who is immunocompromised avoided for the duration of the rash.[25] (See sections 22.5 and 23.5 for eligibility.)

Influenza vaccine

Annual influenza vaccination is recommended but not funded for all children aged 6 months or older and adults, particularly those who are close contacts of an immunocompromised individual.

COVID-19 vaccine

For greater protection of high-risk individuals, it is recommended for close contacts of an immunocompromised individual to be up to date with COVID-19 immunisation with

age-appropriate mRNA-CV from age 5 years, or rCV from age 12 years (for primary course only for ages 12–17 years) or from age 18 years for all other doses.

BCG vaccine

If indicated by the usual BCG eligibility criteria (see section 21.5.2), it is safe to give BCG vaccine to infants of immunocompromised household contacts.

4.3.2 Immune checkpoint inhibitor (immunostimulant) therapy

A person who is currently receiving any of the four immune checkpoint inhibitor medications currently available in New Zealand – namely, nivolumab (Opdivo), pembrolizumab (Keytruda), atezolizumab (Tecentriq) and ipilimumab (Yervoy) – or has received these in the previous six months can receive any non-live vaccine, including influenza, mRNA-CV and rCV, without consulting their specialist prior to vaccination. The administration of live vaccines (MMR and VV) is contraindicated.

4.3.3 Primary immunodeficiency

Primary immunodeficiencies that present in childhood are usually caused by an inherited genetic disorder. They can result in defects in antibody production (B-lymphocyte disorders), defects in the development of cell-mediated immunity (T-lymphocyte disorders), combination defects (disorders or syndromes affecting B- and T-lymphocytes) and defects of complement and phagocytic function.[26]

Children with Down syndrome (trisomy 21) are at increased risk from respiratory and severe infections due to multiple immune deficits in both the innate and adaptive immune systems, as well as anatomical structural differences,[27, 28] and should be considered as primary immune deficiency.

Vaccines for individuals with a primary immunodeficiency

Live vaccines – caution

Diagnosis of primary immunodeficiency is often not made before children start their Schedule vaccinations. For infants who have the potential to be immunodeficient (eg, have a familial history of inherited immunodeficiency) administration of live vaccines such as BCG (see section 21.6.2), rotavirus vaccine, MMR, and/or varicella vaccines may be contraindicated or need to be deferred until specialist consultation is sought.

Live vaccines are contraindicated for all individuals with T lymphocyte-mediated immunodeficiency, a combined B- and T-lymphocyte deficiency or type 1 interferon receptor (IFNAR) signalling pathway defects.[29] Many of these individuals will be on

immunoglobulin replacement therapy, which provides passive protection against most vaccine-preventable infections.

COVID-19 vaccine

Certain individuals from 5 years of age with a primary immunodeficiency are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for all individuals with primary immunodeficiency, particularly for those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16-17 years or given to anyone aged 12-15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label and requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

Influenza vaccine

Influenza vaccine is funded for all individuals with primary immunodeficiency, including Down syndrome, aged 6 months or older. Regardless of their age, all immunodeficient individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart (second dose unfunded), and one funded dose annually after that. A second dose is funded for children aged 6 months to under 9 years when influenza vaccine is being used for the first time.

Pneumococcal vaccines

Infants and children aged under 5 years

Children in this age group with a diagnosed primary immunodeficiency or Down syndrome are eligible to receive extended pneumococcal immunisation for high-risk groups (see section 16.5.2).

A course of PCV13 vaccine at 6 weeks and 3, 5 and 12 months replaces doses of PCV10 vaccine on the usual Schedule (see sections 16.5.2 and 16.5.3) followed by age-appropriate 23PPV vaccinations.

Children aged 5 years or older and adults

Children aged 5 years or older and adults with a diagnosed primary immunodeficiency or inherited complement deficiency are eligible to receive one PCV13 followed by age-appropriate 23PPV vaccinations (see section 16.5.2).

Children with Down syndrome aged 5 years to under 18 years

Children in this age group who **have** received at least two doses of PCV10 and have Down syndrome are recommended and funded to receive one PCV13 followed by up to two doses of 23PPV (see section 16.5.2).

Children in this age group who **have not** received at least two doses of PCV10 and have Down syndrome are recommended and funded to receive up to two doses of 23PPV (see section 16.5.2).

Meningococcal conjugate vaccines

The current funded meningococcal conjugate vaccines are group C and group ACWY meningococcal conjugate vaccines: MenC (NeisVac-C) and MenACWY-D (Menactra).

There is a possibility of blunting of some PCV serotype antibody responses when MenACWY-D (Menactra) is given concurrently with PCV13 because both vaccines contain diphtheria-derived proteins as conjugate. The clinical significance of this blunting, observed in a clinical trial with PCV7,[30] is unknown and the affected serotypes (4, 6B, 18C) are currently rare in New Zealand. The benefits of achieving broad meningococcal protection as early as possible in immunocompromised infants outweigh the theoretical risk of modest reduction of some pneumococcal antibody levels, such that, MenACWY-D is recommended at age 9 months (see Table 4.5 and Table 4.6) rather than waiting until after completion of the PCV13 series. Note: two doses given at least three months apart are recommended as a primary series; ideally, each dose should be given at least four weeks before or after PCV13 to reduce this risk of interference, but PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

Infants aged under 9 months

Infants aged under 9 months who have an inherited complement deficiency are recommended and funded to receive two doses of MenC given a minimum of eight weeks apart. For broader meningococcal group coverage in infants aged 6 weeks to 9 months, MenACWY-T (Nimenrix) is also available but not funded (see section 13.5).

Infants and children aged 9–23 months

Infants and children aged 9–23 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY-D at least three months apart, followed by a booster dose after three years then five-yearly. MenACWY-D is recommended to be given at least four weeks after PCV13.

Children aged 2 years to under 7 years

Children aged 2 years to under 7 years who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart, followed by a booster dose after three years then five-yearly.

Children aged 7 years or older and adults

Children aged 7 years or older and adults who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart, followed by a booster dose every five years.

Group B meningococcal recombinant vaccine (4CMenB)

Vaccination with 4CMenB (Bexsero), to protect against disease caused by the group B meningococci, is recommended and funded for infants, children and adults with an inherited complement deficiency and an increased risk of meningococcal disease.

Infants aged under 12 months

Infants and children aged 6 weeks to <12 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of 4CMenB at least eight weeks apart, followed by a booster dose after 12 months of age given at least six months after the second dose.

Infants from age 12 to 23 months

Infants aged from 12 months to 23 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of 4CMenB at least eight weeks apart, followed by a booster dose given 12–23 months after the second dose.

Children from age 2 years and adults

Children aged from 2 years and adults who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of 4CMenB at least eight weeks apart.

Booster doses of 4CMenB are funded five yearly after the age of 12 months for patients with inherited complement deficiency.

Note: 4CMenB elicits a robust immune response, and sometimes high fevers in infants. Routine use of paracetamol (or ibuprofen if age appropriate) with every dose of 4CMenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain (see section 13.4.4)

Vaccines used to test for a primary immunodeficiency

Hib-PRP, 23PPV and Tdap vaccines may be used in testing for a primary immunodeficiency, on the recommendation of an internal medicine physician or paediatrician. Hib-PRP and Tdap vaccines are funded for primary immunodeficiency testing in children aged under 18 years and eligible adults.

Vaccination advice, by primary immunodeficiency

Below is a summary of the vaccination recommendations for individuals with a primary immunodeficiency.[26] (See also Table A6.1 in Appendix 6.)

Live vaccines are contraindicated for all individuals with T lymphocyte-mediated immunodeficiency, a combined B- and T-lymphocyte deficiency or type 1 interferon receptor (IFNAR1) signalling pathway defects.[29] Many of these individuals will be on immunoglobulin replacement therapy, which provides passive protection against most vaccine-preventable infections.

B lymphocyte deficiencies (humoral)

X-linked agammaglobulinaemia and common variable immune deficiency

- BCG vaccine is contraindicated.
- Only administer live-virus vaccines (rotavirus, MMR, VV) after discussion with the individual's specialist.
- The efficacy of any vaccine that is dependent on a humoral response, such as 23PPV, is doubtful.
- During IVIG therapy, only influenza vaccination is recommended.

Selective IgA deficiency, IgG subclass deficiency and hypogammaglobulinaemia

- BCG vaccine may be contraindicated.
- Live-virus vaccines (rotavirus, MMR, VV) can be administered.
- All vaccines are probably effective.
- Influenza vaccine is recommended.

Combined lymphocyte deficiencies (T and B cell)

Complete defects (eg, SCID or athymia)

- All live vaccines are contraindicated.
- All other vaccines are likely to be ineffective prior to immune reconstitution, and passive protection must be optimised.

Partial defects (eg, most patients with DiGeorge syndrome, Wiskott Aldrich syndrome, ataxia telangiectasia)

- Provision of selected live vaccines is dependent on specialist advice after assessment of degree of immune compromise.
- Hib, pneumococcal (PCV13 and 23PPV), and meningococcal vaccines are recommended, except when the individual receives IVIG therapy.
- Non-live vaccines should be provided as per the usual Schedule, except when the individual receives IVIG therapy.
- Influenza vaccination is recommended, including individuals who receive IVIG therapy.

Complement deficiencies

Deficiency of C1–9, mannose-binding lectin, properdin, factor B

- There are no specific contraindications or precautions.
- The usual Schedule vaccines are probably effective.

- Influenza, Hib, pneumococcal (PCV13 and 23PPV) and meningococcal vaccines are recommended.

Phagocytic function deficiencies

Chronic granulomatous disease and cyclic neutropenia

- BCG and live-bacteria vaccines are contraindicated.
- Live-virus vaccines (rotavirus, MMR, VV) can be administered.
- The usual Schedule vaccines are probably effective.
- Influenza vaccine is recommended.

Leukocyte adhesion defect, myeloperoxidase deficiency

- All live vaccines are contraindicated.
- Influenza, Hib, pneumococcal (PCV13 and 23PPV) and meningococcal vaccines are recommended.

4.3.4 Secondary (acquired) immunodeficiency

Secondary immunodeficiencies are acquired. They occur in individuals with HIV, individuals with malignant neoplasms, solid-organ transplant recipients, and in individuals receiving cancer chemotherapy or other immunotherapies.[26]

The ability of individuals with a secondary immunodeficiency to develop an adequate immunological response depends on the disease and/or the type and intensity of immunosuppressive therapy. After immunosuppressive therapy is discontinued, immune recovery can take weeks to years. Ideally, vaccination should be conducted prior to any planned immunosuppression.

Vaccines for individuals with acquired immunodeficiency

In diseases such as HIV or chronic renal failure, where immune impairment is likely to be progressive, ensuring the individual is up to date with Schedule and additional funded vaccines earlier in their disease and when at optimal disease control may result in better antibody responses.

Before commencing a therapy that would be expected to cause significant immunosuppression, a full vaccination history should be obtained. Then, if circumstances permit, such as prior to commencing immunosuppressive therapy for rheumatological disease or prior to solid organ transplant, vaccination should be completed following the usual Schedule (including HPV from age 9 years). Administration of additional funded vaccines (eg, varicella for children, zoster for certain adults, meningococcal or pneumococcal vaccines) may be appropriate. However, when immediate commencement of therapy is clinically indicated, it is not recommended to delay therapy to allow for vaccination.

Live vaccines – caution

Live vaccines (BCG, rotavirus, MMR and VV) are contraindicated for individuals who are immunosuppressed because of the risk of disseminated vaccine disease.

Individuals who are not considered to be significantly immunodeficient or immunosuppressed can receive live vaccines. For individuals who are due to commence elective immunosuppressive therapy, live vaccines (MMR and VV) should be administered at least four weeks prior to commencement of therapy. Live vaccines should also be administered at least four weeks before a predicted transplant.

On a case-by-case basis with appropriate follow-up in place, a specialist may recommend that VV is administered less than four weeks before a predicted transplant or to a post-transplantation paediatric patient.[31] With specialist input MMR may also be considered in clinically well patients at least 1 year after solid organ transplantation on low level immunosuppression.[32]

See sections 12.5, 22.5 and 23.5 for information about the recommended MMR and VV vaccination schedules and eligibility criteria.

Live zoster vaccine has been discontinued. Individuals from age 18 years with secondary (acquired) immunodeficiency are recommended two doses (unfunded) of recombinant zoster vaccine (rZV, Shingrix). See section 23.5.1.

COVID-19 vaccine

Certain individuals from 5 years of age with a secondary (acquired) immunodeficiency are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for individuals with a secondary (acquired) immunodeficiency, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12-15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given as primary or booster dose from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

Influenza vaccine

Influenza vaccine is funded for all immunodeficient and immunosuppressed individuals aged 6 months or older. Regardless of their age, all immunocompromised individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart (second dose unfunded), and one funded dose annually after that. A second dose is funded for children aged 6 months to under 9 years when influenza vaccine is being used for the first time.

Haemophilus influenzae type b (Hib-PRP) vaccines

Infants and children aged under 5 years

Vaccination against Hib disease for infants and children aged under 5 years is included in the usual Schedule. DTaP-IPV-HepB/Hib vaccine is recommended at 6 weeks, 3 months and 5 months of age followed by a booster dose of Hib-PRP vaccine) at age 15 months.

Children aged 5 years or older and adults

Children aged 5 years or older and adults who have functional asplenia, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-chemotherapy, receiving immunosuppressive therapy for longer than 28 days, or on renal dialysis, are recommended and funded to receive one dose of monovalent Hib-PRP vaccine.

Children and adults post-haematopoietic stem cell transplantation

A three-dose series of Hib-PRP is recommended for children and adults who are post-haematopoietic stem cell transplantation. Children aged under 10 years who are revaccinated using DTaP-IPV-HepB/Hib will receive three doses of Hib-PRP-containing vaccine.

For children aged 10 years or older and adults who receive monovalent Hib-PRP, one dose is funded, and the immunisation benefit can be claimed for vaccine administration. Doses two and three are not funded. Hib-PRP can only be ordered from ProPharma and an immunisation benefit cannot be claimed for vaccine administration.

Pneumococcal vaccines

Infants and children aged under 5 years

Children in this age group who have functional asplenia, HIV, nephrotic syndrome or renal failure, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-haematopoietic stem cell transplantation, or have been receiving high-dose corticosteroid therapy for more than two weeks, other immunosuppressive therapy for longer than 28 days, or radiotherapy are recommended and funded to receive pneumococcal vaccination as part of the extended immunisation programme for high risk groups (see section 16.5.2).

Administration of PCV13 vaccine at 6 weeks, 3, 5 and 12 months replaces PCV10 vaccine on the Schedule (see sections 16.5.2 and 16.5.3) once the eligible condition has been identified followed by age-appropriate 23PPV vaccinations.

Children aged 5 years to under 18 years

Children in this age group who have a condition listed in the *Infants and children aged under 5 years* section above are recommended and funded to receive one PCV13 followed by up to two doses of 23PPV (see section 16.5.2).

Children aged 5 years or older and adults

Children in this age group and adults who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-chemotherapy, post-haematopoietic stem cell transplantation, or on renal dialysis, are recommended and funded to receive one PCV13 followed by age-appropriate 23PPV vaccinations (see section 16.5.2).

It is recommended that individuals in this age group who will be or have been receiving high-dose corticosteroid therapy for more than two weeks or other immunosuppressive therapy for longer than 28 days receive pneumococcal vaccination (this is not funded).

Meningococcal conjugate vaccines

The current funded meningococcal vaccines are group C and group ACWY meningococcal conjugate vaccines: MenC (NeisVac-C) and MenACWY-D (Menactra).

See *Meningococcal conjugate vaccines* in section 4.3.3 for an explanation of the timing of MenACWY-D and PCV13.

Infants aged under 9 months

Infants aged under 9 months who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-splenectomy, pre-/post-solid organ transplantation, or post-haematopoietic stem cell transplantation, or pre/post immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenC a minimum of eight weeks apart.

For broader meningococcal group coverage in infants aged 6 weeks to 9 months, MenACWY-T (Nimenrix) is also recommended but not funded (see section 13.5) to replace the MenC doses.

Infants and children aged 9–23 months

Infants and children in this age group who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY-D at least three months apart, followed by a booster dose after three years then five-yearly.

Infants and children in this age group who are post-haematopoietic stem cell transplantation or will be or have been receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY-D at least three months apart. Booster doses of MenACWY-D after three years and then five-yearly are recommended (although not funded) if immunosuppression is long-term.

Children aged 2 years to under 7 years

Children in this age group who have an acquired complement deficiency, functional asplenia, HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart, followed by a booster dose after three years then five-yearly.

Children in this age group who are post-haematopoietic stem cell transplantation or receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart. If immunosuppression is long-term, booster doses of MenACWY-D after three years and then five-yearly are recommended (although not funded).

Children aged 7 years or older and adults

Children in this age group and adults who have an acquired complement deficiency, functional asplenia, HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart, followed by a booster dose every five years.

Children in this age group and adults who are post-haematopoietic stem cell transplantation or will be or have been receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY-D at least eight weeks apart. If immunosuppression is long-term, a booster dose of MenACWY-D is recommended (but not funded) every five years.

Group B meningococcal vaccine (4CMenB)

Vaccination with 4CMenB (Bexsero), to protect against disease caused by the group B meningococcal serotype, is recommended and funded for infants, children and adults who have an acquired complement deficiency, functional asplenia or HIV, or are pre- and post-splenectomy or pre- or post-solid organ transplantation, or post-haematopoietic stem cell transplantation, or prior to planned and following immunosuppressive therapy for longer than 28 days.

Infants aged under 12 months

Infants and children aged 6 weeks to <12 months who have an acquired immunodeficiency, as listed above, are recommended and funded to receive two doses of 4CMenB at least eight weeks apart, followed by a booster dose at least six months after the second dose, from 12 months of age.

Infants from age 12 to 23 months

Children aged from 12 months to 23 months who are diagnosed with an acquired immunodeficiency are recommended and funded to receive two doses of 4CMenB at least eight weeks apart, followed by a booster dose given 12–23 months after the second dose.

Children from age 2 years and adults

Children aged from 2 years and adults who are diagnosed with an acquired immunodeficiency are recommended and funded to receive two doses of 4CMenB at least eight weeks apart.

Booster doses are funded five yearly as required after the age of 12 months for patients pre- and post-splenectomy, with functional or anatomical asplenia, HIV, acquired complement deficiency or pre- or post-solid organ transplant.

Note: 4CMenB elicits a robust immune response, and sometimes high fevers in infants. Routine use of paracetamol (or ibuprofen if age appropriate) with every dose of 4CMenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain (see section 13.4.4).

Measles or chickenpox exposure post-transplantation

Specialist advice should be sought if an individual who is immunosuppressed is a suspected or confirmed contact of a measles or chickenpox case. Post-transplantation, the use of passive immunisation with IG after exposure to measles or chickenpox should be based on the documentation of negative antibody titres, or where immune status is unknown. See *Human normal immunoglobulin prophylaxis for contacts* and *Prophylaxis with intravenous immunoglobulin* in section 12.8.2 and *Post-exposure prophylaxis with zoster immunoglobulin* in section 22.8.2.

4.3.5 Individuals receiving corticosteroids

Corticosteroids reduce inflammation and generally suppress the immune system. The minimum amount of corticosteroid administration sufficient to cause immunosuppression is not well defined, and is dependent on the treatment used, dose, route of administration and duration. A daily dosage equivalent to 2 mg/kg oral prednisone or greater, or a total daily dosage of 20 mg or greater, particularly when given for 14 days or more, is considered sufficient to raise concern about the safety of live vaccines. Individuals receiving fludrocortisone or long-term dexamethasone should not receive live vaccines during treatment and for three months after discontinuation.

A single dose of dexamethasone for management of an acute respiratory illness in children is not associated with a decrease in endogenous corticosteroid levels[33] or immunosuppression. No minimum interval is required between administration of a single dose of dexamethasone and a live vaccine, as long the individual is not acutely unwell.

Rotavirus vaccine can be given to preterm infants born who are receiving corticosteroids.

Live vaccines *can be* administered to individuals who:

- are using topical corticosteroid therapy, including on the skin or respiratory tract (by aerosol), or receiving local intra-articular, bursal or tendon corticosteroid injections because such therapies do not usually result in immunosuppression
- are receiving maintenance *physiological* doses of corticosteroids
- are receiving oral budesonide or fluticasone to treat an inflammatory bowel condition
- received a single dose of dexamethasone for management of an acute respiratory illness
- are receiving low to moderate doses of systemic steroids given daily or on alternate days
- are receiving high-dose corticosteroids for fewer than 14 days.

Live vaccines *should not* be administered to individuals:

- receiving high dose corticosteroids daily or on alternate days for more than 14 days
- receiving long-term dexamethasone or hydrocortisone that is not for physiological maintenance or fludrocortisone
- who have a disease process that causes immunosuppression, except in special circumstances after discussion with the individual's specialist.

See Table 4.1 for guidelines according to each corticosteroid agent.

Table 4.1: Guidelines for live vaccine administration for individuals receiving corticosteroid agents

Corticosteroid agent	Dose regime	Administration of live vaccines
Topical or local corticosteroid doses	Any agent, any dose • applied to the skin • inhaled • injected locally into a joint, bursa or tendon	Any time before, during or after treatment
Budesonide	Oral or inhaled, any dose	Any time before, during or after treatment
Dexamethasone	Single dose for an acute respiratory illness	Any time before or after dose
	Physiological maintenance doses	Any time before, during or after treatment
	Long-term treatment not for physiological maintenance	Delay for 3 months after discontinuation
Fludrocortisone	Any dose	Delay for 3 months after discontinuation
Fluticasone	Oral or inhaled, any dose	Any time before, during or after treatment
Hydrocortisone	Physiological maintenance doses	Any time before, during or after dose
	Long-term treatment not for physiological maintenance	Delay for 3 months after discontinuation

Corticosteroid agent	Dose regime		Administration of live vaccines
Prednisone / Prednisolone[34]	*Infants and children <10kg*	*Children and adults ≥10kg*	
	<2mg/kg per day, any duration	<20mg per day, any duration	Any time before, during or after treatment
	≥2mg/kg per day for <14 days	≥20mg per day for <14 days	Immediately on discontinuation
	≥2mg/kg per day for ≥14 days	≥20 mg per day for ≥14 days	Delay for 1 month after discontinuation

Note: The guidelines in this table are intended to ensure safety of administration of the live vaccines to individuals receiving corticosteroids; optimal vaccine immunogenicity may not be achieved.

COVID-19 vaccine

Certain individuals from 5 years of age receiving corticosteroids agents are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for individuals receiving corticosteroid agents, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions, and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

4.3.6 Individuals receiving non-corticosteroid immunomodulatory agents

Non-biologic agents

Hydroxychloroquine, mesalazine/5-ASA, olsalazine and sulfasalazine act on the immune system and reduce the inflammatory responses associated with immune-mediated inflammatory disease (IMID, also known as autoimmune diseases) but do not cause immunosuppression.[35]

Azathioprine, 6-mercaptopurine, methotrexate, cyclophosphamide, cyclosporine, leflunomide, mycophenolate mofetil and tacrolimus suppress immune system function to varying degrees, dependent on the agent and intensity of therapy, to reduce symptoms and tissue damage associated with IMID or prevent rejection of a transplanted organ.[35]

See Table 4.2 for guidelines for administration of live vaccines according to each non-biologic agent.

Biologic agents

Immunotherapeutic treatment of disease has increased rapidly over recent years. The treatment relies on administration of biologic agents that selectively target components of the immune system (eg, antibodies, cytokines and proteins) to alter an individual's immune response to treat disease.[35]

In IMID, such as rheumatoid arthritis and inflammatory bowel disease, biologic agents target a specific part of the individual's immune response against 'self' to stop the immune response creating inflammation and damage.[35] However, they also affect the immune response against genuine antigens and cause immunosuppression. Use of a combination of therapies may have a cumulative effect that increases the level of immunosuppression in an individual.

In atopic conditions and inflammation such as chronic spontaneous urticaria and allergic asthma, biologic agents inhibit the activation of allergen specific IgE antibodies and mast cells or decrease the number of eosinophils that contribute to allergy related inflammation.[35] These treatments do not cause immunosuppression.

Other biologic agents stimulate an individual's immune response by blocking immune checkpoints on healthy cells and cancer cells to increase their anti-tumour response, see section 4.3.2.
Live vaccines *can be* administered to individuals:

- receiving hydroxychloroquine, mesalazine/5-ASA, olsalazine and sulfasalazine
- with low-level immunosuppression regimens of azathioprine, 6-mercaptopurine or methotrexate
- receiving intra-ocular biologic therapy because such therapy does not usually result in immunosuppression
- taking omalizumab or mepolizumab to manage allergic conditions such as chronic spontaneous urticaria and allergic asthma.

Live vaccines *should not* be administered to individuals:

- with high-level immunosuppression regimens of azathioprine, 6-mercaptopurine or methotrexate
- receiving treatment with any dose of cyclophosphamide, cyclosporine, leflunomide, mycophenolate mofetil, or tacrolimus
- receiving treatment with monoclonal antibody inhibitors, TNF inhibitors and kinase inhibitors, and immune checkpoint inhibitors.

See Table 4.2 for guidelines for administration of live vaccines according to each biologic agent.

Table 4.2: Guidelines for live vaccine administration for individuals receiving non-corticosteroid agents

	Dose regime	Administration of live vaccines	Dose regime	Administration of live vaccines
Non-biologic agent				
Hydroxychloroquine Mesalazine/5-ASA Olsalazine Sulfasalazine	Any dose	Any time before, during or after treatment		
Azathioprine	≤3 mg/kg per day	Any time before, during or after treatment	>3mg/kg per day	Delay for 3 months after discontinuation
6-mercaptopurine	≤1.5 mg/kg per day		>1.5mg/kg per day	
Methotrexate	≤0.4 mg/kg per week		>0.4mg/kg per week	
Cyclophosphamide Cyclosporine Mycophenolate mofetil Tacrolimus			Any dose	Delay for 3 months after discontinuation
Leflunomide Teriflunomide			Any dose	Delay for 6 months after discontinuation
Axitinib Imatinib Ruxolitinib Tofacitinib			Any dose	Delay for 12 months after discontinuation
Biologic agent				
Locally injected biologic dose	Any agent, any dose Intra-ocular injection	Any time before, during or after dose		
Omalizumab Mepolizumab	Any dose	Any time before, during or after dose		
Fingolimod Natalizumab			Any dose	Delay for 3 months after discontinuation
Atezolizumab Ipilimumab Nivolumab Pembrolizumab Sirolimus			Any dose	Delay for 6 months after discontinuation

	Dose regime	Administration of live vaccines	Dose regime	Administration of live vaccines
Abatacept Adalimumab Anakinra Etanercept Infliximab Rituximab Tocilizumab Trastuzumab			Any dose	Delay for 12 months after discontinuation
Ocrelizumab			Any dose	Delay for 3 years after discontinuation

For children aged under 18 years, see the Starship Clinical Guidelines *Immunosuppression and Immunisation in Rheumatology* (available at **www.starship.org.nz/guidelines/immunosuppression-infection-and-immunisation-in-rheumatology**).

For adults, see the IMAC factsheet *Immunisation for adults with immune-mediated inflammatory disease (IMID) who require immunosuppressive treatment* (available at **immune.org.nz/resources/written-resources**).

COVID-19 vaccine

Individuals from 5 years of age receiving certain biologic and non-biologic immunosuppressive agents are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for individuals receiving immunosuppressive agents, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions, and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

Infants of mothers who received immunomodulatory biologic agents during pregnancy

> For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with infant's mother or specialist, or contact IMAC (on 0800 IMMUNE / 0800 466 863) before administration of rotavirus, BCG, MMR or VV vaccines.

In recent years there has been rapid development of targeted immunomodulatory biologic agents (also known as biologic response modifiers; BRM), and an increasing number of pregnant women are receiving such therapies. Common examples include adalimumab, infliximab and rituximab. Studies of the effects of these agents on the infant's immune system and ability to respond to vaccination are limited.[36]

Multiple factors influence the potential for these agents to be detected and/or cause immunosuppression in an infant for months after they are born. These include, the agent or combination of agents used, gestational age(s) when administered, ability of the agent(s) and/or their metabolites to cross the placenta, and time between administration of the last antenatal dose and the chronological age of the infant.[37]

A recent study analysing a US vaccine safety database is encouraging regarding the safety of rotavirus vaccine in the first year of life, and measles-containing vaccine in the first two years of life, in infants exposed in utero to immunomodulatory biologic agents, with no increased rates of adverse events.[38] The commonest agents represented were anakinra, adalimumab, infliximab and etanercept, but other agents were only used in a few women so the safety of these remains unknown.

Rotavirus vaccine

There is limited data on rotavirus vaccination safety when given to infants born to mothers receiving immunomodulatory therapy during pregnancy.[20, 36, 39] Although in most cases it is likely to be safe, caution is required. The level of circulating wild-type rotavirus is currently very low in New Zealand, therefore, the risk of gastroenteritis following rotavirus vaccination in this cohort of infants may be greater than the risk of acquiring the disease. The decision to administer rotavirus vaccine to infants born to mothers who received immunomodulatory biologic agents during pregnancy should be determined case by case.

If an infant turns 15 weeks of age before the first rotavirus vaccine dose can be administered, they will not be able to receive any rotavirus vaccine doses.

BCG

Infants born to mothers who received immunomodulatory biologic agents during pregnancy must not be vaccinated with a BCG vaccine without specialist consultation (see box above).

MMR and VV

Infants aged under 12 months born to mothers who received immunomodulatory biologic agents during pregnancy should not be vaccinated with MMR or VV unless specialist consultation has been sought. Normally, it is only recommended to give MMR and VV before age 12 months if there is an increased risk of exposure, such as during an outbreak or following close contact with a case (see sections 12.5.1, 12.8 and 22.8.3) or if an infant is on an accelerated vaccination schedule prior to solid organ transplantation (see section 4.3.11).

4.3.7 Vaccination prior to planned immunosuppression

A variety of immune-mediated inflammatory diseases (IMID), across many subspecialties (eg, rheumatology, dermatology, gastroenterology etc), require treatment escalation to immunosuppressive therapy over a variable time course. Routine and additional vaccinations should be given prior to any planned immunosuppression where clinically possible.

- Complete all age-appropriate vaccinations according to the Schedule; previous doses do not need to be repeated prior to immunosuppression.
- Live viral vaccines are recommended to be administered prior to planned immunosuppression, if time permits, as they cannot be given once immunosuppression has commenced. Clinically indicated immunosuppression should not be delayed in order to give live vaccines.
- Whilst non-live vaccines can be given safely when receiving immunosuppression, the immune response is likely to be reduced.
- Administration of non-live vaccines (eg, completion of meningococcal vaccines) can resume once immunosuppression has been reduced or stopped.
- The required interval before resuming live vaccination varies with the agents given – see Table 4.1 and Table 4.2, and seek specialist advice.

For additional and accelerated recommendations for the immunisation of infants and children diagnosed with conditions requiring immunosuppression for 28 days or longer, see Table 4.3.

For infants aged under 12 months of age, seek specialist advice.

For additional recommendations for the immunisation of adults see IMAC factsheet *Immunisation for adults with immune-mediated inflammatory disease (IMID) who require immunosuppressive treatment* (available at **immune.org.nz/resources/written-resources**).

Table 4.3: Additional vaccine recommendations for children (12 months to 18 years) when diagnosed with a condition requiring immunosuppression for than 28 days or longer, or having completed immunosuppression

Refer to the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions. Children should receive the usual Schedule vaccines, including rotavirus vaccine for infants prior to planned immunosuppression.

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Ages 12 months to 18 years when diagnosed with a condition requiring immuno-suppression	PCV13	• Children aged 12–59 months, who have not yet received any PCV13 – give 2 doses of PCV13 at least 8 weeks apart[a] • Children aged 5 years to under 18 years: – give 1 dose of PCV13 even if fully vaccinated[a]
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years.[b] Revaccinate once after 5 years.
	MenACWY-D (Menactra)[b]	• If aged 12 months to under 7 years at diagnosis, give 2 doses of MenACWY-D at least 3 months apart followed by a booster dose after 3 years, then 5-yearly[c] • If aged 7 years or older give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose 5-yearly[c]
	4CMenB (Bexsero)[d]	• From age 12 to 23 months, give 2 doses 8 weeks apart followed by a booster given 12–23 months after second dose. • From age 2 years, give 2 doses 8 weeks apart. • Give booster doses 5-yearly[e]
	Hib-PRP-T (Hiberix)	• If child is aged 12–15 months, give 1 dose at age 15 months as per the Schedule • If aged 16 months to under 5 years and has not received a single Hib-PRP-T dose after age 12 months, give 1 dose • If aged 5 years or older, give 1 dose, unless fully vaccinated
	Influenza (age-appropriate vaccine)[f]	Give annually • In previously unvaccinated children age <9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year
	MMR	• 2 doses given 4 weeks apart, if time permits, to be given at least 4 weeks prior to planned immunosuppression[g]
	Varicella (VV)	• 2 doses given 4 weeks[h] apart, if time permits, and to be given at least 4 weeks prior to planned immunosuppression[h]

a. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

b. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).

c. Where possible give MenACWY-D at least 4 weeks after PCV13 (see section 4.3.3). PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required (see section 4.3.3).

d. It is recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.3).

e. Although, the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

f. Check **influenza.org.nz** for most recent influenza vaccine brands and appropriate age ranges.

g. Live viral vaccines are recommended to be administered prior to planned immunosuppression. Clinically indicated immunosuppression should not be delayed in order to give live vaccines.

h. Accelerated timing for VV differs from Table 22.1. For vaccination **after** immunosuppression, standard interval of 6 weeks would apply.

4.3.8 (Re)vaccination following immunosuppression

All vaccines on the Schedule are funded for vaccination or re-vaccination of individuals following immunosuppression. Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days. The timing and number of doses should be discussed with the individual's specialist. Ideally, vaccination should be conducted prior to any planned immunosuppression. See also the relevant disease chapters.

4.3.9 Oncology

This section provides general guidelines for vaccination during and after cancer treatment. Specific vaccination questions should be discussed with an expert paediatrician, infectious diseases physician or oncologist.

Note: The exception to these guidelines is individuals being treated with immune checkpoint inhibitors for whom vaccination may be contraindicated (see section 4.3.2).

Vaccination during cancer chemotherapy

While administration of inactivated and subunit (non-live) vaccines is safe for individuals undergoing cancer chemotherapy, their response and subsequent protection may be reduced compared with healthy individuals.

Influenza vaccination is recommended for children and adults prior to planned or when undergoing cancer chemotherapy as soon as the vaccine becomes available; there is no need to wait until three months after the individual's last treatment.[40, 41] Influenza vaccination can be administered at any time during a cancer chemotherapy cycle.[42]

In both children and adults, administration of two influenza vaccine doses a minimum of four weeks apart could improve the immune response to vaccination.[43]

Administration of live vaccines during cancer chemotherapy is absolutely contraindicated because of the risk of disseminated vaccine disease. For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

Vaccination after cancer chemotherapy

In general, booster dose(s) of a diphtheria/tetanus/pertussis-containing vaccine, and hepatitis B, polio (IPV) and pneumococcal vaccines (PCV13 followed by 23PPV) should be given, from not less than three months after cancer chemotherapy has ended (when the lymphocyte count is >1.0 × 10^9/L).

In general, administration of age-appropriate live vaccines should be delayed for at least six months after cancer chemotherapy. This interval may need to be extended according to:

- the intensity and type of therapy
- receipt of blood products or immunoglobulin (see Table A6.1 in Appendix 6)
- underlying disease.

MMR vaccination is not required post-chemotherapy for adults born prior to 1969 or who have documented evidence of measles, mumps and rubella immunity (see section 12.8.3). Adults born in 1969 or later who do not have documented evidence of immunity to measles, mumps and rubella should receive up to two documented doses of MMR, as per the usual adult catch-up Schedule, at least six months post-chemotherapy and when their lymphocyte count is >1.0 x 10^9/L.

For children aged under 18 years, see the Starship Clinical Guideline *Immunisation of children during and after cancer therapy* for age-appropriate schedules and worksheets (available at **www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy**).

For adults, see the IMAC factsheet *Immunisation for adults post-chemotherapy who are not taking immunosuppressive disease modifying drugs* (available at **immune.org.nz/resources/written-resources**).

Vaccination and radiotherapy

Individuals who are only receiving localised radiotherapy to treat a tumour or lesion can be vaccinated with subunit vaccines and live vaccines at any time prior to, during, or after radiotherapy.[44]

4.3.10 Haematopoietic stem cell transplantation

Haematopoietic stem cell transplantation (HSCT) is used to treat haematological disease, such as acute leukaemia, and some immunodeficiency syndromes, such as severe combined immunodeficiency. Transplant recipients undergo a conditioning regime to destroy their immune system and underlying disease then receive an infusion of cells to reconstitute a new immune system. The transplanted cells may be collected from bone marrow, umbilical cord blood, or peripheral blood. They may be donated by another person (called an allogeneic transplant), or may be the recipient's

own cells that have been processed to ensure they are disease free (called an autologous transplant).[45]

After HSCT, it takes months to years for the recipient's new immune system to reconstitute and become functional. However, the age of the recipient, underlying disease, conditioning regime, type of transplantation and complications such as graft versus host disease (GVHD) can affect and prolong recovery time.[45, 46]

Vaccination of individuals post-HSCT

Initially, the recipient may have temporary measurable donor-derived protection against some diseases, but their reconstituted immune system will need full (re)vaccination to provide long-term protection against vaccine-preventable diseases. Administration of subunit vaccines, such as PCV13, may be recommended as early as three months post-HSCT. Annual influenza vaccination may be recommended from six months post-HSCT. It is generally recommended to commence immunisation with live viral vaccines no less than 24 months post-HSCT and in the absence of GVHD and immunosuppressive therapy.[46, 47]

For children aged under 18 years, see the Starship Clinical Guideline *Immunisation of children during and after cancer therapy* for age-appropriate schedules and worksheets (available at **www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy**).

For adults, see the vaccination protocol provided by the person's New Zealand-based haematology clinic or the IMAC factsheet *Immunisation for adults post-haematopoietic stem cell transplantation (HSCT)* (available at **immune.org.nz/resources/written-resources**).

For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

COVID-19 vaccine

Individuals aged from 5 years who have received HSCT since receiving their first COVID-19 vaccination course can be revaccinated with two or three primary doses and a booster, as age appropriate.

A third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate), to be given at least 8 weeks after dose two, is available for individuals aged from 5 years who have received HSCT in the previous 24 months or with ongoing immunosuppression or graft-versus-host disease for more than 24 months (see section 5.5.8 for details).

A booster dose of mRNA-CV (30 µg), given at least three calendar months after completion of the primary course, is recommended for recipients of HSCT, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions, and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

4.3.11 Solid organ transplantation

Vaccination of individuals pre-/post solid organ transplantation

In addition to the usual Schedule vaccines, individuals who are pre-/post-solid organ transplantation are eligible to receive additional funded vaccines. Ideally, vaccination should be conducted prior to any planned immunosuppression.[48] An accelerated immunisation schedule is provided for infants with congenital biliary or renal conditions requiring transplant (see Table 4.4).

Additional funded vaccines may include hepatitis A vaccine; hepatitis B vaccine if the person was not previously vaccinated or does not have evidence of immunity (see section 9.5.4); *Haemophilus influenzae* type b (Hib-PRP), influenza, pneumococcal, meningococcal and varicella vaccines.

COVID-19 vaccine

A third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate), to be given at least 8 weeks after dose two, is available for individuals aged from 5 years receiving or having received immunosuppressive therapy in the previous 6 months following a solid organ transplant (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for recipients of a solid organ transplant, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions, and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

Based on clinical discretion, if all scheduled doses have been completed prior to commencement of chemotherapy or solid organ transplant, a single further dose of mRNA-CV can be given from the age of 5 years.

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

Live vaccines – caution

Live vaccines should also be administered at least four weeks before a predicted transplant. Administration of live vaccines (MMR and VV) is generally contraindicated post-transplantation due to immunosuppression. However, on a case-by-case basis with appropriate follow-up in place, a specialist may recommend that VV is administered less than four weeks before a predicted transplant or to a post-transplantation paediatric patient.[31] With specialist input MMR may also be considered in clinically well patients at least 1 year after solid organ transplantation on low level immunosuppression.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.4 for precautions and contraindications for the administration of live vaccines (MMR and VV), eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines, and recommendations when an individual who is immunosuppressed/post-solid organ transplantation is a contact of a measles or chickenpox case.

It is recommended to follow an accelerated schedule of vaccinations for infants and children likely to be listed for solid organ transplantation, see Table 4.4 for infant recommendations.

> For pre-/post-solid organ transplantation advice for adult immunisation, see the IMAC factsheet *Immunisation for adults pre-/post-solid organ transplantation (excluding kidney transplantation)* or *Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant* (both available at **immune.org.nz/resources/written-resources**).

For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

Table 4.4: Accelerated vaccination schedule with additional vaccine recommendations for infants likely to require liver or kidney transplantation

Funded vaccines are in shaded rows. Refer to the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions.

Age	Vaccination	Comments
Do not start earlier than age 6 weeks.		
6 weeks	RV1 (Rotarix) PCV13[a] (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	PCV13 replaces PCV10 (Synflorix)
2 months	MenC (NeisVac-C) 4CMenB (Bexsero)[b]	If MenACWY-T (Nimenrix) not given
	MenACWY-T (Nimenrix)[c]	Not funded, need to be prescribed and purchased
3 months	RV1 PCV13[a] (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	PCV13 replaces PCV10
4 months	MenC (NeisVac-C) 4CMenB (Bexsero)[b]	If MenACWY-T (Nimenrix) not given
	MenACWY-T (Nimenrix)[b]	Not funded; need to be prescribed and purchased
5 months	PCV13[a] (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	PCV13 replaces PCV10

Continued overleaf

6 months	Influenza (junior formulation)[d]	Give two doses 4 weeks apart in the first year receiving influenza vaccine, and one dose in subsequent years Give annually
	MMR (Priorix)[e]	MMR should not be given less than 4 weeks before the predicted transplant
	HepA (Havrix Junior)	
	Check Anti-HBs serology	If anti-HBs is negative, give a further three doses of monovalent HepB vaccine (Engerix-B 20 µg) 4 weeks apart
9 months	Varicella (Varilrix)[e,f]	In general, VV should not be given less than 4 weeks before the predicted transplant but may be given closer at the discretion of the specialist
	MenACWY-D (Menactra)[g]	If MenACWY-T (Nimenrix) not given previously
12 months	PCV13 (Prevenar 13)[a]	PCV13 replaces PCV10
	MMR[e]	MMR should not be given less than 4 weeks before the predicted transplant
	Varicella (Varivax)[e]	In general, VV should not be given less than 4 weeks before the predicted transplant but may be given closer at the discretion of the specialist
	4CMenB (Bexsero)[b]	At least 6 months after second dose, give 1 dose to those who received two primary doses in infancy, followed by booster dose 5-yearly If previously unvaccinated, give 2 doses 8 weeks apart, then a booster 12–23 months after dose two followed by booster doses given 5-yearly
13 months	DTaP-IPV-HepB/Hib (Infanrix-Hexa)	
	MMR (Priorix)	MMR should not be given less than 4 weeks before the predicted transplant
	MenACWY-D[g]	Give a booster after 3 years, then 5-yearly
	HepA (Havrix Junior)	
2 years	23PPV (Pneumovax 23)	Give one dose Revaccinate once after 5 years
4 years	DTaP-IPV (Infanrix-IPV)	
From age 9 years	HPV9 (Gardasil 9)	Give 3 doses at 0, 2 and 6 months
11 years	Tdap (Boostrix)	

Continued overleaf

6 months post-transplant	HepB (Engerix-B), plus anti-HBs serology before and 4 weeks after the initial HepB series	Give 3 doses of monovalent HepB vaccine (Engerix-B 20 ug) If there is an inadequate immune response to the initial 3-dose HepB series, give a further 3 doses
	23PPV (Pneumovax 23)	If child is at least 24 months old and dose not given pre-transplant Revaccinate once after 5 years
	Influenza (age appropriate vaccine)[d]	For infants and children aged 6 months to under 9 years, give 2 doses 4 weeks apart in the first year of receiving the influenza vaccine, and 1 dose in subsequent years Give annually
12 months post-transplant	Resume the usual Schedule, except live vaccines	Live vaccines[h] are contraindicated post-transplantation
Household contacts of transplant recipients	National Immunisation Schedule vaccines	Immune-competent siblings and other household contacts may receive all the Schedule vaccines and should be fully vaccinated for their age.
	Influenza (with age-appropriate vaccine)[d]	Recommended annually for all family members[i].
	Varicella	Two doses of VV are funded for susceptible household contacts of transplant recipients.

a. A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, replaces PCV10 on the usual Schedule.

b. Recommended to administer prophylaxic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (section 13.7.3).

c. As MenACWY-D (Menactra) is only licensed from age 9 months, MenACWY-T (Nimenrix) can be used to give broader serotype protection to infants than MenC (NeisVac-C), but is not funded.

d. Check **influenza.org.nz** website for most recent updates on funded influenza vaccine and appropriate age ranges.

e. MMR and VV can be given on the same day; if not, seek 4 weeks of separation between them.

f. Only Varilrix is available from hospital at ages 9 to <12 months; Varivax is not licensed under the age of 12 months.

g. Where possible give MenACWY-D at least 4 weeks after PCV13 (see section 4.3.3). PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

h. On a case-by-case basis, a specialist may recommend that VV is administered to their post-transplantation paediatric patient.

i. Funded for all children aged 3–12 years until 31 December 2022 and for individuals aged from 55 years of Māori and Pacific ethnicity.

4.3.12 Functional asplenia, hyposplenia and pre-/post-splenectomy

The spleen has an important role in initiating the immune response to encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b (Hib), and removing them from the circulatory system.

There are three main reasons why an individual may not have a fully functioning spleen:

- congenital disorders (eg, asplenia, hyposplenia or polysplenia associated with a congenital syndrome)
- disease (eg, Coeliac disease, acute leukaemia)
- surgical removal (eg, trauma, autoimmune haemolytic anaemia).

Individuals with reduced spleen function or an absent spleen are at increased risk of overwhelming infection by encapsulated bacteria.[49] This is a medical emergency and carries a high mortality rate. The risk of overwhelming infection after splenectomy is more than 50 times higher than the risk in the general population. Opinion is divided on whether this level of risk is life-long or decreases over time after the splenectomy.

Vaccination of individuals with asplenia or hyposplenia or pre-/post-splenectomy

No vaccines are contraindicated for individuals with functional or anatomical asplenia (pre-/post-splenectomy), and they are eligible for additional funded influenza, Hib, pneumococcal and meningococcal vaccines. Providers should also ensure that they are up to date with Schedule vaccines, including Tdap and MMR.

When a splenectomy is planned, individuals should ideally complete the vaccinations they require up to two weeks prior to their surgery. If this is not possible, preferably administer vaccines until 14 days before the splenectomy and continue from seven days after the splenectomy, or prior to discharge from hospital, if sooner. When the splenectomy is unexpected, for example due to trauma, commence vaccination from seven days after surgery or prior to discharge from hospital. In all cases a vaccination plan must be formulated and communicated to the GP for completion (see Table 4.5).

Individuals with reduced spleen function (eg, because of disease or partial splenectomy), are recommended (but not funded) to receive pneumococcal and meningococcal vaccines and annual influenza vaccination.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.4 for eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines.

Table 4.5 summarises the additional vaccine recommendations and schedules for infants and children aged under 18 years with functional or anatomical asplenia. The funded vaccines are shown in shaded rows.

> For adults, see the IMAC factsheet *Immunisation for adults pre-/post-splenectomy or with functional asplenia* (available at **immune.org.nz/resources/written-resources**).

Table 4.5: Additional vaccine recommendations for infants and children aged under 18 years with functional or anatomical asplenia

Funded vaccines are in the shaded rows.
Refer to the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions.

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Under 12 months when diagnosed with functional asplenia or pre- or post-splenectomy[a]	PCV13 (Prevenar 13)[b]	Give PCV13 [b] at ages 6 weeks, and 3, 5 and 12–15 months or an age-appropriate catch-up schedule: • **If aged under 7 months**, replace PCV10 with PCV13 from the next visit. Give PCV13 [b] at ages 6 weeks, 3 months, 5 months and 12 months • For those who **have not been immunised** age 7–11 months: give 2 doses of PCV13 (8 weeks apart) and a further dose at least 8 weeks later, from age 12 months • For children aged 7–11 months **who have completed** a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) at least 8 weeks later, from age 12 months
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years • Revaccinate once after 5 years
	MenC (NeisVac-C) and MenACWY-D (Menactra)[c]	• If aged under 9 months, give 2 doses of MenC 8 weeks apart, followed by MenACWY-D [c] at ages 9 and 13 months. Administer one MenACWY-D booster dose after 3 years, then 5-yearly. See alternative unfunded MenACWY-T (Nimenrix) option below • If aged 9–11 months, give 2 doses of MenACWY-D[c] at least 3 months apart, followed by a booster dose after 3 years, then 5-yearly
	4CMenB (Bexsero)[d]	• Give two doses at least 8 weeks apart followed by a booster dose at least 6 months later, from age 12 months • Give a booster dose 5-yearly.
	MenACWY-T (Nimenrix)	Licensed from 6 weeks; can be used in place of MenC doses to offer broader protection. Not funded; needs to be prescribed and purchased. Give 2 doses at least 8 weeks apart. A booster dose of MenACWY-D[c] (funded) or MenACWY-T (unfunded) is recommended at age 12 months or older
	Influenza (junior formulation)[e]	Annual vaccination from age 6 months. • In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year

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Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Aged 12 months to under 18 years when diagnosed with functional asplenia or pre- or post-splenectomy[a]	PCV13	• Children aged 12–59 months, who have not yet received any PCV13: – give 2 doses of PCV13 at least 8 weeks apart[f] • Children aged 5 years to under 18 years: – give 1 dose of PCV13 even if fully vaccinated[g]
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years. Revaccinate once after 5 years.
	MenACWY-D (Menactra)[c]	• If aged 12 months to under 7 years at diagnosis, give 2 doses of MenACWY-D at least 3 months apart followed by a booster dose after 3 years, then 5-yearly[c] • If aged 7 years or older give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose 5-yearly[c]
	4CMenB (Bexsero)[d]	• From age 12 to 23 months, give 2 doses 8 weeks apart followed by a booster given 12–23 months after second dose. • From age 2 years, give 2 doses 8 weeks apart. • Give booster doses 5-yearly[h].
	Hib-PRP-T (Hiberix)	• If child is aged 12–15 months, give 1 dose at age 15 months as per the Schedule • If aged 16 months to under 5 years and has not received a single Hib-PRP-T dose after age 12 months, give 1 dose • If aged 5 years or older, give 1 dose, unless fully vaccinated
	Influenza (age appropriate vaccine)[e]	Give annually • In previously unvaccinated children age <9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year

a. Where possible, the vaccines should be administered at least 14 days before elective splenectomy and continue from 7 days after the splenectomy. For emergency splenectomy, the vaccines should be administered from 7 days post-operatively or prior to discharge from hospital.

b. A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, replaces PCV10 on the usual Schedule.

c. Where possible give MenACWY-D at least 4 weeks after PCV13 (see section 4.3.3). PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

d. It is recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.3).

e. Check **influenza.org.nz** for most recent influenza vaccine brands and appropriate age ranges.

f. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

g. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).

h. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

4.3.13 HIV infection

Human immunodeficiency virus (HIV) infects CD4+ T cells leading to a progressive decline in CD4 cell count, increasing immunodeficiency and vulnerability to infection, and suboptimal responses to vaccines.

The efficacy of any vaccine may be reduced in HIV-positive individuals, and antibody levels within these individuals may wane faster than in individuals who are HIV-negative. Although antiretroviral therapy may improve immune responses, it is unlikely these individuals will achieve the levels of antibodies seen in individuals who are HIV-negative. Serological testing and the need for additional doses (eg, HepB: see section 9.5.7 and Table 9.6) should be discussed with the individual's specialist.

Vaccination of individuals with HIV infection

In addition to the usual Schedule vaccines, individuals who are HIV-positive to receive additional funded vaccines including Hib, pneumococcal, and meningococcal vaccines. Individuals who are HIV-positive are also eligible to receive funded influenza vaccination.

COVID-19 vaccine

Individuals aged from 5 years with active HIV infection or AIDS (with CD4 count <200 cells per µl) are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV, given at least three calendar months after completion of the primary course, is recommended for individuals living with HIV infection, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is available for individuals with immunocompromising conditions, and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

Live vaccines – caution

It is recommended that infants who are HIV-positive receive rotavirus vaccine as per the Schedule. Administration of BCG vaccination is contraindicated for all HIV-positive individuals regardless of their CD4+ percentage/count.[50]

MMR and VV may be administered as per the Schedule to:

- children aged 1–13 years who have a recent CD4+ lymphocyte percentage of ≥15 percent
- children aged 14 years to under 18 years who have a recent CD4+ count of ≥200 cells/ml
- MMR and VV can be administered as per the Schedule to adults aged 18 years or older who have a recent CD4+ lymphocyte count of ≥200 cells/mm^3.[49]

Live zoster vaccine has been discontinued. Individuals from age 18 years with HIV infection are recommended two doses (unfunded) of recombinant zoster vaccine (rZV, Shingrix). See section 23.5.1.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.4 for eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines.

Table 4.6 (for children aged under 5 years when diagnosed) and Table 4.7 (for children aged 5 to under 18 years) summarise additional vaccine recommendations and schedules for HIV-positive children. The funded vaccines are shown in shade rows.

For adults, see the IMAC factsheet *Immunisation for adults with HIV infection* (available at **immune.org.nz/resources/written-resources**).

Table 4.6: Additional vaccine recommendations for children aged under 5 years when diagnosed with HIV

Note: HIV-positive children should receive the usual Schedule vaccines, including rotavirus vaccine for infants; BCG should not be given; MMR and VV may be administered as per the recommendations below. **Funded vaccines are in shaded rows.** Refer to the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions.

Relevant age	Vaccine (trade name)	Recommended vaccine schedule
Infants aged under 12 months when diagnosed	PCV13 (Prevenar 13)[a]	Give PCV13[a] at ages 6 weeks and 3, 5 and 12–15 months or an age-appropriate catch-up schedule: • **If aged under 7 months**, replace PCV10 with PCV13 from the next visit. Give PCV13[a] at ages 6 weeks, 3 months, 5 months and 12 months • For those **who have not been immunised** age 7–11 months: give two doses of PCV13 (8 weeks apart) and a further dose at least 8 weeks later, from age 12 months • For children aged 7–11 months **who have completed** a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) at least 8 weeks later, from age 12 months
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give one dose at least 8 weeks after the last PCV13 dose, from age 2 years Revaccinate once after 5 years

Continued overleaf

Relevant age	Vaccine (trade name)	Recommended vaccine schedule
	MenC (NeisVac-C) and MenACWY-D (Menactra)[b]	• If aged under 9 months, give 2 doses of MenC 8 weeks apart, followed by MenACWY-D at ages 9 and 13 months[b] Administer one MenACWY-D booster dose after 3 years, then 5-yearly See alternative unfunded MenACWY-T (Nimenrix) option below • If aged 9–11 months, give 2 doses of MenACWY-D at least 3 months apart, followed by a booster dose after 3 years, then 5-yearly
	4CMenB (Bexsero)[c]	Give 2 doses at least 8 weeks apart followed by a booster dose at least 6 months later, from age 12 months. Give further booster doses 5-yearly.
	MenACWY-T (Nimenrix)	Licensed from age 6 weeks, can be used in place of MenC doses. Not funded; needs to be prescribed and purchased. Give 2 doses at least 8 weeks apart A booster dose of MenACWY-D[b] (funded) or MenACWY-T (unfunded) is recommended at age 12 months or older
	Influenza (junior formulation)[d]	Annual vaccination from age 6 months In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year
Children aged 12 months to under 5 years when diagnosed	PCV13	• Children aged 12–59 months, who have not yet received any PCV13, give 2 doses of PCV13 at least 8 weeks apart[e] • Children aged 5 years to under 18 years, give 1 dose of PCV13 even if fully vaccinated[f]
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years Revaccinate once after 5 years
	Influenza (age appropriate vaccine) [d]	Give annually In previously unvaccinated children, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.
	MMR[g] (Priorix)	If CD4+ lymphocyte percentage is ≥15%: • give the first MMR dose at age 12 months, followed by the 2nd dose 4 weeks later
	Varicella[g] (Varivax)	If CD4+ lymphocyte percentage is ≥15%: • give 2 doses (starting 4 weeks after the 2nd MMR), at least 3 months apart
	MenACWY-D[b] (Menactra)	Give 2 doses of MenACWY-D at least 3 months apart followed by a booster dose after 3 years, then 5-yearly[b]
	4CMenB (Bexsero)[c]	• From age 12 to 23 months, give 2 doses 8 weeks apart followed by a booster given 12–23 months after second dose. • From age 2 years, give 2 doses 8 weeks apart. • Give booster doses 5-yearly[h].

a. A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, replaces PCV10 on the usual Schedule.

b. Where possible give MenACWY-D at least 4 weeks after PCV13 (see section 4.3.3). PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

c. Recommended to administer prophylaxic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.3)

d. Check **influenza.org.nz** for most recent influenza vaccine brands and appropriate age ranges.

e. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

f. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).

g. Only a single live vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.

h. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

Table 4.7: Additional vaccine recommendations for children aged 5 to under 18 years when diagnosed with HIV

Note: HIV-positive children should receive the usual Schedule vaccines, MMR and varicella vaccines may be administered as per the recommendations below. **Funded vaccines are in shaded rows.**

Refer to the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions.

Vaccine (trade name)	Recommended vaccine schedule
HPV9 (Gardasil 9)[a]	From age 9 years, give 3 doses of HPV at 0, 2 and 6 months[a]
PCV13 (Prevenar 13)[b]	For children who have not previously received PCV13, give 1 dose of PCV13[b]
23PPV (Pneumovax 23)	Give 1 dose of 23PPV at least 8 weeks after the PCV13 dose. Revaccinate once with 23PPV, 5 years after the first 23PPV
MenACWY-D (Menactra)[c]	• If aged 5 years to under 7 years give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose after 3 years and then 5-yearly[c] • If aged 7 years or older give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose followed by a booster dose 5-yearly[c]
4CMenB (Bexsero)	Give 2 doses 8 weeks apart followed by a booster[e] dose 5-yearly
MMR[d] (Priorix)	If aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 2 doses of MMR at least 4 weeks apart
Varicella[d] (Varivax)	If no history of varicella disease or vaccination, and • if aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or • if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm^3: – give 2 doses (starting 4 weeks after 2nd MMR) at least 3 months apart
Influenza (Afluria Quad)	• If aged under 9 years give 2 doses 4 weeks apart in the first year receiving influenza vaccine (both doses are funded), and 1 dose in subsequent years • If aged 9 years or older give 1 dose • Give annually

Continued overleaf

Vaccine (trade name)	Recommended vaccine schedule
COVID-19 (Comirnaty)	• Two doses given 8 weeks apart (minimum 21 days apart) from age 5–11 years (mRNA-CV 10ug) or from age 12 years (mRNA-CV 30 µg) • Booster dose can be offered (ages 12–15 years off-label, requires prescription).

a. HPV9 is approved for use from age 9 years.

b. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 1 year before administering PCV13.

c. Give MenACWY-D at least 4 weeks after PCV13 (see section 13.4.4). PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

d. Only a single live vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.

e. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

Source: Starship Child Health

4.4 Chronic kidney disease

Individuals immunised during the early stages of chronic kidney disease (CKD) generally respond to vaccination. However, the immune system response to vaccination decreases with advancing kidney disease.[51, 52] Cases of children developing a disease for which they have serological evidence of immunity have been reported.[52]

Individuals with nephrotic syndrome, kidney failure or end-stage kidney disease (CKD stages 4–5) have an increased risk of peritonitis and/or sepsis caused by encapsulated bacteria, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and *Neisseria meningitidis*.[51, 52, 53] Individuals on haemodialysis have an increased risk of exposure to hepatitis B virus. Adults with CKD also have an increased risk of zoster.[54]

Vaccination of individuals with chronic kidney disease

Individuals with CKD who are not receiving immunosuppressive therapy to manage their condition can receive vaccination as per the usual Immunisation Schedule. In addition to the usual Immunisation Schedule vaccines, individuals with CKD may be eligible to receive additional funded vaccines. These should be given as soon as the individual meets the eligibility criteria (eg, CKD stages 4–5: pre-dialysis, on dialysis, pre-kidney transplant, post-kidney transplant).

Additional funded vaccines may include hepatitis A, hepatitis B, *Haemophilus influenzae* type b (Hib), pneumococcal, and meningococcal vaccines. Individuals with CKD are also eligible to receive funded influenza vaccination.

Live vaccines – caution

Administration of live vaccines (MMR and VV or ZV) are generally contraindicated for individuals who are immunosuppressed because of the risk of disseminated vaccine disease. However, individuals with CKD who are considered to have minimal immunosuppression may be able to receive VV.[34]

Live zoster vaccine has been discontinued. Two doses of recombinant zoster vaccine (rZV, Shingrix) are recommended for adults with CKD stages 4–5 from age 18 years (unfunded).

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.4 for eligibility and recommendations for influenza, *Haemophilus influenzae* type b (Hib), pneumococcal and meningococcal vaccines.

There is no relationship between vaccination and deterioration of renal function or a reduction in the efficacy of dialysis.[52]

For children aged under 18 years, see the Starship Clinical Guideline *Renal vaccination record for Starship paediatric CKD* (available at **www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd**).

For adults, see the IMAC factsheet *Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant* (available at **immune.org.nz/resources/written-resources**).

COVID-19

Individuals from 5 years of age receiving long term haemodialysis or peritoneal dialysis are eligible to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age appropriate) to be given at least 8 weeks after the second dose (see section 5.5.8 for details).

A booster dose of mRNA-CV (30 µg), given at least three calendar months after completion of the primary course, is recommended for individuals with chronic kidney disease, and in particular those eligible for a third primary dose. A booster dose given earlier than six months to individuals aged 16–17 years or given to anyone aged 12–15 years is considered an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981) (see section 5.5.10).

A second booster dose given six months after the previous booster dose is recommended for individuals with chronic kidney disease and is particularly recommended for individuals aged from 16 years who were eligible for a third primary dose (ie, a fifth dose; see section 5.5.10).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be given from age 18 years or age 12–17 years (off-label, requires a prescription), if not contraindicated: in this situation it is recommended to seek advice from IMAC.

4.5 Chronic liver disease

Chronic liver disease in infants and children may present as part of a congenital syndrome. They may have other conditions (eg, infants with biliary atresia may also have a non-functioning spleen) and eligibility for additional funded vaccines.

4.5.1 Vaccination of individuals with chronic liver disease

Individuals with chronic liver disease who are not receiving immunosuppressive therapy to manage their condition can receive vaccination as per the usual Schedule.

In addition to the usual Schedule vaccines, infants and children with chronic liver disease are eligible to receive funded hepatitis A vaccination from 12 months of age (see section 8.5.1). However, if they are likely to require a liver transplant an accelerated vaccination schedule may be advised as per Table 4.4. The aim of the accelerated schedule is to maximise protection against vaccine-preventable diseases and to deliver live vaccines prior to transplantation and immunosuppression. Prior to transplantation, hepatitis A vaccine could be administered from as early as 7 months of age. Additional pre-transplantation funded vaccines include influenza, pneumococcal, meningococcal, and varicella vaccines (see section 4.3.1).

It is recommended that adults with chronic liver disease receive influenza vaccination annually but this is not currently funded. Adults who are likely to require a liver transplant are eligible for additional funded vaccines, including hepatitis A vaccine; hepatitis B vaccine, if the individual was not previously vaccinated or does not have evidence of immunity; *Haemophilus influenzae* type b (Hib), influenza, pneumococcal, meningococcal and varicella vaccines (see section 4.3.11).

4.6 Other special groups

It is recommended that all individuals receive vaccination as per the usual Schedule except when pre-vaccination screening identifies a contraindication for a specific vaccine (see section 2.1.4). Additional vaccines may be recommended (but are not always funded) for individuals with some conditions or in some circumstances not previously discussed in this chapter.

Table 4.8 lists other special groups and recommended additional vaccines. Funded vaccines are shown in shaded rows.

Table 4.8: Additional vaccine recommendations for other special groups

Funded vaccines are in shaded rows. See the table footnotes for more information when indicated. Vaccinators are advised to check the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to funding decisions.

Special group	Recommended vaccines
Individuals: • with cerebrospinal fluid (CSF) leak • chronic pulmonary disease, including asthma treated with high-dose corticosteroid therapy and cystic fibrosis • receiving corticosteroid therapy for more than two weeks and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater • diabetes • intracranial shunt • receiving radiotherapy • living in boarding schools, hostels, university halls of residence, or other close quarters[a]	Children, aged under 5 years • PCV13, 23PPV • Influenza, annually Children aged 5 years to under 18 years, (including for those who received four doses of PCV10) • PCV13, 23PPV • Influenza, annually MenACWY[a] MMR (if susceptible)
	4CMenB Hepatitis B (if susceptible) VV (if susceptible) Influenza, annually
• with cochlear implants	*Haemophilus influenzae* type b (Hib-PRP-T) Influenza, annually Pneumococcal (PCV13, 23PPV)
• living in correctional facilities[a]	MenACWY[a] MMR (if susceptible)
	4CMenB Hepatitis B (if susceptible) Influenza, annually
• with error of metabolism at risk of major metabolic decompensation	Influenza, annually Varicella (VV)
• with rheumatic heart disease	Influenza, annually
• who are case contacts of an individual with hepatitis A	Hepatitis A (if susceptible)
• with hepatitis B infection	Hepatitis A (if susceptible)
• who are household or sexual contacts of an individual with hepatitis B	Hepatitis B (if susceptible)
• with hepatitis C infection	Hepatitis A (if susceptible) Hepatitis B (if susceptible)
• with a needle-stick injury	Hepatitis B (if susceptible)

Continued overleaf

Special group	Recommended vaccines
• who have had non-consensual sexual intercourse	Hepatitis B (if susceptible)
Intravenous drug users	Hepatitis A (if susceptible) Hepatitis B (if susceptible) Influenza, annually
Men who have sex with men	HPV[b] Hepatitis A (if susceptible) Hepatitis B (if susceptible)
Case contacts of an individual with meningococcal disease of any group	MenACWY[c] 4CMenB
Individuals who have previously had meningococcal disease of any group	MenACWY[c] 4CMenB
Children at risk of exposure to tuberculosis	BCG vaccination for children aged under 5 years who: • will be living in a house or family/whānau with a person with either current TB or a history of TB • have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥40 per 100,000 • during their first five years will be living for three months or longer in a country with a TB rate ≥40 per 100,000. See section 21.5.2

a. One dose of MenACWY-D (Menactra) is funded for individuals aged 13–25 years inclusively who are entering within the next 3 months, or who are in their first year of living in a boarding school hostel, tertiary education halls of residence, military barrack, or prison. Both MenACWY-D (Menactra) and MenACWY-T (Nimenrix) are available but unfunded for individuals who do not meet these criteria.

b. Three doses are funded for those aged 26 years or under.

c. As age-appropriate: those aged under 9 months can either receive MenC (NeisVac, funded) or MenACWY-T (Nimenrix, unfunded).

4.7 Immigrants and refugees

Adults and children who enter New Zealand as refugees or immigrants will need an assessment of their **documented** vaccination status and an appropriate planned catch-up programme. The programme may require modification based on **documented** doses: only clearly documented doses should be considered as given. If there is no documented vaccination history, plan the catch-up schedule assuming the vaccines have not been given, see Appendix 2 for catch-up schedules.

Immunisation schedules vary from country to country. Check all migrant and former refugee children immunisation records to ensure they are up to date with the New

Zealand Schedule, in particularly ensure they have received MMR as opposed to a measles-rubella vaccine only.

For assistance with planning catch-up schedules, contact your local immunisation coordinator; or call IMAC on 0800 IMMUNE/0800 466 863, or discuss with an experienced colleague.

All children aged under 18 years are eligible to receive Schedule vaccines and Well Child Tamariki Ora services regardless of their immigration and citizenship status, and providers can claim the immunisation benefit for administering the vaccines.

Adult refugees aged 18 years or older are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines. Non-residents who were aged under 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. Other adults aged 18 years or older must meet all the applicable eligibility criteria described in the *Health and Disability Services Eligibility Direction 2011* to receive funded healthcare services, including Schedule vaccines. For more information about eligibility for publicly funded services, see the Ministry of Health website (**www.health.govt.nz/eligibility**).

See also the *Recommendations for Comprehensive Post-Arrival Health Assessment for People from Refugee-like Backgrounds (2016 edition)*, available on the Australasian Society for Infectious Diseases website (**www.asid.net.au/resources/clinical-guidelines**).

Tuberculosis

In New Zealand, BCG vaccination is recommended and funded for infants and children aged under 5 years at increased risk of tuberculosis (TB). For further details, see section 21.5.2 and the Ministry of Health *Guidelines for Tuberculosis Control in New Zealand, 2019* (available at **www.health.govt.nz/publication/guidelines-tuberculosis-control-new-zealand-2019**).

Quota refugees are screened for active TB prior to arrival in New Zealand. If they are found to have active TB, their arrival is delayed until they are treated. The requirement for active TB screening of visitors and immigrants to New Zealand varies, dependent on the country they are coming from and/or how long they intend to stay in New Zealand.[55] In New Zealand over 2010–2016, the highest number of new TB cases were in people born overseas followed by people living with a person born overseas. Over 2012–2016, the average time between arrival in New Zealand and a new diagnosis of TB was around five years.[56] See section 21.3.2 for risk factors and for countries with high incidence of TB.

Medical practitioners and laboratories are required to notify the Medical Officer of Health of suspected or confirmed cases of active TB. A person who has, or is suspected to have, active TB is entitled to the same level of funded health services as New Zealand citizens can expect.[55]

Hepatitis B

If a member of a refugee or immigrant family is found to be a hepatitis B carrier, it is recommended that all the family be screened, and vaccination offered to all those who are non-immune. Even if no one in the family is a hepatitis B carrier, it is recommended that all children aged under 18 years be vaccinated against hepatitis B. See chapter 9 for more information and Appendix 2 for catch-up schedules.

Varicella

Individuals who have grown up in the tropics are less likely to have had chickenpox in childhood and may be non-immune as adolescents and adults. Adult chickenpox can be severe, and maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 22.4). If there is no history of chickenpox, VV should be offered (although it is currently not funded).

COVID-19

All individuals aged from 5 years living in New Zealand are eligible for COVID-19 vaccination (age-appropriate mRNA-CV [10 µg or 30 µg], or adjuvanted rCV from age 12 years), regardless of health and disability services eligibility. See section 5.5.7 for timing of COVID-19 vaccination following prior COVID-19 infection.
For information about up to date COVID-19 vaccination in relation to documented partial immunisation with different vaccines given elsewhere see **www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/my-covid-record-proof-vaccination-status/covid-19-overseas-vaccinations-and-my-vaccine-pass**

4.8 Occupation-related vaccination

Certain occupations result in increased risk of contracting some vaccine-preventable diseases. Some infected workers, particularly health care workers and those working in early childhood education services, may transmit infections such as influenza, rubella, measles, mumps, varicella and pertussis to susceptible contacts, with the potential for serious outcomes.

Where workers are at significant occupational risk of acquiring or transmitting a vaccine-preventable disease, the employer should implement a comprehensive risk-based occupational vaccination programme, including vaccination policies, staff vaccination records, information about the relevant vaccine-preventable diseases and the management of vaccine refusal. Employers should take all reasonably practicable steps to encourage workers to be immunised as appropriate for the workplace environment and tasks. For information on what is required as evidence of immunity against vaccine preventable diseases, see the IMAC factsheet *Occupation related immunisation* (available at **immune.org.nz/resources/written-resources**).

The vaccines in Table 4.9 are recommended for certain occupational groups. In addition to the vaccines listed here, all adults should be up to date with age-

appropriate Schedule vaccines (see section A2.3 in Appendix 2 for catch-up vaccination advice for adults aged 18 years or older) and includes COVID-19 vaccines.

If a non-immune individual is exposed to a vaccine-preventable disease, post-exposure prophylaxis and control measures should be administered where indicated (see the relevant disease chapters and in the *Communicable Disease Control Manual,* available at **health.govt.nz/publication/communicable-disease-control-manual**).

Table 4.9: Recommended vaccines, by occupational group

Occupation	Recommended vaccines
Workers in health care settings	
Health care staff who work with patients or are working in clinical areas where patient care is being administered. For example, medical staff, nursing staff, lead maternity carers, radiography staff, dentists, other health professional staff and students, and allied staff in health care settings, such as cleaning and catering staff.	Tdap – at least every 10 years MMR Varicella Hepatitis B Influenza, annually COVID-19
Carers	
Health care assistants, long-term facility carers and nursing home staff	Tdap – at least every 10 years MMR Varicella Hepatitis B Influenza, annually COVID-19
Individuals who work with children	
Early childhood education services staff	Tdap – at least every 10 years IPV MMR Varicella Hepatitis A Hepatitis B Influenza, annually COVID-19
Other individuals working with children, including: • correctional staff working where infants/children live with mothers • school teachers (including student teachers) • outside school hours carers • child counselling services workers • youth services workers	Tdap – at least every 10 years IPV MMR Varicella Influenza, annually COVID-19

Continued overleaf

Occupation	Recommended vaccines
Emergency and essential service workers	
Police and emergency workers	Tdap – at least every 10 years IPV MMR Varicella Hepatitis B Influenza, annually COVID-19
Armed forces personnel	Tdap – at least every 10 years IPV MMR Varicella Hepatitis A (if deployed to high-risk countries) Hepatitis B Influenza, annually COVID-19 MenACWY[a] (if living in close quarters and/or deployed to high-risk countries) 4CMenB (if living in close quarters) Yellow fever, rabies, typhoid, Japanese encephalitis (as appropriate, if deployed to high-risk countries)
Staff of correctional facilities	Tdap – at least every 10 years IPV MMR Varicella Hepatitis B Influenza, annually COVID-19
Staff of immigration/refugee centres	Tdap – at least every 10 years IPV MMR Varicella Hepatitis B Influenza, annually COVID-19
Border staff and those working in managed quarantine facilities (eg, cleaners, security staff, custom and border officials, hotel workers, airline staff, port authorities, police, defence force staff and health professionals)	Influenza, annually MMR COVID-19

Continued overleaf

Occupation	Recommended vaccines
Individuals who work with animals	
Veterinarians, veterinary students and veterinary nurses	Tdap IPV MMR Influenza, annually
Zoo staff who work with primates	Tdap IPV MMR Hepatitis A Influenza, annually
Poultry workers and others handling poultry, including those who may be involved in culling during an outbreak of avian influenza, and swine industry workers	Tdap IPV MMR Influenza, annually
Individuals exposed to human tissue, blood, body fluids or sewage	
Laboratory staff	Tdap MMR Varicella Hepatitis A (if exposed to faeces) Hepatitis B Influenza, annually MenACWY and 4CMenB (if regularly working with *Neisseria meningitidis* cultures) IPV (10-yearly booster doses if handling faecal samples from those coming from high-risk countries) COVID-19
Workers who perform skin penetration procedures (eg, tattooists, body-piercers) Funeral workers, embalmers and other workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes	Tdap IPV Hepatitis B
Sewage workers, plumbers or other workers in regular contact with untreated sewage	Tdap IPV MMR Hepatitis A Hepatitis B
Sex workers	Tdap IPV MMR Hepatitis B HPV

a. One dose of MenACWY-D (Menactra) is funded for individuals aged 13–25 years inclusively who are entering within the next 3 months, or who are in their first year of living in a boarding school hostel, tertiary education halls of residence, military barracks, or prison.

4.9 Travel

All travellers should be encouraged to consider vaccination requirements well in advance of overseas travel, including those who travel frequently for work or to visit family. It is recommended that they are up to date with age-appropriate Schedule vaccines (see Appendix 2 for advice on planning catch-up vaccination) and receive current information on overseas travel requirements (eg, COVID-19, typhoid, yellow fever, rabies, Japanese encephalitis vaccination).

Travellers can seek advice from a primary care practice with expertise in travel medicine or a specialist travel medicine clinic. Information is also available on the New Zealand Safe Travel (**safetravel.govt.nz**) and WHO (**who.int/travel-advice**) websites.

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5 Coronavirus disease (COVID-19)

Key information

Mode of transmission	Aerosolised droplets.
Incubation period	Most commonly 2–5 days (range 1–14 days).
Period of communicability	From 1–2 days before, and typically transmissibility peaks 5 days after symptom onset. Asymptomatic spread is documented.
Incidence and burden of disease	Global pandemic ongoing. The burden of disease predominantly lies with older adults, those with comorbidities and health care workers exposed to patients with high viral loads. Children generally experience milder disease.
Funded vaccines	mRNA-CV: Comirnaty (manufacturer Pfizer/BioNTech). Adjuvanted rCV: Nuvaxovid (manufacturer Novavax).
Dose, presentation, route (see sections 5.4.4 and 5.4.5)	**mRNA CV: Comirnaty** mRNA-CV (30 µg) • purple cap • 0.3 mL dose • multi-dose vial, to be diluted before use • intramuscular injection • Storage once thawed: – undiluted, +2° to 8°C expiry 1 month (31 days) – diluted (in vial or drawn up), +2° to 30°C expiry 6 hours mRNA-CV (10 µg) • orange cap • 0.2 mL dose • Multi-dose vial, to be diluted before use • Intramuscular injection • Storage once thawed: – undiluted, +2° to 8°C expiry 10 weeks – diluted, in vial +2° to 8°C expiry 12 hours or drawn up +2° to 30°C expiry 6 hours

Dose, presentation, route (continued)	**Adjuvanted rCV: Nuvaxovid** • 0.5 mL dose • Blue cap • multi-dose vial, no dilution required • intramuscular injection • storage: +2° to 8°C (up to 6 months) – Use opened vial within 6 hours of first use, store at +2° to 8°C – drawn up vaccine within 6 hours (and before expiry)
Funded vaccine indications and schedule (see section 5.4.5)	<u>mRNA-CV (30 µg)</u> • Two doses, recommended to be given 6–8 weeks apart, can be given at least 21 days apart • For use from age 12 years • A third primary dose given at least 8 weeks after first two doses for those with severe immunocompromise from age 12 years (see section 5.5.8) • A booster dose given at least 3 calendar months to those aged 18 years or at least 6 months to those aged 16–17 years after completion of primary course (see section 5.5.10) • Certain individuals from age 16 years are recommended a second booster dose given at least 6 months after previous dose (see section 5.5.10) <u>mRNA-CV (10 µg)</u> • Two doses recommended to be given at least 8 weeks apart, can be given at least 21 days apart • For use in children aged 5 to 11 years, inclusively • A third primary dose given at least 8 weeks after first two doses for those with severe immunocompromise from age 5 years (see section 5.5.8)
Other funded vaccine indication and schedule	Two doses of adjuvanted rCV, given at least 21 days apart for use from age 12 years This vaccine can be used for a two-dose primary course without prescription. If this vaccine is used as second or third primary dose after mRNA-CV, a prescription is required. A prescription is not required for use of rCV as a booster dose from age 18 years.
Contraindications (see section 5.6.1)	mRNA-CV and rCV: A history of anaphylaxis to any component or previous dose.
Precautions (see section 5.6.2)	mRNA-CV and rCV: A definite history of anaphylaxis to any other product is a precaution not contraindication. Defer further doses if individual develops myocarditis/pericarditis after first or second dose of mRNA-CV or rCV. Seek specialist immunisation advice regarding future COVID-19 vaccination doses.
Potential responses to vaccine (see section 5.7.1)	mRNA and rCV: Generally mild or moderate: injection site pain, headache, fever, muscle aches, dizziness and nausea, a day or two after vaccination. These responses are more commonly reported after second dose and in younger adults (<55 years).

Vaccine effectiveness (see section 5.4.3)	mRNA-CV (30 µg): Clinical trial data showed efficacy against confirmed symptomatic COVID-19 of 90–98% after two doses. mRNA-CV (10 µg): Clinical trial data showed efficacy against confirmed, symptomatic COVID-19 of 68–98% after two doses in children aged 5-11 years. rCV: Clinical trial data gave efficacy of 80–95% against symptomatic COVID-19. Effectiveness of these vaccines is maintained against severe disease with recommended boosters but wanes for mild disease over a period of weeks after the primary course.
Public health measures	Ongoing testing for all suspected cases. Quarantine and isolation of household contacts and cases.

5.1 Virology

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a member of the Coronaviridae family and the *Betacoronavirus* genus. This enveloped, positive-strand RNA virus encodes four major structural proteins – spike (S), membrane (M), envelope (E) and a helical nucleocapsid (N). To enter host cells, the spike protein, which forms the characteristic crown-like (Latin: *corona*) surface structures, binds to the angiotensin-converting enzyme-2 (ACE2) receptor most frequently found on human respiratory tract epithelium.[1, 2]

The precise origin of this virus is unknown. First identified in humans in Wuhan, China, this virus shares a strong genetic sequence similarity to bat coronaviruses found in China,[3] and is a suspected zoonosis from bats via an intermediary animal, such as a pangolin.[4] As with most RNA viruses, mutations occur and variant strains of SARS-CoV-2 have been identified.

5.2 Clinical features

Coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 virus, which infects the respiratory tract and is transmitted human to human primarily through respiratory droplets and aerosols. Documented transmission has also occurred through direct contact and rarely fomites (objects or materials that can carry infection).

The reproduction number (R_0) (see section 1.2.1) was initially estimated to be around 2–3.[5, 6] Transmissibility varies by setting, and recently identified variant strains of SARS-CoV-2 have been well beyond the initial estimated R_0 values.[7, 8] The formerly dominant Delta (B1.617.2) variant was twice as transmissible as the ancestral strain (R_0 5–6).[9] The Omicron variants have even higher R_0 values.[10]

The symptoms of COVID-19 range widely from asymptomatic or a mild respiratory tract infection to severe and pneumonia, which can lead to severe inflammatory disease and respiratory failure. The most common symptoms of COVID-19 are like

those of other common respiratory illnesses and include a new or worsening dry cough, sneezing and rhinorrhoea or nasal congestion, fever, sore throat and shortness of breath. Unlike other respiratory viral infections, COVID-19 was frequently associated with a temporary loss of smell or altered sense of taste, and sometimes this is the only symptom; this symptom is less common with Omicron variant infections than reported with Delta.[11]. Some cases have reported gastrointestinal symptoms including nausea, diarrhoea, vomiting and abdominal pain, headache, muscle aches, malaise, chest pain, joint pain, and confusion or irritability; these symptoms almost always occur with one or more of the common symptoms. For around 80 percent of cases, COVID-19 is a mild disease, but some develop more severe disease or exacerbation of comorbidities, particularly older adults, in pregnancy, and those with comorbidities, which can progress to multi-organ and respiratory failure. As for influenza and other respiratory viruses, many of those with laboratory-confirmed infection remain asymptomatic.

In the early stages, it is difficult to distinguish COVID-19 symptoms from other common viral infections. The most reliable common diagnostic test has been detection of viral mRNA from a nasopharyngeal swab, using PCR assay and rapid antigen tests (RATs).

The incubation period is typically around two to five days (up to 14 days). Individuals may be infectious from up to two days before becoming symptomatic, with infectiousness typically peaking within five days of symptom onset.[12] High viral loads are detected in the nose at time of symptom onset.[13] Viable virus is not usually detectable for more than ten days after symptom onset, although SARS-CoV-2 mRNA has been detected for up to 83 days in respiratory and stool samples.[12, 14] Unlike previous coronavirus outbreaks (SARS and MERS), transmission of SARS-CoV-2 can also occur before the onset of symptoms or from asymptomatic individuals.[15] Viral loads and infectiousness are highest immediately after symptom onset, and most transmission occurs in household settings.[16, 17]

It is currently unclear what protection previous infection with SARS-CoV-2 provides. A study in the UK in health care workers found protection against symptomatic COVID-19 to be similar to that reported for mRNA COVID-19 vaccine.[18] A previous history of SARS-CoV-2 infection was associated with an 83 percent lower risk of infection, with a median time to re-infection of over five months.[19] Only about one third of the reinfections in health care workers presented as typical COVID-19 symptoms, as compared with 78 percent of new infections.[18] Neutralising antibodies have been detected and remained relatively stable between eight to 11 months after primary infection, even without natural boosting as was the situation early in the pandemic in New Zealand.[20, 21]

5.2.1 Children and young adults

Initially, the rate of SARS-CoV-2 symptomatic infection in children appeared to be lower than in adults,[22, 23, 24] but since adults are increasingly being vaccinated, the proportion of cases in children being detected has increased and severe outcomes are emerging.[25] Commonly, children have mild or no symptoms of COVID-19 with a short duration of illness; symptoms typically include headache, fever, cough, and may include sore throat, nasal congestion, sneezing, muscle aches and fatigue.[26] Around one in five

children with symptomatic COVID-19 present with gastrointestinal symptoms, such as nausea, vomiting, abdominal pain and diarrhoea. A systematic review found that diarrhoea was significantly associated with a severe clinical course (odd ratio 3.97; 95% CI 1.80-8.73).[26]

The incidence of severe or fatal disease in children is significantly lower than in adults.[27] Children at risk of more severe disease include those living with pre-existing health conditions and socioeconomic barriers to accessing health care. These risk factors are prevalent in New Zealand children, particularly children of Māori and Pacific ethnicity.[28, 29] Pre-existing conditions associated with higher risk from COVID-19 in children include obesity, diabetes, asthma, cardiac and pulmonary diseases, immune disorders, metabolic disease, cancer, neurological, neurodevelopmental (in particular, Down syndrome [trisomy 21]) and neuromuscular conditions.[30, 31] A systematic review found children with comorbidities were 25 times more likely to have severe COVID-19 than those without (5.1 percent vs 0.2 percent) and have a 2.8 times higher relative risk of death.[31] Children who develop pulmonary complications (eg, pneumonia) have a similar progression of disease as seen in adults, requiring oxygenation in hospital and in some cases corticosteroids treatments.[32] In the US, as of 24 February 2022, over 12.6 million cases of COVID-19 have been reported in children aged under 18 years (19 percent of all reported cases), and among reporting states, 0.1–1.5 percent of cases in children resulted in hospitalisation and mortality was zero to 0.01 percent of all child cases.[25]

5.2.2 Transmission

The role children play in transmitting SARS-CoV-2 is still unclear and is changing as new variants evolve and older populations are highly vaccinated. Transmission within educational settings is limited and is influenced by broader transmission in the community.[33, 34] Although children are susceptible to infection, transmission is more likely to occur between adults and from adults to children; the risk of child to child or child to adult transmission is considerably less.[33, 34, 35] The risk of transmission within education settings is highest for children aged 10–19 years.[36] Non-pharmaceutical interventions (masks, ventilation, spatial and temporal distancing, 'stay at home' polices and hygiene) can help to protect children from infection in schools.[27]

Transmission in households is common, particularly with the more infectious variants Delta and Omicron.[10] The potential for households to be a significant source of transmission likely reflects the self-isolation of confirmed or suspected COVID-19 cases at home.[37, 38] In England, children were at a lower risk of transmission or being the index case within households,[39, 40] but unpublished data found that households with at least one child had higher prevalence of COVID-19 than those without children (3.0 percent vs 0.75 percent).[41]

5.2.3 Risk groups

Risk factors for severe disease include older age, male, smoking,[42] obesity and chronic medical conditions, including diabetes,[43] cancer, chronic respiratory disease,

cardiovascular disease, chronic kidney disease, hypertension and being immunocompromised.[44] Increased incidence is well documented in some ethnic groups but seems primarily related to prevalence of the risk factors listed above. Increasing age is the most important risk factor for severe disease, due to declining immune function and high prevalence of comorbidities. The highest rates of mortality are in the oldest age groups, especially those aged over 80 years (at a rate 20-fold higher than for those aged 50–59 years in the United Kingdom).[44]

Health care workers

Patient-facing health care workers caring for patients with COVID-19 are likely to be exposed to higher viral loads, placing them and their household members at greater risk of developing COVID-19 than the general population.[45] In Scotland, one-sixth of the COVID-19 cases admitted to hospital were health care workers and their household members.[45] Health care workers have also been implicated in the spread of SARS-CoV-2 within health and long-term care facilities.[45, 46, 47] However, the use of personal protective equipment (PPE) and other measures aimed at reducing nosocomial viral transmission have been shown to be effective, such that, where COVID-19 is prevalent in the community, health care workers are more likely to catch COVID-19 from an infected household member.[17]

Pregnancy

Although pregnant women are not at increased risk of SARS-CoV-2 infection, they are at increased risk of severe disease and death compared with age-matched non-pregnant women.[48, 49, 50, 51] While the absolute risk of severe outcomes among pregnant women is low compared with absolute risk due to advanced age, the risk of hospital admissions is three times higher and the rate of ICU care for COVID-19 has been found to be five times higher (relative risk 5.04; 95% CI 3.13–8.10) for pregnant women than for non-pregnant women.[50] Obesity, hypertension, asthma, autoimmune disease, diabetes and older age are also associated with severe COVID-19 in pregnant women.[52]

Infants of mothers with COVID-19 are at increased risk of preterm birth, particularly due to early delivery, and neonatal ICU admission.[49, 52] Early studies do not suggest intrauterine transmission, but transmission during birth has been shown in around 3 percent of neonates.[53] Most neonatal infections are asymptomatic or mild, but around 12 percent experience severe disease with dyspnoea and fever as the most commonly reported signs.[54]

5.2.4 Post-infection complications

Post-acute COVID-19 sequalae or commonly called 'long COVID' is characterised by persistent symptoms lasting for more than three months and appears to affect around 10 percent of those infected, particularly those with at least five symptoms in the first week of illness.[55, 56, 57] Post-acute manifestations include cardiovascular, pulmonary and neurological effects, including chronic fatigue, dyspnoea, specific organ dysfunction and depression.[58]

Long COVID-19 is not well described in children but appears to be less common, particularly under the age of 12 years, than in adults.[32, 59, 60, 61] Similar symptoms are seen in children following other viral infections and some symptoms could be related to social restrictions during lockdowns.

For further information see the Ministry of Health Long COVID-19 website: **health.govt.nz/covid-19-novel-coronavirus/covid-19-health-advice-public/about-covid-19/long-covid**

Paediatric multisystem inflammatory syndrome

Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS or MIS-C) is a rare, delayed complication of COVID-19 following largely asymptomatic SARS-CoV-2 infection in children and adolescents.[62, 63] PIMS-TS can occur approximately one month after symptomatic or asymptomatic SARS-CoV-2 infection affecting different parts of the body and usually presents as a fever, rash and abdominal pain, although in more severe cases, myocarditis and low blood pressure can occur.[64] Early diagnosis and appropriate treatment improve outcomes. Data from the US has shown that the risk PIMS-TS is highest in marginalised and ethnic minority groups.[65]

5.2.5 SARS-CoV-2 variants

As with all viruses, new variants have evolved. Most recently, certain variants have been shown to bind the ACE2 receptor more readily, making the variants more transmissible. The greater numbers of people becoming infected is increasing the burden of the disease.[7, 8] There is evidence that recent Omicron variants are more infectious than the former strains.[9, 66] WHO has classified genetic variants in to three classes:[67]

- Variants of interest – genetic changes that are predicted or known to affect transmission, diagnostic, therapeutic or immune escape (for example, reduced antibody neutralisation) and identified to cause significant community transmission or COVID-19 clusters, in multiple countries with increasing prevalence or other epidemiological impacts, suggesting emerging risk to global public health
- Variants of concern – meet variant of interest definition with evidence of increased transmissibility or detrimental change in COVID-19 epidemiology, change in clinical disease or virulence, reduced vaccine or treatment efficacy or diagnostic detection failures.
- Variants under monitoring – genetic changes that are suspected to affect SARS-CoV-2 characteristics with indication of potential risk, but evidence of impact unclear.

5.3 Epidemiology

5.3.1 Global burden of disease

Clusters of distinctive pneumonia cases were observed in Wuhan, China during December 2019. The cause was identified in January 2020 as a novel coronavirus that had genetic and clinical similarity to the coronavirus causing the severe acute respiratory syndrome (SARS) epidemic from 2002 to 2004. Consequently, the novel coronavirus was named SARS-CoV-2 and the associated disease named Coronavirus Disease 2019 (COVID-19). Due to the rapid spread, a public health emergency of international concern (PHEIC) was announced in late January 2020. By the time the COVID-19 pandemic was declared by the World Health Organization (WHO) on 11 March 2020, there were 118,000 reported COVID-19 cases and 4,291 associated deaths in 114 countries. The global death toll surpassed one million by late September 2020.

As of 7 September 2022, 6.5 million deaths and over 600 million confirmed cases were reported to the WHO, 4 million new cases per week continue to be reported. Cases numbers increased rapidly from the end of December 2021 as the Omicron variant spread, peaking at a 12.7 percent increase per week. See the WHO Coronavirus Disease (COVID-19) Dashboard (**covid19.who.int**) for the latest official data. Actual rates are expected to be considerably higher than officially reported rates, especially since milder infections may not be reported.

The infection-fatality rate, while still high particularly in the older age groups, has reduced since the start of the pandemic, with vaccination, improved clinical recognition and management and the use of therapies of demonstrated value, such as dexamethasone and antiviral medications such as Paxlovid (nirmatrelvir and ritonavir) and molnupiravir.[68, 69]

The use of vaccines has reduced the global burden of COVID-19 significantly. The first phase I clinical trial for a COVID-19 vaccine commenced in March 2020. The first public vaccination dose was given as part of a mass campaign in the United Kingdom on 8 December 2020. As of 3 September 2022, around 12.5 billion doses had been administered with 4.9 billion people fully vaccinated, globally. Eleven COVID-19 vaccines have been granted emergency use listing by the WHO.

See the WHO Coronavirus Disease (COVID-19) Dashboard (**covid19.who.int**) and the Our World in Data website (**ourworldindata.org/covid-vaccinations**) for the latest official data.

5.3.2 New Zealand epidemiology

Prior to the outbreak of the Delta variant in August 2021, during 2021 most of the reported cases were imported from overseas (over 95 percent from 1 January to 9 August 2021). From 16 August 2021, the number of cases in New Zealand began to increase sharply due initially to the highly infectious Delta variant. From January 2022, when the even more infectious Omicron variant entered the community, case numbers rose rapidly. By 10 September 2022, over 1.7 million cases had been notified and 2,830 people had died within 28 days of being reported as a case and of these, 1,235 had COVID-19 coded as the underlying cause of death. From August 2021 to end of August 2022, as a proportion of the total number of cases per ethnicity, the higher rates of hospitalisation were reported for Pacific peoples (1.1 percent), Māori (0.9 percent) and MELAA (0.75 percent) than European (0.7 percent) and Asian (0.45 percent). For current details on case demographics see **health.govt.nz/covid-19-novel-coronavirus/covid-19-data-and-statistics**

Strategy for prevention

The first case of COVID-19 was reported in New Zealand on 28 February 2020. During March, cases numbers increased, and clusters of transmission were identified. Border restrictions were implemented on 16 March 2020. On 25 March 2020, New Zealand entered a nationwide lockdown (alert level four). New Zealand implemented an elimination strategy with four defined levels of pandemic response to prevent the spread of SAR-CoV-2. A mobile phone app aided rapid contact tracing. These strategies were effective in containing the spread of SARS-CoV-2 in New Zealand and restrictions were able to rapidly stop the spread of the virus within the country. Only 19 percent of the introductions of virus in 2020 resulted in ongoing transmission or more than one additional case.[5] Subsequently on 3 December 2021, once around 90 percent of the eligible population had been vaccinated in most regions, a revised COVID-19 protection framework using 'traffic lights' was introduced to manage infection spread; it was discontinued in September 2022.

5.4 Vaccines

5.4.1 Introduction

Clinical trials for COVID-19 vaccine candidates began shortly after the pandemic was announced in March 2020. Between October to December 2020, the New Zealand Government signed advanced purchase agreements for four vaccine candidates, with purchase dependent on approval for use from the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). This is an ongoing process and, therefore, the availability and eligibility for these different vaccines may change.

5.4.2 Available vaccines

Vaccines for COVID-19 continue to undergo phase III clinical trials, and the Medsafe review process is ongoing for each vaccine candidate examining clinical trial and post-marketing surveillance data. The first vaccine to receive approval for use in New Zealand was an mRNA-based COVID-19 vaccine (mRNA-CV, trade name Comirnaty) manufactured by Pfizer/BioNTech. Provisional consent approval was granted on 3 February 2021. Two adenoviral vector COVID-19 vaccines were granted provisional approval in July 2021: Vaxzevria (manufactured by AstraZeneca and was available from late November 2021 to September 2022) and COVID-19 Vaccine Janssen (not available in New Zealand). On 4 February 2022, provisional approval was granted to an adjuvanted recombinant spike protein subunit COVID-19 vaccine (rCV; trade name Nuvaxovid) manufactured by Serum Institute of India on behalf of Novavax and sponsored in New Zealand by Biocelect (available from March 2022).

Provisional consent imposes conditions on these vaccines to restrict their use by health professionals according to the available data at time of approval. This approval status allows New Zealanders early access to medicines with significant unmet clinical need under the Medicines Act.

Funded vaccines

The mRNA-CV, Comirnaty, consists of messenger ribonucleic acid (mRNA) encoding the full-length spike glycoprotein of the SARS-CoV-2 virus inside a lipid nanoparticle (named tozinameran). The spike protein has an adjuvant effect, so no additional adjuvant is included. It is designated BNT162b2 in clinical trials conducted by Pfizer and BioNTech. This mRNA vaccine delivers the instructions for human cells to build the viral antigen, SARS-CoV-2 spike protein. The mRNA is temporarily protected from degradation by the lipid nanoparticle that also facilitates fusion with the recipient's cell wall.[70, 71]

The adjuvanted recombinant COVID-19 vaccine (abbreviation rCV), Nuvaxovid, contains recombinant SARS-CoV-2 spike protein in a stabilised prefusion conformation. The spike protein is produced by an insect cell-line that has been infected with an insect baculovirus expressing SARS-CoV-2 spike protein genes. Together, the purified spike proteins and the adjuvant matrix are formed into immunogenic nanoparticles. The proprietary adjuvant (Matrix-M) contains two purified saponin fractions from *Quillaja saponaria* (soapbark tree) which enhances the innate immune response and activates the production of neutralising antibodies and T and B cell immunity. The vaccine was designated NVX-2373 in clinical trials conducted by Novavax and is sponsored in New Zealand by Biocelect.

mRNA-CV – Comirnaty (Pfizer/BioNtech)

mRNA-CV (30 µg) for ages from 12 years (purple cap)

Each 0.3 mL dose of mRNA-CV contains:

- 30 µg of tozinameran, a single-stranded 5'-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein embedded in a

lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.

- The lipid nanoparticle contains ALC-0315 ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)), ALC-0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), distearoylphosphatidylcholine (DSPC)) and cholesterol.
- Also contains potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, sucrose and water for injection.

mRNA-CV (10 µg) for children aged 5 to 11 years (orange cap)

Each 0.2 mL dose contains:

- 10 µg of tozinameran, a single-stranded 5′-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein embedded in a lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.
- The lipid nanoparticle contains ALC-0315 ((4 hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)), ALC 0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), distearoylphosphatidylcholine (DSPC)) and cholesterol.
- Also contains Tris/sucrose buffer: tromethamine (also known as Tris), tromethamine hydrochloride, sucrose and water for injection

The 10 µg paediatric formulation of mRNA-CV (with orange cap) uses a Tris/sucrose buffer to improve the stability at +2° to 8°C.

Adjuvanted rCV – Nuvaxovid (Novavax)

Each 0.5 mL dose of adjuvanted rCV contains:

- 5 µg of recombinant SARS-CoV-2 spike protein (produced in insect cell line, Sf9)
- 50 µg adjuvant Matrix M - fraction A and fraction C saponins from *Quillaja saponaria* formed into lipid nanoparticles containing cholesterol, phosphatidyl choline, monobasic potassium phosphate and potassium chloride
- Also contains: dibasic sodium phosphate heptahydrate, monobasic sodium phosphate monohydrate, sodium chloride, polysorbate 80, sodium hydroxide (for adjustment of pH), hydrochloric acid (for adjustment of pH) and water for injections

Other vaccines

An adenoviral vector COVID-19 vaccine, Vaxzevria (abbreviation ChAd-CV), was provisionally approved for use in New Zealand on 29 July 2021. This vaccine, based on a recombinant non-replicating chimpanzee adenovirus ChAdOx1-S, contains a transgene encoding the prefusion SARS-CoV-2 spike glycoprotein. The adenovirus delivers the instructions to make replicas of the SARS-CoV-2 viral protein. It has been modified to be unable to replicate and only the gene encoding the spike protein (the antigen) can be expressed. The virus is destroyed once the protein instructions have

been delivered virus is destroyed. This vaccine is manufactured by AstraZeneca (clinical trial designation AZD122). As of 5 September 2022, it is no longer available in New Zealand.

Another adenoviral vector COVID-19 vaccine (Ad26.COV2.S, brand names Jcovden or COVID-19 Vaccine Janssen) was approved for use in New Zealand on 7 July 2021. Using a similar platform to ChAd-CV, this vaccine (abbreviated here to Ad26-CV) contains a modified non-replicating human adenovirus, Ad26, that carries a transgene coding for the COVID-19 prefusion SARS-CoV-2 spike protein. This vaccine is not available in New Zealand.

5.4.3 Efficacy and effectiveness

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Immunogenicity

Before the phase III efficacy studies were conducted, immunogenicity was a key indicator in the early-phase clinical trials of COVID-19 vaccines in 2020. Virus neutralising antibody responses measured the killing of live SARS-CoV-2 and/or pseudovirus in cell culture, and humoral responses were compared with human convalescent sera collected from patients who had recovered from COVID-19. The initial phase I and II clinical trials evaluated two vaccine candidates (BNT162b1 and BNT162b2) in adults. Both induced dose-dependent neutralising antibody titres similar or higher to the titres in convalescent sera.[72] The antibody response was lower in older people (aged 55–85 years) than in younger people (aged 18–55 years), but both groups had higher average neutralising antibody levels than those who had SARS-CoV-2 infection.

Similar immunogenicity was shown in a phase III trial in participants aged 12–15 years and those aged 16–25 years given 30 µg dose of mRNA-CV, with the neutralising antibody responses higher in the younger adolescents (geometric mean ratio 1.76; 95% CI 1.47–2.10).[73] In 264 children aged 5-11 year, a phase II/III clinical trial found that the immunogenicity of 10 µg doses of mRNA-CV was similar to that seen in young people aged 16–25 years given 30 µg doses.[74] At one month after two doses given 21 days apart, the neutralising antibody geometric mean ratio was 1.04 (0.93–1.18) between the children and young adults.

Efficacy – clinical trial data

Efficacy of 30 µg mRNA-CV (BNT162b2) was assessed in the phase III component of a large, ongoing clinical trial in which 43,448 participants aged 16–85 years across six countries were randomised to receive vaccine or saline placebo, with two doses given 21 days apart.[75] Interim data, based on the early SARS-CoV-2 variants, indicated:

- vaccine efficacy (VE) against symptomatic PCR-confirmed COVID-19 was 94.8 percent (95% CI: 89.8–97.6 percent)
- evidence of previous SARS-CoV-2 infection did not alter this efficacy (VE 95.0 percent without and 94.6 percent with and without previous infection)

- similar efficacy (90–100 percent) was observed across all subgroups as defined by age, sex, race, ethnicity, baseline body-mass index (35 percent of participants were obese, BMI ≥ 30) and the presence of at least one co-existing medical condition (in 21 percent of participants)
- moderate protection against COVID-19 was observed before the second dose.[75]

For adolescents aged 12-15 years, observed vaccine efficacy for mRNA-CV (30 µg) in a 2020/21 phase III clinical trial was 100 percent (95% CI 75.3–100) against symptomatic COVID-19. A total of 2,220 randomised participants received two doses of vaccine or saline placebo given 21 days (19–42 days) apart. No cases of severe COVID-19 were observed in this age group.[73]

In children aged 5-11 years, vaccine efficacy of 90.7 percent (95% CI 67.7–98.3) against symptomatic COVID-19 was seen from seven days after dose two in 1,305 children (without evidence of previous infection) who received mRNA-CV (10 µg) when compared with 663 who received placebo in the phase II/III clinical trial.[74]

Effectiveness of primary course – real-world experience

Early data from Israel at the start of its national COVID-19 immunisation programme, which included around 1.2 million vaccinated and unvaccinated individuals aged from 16 years, demonstrated that mRNA-CV was highly effective at preventing COVID-19 and severe disease, and these data were in line with those observed during clinical trials.[76] At the start of the programme in the UK in older adults, a significant reduction in symptomatic COVID-19 cases aged from 70 years was seen for at least six weeks after a single dose of mRNA-CV, with effectiveness of 70 percent (95% CI 59–78 percent) by days 28–34, plateauing to 61 percent (51–69 percent). Additionally, those that had been vaccinated were 43 percent (33–52 percent) less likely to require emergency hospitalisation and at 51 percent (37–62 percent) lower risk of death. At day 14 after a second dose (given 12 weeks after dose one), vaccine effectiveness reached 89 percent (85–93 percent).[77]

Effectiveness of mRNA-CV against symptomatic COVID-19 caused by the Delta variant was reduced in comparison with previous variants (ranging from around 78–93 percent),[78] but the vaccine remained highly effective against hospitalisation (73–94 percent), severe disease and death (80-97 percent) in a range of groups.[79] The risk of infection with Delta was also significantly lower in fully vaccinated compared with unvaccinated individuals (hazard ratio 0.35; 95% CI 0.32–0.39).[80]

Effectiveness of the two-dose primary course against Omicron variant was found to wane rapidly and booster doses were required to prevent symptomatic infection (see below).

Effectiveness against transmission

Effectiveness of mRNA-CV against transmission of SARS-CoV-2 is unclear and likely to depend on a range of factors, including rate of viral growth once infected and the infectivity of variant of the virus. It was expected the spread of the virus would decrease as the number of people who were vaccinated increased. During the Delta wave, evidence from the UK showed that vaccination against COVID-19 reduced the risk of infection and accelerated the viral clearance. Although peak viral loads were

similar between infected vaccinated and unvaccinated individuals, the secondary attack rate between household contacts was 25 percent (95% CI 18–33 percent) in fully vaccinated individuals compared with 38 percent (24–53 percent) in unvaccinated individuals.[81] Transmission to non-immune individuals in households in Sweden was shown to be significantly reduced and correlated with the proportion of family members vaccinated.[82] The ability of the vaccine to prevent infection and transmission was further reduced with the emergence of the Omicron variants.

Effectiveness in adolescents and children

Interim effectiveness against Delta variant SARS-CoV-2 infection, irrespective of symptoms, was estimated to be 92 percent (95% CI 79–97) in adolescents aged 12-17 years in Arizona.[83] A test-negative case-control study in the US showed vaccination with mRNA-CV (30 µg) to be protective against PIMS-TS in adolescents aged 12–18, with an estimated effectiveness of 91 percent (95% CI 78–97 percent), a median of 84 days (range 52–122) after vaccine dose two.[84]

Vaccination with mRNA-CV in pregnancy reduces the risk of severe COVID-19 and provides passive immunity to the infant for the first few months of life.[85, 86, 87]

Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

Immunogenicity

Two doses of adjuvanted rCV were immunogenic in adults aged 18–59 years and 60–84 years. At 14 days after two doses given 21 days apart, neutralising antibody levels in both groups were higher than those in a panel of convalescent sera and all participants who received rCV seroconverted. At total of 1,283 participants were randomised 1:1:1:1 to receive one or two doses of vaccine (5 µg spike protein), a higher dose (25 µg) or placebo, and were stratified by age in the US and Australia. Both age groups had robust immune responses, although the older participants had lower antibody titres of anti-spike protein IgG or wild-type neutralising antibody than the younger group.[88]

Coadministration with influenza vaccines

Coadministration with influenza vaccine was investigated in a small phase I/II sub-study in UK hospitals. Around 400 participants were randomised to receive rCV and inactivated quadrivalent influenza vaccine for those aged 18–64 years or adjuvanted trivalent influenza vaccine for those aged 65 years or over, or rCV alone. Immunogenicity showed no change in the response to influenza vaccine but a reduction in antibody response to SARS-CoV-2. There was no difference in the seroconversion rates. Although the anti-spike protein IgG responses were 0.6-fold lower in the groups that received both vaccines, when post-hoc analysis of efficacy was considered, this reduction was not suggested to be clinically meaningful and in the younger age group, the anti-spike antibody levels were three-fold greater than found in convalescent serum.[89]

Efficacy – clinical trial

Data from two phase III clinical trials of adjuvanted rCV gave overall vaccine efficacy of 90 percent (95% CI 82.9-94.6 in PREVENT-19 study in US/Mexico and 80.2-94.6 percent

in UK trial) against symptomatic COVID-19 from at least seven days after dose two. [90, 91] By age group, in approximately 10,000 vaccinated and placebo participants in the UK (randomised 1:1), vaccine efficacy against COVID-19 in those aged 18-64 years was 89.8 percent (79.7-95.5) versus 88.9 percent (20.2-99.7) in approximately 4,000 participants aged 65– 84 years[91] In a subgroup of approximately 6,000 participants with coexisting illness, vaccine efficacy was 90.9 (70.4-97.2)[91] These clinical trials were conducted during early 2021, against predominantly Alpha not Delta or Omicron variants.

Effectiveness – real-world

This vaccine has only been recently approved for use and real-world effectiveness is beginning to be evaluated. There is no published effectiveness data to date.

Duration of immunity

Especially with the emergence of more infectious variants, there has been insufficient time since the commencement of clinical trials and vaccination campaigns to assess fully how long-lived immunity lasts following immunisation or natural infection. A decline in vaccine efficacy was observed against SARS-CoV-2 infection and mild disease, particularly with emerging variants such as Delta and Omicron, but protection against severe disease has been maintained and enhanced with the use of booster doses. Waning in neutralising antibody levels has been correlated with predominantly mild or asymptomatic breakthrough infections in health care workers.[92] The greatest waning was observed in those aged over 65 years and those aged 40–64 years with underlying medical conditions compared with healthy adults.[93] Data indicated that vaccine effectiveness with the primary course against symptomatic infection caused by Omicron variant declines more rapidly than was seen against Delta.[94]

Although neutralising antibody levels wane,[95] and lower levels are less effective against the emerging variants such as Omicron, T cell responses and memory are maintained in vaccine recipients (for mRNA-CV and rCV).[96, 97]

Booster doses

To prolong protection many countries introduced a booster dose after the primary course. Booster dose programmes were accelerated following the emergence of the Omicron variant from late 2021, including in New Zealand.

mRNA COVID-19 vaccine

Booster doses, given from five months after the primary course, were shown to reduce the rates of symptomatic COVID-19 by a factor of 11.3 (95% CI 10.4–12.3) and severe illness by a factor of 5.4 (4.8–6.1) in older adults aged from 60 years in Israel.[98] The UK Health Security Agency reported that vaccine effectiveness against symptomatic infection was significantly lower against Omicron than Delta variant, such that by 15 weeks vaccine effectiveness had declined to between 34–37 percent after two doses of mRNA-CV. At more than 25 weeks after two primary doses, mRNA-CV vaccine effectiveness was 25–35 percent against hospitalisations due to Omicron variant. From

two weeks after a booster dose of mRNA-CV (30µg) given from 25 weeks after the primary course, effectiveness against mild infection was increased to 70–75 percent: 75.5 percent (95% CI 56–86) in those mRNA-CV primed and 71 percent (42–86) in those primed with ChAd-CV.[94] A booster with mRNA-CV increased effectiveness against hospitalisation to over 90 percent within two weeks but then declined to 75 percent after 10–14 weeks.[99]

These findings were supported by data from Canada, which showed vaccine effectiveness waned more rapidly after the primary series against symptomatic infection with Omicron compared with Delta variant. Vaccine effectiveness was significantly improved against symptomatic infection with Omicron variants, from <1% (-8 to 10 percent) to 61 percent (56–65 percent), by a booster dose of an mRNA COVID-19 vaccine given from 240 days after the second dose of primary course (with at least one dose of an mRNA vaccine). The booster dose was highly effective against severe outcomes of Delta or Omicron (98–99 percent and 87–98 percent, respectively).[100]

Second booster doses (ie fourth doses) are recommended for certain groups. Fourth doses boosted both humoral and cellular immunity when given approximately seven months after a third dose booster in the UK. Anti-spike protein IgG titres were higher 14 days after a fourth dose than seen 28 days following the third dose (11–20 fold increase from day 0 to day 14 post fourth dose).[101] In an Israeli study, a fourth dose of mRNA-CV, given at least four months after the third dose to adults aged from 60 years, provided additional protection for at least six weeks and reduced the rate of severe COVID-19 by a factor of 3.5 (95% CI 2.7-4.6) compared with those who had received three doses, and reduced the rate of confirmed SARS-CoV-2 infection by a factor of two (1.0 –2.1) at four weeks. The study included over 1.2 million participants (1:1 received fourth and third doses).[102] There is marginal evidence that a fourth dose prevents infection in health care workers (given 4 months after dose three) – data from an open-label nonrandomised clinical trial in Israel, gave vaccine efficacy of 30 percent (-9 to 55) against Omicron infection and estimated 43 percent against symptomatic illness. Those who were infected were shown to have relatively high viral loads and likely to be infectious.[103]

Adjuvanted recombinant COVID-19 vaccine

Immunogenicity of homologous booster doses of rCV, evaluated during a secondary analysis of a phase II clinical trial, showed that antibody levels induced by the booster dose in healthy adults were higher than levels associated with efficacy in the primary response phase III trials.[95] In the phase II clinical trial, conducted in the US and Australia, a single booster dose was given approximately six months after two-dose primary course of rCV to 105 healthy adults aged 18 to 84 years. Immune responses at 28 days post booster (day 217) were compared with those at 14 days post dose two (day 35). Serum IgG GMTs increased 4.7-fold from day 35 to day 217 against ancestral SARS-CoV-2, and 4.1-fold in the neutralisation assay. Increases in functional ACE2 receptor binding inhibition were also observed from day 189 to day 217 (pre and post booster) against various variants, including a 24-fold increase against Delta and 20-fold increase against Omicron. Anti-spike IgG activity also showed improved titres against a range of variants, including 92.5-fold increase against Delta and 73.5-fold increase against Omicron.[95]

Mixed COVID-19 vaccine schedules

Heterologous priming

Much of the evidence available around mixed (heterologous) COVID-19 vaccine schedules investigated ChAd-CV (Vaxzevria) followed by mRNA-CV (Comirnaty) as the second dose (heterologous prime-prime schedules) in 2021.[104, 105] The humoral immune response was shown to be stronger with a ChAd/mRNA primary schedule than homologous ChAd-CV schedule against different SARS-CoV-2 variants including Delta.[104, 106] The T cell response was also found to be higher following heterologous dosing.[107] The ComCOV study in the UK found that when ChAd-CV was given 4 weeks after mRNA-CV, the anti-S protein IgG antibody response was lower than homologous mRNA-CV dosing (geometric mean ratio [GMR] 0.51; 95% CI 0.43–∞), but higher than ChAd/ChAd. Giving mRNA-CV after ChAd-CV first dose, produced a higher response than ChAd/ChAd dosing (GMR 9.2; 7.5–∞). Taking age, comorbidity and different immunological outcomes into consideration, the overall humoral response of mRNA/mRNA was favoured over mRNA/ChAd dosing and ChAd/mRNA was favoured over ChAd/ChAd.[108]

A phase II clinical trial (ComCOV 2) conducted in the UK investigated the safety and immunogenicity of mixed priming schedules with rCV. Between April and May 2021, 1,072 participants aged 50–78 years received a second dose of one of three COVID-19 vaccines a median of 9.4 weeks after receipt of a single dose of ChAd-CV or mRNA-CV.[109] Although when rCV was given as the second dose the antibody response was inferior to a second dose of mRNA-CV (GMR 0.5; 95% CI 0.4 to 0.7), rCV induced an 18-fold rise in anti-spike antibody concentration 28 days after vaccination, which were high than ChAd-CV. For those who received a first dose of ChAd-CV, a second dose with rCV antibody concentration was non-inferior to a second dose of ChAd-CV (GMR 2.8; 2.2 to 3.4).[109]

Heterologous boosting

As part of the UK COV-BOOST study, all vaccines used as third-dose boosters demonstrated superior immunogenicity compared with control (except an inactivated virus COVID-19 vaccine in mRNA-CV primed group) as measured by anti-spike IgG and neutralising assays.[110] Participants aged 30 years or over with no history of laboratory-confirmed SARS-CoV-2 infection were given a booster dose at least 84 days post two doses of mRNA-CV (30µg Comirnaty) or at least 70 days post two doses of ChAd-CV. Participants received one of six vaccines including rCV, half dose rCV, ChAd-CV, mRNA-CV (Comirnaty), mRNA-CV (Spikevax) or MenACWY as control. Cellular responses in ChAd-CV primed individuals were better boosted by rCV than in those primed with mRNA-CV. Optimal timing of the dosing intervals remains unclear.[110]

5.4.4 Transport, storage and handling

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

mRNA-CV (30 µg) for ages 12 years and over

To preserve the integrity of the mRNA in this vaccine, storage at ultra-low temperature freezer (between -90°C and -60°C) is required. At these ultra-low temperatures, the shelf-life is 15 months. Trays of unopened vials may be stored and transported at -25°C to -15°C for a total of two weeks on one occasion only. Once an individual vial has been removed from the vial tray, it should be thawed for use.

The vaccine will be thawed in batches, packed into cartons and distributed from the central warehouse. Each carton will have a label with an updated batch number and expiry date and time. Expiry reduces from 15 months to 31 days once thawed. Thawed vaccines will be shipped to vaccination sites as per the standard cold chain distribution process.

Store undiluted vials (with purple cap) at +2°C to +8°C for up to 31 days (including up to 48 hours for transportation) including up to two hours at room temperature (up to +30°C). After dilution, store vials between +2°C and +30°C and use within six hours. Any remaining vaccine in the vial must be discarded after six hours. Do not refreeze. See 2021 Addendum to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/2021-addendum-national-standards-vaccine-storage-and-transportation-providers-2017-2nd-edition**). See also '*Guidance supporting the administration of mRNA-CV vaccine*' factsheet available from **covid.immune.org.nz**.

mRNA-CV (10 µg) for ages 5–11 years

This vaccine requires storage at ultra-low temperatures (-90°C to -60°C) and at this temperature has a shelf-life of 12 months. Store unopened, undiluted vials (with orange cap) at at +2°C to 8°C for up to 10 weeks within the 12 months shelf-life. Do not freeze. Transport according to the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition) **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**

Store diluted vaccine in vials at +2°C to 8°C for a maximum of 12 hours, or store vaccine drawn-up in syringe for a maximum of six hours at +2°C to 30°C. Prior to use, once an undiluted vial is taken out of the refrigerator, allow time (up to 2 hours) for the vaccine to reach room temperature and to be diluted. Discard any vaccine exceeding these times, accordingly. See also the IMAC COVID-19 Education factsheet '*Paediatric Pfizer/BioNTech mRNA-CV 10µg Vaccine Preparation*' available from **covid.immune.org.nz**.

Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

Transport and store according to the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)
health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017

Store at +2°C to +8°C. Do not freeze. Protect vials from light. Unopened vials (with blue cap) have a shelf-life of up to six months. Opened vials should be used within six hours of first use. Vaccines should ideally be used within an hour of being drawn up. The maximum time the vaccine can be stored in a syringe is six hours when stored at +2°C to 25°C, and before the vial six-hour expiry is reached, whichever is soonest. To ensure optimum use, in New Zealand, the vaccine is recommended to be always stored in the fridge and, where practical, doses are drawn up as required.

See also the IMAC COVID-19 education factsheet, '*Guidance for Nuvaxovid (Novavax) COVID-19 Vaccine Preparation*' available from **covid.immune.org.nz**.

5.4.5 Dosage and administration

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

mRNA-CV (30 µg) for ages from 12 years

Each dose of mRNA-CV is 0.3 mL (30 µg) to be administered intramuscularly. Two doses are given at least 21 days apart for individuals aged 12 years or older. All individuals from the age of 12 years are recommended to receive two doses of mRNA-CV (30 µg) given from eight weeks apart.

Each multi-dose vial (with purple cap) contains 0.45 mL of vaccine and should be diluted with 1.8 mL of 0.9% NaCl. Once diluted, each reconstituted vaccine will supply six (up to seven) doses of 0.3 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.3 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

mRNA-CV (10 µg) for ages 5 to 11 years

Each 0.2 ml dose (10 µg) is to be administered intramusclarly. Two doses are given at least 21 days apart for individuals aged 5 to <12 years. An interval of at least 8 weeks is recommended between doses for this age group partly because it is expected give an optimal immune response.

Each multidose vial (with an orange cap) contains 1.3 ml and should be diluted with 1.3 ml 0.9% NaCl. Once reconstituted, each reconstituted vials will supply ten doses of 0.2 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.2 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

Preparing mRNA-CV multi-dose vial

Note that the process for drawing up mRNA-CV differs from the recommendations for other multi-dose vial vaccines as described in section A7.2 in Appendix 7. To follow international guidance around the use of low dead space needles, the needle used to draw up mRNA-CV is also used to administer the injection. Unless you plan to administer the vaccine dose immediately, carefully replace the needle guard and place syringe onto a ridged tray for storage, for example, if all six doses are prepared at one go in a mass vaccination setting.

For detailed instructions for mRNA-CV multi-dose vial preparation and administration see the most current IMAC COVID-19 education factsheets '*Instructions for multi-dose vial Pfizer/BioNTech vaccine: preparation and administration*' and '*Paediatric Pfizer/BioNTech mRNA-CV 10µg Vaccine Preparation*' available from **covid.immune.org.nz**.

Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

A primary course of two 0.5 ml doses of adjuvanted rCV are given intramuscularly at least 21 days apart. All individuals from the age of 12 years, who cannot have mRNA-CV, are recommended to receive two doses of rCV from eight weeks apart.

This vaccine has been approved by Medsafe for use as a primary course for individuals aged 12 years and older. See section 5.5.2 for prescribing information.

The ready-to-use multidose vials (with blue cap) contain ten doses. The vials do not require dilution or reconstitution. Do not pool excess from multiple vials. For detailed instructions for adjuvanted rCV multidose vial administration see the most current IMAC COVID-19 education factsheet, '*Guidance for Novavax COVID-19 vaccine preparation*' available from **covid.immune.org.nz**.

This vaccine is latex-free. The vial stopper is made with bromobutyl or chlorobutyl rubber, not natural rubber latex.

Coadministration with other vaccines

There are no anticipated safety concerns regarding coadministration any of the currently available COVID-19 vaccines (mRNA-CV (10 µg or 30 µg) or rCV) with other vaccines. These vaccines can be administered at any time before, after or simultaneously (in separate syringes, at separate sites) with other Schedule vaccines including MMR, varicella, influenza, HPV, Tdap and meningococcal vaccines. Note: Due to limited experience at this time, it is recommended to allow spacing of at least three days between rCV and rZV (Shingrix) and adjuvanted influenza vaccine (Fluad Quad).

TST/Mantoux testing for tuberculosis can also be conducted at any time before, after or simultaneously with mRNA-CV or rCV.

5.5 Recommended immunisation schedule

The COVID-19 vaccines were initially only available according to a prioritisation schedule for defined groups, however, since January 2022, all individuals in New Zealand aged from 5 years are eligible to be vaccinated. See Table 5.1 for the recommended schedule.

For up-to-date details around vaccine policy statements and further clinical guidance for the COVID-19 Vaccine Immunisation Programme refer to **health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance**.

Table 5.1: Recommended schedule for COVID-19 vaccination

Shade boxes – recommended but off-label and requires prescription and written consent preferred; dash = not required

Group	Age[a]	Primary doses 1 and 2[b]	Primary dose 3[c]	Booster dose 1	Booster dose 2
General population	5-11 years	8 weeks apart[b]	-	-	-
	12-15 years	8 weeks apart[b]	-	-	-
	16-17 years	8 weeks apart[b]	-	give from 6 months after previous dose	-
	18-64 years	8 weeks apart[b]	-	give from 3 months after previous dose	can be given age 50 and over years, from 6 months after previous dose
Pregnant women	any age	8 weeks apart[b]	-	as age appropriate	-
Older adults	from 65 years	8 weeks apart[b]	-	give from 3 months after previous dose	recommended, give from 6 months after previous dose
Māori or Pacific People	from 50 years				
Resident of age or disability care facility	from 16 years				
Frontline health care, age care or disability workers	from 16 years	8 weeks apart[b]	-	give from 3 months after previous dose	can be given age 30 years and over, from 6 months after previous dose
Severely immune compromised[c,d]	5–11 years	8 weeks apart[b]	give 8 weeks after dose two[d]	-	
	12–15 years	8 weeks apart[b]		See footnote [e]	
	from 16 years			give 3 months after previous dose	recommended, give from 6 months after previous dose
Additional groups at increased risk of severe COVID-19[f]	from 16 years	8 weeks apart[b]	give 8 weeks after dose two[d]	give 3 months after previous dose	recommended, give from 6 months after previous dose
Following SARS-CoV-2 infection	from age 5 years	Complete vaccination course as above. Defer next dose for 3 calendar months after recovery from acute illness or positive SARS-CoV-2 test if asymptomatic (see sections 5.5.7 and 5.5.10)			

a. mRNA-CV can be given from age 5 years. rCV can be given from age 12 years, if preferred or indicated (note that when these vaccines are given as part of a mixed primary or booster schedule, a prescription may be required for off-label use, and written consent recommended (see sections below).

b. Ideally, give 8 weeks apart. Give mRNA-CV or rCV a minimum of 21 days apart if a shortened schedule is required (eg, due to planned immunosuppression, required for international travel or at very high risk from exposure to COVID-19).

c. Certain individuals with severe immunosuppressive conditions or treatments are eligible for up to five doses (three primary and two booster doses). See section 5.5.8.

d. The timing of this dose also needs to consider current or planned immunosuppressive therapies. If the period of least immunosuppression is less than eight weeks, the vaccination can be given any time from four weeks after dose two. See section 5.5.9.

e. A booster dose may be considered for individuals aged 12–15 years if clinically indicated, this dose will require a prescription. Give 3-6 months after previous dose. See section 5.5.10.

f. Including those with medical condition or living with disability with significant or complex health needs. See section 5.5.10 and Table 5.4 for further groups recommended a second booster dose due to increased risk of severe breakthrough COVID-19.

5.5.1 mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

mRNA-CV (30 µg) for ages from 12 years (purple cap)

All individuals from the age of 12 years are recommended to receive two doses of mRNA-CV given six to eight weeks apart. In situations where the longer interval is not possible (eg, prior to planned immunosuppression, required for urgent international travel or at very high risk from exposure to SARS-CoV-2), give the second dose a minimum of 21 days after first.

Full immunity from the primary course develops from around seven days after the second dose. For booster doses, see section 5.5.10.

mRNA-CV (10 µg) for ages 5 to 11 years (orange cap)

Two doses mRNA-CV (10 µg) given at least 8 weeks apart to children aged from 5 years up to 11 years. In situations where the longer interval is not possible (eg, prior to planned immunosuppression, required for urgent international travel or at very high risk from exposure to SARS-CoV-2), give the second dose a minimum of 21 days after first.

For children who turn 12 years after their first dose, it is recommended to give an age-appropriate vaccine (ie, mRNA-CV (30µg) for the second or subsequent doses, maintaining an eight-week gap between doses.

To date, mRNA-CV has not been approved for use in children aged younger than 5 years in New Zealand. Clinical trials are ongoing in younger age groups.

5.5.2 Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

The preferred vaccine for the Schedule is mRNA-CV, however, adjuvanted rCV can be offered (if not contraindicated, see section 5.6), where available, to individuals aged from 12 years who are contraindicated mRNA-CV or have experienced an adverse reaction to the first dose of mRNA-CV. It can also be offered to individuals who have declined mRNA-CV and would prefer an alternative vaccine. Individuals opting for this vaccine are recommended to discuss the benefit and potential risks of receiving this vaccine with a health professional.

The following gives details of approved and off-label use of rCV.

- A (homologous) primary course two doses of rCV from age 12 years – no prescription is required.
- For a mixed (heterologous) primary course when a different COVID-19 vaccine dose was given previously – a further primary dose with rCV (if considered appropriate by a clinician, see section 5.5.10) is an off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981).
- Booster dose(s) following any previous COVID-19 vaccine for individuals aged 18 years or older – no prescription required.
- Booster doses are not yet approved for ages 12–17 years.

Written consent is recommended when a prescription for any doses is required.

5.5.3 Breastfeeding

As with all schedule vaccines, there are no safety concerns about giving mRNA-CV to those lactating. There is limited data to date around the use of adjuvanted rCV in lactation.

5.5.4 Pregnancy

Anyone who is pregnant or planning pregnancy is encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy. The risk of an adverse outcomes from COVID-19 infection during pregnancy is significantly higher compared to age-matched non-pregnant adults (see section 5.2.3).[52] International evidence from large quantities of safety surveillance has found no safety concerns with administering mRNA-CV in any stage of pregnancy including no safety concerns of the infant. [111, 112, 113, 114] There is also evidence of antibody transfer in cord blood and breast milk which can offer protection to infants through passive immunity. [87, 115, 116, 117] Infants born to those vaccinated in pregnancy have some protection from COVID-19-associated hospitalisation for up six months.[118]

Those who are pregnant and have questions or concerns are encouraged to discuss them with their health professional. People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

There are no known safety concerns, but due to limited experience, rCV is not currently recommended for use in pregnancy – see Precautions (section 5.6.2).

For information about booster doses in pregnancy, see section 5.5.10.

5.5.5 Frail elderly individuals

In general, it is recommended that all eligible adults, including the frail and elderly with comorbidities are offered vaccination against COVID-19, if there are no contraindications to its administration (see section 5.6.1), to provide protection for the individual as well as their community.

5.5.6 Individuals receiving cardiology care

It is recommended that all individuals from age 12 years receive two doses of mRNA-CV (30 µg) given at least 21 days apart, preferably six to eight weeks apart. Children aged 5–11 years are recommended two doses of paediatric mRNA-CV (10 µg) given at least eight weeks apart. Pre-existing cardiac conditions, in general, **are not** regarded as precautions or contraindications to vaccination. This includes pre-existing rheumatic heart disease. Note that many cardiac conditions increase the risk from COVID-19 disease. Those with a history of pericarditis or myocarditis, unrelated to mRNA-CV, can have the vaccination if the condition is completely resolved, (ie, no symptoms and no evidence of ongoing cardiac inflammation). See section 5.6.2 for those who have myocarditis associated with mRNA-CV.

For those with a history of myocarditis and pericarditis related to mRNA-CV, seek specialist immunisation advice on a case-by-case basis to consider an appropriate alternative vaccine (eg, rCV from age 12 years) or no further vaccination, and about timing of further doses.

5.5.7 Vaccination following SARS-CoV-2 infection

Vaccination should be offered regardless of an individual's history of symptomatic or asymptomatic SARS-CoV-2 infection. As the duration of protection post infection is currently unknown, vaccination is recommended. Although, there are no specific safety concerns around giving mRNA-CV to individuals with a history of SARS-CoV-2 infection or symptomatic COVID-19, those who have had recent infection can experience more systemic reactogenicity after the first dose of mRNA-CV (see section 5.7.1).[119] Viral or serological testing is not required before vaccination.

A person aged from 5 years who has had prior SARS-CoV-2 infection is recommended to complete the full vaccination course of mRNA-CV (or another COVID-19 vaccine, as available). In these individuals, vaccination is recommended to be continued from three calendar months after recovery from acute illness, or three months from the first confirmed positive test if asymptomatic. This applies to any dose of the primary course or booster doses, as age appropriate. Based upon clinical discretion, where the individual is at high risk of severe disease from reinfection and has not completed the full course, vaccination can be delivered sooner than three months after SARS-CoV-2 infection and completed with the recommended spacing between doses.

For all other vaccines, vaccination can commence as soon as the individual is no longer acutely unwell and when cleared to leave isolation.

5.5.8 Individual with immunodeficiencies or receiving immunosuppressive agents

There are no safety concerns around administering mRNA-CV or rCV to individuals who are immunocompromised and/or receiving immunosuppressive agents. As with other non-live vaccines, the antibody response to these vaccines may be reduced and protection may be suboptimal but, it is likely to be adequate to protect against severe disease. It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointment for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.7).

It is important that all close contacts of immunocompromised individuals aged from 5 years are up to date with immunisations. Close contacts aged from 18 years should also receive a booster dose at least three calendar months after their primary course and those aged 16–17 years should receive a booster dose at least six months after their primary course. For booster doses, see section 5.5.10.

Individuals who are severely immunocompromised

A third primary dose of mRNA-CV (10 µg or 30 µg, as age-appropriate) is indicated for certain individuals aged from 5 years who are severely immunocompromised who are likely to have not responded adequately to the first two doses. Serology is not recommended. This third primary dose is distinct from the booster dose (for booster doses see section 5.5.10).

Preferably, this third dose should be administered at least eight weeks after the second dose. However, the timing also needs to consider current or planned immunosuppressive therapies. If the period of least immunosuppression is less than eight weeks, the vaccination can be given any time from four weeks after dose two. Where possible, delay the third dose until two weeks after the period of immunosuppression (in addition to the clearance time-period of therapeutic). If this is not possible, consider vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.

These additional doses are currently considered off label and can only be offered by an authorised prescriber with informed, preferably written, consent (under regulation s25 of the Medicines Act 1981). This is under review with Medsafe. For further guidance see **health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance**.

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then rCV may be considered for those aged from 12 years (if not contraindicated). This also requires prescription and written consent is recommended. It is recommended to seek advice from IMAC.

Table 5.2 provides guidance on types of immunocompromise for which a third primary dose is recommended. For further information on corticosteroid indicative dosages

and examples of non-corticosteroid agents considered immunosuppressive, see section below and Table 5.3.

Table 5.2: Individuals (aged 5 and older) with severe immunocompromise recommended to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age-appropriate)

Note: This list is not exhaustive but provides guidance on scenarios where a third primary dose is recommended. There is variation between individuals in response to immunosuppressive or immunomodulating therapy**. Clinicians may use their judgement** for conditions or medications that are not listed here that are associated with severe immunocompromise.

Eligible group / indication	Treatments or health status
Individuals with primary or acquired immunodeficiency states at the time of vaccination	
Acute and chronic leukaemia and clinically aggressive lymphomas (including Hodgkin's lymphoma)	under treatment, or within 12 months of achieving cure or remission
Chronic lymphoproliferative disorders, including haematological malignancies[a] and plasma cells dyscrasias	under specialist follow up
Active HIV infection / AIDS	current CD4 count <200 cells/µl
Primary or acquired cellular and combined immune deficiencies	lymphopenia (<1,000 lymphocytes/µl) or functional lymphocyte disorder.
Allogenic or autologous haematopoietic stem cell transplant	received in previous 24 months or received >24 months ago but had ongoing immunosuppression or graft-versus-host disease.
Persistent agammaglobulinaemia due to primary immunodeficiency and secondary to disease/therapy	IgG <3 g/L
Individuals on, or recently on, immunosuppressive therapy at the time of vaccination	
Following a solid organ transplant	receiving therapy
B cell depleting biologic therapy, including rituximab	receiving or received therapy in the previous 6 months
Biologics or targeted therapy[b] for autoimmune or autoinflammatory disease	received within the previous 3 months
Immunosuppressive cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication	received within the previous 6 months

Continued overleaf

Eligible group / indication	Treatments or health status
Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination	
High-dose or long-term moderate dose corticosteroids (for indicative dosages, see below)	for more than a week in the month before vaccination
For select immunosuppressant drugs[b,c]	in previous 3 months
Certain combination therapies at where cumulative effect is severely immunosuppressive, as determined by clinical judgment	in previous 3 months
Individuals receiving long term haemodialysis or peritoneal dialysis	

a. Such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias. **Note** this list is not exhaustive but provides an indication of conditions where an individual is recommended to receive a third primary dose.

b. For examples, see Table 5.3

c. Excluding hydroxychloroquine, sulfasalazine, or mesalazine, when used as monotherapy.

Individuals receiving corticosteroids

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory disease who are receiving or have received high dose or long-term moderate doses of corticosteroids prior to vaccination, for example:

- high dose – equivalent to at least 20 mg prednisolone per day for more than ten days, in previous month
- moderate dose – equivalent to at least 10 mg prednisolone per day for more than four weeks, in previous three months
- also includes for those who received high dose corticosteroids for any reason – equivalent to at least 40 mg per day for more than a week, in the previous month.

Individuals for whom third primary dose **is not** routinely recommended include those who require:

- brief corticosteroid therapy, for example for asthma, chronic obstructive pulmonary disease or COVID-19 – equivalent to 40mg or less prednisolone per day
- low locally acting corticosteroids, inhaled or topical
- replacement corticosteroid treatment for adrenal insufficiency.

Clinical judgement is required to determine the level of immunosuppression and these dosages are only indicative examples. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

Individuals receiving non-corticosteroid immunomodulatory agents

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory diseases who were receiving or had received immunosuppressive therapy prior to primary COVID-19 vaccination. Indicative examples are given in Table 5.3. Clinical judgement is required to determine the level of immunosuppression. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

Table 5.3: Examples of non-corticosteroid immunosuppressant therapies for which a third primary dose of mRNA-CV is recommended or not routinely recommended

Clinicians may use their judgement for conditions or medications that are not listed here that are associated with severe immunocompromise and in some cases based on dosages or combinations of therapies

Examples of non-corticosteroid agents for which a third dose is recommended	
Agent	**Example**
Mycophenolate, methotrexate, leflunomide, 6-mercaptopurine	
Thiopurines	azathioprine
Alkylating agents	cyclophosphamide
Systemic calcineurin inhibitors	cyclosporin, tacrolimus
BTK inhibitors	ibrutinib
JAK inhibitors	ruxolitinib
Anti CD20 antibodies	rituximab, obinutuzumab, ocrelizumab
Sphingosine 1-phosphate receptor modulators	fingolimod
Anti-CD52 antibodies	alemtuzumab
Anti-complement antibodies	eculizumab
Anti-thymocyte globulin	

Continued overleaf

Examples of non-corticosteroid agents[a] for which third primary dose is not routine recommended	
Agent	**Example**
Anti-integrins	natalizumab
Anti-TNF-α antibodies	infliximab, adalimumab, etanercept
Anti-IL-1 antibodies	anakinra
Anti-IL-6 antibodies	tocilizumab
Anti-IL-17 antibodies	secukinumab
Anti-IL-4 antibodies	dupilumab
Anti-IL-23 antibodies	ustekinumab

a. For immune checkpoint inhibitors see section 4.3.2

5.5.9 Revaccination

Individuals from age 5 years who have undergone haematopoietic stem cell transplantation since their first course can be revaccinated with a full (three dose) primary course of a COVID-19 vaccine, plus booster as age appropriate (preferably with age-appropriate mRNA-CV).

Based on clinical discretion, if all scheduled doses have been completed prior to commencement of chemotherapy or solid organ transplant, a single further dose of mRNA-CV can be given from the age of 5 years.

5.5.10 Booster doses

All individuals aged 16 years and over are recommended to receive a booster dose. For those aged 18 years and above, a single dose of mRNA-CV (30 µg) is recommended to be given at least three calendar months after completion of the two-dose primary course. In cases where confirmed SARS-CoV-2 infection occurs between dose two of the primary course and booster dose, give a single dose of mRNA-CV from three calendar months after recovery from COVID-19, or at least three calendar months from the first confirmed positive PCR test if asymptomatic (see section 5.5.7).

For those aged 16–17 years, a single dose of mRNA-CV (30 µg) is recommended to be given at least six months after completion of the primary course. If SARS-CoV-2 infection occurs later than three months after primary course, give a booster dose at least three calendar months after recovery from acute illness or positive test in asymptomatic (see section 5.5.7) to provide the longest gap.

A booster dose is particularly recommended for individuals most at risk of exposure to SARS-CoV-2 or most at risk of serious COVID-19, as outlined below.

- Frontline health care workers, particularly those most likely to be exposed to COVID-19 in the community or in regions where further risk of spread of SARS-CoV-2 is high.

- All individuals who are aged 65 years or over.
- Māori and Pacific People due to a greater risk of severe disease, especially if aged from 50 years or over.
- Anyone aged 16 years or over at increased risk of severe COVID-19:
  - eligible for funded influenza vaccine, including pregnancy (See Booster doses in pregnancy)
  - disabled or caring for a person with a disability
  - severely obese (BMI ≥40 kg/m^2)
  - hypertension, requiring two or more medications to control
  - in a custodial setting
  - have been diagnosed with a severe mental illness (including schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder, and adults currently accessing secondary and tertiary mental health and addiction services).

Individuals aged from 16 years who are severely immunocompromised who received a third primary dose are recommended to also be given the booster dose at least three calendar months later, taking in consideration current or planned immunosuppressive therapies. A booster dose given prior to six months after the primary course to those aged 16–17 years is considered off-label and requires a prescription.

A booster dose is not currently approved as part of the COVID-19 vaccination programme for individuals aged under 16 years. A booster dose can be considered for those aged 12–15 years who are at higher risk of severe COVID-19, to be given from three to six months after completing the primary course. This is an off-programme use requiring a prescription and written consent is recommended. For underlying health conditions that increase risk for severe COVID-19 in children see **starship.org.nz/guidelines/covid-19-disease-in-children/**. This list is not exhaustive and clinicians may use their judgement for conditions that are not listed.

Although mRNA-CV is the preferred vaccine, rCV can also be used as a booster dose, if not contraindicated for those aged from 18 years. A prescription is not required for this use.

Certain individuals with severe immunosuppression are recommended to receive three primary doses with the third dose given at least eight weeks after dose two (see section 5.5.8; this is not the same as booster doses).

Second booster dose

Due to the risk from waning protection, notably during the winter season, certain individuals aged from 16 years who are at highest risk from severe breakthrough COVID-19 are recommended to have a second booster dose of mRNA-CV to be given at least six months since their previous booster dose. These include:

- people of Māori or Pacific ethnicities aged 50 years and over
- all other individuals aged 65 years and over
- residents aged 16 years or over living in aged care and disability care facilities

- severely immunocompromised people who were eligible to receive a third primary dose and fourth dose as a first booster (see section 5.5.8; ie, this group is eligible for five doses)
- individuals aged from 16 years who have certain medical conditions (see Table 5.4) that increase the risk of severe breakthrough COVID-19 illness.
- individuals aged from 16 years who live with disability with significant or complex health needs or multiple comorbidities (see Table 5.4).

A second booster dose is also available for:

- all people aged 50 years and over
- health care, aged care and disability workers aged 30 years and over.

As with previous doses, a second booster dose, if due, should be postponed for three months after SARS-CoV-2 infection. Ideally, to be given from six months after previous vaccination or three months after infection whichever is the longest time since exposure to SARS-CoV-2 antigens. Clinical discretion can be applied when considering vaccination prior to 3 months after infection. This may be appropriate for those individuals considered to be at high risk of severe disease from COVID-19 re-infection.

If indicated or preferred, rCV can be given as a second booster dose from age 18 years instead of mRNA-CV.

Table 5.4: Additional groups recommended for a second booster dose of COVID-19 vaccine (adapted from ATAGI)

People in these groups are likely to have ongoing increased risk of severe COVID-19 even after primary vaccination. These examples are not exhaustive, and providers may include individuals with conditions similar to those listed below, based on clinical judgement.

Category	Examples
Immunocompromising conditions	including people living with HIV infection
Cancer	Non-haematological cancer including those diagnosed within the past 5 years or on chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy (active treatment or recently completed) or with advanced disease regardless of treatment. Survivors of childhood cancer.
Chronic inflammatory conditions requiring medical treatment with disease-modifying anti-rheumatic drugs (DMARDs) or immune-suppressive or immunomodulatory therapies.	Systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, ulcerative colitis, and similar who are being treated.

Continued overleaf

Chronic lung disease	Chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and severe asthma (defined as requiring frequent hospital visits or the use of multiple medications).
Chronic liver disease	Cirrhosis, autoimmune hepatitis, non-alcoholic fatty liver disease, alcoholic liver disease.
Severe chronic kidney disease (stage 4 or 5)	
Chronic neurological disease	Stroke, neurodegenerative disease (eg, dementia, motor neurone disease, Parkinson's disease), myasthenia gravis, multiple sclerosis, cerebral palsy, myopathies, paralytic syndromes, epilepsy.
Diabetes mellitus requiring medication	
Chronic cardiac disease	Ischaemic heart disease, valvular heart disease, congestive cardiac failure, cardiomyopathies, poorly controlled hypertension, pulmonary hypertension, complex congenital heart disease.
People with disability with significant or complex health needs or multiple comorbidities which increase risk of poor outcome from COVID-19	Particularly those with trisomy 21 (Down Syndrome) or complex multi-system disorders.
Severe obesity with BMI ≥40 kg/m^2	
Severe underweight with BMI <16.5 kg/m^2	

Booster doses in pregnancy

Pregnant women aged from 16 years can receive a booster dose of mRNA-CV at any stage of pregnancy (from three calendar months after a primary course if aged 18 years or over, or from six months if aged 16–17 years). Although the use of booster doses in pregnancy is limited to date, as with the primary course, it is expected to be safe and effective. If the full primary course has been given in pregnancy, a booster can be given as time-appropriate before or after delivery, and at least three calendar months after completion of their primary course. Those who are pregnant are encouraged to discuss timing of a booster dose with their health professional. A booster dose given earlier than six months after the primary course to those aged 16–17 years, is considered off-label and requires a prescription and written consent is recommended. Second booster doses are not currently recommended to be given during pregnancy to healthy individuals without medical conditions or who do not meet other criteria given above (see Second booster dose and Table 5.4).

5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

5.6.1 Contraindications

Vaccination with mRNA-CV or rCV is contraindicated for individuals with a history of anaphylaxis to any component or previous dose the same vaccine.

5.6.2 Precautions

A definite history of immediate allergic reaction to any other product is considered as a precaution but not a contraindication to vaccination with COVID-19 vaccines (mRNA-CV or rCV). A slightly increased risk of a severe allergic response in individuals who have had a previous anaphylaxis-type reaction needs to be balanced against the risk of SARS-CoV-2 exposure and severe COVID-19. These individuals can still receive a COVID-19 vaccines, if not contraindicated, and observation extended to 30 minutes after vaccination in health care settings, where anaphylaxis can be immediately treated with adrenaline.

When vaccinating an elderly person who has an intercurrent or comorbid condition, ensure they are stabilised or as well as possible before they have the vaccine. Following vaccination ensure good hydration and careful management of potential systemic adverse events, such as fever. It is advisable for them to be with someone else for 24 hours after receipt of the vaccine to help manage potential adverse events.

Myocarditis or pericarditis

If myocarditis, myopericarditis or pericarditis occurs after a dose of mRNA-CV or rCV, defer further doses of COVID-19 vaccination. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccine or no further vaccination, and about timing for further primary or booster doses. Vaccination is not recommended for anyone with current active cardiac inflammation.

Pregnancy

There is insufficient safety data to recommend rCV for use during pregnancy. Those who are pregnant are advised to discuss the benefit and potential risks of receiving this vaccine in pregnancy with their health professional. There are no safety concerns should it be given inadvertently in pregnancy.

5.7 Potential responses and AEFIs

5.7.1 Potential responses

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Commonly reported responses to mRNA-CV (30 µg) during clinical trials and post-licensure surveillance are injection-site pain, headache, dizziness and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, chest discomfort, joint pain, nausea and axillar lymph node swelling. These occurred most often after dose two and in younger adults (aged 18–55 years), and within one or two days of vaccination. Most are mild or moderate in severity and are self-limiting.[75, 120] Analgesia, such as paracetamol or ibuprofen (as appropriate), can be taken for pain and discomfort following vaccination. It is advisable to limit vigorous exercise if feeling unwell.

During clinical trials, the responses in children aged 5–11 years given paediatric formulation mRNA-CV (10 µg) were similar to those seen for the adult formulation mRNA-CV (30 µg) in those age 16–25 years. Generally, reactions were mild to moderate and short-lived. Pain at injection site was commonly reported (by over 70 percent) after dose one and two. Overall fewer children reported systemic reactions than seen after the 30 µg dose in adults, with fever, fatigue, headache, chills and muscle ache as the most common and more frequent after the second dose.[74] These responses were mirrored in reports to VAERS and V-safe after 8.7 million doses given routinely to children in the US.[121]

See chapter 2 (section 2.3.3) for immunisation-stress related responses (ISRR).

Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

The most reported responses to rCV in clinical trials were injection-site tenderness and pain, headache, fatigue, myalgia, malaise, arthralgia, nausea and vomiting. These reactions were more common after dose two, lasting for one to three days, and occurred at higher incidence in younger age groups (less than 65 years).[91]

Breast screening and CT scans

Transient unilateral axillary adenopathy, a known response to vaccination, was particularly noted following vaccination with mRNA-CV due to the scale of the roll-out and age groups being immunised. Early estimates suggest that 12–16 percent of vaccine recipients experience axillary adenopathy after vaccination with mRNA-CV, starting one or two days after vaccination and which can persist for several weeks.[122, 123] Lymphadenopathy has also been commonly reported after booster doses of mRNA-CV.[124]

When attending breast screening and mammography appointments, it is recommended that individuals advise the radiographer or doctor that they have received a COVID-19 vaccine recently. It is advised to monitor any lymph node changes that persist for longer than six weeks after vaccination.[122]

Likewise, individuals undergoing FDG PET/CT scans for cancer screening are advised to inform the radiologist or their oncologist that they have been recently vaccinated, or, if possible, to have COVID-19 vaccination at least two weeks before a scheduled scan or as soon as possible afterwards. Treatment should not be delayed.

5.7.2 AEFIs

Adverse events following immunisation (AEFIs) with the COVID-19 vaccines are being closely monitored during clinical trials and by post marketing surveillance. A dedicated COVID-19 vaccine AEFI reporting tool is available online from CARM (see section 1.6.3). Medsafe reports weekly on the AEFI reported to CARM after COVID-19 vaccinations (see **medsafe.govt.nz/COVID-19/vaccine-report-overview.asp**).

A list of adverse events of special interest (AESIs), including those previously associated with immunisation in general and with the particular vaccine platforms, was created by Safety Platform for Emergency Vaccines (SPEAC) in collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) and based on existing and new Brighton Collaboration case definitions. For further information, see **brightoncollaboration.us/covid-19**. Global pharmacovigilance and active safety monitoring systems continue to watch for both AESI and unexpected AEFI.

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Overall, no AESI signals were detected by the Vaccine Safety Datalink in the US up to 21 days after vaccination, following the administration of over 13 million doses of mRNA-CV (Comirnaty), however, subgroup analyses did find mRNA-CV to be associated with a slight increase in myocarditis and pericarditis in younger people (aged under 30 years).[125, 126]

Preliminary phase II/III clinical trial safety data reported lymphadenopathy in 64 (0.3%) vaccine recipients and six (<0.1%) placebo recipients (follow-up of up to 14 weeks after second dose of a subset of 18,860 participants who received at least one dose of mRNA-CV). Four vaccine-related adverse events were recorded (namely, shoulder injury related to vaccine administration, lymphadenopathy local to injection site, paroxysmal ventricular arrhythmia and right leg paraesthesia). No deaths were related to either the vaccine or the placebo.[75] During clinical trial follow-up to 1 February 2021, acute peripheral facial paralysis (Bell's palsy) was reported by four vaccinated participants and none in the placebo group.[127] No safety signal has been detected for this condition as an AESI,[128] and safety monitoring is ongoing.

No vaccine-related severe adverse events were seen during the phase II/III clinical trial of mRNA-CV (10 µg) in 1,518 children aged 5–11 years. Lymphadenopathy was reported in ten (0.9 percent) of mRNA-CV (10 µg) recipients. Rashes, with no consistent

pattern, considered related to the vaccination were observed in four participants; these were mild and self-limiting with typical onset seven or more days after vaccination. No differences were apparent in vaccine safety between the children who had baseline evidence of previous SARS-CoV-2 infection.[74] As of 19 December 2021 following administration of approximately 8.7 million doses of mRNA-CV (10 µg) in children aged 5–11 years in the US, the majority of reports to VAERS (97.6 percent) were non-serious and 2.4 percent were serious. The most common non-serious reports were due to vaccine administration errors. Of the serious reports, 11 verified cases of myocarditis were reported to VAERS but no chart-confirmed myocarditis cases were reported through the Vaccine Safety Datalink in this age group.[121] Post-licensure surveillance is ongoing internationally.

Myocarditis and pericarditis

A small increase in incidence of myocarditis, myopericarditis and pericarditis has been observed following the second dose of mRNA-CV vaccination (40.6 cases per million doses in young males and 4.2 cases per million in young females, aged 12–29 years, decreasing to 2.4 and 1.0 per million, respectively, in men and women aged over 30 years).[129] Most cases occur within 14 days of vaccination typically with full recovery after standard treatment and rest.[130, 131] A review of clinical records in the US observed the median time to onset for myocarditis was 3.5 days (interquartile range 3.0–10.8 days) after vaccination and a median of 20 days (range 6.0–41 days) for pericarditis.[131] Wider spacing between doses (ie, eight weeks) has been shown to significantly lower the risk of myocarditis in young adults in Canada.[132]

Myocarditis and pericarditis are uncommon conditions considered to be associated with viral infection, including COVID-19. Recently vaccinated individuals should seek immediate medical attention if they experience new onset of (acute and persisting) chest pain, shortness of breath or arrhythmia (palpitations). Diagnosis is based on elevated troponin, C-reactive protein and electrocardiogram and/or MRI findings. Report all suspected cases to CARM as Medsafe continues to monitor this AEFI closely. Defer further doses of mRNA-CV if myocarditis or pericarditis occurs after vaccination. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccination option, and timing for further primary or booster doses (see section 5.6.2).

Anaphylaxis

Following approval for use in the US, the VAERS detected 47 cases of anaphylaxis after administration of just under ten million doses (around five cases per million doses) mRNA-CV (Pfizer/BioNTech). The median interval to symptom onset was ten minutes (range <1–1140 minutes), almost 90 percent occurred within 30 minutes of vaccination.[133] All were successfully treated with adrenaline. See section 5.6 for contraindications and precautions.

Frail elderly

A follow-up, after approximately two million doses of mRNA-CV were delivered through long-term residential care facilities to elderly and frail residents in the US found no increase in deaths post vaccination.[43] Deaths were to be expected and consistent with the all-cause mortality rate and causes of death for these individuals,

who have multiple comorbidities, declining health and require end-of-life care.[43] There are no added safety concerns about the use of this vaccine in the elderly.[134]

History of Guillain-Barré Syndrome

There is no evidence of a higher rate of reporting of Guillain-Barré syndrome (GBS) following COVID-19 vaccination in individuals who have previously had GBS. Vaccination with mRNA-CV is preferred.

Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

Uncommon AEFI reported during clinical trials were lymphadenopathy, hypertension (observed in 1 percent of older adults for three days following vaccination), rash and injection site pruritus. One case of myocarditis was observed in a clinical trial occurring three days after second dose was deemed by the independent safety monitoring committee to most likely be viral myocarditis. No episodes of anaphylaxis were reported.[91] Three cases of myocarditis or myopericarditis and two cases of pericarditis were reported during two clinical trials (one case in placebo group) and in two cross-over studies. Although a causal relationship to the vaccine could not be confirmed, the European Medicines Agency listed heart inflammation as a potential risk.[124]

In a clinical trial, when rCV was given as a second dose after a first dose of mRNA-CV, similar systemic responses were observed to those given mRNA-CV as a second dose and local reactions were generally less frequent.[109]

A slightly increased incidence of local adverse events such as injection site tenderness and pain were reported during a clinical trial of rCV given concurrently with seasonal influenza vaccine (65 percent rCV plus influenza vs 53 percent for rCV alone of participants reported tenderness). This component of a randomised, placebo controlled clinical trial included 201 people who received rCV and QIV concurrently and 16 participants aged 65 years or older who received adjuvanted TIV.[89]

5.8 Public health measures

There is an ongoing COVID-19 pandemic globally. New Zealand has implemented strict pandemic response control measures to limit the spread of SARS-CoV-2 in the community as described at **covid19.govt.nz**.

All individuals with symptoms of COVID-19 are expected to self-isolate, seek medical advice and be tested for infection. Rapid antigen testing and nasopharyngeal PCR testing continue to be fundamental components of the public health measures.

Immunisation using COVID-19 vaccines is part of the public health strategy aimed at reducing the risk of severe disease to minimise the burden on the health care system and slowing the rate of transmission during community outbreaks.

5.8.1 Post-exposure prophylaxis and outbreak control

Currently, there is no information on the use of COVID-19 vaccines for post-exposure prophylaxis or outbreak control. Vaccination is available to everyone in New Zealand aged 5 years or older.

5.9 Variations from the vaccine data sheet

Spacing of at least eight weeks between first and second dose is recommended for mRNA-CV and rCV. This differs from the data sheets which recommend an interval of at least 21 days.

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6 Diphtheria

Key information

Mode of transmission	Contact with respiratory droplets or infected skin of a case or carrier or, more rarely, contaminated objects.	
Incubation period	Usually 2–5 days, occasionally longer.	
Period of communicability	Variable; usually 2 weeks or less, seldom more than 4 weeks. Carriers may shed for longer. Effective antimicrobial therapy promptly terminates shedding.	
Funded and available vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation) for pertussis protection	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or specialist baby care units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth for pertussis protection	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	
Vaccine effectiveness	Protection of 87–98 percent has been demonstrated using population-based analysis. Immunised cases have been shown to have less severe disease To prevent major community outbreaks at least 70 percent of the childhood population must be immune to diphtheria	
Public health measures	All cases of diphtheria must be notified immediately on suspicion (see section 6.8).	

6.1 Bacteriology

Diphtheria is a serious, often fatal, toxin-mediated disease caused by *Corynebacterium diphtheriae*, a non-sporulating, non-encapsulated, gram-positive bacillus. Rarely, it may also be caused by other toxin-carrying Corynebacteria species, such as *Corynebacterium ulcerans*. Both toxigenic and non-toxigenic strains can occur during outbreaks, during which non-toxigenic strains can convert to toxigenic strains by infection with *tox*-gene containing β-corynebacteriophage.[1]

6.2 Clinical features

Classic diphtheria characteristically involves membranous inflammation of the upper respiratory tract with involvement of other tissues, especially the myocardium and peripheral nerves. The organism itself is rarely invasive, but a potent exotoxin, diphtheria toxin, is produced by some toxigenic strains that causes tissue damage through local and systemic actions. There is also a cutaneous form of diphtheria, which is typically less severe. The detection of either *C. diphtheriae* or *C. ulcerans* is notifiable to the medical officer of health, and the isolates should be referred to the Institute of Environmental Science and Research (ESR) for toxin detection. Non-toxigenic diphtheria strains can circulate but these do not secrete diphtheria toxin and are not associated with disease nor preventable by immunisation with diphtheria toxoid vaccine.

Transmission is by respiratory tract droplets, or by direct contact with skin lesions or contaminated articles. Cutaneous toxigenic diphtheria is more efficiently transmitted than respiratory toxigenic diphtheria and can cause respiratory infection in others.[2, 3] Humans are the only known host for diphtheria, and the disease is usually spread by close personal contact with a case or carrier, or occasionally by fomites or food. The disease remains communicable for up to four weeks after infection, but carriers of *C. diphtheriae* may continue to shed the organism and be a source of infection for much longer.

Classic diphtheria has a gradual onset after an incubation period of two to five days. Symptoms and signs may be mild at first, but progress over one to two days with the development of a mildly painful tonsillitis or pharyngitis with an associated greyish membrane. Diphtheria should be suspected particularly if the membrane extends to the uvula and soft palate. The nasopharynx may also be obstructed by a greyish membrane, which leaves a bleeding area if disturbed. The breath of a patient with diphtheria has a characteristic mousy smell.

The major complication of diphtheria is respiratory obstruction, although most deaths result from the effects of diphtheria toxin on various organs. Of importance is the toxicity to the myocardium (leading to myocarditis and heart failure), peripheral nerves (resulting in demyelination and paralysis), and kidneys (resulting in tubular necrosis). The neuropathy begins two to eight weeks after disease onset, while the myocarditis can be early or late. Neurological complications occur in 15–20 percent of cases and can cause paralysis up to two months after disease onset.[1]

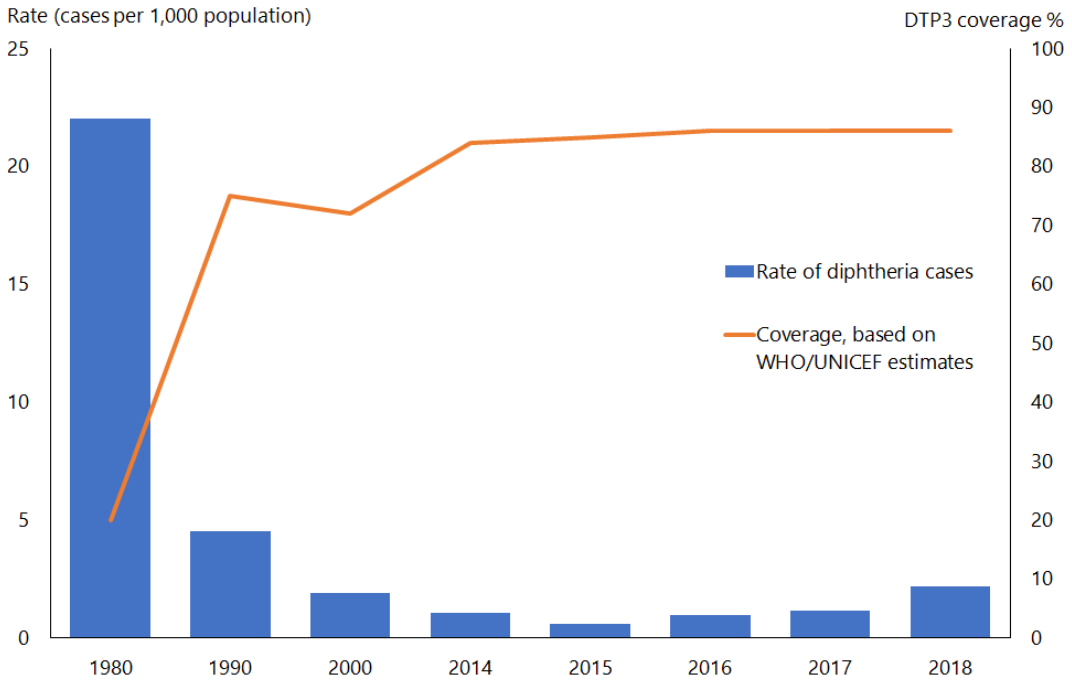
6.3 Epidemiology

6.3.1 Global burden of disease

In the pre-immunisation era, diphtheria was predominantly a disease of children aged under 15 years; most adults acquired immunity without experiencing clinical diphtheria. Asymptomatic carriage was common (3–5 percent) and important in perpetuating both endemic and epidemic diphtheria. The global incidence of diphtheria dropped dramatically during the 20th century. Immunisation played a large part but may not be wholly responsible for this reduction (see Figure 6.1). The estimated total number of diphtheria cases globally fell from just under 100,000 cases in 1980 to around 4,500 in 2015, but increased to over 16,500 cases in 2018.[4]

Diphtheria remains a significant health issue in countries with low immunisation coverage. Around 14 percent of children globally are not fully immunised against diphtheria and all countries have pockets of unvaccinated children.[5] Most cases of diphtheria reported during 2011–2015 were in South-East Asia, in particular India and Indonesia, but under-reporting has been shown for Africa and Eastern Mediterranean regions.[5]

Figure 6.1: Diphtheria global annual reported cases and DTP3* immunisation coverage, 1980–2018



* Three doses of diphtheria, tetanus and pertussis vaccine in infancy.

Source: WHO/UNICEF as of December 2019

Immunisation leads to the disappearance of circulating toxigenic strains, but non-toxigenic strains infected with the β-corynebacteriophage can become toxigenic during outbreaks. The return of epidemic diphtheria is a real threat when herd immunity is insufficient, as happened in the states of the former Soviet Union during 1990–1997. Factors contributing to this epidemic included a large population of susceptible adults, decreased childhood immunisation, suboptimal socioeconomic conditions and high population movement.[6]

Most reported cases were unvaccinated or incompletely vaccinated adolescents and adults (40 percent of cases were age over 15 years in high-incidence countries and 66 percent in low incidence countries) due to historically low coverage and a lack of booster doses to maintain protection in adolescents and adults. This vulnerability in adults was highlighted by a recent outbreak in Indonesia.[7] However, continuing endemic cutaneous diphtheria in indigenous communities has been reported from the US, Canada and Australia. Small diphtheria outbreaks occurring in high-income countries often appear to be caused by non-immune individuals travelling to endemic countries.[1]

The overall case fatality rate for clinical diphtheria is 5–10 percent, with higher death rates (up to 20 percent) among persons younger than 5 and older than 40 years. The case-fatality rate for diphtheria has changed very little during the last 50 years.[8]

Diphtheria remains rare in high-income countries such as New Zealand due to high coverage with diphtheria toxoid-containing vaccines.

6.3.2 New Zealand epidemiology

Diphtheria infection was common in New Zealand until the 1960s. The last case of toxigenic respiratory diphtheria was reported in 1998.[9] Low numbers of cutaneous toxigenic diphtheria are regularly notified in New Zealand: two confirmed cases were notified in 2015 in refugees from Afghanistan[10] and one case was notified in 2019 in an immunised child from Papua New Guinea.

Non-toxigenic *C. diphtheria* isolates continue to be identified; for example, there were seven throat and 41 cutaneous non-toxigenic isolates and seven from other sites in 2019 (ESR, 8 June 2020). These strains do not cause diphtheria disease.

Travel to endemic countries is an important risk factor for infection, but transmission within New Zealand can occur to susceptible contacts of cutaneous cases. Tattooing practices in the Pacific Islands have also been implicated in outbreaks in New Zealand.[11]

The 2005–2007 National Serosurvey of Vaccine Preventable Diseases found that 61 percent of 6–10-year-olds, 77 percent of 11–15-year-olds, 71 percent of 16–24-year-olds, 48 percent of 25–44-year-olds and 46 percent of ≥45-year-olds had presumed protective levels of diphtheria antibody.[12] The decline apparent with age suggests there is likely to be a large and increasing pool of older adults who may be susceptible to diphtheria in New Zealand, despite the introduction of adult tetanus and diphtheria (Td) vaccination in 1994.

For details of diphtheria notifications, refer to the most recent ESR notifiable disease annual tables and reports (available at **https://surv.esr.cri.nz/surveillance/surveillance.php**).

6.4 Vaccines

Diphtheria toxoid is prepared from cell-free purified diphtheria toxin treated with formaldehyde. It is a relatively poor immunogen, which, to improve its efficacy, is usually adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide.

Diphtheria toxoid is only available as a component of combination vaccines (in New Zealand as DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap).

See Appendix 1 for the history of diphtheria toxoid-containing vaccines in New Zealand.

6.4.1 Available vaccines

Funded diphtheria vaccines

The diphtheria toxoid-containing vaccines funded as part of the Schedule are as follows.

DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine, which contains:

- not less than 30 IU of diphtheria and 40 IU of tetanus toxoids and three purified Bordetella pertussis antigens (25 µg of pertussis toxoid; 25 µg of filamentous hemagglutinin; 8 µg of pertactin, a 69 kilodalton outer membrane protein) adsorbed onto aluminium salts
- three types of inactivated polio viruses: 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett)
- 10 µg of purified major surface antigen (HBsAg) of the hepatitis B virus (HBV)
- 10 µg of purified polyribosylribitol phosphate (PRP) capsular polysaccharide of *Haemophilus influenzae* type b (Hib), covalently bound to 20–40 µg tetanus toxoid, adsorbed onto aluminium salts
- lactose, sodium chloride, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate, which are also present as other components or as trace residuals from the manufacturing process.

DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine, in the same quantities as for Infanrix-hexa above. Other components and residuals include sodium chloride, aluminium salts, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate.

Tdap (Boostrix, GSK): a smaller adult dose of diphtheria toxoid and pertussis antigens together with tetanus toxoid. Tdap contains not less than 2 IU of diphtheria toxoid, not less than 20 IU of tetanus toxoid, 8 µg of pertussis toxoid, 8 µg of filamentous hemagglutinin and 2.5 µg of pertactin, adsorbed onto aluminium salts. Other components and trace residuals include sodium chloride, formaldehyde, polysorbate 80 and glycine.

Other vaccines

Other diphtheria toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

6.4.2 Efficacy and effectiveness

Immunity against toxigenic diphtheria occurs via an antibody-mediated response to the diphtheria toxin and is primarily of the IgG type. Antitoxin antibodies can pass through the placenta to provide passive immunity to the newborn.

Although there are no randomised controlled studies on the efficacy of the vaccine, between 87 and 98 percent protection has been demonstrated using population-based analyses. Immunised cases have been shown to have less severe disease, as highlighted during the outbreak in the former Soviet Union.

Vaccines combining pertussis antigens with diphtheria and tetanus toxoids have been gradually introduced into immunisation schedules throughout the world. Immunogenicity data for these combination vaccines is discussed in section 15.4.2.

Herd immunity

Immunisation is more effective at preventing disease, by neutralising diphtheria toxin, than preventing infection. Herd immunity is created by reducing carriage and transmission from symptomatic patients.[13, 14] To prevent major community outbreaks, it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria.[15, 16] Herd immunity in adults is likely to depend on the size of the reservoir of disease in children.[1] This may explain the control of diphtheria in New Zealand despite historically relatively poor coverage.

Duration of immunity

Diphtheria antitoxin levels decline over time in children after they have received a primary series of vaccines, and a booster dose is required. In countries where diphtheria immunisation is common practice and high coverage rates are achieved, there will be no natural boosting from circulating disease, and antitoxin levels declining with increasing age may result in a susceptible older adult population.[5] WHO identified that adults in countries with long-standing childhood immunisation programmes were likely to be susceptible without booster doses to overcome waning immunity due to lack of exposure to diphtheria. Waning immunity contributed to the high number of cases in adults observed during the outbreak in the former Soviet Union.[17]

Despite apparent immunity gaps, there has been minimal disease in high-income countries, suggesting that the established correlates of seroprotection based on antitoxin levels may not be reliable guides for protection and that other factors may be operating.[18] For example, a high proportion of the adult German population have low antibody levels, indicating susceptibility, yet diphtheria outbreaks have not occurred despite Germany's relative geographical proximity to high rates of disease in the former Soviet Union.[19]

The duration of protection after Tdap boosters is unknown, but the results of an Australian study have shown that five years after the Tdap booster dose, 94.4 percent of adults had seroprotective levels of antibodies against diphtheria, compared with 93.7 percent who received Td vaccine.[20] It has been predicted that 95 percent of the adult population in the US would maintain seroprotection for more than 30 years without requiring further booster doses.[21]

6.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and Tdap should be stored in the dark.

> DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

6.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap vaccine is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap vaccine can be administered simultaneously (at separate sites) with other vaccines or IGs.

6.5 Recommended immunisation schedule

Table 6.1: Immunisation schedule for diphtheria-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
Pregnant women – recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother[a] Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

a Tdap booster during pregnancy is to protect against mother and newborn against pertussis (see section 4.1.2).

6.5.1 Usual childhood schedule

A primary course of diphtheria vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 6.1). A booster is given at age 11 years (school year 7), which includes a pertussis component given as the vaccine Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

6.5.2 Catch-ups for individuals aged 10 years and older

For previously unimmunised individuals aged 10 years and older, a primary immunisation course consists of three doses of a diphtheria toxoid-containing vaccine at intervals of not less than four weeks (see Appendix 2). For children aged under 18 years, a booster dose is recommended at least six months after the third dose.

Children aged under 18 years may receive Tdap (funded from age 7 to under 18 years); adults aged 18 years and older may receive Td (funded) or Tdap (unfunded). Although Tdap and Td are not approved for use (registered) as a primary course, there are expected to be no safety concerns.

6.5.3 Booster doses for adolescents and adults

Studies overseas show that many adults lack protective levels of the antitoxin, and this has led to concern about waning immunity and recommendations for booster doses beyond childhood (see also section 6.3.2). Most authorities recommend maintaining diphtheria immunity by periodic reinforcement using a combined Td vaccine.[1] A single booster dose of Tdap induces seroprotective levels of antibodies to diphtheria and tetanus in virtually all children and adolescents, and in a high proportion of adults and elderly individuals at approximately one month post-vaccination, irrespective of their vaccination history.[22]

Tdap is recommended and funded:

- as a booster dose to all adolescents at school year 7 or age 11 years
- as a booster dose for vaccination of individuals aged 65 years old
- as a single dose for catch-up vaccination of individuals aged 45 years old who have not had four previous tetanus-containing doses.

These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures.

Booster doses before travel

If someone is travelling to an area endemic for diphtheria, or there is another reason to ensure immunity, a booster dose is recommended (but not funded) if it is more than 10 years since the last dose. For website sources on travel vaccines, see Appendix 8.

6.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide pertussis protection from birth (funded when given

any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis (see section 16.5.2).[23]

Tdap vaccine may also be given to pregnant women when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound (see section 20.5.5).[23, 24]

Tdap vaccines can be given to breastfeeding women.[24]

6.5.5 (Re)vaccination

Diphtheria toxoid-containing vaccines are funded for (re)vaccination of eligible patients as follows, including prior to planned or following immunosuppression. See also section 4.3.2.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

6.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

6.6.1 Contraindications

There are no specific contraindications to diphtheria vaccine (as Tdap or DTaP), except for anaphylaxis to a previous dose or any component of the vaccine.

Most other cases of hypersensitivity that have been reported for tetanus-containing vaccines were in individuals who have had an excessive number of booster injections outside the guidelines noted above (see section 20.6.2).

6.6.2 Precautions

See section 15.6.2 for precautions for pertussis-containing vaccines and section 20.6.2 for precautions for tetanus-containing vaccines.

6.7 Potential responses and AEFIs

Despite the widespread use of diphtheria toxoid, the 1994 Institute of Medicine review of vaccine reactions did not identify any reaction for which the evidence favoured or established a causal relationship with diphtheria toxoid.[25] However, local and systemic reactions do occur with diphtheria toxoid-containing vaccine, especially when the infant vaccine is used in older children and adults. Mild discomfort or pain at the injection site persisting for up to a few days is common.[24]

See also sections 15.7 and 20.7 for potential responses and AEFIs to DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap.

6.8 Public health measures

It is a legal requirement that all cases of diphtheria be notified immediately on suspicion to the local medical officer of health.

Alert the laboratory that the sample is from a suspected case of diphtheria. All isolates of *C. diphtheriae* and *C. ulcerans* are notifiable until toxigenicity is determined, including cutaneous isolates. If the isolate is determined to be nontoxigenic (ie, does not have the ability to produce diphtheria toxin), the case should be denotified.

All patients with *C. diphtheriae* or *C. ulcerans* isolated from a clinical specimen should be discussed with the medical officer of health urgently.

All contacts should have cultures taken.

6.8.1 Antimicrobial prophylaxis

All close contacts, after cultures have been taken and regardless of immunisation status, should receive:

- a single intramuscular dose of benzathine penicillin (450 mg for children aged under 6 years; 900 mg for contacts aged 6 years or older), or
- 7 to 10 days of oral erythromycin (children: 40 mg/kg per day; adults: 1 g per day, in four divided doses).

Benzathine penicillin is preferred for contacts who cannot be kept under surveillance.

In contacts with a positive culture: two follow-up cultures should be obtained at least 24 hours after completion of therapy. If cultures are still positive, discuss further management with an infectious disease physician. The primary health care practitioner should be kept informed of the management of contacts and laboratory results.

6.8.2 Vaccination of contacts

All close contacts should also be offered a complete course of vaccine or a booster according to the following schedule.

- Fully immunised children aged under 10 years who have only received three doses of diphtheria toxoid-containing vaccine: give one injection of a diphtheria toxoid-containing vaccine.
- Fully immunised individuals aged 10 years and older who have not received a booster dose of a diphtheria toxoid-containing vaccine within the last five years:

give one injection of Tdap – funded if aged 10–17 years; unfunded if aged 18 years or older (see section 6.5).

- Unimmunised individuals: see Appendix 2.

6.8.3 Exclusion of contacts

Child contacts should be excluded from school, early childhood services and community gatherings until they are known to be culture negative. Adult contacts who are food handlers or who work with children should be excluded from work until known to be culture negative. Cases should be excluded from school until recovery has taken place and two negative throat swabs have been collected one day apart and one day after cessation of antibiotics.

For more details on control measures, see the 'Diphtheria' chapter of the *Communicable Disease Control Manual*[26] *(*available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

6.9 Variations from the vaccine data sheets

See section 15.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

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7 *Haemophilus influenzae* type b (Hib) disease

Key information

Mode of transmission	By inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions.
Incubation period	Unknown, but probably 2–4 days.
Period of communicability	May be prolonged. Non-communicable within 24–48 hours after starting effective antimicrobial therapy.
Burden of disease	Children aged under 5 years, particularly those aged under 1 year: meningitis, epiglottitis, pneumonia and bacteraemia.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). Hib-PRP-T (Hiberix).
Dose, presentation, route	DTaP-IPV-HepB/Hib and Hib-PRP-T: • 0.5 mL per dose after reconstitution • pre-filled syringe and glass vial – the vaccines must be reconstituted prior to injection • intramuscular injection (Hib-PRP-T can also be administered subcutaneously).
Funded vaccine indications and schedule	Usual childhood schedule: • at ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib • at age 15 months: Hib-PRP-T. For (re)vaccination of eligible patients: • up to 4 additional doses of DTaP-IPV-HepB/Hib (for eligible children <10 years); or • 1 additional dose of Hib-PRP-T. For children <10 years receiving solid organ transplantation: up to 5 doses of DTaP-IPV-HepB/Hib. For testing for primary immune deficiencies: Hib-PRP-T.
Vaccine effectiveness	Hib disease has been almost eliminated in countries where Hib vaccine is used.
Public health measures	All cases of Hib disease be notified immediately on suspicion. All contacts should have their immunisation status assessed and updated as appropriate.
Post exposure prophylaxis	Rifampicin prophylaxis should be administered to contacts as appropriate.

7.1 Bacteriology

Haemophilus influenzae is a gram-negative coccobacillus, which occurs in typeable and non-typeable (NTHi) forms. There are six antigenically distinct capsular types (a–f), of which type b is the most important. Before the introduction of the vaccine, *H. influenzae* type b (Hib) caused 95 percent of *H. influenzae* invasive disease in infants and children.

7.2 Clinical features

Transmission is by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions. Hib causes meningitis and other focal infections (such as pneumonia, septic arthritis and cellulitis) in children, primarily those aged under 2 years, while epiglottitis was more common in children over 2 years. Invasive Hib disease was rare over the age of 5 years, but could occur in adults. In the absence of vaccination these presentations may still occur. There have always been a small number of cases of *H. influenzae* invasive disease in adults, and these continue to occur. The incubation period of the disease is unknown, but is probably from two to four days.

Immunisation against Hib does not protect against infections due to other *H. influenzae* types or NTHi strains. Non-typeable *H. influenzae* (NTHi) organisms usually cause non-invasive mucosal infections, such as otitis media, sinusitis and bronchitis, but can occasionally cause bloodstream infection, especially in neonates. They are frequently present (60–90 percent) in the normal upper respiratory tract flora.

Young infants (aged under 2 years) do not produce an antibody response following Hib invasive disease, so a course of Hib-PRP vaccine is recommended when they have recovered (see section 7.5.3).

Hib and NTHi strains also cause diseases (including pneumonia and septicaemia) in the elderly.

7.3 Epidemiology

7.3.1 Global burden of disease

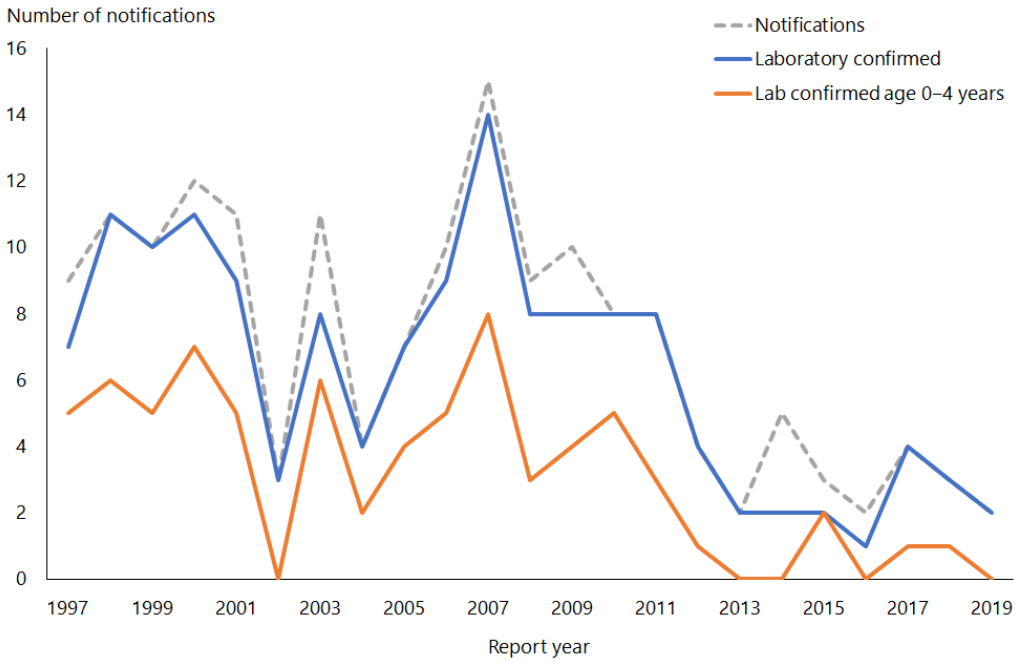
The source of the organism is the upper respiratory tract. Immunisation with a protein conjugate vaccine reduces the frequency of asymptomatic colonisation by Hib. Before the introduction of the vaccine, Hib was the most common cause of bacterial meningitis in children. Worldwide immunisation coverage is increasing, with approximately 194 countries having fully or partially introduced Hib onto their schedules by July 2019 (98 percent of all WHO member states).[1] The estimated global coverage for three doses of Hib is 72 percent as of July 2019.[2]

7.3.2 New Zealand epidemiology

Hib-PRP was introduced in 1994 (see Appendix 1). In 1993, 101 children aged under 5 years had laboratory-confirmed invasive Hib disease (an age-specific rate of 36.4 per 100,000 population). By 1999 only five children in this age group had laboratory-confirmed disease (1.7 per 100,000) (Figure 7.1).

Two cases of Hib were notified and laboratory confirmed in 2019 (ESR, 8 June 2020). The cases were aged 50–59 and 60–69 years, both were unvaccinated. There were seven deaths from Hib between 1997 and 2019 (ESR, 8 June 2020), the most recent was in 2012 in an adult over 70 years of age.[3]

Figure 7.1: Number of notifications and culture-positive cases of *Haemophilus influenzae* type b invasive disease, 1997–2019



Source: ESR

For details of Hib notifications, refer to the most recent ESR notifiable disease annual tables and reports (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

7.4 Vaccines

Antibodies to PRP, a component of the polysaccharide cell capsule of Hib, are protective against invasive Hib disease. To induce a T-cell dependent immune response, the polyribosylribitol phosphate (PRP) polysaccharide has been linked (conjugated) to a variety of protein carriers. These conjugate Hib vaccines are immunogenic and effective in young infants (see also section 1.4.3). The protein carriers used are either an outer membrane protein of *Neisseria meningitidis* (Hib-PRP-OMP vaccine), or a tetanus toxoid (Hib-PRP-T vaccine).

Note that the protein conjugates used in Hib vaccines are not themselves expected to be immunogenic and do not give protection against *N. meningitidis* or tetanus.

7.4.1 Available vaccines

Funded vaccines

The Hib vaccines funded as part of the Schedule are:

- Hib-PRP-T, given as the hexavalent vaccine DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK). It contains diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and Haemophilus influenzae type b vaccine (see section 6.4 for more information)
- Hib-PRP-T given as monovalent Hib vaccine (Hiberix, GSK). It contains 10 µg of purified Hib capsular PRP polysaccharide conjugated to 25 µg of inactivated tetanus toxoid. Other components (excipients) include lactose in the vaccine and sterile saline solution in the diluent.

Other vaccines

No other Hib vaccines are available currently. Hib-PRP-T (Act-HIB, Sanofi) was the funded vaccine prior to the 1 July 2017 Schedule change.

7.4.2 Efficacy and effectiveness

The high efficacy and effectiveness of Hib-PRP vaccines have been clearly demonstrated by the virtual elimination of Hib in countries implementing the vaccine,[4, 5, 6] including New Zealand. Hib-PRP vaccines are highly effective after a primary course of two or three doses.[7, 8, 9] Disease following a full course of Hib-PRP is rare.

Conjugate vaccines reduce carriage in immunised children and as a result also decrease carriage and disease in unimmunised people (herd immunity). These vaccines will not protect against infection with NTHi strains, and therefore do not prevent the great majority of otitis media, recurrent upper respiratory tract infections, sinusitis or bronchitis.

(See also section 15.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.)

Duration of immunity

A primary series followed by a booster dose in the second year of life should provide sufficient antibody levels to protect against invasive Hib disease to at least the age of 5 years.[10]

7.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib should be stored in the dark.

> DTaP-IPV-HepB/Hib vaccine (Infanrix-hexa) must be reconstituted by adding the entire contents of the pre-filled syringe containing DTaP-IPV-HepB vaccine to the vial containing the Hib powder. After adding the vaccine to the powder, the mixture should be shaken until the powder is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.
>
> Hib-PRP-T vaccine (Hiberix) must be reconstituted with the supplied diluent and used immediately after reconstitution.

7.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib and Hib-PRP-T vaccines is 0.5 mL administered by intramuscular injection. Hib-PRP-T can also be administered subcutaneously if indicated (see section 2.2.3).

Co-administration

DTaP-IPV-HepB/Hib and Hib-PRP-T vaccines can be co-administered with other routine vaccines on the Schedule, in separate syringes and at separate sites.

7.5 Recommended immunisation schedule

7.5.1 Usual childhood schedule

Hib vaccine is funded for all children aged under 5 years. Three doses of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine are given as the primary course, with a booster of Hib-PRP-T (Hiberix) at age 15 months (see Table 7.1).

Table 7.1: Usual childhood Hib schedule (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
15 months	Hib-PRP-T	Booster

For children aged under 5 years who, for whatever reason, have missed out on Hib vaccine in infancy, a catch-up schedule is recommended. The total number of doses of Hib vaccine required is determined by the age at which Hib immunisation commences. Where possible, the combined available vaccines should be used, but individual immunisation schedules based on the recommended national schedule may be required for children who have missed some immunisations (see Appendix 2).

7.5.2 Special groups

Children

Because of an increased risk of infection, it is particularly important that the following groups of children, whatever their age, receive the Hib vaccine as early as possible (see also sections 4.2 and 4.3):

- children with anatomical or functional asplenia, or who are suffering from sickle cell disease (if possible, it is recommended that children be immunised prior to splenectomy)
- children with partial immunoglobulin deficiency, Hodgkin's disease or following chemotherapy (note, however, that response to the vaccine in these children is likely to be suboptimal)
- children with nephrotic syndrome
- HIV-positive children.

Recommendations for Hib vaccine for older children and adults with asplenia

Although there is no strong evidence of an increased risk of invasive Hib disease in asplenic older children and adults, some authorities recommend Hib immunisation for these individuals.[11, 12] The Hib PRP-T vaccine has been shown to be immunogenic in adults.

- Hib-PRP-T vaccine (Hiberix) is funded for older children and adults pre- or post-splenectomy or with functional asplenia; one dose of vaccine is recommended (see also section 4.3.4) if childhood vaccine schedule is incomplete or unknown.

Note: Pneumococcal, meningococcal, influenza, varicella and pertussis-containing vaccines are also recommended for these individuals; see section 4.3 and the relevant disease chapters.

7.5.3 Children who have recovered from invasive Hib disease

Children aged under 2 years with Hib disease do not reliably produce protective antibodies and need to receive a complete course of Hib-PRP-T. The number of doses required will depend on the age at which the first dose after the illness is given, **ignoring** any doses given before the illness (follow the age-appropriate catch-up schedules in Appendix 2).

Commence immunisation approximately four weeks after the onset of disease.

Any immunised child who develops Hib disease or who experiences recurrent episodes of Hib invasive disease requires immunological investigation by a paediatrician.

7.5.4 (Re)vaccination

Hib-PRP-containing vaccines are funded for vaccination and revaccination of eligible patients, as follows. See also section 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa)

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for vaccination or revaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib are funded for children aged under 10 years receiving solid organ transplantation.

Hib-PRP-T (Hiberix)

One additional dose of Hib-PRP-T (Hiberix) is funded for vaccination or revaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy or with functional asplenia
- pre- or post-solid organ transplant
- pre- or post-cochlear implants
- undergoing renal dialysis
- prior to planned or after other severely immunosuppressive regimens.

7.5.5 Pregnancy and breastfeeding

Hib-PRP is not routinely recommended for pregnant or breastfeeding women. However, for women with asplenia see the 'Recommendations for Hib vaccine for older children and adults with asplenia' in section 7.5.2.

7.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications. Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.

See section 15.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

Hib-PRP-T vaccines should not be administered to people with a history of an anaphylactic reaction to a prior dose of Hib vaccine or to a vaccine component. Significant hypersensitivity reactions to Hib vaccines appear to be extremely rare.

7.7 Potential responses and AEFIs

See section 15.7.1 for potential responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

7.7.1 Potential responses

Adverse reactions to Hib-PRP conjugate vaccines are uncommon. Pain, redness and swelling at the injection site occur in approximately 25 percent of recipients, but these symptoms typically are mild and last less than 24 hours.[13]

7.7.2 AEFIs

A meta-analysis of trials of Hib-PRP vaccination from 1990 to 1997 found that serious adverse events were rare.[14] No serious vaccine-related adverse experiences were observed during clinical trials of Hib vaccine alone. There have been rare reports, not proven to be causally related to Hib vaccine, of transverse myelitis, thrombocytopenia and Guillain-Barré syndrome (GBS).[15]

7.8 Public health measures

It is a legal requirement that all cases of Hib disease be notified immediately on suspicion to the local medical officer of health, who will arrange for contact tracing, immunisation and administration of prophylactic rifampicin, where appropriate.

For further information see the *Communicable Disease Control Manual*.[16]

7.8.1 Management of contacts

All child contacts should have their immunisation status assessed and updated, as appropriate.

Immunisation reduces – but does not necessarily prevent – the acquisition and carriage of Hib. Therefore, immunised children still need rifampicin prophylaxis, when indicated, to prevent them transmitting infection to their contacts. Careful observation of exposed household and early childhood service contacts is essential. Exposed children who develop a febrile illness should receive prompt medical evaluation.

Rifampicin chemoprophylaxis

To eradicate the carrier state and protect susceptible children, antimicrobial prophylaxis should be given to contacts as soon as possible, and ideally within seven days of the index case developing the disease, irrespective of their own immunisation status. Prophylaxis started after seven days may still be of benefit and is recommended. Note that the prophylaxis for Hib is different from that for meningococcal disease (see chapter 13).

Rifampicin recommendations

Chemoprophylaxis with rifampicin is recommended for the following contacts of an index case of Hib:

- all members of the case's household (including adults) where there is at least one contact aged under 4 years who is either unimmunised or partially immunised
- all members of a household where there is a child aged under 12 months, even if the child has had three doses (primary series) of the Hib-PRP vaccine
- all members of a household where there is an immunosuppressed person
- all staff and children at an early childhood service where two or more cases of Hib have occurred within 60 days.

Use oral rifampicin 20 mg/kg (maximum 600 mg) daily for four days. The dose for infants aged under 4 weeks has not been established, but a dose of 10 mg/kg per day is recommended. This is a different regimen to that recommended for prophylaxis from meningococcal disease (see chapter 13).

The index case should also receive rifampicin unless treated with cefotaxime or ceftriaxone.

Rifampicin is not recommended for:

- occupants of households where there are no children aged under 4 years, other than the index case
- occupants of households where all contacts aged 12 months to under 4 years have completed their immunisation series, including the second-year-of-life dose
- pregnant women – rifampicin is contraindicated in pregnant women; pregnant women who are a household contact of an index case should receive ceftriaxone.

For more details on control measures, refer to the '*Haemophilus influenzae* type b invasive disease (Hib)' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**).[16]

7.9 Variations from the vaccine data sheets

The Hib-PRP-T (Hiberix) data sheet states that the vaccine is not intended for use in adults. However, the Ministry of Health recommends that asplenic adults (see section 7.5.2) or adults with specified immunocompromised conditions (see section 7.5.4) receive Hib-PRP-T vaccine.[11, 17] There are not expected to be any safety concerns in regard to use in older age groups.

See section 15.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

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8 Hepatitis A

Key information

Mode of transmission	Faecal–oral route, either from person-to-person contact or through contaminated food or drink. It is also occasionally spread by injected drug use.
Incubation period	28–30 days average (range 15–50 days).
Period of communicability	The 1–2 weeks before and the first few days after the onset of jaundice.
Burden of disease	Infants and children are usually asymptomatic. Severity in adults increases with age. The disease is more serious in those with chronic liver disease and the immunocompromised. There is no carrier state.
Funded vaccines	Monovalent inactivated hepatitis A virus (HAV) vaccine: Havrix.
Other available vaccines	Monovalent inactivated hepatitis A virus (HAV) vaccine: Avaxim. Combined inactivated HAV-recombinant HBsAg protein vaccine: Twinrix. Combined HAV-purified *Salmonella typhi* Vi polysaccharide vaccine: Vivaxim.
Dose, presentation, route	Havrix, Twinrix, Vivaxim: 1.0 mL per dose. Havrix Junior, Twinrix Junior, Avaxim: 0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded vaccine indications and recommended schedule	HepA vaccine (Havrix) is recommended and funded for: • transplant patients – 2 doses • children with chronic liver disease – 2 doses • close contacts of hepatitis A cases – 1 dose.
Recommended, unfunded	Individuals working with children, exposed to faeces or contaminated water, or with non-human primates Armed forces personnel and travellers visiting high-risk countries Adults with chronic liver disease, including with chronic hepatitis B and C infection Men who have sex with men Food handlers during community outbreaks
Vaccine efficacy	High efficacy: HAV infection has been almost eliminated in immunised populations.
Public health measures	All cases of hepatitis A must be notified immediately on suspicion to local medical officer of health
Post-exposure prophylaxis	In an outbreak (if within 2 weeks of exposure): • age <12 months: human normal immunoglobulin is recommended • ≥12 months: age-appropriate vaccination is recommended.

8.1 Virology

Hepatitis A virus (HAV) is a ribonucleic acid (RNA) virus belonging to the picornavirus group, which also contains enteroviruses and rhinoviruses. The virus is usually transmitted by the faecal–oral route, either from person-to-person contact or through contaminated food or drink.

HAV primarily replicates in the liver and is excreted in large quantities via the biliary tract into the faeces. It is a hardy virus and can survive outside the body for prolonged periods in food and water. It causes a self-limiting illness with no carrier state.

8.2 Clinical features

The incubation period between ingestion of the virus and clinical symptoms is 15 to 50 days, with an average of 28 to 30 days. The virus can be detected in blood and faeces within a few days of ingestion, and it increases to a peak in the two weeks prior to the onset of clinical illness, which is the time that subjects are most likely to spread the infection. Faecal viral shedding continues for one to three weeks in adults, but has been reported to last longer in young children. Virus excretion falls sharply in the week following the onset of hepatitis.

In infants and preschool children, most infections are either asymptomatic or cause only mild, non-specific symptoms without jaundice. Most adults and adolescents develop symptomatic disease, the severity of which generally increases with age. Symptomatic HAV infection is characterised by an acute febrile illness with jaundice, anorexia, nausea, abdominal discomfort, malaise and dark urine. Signs and symptoms usually last less than two months, although 10–15 percent of symptomatic persons have prolonged or relapsing illness lasting up to six months. Liver enzymes almost always return to normal by six months after the illness, and often much sooner. The disease is more serious in people with chronic liver disease or those who are immunocompromised (including people with HIV infection). Chronic carrier states do not occur following hepatitis A infection and persisting liver damage is very rare.

8.3 Epidemiology

8.3.1 Global burden of disease

HAV is common in areas with poor sanitary conditions and limited access to clean water.[1] In highly endemic areas, such as parts of Africa and Asia, the disease is virtually confined to early childhood and is not an important cause of morbidity.[1, 2] Almost all adults in these areas are immune, and hepatitis A epidemics are uncommon. In intermediate endemicity areas, such as Central and South America, Eastern Europe and parts of Asia, children may not be infected in early childhood and reach adulthood without immunity. A high proportion of adolescents and adults are susceptible and large outbreaks are common. In low endemicity areas, such as the US and Western Europe, infection is less common but can occur in high-risk groups. Large outbreaks are rare, due to high levels of sanitation that stops person-to-person transmission.

Viral spread occurs readily in households, in early childhood services and in residential facilities that care for the chronically ill, disabled or those with a weakened immune system. In early childhood services, typically the adult guardian develops symptomatic disease while the primary source, the infected young child, is asymptomatic. The risk of spread in early childhood centres is proportional to the number of children aged under 2 years wearing nappies. Infection in these early childhood services is an important source of outbreaks for whole communities.

Other groups at the highest risk of contracting the disease include people in close contact with an infected person, and travellers to areas with high or intermediate rates of hepatitis A infection. Others also at greater risk of contracting HAV are people who have oral–anal sexual contact, illicit drug users, those with chronic liver disease, food handlers and laboratory staff working with the virus.

Universal and targeted programmes for childhood immunisation have been introduced in several countries, including Israel, the US and Australia. Acute HAV infection has almost been eradicated in areas with HAV immunisation programmes.

8.3.2 New Zealand epidemiology

The rate of HAV in New Zealand declined from 145.7 per 100,000 in 1971 to 1.2 per 100,000 in 2019 (ESR, 8 June 2020).[3, 4] This fall in rate is attributable to the use of HAV vaccination in travellers and a reduction in HAV prevalence overseas.

In 2019, 58 cases were notified compared with 68 in 2018 (ESR, 8 June 2020). Hospitalisation status was recorded for 57 cases, of which, 36 (63 percent) were hospitalised.

The highest rates occurred in the 15–19 years (2.2 per 100,000) and 1–4- and 20–29-years age groups (both 2.0 per 100,000). Of the 56 cases with ethnicity information

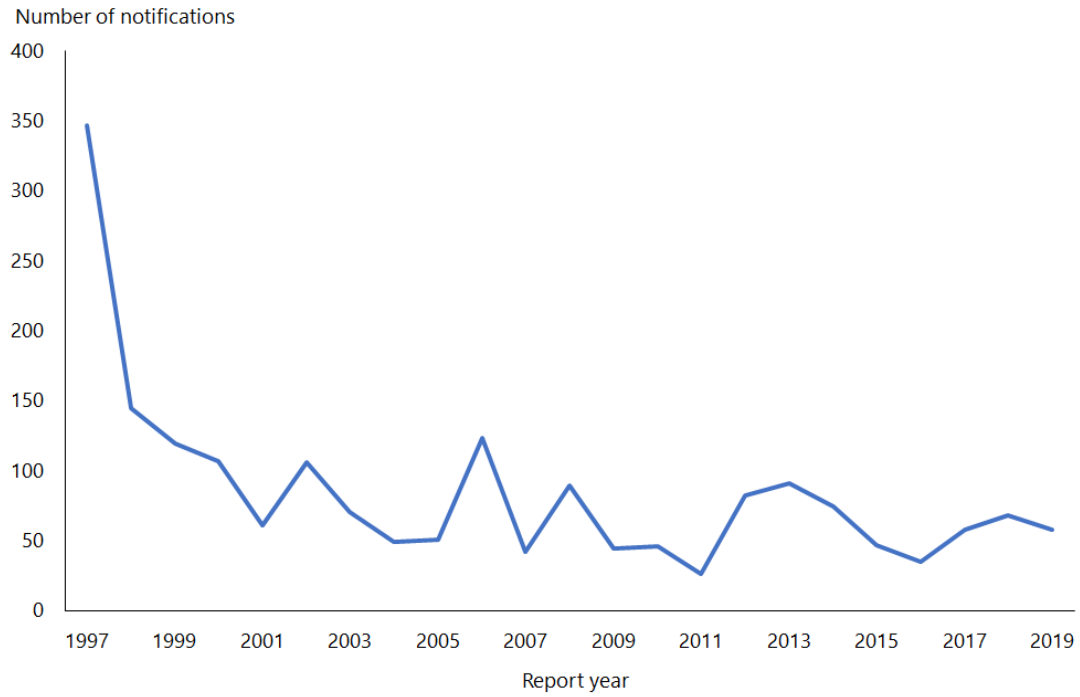
recorded, Pacific peoples had the highest notification rate (5.4 per 100,000), followed by the Asian (3.1 per 100,000) ethnic groups (ESR, 8 June 2020).

Overseas travel information was recorded for 55 cases: 32 cases (58.2 percent) had travelled overseas during the incubation period of the disease (ESR, 8 June 2020). The countries most frequently visited included India and Samoa (7 cases each), Fiji (5 cases), Indonesia (4 cases) and Tonga (3 cases). Four cases reported travel to more than one country.

Hepatitis A outbreaks continue to occur. There was one outbreak in 2019, involving 10 cases (ESR, 8 June 2020).

Figure 8.1 illustrates the overall national downward trend since a peak of notifications in 1997.

Figure 8.1: Hepatitis A notifications, by year, 1997–2019



Source: ESR

For further details of hepatitis A notifications in New Zealand, refer to the most recent notifiable disease annual reports from ESR (available at **surv.esr.cri.nz/surveillance/annual_surveillance.php**).

8.4 Vaccines

8.4.1 Available vaccines

Two inactivated HAV vaccines (HepA) are currently registered (approved for use) and available (marketed) in New Zealand, as well as a combined HepA-HepB vaccine and a combined HepA-typhoid vaccine.

Funded vaccine

Hepatitis A vaccine (HepA) is not on the Schedule, but is recommended and funded for certain high-risk groups, as shown in Table 8.1.

> Each 1.0 mL dose of Havrix (GSK) contains 1,440 EU (enzyme-linked immunosorbent assay units) of inactivated HAV adsorbed onto aluminium hydroxide. Each 0.5 mL dose of Havrix Junior contains 720 EU of inactivated HAV. Other components and residuals include neomycin sulphate, 2-phenoxyethanol, polysorbate 20, amino acid supplement in a phosphate buffered saline solution.

Other vaccines

Inactivated HAV vaccine

Avaxim (Sanofi) contains 160 antigen units of inactivated HAV in each 0.5 mL dose; other components and residuals include aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

Combined HAV and HBV vaccine

Twinrix (GSK) contains 720 EU of inactivated HAV and 20 µg of recombinant DNA HBsAg vaccine in each 1.0 mL dose. The Twinrix Junior preparation (0.5 mL per dose) contains half these amounts. The vaccines are adsorbed onto aluminium adjuvants. Other components and residuals include aluminium hydroxide, aluminium phosphate, sodium chloride, amino acids, dibasic sodium phosphate, formaldehyde, monobasic sodium phosphate, neomycin sulphate, polysorbate 20 and trometamol.

Combined HAV and typhoid vaccines

Vivaxim (Sanofi) contains 160 antigen units of inactivated HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide in each 1.0 mL dose; other components and residuals include sodium chloride, sodium phosphate, aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

8.4.2 Efficacy and effectiveness

After one dose of monovalent HepA in healthy people, protective levels of antibody have been demonstrated by two weeks, and 94–100 percent of people vaccinated will seroconvert by four weeks.[5]

A second dose 6 to 18 months after the first is thought to be important for long-term protection, particularly in the absence of exposure to HAV.[6, 7] In subjects with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Hep A vaccines have not yet been approved for children aged under 12 months. This is due to the potential interference from maternal antibody which may affect long term immunity.[8] However, HepA vaccines have been shown to be safe and efficacious in infants as young as 2 months.[9] Such that the CDC recommends HepA vaccination for infants aged 6–11 months travelling outside of the US.[10]

HepA vaccines are highly effective in preventing clinical disease, with recorded efficacy measures of around 94–100 percent from six weeks post-vaccination. Where children, adolescents and young adults have been vaccinated in targeted and/or national programmes, there has been a rapid decline in disease incidence. This decline is through both direct and indirect (herd immunity) effects.[6]

Duration of immunity

Antibodies to two doses of HepA have been shown to persist in vaccinated adults for at least 17 years after vaccination, and up to 15 years in vaccinated children and adolescents.[11] Mathematical models estimate that following completion of a two-dose series, protective levels of antibody persist for 40 years or longer in adults and 14–20 years in children.[11] Given that HAV has a long incubation period, it is possible that immune memory with no detectable circulating antibody may be sufficient for protection, as is the case with HBV and HepB.

8.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze.

8.4.4 Dosage and administration

See Table 8.2 for dosage and scheduling information.

The monovalent HepA and HepA combination vaccines should be administered by intramuscular injection into the deltoid region of the upper arm in adults and older children, or the anterolateral aspect of the thigh in younger children (see section 2.2.3).

Co-administration with other vaccines

The monovalent HepA and HepA-combination vaccines may be administered concurrently with other vaccines.[11, 12] The vaccines should be given in separate syringes and at different injection sites.

Interchangeability of hepatitis A vaccines

The monovalent HepA vaccines may be used interchangeably to complete a two-dose course.[12]

8.5 Recommended immunisation schedule

8.5.1 Recommendations

Hepatitis A vaccines are not on the Schedule, but are funded for the high-risk groups as shown in the shaded section of Table 8.1. They may also be employer-funded or funded during an outbreak (see section 8.8).

Table 8.1: Hepatitis A vaccine recommendations

Note: **Funded individuals are in shaded rows**. See the Pharmaceutical Schedule (**pharmac.govt.nz/**) for any changes to the funding decisions.

Recommended and funded
Transplant patients[a]
Children with chronic liver disease[a]
Close contacts[b] of hepatitis A cases
Recommended but not funded
Adults with chronic liver disease: • chronic hepatitis B or C infection • other chronic liver disease
Men who have sex with men
Travellers – including occupational[c] and recreational travel
Occupational groups[c] exposed to faeces, including: • employees of early childhood services, particularly where there are children too young to be toilet trained • sewage workers • those who work with non-human primates (eg, zoos, research laboratories).
Food handlers[c] during community outbreaks.
Armed forces personnel[c] who are likely to be deployed to high-risk areas.

a. See also section 4.3.11.

b. Only one dose is funded for close contacts as protection is only required for the duration of the outbreak. For long-term protection, contacts may seek a second (unfunded) dose, after an interval of at least 6 months. See the *Communicable Disease Control Manual*[13] for a definition of contacts.

c. May be employer-funded. See also section 4.8.

Individuals with chronic liver disease

HepA is recommended and funded for children with chronic liver disease and for children and adults undergoing transplants (see sections 4.3.11 and 4.5). People with chronic liver disease are not at increased risk for hepatitis A, but acute hepatitis A can have serious or fatal consequences.[6]

Chronic hepatitis B or C infection

Studies have shown that in these individuals, super-infection with HAV leads to increased morbidity and mortality.[6]

Other chronic liver disease

Non-immune individuals who have not been vaccinated should receive HepA before liver decompensation. It should be given as early as possible before liver transplantation; vaccination may be performed after transplantation, although the response is unlikely to be as good as early in liver disease.[14, 15]

Travellers

The first dose of HepA should be given as soon as travel is considered.[11] The high and intermediate endemicity areas listed in section 8.3.1 may be used as a guide for recommending hepatitis A vaccination for travel, but there are limits to the data that informs these listings, and variation within countries. Even in low prevalence countries there is a risk of foodborne hepatitis A. In addition, decreasing prevalence in formerly endemic countries leads to large numbers of susceptible people and the risk of large outbreaks, as has recently been reported. The vaccine may be considered for all travellers. Although licensed from age 1 year, HepA could also be considered for use in infants younger than 1 year if at significant risk of infection.[10]

Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.

Certain occupational groups

Immunisation with HepA is recommended (but not funded) for people in occupational groups exposed to faeces, as listed in Table 8.1 above.

Others at higher risk

Pre-immunisation screening for anti-HAV antibodies is not routinely recommended. There is no danger in vaccinating an already immune person, but some groups with higher probability of prior infection may wish to avoid the expense of vaccination. These include:

- those who are likely to have been exposed as children (born in a country of high endemicity) or in the course of their employment
- those with a history of jaundice.

Consider HepA for the following groups:

- intravenous drug users (who account for 30 percent of cases in communities during outbreaks)[6]
- men who have sex with men.

Routine immunisation for children

HepA is not routinely recommended and is not on the Schedule for children in New Zealand. It should, however, be considered during community outbreaks (see section 8.8).

8.5.2 Immunisation schedule

Immunisation schedules for HAV-containing vaccines are provided in Table 8.2. See the manufacturers' data sheets for more information. For monovalent HepA, the first dose is for primary immunisation and the second dose is a booster.

Table 8.2: Hepatitis A-containing vaccines: by age, dose and schedule

Note: Havrix and Havrix Junior are funded for eligible individuals[a] (see Table 8.1).

Age	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Hepatitis A vaccines					
1–15 years	Havrix Junior[a]	720 EU	0.5	2	0 and 6–12 months[b]
2 years–adult	Avaxim	160 antigen units	0.5	2	0 and 6–36 months
≥16 years	Havrix 1440[a]	1,440 EU	1	2	0 and 6–12 months[b]
Hepatitis A–Hepatitis B combined vaccine					
1–15 years	Twinrix[c]	720 EU of HAV and 20 µg of HBsAg	1.0	2	0 and 6–12 months
	Twinrix Junior[d]	360 EU of HAV and 10 µg of HBsAg	0.5	3	0, 1 and 6 months
≥16 years	Twinrix	720 EU of HAV and 20 µg of HBsAg	1.0	3	0, 1 and 6 months; or 0, 7, and 21 days plus a booster at 1 year
Hepatitis A–Typhoid combined vaccines					
≥16 years	Vivaxim	160 antigen units of HAV and 25 µg of Vi	1.0	1	At least 14 days before departure; then boost with HepA at 6–36 months[e]

Key: EU = enzyme-linked immunosorbent assay (ELISA) units of hepatitis A virus protein; HAV = hepatitis A virus; HBsAg = recombinant hepatitis B surface antigen; Vi = *Salmonella typhi* polysaccharide

Notes

a. Note that two doses of HepA are funded for transplant patients and children with chronic liver disease (see sections 4.3.11 and 4.5); one dose is funded for close contacts of hepatitis A cases.

b. Even after a longer interval between the first and second doses, there is no need to restart the series. A substantial anamnestic response occurs after a second dose given up to 8 years after the initial dose.[16]

c. For children not previously exposed to the hepatitis A or B viruses. Source: GlaxoSmithKline NZ Ltd. 2016. Twinrix and Twinrix Junior New Zealand Data Sheet. URL: **www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf** (accessed 19 June 2020).

d. Use when the child is at immediate risk of exposure to hepatitis B (eg, travellers) and did not receive a primary course of HepB as an infant. Source: GlaxoSmithKline NZ Ltd. 2019. Twinrix and Twinrix Junior New Zealand Data Sheet. URL: **www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf** (accessed 19 June 2020).

e. If the individual remains at risk from typhoid fever, a single dose of the typhoid vaccine is recommended every 3 years.

8.5.3 Pregnancy and breastfeeding

The safety of HepA during pregnancy and while breastfeeding has not been determined. However, because HepA is produced from inactivated HAV, there is not expected to be any risk to the developing fetus and infant. As a precaution, HepA should be used during pregnancy only when clearly needed, such as when travelling to a country where HAV is endemic.

8.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

8.6.1 Contraindications

Administration of HepA should be delayed in individuals suffering from acute febrile illness. HepA should not be administered to people with a history of an anaphylactic reaction to a prior dose of HepA or to a vaccine component.

8.6.2 Precautions

In individuals with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Pregnancy is a precaution – see section 8.5.3.

8.7 Potential responses and AEFIs

8.7.1 Potential responses

Soreness, redness and swelling at the injection site; fever; malaise; headache; nausea; and loss of appetite have been reported for monovalent HepA, but these responses are usually mild and brief.[17] Similar responses are seen with HepA–HepB combination vaccines, and HepA–typhoid combination vaccines.

8.7.2 AEFIs

Review of data from multiple sources has not identified any serious adverse events among children and adults that could be attributed to HepA.[17]

8.8 Public health measures

It is a legal requirement that all cases of hepatitis A be notified immediately on suspicion to the local medical officer of health.

8.8.1 Post-exposure prophylaxis and outbreak control

Vaccination

Age-appropriate vaccine is recommended for all close contacts aged older than 1 year. If time allows, consider pre-vaccine serology if there is a history or likelihood of previous HepA vaccination or infection (eg, previous residence in an endemic country). Post-exposure prophylaxis with vaccine should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case. The efficacy of vaccine when administered more than two weeks after exposure has not been established.

Immunoglobulin

Where vaccine is contraindicated (or not immediately available), human normal immunoglobulin may be offered to a close contact who may have a reduced response to vaccine or has risk factors for severe disease. The dose is 0.03 mL/kg given by intramuscular injection. Post-exposure prophylaxis should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case.

For post-exposure prophylaxis, close contacts aged under 1 year may require human normal immunoglobulin. This should be discussed with the appropriate infectious disease physician.

Human normal immunoglobulin is available from the New Zealand Blood Service. For further information, see the medicine data sheets or the New Zealand Blood Service website (**nzblood.co.nz**).

Early childhood services and other institutional outbreaks

If an outbreak occurs in an early childhood service, vaccination (and/or immunoglobulin if appropriate) may be indicated for all previously unimmunised staff and children at the service and unimmunised new staff and children for up to six weeks after the last case has been identified, including cases in the household of attendees. The number of infected cases should determine the extent of intervention.

Vaccination and/or immunoglobulin may also be indicated for adults and children at a school, hospital or custodial-care institution where an outbreak of hepatitis A is occurring. For sporadic cases in hospitals, schools or work settings, post-exposure prophylaxis is not routinely indicated, but careful hygiene practices should be maintained.

Community-wide outbreaks of hepatitis A infection

HepA is effective in controlling community-wide epidemics and common-source outbreaks of HAV infection.[18] Before the vaccine is used for outbreak control, consideration should be given to the current epidemiology in the community, the population at risk should be defined, and the feasibility and cost of delivering a programme should be assessed.

For more details on control measures, see the 'Hepatitis A' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**).

8.9 Variations from the vaccine data sheets

Havrix Junior is licensed from ages 1 to 15 years of age. However, for infants travelling to areas at high risk of hepatitis A infection and pre-exposure prophylaxis, the Ministry of Health recommends that HepA vaccination (Havrix Junior) can be given under 1 year of age at least two weeks prior to departure.

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9 Hepatitis B

Key information

Mode of transmission	Contact with infected blood or body fluids during childbirth (vertical transmission); sexual intercourse, intravenous drug use or contact with broken skin (horizontal transmission).
Incubation period	45–180 days, commonly 60–90 days.
Period of communicability	Potentially infectious 2–3 weeks before the onset of symptoms, during the clinical disease and usually for 2–3 months after acute hepatitis B illness; or for as long as HBsAg continues to be present in blood (chronic hepatitis B carrier state).
Incidence and burden of disease	New Zealand is a country with a low overall prevalence of hepatitis B carriage, but it contains certain populations with high prevalence. All pregnant women and high-risk groups should be screened for chronic HBV infection. HBV acquisition in infancy is very likely to lead to chronic infection. Chronic HBV infection can progress to cirrhosis and liver cancer.
Funded vaccines	HepB (Engerix-B) DTaP-IPV-HepB/Hib (Infanrix-hexa).
Dose, presentation, route	HepB: • 20 µg presentation – 1.0 mL per dose, pre-filled syringe • 10 µg presentation – 0.5mL per dose, pre-filled syringe (paediatric dose) • intramuscular or subcutaneous injection. DTaP-IPV-HepB/Hib: • 0.5 mL per dose • pre-filled syringe and glass vial – the vaccine must be reconstituted prior to injection. • intramuscular injection.
Funded vaccine indications and schedule	At ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. Infants born to HBsAg-positive mothers should receive HepB vaccine plus HBIG at birth, then the usual childhood schedule. Serological testing at age 9 months (anti-HBs and HBsAg). Individuals with eligible conditions or close household contacts of infected individuals: HepB (see section 9.5).
Recommended, unfunded	Those with increased risk from occupational or sexual exposure to body fluids and faeces, or receiving regular blood products. Those with developmental disability, current or prior injectable drug users, prison inmates, and travellers to and from high-prevalence countries.
Vaccine effectiveness	In general, efficacy is 85–95 percent in high risk groups, though likely to be lower in older individuals and those with immunocompromise. Protection is expected to be lifelong and boosters are not required.
Public health measures	Notify all cases of acute hepatitis B infection (see section 9.8).

9.1 Virology

The hepatitis B virus (HBV) is a partially double-stranded DNA virus belonging to the Hepadnaviridae family. Three major subunits make up the structural components:

- the HBV genome, a small, circular, partially double-stranded DNA molecule, in association with a polymerase enzyme
- the nucleocapsid core, which surrounds the genome and consists of core protein (hepatitis B core antigen, HBcAg)
- the outer lipoprotein envelope, which contains the hepatitis B surface antigen (HBsAg).

The genome has four genes (S, C, X and P). Both the core nucleocapsid protein (HBcAg) and the 'early' protein (which makes HBeAg) are translated from the C gene. HBcAg is essential for viral packaging and is an integral part of the nucleocapsid. HBeAg is a soluble protein that is not part of the virus particle. Detection of HBeAg in the serum is correlated with viral replication and is a marker for severe disease. It is most commonly found in those with acute hepatitis B and those with chronic HBV infection with high viral load.[1]

9.2 Clinical features

There is a broad spectrum of clinical disease with HBV infection, from subclinical through to fulminant hepatitis. Persistent infection can lead to chronic liver disease, potentially causing cirrhosis or hepatocellular carcinoma.

9.2.1 Serological markers of infection

The HBV antigens and their associated antibodies are serological markers of HBV infection or vaccination (Table 9.1). At least one serological marker is present during the different phases of infection (Table 9.2).

Table 9.1: HBV antigens and their respective antibodies

Antigen	Antibody (IgM, IgG and total)
HBsAg (hepatitis B surface antigen)	Anti-HBs
HBcAg (hepatitis B core antigen)	Anti-HBc
HBeAg (hepatitis B e antigen)	Anti-HBe

Table 9.2: Interpretation of serology for HBV infection

Serological marker				Interpretation
HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	
–	–	–	–	Never infected
+	–	–	–	Early acute infection; transient (up to 18 days) after vaccination
+	+	+	–	Acute infection
–	+	+	+ or –	Acute resolving infection
–	+	–	+	Recovered from past infection and is immune
+	+	–	–	Chronic infection[a]
–	–	–	+	Immune if ≥10 IU/L vaccinated or natural infection

Key: Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen (HBsAg); IgM = immunoglobulin M; + = positive test result; – = negative test result.

a HBeAg positive (HBeAg+) correlates with high viral load and increased risk of transmission; HBeAg negative (HBeAg–) correlates with lower viral load and reduced risk of developing cirrhosis or cancer.

Adapted from: Van Damme P, Ward J, Shouval D, et al. 2018. Hepatitis B vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Plotkin's Vaccines* (7th edition). Philadelphia, US: Elsevier. Table 25.1.

Any difficulties with interpreting serological results for cases and contacts should be discussed with an infectious diseases physician or the laboratory. See the 'Hepatitis B' chapter of the *Communicable Disease Control Manual* for recommendations for HBV case and contact management (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

9.2.2 Acute hepatitis

The virus preferentially infects liver cells, multiplying in the liver and releasing large amounts of HBsAg, which is present in the blood of people with active infection. The incubation period varies between 45 and 180 days and is commonly 60 to 90 days.

HBV is not directly cytopathic; the host's immune response leads to death of infected liver cells. Most infected people mount an effective immune response that leads to eradication of infection over a period of several months. Approximately 80 percent of adults with acute infection have symptomatic hepatitis, and the remaining 20 percent can be asymptomatic (but these proportions vary).[2]

The common symptoms of acute hepatitis B illness are fever, jaundice, malaise, anorexia, nausea, vomiting, myalgia and abdominal pain. Jaundice usually develops within two weeks of onset of the illness, and dark urine and/or clay coloured stools might appear up to five days before clinical jaundice. Clinical signs and symptoms of acute hepatitis B usually resolve one to three months later.[1]

There is a small risk of liver failure (less than 1 percent) with acute infection; if failure occurs, almost half will die or require emergency liver transplantation.

9.2.3 Chronic HBV infection

The main burden of HBV disease occurs in people with chronic HBV infection. Chronically infected people are identified by presence and persistence of HBsAg in their serum for at least six months. The age of acquisition of HBV is strongly associated with the risk of developing chronic HBV infection. Approximately 90 percent of those infected perinatally or in infancy develop chronic HBV infection, compared with 30 percent of children infected between ages 1 and 4 years and less than 5 percent of people infected as adults.

Infants seldom mount an immune response to HBV infection, and infection in infancy is often asymptomatic. Asymptomatic chronic infection stimulates persistent immune responses that may eventually lead to cirrhosis (decades later); cirrhosis and chronic infection increase the risk of development of hepatocellular carcinoma.

Table 9.3: Characteristics and phases of chronic hepatitis B virus infection

Phases of HBV infection	Features
Immune tolerance phase	Prolonged period of active viral replication without active liver disease. Seen in children who acquire infection perinatally.
Immune clearance phase	Active viral replication and active liver disease
Inactive chronic HBV infection	Low or absent viral replication and remission of active liver disease
Reactivation	HBV replication after inactivity, seen in some patients

There are up to four phases of chronic infection as in Table 9.3 show; not all are present in all infections.[1] The initial phase of infection may last 10 to 30 years, during which spontaneous clearance rates of HBeAg in the serum are less than 1 percent per year.

Chronically infected people who are HBsAg positive can also have detectable HBeAg in the serum; this combination is considered most infectious. Although recent evidence suggests HBeAg negative patients are less infectious, it is dependent on HBV DNA levels. Whatever the case, both groups can be an ongoing source of infection to susceptible individuals. In the early years of chronic infection, high rates of viral replication are common, and both HBeAg and high levels of HBV DNA are present in the blood. In later years, HBeAg may be absent from the blood, and HBV DNA levels (viral load) are usually lower, both of which correspond with lower rates of viral replication.

It is estimated that 4.5 percent of HBsAg positive individuals (12 million people worldwide) have been co-infected with hepatitis D virus (HDV), which is a significant contributor to HBV-associated cirrhosis and hepatocellular carcinoma.[3] The highest prevalence is seen in those with hepatitis C and HIV, and in certain geographic areas.

9.2.4 Routes of transmission

HBV is usually transmitted through contact with infected blood or body fluids during childbirth, contact with broken skin, sexual intercourse or intravenous drug use. Although HBV can be found in all body fluids, blood has the highest concentration and saliva the lowest. HBV in dried blood remains infective for at least one week.[4]

Perinatal (vertical) transmission

The primary source of HBV infection is perinatal exposure from mothers with chronic HBV infection. Transmission usually occurs at the time of birth. The *in utero* transmission of HBV is relatively rare, accounting for less than 2 percent of infections transmitted from mother to infant.[5]

If no prophylaxis is given to the infant, the baby of an HBeAg positive mother has a 70–90 percent risk of infection, while the baby of an HBeAg negative HBsAg positive carrier mother has a 5–20 percent risk of infection. Over 90 percent of infants who acquire infection perinatally become chronic carriers.

Person-to-person (horizontal) transmission

Non-sexual person-to-person transmission probably occurs from inadvertent percutaneous or mucosal contact with blood or infectious body fluids among people in close daily contact (household members).

The main sources of transmission are:

- sexual contact with an infected individual
- percutaneous exposure to blood or infectious body fluids
- needle-stick injuries or sharing needles.

Those travelling to high endemic countries are at higher risk of exposure (see below).

9.3 Epidemiology

9.3.1 Global burden of disease

Approximately two billion people worldwide had been exposed to HBV in 1995. In 2015, based on serological data, around 3.5 percent of the general population globally were infected with HBV and more than 250 million people were estimated to have chronic infection and these people remain at risk of developing cirrhosis and hepatocellular carcinoma.[6, 7] More than 90 percent of individuals with chronic HBV resided in the Asia–Pacific region, where most countries have high prevalence rates of HBV infection (the population rate of HBsAg positivity is between 5 and 20 percent) and more than 99 percent of HBV-infected people in this region acquired infection through vertical transmission from their mother (usually at the time of delivery) or in early childhood.[8] As an example of this risk, 22.8 million out of 80 million people living in China with chronic HBV infection are women of child-bearing age.[9] Acquisition of HBV during adulthood (usually via sexual transmission or injecting drug use) is associated with a high rate of symptomatic hepatitis but a low rate of chronic infection.

The introduction of universal childhood HBV immunisation has changed the epidemiology of chronic infection in many countries, but it will be several decades (one to two human generations) before the full benefits are realised. In China, for example, within 20 years since the introduction of HBV immunisation, mother-to-child transmission has been cut by 97 percent; 120 million new HBV infections and 28 million chronic infections have been averted.[9] Thirty years after the introduction of a HepB immunisation programme for newborns in Taiwan, infant fulminant hepatitis mortality and, in those aged 5 to 29 years, chronic liver disease and hepatocellular carcinoma mortality had all decreased by more than 90 percent.[10]

The world can be divided into regions with high (8 percent and over), high-moderate (5–7 percent), low-moderate (2–4 percent) and low (less than 2 percent) prevalence of chronic infection, defined as the presence of HBsAg in serum.[11, 12] In regions with a high prevalence of chronic infection, the lifetime risk of exposure to HBV is almost 80 percent, with most infections occurring in the first decade of life. The Pacific Islands and most of Asia (except Japan and India) are high-prevalence regions. Other high-prevalence regions include Sub-Saharan Africa and Latin America.[12] In contrast, in countries with a low HBsAg prevalence, the lifetime risk of HBV exposure is less than 20 percent, with most infections acquired in adulthood. New Zealand has a low overall prevalence of hepatitis B carriage but contains certain populations with high prevalence (see section 9.3.2 below).

9.3.2 New Zealand epidemiology

Before the introduction of HBV immunisation in New Zealand, HBV transmission was common among preschool and school-aged children. The exact mode of transmission is uncertain, but is thought to be related to close contact. In the eastern Bay of Plenty region almost half of the population were infected by age 15 years.[13, 14] Even after the introduction of universal HepB in 1988 (see Appendix 1), there were regions in New Zealand where children were still at risk of HBV infection due to poor immunisation coverage rates.[15, 16, 17]

Acute HBV infection

Only acute hepatitis B is a notifiable disease in New Zealand; notification rates do not describe the burden of chronic HBV infections.

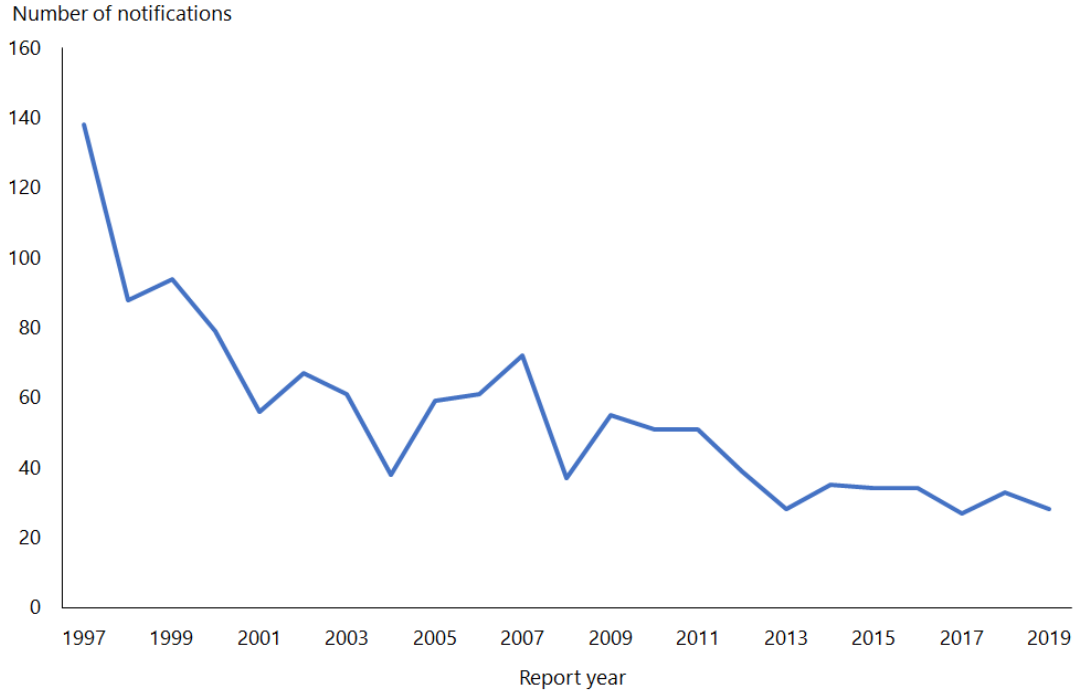
The HBV notification rate in 2019 was 0.6 per 100,000 population (28 cases), similar to the 2018 rate (0.7 per 100,000, 33 cases). The highest notification rate was in the 30–39 years age group (1.1 per 100,000) followed by 50–59 years and 70 years and over (both 0.8 per 100,000). The notification rate was higher for males (0.9 per 100,000) than for females (0.3 per 100,000) (ESR, 8 June 2020).

Ethnicity was recorded for all cases. The Māori (1.3 per 100,000) ethnic group had the highest hepatitis B notification rate followed by the Asian (0.7 per 100,000) ethnic group.

The most common reported risk factors were overseas travel, migration and sexual contact with a confirmed case or carrier.

Hepatitis B notifications have declined from 609 cases in 1984 to 28 cases in 2019 (see Figure 9.1). While difficult to quantify accurately, the introduction of universal infant immunisation in 1988 has contributed to the dramatic decline in the number of newly notified cases of HBV infection.

Figure 9.1: Notifications of hepatitis B, 1997–2019



Source: ESR

For recent data on acute hepatitis B notifications, refer to the most recent notifiable disease annual reports from ESR (available at **surv.esr.cri.nz/surveillance/annual_surveillance.php**).

Chronic HBV infection

The Hepatitis Foundation of New Zealand reports that around 120,000 people in New Zealand are living with chronic HBV infection, around 50 percent are diagnosed, but only around 7,000 are being treated. Based on 2016 data, around 1,000 new cases are diagnosed each year nationally. Mathematical modelling anticipated that the prevalence of chronic HBV infection would drop from 3.3 percent in 2016 to 2.4 percent by 2030, falling short of the elimination targets set by the WHO in 2016.[18]

The National Hepatitis B Screening Programme found that between 1999 and 2002 in the North Island, the highest rates of chronic HBV infection were among Chinese (9.1 percent), Pacific peoples (8.5 percent) and Māori (5.8 percent). Although Europeans were not specifically targeted in this screening programme, they have an estimated prevalence rate of 1 percent (higher than in Australia, North America and Europe), reflecting an increased risk of childhood horizontal transmission.[19]

A New Zealand-based modelling study estimated that until the year 2100, people with chronic HBV infection will continue to provide a source of infection to susceptible people.[20] Increased immigration from high-prevalence countries in the Asia–Pacific region is also likely to influence HBV prevalence in New Zealand.

Because people who acquire chronic HBV infection in childhood usually do not develop hepatocellular carcinoma until aged 40 years or older, the introduction of a universal HBV vaccination in 1988 is unlikely to have a significant effect on the incidence of hepatocellular carcinoma until approximately 2030.

A retrospective laboratory data study of antenatal HBsAg tests from the Midlands region (Bay of Plenty, Eastern Bay of Plenty, Waikato and Rotorua) between 1997 and 2009 found a declining prevalence of HBV infection. This decrease was seen across all age groups, but was most marked in antenatal tests of women aged under 20 years, due to receipt of funded HepB in childhood.[21]

A long-term follow-up study in New Zealand showed that horizontally acquired HBV infection during childhood in Māori and Pacific peoples correlates with increased rates of hepatocellular carcinoma and liver-related mortality.[22] This study emphasises the importance of early protection of the infant with vaccination.

Strategy for prevention

In 1988 New Zealand was one of the first countries to introduce universal infant hepatitis B immunisation. As of 31 December 2019, 93 percent of New Zealand children aged 2 years had completed a primary course of HepB, which confers lifelong immunity in approximately 95 percent of those vaccinated.

9.4 Vaccines

9.4.1 Available vaccines

The specific monovalent and combination HepB vaccines licensed (approved for use) and available (marketed) in New Zealand contain recombinant HBsAg (HepB).

Funded vaccines

- HepB (Engerix-B, GSK): contains 20 µg HBsAg per dose; it does not contain a preservative. Other components and residuals include aluminium hydroxide, sodium chloride, sodium phosphate dehydrate, sodium dihydrogen phosphate and traces of polysorbate 80.
- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and Haemophilus influenzae type b vaccine (see section 6.4.1 for more information).

Other vaccines

HepA-HepB (hepatitis A and hepatitis B vaccine): Twinrix and Twinrix Junior (GSK) (see also section 8.4.1).

9.4.2 Efficacy and effectiveness

Clinical trials in high-risk groups have shown a vaccine efficacy of 85–95 percent for HepB vaccines.[8]

See also section 15.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.

Immunogenicity

Serum anti-HBs antibody ≥10 IU/L, measured 1–2 months after immunisation, is considered by WHO as a correlate of long-term protection.[8] In the primary care setting, individuals who have had a documented seroconversion after three injections are expected to have lifelong immunity with no need for further boosters, even if circulating antibody is subsequently not detectable.

Smoking, obesity, HIV infection and chronic disease (including renal failure) all reduce vaccine efficacy, but age is the primary factor affecting the response. At least 98 percent of infants, 95 percent of children and 90 percent of adolescents develop protective levels of antibody after three doses of vaccine. Some non-responders will not produce adequate antibody levels to the initial vaccination course, but most respond to further vaccine doses.

However, some people are persistent non-responders. Persistent non-responders often have an impaired immune system, such as organ transplant recipients and those with HIV infection or chronic disease, including advanced cirrhosis, renal failure or those undergoing haemodialysis. A small percentage (approximately 2–3 percent) of the immunocompetent population may also fail to elicit an antibody response. High-risk individuals who fail to respond adequately are recommended further vaccinations (see section 9.5.7).

Effectiveness of birth dose given to babies born to HBsAg-positive mothers

Infants vaccinated at birth born to infected mothers were 3.5 times less likely to be infected with HBV than those who did not receive a birth vaccination.[8, 23] For babies of HBeAg-positive mothers, controlled trials have shown that vaccine at birth provides 75 percent protection from infection, while administration of HBIG in addition to vaccination provides 85–95 percent protection against transmission.[23, 24] Transmission following HBIG/HepB prophylaxis at birth almost exclusively occurs in HBeAg-positive mothers with high HBV DNA levels (above 2 x 10^5 IU/ml or 1 million copies/ml) and/or HBsAg levels above 4-4.5 $\log_{10}$ IU/ml.[25] In this situation, administration of tenofovir (an antiviral agent) to the mother during the last trimester is recommended and funded.

Duration of immunity

The development of anti-HBs antibodies after a primary vaccination course (three injections and seroconversion) indicates development of immune memory. The quantity of antibody in serum is thought to determine the length of time the antibody titre can be detected in the blood, although any reading ≥10 IU/L post-vaccination course is considered protective.[26, 27] Children who are given booster doses up to 12 years after the primary series show strong anamnestic (secondary) responses, indicating that booster is unnecessary once a seroprotective level is reached after the three-dose primary vaccination course.[26, 27]

Long-term protection from clinical infection, despite loss of detectable neutralising antibody, is thought to reflect a strong cellular memory immune response following HBV vaccination.[28] Even though a large proportion of vaccine recipients may have undetectable antibody within seven years of vaccination, there is evidence from Germany,[28] Taiwan,[29] Alaska[30] and Hawaii[31] that boosters of HepB are unnecessary following completion of infant immunisation.

Sustained immune memory, including circulating memory B and T cells, and long-term protection have been shown 20–30 years after complete primary immunisation of immune competent adults in the absence of natural or artificial boosting.[24]

In general, vaccine recipients who are subsequently infected with HBV do not develop clinical illness but may have anti-HBc present in plasma.[1]

Impact on chronic HBV infection

In all populations, where it has been measured, immunisation has led to a dramatic drop in HBV chronic infection.[32] For example, chronic HBV infection dropped from 16 percent to zero in Alaska as a result of 96 percent immunisation coverage. In Taiwan, the incidence of hepatocellular carcinoma also decreased as a result of the immunisation programme in children.[33, 34] Adolescents and adults who were offered universal HBV vaccination in infancy had more than 75 percent lower prevalence of HBV infection and anti-HBc prevalence than those for whom immunisation was unavailable.[35]

9.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at

health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and HepB vaccines should be stored in the dark.

> DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

9.4.4 Dosage and administration

DTaP-IPV-HepB/Hib

Each 0.5 mL dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine contains 10 µg of HBsAg, and is administered by intramuscular injection (see section 2.2.3).

HepB

The dose of HepB vaccine varies according to the vaccine manufacturer, the age of the individual and/or their health status (see section 9.5 for recommendations):

- Engerix-B 20 µg (GSK): 20 µg HBsAg per 1.0 mL
- Engerix-B paediatric 10 µg (GSK): 10 µg per 0.5 mL.

HepB vaccine is administered by intramuscular injection. It can be also administered by subcutaneous injection, if indicated for bleeding disorders (see section 2.2.3).

Co-administration with other vaccines

Hepatitis B vaccines may be given at the same time as all other vaccines on the Schedule, including measles, mumps and rubella (MMR) vaccine.

If a course of vaccine is interrupted, it may be resumed without repeating prior doses (see Appendix 2).

9.5 Recommended immunisation schedule

Table 9.4: Hepatitis B vaccine recommendations, funded and unfunded

Note: **Funded individuals and situations are in the shaded rows.** See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to funding decisions.

Recommended and funded
Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Babies of HBsAg-positive mothers (ie, mothers with acute or chronic HBV infection) – require a birth dose plus the three-dose primary series (HBIG is also given to these babies at birth)
Children and adolescents aged under 18 years who are considered not to have achieved a positive serology by 1 month after vaccination and require additional vaccination or require a primary course of vaccination[a]
Individuals who are HIV-positive[b]
Individuals who are hepatitis C-positive[c]
Following non-consensual sexual intercourse
Prior to planned or following immunosuppression[b,d]
Prior to or following solid organ transplant[b,d]
Individuals post-HSCT[b]
Following needle-stick injury
Patients on dialysis[b,d]
Recommended, not funded
Adults at occupational risk (see section 4.8)
Adults at risk of infection by sexual exposure: • people seeking evaluation or treatment for a sexually transmitted infection • people with a high number of sexual partners • people who have sex with commercial sex workers • men who have sex with men
Individuals with haemophilia and other regular recipients of blood products
Prison inmates
Current or recent injecting drug users
Individuals with developmental disabilities
Migrants from HBV endemic countries (HBsAg prevalence ≥2 percent)[f]
Travellers to HBV endemic regions (HBsAg prevalence ≥2 percent)[f]

a. Serological testing is not routinely recommended, see Figure 9.3.

b. See also section 4.3.3.

c. Hepatitis C patients should also receive hepatitis A vaccine, although this is not currently funded.

d. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

e. 40 µg of HepB is recommended for adult dialysis patients or for adult liver or kidney transplant patients.[36] See Table 9.5.

f. See the Centers for Disease Control and Prevention website for countries with an HBsAg prevalence ≥2 percent (**https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-b**). Consider combined Hep A and B vaccination for travellers to these regions.

9.5.1 Usual childhood schedule

A primary course of hepatitis B vaccination is given as three doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months (Table 9.5). If a course of immunisation is interrupted for any reason, it may be resumed without repeating prior doses (see section 9.5.3 and Appendix 2).

Table 9.5: Usual childhood schedule for hepatitis B-containing vaccine (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series

Preterm infants of HBsAg-negative women

Some low birthweight or preterm infants may have a reduced response to HepB vaccine at birth.[37] However, by the chronological age of 1 month, all medically stable preterm infants, regardless of initial birthweight or gestational age, respond to HepB as well as term and larger infants.[38] Because New Zealand's Schedule starts at age 6 weeks, low birthweight and preterm infants are expected to respond to HepB content in the DTaP-IPV-HepB/Hib vaccine. (See also sections 4.2.1 and 4.2.2.)

Infants with liver or renal disease

HepB vaccine is funded for liver or kidney transplant patients and for dialysis patients. For infants requiring transplants, see 'Solid organ transplantation' in section 4.3.11. For infants undergoing dialysis, see 'Chronic kidney disease' in section 4.4.

9.5.2 Infants born to HBsAg-positive mothers

The routine schedule for these infants is a birth dose of monovalent HepB plus HBIG, then three routine doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months.

All pregnant women should receive antenatal screening for hepatitis B infection by testing for HBsAg. Infants of HBsAg-positive mothers are to be notified at birth using the form ***HE1446: Consent for hepatitis B vaccine and hepatitis B immunoglobulin and notification to the Medical Officer of Health***, available from **healthed.govt.nz** or the local authorised health education resource provider or public health unit.

Infants born to HBsAg-positive mothers should receive:

- 100–110 IU HBIG neonatal, at or as close as possible to birth
- a birth dose of HepB which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice.

These infants should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see below).

The vitamin K injection may also be given at the same time, in the same limb as the HBIG, but not at the same site.

Occasionally women have not been tested for their HBsAg status during the antenatal period. If a woman's HBsAg status is unknown at the time of delivery, the baby should be given HepB at the time of delivery while waiting for the result of an urgent HBsAg test on the mother. If she is found to be HBsAg positive, the baby should be given HBIG as soon as possible, up to seven days post-delivery. Immunoprophylaxis is most effective when given within 12 hours of delivery.[38] Subsequent vaccine doses are given as per the Schedule.

It is essential to take blood to determine whether the baby has seroconverted (anti-HBs positive) or has become infected despite immunoprophylaxis (HBsAg positive), or is neither infected nor immune (ie, HBsAg negative and anti-HBs negative). Testing should be performed at 9 months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximise the likelihood of detecting late onset HBV infections.[38] Infants of HBsAg-positive mothers should be placed on a practice recall system to have their blood tested at 9 months of age. Check at the 12-month immunisation event to ensure that testing has occurred. The serology results should be interpreted as in Figure 9.2.

Figure 9.2: Management of an infant of an HBsAg-positive woman

Screen all women in early pregnancy for hepatitis B carriage

Woman is HBsAg positive **No** ⋯⋯› See section 9.5.1: 'Usual childhood schedule'

Yes

All HBsAg-positive pregnant women should also be tested for HBeAg and should have HBV DNA measured. The results should be discussed with a specialist or the woman should immediately be referred to a specialist for ongoing care.

Give the baby hepatitis B protection as follows.

At age	Action to be taken
Birth	Give HBIG 100–110 IU **and** HepB
6 weeks	DTaP-IPV-HepB/Hib
3 months	DTaP-IPV-HepB/Hib
5 months	DTaP-IPV-HepB/Hib
9 months	Take a blood test to check for hepatitis B infection (HBsAg) and for vaccine-induced immunity (anti-HBs). If HBsAg is negative and anti-HBs level is ≥10 IU/L at age 9 months, immunity is proven. If HBsAg is positive, the infant has become infected despite prophylaxis: refer to an appropriate specialist. If HBsAg is negative and anti-HBs level is <10 IU/L at age 9 months, give a further 3 doses of HepB at least 4 weeks apart. Recheck serology 4 weeks after the last dose. If there is no seroconversion after the third further dose of HepB (ie, if anti-HBs is still <10 IU/L), discuss with a specialist.

All other vaccines should be administered as per the Schedule.

Neonatal HBIG plus vaccine will fail to prevent vertical HBV transmission in up to 20 percent of infants born to HBsAg-positive mothers with serum HBV DNA levels greater than 10^8 IU/mL (or 2 x10^7 copies/mL). These mothers are usually young, with normal alanine transaminase, and are HBeAg-positive. If the mother's HBV DNA level is greater than 200,000 IU/mL[39, 40, 41], administration of tenofovir (an antiviral agent) during the last trimester is funded.

The number of such high-risk pregnancies appears to be increasing in this country as a result of the immigration of young Asian women of childbearing age, of whom approximately 8 percent are HBsAg-positive with the majority of those also HBeAg-positive. In contrast, the number of HBsAg-positive Māori and Pacific women of childbearing age has decreased markedly due to infant vaccination. In addition, most HBsAg-positive Māori and Pacific women are HBeAg-negative, with lower HBV DNA levels (below 10^8 IU/mL).

Infants born to mothers who received oral antiviral therapy for chronic HBV must still receive the recommended neonatal HBIG/vaccine schedule. All other vaccines are administered as per the Schedule.

See Appendix 6 and section 9.8.1 for more information about passive immunisation and HBIG.

Preterm and low birthweight infants of HBsAg-positive women

Preterm and low birthweight infants of HBsAg-positive women should be managed as above, regardless of birthweight or gestation.

9.5.3 Catch-ups for children and adolescents

HepB is recommended and funded for everyone aged under 18 years. If HepB is not given during the first year of life, three doses of vaccine are recommended given 0, 1 and 6 months.

For adolescents aged 11–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using the monovalent HepB with the second dose given four to six months after the first.

See Appendix 2 for catch-up schedules.

Children and adolescents with liver or kidney disease

HepB vaccine is funded for liver or kidney transplant patients (recommend six months post-transplant) and for dialysis patients.

See Figure 9.3 and Figure 9.4 for serological testing and vaccination recommendations. If non-immune, children aged under 16 years should receive three doses of HepB; those aged 16 years and older should receive four doses of HepB given at 0, 1, 2 and 12 months. If there is an inadequate immune response to the initial three-dose HepB series (see Figure 9.4), give a further three doses, as appropriate for age.

See also 'Solid organ transplantation' in section 4.3.11, 'Chronic kidney disease' in section 4.4 and 'Chronic liver disease' in section 4.5.

9.5.4 Eligible adults aged 18 years and older

Table 9.6: Hepatitis B vaccine schedules for eligible adults aged 18 years and older

Who	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Dialysis patients, liver or kidney transplant patients	HepB	40 µg	1.0	3	0, 1 and 6 months
HIV patients	HepB	20 µg	1.0	4	0, 1, 2 and 12 months
Other eligible adults (see Table 9.4)	HepB	20 µg	1.0	3	0, 1 and 6 months

Adult dialysis or adult liver or kidney transplant patients

These adults may have a reduced response to HepB,[36, 42] so three higher doses (40 µg per dose) are recommended and funded.

See section 9.5.7 for information about post-vaccination serology.

(See also 'Solid organ transplantation' in section 4.3.11 and recommendations provided in IMAC factsheet '*Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant*' available at **immune.org.nz**.)

Adult HIV patients

Adult HIV patients should receive four doses of HepB (20 µg per dose) at 0, 1, 2 and 12 months.

(See also 'HIV infection' in section 4.3.13 and recommendations provided in IMAC factsheet *Immunisation for adults with HIV infection* available from **immune.org.nz**.)

Other eligible adults

The optimal dosing regime is three doses of 20 µg HepB given at 0, 1 and 6 months. See the manufacturer's data sheet for sub-optimal accelerated HepB schedules if dosing is time constrained. For other eligible adults, see

Table 4.8, 'Other special groups' in section 4.6.

9.5.5 Pregnancy and breastfeeding

HepB may be given during pregnancy and while breastfeeding. Acute HBV infection in pregnant women may result in severe acute hepatitis for the mother, with associated increased risk of fetal loss or neonatal infection. Vaccination should not be withheld from a susceptible pregnant woman at increased risk of acquiring hepatitis B (eg, the sexual partner of an injecting drug user, or known infected male).

9.5.6 (Re)vaccination

Hepatitis B-containing vaccines are funded for vaccination and revaccination of eligible children, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for vaccination or revaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib are funded for children aged under 10 years receiving solid organ transplantation.

Monovalent HepB

HepB is funded for children aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination.

9.5.7 Serological testing

- Serological testing is **not** routinely recommended – immunisation is highly effective.
- Most people with documented evidence of three HepB vaccinations will be immune for life.
- Unnecessary testing leads to unnecessary extra vaccination.

- Infants born to HBsAg-positive mothers and some individuals who require protection in relation to their employment (eg, health care professionals) require post-vaccination serology.
- Where there is concern about immunity follow Figure 9.3.

Screening for chronic infection

Screening for the antigen (HBsAg) is useful where there is increased likelihood of the individual already being infected.

The Hepatitis Foundation of New Zealand recommends that the following individuals are most at risk of HBV:[43]

- people of Māori, Pacific or Asian ethnicity, unless fully vaccinated with HepB vaccine as an infant
- people born in an area of high hepatitis B endemicity, including Asia, the Pacific Islands, Africa, the Middle East, southern Europe or the northern or eastern parts of New Zealand's North Island
- people born to a mother or who have a close family member who has chronic HBV infection
- people who live with someone who has HBV
- people who have had unprotected sexual contact with an HBV-infected person
- people who have ever injected drugs
- people who have received a tattoo using unsterile equipment.

Screening for HBsAg is also part of routine antenatal care (see section 9.5.2).

All HBsAg-positive individuals should be offered follow-up under the Hepatitis Foundation Hepatitis B Follow-up Programme to enable early diagnosis and treatment of the complications of severe liver disease and hepatocellular carcinoma. Vaccination is funded for household or sexual contacts of HBsAg-positive people (ie, contacts of people with acute or chronic HBV infection).

To confirm chronic HBV status, repeat testing after 6 months and if still positive, refer patient to The Hepatitis Foundation.

Serological testing for high-risk groups

Serological testing is **not** routinely recommended – immunisation is highly effective.

- Serological testing is only indicated in high-risk groups (see Table 9.7). These high-risk groups are at higher risk of exposure to HBV, at higher risk of having severe disease or are more susceptible to disease.
- A flow diagram (Figure 9.3) is included to assist in deciding whether pre- and/or post-vaccination serological testing is indicated. Figure 9.3 may be

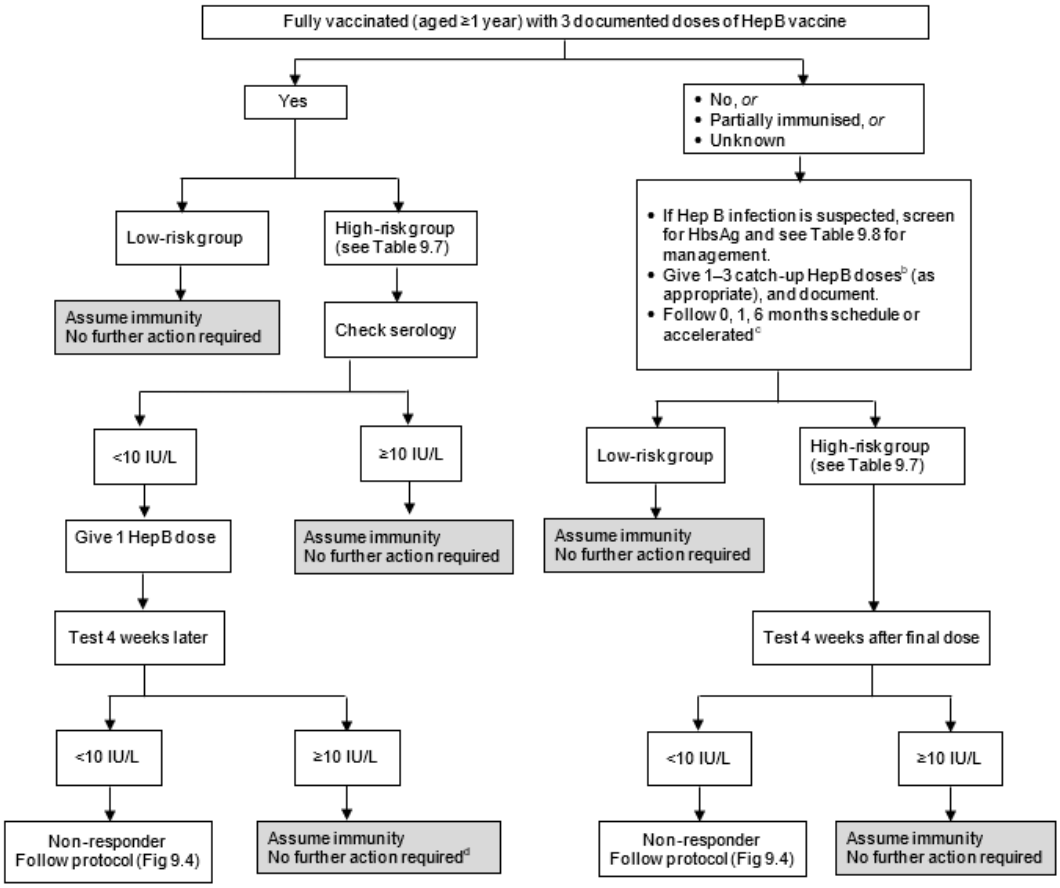
used for any individual aged 12 months or older, such as for the management of blood and body fluid exposures, or when an adult presents to primary care.

Table 9.7: Individuals at high-risk of hepatitis B infection, for whom serological testing is indicated

Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Current or recent injecting drug users
Individuals who change sexual partners frequently (eg, sex workers)
Immunocompromised individuals, including HIV-positive patients
Following non-consensual sexual intercourse
Individuals prior to planned immunosuppressive therapies for 28 days or more
Individuals following immunosuppressive therapies for 28 days or more
Solid organ and post-HSCT patients
Following percutaneous injury (eg, needle-stick injury)
Adults at occupational-related risk (see section 4.8)
Individuals with haemophilia and other regular recipients of blood products
Inmates of custodial institutions
Individuals with developmental disabilities
People with chronic disease (eg, chronic renal failure requiring haemodialysis, or chronic liver disease)
Migrants from HBV endemic regions (where HBsAg prevalence is ≥2 percent)*

* See the Centers for Disease Control and Prevention website for countries with an HBsAg prevalence ≥2% (**https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-b**). Consider combined Hep A and B vaccination for individuals travelling to these regions.

Figure 9.3: Flow diagram for serological testing for hepatitis B



a. HBIG may be recommended for non-immune individuals. See Table 9.8.

b. Do not count any birth doses of HepB vaccine. See Table 9.4 for the list of funded conditions for HepB vaccine.

c. See the manufacturer's data sheet for accelerated HepB schedules.

d. Haemodialysis patients need annual testing and boosting if required.

The non-responder protocol

Most vaccine recipients will develop a high anti-HBs titre, usually greater than 100 IU/L, which usually wanes over time.

Fully vaccinated individuals (ie, those who have received three documented doses of HepB) who have at any time had anti-HBs ≥10 IU/L do not need any booster doses, even if antibodies subsequently wane to undetectable levels, which occurs in most individuals by seven years after the last vaccination. Adults have been shown to have an anamnestic antibody and cellular immune response to a HepB dose given 20–30 years after the primary immunisation.[24] If exposed to HBV, they will have a secondary anamnestic immune response that will prevent replication of the virus.[1, 44]

Note: Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

If a high-risk individual does not achieve a titre of ≥10 IU/L by four weeks following one HepB dose, they should be considered a non-responder and follow the non-responder protocol (Figure 9.4).

Figure 9.4: The non-responder protocol

Individual is high-risk (see Table 9.7), has received three documented doses of HepB plus a booster dose and has an anti-HBs <10 IU/L:

- Complete a second course of three HepB vaccine doses.
- Repeat the serology four weeks after the final HepB vaccine dose.
- If anti-HBs ≥10 IU/L, assume immunity. No further action is required.
- A third course of three doses of 40µg HepB vaccine (ie, two injections per visit of Engerix-B 20 µg) is advised for high risk individuals who fail to respond to a second course.[45] Alternatively, there is also some evidence that using a double dose of HAV-HepB (Twinrix) at 0, 1 and 6 months can correct this hyporesponsiveness, using the bystander carrier effect of the HAV component,[46] but this is not funded.
- Repeat serology four weeks after final HepB dose.
- If, after the third course of three HepB vaccine, a person has not achieved anti-HBs ≥10 IU/L, they should be considered a persistent non-responder to vaccination.
- Persistent non-responders with no immunocompromise who have completed the primary series and further courses of three vaccine doses should be monitored for wild-type disease, but literature reports disease from vaccine failures are rare. They should be considered 'unprotected' against hepatitis B and advised to minimise the chance of exposures. Parenteral or mucosal exposure to HBV requires HBIG within 72 hours.

Intradermal injections to correct this hypo-responsiveness have been used in the past, but they are technically difficult and not recommended.

9.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

The only specific contraindication to HepB is anaphylaxis following a previous dose, or individuals with a history of allergic reactions to yeast or any of the vaccine's components. Immunisation of previously infected subjects is wasteful, but not harmful.

See section 15.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

9.7 Potential responses and AEFIs

See section 15.7 for potential responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

9.7.1 Potential responses

Minor side-effects – including local tenderness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than in children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after receiving the vaccine include a temperature >37.7°C in 1–6 percent; pain in 3–29 percent; and erythema, headache or swelling in 3 percent of vaccine recipients.

9.7.2 AEFIs

Allergic reactions have been reported but are rare. Anaphylaxis following vaccination is extremely rare (estimated to be 1.1 cases per million doses).[47]

A number of studies have examined and failed to find disease events linked to hepatitis B immunisation.[48] These studies have documented no increased risk of multiple sclerosis,[49, 50, 51] diabetes, chronic fatigue syndrome,[52] encephalomyelitis or hair loss.[53] Rarely, transient thrombocytopenia[54] and myalgia and arthralgia[55, 56] have been reported after HepB vaccination.

9.8 Public health measures

The elimination of HBV transmission is now a realistic public health goal[7, 57] especially with the proven effectiveness and safety record of HepB.[58] Achievement of this goal is being facilitated by the implementation of triple elimination strategies in the Western Pacific Region to prevent mother-to-child transmission of HIV, HBV and syphilis,[8] and the use of birth dosing HepB regimes, either universally or as directed.

It is important to ensure vaccination programmes are maintained for the at-risk populations, especially babies of mothers with chronic hepatitis B infection.

> It is a legal requirement that all cases of acute hepatitis B infection be notified to the local medical officer of health.

Babies born to HBsAg-positive mothers should be notified at birth. The prevention of perinatal transmission is covered in section 9.5.2.

9.8.1 Passive immunisation

HBIG is prepared from donated blood plasma and contains high levels of anti-HBs antibody (see Appendix 6). It is given after exposure to HBV and provides passive anti-HBs antibody protection against acute and chronic HBV disease. HBIG prophylaxis should be given in combination with the HepB to confer both passive and active immunity after exposure.

The efficacy of HBIG alone in preventing clinical hepatitis B infection is about 75 percent in adults, but the protection lasts only for a few months.[1]

Whenever immediate protection is required, immunisation with a vaccine should be combined with simultaneous administration of HBIG at a different site. It has been shown that passive immunisation with HBIG does not suppress the active immune response to vaccination. A single dose of HBIG is sufficient (usually 400 IU for adults, 100–110 IU for newborns).[59] If infection has already occurred at the time of the first immunisation, virus replication is unlikely to be inhibited completely, but severe illness and, more importantly, the development of chronic HBV infection may be prevented, particularly in the infants of HBsAg-positive mothers.

The management of contacts is summarised in Table 9.8.

Table 9.8: Management of contacts of hepatitis B cases

Contact	Serological testing of contact (HBsAg, anti-HBs, anti-HBc, IgM and IgG)	Immunoglobulin (if within 7 days of onset of case's symptoms)	Immunisation
Any sexual contact, including protected sex	Yes	Yes, immediately after blood taken	Yes, immediately after blood taken
Household, mucosal or percutaneous	Yes	Yes, if serology negative	Yes, if serology negative
Other	Yes	No	Yes, if serology negative

Source: Ministry of Health. 2012. *Communicable Disease Control Manual*. Wellington: Ministry of Health. URL: **www.health.govt.nz/publication/communicable-disease-control-manual** (accessed 30 June 2020).

For more details on control measures, refer to the 'Hepatitis B' chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/publication/communicable-disease-control-manual-2012**).

9.9 Variations from the vaccine data sheet

See section 15.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

Ministry of Health advises that two doses Engerix-B 20 µg, given four to six months apart, may be given to adolescents aged 11–15 years. The manufacturer's data sheet recommends three doses of 10 µg given at 0, 1 and 6 months, but in circumstances where compliance may not be assured, giving 20 µg per dose increases the proportion of recipients protected after the first and second doses.

Although the Ministry of Health and the data sheet recommend 0.5 ml Engerix-B 10 µg (paediatric formulation) for neonates born to HBV infected mothers, where the paediatric presentation is unavailable, the data sheet advises that Engerix-B 20 µg can be given to children from birth up to the age of 10 years.

The Ministry of Health recommends giving three doses of 40 ug HepB (ie, two doses of Engerix-B 20 µg per visit) to be given 0, 1, and 6 months for adult renal dialysis patients, liver or kidney transplant patients. For adults with HIV, four doses of Engerix-B 20 µg is recommended given at 0, 1, 2 and 12 months. The data sheet advises four doses of 40 µg (ie, two doses for Engerix-B 20 µg per visit) given at 0, 1, 2 and 6 months for chronic haemodialysis patients and other individuals who have an impairment of their immune system.

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10 Human papillomavirus

Key information

Mode of transmission	Skin-to-skin contact, predominantly sexual, with a person with human papillomavirus (HPV) infection.
Period of communicability	HPV infection is very common, with initial infection occurring soon after sexual debut and a lifetime risk of over 80%. Recurrent infection and co-infection with multiple types are possible.
Incidence and burden of disease	HPV is linked to almost all cervical cancers and to about 69% of vulvar, 75% of vaginal, 63% of penile, 90% of anal and 70% of oropharyngeal cancers.
Funded vaccine	HPV9 (Gardasil 9) is a recombinant subunit vaccine containing virus-like particles (VLPs). HPV9 contains HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58.
Dose, presentation, route	0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded indications and recommended schedules	2 doses, at 0 and 6–12 months for children aged 14 years and under. 3 doses, at 0, 2 and 6 months, for individuals: • aged 15–26 years inclusive • aged 9–26 years inclusive: – with confirmed HIV infection or – who are transplant (including stem cell) patients An additional dose for individuals aged 9–26 years post-chemotherapy. NB: Individuals who were previously fully vaccinated with HPV4 are not eligible for HPV9.
Vaccine effectiveness	The incidence of HPV infection, precancerous lesions and genital warts is significantly reduced in immunised populations (in women and men). There is evidence for herd immunity (reductions in HPV infection and genital warts in unimmunised populations).
Precautions and special considerations	HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.
Potential responses to vaccine	Syncope (fainting) and other immunisation-related stress reactions are associated with giving vaccine to adolescents.
Public health measures	Measures for cancer prevention (see section 10.8): • HPV immunisation. • Regular cervical screening for women. • Safer sex approaches.

10.1 Virology and the causal link to cancer

Human papillomaviruses (HPVs) are small, non-enveloped DNA viruses from the Papillomavirus family. There are about 150 different HPV serotypes. They vary in their preference for infecting squamous epithelium at different sites, thereby causing the various types of HPV infection (eg, common, palmar, plantar or anogenital). More than 40 HPV types can infect the anogenital tract.[1, 2]

Data from the US cancer registry indicates that HPV is causally associated with almost all cervical cancers, about 69 percent of vulvar, 75 percent of vaginal, 63 percent of penile, 90 percent of anal and 70 percent of oropharyngeal cancers (see Table 10.1).[3]

Based on their causal link to cancer, HPVs are divided into low-risk and high-risk types. There are approximately 12 high-risk types, which include 16, 18 and types 31, 33, 52, 58 and 45 that are genetically related to 16 and 18.[4] Types 16 and 18 are most frequently associated with cervical cancer but are also causally associated with other cancers. In the US, HPV types 16 and 18 are estimated to cause 66 percent of invasive cervical cancers, 80 percent of anal, 49 percent of vulvar, 55 percent of vaginal, 48 percent of penile and 60 percent of oropharyngeal cancers annually (Table 10.1).[3]

Low-risk types (especially types 6 and 11) are predominantly associated with non-malignant lesions, such as genital warts, and recurrent respiratory papillomatosis.

Table 10.1: Average annual percentage of cancer cases attributable to HPV, by anatomic site and sex, United States, 2008–2010

Anatomic site[c]	Cancers attributable to any HPV[a, b] %	Cancers attributable to HPV 16, 18[a, b] %	Cancers attributable to HPV 31, 33, 45, 52, 58[a, b] %
Cervix	90.6[d]	66.2	14.7
Vulva	68.8	48.6	14.2
Vagina	75.0	55.1	18.3
Penis	63.3	47.9	9.0
Anus			
• women	92.5	79.5	10.8
• men	88.7	79.1	3.8
Oropharyngeal			
• women	63.3	50.8	9.5
• men	72.4	63.4	4.4

a. Data is from 2008–2010 diagnosis years from population-based cancer registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results Program.

b. These estimates do not consider future changes in incidence, population structure or the percentage of cancers that are HPV positive.

c. International Classification of Diseases (ICD) codes: Cervix C53; Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharyngeal (includes cancers of the soft palate, walls of pharynx, tonsils and base of tongue) C01.9, C02.4, C02.8, C05.1, C05.2, C05.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.2, C10.8, C10.9, C14.0, C14.2, and C14.8.

d. Although HPV is accepted to be a necessary factor in the causal pathway to invasive cervical cancer, HPV is not always detected in tumour specimens from women who receive a diagnosis of invasive cervical cancer due to a variety of reasons, including misclassification of tissue specimens as cervix, quality of tissue specimens, assay sensitivity, and a small proportion of HPV-negative, cervical cancers.

Adapted from: Saraiya M, Unger ER, Thompson TD, et al. 2015. US Assessment of HPV types in cancers: Implications for current and 9-valent HPV vaccines. *Journal of the National Cancer Institute* 107(6), DOI: 10.1093/jnci/djv086 Table 4.

10.2 Clinical features

10.2.1 Infection

Infection results from predominantly sexual skin-to-skin contact with a person with HPV infection. Transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse. HPV may also be transmitted perinatally from mother to newborn baby.

Clinically apparent warts are probably more infectious than subclinical infection. The virus penetrates micro-abrasions in the epithelium to reach the basal epithelial cells, where it causes the infected cells to produce proteins that delay cellular maturation. Continued replication of these infected cells in the intermediate epithelial layer, followed by virus replication in the superficial epithelial layer, results in the cellular overgrowth typical of warts.

For most people, HPV infection is transient and becomes undetectable by DNA testing within 6 to 12 months, but in some cases, HPV infection remains latent and may reactivate years later. As it is difficult to detect HPV in its latent stage, it is impossible to know whether the immune system can completely clear the virus or whether, in some cases, undetectable latent virus is capable of later re-emerging.

Acquisition of HPV

Infection with oncogenic serotypes of HPV is common, with an estimated 70–80 percent of sexually active individuals becoming infected at some stage during their life. Initial infection occurs soon after sexual debut.

Most episodes of infection become undetectable by DNA testing within two years of acquisition; the average duration of infection is one year. Previous infection does not necessarily create long-term immune memory so does not prevent future re-infection with the same HPV type.

At any one time, approximately 10 percent of women have at least one HPV infection. The HPV serotypes that cause more prolonged infection tend to be those that more frequently result in the development of histological abnormalities.[5, 6]

Two US studies found that incidence of genital HPV infection was higher in men than for similar cohorts of young women. In university students (age 18–20 years), the cumulative incidence of first-time infection at 24 months was 32 percent (95% CI: 28.0–37.1) for females compared with 62.4 percent (95% CI: 52.6–72.2) in heterosexually active male students. Frequent new sexual partners and a history of smoking were associated with an elevated risk of HPV acquisition for both.[7, 8]

There are differences between the sexes in the immune response to HPV. A smaller proportion of men are HPV-seropositive, and men have lower antibody titres than women.[9] In contrast to women, for whom the risk for HPV acquisition increases with age through the early 20s and then decreases, studies have demonstrated HPV prevalence in men seems to peak at slightly older ages and remains constant or decreases slightly with increasing age, suggesting persistent HPV infection or a higher rate of re-infection.[10, 11]

Men who have sex with men, especially those who are HIV-positive, are at higher risk for HPV infection, anal cancer and high-grade anal intraepithelial neoplasia.[12] In teenage men who have sex with men (aged 16–20 years), early and high per-partner HPV transmission occurs between men soon after their first sexual experiences.[13]

Individuals who are immunocompromised (due to medical conditions or treatment) are more likely to develop a persistent HPV infection and to subsequently progress to HPV-related disease.[14, 15] Those with confirmed HIV infection are more at risk of HPV infection.[16] HPV is less likely to become undetectable in individuals coinfected with HIV.[17, 18] A direct relationship has been identified between low CD4+ cell count and an increased risk of cervical cancer in HIV-infected women.[19]

10.2.2 Cervical cancer

HPV rapidly becomes undetectable in the first 6–12 months of acquisition of infection, with 80–90 percent undetectable by two years. Following this, a very small fraction of persistent infection progresses to cervical intraepithelial neoplasia (CIN); these are non-invasive precancerous lesions, which are categorised as either low- or high-grade CIN. Invasive cervical cancer occurs when the lesions invade the cervical tissue, and is graded from stage I to IV, depending on how far the cancer has spread beyond the cervix into surrounding tissue or organs.

Cervical cancer does not usually develop until decades after acquisition of infection with an oncogenic (cancer-causing) HPV serotype. Persistent HPV infection is detected in almost all women with cervical cancer.[20]

HPV infection is essential, but not sufficient by itself, for the development of cervical cancer. Other factors have been described that may be associated with HPV persistence and high-grade lesions including smoking, early onset sexual activity, older age, contraceptive use, multiple sexual partners and genetic factors.[21, 22]

10.2.3 Oropharyngeal and other cancers

The clinical features of other HPV-associated cancers and their precancerous lesions in the anogenital and oropharyngeal regions vary, and also depend on the anatomical site. The progression from HPV-associated precancer lesions to cancers in these sites is less well understood than the process in the cervix.

Oropharyngeal cancers include cancers of the soft palate, the walls of the pharynx, the tonsils and the base of the tongue. The risk factors for oropharyngeal cancer are similar to those for cervical cancer, including the number of sexual partners, younger age at first sexual intercourse, practice of oral sex, history of genital warts and younger age.[23]

10.2.4 Genital warts and recurrent respiratory papillomatosis

HPV 6 and 11 account for around 90 percent of all genital wart cases. Most warts cases are self-limited, although some may persist for several years. Persistence is more common in patients with impaired cell-mediated immunity.[2]

Perinatal transmission of HPV (usually types 6 or 11) can cause laryngeal infection in infants, which in rare cases can result in recurrent respiratory papillomatosis in children. Respiratory papillomatosis is characterised by multiple warty growths on the mucosal surface of the respiratory tract, which can cause hoarseness and significantly obstruct the airways and require repeated surgery.[2]

10.3 Epidemiology

10.3.1 Global burden of disease

HPV is an important carcinogenic infection. The 12 high-risk types are reported to be the second most common infectious cause of cancer worldwide after *Helicobacter pylori*.[24] It has been estimated that 4.5 percent of all cancers (630,000 new cancer cases per year) are attributable to HPV; over 70 percent are attributable to HPV types 16 and 18, and 90 percent to types contained within the HPV9 vaccine. The greatest burden is in India and sub-Saharan Africa, where there is limited access to both screening and vaccination, and more than 20 percent of cancers in women are attributable to HPV infection.[25]

Onset of sexual activity

Most HPV infections occur within the first two years of onset of sexual activity; more than 40 percent of individuals become infected during this period. The first sexual relationship carries a substantial risk.[26]

Cervical cancer

Cervical cancer is the fourth cause of female cancer and cancer deaths in the world and is the second most common cause of female cancer and cancer deaths in women aged 15–44 years; the estimated incidence rate of cervical cancer cases attributable to HPV across Oceania was 10.1 (range 5.6–28.3) per 100,000 across all ages; the estimated annual mortality was 4.6 (range 1.6–18.6) per 100,000 in 2020.[27]

Persistent HPV infection can lead to high-grade CIN. Approximately one-third of CIN3 progresses to invasive cervical cancer within 10–20 years. A 2010 study reported that more than one-quarter (26.7 percent; 95% CI: 21.1–31.8) of those with persistent HPV16 and nearly one in five (19.1 percent; 95% CI: 10.4–27.3) of those with persistent HPV18 developed CIN3 or cancer within 12 years.[28] A multi-national study across 38 countries found HPV types 16, 18, 31, 33, 45, 52 and 58 in 85 percent of invasive cervical cancer cases, 71 percent (95% CI: 70-72) of cervical adenocarcinomas were positive for HPV16 and 18 and 94 percent (95% CI: 92-96) were positive for HPV16, 18 and 45.[20]

Other HPV-related cancers

Oncogenic HPV types are linked to other cancers in women and men, including vulval, vaginal, penile, anal and oropharyngeal cancers (see Table 10.1).

Anal cancers

Anal cancer remains relatively rare compared to other cancers, but the global incidence has increased among both men and women, particularly in high-income regions (the average worldwide incidence is 0.5 per 100,000 population in 2020).[27] Women have a higher incidence of anal cancer than men. The incidence is highest among men who have sex with men, women with history of cervical or vulvar cancer, and immunosuppressed populations, including those who are HIV-infected and patients with a history of organ transplantation.[27]

Oropharyngeal cancers

There has been an increase in the incidence of head and neck cancers over the past few decades. This increase is mainly due to an unexpected increase in HPV-related oropharyngeal cancers, primarily in males aged 40–55 years with exposure to alcohol and tobacco.[29]

Most recent data suggest that around one-quarter of all oropharyngeal cancers are attributable to HPV infection; the most frequent type is HPV16.[25, 27] (see Table 10.1).

Vulval and vaginal cancer

Vulval and vaginal cancers are rare worldwide, representing 4 percent and 2 percent of all gynaecological cancers. Incidence is highest in less developed countries.[27]

Genital warts

Genital warts, which are most commonly due to infection with HPV6 or HPV11, have a prevalence of approximately 1 percent of adults in the US.[30, 31] Scandinavian countries have reported rates as high as 10 percent.[32]

10.3.2 New Zealand epidemiology

Onset of sexual activity

Data from the Youth'12 survey suggests that approximately 8 percent of New Zealand adolescents may have had sexual intercourse before the age of 13 years.[33, 34] This increases to 24 percent by the age of 15 years and 46 percent by age 17 years.

Compared to 2001, students were more likely to delay sexual debut in 2012 but less likely to use condoms and contraception consistently.[35] Māori (OR 0.7; 95% CIs: 0.6–0.8) and Pacific (OR 0.5; 95% CIs: 0.4–0.7) students used condoms less frequently than NZ European students; those from socioeconomically deprived communities (school decile 1) used condoms less frequently (OR 0.7; 95% CIs: 0.5–0.9) than students from wealthier communities (school decile 10).[35]

Cervical cancer

HPV prevalence in precancerous lesions and invasive cervical cancer

The prevalence of HPV infection and distribution of HPV types among New Zealand women with histologically confirmed CIN 2/3[36, 37] or invasive cervical cancer[38] was broadly consistent with that seen internationally. During 2011–2012, 97 percent (95% CI: 94–98) of women with histologically confirmed CIN 2/3 were HPV-positive, and the prevalence of any high-risk HPV was 96 percent (95% CI: 91–99).[36] In women with histologically confirmed invasive cervical cancer during 2004–2010, 88.5 percent (95% CI: 83.7–92.4) were HPV-positive, and the prevalence of any high-risk HPV was 87.2 percent (95% CI: 82.2–91.3).[38] For both CIN 2/3 and invasive cervical cancer, the overall distribution of HPV types was similar in Māori and non-Māori women, with HPV16 being the most commonly detected HPV type in both groups.[36, 38]

Cervical cancer registrations and deaths

In 2018 (provisional), there were 191 new cervical cancer registrations, an increase from 164 in 2017.[39] In 2017, the age-standardised registration rate was 6.0 per 100,000 population, similar to the 2016 rate (6.4 per 100,000). The registration rate for Māori women was 9.4 per 100,000, 1.7 times greater than the rate for non-Māori women (5.4 per 100,000).[39]

There were 55 cervical cancer deaths in 2016. In 2014, when there were 46 deaths (1.4 deaths per 100,000 population) and the mortality rate for Māori women was 3.0 per 100,000, 2.7 times greater than for non-Māori women (1.1 per 100,000).[40]

Other HPV-related cancers

The most recent New Zealand data available for other HPV-related cancers is from 2017 (see Table 10.2). Note that this data is for new cancer registrations only; the tumours have not been analysed for the presence of HPV.

Table 10.2: Number and age-standardised rate of new registrations for other cancers known to be associated with HPV in New Zealand, 2017

Anatomic site*	Number of new registrations	Rate of new registrations (per 100,000)
Vulva	52	1.2
Vagina	19	0.5
Penis	18	0.5
Anus		
• women	40	1.1
• men	21	0.6
Oropharynx		
• women	4	0.1
• men	10	0.3
Tonsils		
• women	21	0.6
• men	85	2.7

* ICD codes: Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharynx C10; Tonsils C09. (Note that in Table 10.1, the US definition for oropharyngeal cancer combines multiple cancers, using 4-character ICD codes. At the time of writing, New Zealand data for 2017 was only available at the 3-character ICD code level.)

Source: Ministry of Health. 2019. *New cancer registrations 2017*. Wellington: Ministry of Health URL: **https://www.health.govt.nz/publication/new-cancer-registrations-2017** (accessed 20 June 2020).

Anal cancers

For the period 2008–2012, the age-standardised rate for anal cancer was 0.6 and 1.1 per 100,000 persons per year among men and women in New Zealand, respectively.[27] It remained the same in 2017 (see Table 10.2).

Oropharyngeal cancers

A retrospective review of New Zealand cancer registry data for the period 1981–2010 showed a rapid rise in oropharyngeal cancers in men (mainly in those aged 40 years or older), particularly from 2005 onwards.[41] The rate of oropharyngeal cancers was almost four times greater in men (1.87 per 100,000) than in women (0.47 per 100,000). The incidence rates for oral cavity cancer, which is generally associated with alcohol and tobacco consumption, remained relatively stable in both sexes during that time. (Note that this study included both oropharyngeal and oral cavity cancers.)

A significant increase in HPV-positive oropharyngeal cancer (OR 5.65; 95% CI: 2.60–12.30 was detected in biopsies taken during 1996-1998 and 2010-2012 and occurring at a younger age (OR 0.55; 95% CI: 0.33-0.99 aged 61 or older and age 60 years or younger). Most cases attributable to HPV were HPV16-positive (98.5 percent); there was also one case each of HPV 33 and 35.[42]

Genital warts

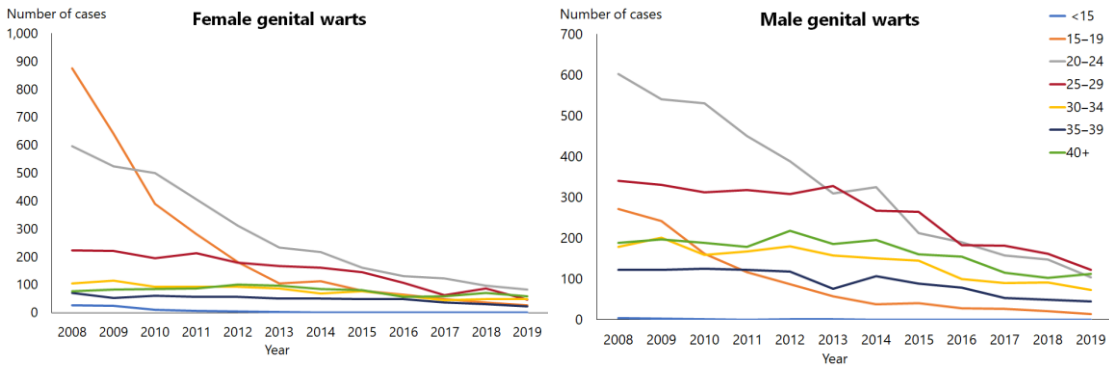
Many sexually transmitted infections (STIs), including genital warts, are not notifiable in New Zealand. ESR cautions that the number of cases of genital warts reported through the clinic-based surveillance system likely underestimates the true burden of disease in New Zealand because a substantial percentage of STIs are diagnosed by other health care providers.

Following the introduction of HPV4 vaccine to females in 2008 and the introduction of HPV9 vaccine for males and females in 2017, from 2008 to 2019 genital warts clinical case counts reported by sexual health clinics have decreased by 79.5 percent (from 3,681 to 756 cases) and case counts reported by family planning clinics decreased by 77.8 percent (from 573 to 127 cases) (ESR 26 June 2020). Since the introduction of the HPV vaccination programme, there have been decreases in the number of genital warts diagnoses in all ethnic groups in sexual health clinics and in all ethnic groups, except 'Other', in family planning clinics.

In sexual health clinics, the decrease was most notable in the 15–19 years and 20–24 years age groups, and there was a moderate decrease in the 25–29 years age group, in both sexes (Figure 10.1). A marked decrease was following the extension of vaccination to males in 2017. From 2016 to 2019, reported cases decreased by 50 percent (from 28 to 14 cases) in the younger males aged 15–19 years and 45.3 percent (from 190 to 104 cases) in those aged 20–24 years (ESR, 26 June 2020). A decrease in cases seen in older age groups suggests that immunisation is also providing some herd immunity to unvaccinated individuals. A decline in the number of prescriptions for treating genital warts (imiquimod and podophyllum resin-based products) supports this evidence for a herd immunity effect.[43] The largest decline was seen in women aged under 20 years.

A study in Auckland sexual health clinics found a similar population effect in genital wart cases over five years following the introduction of HPV4 to women in 2009. A significant reduction in new genital warts cases was observed in a vaccine-eligible age group of females (aged <20 years), not observed in older age-groups (those aged over 20 years) or in males, not eligible to receive vaccination at that time. There was a smaller but not statistically significant decrease in genital warts cases in younger males (age <20 years) compared with that seen in older males.[44]

Figure 10.1: Number of genital warts (first presentation) in sexual health clinics, by sex and age group, 2008–2019



Source: ESR

For further details of genital wart notifications, refer to the most recent STI quarterly and annual reports from ESR (available **surv.esr.cri.nz/surveillance/surveillance.php**).

10.4 Vaccines

10.4.1 Available vaccines

One HPV vaccine, HPV9 (Gardasil 9, Seqirus/MSD), is approved for use (registered) and is available for distribution (marketed) in New Zealand.

HPV9 is registered for use in females aged 9–45 years and in males aged 9–26 years as a two-dose schedule in individuals aged 14 years and under, and as a three-dose schedule in older individuals and immunocompromised individuals from age 9 years.

The vaccine contains HPV virus-like particles (VLPs), which are composed of the L1 protein (a component of the virus outer layer) aggregated into clumps that mimic the outer structure of the HPV virion. The VLPs do not contain viral DNA and are incapable of causing infection. The L1 proteins are produced by genetically engineered yeast cells.

Funded HPV vaccine

Each 0.5 mL dose of HPV9 vaccine (Gardasil 9, Seqirus/MSD) contains:

- 30 µg of HPV6 L1 VLP, 40 µg of HPV11 L1 VLP, 60 µg of HPV16 L1 VLP, 40 µg of HPV18 L1 VLP, 20 µg of HPV31 L1 VLP, 20 µg of HPV33 L1 VLP, 20 µg of HP45 L1 VLP, 20 µg of HPV52 L1 VLP and 20 µg of HPV58 L1 VLP
- 500 µg of aluminium hydroxyphosphate sulphate.

The vaccine does not contain any preservative or antibiotics.

Other vaccine

HPV4 (Gardasil) was used prior to the introduction of HPV9 (Gardasil 9) in January 2017. See also section A1.3.4 in Appendix 1 for the history of HPV vaccines in New Zealand.

In other countries, including Australia and in Europe, a bi-valent HPV vaccine (Cervarix, GSK) is available to protect against HPV types 16 and 18 only. This vaccine is unavailable in New Zealand.

10.4.2 Efficacy and effectiveness

Most HPV vaccine clinical trials do not collect direct data about clinical outcomes, like cancer or precancer, for young adolescents, because it is unethical to collect samples from the cervix of vaccinated girls who are sexually naïve and because precancerous lesions do not appear for years after the HPV infection has occurred. Also, since treatment is offered as precancers develop, progression to cervical cancer is rare even in those not vaccinated and requires a very long time for follow-up. Therefore, immunological bridging is used to infer efficacy against cervical and anal cancer. Efficacy is also inferred for the younger age group because immunogenicity (antibody responses) is non-inferior to that seen in older age groups.

Immunogenicity

Although there is no known correlate of protection (ie, an established antibody level required for protection against HPV-related disease), HPV vaccines generate excellent antibody responses in most recipients.

HPV4

Immunisation with three doses of HPV4 vaccine produces antibody responses against HPV16, HPV18, HPV6 and HPV11 in more than 99 percent of vaccine recipients. The peak antibody titres following three doses of HPV vaccine are greater than that following natural infection.

A Cochrane systematic review found the immunogenicity of two- and three-dose HPV vaccination schedules in young females to be comparable.[45] Two doses of HPV4 are more immunogenic in recipients aged between 9 and under 15 years than in older groups aged over 15 years and comparable to three doses in older recipients (those over 15 years).[46] In young females, two doses have been found to be non-inferior to three doses for at least 21 months after vaccination, particularly when the interval between doses is at least six months.[47, 48] The immunogenicity of three doses of HPV4 vaccine has been established to be robust and long-lasting.[49, 50, 51] Anamnestic responses have been demonstrated out to at least 8.5 years.[51]

Differences in seroconversion rates and antibody titres were seen in immunocompromised individuals. The immune response to HPV4 among immunocompromised children appears adequate,[52, 53] although antibody titres were lower than those in healthy children of the same age groups.[52] Seroconversion among HIV-infected individuals has been demonstrated to be robust and higher among those with lower HIV loads or on antiretroviral therapy.[54, 55, 56]

While some immunosuppression regimes can attenuate the immune response to HPV4, patients with autoimmune diseases generally appear to respond well to the vaccine.[57] In contrast, adult solid organ transplant recipients produce suboptimal responses to HPV4.[58]

HPV9

The immunogenicity of HPV9 vaccine was initially assessed in women aged 16–26 years.[59] Antibody responses generated by the HPV9 were non-inferior to HPV4 against HPV types 6, 11, 16 and 18; and in girls and boys aged 9–15 years.[60] Antibody responses to all nine vaccine HPV types in girls and boys aged 9–15 years and men aged 16–26 years were non-inferior to women aged 16–26 years.[61, 62]

Men who have sex with men appear to produce lower antibody titres than heterosexual men (although seroconversion rates to all nine vaccine types were greater than 99 percent in both groups).[61] This lower antibody response is possibly due to greater exposure to the virus, highlighting the importance of vaccination at a young age.

The immunogenicity of two doses of HPV9 in girls and boys aged 9–14 years was non-inferior to three doses in women aged 16–26 years, the age group in which efficacy was demonstrated.[63]

Efficacy

HPV-related cancers

HPV4 and HPV9 vaccines offer similar protection against cervical, vaginal and vulval precancerous lesions or cancer in women vaccinated at 15–26 years.[45] Protection is greatest among young women not initially infected with HPV 16/18 prior to vaccination (vaccine efficacy of 95 percent [95% CI: 83–99] against vaginal and vulval lesions).[64]

HPV9 efficacy was studied in women aged 16–26 years and compared with HPV4.[59] HPV9 prevented cervical, vulvar and vaginal disease and persistent infection related to HPV types 31, 33, 45, 52 and 58 (the five additional serotypes in HPV9). The antibody response and incidence of disease related to HPV types 6, 11, 16 and 18 were similar in the two vaccine groups.

Protection against CIN 2/3 or adenocarcinoma *in situ* is widely accepted as a surrogate for protection against invasive cancer, since study participants who develop these precancerous lesions require treatment to prevent progression to invasive cancer. Bivalent and quadrivalent HPV vaccines have been shown to be highly effective in preventing these HPV16- and HPV18-related precancerous lesions in females.[1, 65] In the pivotal efficacy trial in women aged 15–26 years, HPV4 vaccine efficacy for the prevention of precancerous lesions related to HPV16 or HPV18 was 98 percent (95% CI: 86–100) in the per-protocol susceptible population.[66]

A phase III clinical trial among Asian and Latin American women found population-specific vaccine efficacy to be more than 96 percent against any grade of cervical, vulvar and vaginal disease and more than 93 percent efficacy against six-month persistent HPV infection.[67]

Studies in males, including men who have sex with men, have shown that HPV4 vaccine is efficacious against anal HPV infection and associated precancerous lesions.[9, 68, 69] HPV4 protects men vaccinated between ages 16–26 years against genital warts or external genital lesions compared with unvaccinated dummy controls.[45]

Effectiveness

A 2016 systematic review of published literature summarised the global experiences with HPV4 from 1 January 2007 to 29 February 2016.[70] It assessed the global effect of HPV4 vaccine on HPV infection, genital warts and cervical abnormalities based on 57 publications across nine countries. The greatest impact was seen in countries with high vaccine uptake and among girls vaccinated prior to HPV exposure. Maximal reductions of around 90 percent were reported for vaccine-type HPV infections (6, 11, 16, 18) and genital wart cases.

For women vaccinated before the age of 20 years, the risk of CIN2+ was significantly lower than in unvaccinated women (effectiveness of at least one dose is 58–77 percent).[71, 72, 73]

Duration of protection

As vaccination programmes have only been in place for little over a decade, the duration of protection is not yet fully known. Follow-up studies 8–10 years after HPV vaccination have shown no waning of protection.[1] Long-term studies are ongoing to determine the duration of efficacy for all HPV vaccines.

Herd immunity and population impact

In January 2019, WHO began considering a global strategy to eliminate cervical cancer and established clear targets to 2030. This is only achievable with high vaccination coverage and access to regular screening for all women.[74, 75]

Australia saw a reduction in the prevalence of vaccine-type HPV infections (6, 11, 16, 18) in unvaccinated young men after the introduction of the vaccine to young women, supporting the role of herd immunity.[76, 77, 78] There was also a significant decrease in the prevalence of vaccine-type HPV infections in unvaccinated women (aged 25 years or younger).[79] Vaccination of females has provided herd immunity against oropharyngeal HPV16 prevalence in unvaccinated males in the UK.[80]

In a study of sexual health clinic data in Melbourne, the researchers noted the near disappearance of genital warts in women and heterosexual men aged under 21 years.[78] In addition, the data indicated that the basic reproductive rate (see section 1.2.1) had fallen below one. This reduction in cases occurred without any corresponding reduction in women aged over 30 years, men who have sex with men and non-residents. Similar trends were noted in the data from the Australian genital warts national surveillance network.

Eleven years after the introduction of HPV4 vaccine in the US, HPV4 types declined by 81 percent in vaccinated women and 40 percent in unvaccinated women. As well as direct protection from HPV9 vaccine, potential cross-protection from HPV4 was also observed in vaccinated women with a 71 percent decline in prevalence of the additional, genetically related HPV9 types.[4]

Previous exposure to HPV

While efficacy is unclear, there are no safety concerns in offering vaccination to women who have had HPV-related disease and would like to use the vaccine to reduce the risk of further disease.

A retrospective analysis of the HPV4 vaccine's pivotal efficacy trial data (Future I and Future II) studied a group of women who were vaccinated before they had their first treatment for HPV-related disease.[81] This showed a reduction in subsequent HPV-related disease in vaccinated women aged 15–26 years who had received treatment for cervical, vulvar or vaginal disease during the trial. The study showed a 46.2 percent reduction (95% CI: 22.5–63.2) after cervical surgery of any HPV-related disease and 35.2 percent reduction (95% CI: 18.8–51.8) after diagnosis of genital warts or vaginal or vulvar disease.

In contrast, a systematic review found that there was no evidence that HPV vaccines were effective in preventing vaccine-type HPV-associated precancer in pre-exposed women. This review explored efficacy against CIN3+ precancers in women with evidence of prior vaccine-type HPV exposure in three randomised controlled trials and two post-trial cohort studies.[82] Despite these findings, it was concluded that longer-term benefits in preventing re-infection could not be excluded (ie, the vaccine is not therapeutic but may prevent future infection, emphasising the importance of vaccination prior to sexual debut).

10.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store in the dark at +2°C to +8°C. Do not freeze.

10.4.4 Dosage and administration

The dose of HPV vaccine is 0.5 mL, administered by intramuscular injection in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

HPV vaccine may be co-administered with any live or inactivated vaccine indicated at the same visit.[1]

Interchangeability

All HPV vaccines may be used interchangeably for completion of a course.[83]

10.5 Recommended immunisation schedule

10.5.1 Recommended and funded

From 1 January 2017 males and females aged 26 years and under became eligible for HPV vaccine. Including males in a routine vaccination programme is expected to increase the benefit to the population in terms of reduction for both HPV-related cancer outcomes and genital warts.

Immunisation should preferably be completed before the onset of sexual activity. The optimal time for HPV administration is at age 9–13 years, as the immunogenicity is more effective when given younger and as most males and females in this age group would be naïve to all HPV types. However, individuals who have begun sexual activity may still benefit from vaccination. The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

See Table 10.3 for HPV vaccine recommendations and schedules. A two-dose schedule of HPV at 0 and 6–12 months is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose. Three doses are required for this age group if they have confirmed HIV infection or are transplant or chemotherapy patients, or if the minimum dosing interval is not met (see below). Older individuals from age 15 years receive three doses of HPV vaccine, at 0, 2 and 6 months.

Table 10.3: HPV vaccine recommendations and schedules

Note: HPV vaccine may be offered from age 9 years, but the usual Schedule will be at age 11/12 years (school years 7/8). **Funded individuals are in shaded rows**. See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to the funding decisions.

Recommended and funded	Doses	HPV Schedule[a]
Children aged 14 years and under[a]	2[a]	0 and 6–12[a] months
Individuals aged 15–26 years[a,b]	3	0, 2 and 6 months[c]
Individuals aged 9–26 years: • with confirmed HIV infection[d]	3	0, 2 and 6 months

• transplant (including stem cell)[d] • post-chemotherapy patients[d]	An additional dose	At least 1 month after the last dose of chemotherapy
Recommended but not funded	**Doses**	**HPV Schedule**
Individuals aged 27 years and older:[a,b,e] • who have had little previous exposure to HPV and are now likely to be exposed • who are men who have sex with men • with HIV.	3	0, 2 and 6 months[e]

a. See note in text for two-dose schedules, age groups and continuation of courses.

b. The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

c. If a shortened schedule is required, the three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.

d. For more information see sections 4.3.9 and 4.3.10.

e. HPV vaccines are registered for use in females aged 9–45 years and males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

Note

For the two-dose HPV schedule for children aged 14 years and under:

- a two-dose schedule at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose
- the second dose is preferably given at least six months after the first; however, if the second dose is given less than five months after the first, a third HPV dose is recommended and funded – give the third HPV dose at least five months after the first.

Individuals who started with HPV4 may complete their remaining doses with HPV9.

Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the three-dose course, even if they are older than 27 years when they complete it.

HPV9 is not funded for those individuals who were previously fully vaccinated with HPV4.

Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are older than 18 years when they complete it.

10.5.2 Recommended but not funded

Individuals aged 27 years and older

The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

The data from the pivotal studies for HPV4 has demonstrated potential benefit to some women older than 25 years and the vaccine was shown to be effective at preventing infection and disease from the vaccine types in women aged 24–45 years who were uninfected at baseline.[84] However, pre-vaccination testing for cervical cytological abnormalities or for HPV infection is not recommended.

HPV9 is registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

10.5.3 Pregnancy and breastfeeding

HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.[85]

Data to date shows no adverse effects of HPV vaccines on pregnancy outcomes.[1, 86, 87] However, if a vaccine dose has been administered around the time of conception or during pregnancy, health professionals are advised to report this to CARM (see section 1.6.3) and the vaccine manufacturer to assist with ongoing safety monitoring. If a woman is found to be pregnant after starting the HPV vaccine schedule, the remaining doses should be delayed until after pregnancy.

HPV vaccines may be given to breastfeeding women.[88]

10.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

10.6.1 Contraindications

HPV vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of HPV vaccine or to a vaccine component. HPV vaccines contain HPV proteins produced by genetically engineered yeast cells. They should not, therefore, be given to people with a history of an immediate hypersensitivity to yeast.

10.6.2 Precautions

Pregnancy is a precaution – see section 10.5.3.

10.7 Potential responses and AEFIs

HPV vaccines have excellent safety profiles internationally. There have been no safety signals raised since the vaccines were licensed, and a number of large investigations have been carried out to assess specific outcomes, particularly autoimmune conditions.[89, 90, 91, 92, 93] Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.[94, 95, 96] The WHO's Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.[97, 98] The main challenge with HPV vaccine is communicating its excellent safety profile.[99] (See also the HPV discussion in section 3.2.4.)

Syncope (fainting) occurs frequently in adolescents following vaccination, but this is a stress response to being vaccinated, not a reaction to the vaccine.[2, 100, 101] WHO recognises immunisation-related stress responses as potential responses to HPV vaccination (see section 2.3.3).[102]

Safety has been evaluated in approximately 15,000 subjects in the HPV9 clinical development programme and no new safety signals have been shown through post-marketing surveillance.[83, 103] The vaccine is well-tolerated, and most adverse events were injection-site-related pain, swelling, and erythema that were mild to moderate in intensity. The safety profile of HPV9 is like HPV4. Female HPV9 recipients had more injection-site adverse events than female HPV4 recipients, including swelling (40.3 percent compared to 29.1 percent in HPV4 recipients) and erythema (34 percent compared to 25.8 percent in HPV4 recipients). Male recipients had fewer injection-site adverse events and were similar following either vaccine. Rates of injection-site swelling and erythema both increased following each successive dose of HPV9.

In summary, HPV9 is well-tolerated in all age groups, although it is slightly more reactogenic than HPV4.[59, 61, 83] The most common adverse events are pain, swelling, erythema, pruritus, headache and pyrexia. The frequency of these common adverse events is increased slightly (up to two-fold) when concurrent vaccinations are given.[104]

10.8 Cancer prevention measures

For women, HPV immunisation is part of a three-pronged approach to cervical cancer prevention that also includes regular cervical screening and safer sex approaches. For men, HPV immunisation and safer sex approaches are expected to contribute to the prevention of HPV-related cancers and disease that affect men, as well as cervical cancer prevention in women.

10.8.1 HPV immunisation

By preventing infection with oncogenic HPV types, HPV vaccination can reduce the incidence of precursor lesions that may lead to cancer. Vaccination needs to be administered before HPV infection occurs to prevent atypia and malignancy. Because genital HPVs are so common and so readily transmitted, in practical terms vaccination should be offered before the onset of sexual activity; that is, during or prior to early adolescence.

HPV immunisation does not reduce the progression of established disease but can be used in therapeutic situations by preventing the reactivation of latent infection or acquiring new infections.

10.8.2 Regular cervical screening for women

A successful HPV immunisation programme for men and women will reduce the community prevalence of HPV infection and thus the incidence of cervical cancer in women. However, HPV immunisation alone will not completely eliminate cervical cancer, because some women will not have been vaccinated, a few will not develop immunity despite vaccination, and some will be infected prior to vaccination or with oncogenic types not included in the vaccine.

Consequently, women will need to continue to undergo regular cervical screening to detect those precancerous lesions that occur despite vaccination. Cervical screening programmes are based on regular cytological screening or HPV testing to detect, monitor and treat at an early stage precancerous lesion, or CIN. These programmes have been successful in reducing invasive disease and mortality.

> Although the frequency of abnormal cytology is lower in the vaccinated group, women who have received HPV immunisation should still take part in the National Cervical Screening Programme. Three-yearly cervical smears are recommended for women between the ages of 25 and 70 years who have ever been sexually active.

10.8.3 Safer sex approaches

To minimise the risk of HPV infection (plus other sexually transmitted infections), practitioners should remind individuals of safer sex approaches, including sexual abstinence, monogamous relationships, delayed sexual debut and minimising the number of sexual partners.[1] Consistent and correct use of condoms can decrease the risk of anogenital HPV infection when infected areas are covered or protected by the condom. However, HPV transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse.[8]

10.9 Variations from the vaccine data sheets

HPV vaccines are registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males (see section 10.5.2).

For the three-dose schedules, the HPV vaccine data sheets recommend that all three doses are given within a 12-month period. The Ministry of Health recommends that if the three-dose schedule has been interrupted, prior doses do not need to be repeated regardless of how long ago the previous doses were given (see Appendix 2).

The HPV9 data sheet states that there are no studies on the interchangeability of HPV vaccines. The Ministry of Health recommends that all HPV vaccines may be used interchangeably for completion of a course.[83] Those individuals who started with HPV4 may complete their remaining doses with HPV9.

References

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11 Influenza

Key information

Mode of transmission	Spread by droplets generated by sneezing and coughing, by direct or indirect contact, or by the aerosol route.
Incubation period	Usually 1–3 days (range 1–7 days).
Period of communicability	From 1–2 days before symptoms start until about day 5 of illness; may be longer in young children and if immunocompromised. Asymptomatic spread is common.
Incidence and burden of disease	Influenza epidemics occur each year. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low-income groups and Māori and Pacific ethnic groups.
Funded vaccines	• Quadrivalent inactivated split virion influenza vaccine: children aged 6 months to under 3 years (ie, aged 6–35 months): Afluria Quad Junior • adults and children aged 3 years and older: Afluria Quad.
Dose, presentation, route	0.25 mL for young children (age from 6–35 months) and 0.5 mL for older children and adults per dose Pre-filled syringe Intramuscular injection, or subcutaneous injection (if indicated)
Funded vaccine indications and recommended schedule	1 dose is recommended and funded annually from 1 April for: • pregnant women • individuals aged 65 years and older • individuals aged from 55 years and of Māori or Pacific ethnicity • individuals aged 6 months to under 65 years with eligible conditions (Table 11.3) • all children aged 3–12 years (from 1 July to 31 December 2022) • children aged 4 years or under who have been hospitalised for respiratory illness (including measles) or have a history of significant respiratory illness • individuals with serious mental health or addiction. Children aged under 9 years who have not previously received influenza vaccine require 2 doses 4 weeks apart (funded for children with eligible conditions).
Recommended, unfunded	Occupational: recommended for health care workers, teachers and support staff in schools and early childhood education and staff in long-term care and aged-care facilities. Recommended particularly for all close contacts (eg, caregivers, family members) of those at high risk from influenza. Universally recommended for anyone age from 6 months, annually.
Vaccine effectiveness	Depends on the match of the strains in the vaccine with circulating strains, the age of the individual and whether they have any underlying medical conditions. Vaccination can prevent disease or reduce severity.

Precautions and special considerations	There may be a small increased risk of fever and febrile convulsions with concomitant delivery of PCV13 and influenza vaccine in children aged 6 months to under 5 years.
Potential response to vaccine	Mild fever, headache, muscle aches, local swelling and mild pain at injection site. Children aged under 5 years are more likely than older children or adults to have a febrile reaction to influenza vaccine.

11.1 Virology

Influenza viruses belong to the Orthomyxoviridiae family, and are classified into influenza virus types A, B and C. Influenza A virus subtypes are classified based on two surface antigens:

- haemagglutinin (H), responsible for cell surface attachment during infection
- neuraminidase (N), which potentiates the release of new virions from the cell.

Subtypes which have in the past caused pandemics include the influenza A H1N1, H2N2, H3N2 and H1N1pdm09 viruses, while the H3N2 and H1N1pdm09 viruses continue to cause epidemics as seasonal influenza viruses. Influenza B has two lineages of viruses: B/Victoria and B/Yamagata, which are also associated with outbreaks and epidemics, and account for a significant proportion of the overall burden of influenza.[1] Influenza C is associated with mild cases of upper respiratory infection.

11.1.1 Antigenic drift

Influenza A and B viruses undergo frequent small changes (mutations) in their segmented RNA genome over time. The mutations can occur in the coding regions responsible for H and N surface antigens. This 'antigenic drift' leads to the emergence of new antigenic variants or virus strains.

These new strains are described by the geographic site of isolation, laboratory number and year of isolation; for example, A/Hong Kong/4801/2014 (H3N2). Because of this ongoing antigenic drift, seasonal influenza virus vaccine formulations are reviewed by the WHO bi-annually.

11.1.2 Antigenic shift

New influenza A virus subtypes emerge periodically that have caused pandemics in humans. The new virus subtype has novel H and N surface antigens result from the mixing of genomic segments of two or more influenza A viruses. This is known as 'antigenic shift'. Other possible mechanisms for the emergence of new influenza viruses are through the adaptation of avian influenza viruses to infect humans and the re-assortment of the genomic segments of multiple viruses (ie, human, avian and pig influenza viruses).

11.2 Clinical features

Influenza is contagious, with a reproductive number (R0) estimated at 1.4–4 (see section 1.2.1).[2] The virus is transmitted by respiratory droplets generated by sneezing and coughing that land directly on respiratory mucous membranes by aerosolised droplets or by direct or indirect contact (via contaminated hands or fomites).[2, 3, 4] The incubation period can range from one to seven days (average one to three days), during which time the virus replicates in the ciliated columnar epithelial cells of the upper and lower respiratory tract. An infected person is contagious from one to two days before symptoms start until about day five of the illness. Peak viral shedding occurs one to three days after the development of symptoms, diminishing to low levels by five days. Children shed more virus and remain infectious for longer than adults.

There is a wide range of symptoms, from asymptomatic to severe disease. Mild influenza with non-specific symptoms is common, resulting in a large proportion of viral transmission and undetected infections.[5] In older children and adults, the illness characteristically begins abruptly with fever and a variety of clinical symptoms, including chills, malaise, headache, myalgia, non-productive cough, rhinitis, sore throat and mild conjunctivitis. Vomiting and diarrhoea may be present. While children aged under 5 years have fever, cough and rhinitis, infants may present with unexplained fever or sepsis-like syndrome only.[3] In the young, influenza virus may cause croup, bronchiolitis and pneumonia. Fever is often less evident in the elderly, who may present with other symptoms, such as anorexia, fatigue or confusion. Influenza typically resolves after several days in most people, although cough and malaise may persist for two or more weeks.

Infections due to pandemic influenza A strains are more likely to lead to severe morbidity and increased mortality than influenza B or seasonal influenza A strains.

Influenza B infections were previously thought to generally cause more mild illness, but numerous studies indicate that there is little difference between clinical symptoms and outcomes of influenza B compared to influenza A.[1] Influenza B-associated hospitalisations and mortality may have previously been underestimated; studies have reported higher mortality following influenza B infection than A in some years.[1] Influenza B infection is more common in children aged 5–17 years than in other age groups, and disease is likely to be more severe in children than in adults.[6]

Influenza can exacerbate underlying medical conditions, such as pulmonary, cardiac or metabolic disease. Some of the many reported complications associated with influenza include pneumonia, respiratory failure, myositis, encephalopathy, myocardial infarction, myocarditis and pericarditis, Reye syndrome (associated with aspirin use in children), bronchitis, otitis media and death. The risk of complications is increased in pregnancy.[7] Also associated with influenza infection is increased frailty and cognitive decline in older people and incidence of cardiovascular disease are also associated with influenza infection.[8, 9] Influenza during pregnancy can result in poorer outcomes for the mother and her fetus, including preterm birth and fetal loss.[10, 11]

Asymptomatic influenza

The majority of influenza infections are asymptomatic, and most symptomatic cases self-manage without seeking medical help.[12, 13] Results from the 2015 New Zealand Southern Hemisphere Influenza and Vaccine Effectiveness, Research and Surveillance (SHIVERS) serosurvey showed that around 32 percent of people surveyed had serologically confirmed influenza over the 2015 season (adjusted for age and ethnicity).[5, 14] Overall only one-quarter of those reported influenza-like illness; three out of four people were asymptomatic; only 1 out of 47 visited their GP and 1 in 680 were hospitalised. Young children and Pacific people experienced the highest influenza infection attack rates.[15]

11.3 Epidemiology

11.3.1 Global epidemiology

Influenza is an important cause of disease worldwide. Annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290,000 to 650,000 respiratory deaths globally.[16, 17] For example, it was estimated globally that 11.5 percent of lower respiratory tract infections (LRTI), 5.6 percent of LRTI deaths and 9.5 million LRTI hospitalisations were attributable to influenza in 2017.[18]

In temperate climates, seasonal epidemics occur mainly during winter, while in tropical regions, influenza occurs throughout the year causing outbreaks more irregularly.[16]

From time to time, pandemics occur when a new virus arises and spreads globally (see section 11.3.3). The last influenza pandemic was caused by the A(H1N1)pdm09 virus. More than 214 countries and overseas territories reported laboratory-confirmed influenza, including over 18,449 deaths.[19] Many more deaths were found to associated with the pandemic due to respiratory and cardiovascular complications.[20]

11.3.2 New Zealand epidemiology

New Zealand experiences the typical temperate climate epidemiology of influenza, with the peak incidence occurring during the winter months, however, influenza activity occurs throughout the year.

The impact of influenza in New Zealand is substantial in terms of general practice consultations, hospitalisations and deaths. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low-income groups, and Pacific and Māori ethnic groups.

Influenza surveillance

The New Zealand influenza surveillance system compiles information from a variety of sources, including:

- national sentinel general practice-based influenza-like illness surveillance (part of the WHO's Global Influenza Programme)
- year-round laboratory-based surveillance by the regional virus diagnostic laboratories
- hospital-based severe acute respiratory infection surveillance in Auckland and Counties Manukau DHBs
- data from Healthline, HealthStat, publicly funded hospital discharges, the NIR and the AIR.

Influenza prevalence and circulating strains are monitored through general practice surveillance for influenza-like illness (ILI); hospitalisations are monitored for severe acute respiratory infection (SARI) admissions; and severity is determined by the proportion of hospitalisations requiring intensive care unit (ICU) admission.[21]

For example, during the 2019 season the levels of influenza-like illness and the overall impact were low and generally just above seasonal baseline.[22] However, SARI hospitalisation rates increased earlier than in previous years and, during the winter, a higher than usual proportion of viral respiratory illnesses were due to influenza. A(H3N2) and B/Victoria strains were co-circulating. Seriousness was similar to other A(H3N2) predominant years. Influenza A viruses were detected most frequently in hospitalised patients whereas influenza B was detected more in the community. In contrast, in 2018 the predominant strain was A(H1N1)pdm09 strain which is associated with high severity in those aged younger than 65 years.[23] Over one-half of those admitted to ICUs with influenza-associated SARI in 2018 did not report any pre-existing medical risk factors, consistent with being younger.[23]

In 2020 and 2021, due to COVID-19 pandemic restrictions, transmission of influenza in the community was interrupted: no cases with ILI symptoms and 0.6 percent of hospitalised SARI cases had detectable influenza virus in 2020 and no community influenza cases were detected during 2021.[24, 25]

For detailed information, including influenza surveillance and influenza reports, see the ESR website (**www.surv.esr.cri.nz/virology/virology.php**).

Influenza immunisation uptake

More than 1.43 million doses of influenza vaccine were distributed to 24 September 2021. This equated to around one third of the whole population (approximately 275 doses per 1,000 population).[24] According to Ministry of Health data, based on reporting from funding claims, publicly funded influenza vaccine uptake for individuals aged 65 years and older was around 63.5 percent in 2021; this is likely to be an underestimate of the coverage. After progressive increases, the national influenza immunisation coverage for DHB staff decreased from 77 percent overall (17 DHBs achieved coverage of over 70 percent and six of over 80 percent) in 2020[26] to 47 percent in 2021 with no DHBs reaching 80 percent.

11.3.3 Pandemic influenza

The natural ecology of influenza type A viruses is among wild aquatic avian species, and from time to time, these viruses spill over into other species, including humans. These avian influenza virus infections are usually severe and associated with a high mortality; however, they are rarely transmitted from human to human. In the past, avian viruses have become transmissible either through adaptation or the acquisition of swine or human genomic material, and when natural immunity has been lacking in the population, have resulted in a pandemic with global spread. There have been four influenza pandemics recorded since 1918.

Pandemics have the potential to result in large numbers of severe infections, but the degree of severity is hard to predict and will depend upon many factors, including whether there is any previous community immunity. The most severe recorded influenza pandemic was the 'Spanish flu' A(H1N1) pandemic of 1918–1920, which caused an estimated 20–50 million deaths worldwide. The most recent pandemic was the 2009 A(H1N1)pdm09 strain. It was estimated that 18 percent (800,000) of the New Zealand population were infected with the virus during the first wave, including one in every three children.[27] Risk factors for severe outcomes included obesity, pregnancy,[28] diabetes mellitus and Pacific or Māori ethnicity.[27] This strain is now established as a circulating seasonal influenza strain.

Globally, in the first 16 months of the 2009 H1N1 influenza pandemic, 18,500 deaths were attributed to laboratory-confirmed influenza. When investigated further, it was estimated that over 201,000 respiratory deaths and an additional 83,300 cardiovascular deaths were associated with the pandemic – producing a rate 15 times higher than the laboratory-confirmed deaths. Of these deaths, 80 percent were younger than 65 years of age.[20]

Monitoring, surveillance and response for new pandemic strains are in place. See section 11.8.3.

11.4 Vaccines

Annual influenza vaccination is a most important measure for preventing influenza infection and mortality. New Zealand's annual National Influenza Immunisation Programme campaign includes an annual influenza kit for health care professionals (available from **influenza.org.nz**) and a national education and communication programme.

11.4.1 Available vaccines

Funded vaccines

Two quadrivalent split virion influenza vaccines are funded.

- **Afluria Quad (Seqirus) for adults and children from 3 years of age[29]**

Each 0.5 mL dose contains 15 µg of each of the four recommended influenza strains; other components and excipients include sodium chloride, dibasic sodium phosphate, monobasic sodium phosphate, potassium chloride, monobasic potassium phosphate, calcium chloride dihydrate and water for injections to 0.5 mL. Trace amounts of the following may also be present in each 0.5 mL dose: sodium taurodeoxycholate, ovalbumin (<0.1 µg), sucrose, neomycin sulphate, polymyxin B sulphate and propiolactone

- **Afluria Quad Junior (Seqirus) for infants and children aged 6 months to under 3 years (ie, aged 6–35 months)**

Each 0.25 ml dose of Afluria Quad Junior (Seqirus) contains 7.5 µg of haemagglutinin of each of the same four influenza strains that are in Afluria Quad.

Availability of influenza vaccines, particularly the unfunded vaccines, can vary during the season depending on demand and supply (see **influenza.org.nz**).

Vaccine preparations and potential future options

Influenza vaccine preparations vary by their type, the number of influenza strains contained in the vaccine and their delivery systems. There are a range of delivery mechanisms available internationally, including intradermal injection and intranasal mists. Live attenuated influenza vaccines are delivered by intranasal spray. Some data suggest that intradermal vaccines may induce improved immune responses, particularly in older adults.[30, 31]

The seasonal influenza vaccine strains vary each year depending on the prevailing viruses. WHO conducts technical consultations in February/March and September each year to recommend viruses for inclusion in both trivalent and quadrivalent vaccines for the northern and southern hemisphere influenza seasons, respectively. In recent years, the southern hemisphere recommendations include the two influenza type A (H1N1pdm09 and H3N2) and two B (Victoria and Yamagata) strains likely to circulate in New Zealand over the coming influenza seasons.[32]

Split virion influenza vaccines

Only quadrivalent split virion influenza vaccines were available in New Zealand for the 2020 influenza season.

Quadrivalent influenza vaccines (QIVs) contain two type A and two type B influenza strains. They are split virion vaccines prepared from virus grown in embryonated hens'

eggs. The virus is purified, disrupted and inactivated by splitting with beta-propiolactone or formaldehyde. QIVs offer broader protection against co-circulating B-strains and better effectiveness in seasons of B-strain mismatch than trivalent influenza vaccines (TIVs), which contain two influenza type A strains and one type B strain.[1]

Adjuvanted vaccines

For the 2022 influenza season, an adjuvanted QIV (aQIV; Fluad Quad, Seqirus) is available (unfunded) to those aged 65 years and over.

Adjuvants enhance the immune response to an antigen and require less antigen (antigen sparing). Internationally, there are three adjuvants licensed for use in influenza vaccines: two oil-in-water emulsions and a third that uses immunopotentiating reconstituted influenza virosomes.[3] Vaccines with these adjuvants show modestly improved immune responses, which may be particularly useful for the elderly and young children, but may also cause more local and systemic reactions than unadjuvanted vaccines.[3, 33]

The adjuvanted influenza vaccine available in New Zealand, FluAd Quad, contains a squalene-based oil-in-water emulsion adjuvant (designated MF-59). This adjuvant has been used in influenza vaccines since 1997 and has a good safety record. Since there are limited head-to-head studies, a systematic review, comparing vaccine effectiveness of adjuvanted vaccine with the vaccine effectiveness of standard TIV or QIV or no vaccination, found that adjuvanted TIV modestly improved vaccine effectiveness in adults aged 65 years or older.[34] During an A/H3N2 predominant season, a clinical trial comparing adjuvanted TIV (aTIV) with standard TIV in nursing home settings in the US, with mean age of 79 years, reported that, while respiratory hospitalisation rates were similar in both groups, significant reductions in all-cause hospitalisations (unadjusted HR 0.94; 95% CI 0.87-1.0) and pneumonia/influenza hospitalisations (unadjusted HR 0.79; 0.65-0.96).[35]

Live attenuated influenza vaccines

At the time of writing, live attenuated influenza vaccines (LAIVs) were not registered in New Zealand.

LAIVs may induce stronger immune responses than TIV or QIVs, particularly in children, by mimicking natural influenza infection and evoking both mucosal and systemic immunity, including broader cellular immune responses.[36] Trivalent and quadrivalent LAIVs are licensed for use in North America for healthy non-pregnant individuals aged 2–49 years and in Europe for children aged 2–18 years.[37] LAIVs have been shown to be effective in children aged 6 months to 7 years.[38]

During the 2013/14 and 2015/16 influenza seasons, effectiveness of LAIV against the predominant A(H1N1) strain was lower in the US in children age 2–17 years than that observed in the UK during the same seasons, such that the US Advisory Committee on Immunization Practices (ACIP) temporarily withdrew its recommendations for LAIVs use during 2016/17 influenza season.[37, 39] LAIVs were reinstated during the 2019/2020 season.

UK data from the 2018/19 season showed that LAIV effectiveness in children aged 2–17 years was at least as good as QIV in children for whom LAIV is contraindicated, particularly against A(H1N1)pdm09.[39, 40, 41] It is remains unclear why there were such significant differences in effectiveness for different regions, although variations in circulating strain matches, the make-up of the LAIV itself and previous vaccination history may all have some effect.[39]

High dose vaccines

For the 2022 season, high-dose influenza vaccine formulations will not be available in New Zealand. High-dose influenza vaccines containing four times more haemagglutinin antigen than standard vaccines have been shown to be more effective against influenza-related death and all-cause hospitalisation in the elderly than standard-dose trivalent vaccines.[42] Evidence to compare high-dose and standard quadrivalent vaccines is currently limited and research is ongoing to evaluate their application.

11.4.2 Efficacy and effectiveness

International data

The efficacy (prevention of illness among vaccinated individuals in controlled trials) and effectiveness (prevention of illness in vaccinated populations) of influenza vaccine depends on several factors. The age and immune competence of the vaccine recipient are important factors, as well as the match between the virus strains in the vaccine and those in circulation each year. Mismatches can evolve during a season or due to mutations occurring during vaccine manufacture (egg adaptation).[40] Previous vaccination history has been suggested to reduce the vaccine effectiveness in some cases; possibly more so when the previous vaccination was mismatched with the circulating strains at the time.[43] More recently, prior-season vaccination history has not been associated with reduced vaccine effectiveness in children or adults, and findings support annual revaccination.[40, 44, 45, 46, 47] With increasing complexity, this continues to be researched.

Two influenza B strains can frequently co-circulate, and due to the challenges involved in predicting which B strains will circulate in the upcoming season, mismatches between the B strain selected for TIVs and the circulating B strains have occurred in up to one-half of influenza seasons. The capacity of QIVs (containing two B influenza strains) to provide broader immune responses against B strains and cross-protection during B-mismatched seasons is expected to prevent more influenza cases, hospitalisations and deaths than TIVs.[1]

Data for vaccine efficacy and effectiveness of TIVs is summarised in Table 11.1.

Table 11.1: Current estimates of TIV influenza vaccine efficacy and effectiveness

Population	Type of outcome	Level of protection (95% confidence intervals)	Ref
Pregnant women	Effectiveness		
	• against confirmed influenza	50% (15–71%)	48
	• against acute respiratory illness		49
	– requiring an ED visit	81% (31–95%)	
	– or hospitalisation	65% (3–87%)	
Infants aged under 6 months whose mothers received an influenza vaccination during pregnancy	Effectiveness		
	• against confirmed influenza	41% (7–63%) to 49% (12–70%)	50 48
	• against influenza-related hospitalisation	47% (12–68%)	51
Healthy children	Effectiveness		
• aged under 2 years	• against confirmed influenza	Insufficient data under 2 years	38, 52
		66% (9–88%)	53
• aged 6–35 months		66% (29–84%)	53
• aged 6 months to 17 years	• against influenza-related death	65% (47–78%)	54
• aged 2–15 years	Efficacy against confirmed influenza	64% (52–72%)	52
	Effectiveness		
	• against influenza-like illness	28% (21–35%) to 47% (33–58%)	52
	• against influenza-related hospitalisation	56% (12–78%)	55
Children with high-risk conditions aged 6 months to 17 years	Effectiveness against influenza-related death	51% (31–67%)	54
Healthy adults (aged 18–64 years)	Effectiveness		
	• against confirmed influenza	59% (53–64%) to 66% (55–75%)	56
	• and influenza-like illness	16% (5–25%) to 18% (2–31%)	
	• against influenza-related hospitalisation in New Zealand	61% (34–77%)	57
	• against influenza-like illness general practice visit in New Zealand	55% (24–73%)	

Continued overleaf

Population	Type of outcome	Level of protection (95% confidence intervals)	Ref
Adults with high-risk conditions: • heart failure	Risk of: • all-cause mortality	17% reduced risk	58
• diabetes (newly diagnosed, aged 65 years or older)	• all-cause mortality • influenza-related hospitalisation	56% reduced risk 11% reduced risk	59
• chronic obstructive pulmonary disease	Effectiveness against influenza-related hospitalisation	22% (15–27%) to 43% (34–52%)	60
Adults aged 40 years or older	Effectiveness against acute myocardial infarction	29% (9%–44%)	61
Adults aged 65 years or older	Effectiveness • against confirmed influenza	49% (33–62%) 58% (34–73%)	62 63
	• against influenza-like illness	39% (35–43%) 41% (27–53%)	62 63
	• against non-fatal and fatal complications	28% (26–30%)	63

Vaccine effectiveness in New Zealand

New Zealand data is consistent with international data. While there is some variability from year to year and with different strains, the data overall show that the point estimate for influenza vaccine effectiveness is approximately 50 percent for preventing general practice visits, hospitalisations and for both influenza type A and B strains.[57, 64, 65, 66] Estimates for vaccine effectiveness tend to be higher in children and healthy midlife adults, and lower in the elderly. Influenza vaccination significantly reduces influenza-associated ICU admissions and attenuates disease severity in adults who were infected despite vaccination.[67]

Low influenza activity over recent years in New Zealand can cause imprecision in estimating annual vaccine effectiveness.[23, 68]

Pregnant women, the fetus and neonates

A pregnant woman and her fetus are at increased risk of influenza complications.[7] Physiological and immunological changes in pregnant women increase susceptibility to influenza.[69] Hospitalisation from influenza-related cardiorespiratory disorders during the second and third trimesters was especially apparent in the 2009 pandemic.[70] Influenza immunisation is therefore recommended during every pregnancy to reduce this risk, with similar effectiveness in healthy pregnant women as in other healthy adults against laboratory-confirmed influenza.[71] During the 2012–2013 seasons in Australia, women vaccinated in pregnancy were 81 percent less likely to attend emergency departments and 65 percent less likely to be hospitalised with acute respiratory illness than those unvaccinated.[49]

Influenza immunisation during pregnancy may reduce the incidence of stillbirth. Stillbirth was half as likely among vaccinated mothers compared to unvaccinated mothers in an Australian study.[11]

Maternal influenza immunisation offers protection to the newborn through maternal antibody transfer.[36, 51, 70, 72] Influenza vaccines are not registered and have not been shown to be effective in infants aged under 6 months: therefore, immunisation during pregnancy confers protection to newborns and infants who are too young to be vaccinated.[10, 50] Maternal influenza immunisation is significantly associated with reduced risk of influenza virus infection and influenza-related hospitalisation in infants up to 6 months of age and increased influenza antibody titres are maintained in infants through to age 2–3 months.[50, 73]

Children

Influenza vaccination in children provides similar protection to that seen in healthy adults. Effectiveness against laboratory-confirmed influenza is around 65 percent in young children aged 6 months to 5 years when vaccine and circulating strains are well-matched.[52, 53, 54] Influenza vaccination offers the greatest protection against influenza-related hospitalisation to children who are fully immunised with routine vaccines.[74] QIV vaccine effectiveness against influenza hospitalisation of children in the 2018 season in Australia was estimated to be 78.8 percent (95% CI 66.9–86.4); this was when Australia expanded the funded influenza vaccination programme to preschool children, those with comorbid medical conditions and all indigenous children.[75]

The additional benefit of vaccinating children is protection of those around them, including grandparents and infants.

Healthy adults

Generally, randomised placebo-controlled trials of TIV in healthy adults support good protection against laboratory-confirmed influenza.[56] Effectiveness against laboratory-confirmed influenza is around 60 percent in adults, but varies with the match of vaccine with circulating strains (see Table 11.1).

Adults aged over 65 years

Although currently available influenza vaccines are less effective at preventing clinical illness in older people,[76] influenza vaccination does reduce hospitalisation and deaths.

Effectiveness in community-dwelling adults aged over 60 years depends on how well the vaccine matches the circulating strains.[3] Influenza vaccine was moderately effective against laboratory-confirmed influenza during an epidemic season in community-dwelling adults age 65 year or older, irrespective of vaccine strain match. Significance was less during non-epidemic seasons and varied with virus type (the highest effectiveness was against A[H1N1] and the lowest against B).[77]

Vaccination has been demonstrated to prevent hospitalisation and death in older nursing home residents.[78, 79, 80, 81] A meta-analysis across 11 studies estimated influenza vaccination effectiveness to 37 percent (95% CI: 18–53; p=0.001) against pneumonia and 34 percent (95% CI: 10–53; p=0.01) against death due to pneumonia or influenza in institutionalised older adults.[82] A 2010 Cochrane review concluded that there was insufficient evidence to support influenza vaccine effectiveness in the elderly;[83] however, reanalysis of that review and its methodology argued that there is substantial evidence for the ability of influenza vaccine to reduce the risk of influenza infection and influenza-related disease and death in the elderly.[52, 62]

Severity of influenza symptoms are modestly attenuated by influenza vaccination in the elderly.[84] Therefore, by reducing severity of disease, vaccination can reduce the risk or duration of hospitalisation. Hospitalisation and immobility in the elderly leads to physical and mental decline, increased frailty and loss of independence.[8, 84, 85, 86]

Co-morbid conditions in adults and children

Influenza vaccination has been associated with reductions in hospitalisations and deaths among adults with risk factors for influenza complications, including diabetes,[87, 88] chronic obstructive pulmonary disease[89, 90] and heart failure.[58] Obese adults have a similar risk of influenza-associated hospitalisations as those with cardiovascular disease and diabetes.[91] Among Danish adults aged under 65 years with underlying medical conditions, vaccination reduced all-cause deaths by 78 percent and hospitalisations attributable to respiratory infections or cardiopulmonary diseases by 87 percent.[92] An Australian study of adults aged 40 years and older showed that unvaccinated adults are almost twice as likely as vaccinated adults to have an acute myocardial infarct.[93, 94]

Influenza vaccination is as effective as other preventative coronary care therapies (eg, smoking cessation, statins and antihypertensives) in protection against cardiovascular events.[94]

During the 2018 season in Australia, QIV vaccine effectiveness against influenza-related hospitalisation for children with comorbidities was estimated to be 77.3 percent (95% CI 59.8–87.2%).[75]

This highlights the importance of vaccinating children, as well as adults, with comorbidities against influenza.

Herd immunity

Influenza vaccination can provide indirect protection to those who are unimmunised or respond less well to the vaccine. This has been shown in certain settings, such as within schools and nursing homes.[3] There is evidence to suggest that herd immunity can be achieved, particularly by vaccinating children.[95]

The UK has progressively rolled-out a vaccination programme using LAIV and QIV, starting with children aged 2–3 years in 2013/14 and extended to children aged 4–7 years in 2015/16. As of the 2019/2020 season, influenza vaccine is offered in the UK to all children aged 2–10 years and up to 18 years for high risk groups. Early results from school-based pilot studies provided evidence of direct effect, indirect effects and overall impact, with decreases in disease incidence and influenza positivity in vaccinated and non-vaccinated groups.[96] A systematic review found that vaccination of children conferred indirect protection in some but not all settings.[97]

Some studies suggest that herd immunity may also be achieved in nursing homes if immunisation coverage of residents is greater than 80 percent.[98] Vaccinating health care workers is likely to be an effective strategy, particularly when in contact with high-risk patients.[13]

As shown by New Zealand SHIVERS data,[5] most people who catch the virus are asymptomatic or have very mild symptoms but are at risk of spreading it, such that increased vaccine uptake (funded and unfunded) across the whole population, from 6 months of age, is likely to achieve the greatest protection.

Duration of immunity

Due to the continual drift of influenza viruses, duration of immunity provided by influenza vaccines is difficult to study. However, when the strains stay the same for consecutive years, vaccination in a previous year appears to confer immunity into the next year for healthy adults and children.[3, 37] However, shorter duration of immunity is likely in other groups, particularly the elderly.[37]

Protection due to LAIVs has been demonstrated to persist beyond a year.[99, 100]

11.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store in the dark at +2°C to +8°C. Do not freeze.

11.4.4 Dosage and administration

The funded quadrivalent influenza vaccine should be administered by intramuscular, or subcutaneous injection, if indicated (see section 2.2.3). The contents of the syringe must be shaken thoroughly before use.

Individuals aged 9 years and older

Individuals aged 9 years and older receive a single 0.5 mL intramuscular dose of a QIV vaccine.

Children aged under 9 years

Children aged under 9 years who have not previously received influenza vaccine require two doses of vaccine four weeks apart to produce a satisfactory immune response. Children aged 6 months to under 3 years (ie, aged 6–35 months) receive a 0.25 mL dose of Afluria Quad junior; children aged 3 years and older receive a 0.5 mL dose of Afluria Quad (see Table 11.2).

Table 11.2: Recommended influenza vaccine doses in children

Age	Vaccine	Dose	Number of doses
6–35 months	Afluria Quad Junior	0.25 mL	1 or 2*
3–8 years	Afluria Quad	0.5 mL	1 or 2*

* Two doses separated by at least four weeks if the vaccine is being used for the first time. The recommended dosages for young children at different ages may vary between vaccine manufacturers, so check the manufacturer's data sheet before administering.

Immunocompromised individuals

Regardless of their age, previously unvaccinated immunocompromised individuals or those who have received a solid organ or haematopoietic stem cell transplant are recommended to receive two doses of influenza vaccine, four weeks apart (the second dose is unfunded).[101] One dose is then given in each subsequent year. (See section 4.3.)

Co-administration with other vaccines

Influenza vaccine can be administered with other vaccines, such as pneumococcal polysaccharide vaccine, tetanus diphtheria acellular pertussis (Tdap) vaccine, COVID-19 vaccines (mRNA-CV and rCV), and the scheduled childhood vaccines. Concurrent administration of influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) carries an increased risk of fever.[102, 103] Separation of the vaccines by two days can be offered, but is not essential. (See also section 16.6.2.)

Due to limited experience of concurrent delivery of liposomal adjuvants, it is recommended to allow three days between doses of non-funded adjuvanted influenza vaccine (FluAd Quad) and recombinant zoster vaccine (rZV; Shingrix) or adjuvanted recombinant COVID-19 vaccine (rCV; Nuvaxovid).

11.5 Recommended immunisation schedule

The optimal time to vaccinate people against influenza, particularly those in high-risk groups, is generally recommended from 1 April, annually, in advance of the usual May to September period of influenza virus activity. The vaccine can be given even when influenza virus activity has been identified, because protective antibody levels develop from four days after immunisation, with full protection after two weeks.[104] The vaccine should be administered annually to maintain immunity and to provide protection against new strains.

Vaccine effectiveness may be reduced in those at highest risk from influenza. Influenza vaccine is therefore recommended annually for everyone from the age of 6 months to reduce the spread of influenza virus and to protect against influenza-related complications. It is particularly important to vaccinate contacts of high-risk individuals, such as family and caregivers, and those working in certain occupations. See Table 11.3 for a summary of the funded and unfunded recommendations for influenza immunisation.

See the National Influenza Immunisation Programme campaign website (at **influenza.org.nz**) for further information.

Table 11.3: Influenza vaccine recommendations

Note: **Funded individuals are in the shaded rows.**

Refer to the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to the funding decisions.

Recommended and funded
All individuals aged 65 years and older. Individuals aged from 55 years and of Māori or Pacific ethnicity. All children aged 3 to 12 years[a]
Individuals aged 6 months to under 65 years who: • have cardiovascular disease (ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease or cerebrovascular disease) • have chronic respiratory disease (asthma if on regular preventive therapy; other chronic respiratory disease with impaired lung function) • have diabetes • have chronic renal disease • have any cancer, excluding basal and squamous skin cancers if not invasive • have other conditions (autoimmune disease, immunosuppression or immune deficiency, HIV infection, transplant recipients, neuromuscular and central nervous system diseases/disorders, haemoglobinopathies, children on long-term aspirin, a cochlear implant, errors of metabolism at risk of major metabolic decompensation, pre- or post-splenectomy, Down syndrome) • are pregnant • are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness (see section 11.5.2) • are patients who are compulsorily detained long-term in a forensic unit within a DHB hospital[b] • have serious mental health conditions (schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder) and/or are currently accessing secondary or tertiary mental health and addiction services.
Recommended but not funded
Generally, this vaccine is recommended annually for all individuals age from 6 months; it is particularly important for: • individuals with asthma not requiring regular preventive therapy • individuals in essential positions, emergency responders and health care workers • individuals with hypertension and/or dyslipidaemia without evidence of end-organ disease. • individuals who may transmit influenza to persons at increased risk of complications from influenza infection, (eg, caregivers, family members, health care staff, child care staff and other close contacts) • travellers • all children aged under 5 years • residents and staff of residential care facilities • the homeless.

a. From 1 July 2022 to 31 December 2022.

b. This is a Pharmaceutical Schedule Section H – Hospital Medicines List funding restriction.

11.5.1 Pregnancy and breastfeeding

The influenza vaccine is strongly recommended, and funded, for women who will be pregnant while the vaccine is available. Pregnant women can receive influenza vaccination at any stage of pregnancy to protect themselves, their fetus and their newborn for each season they are pregnant. When pregnancy spans two influenza seasons, two vaccinations (one from each season) are recommended to protect against all the predicted strains.

Influenza vaccine is safe to administer during any stage of pregnancy or while a woman is breastfeeding. There is no evidence that influenza vaccine prepared from inactivated split virus or subunits causes damage to the fetus or neonate[105] and there is some evidence it may be protective against stillbirth.[11]

Pregnant women are at greater risk from complications associated with influenza illness.[7, 10] When pregnancy is superimposed on high-risk conditions such as asthma or diabetes, influenza-related morbidity is three to four times greater than in non-pregnant women with similar high-risk conditions.

Globally, about one-quarter of influenza-associated hospital admissions and over one-third of in-hospital deaths are in infants under 6 months.[106] Because there is no registered or effective vaccine for children aged under 6 months, vaccination during pregnancy is highly recommended to improve maternal-fetal passive antibody transfer.[10] Influenza vaccination of pregnant women has been shown to significantly decrease influenza in their newborn babies.[36, 51, 70, 72] Breastfeeding is also recommended, to deliver passive immunity to the infant.[36] (See also section 4.1.2.)

11.5.2 Children at increased risk

Influenza vaccine is recommended and funded for all children aged 6 months and older, with chronic illnesses (see Table 11.3); children aged under 4 years a history of significant respiratory disease (including a history of measles); and all children aged from 3 to 12 years (until 31 December 2022). Children with the following conditions should be prioritised to receive influenza vaccine due to their increased risk, including:

- all asthmatics on regular preventive therapy
- other children with chronic respiratory disorders (eg, cystic fibrosis, non-cystic fibrosis bronchiectasis and chronic lung disease of infancy).

Special considerations apply to children, as follows (see also section 4.3):

- Immunisation is occasionally associated with fever between 6 and 24 hours after administration. In children aged 6–24 months with significant chronic medical conditions fever may cause an exacerbation of the underlying condition.
- Children receiving cancer chemotherapy may have a weaker response to influenza vaccine. Vaccination is recommended three to four weeks after the preceding dose of chemotherapy, when the neutrophil and lymphocyte counts are each $\geq 1.0 \times 10^9$/L. Children who are no longer receiving chemotherapy can be expected to show seroconversion to vaccine three months after the cessation of chemotherapy.

11.5.3 Adults at increased risk

Adults aged 65 years and older

In adults aged 65 years and older, influenza vaccine has been shown to be effective against non-fatal and fatal influenza complications, influenza-like illness and laboratory-confirmed influenza (see Table 11.1). Influenza vaccination protects against loss of independence due to increasing levels of frailty associated with hospitalisation.[8, 86, 107]

Adults with underlying medical conditions

Influenza has been associated with increased morbidity and mortality in adults with underlying medical conditions (see Table 11.3). Risk increases with multiple conditions. These also include those with serious mental health conditions and accessing mental health or addiction services.

Adults of Māori or Pacific ethnicity aged 55 years and over

All adults of Māori or Pacific ethnicity aged from 55 years are eligible for funded influenza vaccination. Māori and Pacific people are at greater risk of developing underlying health conditions, such as cardiovascular disease and chronic respiratory disease, at a younger age than other ethnicities,[108] which increases the risk of influenza severity and complications.

11.5.4 Recommended but not funded

Generally, influenza vaccination is recommended annually for all individuals aged from 6 months. It is particularly important for the groups listed in Table 11.2.

There are certain conditions that individually do not render a person eligible for funded influenza vaccine, but when combined, significantly increase the risk of influenza complications (this is described as 'risk stacking'). Such risks are further increased by smoking, alcohol dependency and obesity.

In order to optimise the protection of high-risk infants and toddlers, including those aged under 6 months (see Table 11.3), all household and close contacts should receive influenza vaccine (not funded unless eligibility criteria are met).

Healthy individuals of any age from 6 months and older

Healthy individuals are encouraged to have the vaccine, especially if they are in close contact with individuals at high risk of complications. Employers are encouraged to provide influenza vaccine to avoid illness in their employees, especially those engaged

in health care and other essential community services (see Table 4.9). Immunising healthy individuals has been shown to be cost-effective.

Health care workers

The Ministry of Health strongly recommends, and expects, that all health care workers will receive annual influenza vaccination for their own protection and the protection of those in their care.

Travellers

Influenza vaccine is recommended for people travelling outside New Zealand, especially those who are in the at-risk groups who have not received vaccine during the previous autumn, depending on the season and their destination. In tropical countries, influenza activity can occur throughout the year but is more likely during the winter (wet) and summer seasons, while in the northern hemisphere activity is commonest between the months of December and March. Outbreaks of influenza among organised tourist groups (eg, on cruise ships) can occur throughout the year.

11.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

11.6.1 Contraindications

Influenza vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of influenza vaccine or to a vaccine component. Egg allergy, including anaphylaxis, is **not** a contraindication or precaution: see section 11.6.3.

11.6.2 Precautions

History of Guillain–Barré syndrome

Influenza vaccination has been suggested to increase the risk of GBS. However, no association was found between administering 16 million doses of influenza vaccine and GBS in adults aged from 65 years in the US.[109] Any potential risk increase would be less than one additional case per million doses administered.[3, 37, 110] The risk of developing GBS is increased following influenza infection, and the magnitude of the risk is several times greater than that possibly occurring following influenza vaccination.[3, 110, 111]

New Zealand hospitalisations for GBS showed no increase during the 1990s despite the marked increase in vaccine use during this period but apparent year-to-year variation was observed. In particular, the doubling of vaccine use (with the introduction of funded vaccine) in 1997 was not associated with any increase in GBS hospitalisations. No excess risk for GBS following influenza vaccine in children has been documented. No association between influenza vaccines and any other neurological disease has been substantiated.

The risks and benefits of withholding vaccination should be considered on an individual basis, based on the potential morbidity and mortality associated with influenza for that individual, including the potential risk of recurrent GBS following influenza infection.

Co-administration with PCV13

Individuals (or their parents/guardians) who receive both influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) should be advised of the increased risk of fever following concomitant administration of these vaccines.[102, 103, 112] Separation of the vaccines by two days can be offered, but is not essential (see also section 16.6.2).

11.6.3 Egg allergy

Influenza vaccine can be safely administered to people with a history of egg allergy, including anaphylaxis, at general practices, pharmacies or at the workplace.[113]

Reported cases of anaphylaxis after influenza vaccination in egg-allergic individuals all occurred over 30 years ago, at a time when vaccine egg (ovalbumin) content was much higher than it is now. Recent studies have shown that influenza vaccines containing less than 1 µg of ovalbumin do not trigger anaphylaxis in sensitive individuals.[113]

11.7 Potential responses and AEFIs

Split virion or subunit influenza vaccines are generally well tolerated. The safety profile of quadrivalent vaccines is comparable to that of trivalent vaccines.[37]

Potential responses associated with these influenza vaccines in adults and children include pain, redness and/or swelling at the site of injection (10–64 percent of recipients, lasting less than two days).[3] These local inflammatory responses are almost always mild. Systemic events such as headache, muscle aches and fatigue may occur in adults. Passive reporting of local and systemic reactions to influenza vaccines is more frequent for females (both young and older adults) than males.[114] Australian surveillance data (collected by AusVaxSafety) found that just over 6 percent of adults reported any adverse event following seasonal influenza vaccination, of which less than 1 percent were systemic responses (fever, rash and seizure).[115]

Systemic reactions are more likely in children not previously exposed to the vaccine or virus, these are generally self-limiting and resolve within one to two days.[37] A large post-licensure study in the US, which reviewed more than 250,000 children aged under 18 years given influenza vaccine, showed no increase in clinically important medically attended events for two weeks after vaccination compared to control periods.[116]

In early 2010, an increase in febrile seizures in children in both Australia and New Zealand were all linked to the Fluvax brand influenza vaccine. Active surveillance in Australia continues to monitor for potential safety signals.

Vaccinators need to emphasise to recipients that:

- the split virion vaccine contains components of the virus, not the intact virus, and cannot cause influenza
- local reaction and mild systemic symptoms may occur within a day or two of immunisation
- respiratory viral infections are common, and many individuals will develop one coincidentally following immunisation, and these should not be falsely attributed to the vaccine.

An association was found in 2010 between narcolepsy and one H1N1 pandemic vaccine (Pandemrix, an adjuvanted vaccine not licensed or used in New Zealand). Data from various European countries support a temporal link.[117, 118, 119] The onset of narcolepsy may be confounded by other factors, such as genetic predisposition, A(H1N1)pdm09 influenza and/or other environmental factors.[120, 121, 122] A 2018 systematic review found that although the risk of narcolepsy type 1 increased in association with this particular vaccine, it remains a rare disease and the benefit of the influenza vaccination outweighs the risk.[123]

11.8 Public health measures

Using influenza signs and symptoms to assess the burden of influenza is of limited value. There is also a significant amount of asymptomatic circulation of influenza in the community. The most sensitive diagnostic method is polymerase chain reaction (PCR) of respiratory nasopharyngeal swabs or aspirate samples.

The methods of controlling influenza are:

- immunisation
- hand hygiene (ie, regularly washing hands for at least 20 seconds and drying them for 20 seconds, or regularly using an alcohol-based hand rub)
- respiratory hygiene (ie, cough and sneeze etiquette, and the judicious use of viricidal tissues and wearing of face masks in some settings)
- social distancing (ie, persuading those with symptoms to avoid others in the community by staying away from school and work when sick; in particular, infected individuals should avoid contact with the elderly, the chronically ill, and infants and babies)

- regularly cleaning flat surfaces such as bathroom sinks, bedside cabinets, desks and tabletops
- antiviral therapy, but this has a limited role (see section 11.8.2).

11.8.1 Improving vaccine uptake

Studies in New Zealand and overseas have found that provider attitudes and provider recommendations are key to improving influenza vaccine uptake. Organised registers for recall and opportunistic immunisation are also likely to be important factors in achieving high uptake.

Every effort should be made during April to immunise all people at risk, particularly those aged 65 years and older, those aged under 65 years (including children) who have certain medical conditions, pregnant women and health care workers, and those of Māori or Pacific ethnicity aged 55 to 64 years. During an influenza outbreak, recommend influenza vaccination to anyone at risk who was not immunised during the current season or to those who have not received an influenza vaccination for more than six months. Availability of an appropriate vaccine is the most pertinent of these factors.

Vaccination of all healthy adults and children from age 6 months is encouraged but not funded. Adult vaccination, especially for those in close contact with high-risk groups, may be funded by employers.

11.8.2 Antiviral drugs

Influenza antiviral drugs can be used to treat or to prevent influenza and can be adjuncts to influenza vaccination. Early use of antivirals, especially within the first 48 hours of illness, can reduce the duration of symptoms and the risk of complications from influenza. They are likely to be most effective against severe influenza and for those with high-risk comorbidities.

It has been shown that when patients with influenza-like illness were treated in primary care with oseltamivir, recovery time was shortened compared with usual care. In older patients and those with comorbidities, in particular, even with longer previous symptom duration (48–72 hours), recovery was likely to be 2–3 days sooner following antiviral treatment than it would have been with than standard care alone.[124] Meta-analyses of the effectiveness of oseltamivir in treating uncomplicated influenza show shortened duration of symptoms for healthy adults and adolescents of around one day,[125] a 63 percent (95% CI: 19–83) decrease in risk of hospitalisation for any cause and a 44 percent (95% CI: 25–58) decrease in risk of antibiotic prescription use.[126]

For use with severe influenza, observational studies show early treatment can lead to a decreased risk of death.[127, 128] Early treatment upon hospital admission was significantly associated with reduced length of stay (by 19 percent), regardless of time since symptoms onset, compared with later or no treatment initiation. Greater reductions in

length of stay were seen for pregnant women and obese patients (by 39 percent and 27 percent, respectively).[129]

Antivirals should be particularly considered for unimmunised or recently immunised contacts who are at high risk of severe disease. When used to limit the size of an institutional outbreak, antiviral drugs are usually given for a period of two weeks after immunisation or until one week after the end of the outbreak. Institutional outbreaks should be notified to the local medical officer of health.[130]

11.8.3 Pandemics

At the time of a pandemic, recommended public health advice, priority groups and the timing of vaccination may be quite different from those during inter-pandemic periods. The *New Zealand Influenza Pandemic Plan: A framework for action* (available at **www.health.govt.nz/publication/new-zealand-influenza-pandemic-plan-framework-action**) describes the key phases of a pandemic and the actions and responsibilities within each phase.[131]

11.9 Variations from the vaccine data sheet

Vaccine data sheets state that the vaccine is contraindicated in individuals with a hypersensitivity to egg protein. However, the Ministry of Health recommends that individuals with hypersensitivity to eggs, including anaphylaxis, may receive influenza vaccination: see section 11.6.3.

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12 Measles

Key information

Mode of transmission	By direct contact with infectious droplets or by airborne spread. Measles is one of the most highly communicable of all infectious diseases (R0=12–18).
Incubation period	About 10 days but may be 7–18 days from exposure to onset of fever. The incubation period may be longer in those given IG after exposure.
Period of communicability	From 4 days before to 4 days after rash onset, counting the day of rash onset as day 0.
Incidence and burden of disease	New Zealand was declared free of endemic measles in 2017. Outbreaks continue to occur through imported cases, as occurred in 2019. To prevent recurrent outbreaks of measles, 95 percent of the population must be immune.
Funded vaccine	MMR (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. This includes all adults born in New Zealand from 1 January 1969 without two documented doses of measles-containing vaccine received after age 12 months. For (re)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high risk countries.
Vaccine effectiveness	Measles vaccines are around 95 percent effective after 1 dose and 99 percent effective after two doses.
Duration of protection	Two doses are anticipated to provide lifelong protection. Protection is best achieved through herd immunity from high immunisation coverage.
Contraindications	MMR is contraindicated for immunocompromised individuals and in pregnancy. Priorix is contraindicated for anaphylaxis to neomycin.
Precautions and special considerations	See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions.

Potential responses to vaccine	MMR is generally well tolerated. Fever and rash 6–12 days after vaccination. Salivary gland swelling and joint pain is possible due to mumps and rubella components.
Public health measures	Notify the local medical officer of health immediately on suspicion of wild-type measles. Prevent measles transmission through exclusion and use of personal protective equipment. Promote immunisation to susceptible individuals.
Post-exposure prophylaxis	Management of contacts of measles cases should be discussed with the medical officer of health.

12.1 Virology

The measles virus is an RNA virus, from the genus *Morbillivirus*, in the family Paramyxoviridae. Humans are the only natural host for the measles virus. The virus has a survival time of around two hours and is rapidly inactivated by sunlight, heat and extremes of pH.[1]

12.2 Clinical features

Measles is transmitted by airborne spread as well as direct contact with infectious droplets. It is one of the most highly communicable of all infectious diseases, with an approximate basic reproductive number of 12–18 in high-income countries[2] (see section 1.2.1). There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik's spots on the buccal mucosa. The characteristic maculopapular rash classically appears first behind the ears on the third to seventh day, spreads over three to four days from the head and face, over the trunk to the extremities. It lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is about 10 days, but may be 7–18 days, from exposure to onset of fever, and about 14 days, but may be 7–21 days, from exposure to onset of rash. Measles is highly infectious from four days before to four days after rash onset, counting the day of rash onset as day zero. Incubation may be longer in those given IG after exposure or in infants with residual maternal antibody and can present as a modified, attenuated measles with a mild prodrome and a sparse discrete rash of short duration.[3]

Complications are common, occurring in 10 percent of cases, and include otitis media, pneumonia, croup and diarrhoea. Encephalitis has been reported in 1 in every 1,000 cases, of whom some 15 percent die and a further 25–35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and idiopathic thrombocytopenic purpura (ITP or immune thrombocytopenia).

Measles infection causes acute immune suppression of the cellular and humoral immunity that leads to the depletion of immunological memory and antibody repertoire. This loss in immunity increases the long-term risk of further infections requiring medical treatment.[4, 5, 6, 7, 8] Although there are potential implications for long term effects on immune memory of individuals who have had measles, currently, there is no evidence to recommend reimmunisation.

Sub-acute sclerosing panencephalitis (SSPE) is a rare but fatal degenerative central nervous system disease resulting from persistent measles virus infection. It typically occurs 7–11 years after wild-type measles infection, at an estimated rate of 4–11 per 100,000 measles cases with higher incidence if measles occurs before 2 years of age.[9] Recent literature shows that SSPE is under-reported or under-diagnosed in the US.[10] Cases have occurred following undiagnosed measles or clinically mild disease, particularly when immunisation coverage has been low or where infants too young to have been immunised have acquired the infection while travelling to endemic regions.[11, 12]

The case-fatality rate for reported cases of measles in the US is 1–3 per 1,000.[9] Pneumonia is responsible for approximately 60 percent of deaths, more commonly in young patients. Measles is particularly severe and has a much higher case-fatality rate in the malnourished children with vitamin A deficiency, which is further exacerbated by diarrhoea; in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash;[9] and in pregnant women.[9] Measles during pregnancy can cause miscarriage, stillbirth and preterm delivery.[1]

Measles is also serious in healthy children: over half of all the children who died from measles in the UK between 1970 and 1983 were previously healthy.[13] No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

12.3 Epidemiology

12.3.1 Global burden of disease

Mortality and morbidity

From 2000 to 2016, the annual reported measles incidence decreased by 75 percent worldwide, from 146 to 35 cases per million population, due to increased vaccine coverage.[14] Annual worldwide estimated measles deaths was 89,780 in 2016, representing an 84 percent decline since 2000.[15]

However, there was a worldwide increase in disease during 2019. Over 1.3 million confirmed and suspected cases of measles were reported to WHO from 187/194 member states, resulting from multiple outbreaks, including in the previously measles-free Americas.[16]

Although measles mortality rates have fallen significantly,[17] measles remains an important vaccine-preventable cause of death among children throughout the world, particularly in low-income countries in Africa and Asia. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year. During 2019, the countries with the highest number of cases were Philippines, Madagascar, India, Ukraine, the Nigeria and Brazil.[16] The incidence rate in Samoa was almost 10 times that observed in New Zealand (4525 versus 476 per million population). In Samoa, around 1.5 percent of cases died and one-third were hospitalised (there were 83 deaths, 5,707 cases and 1,868 hospitalised as of 20 January 2020).[18]

Measles elimination

When a country is verified by the Measles Regional Verification Commission as having eliminated measles, it means that the country interrupted transmission of the endemic strain of circulating measles virus for a period of 36 months. Importations of measles virus may have occurred during this period, but circulation of the imported strains of measles virus was interrupted within 12 months of the importation.[19]

In May 2012 the 194 member states of the World Health Assembly endorsed the *Global Vaccine Action Plan 2011–2020*,[20] which aimed to eliminate measles in at least four WHO regions by 2015 and in five WHO regions by 2020. In September 2016, the Region of the Americas was the first WHO region to be declared free of endemic measles and New Zealand was verified as having eliminated measles in 2017.

Disappointingly, no region has sustained measles elimination. Measles cases were reported to have climbed by 300 percent globally in the first three months of 2019.[21] For example, four European countries (Albania, Czechia, Greece and the UK) lost measles elimination status and the US reported it highest number of cases in 25 years.[22] Global coverage for the first measles vaccine dose has stalled at 85 percent and for the second doses at 67 percent, falling short of the 95 percent required to prevent outbreaks.[21]

12.3.2 New Zealand epidemiology

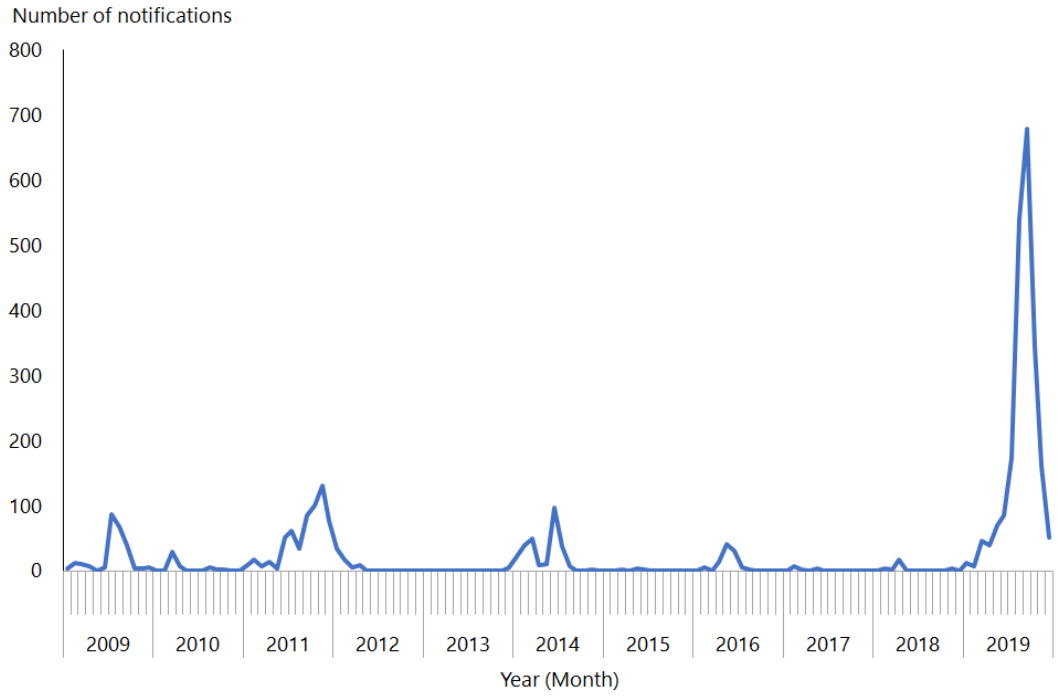
Measles vaccine was introduced in in New Zealand in 1969 and moved to a two-dose schedule (as a combined MMR vaccine) in 1992. Measles became a notifiable disease in 1996. The two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information about the history of the Schedule) and was changed in 2020 to 12 months and 15 months following the 2019 outbreaks.

Historical holes in coverage, due to a combination of issues including historically low immunisation coverage in the childhood programme, unfounded vaccine safety concerns at the turn of the 21st century, changes to the schedule for MMR dose 2 from age 11 years to 4 years and compromised vaccine due to lack of adequate cold chain processes prior to 2004 have meant that young adults and adolescents (ages 15–30 years), in particular, are under immunised against measles.[23]

Prior to the introduction of two-dose MMR schedule, measles epidemics occurred in 1991 (the number of cases was estimated to be in the tens of thousands) and 1997 (when 2,169 cases were identified). In 2019, nine outbreaks occurred, six were linked to imported cases from the Philippines, Japan, Thailand, Australia and Singapore. In 2019, 2,213 cases were notified, of which 775 were hospitalised (ESR, 8 June 2020). The worst affected region was Counties Manukau DHB, which had 1,174 cases, many of whom were of Māori and Pacific ethnicity, children too young to be immunised and unimmunised young adults.[24]

Importation of measles by non-immune people who had travelled overseas was also linked to the smaller measles outbreaks in New Zealand in 2009, 2011, 2014 and 2016 (see Figure 12.1; see also section 12.5.5).

Figure 12.1: Number of measles notifications by month reported, January 2009 to December 2019



Source: ESR

To eliminate measles epidemics, modelling suggests that New Zealand needs to achieve a coverage level of 90 percent or greater for both doses of MMR.[25] If this coverage level is achieved and maintained in those aged 12 months to 50 years, elimination of measles can be maintained. In quarter ending 31 December 2019, the 5-year-old immunisation coverage rate (ie, fully immunised with two doses of MMR) was 89 percent – nearing a target of 90 percent.

For details of measles notifications, refer to the most recent measles and notifiable disease reports from ESR (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

12.4 Vaccines

12.4.1 Available vaccines

The measles vaccine is only available as one of the components of MMR. This vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses.

Funded vaccine

Each 0.5 mL dose of the reconstituted MMR (Priorix, GSK) contains:

- not less than 103.0 CCID50 of the attenuated line of Schwarz strain measles, propagated in chick embryo tissue culture
- not less than 103.7 CCID50 of RIT 4385 mumps strain, derived from the Jeryl Lynn strain and propagated in chick embryo tissue culture
- not less than 103.0 CCID50 of the Wistar RA 27/3 rubella strains, propagated in MRC5 human diploid cells
- lactose, amino acids supplement, mannitol, sorbitol and neomycin sulphate as excipients, and water for injection.

Other vaccines

M-M-R II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change. It contains a attenuated line of measles virus derived from Enders' attenuated Edmonston strain; the Jeryl Lynn (B level) strain of mumps virus; and the Wistar RA 27/3 strain of live attenuated rubella virus.

Two quadrivalent measles, mumps, rubella and varicella vaccines (MMRV: see chapter 22) are also registered but not currently available in New Zealand:

- Priorix-Tetra (GSK) contains n the Schwarz measles, RIT 4385 mumps, Wistar RA 27/3 rubella and Oka/Merck varicella-zoster virus strains.
- ProQuad (MSD) contains Enders' attenuated Edmonston (Moraten) measles virus strain, Wistar RA 27/3 rubella virus, Jeryl Lynn mumps virus and live varicella virus vaccines (Oka/Merck).

12.4.2 Efficacy and effectiveness

Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations.[26] Outbreaks and epidemics continue to occur where low immunisation rates and/or sufficient numbers of susceptible members of communities are present. A 2012 Cochrane review of the safety and effectiveness of MMR concluded that a single dose of MMR is at least 95 percent effective in preventing clinical measles and 92 percent effective in preventing secondary cases among household contacts aged 6 months and older.[27] This was a systematic review of clinical trials and studies, which involved approximately 14.7 million children.

Seroconversion to all three viruses of MMR occurs in 85–100 percent of recipients. 'Primary vaccine failure' refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate an immune response. This occurs in 5–10 percent of recipients after the first dose and is rare after a second dose. More than 99 percent of people who receive two MMR doses (given at least four weeks apart, with the first dose given after age 12 months) develop serologic evidence of immunity to measles.[9] Two doses are required for measles control and elimination in populations.[9] The second MMR dose is not a booster: it is given to increase vaccine efficacy to 98 percent and address primary vaccine failure.

Measles vaccination may have nonspecific effects, reducing mortality from other infectious diseases. Infection with the measles virus causes immune memory loss and predispose people to opportunistic infections for more than three years.[5, 7, 8] Population-level data from the UK, US and Denmark indicates that when measles was common, measles virus infections could have been implicated in as many as half of all childhood deaths from infectious disease.[8] The reduction in measles infections is suggested to be the main factor in reducing overall childhood infectious disease mortality after the introduction of vaccination.

Duration of immunity

Even though antibody levels decline over time, secondary vaccine failure (ie, vaccine failure due to waning of protective immunity) has been documented for measles but remains rare.[28] There were three cases in the recent New Zealand outbreak with documented secondary vaccine failure but no transmission was recorded from these cases. Breakthrough cases, as a result of secondary vaccine failure, appear to be attenuated and less likely to be hospitalised.[29]

In Finland in 1982 a cohort was recruited at the start of the national MMR vaccination programme to study the persistence of vaccine-induced antibodies. By the mid-1990s Finland had eliminated measles, mumps and rubella, and there was little opportunity for natural boosting to occur. The follow-up of this cohort has shown that while antibodies wane over time, 20 years after the second MMR dose, 95 percent of people remained seropositive for measles.[30] The antibody avidity also decreased by 8 percent for measles.[31] Waning of both the concentration and the avidity of antibodies might contribute to measles infections occurring in individuals who have received two doses of MMR. Waning in immunity was suggested in a small proportion of vaccinated cases (less than 1 percent) in the 31–42 year age group reported in an outbreak in Berlin.[32]

12.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

12.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

Co-administration with other vaccines

MMR can be given concurrently with other vaccines, as long as separate syringes are used, and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.) Note that TST/Mantoux testing for tuberculosis must be deferred by at least four weeks after MMR if not given concurrently (see section 12.6.2).

Interchangeability

The two brands of MMR (Priorix and M-M-RII) may be used interchangeably for completion of a course.[33]

12.5 Recommended immunisation schedule

Table 12.1: Recommended MMR vaccination schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 12 months and 15 months
Catch-up[b] for children, adolescents and adults	2 doses: at least 4 weeks apart

a. If MMR is given to children aged 6–11 months for outbreak control, 2 further MMR doses are still required at age 12 months (given at least 4 weeks since the previous dose) and 15 months.

b. For those born from 1 January 1969 who do not have documented evidence of two doses of a MMR-containing vaccine given after age 1 year, or who do not have serological evidence of protection for measles, mumps and rubella. See section 12.5.2.

12.5.1 Usual childhood schedule

A two-dose MMR vaccination schedule (with appropriate documentation) is recommended irrespective of a history of measles, mumps or rubella infection or measles immunisation. A clinical history does not reliably indicate immunity. Positive serology for measles cannot be used as a proxy for mumps or rubella immunity. There are no known ill effects from vaccinating children, even if they have had serologically confirmed infection with any of the viruses.

Measles vaccine is recommended as MMR at age 12 and 15 months. Two doses of measles vaccine are recommended because nearly all the approximately 5 percent who fail to be protected by the first dose will be protected by the second.[9] The second dose of measles vaccine can be given as soon as four weeks after the first dose.

MMR vaccination when aged under 12 months

A dose of MMR (called MMR0 [zero]) may be recommended for infants aged 6–11 months during measles outbreaks if cases are occurring in the very young (see section 12.8). These children still require a further two doses of MMR at ages 12 months (given at least four weeks after previous dose) and 15 months because their immune response and long-term protection from measles is less when the vaccine is given at a younger age.[34, 35] Any recommendations in this regard will be made by the local medical officer of health and the Ministry of Health based on local epidemiology.

Note: Some immigrant children may have received a measles-containing vaccine when aged under 12 months.

12.5.2 Catch-up

Two doses of documented MMR (at least four weeks apart) are recommended and funded for any child, adolescent or adult who is known to be susceptible to one or more of the three diseases.

A second dose of MMR should be given at least four weeks after MMR1 to all children who are older than 15 months but have not yet received their second MMR dose (ie, those who would have been due their second dose at age 4 years).

Adults born in New Zealand prior to the introduction of measles vaccine in 1969 are considered immune to measles as circulating virus and disease were highly prevalent at that time.

Adults born from 1 January 1969

All individuals born in 1969 or later who have documented evidence of two doses of MMR given after age 12 months or who have serological evidence of protection for measles are considered immune to measles.

Some adults may have received one dose of measles-containing vaccine and one dose of MMR or MR during one of the catch-up campaigns (eg, the 1997 campaign, when all those aged up to 10 years were offered MMR, or from international schedules). They will have therefore received the recommended two doses of measles vaccine, but only one of mumps and rubella vaccines. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended and funded. These individuals can receive a second dose of MMR (ie, a third dose of measles vaccine) without any concerns. It is important that women of childbearing age are immune to rubella (see chapter 19).

All persons born from 1 January 1969 with only one documented dose of prior MMR should receive a further dose of MMR; if there are no documented doses of prior MMR or documented evidence of immunity, then two doses should be administered, at least four weeks apart.

Occupational risk groups

Certain occupational groups are at increased risk of exposure to measles; particularly those who travel frequently, such as military personnel and cruise ship staff and aircrew (in this case MMR is funded for those eligible for New Zealand health services). See Table 4.9 for details of relevant occupational groups.

12.5.3 Immunocompromise

Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). These people can be partially protected from exposure to infection by ensuring that all their close contacts, including hospital staff and family members, are fully immunised (this is funded), including hospital staff and family members, through cocoon strategies. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to an immunocompromised individual. See section 12.7.2.

See also '*Vaccination of close contacts of immunocompromised individuals*' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

(Re)vaccination before or following immunosuppression

MMR is funded to be given at least 28 days before planned immunosuppression.

For vaccination or revaccination following immunosuppression (funded), it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.13).

Receipt of MMR, on time at age 12 and 15 months, is recommended for asymptomatic children who are not severely immunocompromised. MMR is recommended for all HIV-positive individuals aged from 12 months, whether they are symptomatic or asymptomatic, if their CD4+ lymphocyte level is over 15 percent or CD4+ lymphocyte count is at least 200 cells/mm^3. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[9]

12.5.4 Pregnancy and breastfeeding

MMR is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.[1, 9]

After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccine recipients (see section A6.4.1).

MMR can be given to breastfeeding women.

(See also sections 4.1.3, 12.6.1 and 19.5.3.)

12.5.5 Travel

International travel is an important factor in reintroducing measles into New Zealand. To avoid importing measles to New Zealand, vaccination with MMR is recommended for all children aged 12 months and older and adults travelling overseas if they have not previously been adequately vaccinated (see Appendix 2 for planning catch-up immunisations). Infants aged 6–11 months can receive one dose of MMR (as MMR0) if they are travelling to a country with an active measles outbreak (see section 12.5.1).

Measles remains endemic in many countries, including areas in Europe, Asia, the Pacific and Africa, and outbreaks are ongoing worldwide. A high rate of measles incidence was reported in the Philippines during 2019 and early 2020.[36] During January to October 2019, 52 (64 percent) out of 81 imported measles cases in the US were residents returning from travel abroad and 73 (90 percent) were unvaccinated or had unknown vaccination status. Eight outbreaks (85 percent of cases of the resulting 1,259 cases) were associated with unvaccinated close-knit populations, such as the Orthodox Jewish community in New York; these began from two single imported cases.[37] Travel was also linked to the measles outbreaks in New Zealand in 2011, 2014, 2016 and 2019.

12.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

12.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR (eg, children with an acute febrile illness should have their immunisation deferred).

Anaphylaxis following a previous dose of MMR or any of the vaccine components is a contraindication to a further dose of MMR. Individuals who have anaphylaxis after receiving MMR should be serologically tested for immunity and referred to, or discussed with, a specialist if they are non-immune to rubella or measles.

MMR is contraindicated for:

- those with proven anaphylaxis to the vaccine or vaccine component (eg, neomycin or gelatin)
- immunocompromised individuals (ie, those with significantly impaired cell-mediated immunity, such as those with untreated malignancy, type 1 interferon receptor (IFNAR) signalling pathway defects, or altered immunity as a result of drug therapy, including high-dose steroids, or receiving high-dose radiotherapy) (see section 4.3)
- individuals who have received another live vaccine, including BCG, within the previous 4 weeks unless given concurrently (for BCG, see chapter 21)
- pregnant women – pregnancy should be avoided for four weeks after immunisation[1, 9]see section 19.5.3)
- individuals who have received IG or a blood transfusion during the preceding 11 months (see Table A6.1 in Appendix 6 for the length of time to defer measles vaccine after specific blood products)
- those with severe immune deficiency from HIV, because vaccine-related pneumonitis (from the measles component) has been reported[9] – discuss vaccination of individuals with HIV infection with their specialists.

Note: Inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.[38]

12.6.2 Precautions

Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response. In the case of children with current ITP, the timing of vaccination should be discussed with their specialist.

Women of childbearing age should be advised to avoid pregnancy for the next four weeks after MMR vaccination (see section 19.5.3).[1, 9]

Measles vaccination may temporarily suppress tuberculin skin test (TST/Mantoux) reactivity, so if required, a TST should be placed on the same day as MMR vaccination or be postponed for four to six weeks after vaccination.[9] TST is not a prerequisite for measles vaccination. An individual with active TB should be established on treatment before administering MMR.

12.6.3 Egg allergy

The measles and mumps components of the MMR are manufactured in chick embryo cell culture, so there may be trace amounts of egg protein in the vaccine. Egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. Various studies have confirmed that children with egg allergy can be vaccinated safely.[9, 39, 40] Other components of the vaccine may be responsible for allergic reactions.[41] Individuals with egg allergy may therefore be safely vaccinated in primary care.[42]

12.7 Potential responses and AEFIs

12.7.1 Potential responses

Some children, around 5–15 percent, may experience fever of 39.4°C or more between 6 and 12 days after immunisation that generally lasts one to two days and is associated with a strong measles antibody response.[9, 43] Rash, often with atypical distribution, can occur in approximately 5 percent of vaccine recipients at the same interval post-vaccination: these individuals are not infectious to others.[9] Fevers, rashes and other systemic symptoms can occur coincidentally after vaccination due to common childhood infections and are not caused by the vaccine.[44]

Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed. During an outbreak, genotyping the sample can help to identify vaccine strain versus wild type disease.

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccine recipients, most often 10–14 days after immunisation.[45] The rubella vaccine can cause a mild rash, fever, joint pain and lymphadenopathy between one and three weeks after immunisation.[9, 46] There were no persisting sequelae associated with the administration of 3 million doses of MMR to 1.5 million children in Finland.[44, 47]

12.7.2 AEFIs

Temporally related reactions, including febrile seizures, nerve deafness, aseptic meningitis, encephalitis, rash, pruritus and purpura, may follow immunisation rarely; however, causality has not been established.[48]

Vaccine virus transmission

MMR vaccine viruses are regarded as being non-transmissible from vaccine recipients. Two historical, poorly documented case of transmission (of a rubella and a mumps vaccine strain) were reported from a vaccine that is no longer in production.[49] Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.[38, 50] There have been no confirmed cases of disease transmission from MMR vaccine viruses.

Idiopathic thrombocytopenic purpura

MMR is the only childhood vaccine with an elevated risk of ITP, which occurs in 1 in 25,000 to 40,000 people, 15 days to six weeks after immunisation.[9] ITP is mild and transient, resolving within six months in 93 percent of cases.[1, 51] If ITP occurs, measles, mumps and rubella serology should be measured, and if the individual is immune to all three infections, a second dose is not required. However, if the individual is susceptible to any of the three infections, a second dose should be administered.[52, 53, 54] The risk of thrombocytopenia is higher after the first dose of vaccine than after the second dose and is much rarer after vaccination than after wild-type infection.[9]

12.7.3 Adverse outcomes not linked to MMR

Over three decades, multiple published epidemiological studies in the UK,[55] Finland[56] and elsewhere[27] have confirmed that there is no link between MMR and the development of autism in young children (see section 3.2.4 for further discussion on this issue).

12.8 Public health measures

> It is a legal requirement that all cases of measles be notified immediately on suspicion to the local medical officer of health – do not wait for a laboratory confirmation as this can delay contact tracing and allow outbreaks to become established if disease is confirmed.

12.8.1 Diagnosis

A single case of measles should be considered an outbreak and result in an appropriate outbreak response. Practitioners should have a low index of suspicion for notification, and all suspected clinical cases should be self-isolated immediately and notified to the medical officer of health.

The standard clinical case definition for measles is 'an illness characterised by all of the following: generalised maculopapular rash, starting on the head and neck; fever (at least 38°C if measured) present at the time of rash onset; and cough or coryza or conjunctivitis or Koplik's spots present at the time of rash onset'.

It is important that the diagnosis be laboratory confirmed, as many viral infections can mimic measles. In the first instance, a nasopharyngeal and throat swab should be taken for viral identification by PCR. Further testing should be discussed with a clinical microbiologist. For instructions on measles specimen collection and transport, see the National Measles Laboratory website (**www.measles.co.nz**)

For more details on diagnosis, refer to the 'Measles' chapter of the online *Communicable Disease Control Manual*[57] (available at **www.health.govt.nz/publication/communicable-disease-control-manual**)

12.8.2 Post-exposure prophylaxis

Management of contacts of a measles case should be discussed with the local medical officer of health.

MMR vaccination

A single dose of MMR when given to an unvaccinated person within 72 hours of first contact with an infectious person may reduce the risk of developing disease as post exposure prophylaxis.[1] If there is doubt about vaccination status, MMR should still be given. MMR will not exacerbate the symptoms of measles if a person is already incubating the disease, but in these situations, any measles-like illness occurring shortly after vaccination is likely to be due to infection.

If MMR is not given within 72 hours of first exposure, it should still be offered at any later interval to provide protection from future exposures, unless the vaccine is contraindicated.

In an outbreak, the use of MMR for infants aged 6–11 months should be considered. If MMR0 is vaccine is given to an infant aged under 12 months, two more doses are still required from age 12 months and at least four weeks apart. This is because the seroconversion rate is lower when MMR is administered to an infant aged under 12 months. Similarly, to optimise early protection, toddlers should be give both doses of MMR four weeks apart.

Human normal immunoglobulin prophylaxis for contacts

Human normal immunoglobulin (HNIG; Normal Immunoglobulin-VF) is recommended for measles-susceptible individuals in whom the vaccine is contraindicated (see section 12.6) and susceptible pregnant contacts. For these individuals, HNIG is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure. All other susceptible contacts should be offered MMR as post-exposure prophylaxis (as described above).

HNIG provides no benefit to those who are already exhibiting symptoms of measles.

HNIG may be recommended for the following contacts of measles cases as soon as possible and up to six days after exposure:

- immunocompromised or immune-deficient people
- susceptible pregnant women
- immune-competent infants aged under 6 months: because maternal antibody wanes in the first six months of life, evidence of maternal vaccination status or serology tests may not predict protection for these infants. Maternal serology may be helpful for neonates. The role of an infant measles IgG test is unclear but may be helpful if available rapidly. Discuss use of HNIG for these infants with a paediatrician
- immune-competent children aged between 6 and 12 months, who are outside the 72-hour exposure window for MMR vaccination
- infants born prematurely <28 weeks' gestation are considered non-immune irrespective of maternal immune status.

For further details for infants under 6 months and immunocompromised children refer to the Starship Child Health guidelines (available at **starship.org.nz/guidelines/measles**).

The recommended dose for pregnant women and immunocompromised or immunodeficient people is 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, usually administered as three 5 mL injections.

Prophylaxis with intravenous immunoglobulin

IVIG (Intragam P) can be considered for: immunosuppressed and immune-deficient measles contacts (who may, for example, have a central venous catheter); individuals with reduced muscle bulk; those whom intramuscular injection is contraindicated; or in individuals for whom large doses are required (see Appendix 6 for more information about passive immunisation). IVIG is not given if a person is already symptomatic.

See the guidance from the Public Health England for further information (available at **www.gov.uk/government/publications/measles-post-exposure-prophylaxis**).[58]

Queries regarding usage and dosage of IVIG for measles prophylaxis can be directed to the New Zealand Blood Service transfusion medicine specialists via the DHB blood bank.

12.8.3 Exclusion

Exclusion of measles cases or contacts should be discussed with the local medical officer of health.

Parents/guardians should be advised that children who are suspected or confirmed measles cases should be excluded from early childhood services, school or community gatherings until at least five days after the appearance of the rash.

Immune contacts (considered to be children aged under 15 months who have received one dose of measles-containing vaccine on or after their first birthday and children aged 15 months and older who have received two doses) need not be excluded from these settings. Non-immune (susceptible) contacts should be excluded because of the risk of developing the disease themselves, and the risk of passing on the disease during the prodromal phase to other susceptible children. Advise susceptible contacts to avoid attending school, early childhood services or community gatherings, and to avoid contact with other susceptible individuals, until 14 days after the last exposure to the infectious case.

Given that post-exposure MMR vaccination cannot guarantee protection, susceptible contacts who have received their first MMR vaccination within the 72-hour period after first exposure should also be excluded for 14 days after the last exposure to the infectious case (unless they subsequently meet the criteria for immunity). Contacts who have previously received one documented dose of MMR and then receive their second dose of MMR within 72 hours after first exposure can go back to school or work.

Individuals who have received IG prophylaxis should also be excluded for 14 days after the last exposure to the infectious case.

Acceptable evidence of immunity:

- was born before 1 January 1969
- has documentation of previous immunity or previous infection
- for children aged 12 months to under 15 months: has documentation of at least one dose of measles-containing vaccine after their first birthday
- for individuals aged 15 months and older: has documentation of two doses of measles-containing vaccine, given at least one month apart and given from 12 months of age.

For more details on control measures, refer to the 'Measles' chapter of the *Communicable Disease Control Manual*[57] (available at **health.govt.nz/publication/communicable-disease-control-manual**).

12.9 Variations from the vaccine data sheet

The vaccine data sheet recommends a single dose of MMR. However, as 2–5 percent of recipients fail to seroconvert after the first dose (see section 12.4.2), the Ministry of Health recommends and funds a second dose of MMR. Two doses are required for measles control and elimination;[9] the second MMR dose is not a booster.

The vaccine data sheet states that individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur. However, various studies have confirmed that egg-allergic children can be vaccinated safely.[9, 39, 40] The Ministry of Health recommends that individuals with egg allergy, including anaphylaxis, may be safely vaccinated in primary care (see section 12.6.3).

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13 Meningococcal disease

Key information

Mode of transmission	By respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.
Incubation period	2–10 days, commonly 3–4 days.
Period of communicability	Commonly 3–4 days without treatment, range 2–10 days. Certain antibiotic therapy eradicates *N. meningitidis* from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Funded vaccines	• Quadrivalent meningococcal conjugate conjugated to diphtheria toxoid (MenACWY-D): Menactra. • Meningococcal group C conjugate (MenC): NeisVac-C. • Meningococcal B recombinant (4CMenB): Bexsero
Other available vaccines	• Quadrivalent meningococcal conjugate conjugated to tetanus toxoid (MenACWY-T): Nimenrix.
Dose, presentation, route	0.5 mL per dose. Presentation: • MenACWY-D: vial • MenACWY-T: vial and pre-filled syringe; must be reconstituted before use • MenC: pre-filled syringe • 4CMenB: pre-filled syringe. Intramuscular injection.
Funded vaccine indications	MenACWY-D (Menactra), MenC (NeisVac-C) and 4CMenB (Bexsero) for: • patients pre- or post-splenectomy or with functional or anatomical asplenia • patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) • pre- or post-solid organ transplant • HSCT (bone marrow transplant) patients • patients prior to planned and following immunosuppression • close contacts of meningococcal cases (any group) • patients with prior meningococcal disease of any group. MenACWY-D (Menactra) for: • adolescents and young adults aged 13–25 years inclusive who will be living or are currently living in a boarding school hostel or university hall of residence, military barracks or prison.
Recommended, unfunded	Laboratory workers handling bacterial cultures Health care professionals in very close contact with cases.

Vaccine effectiveness	MenACWY: 80–85%; effectiveness wanes to 50–60% within 2–5 years after vaccination. MenC: effectiveness of 83–100%; antibody wanes within 2–3 years. 4CMenB: 75% reduction in group B cases in infants over 3 years and cross-protection against group W observed; 71% reduction in group B disease in adolescents.
Potential responses to vaccines	MenC and MenACWY: localised pain, irritability, headache and fatigue, mild fever. 4CMenB: increased risk of fever and fever-related events in children <2 years (prophylaxic antipyretic advised). Older age groups: localised pain, nausea, myalgia, malaise, mild fever and headache.
Contraindications	No specific contraindications or precautions, except prior anaphylaxis to vaccine components.
Public health measures	All cases must be notified if clinically suspected. Parenteral antibiotics should be administered as soon as possible before admission to hospital or in hospital if delays of longer than 30 minutes are likely.
Post-exposure prophylaxis	For chemoprophylaxis of contacts see section 13.8.2.

13.1 Bacteriology

Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative bacterium, causing sepsis, meningitis and some less common clinical syndromes. Groups B, W and C are currently the most important types in New Zealand. Increasingly, group W and Y organisms are the cause of bacteraemia and pneumonia in the elderly. Predominant groups differ between countries; group A is an important epidemic strain, particularly in Africa and the Middle East. Meningococci are spread from person to person by respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.

13.2 Clinical features

Table 13.1 below describes the symptoms and signs of meningococcal disease – individuals may present with some or all of these. Meningococcal septicaemia is more common than meningitis, and presentation varies from a mild non-specific illness to rapid progression with fatal outcome. Symptoms and signs in infants are frequently non-specific. The classical rapidly progressing petechial or purpuric rash may not be present or may initially appear maculopapular. Atypical initial presentations, including gastrointestinal symptoms, septic arthritis and epiglottitis, are more frequently reported with meningococcal W disease, and may contribute to delayed diagnosis and increased case-fatality.[1, 2] Pneumonia is more frequently reported with group Y.

Table 13.1: Symptoms and signs of meningococcal disease

Adolescents and adults	Young infants and children
• Sepsis syndrome, including poor peripheral perfusion and tachycardia • Nausea/vomiting • Meningeal signs • Rash – petechial/purpuric, but may be maculopapular; rash may not be present early and absent in about one-third of cases • Sleepy, difficult to rouse • Occasionally in young adults, irrational behaviour • Arthralgia, myalgia, leg pain • Atypical presentation (particularly group W) may include pneumonia, septic arthritis, myocarditis or diarrhoea	As for adolescents and adults, plus the following: • bulging fontanelle • tachycardia • altered responsiveness • irritability and/or floppiness • refusing drinks or feeds • poor peripheral perfusion • atypical presentation may include epiglottis, diarrhoea or septic arthritis
Notify all suspected cases urgently to local medical officer of health, including out-of-hours.	

Meningococcal disease covers a spectrum, from persistent fever with or without rash and arthritis to rapidly progressive purpuric rash and shock. Meningitis can occur with and without signs of sepsis. In fulminant cases, coma and death can occur within a few hours despite appropriate treatment.

Because of the potential for rapid progression, antibiotics should be administered (Table 13.2) as soon as possible before hospital admission. Antibiotics given prior to transfer should be clearly noted on information accompanying the patient to hospital.

Table 13.2: Recommended antibiotics for suspected cases

Antibiotic	Children <30kg	Children >30kg and Adults (max dose)
Ceftriaxone[a] (first line treatment)	50 mg/kg when given by GP/primary care 100 mg/kg IV (or IM) up to 2g when given in ED	2 g IV (or IM)
Benzylpenicillin[b] (second choice)	50 mg/kg IV (or IM)	2.4 g IV (or IM)

a. Patients allergic to penicillin who do not have a documented history of anaphylaxis to penicillin can be given ceftriaxone.

b. Patients with a documented history of anaphylaxis to penicillin and who are suspected of suffering from meningococcal disease should be sent immediately to hospital without pre-admission antibiotics.

13.3 Epidemiology

13.3.1 Global burden of disease

Incidence and serotypes

The prevalence of meningococcal groups varies geographically. The highest burden of disease occurs in sub-Saharan Africa, where despite a dramatic fall in Group A disease following introduction of a Group A conjugate vaccine this 'meningitis belt', epidemics continue with around 30,000 cases reported annually, now including Group W.

The incidence in Canada, the US and Europe varies substantially from 0.2 to 3 per 100,000 persons per year.[3] Group B has become the predominant capsular group in Europe, Americas and Australia, with incidence typically highest in children aged under 2 years.[4] Group C disease has almost disappeared in countries with universal immunisation programmes, but outbreaks have been observed in men who have sex with men in the US and Europe.

Since 2009 there has been an emerging global incidence of Group W disease, initially in the United Kingdom and South America. Australia has experienced a rapid increase in Group W cases since 2013 with New Zealand also seeing a rapid increase in cases since 2017. Like group C clonal complex ST11 strains, group W ST11 strains have enhanced virulence. Higher rates of carriage of these ST11 strains has been noted within age groups where invasive group W disease is more prevalent (infants and the elderly).[5]

Some parts of the world, particularly in Scandinavia, have reported an increase in group Y disease. In other regions, there is evidence of colonisation, but disease caused by group Y is rare. Patients with group Y strain disease are more likely to develop pneumonia and to be elderly than other strains.[3, 4]

This emergence of group W and Y strains has led to meningococcal C vaccines being replaced by quadrivalent (group A, C, W, Y) meningococcal conjugate vaccines (MenACWY).

Risk groups

The highest incidence of meningococcal disease occurs in children aged under 5 years (especially under 2 years) with a secondary peak in older adolescents (15–19 years).The age distribution for groups W and Y is more likely to include older people that for B and C. A pooled overall case-fatality rate of 8.3 percent (range 4.1–20 percent) is reported internationally, varying by group and age.[6]

Most infection occurs in healthy people, but those with certain rare immune deficiencies (terminal components of complement (C5–9) or properdin) or asplenia are at much higher risk, particularly of recurrent meningococcal disease. Individuals with infection caused by groups other than A, B, C, W, Y and untypeable strains or who experience recurrent disease should be investigated.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as the case's household,[7] early childhood education services,

semi-closed communities, schools, correctional facilities and military recruit camps. Students living in hostel accommodation may also be at higher risk.[8, 9, 10] In health care settings, only those with close exposure to oropharyngeal secretions of patients with meningococcal disease (as may occur during intubation or resuscitation) and microbiology laboratory workers are considered to be at increased risk.

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Secondary cases (ie, in contacts of known cases of meningococcal disease) usually occur within four days, but it can be up to 10 days. The infectivity of patients with meningococcal disease is markedly reduced after 24 hours of antibiotic therapy, although treatment with cefotaxime, ceftriaxone, rifampicin or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage and hence relax infection prevention and control precautions (see section 13.8.2).

In high-income countries in the absence of immunisation, nasopharyngeal carriage of *N. meningitidis* occurs in approximately 10 percent of the overall population, rising from 2 percent in children aged under 4 years to a peak of 24.5 percent to 32 percent among 15–24-year-olds, then declining with increasing age.[3, 11] In adolescents and young adults, the overall and capsular group carriage vary between regions and age groups.[12] The relationship between risk factors for disease and those associated with carriage is incompletely understood.[3] Carriage prevalence does not predict the disease incidence nor the occurrence or severity of outbreaks, as most of the carried strains are non-encapsulated and do not cause disease.[3] Smoking, passive smoking, household crowding and upper respiratory tract infections increase carriage.

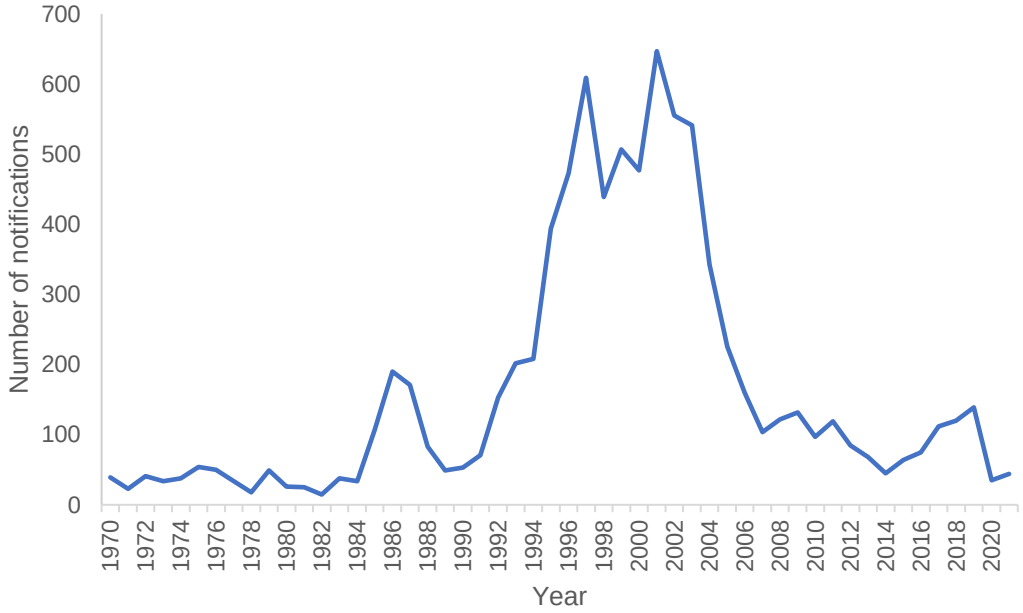
13.3.2 New Zealand epidemiology

Incidence and mortality

In 2021 the notification rate for meningococcal disease was 0.9 cases per 100,000 population, with a total of 44 cases notified (40 laboratory confirmed; ESR, 28 April 2022). Cases remain significantly lower than the peak annual incidence rate of 16.7 per 100,000 for all ages and 200 per 100,000 in children under 12 months as experienced in 2001 during the meningococcal epidemic from 1991 to 2007. The epidemic was largely due to a single Group B subtype (B:4:P1.7-2,4). The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 13.1.

For further details and reports of meningococcal disease in New Zealand refer to the ESR surveillance reports (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

Figure 13.1: Notified cases of meningococcal disease, 1970–2021



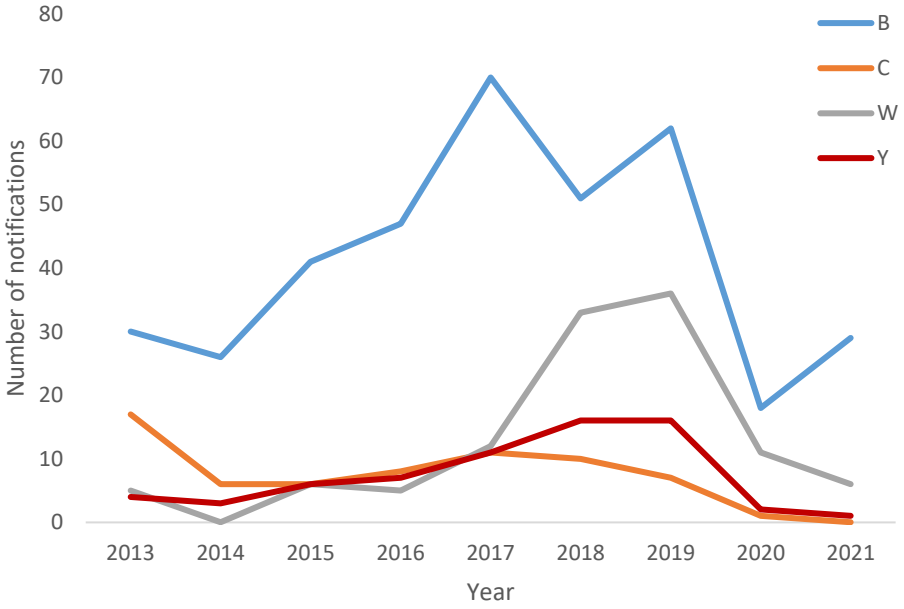
Source: ESR

Meningococcal disease incidence is highest in Māori (2.6 per 100,000, 22 cases in 2021) compared with the total population. Household crowding is an important risk factor for meningococcal disease, independent of ethnicity.[13] In 2021, the highest age-specific disease rates were among those aged under 1 year (27.8 per 100,000, 17 cases) decreasing in ages 1–4 years (2.0 per 100,000, 5 cases). Three deaths occurred in 2021, giving a case fatality rate of 6.8 percent (ESR, 928 April 2022).

Strain types

Strain type was determined for 36 of the 40 laboratory-confirmed cases in 2021. Group B strains were the most prevalent, causing 81 percent of the typed cases (Figure 13.2). The group B strain (B:4:P1.7b,4) responsible for the epidemic caused 22 percent of all meningococcal disease in 2021 (8 of the 36 typed cases). Cases of meningococcal disease caused by group C strains decreased since 2014 (Figure 13.2), while group W increased from five cases in 2016 to 36 in 2019. Cases in groups C, W and Y decreased in 2021, likely in part, due to the public health measures implemented to control the COVID-19 pandemic. Only group B increased from 2020.

Figure 13.2: Meningococcal disease notifications by group, 2014–2021



Source: ESR

13.4 Vaccines

13.4.1 Available vaccines

Internationally, meningococcal vaccination programmes were revolutionised by the development of conjugate vaccines, which allow vaccination in younger children and induced herd immunity when used in population-wide programmes due to reduced nasopharyngeal carriage (see section 1.4.3).

The monovalent (C) and quadrivalent (ACWY) conjugate vaccines are conjugated to a protein, either CRM_{197} (diphtheria toxin-derived), diphtheria toxoid or tetanus toxoid. Previously used, polysaccharide-only vaccines provided three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines and are no longer available or registered in New Zealand. Those travelling to Africa, the Middle East and other areas with wide serogroup prevalence, including group A, require MenACWY vaccine for broad protection. In 2018, a multicomponent meningococcal group B recombinant vaccine (4CMenB) was registered in New Zealand to protect against group B disease.

With the current New Zealand epidemiology, neither MenACWY nor 4CMenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. The meningococcal vaccines registered and available are summarised in Table 13.3 below.

Table 13.3: Meningococcal vaccines registered and available in New Zealand

Name (manufacturer)	Vaccine type
Bexsero (GSK)	Meningococcal group B four-component recombinant (4CMenB)
Menactra (Sanofi)	Quadrivalent meningococcal conjugate (MenACWY-D): contains group A, C, W and Y polysaccharides conjugated to diphtheria toxoid
NeisVac-C (Pfizer NZ Ltd)	Meningococcal group C conjugate (MenC): contains group C polysaccharide conjugated to tetanus toxoid
Nimenrix (Pfizer NZ Ltd)	Quadrivalent meningococcal conjugate (MenACWY-T): contains group A, C, W and Y polysaccharides conjugated to tetanus toxoid

Funded vaccines

No meningococcal vaccines are on the routine Schedule. See section 13.5 for funded vaccine for special groups.

Three meningococcal vaccines are funded for certain special groups (see section 13.5).

- Meningococcal group C conjugate vaccine MenC (NeisVac-C, Pfizer NZ Ltd) contains 10 µg of polysaccharide derived from the group C capsule, conjugated to 10–20 µg of tetanus toxoid. Other components include aluminium hydroxide and sodium chloride.
- Quadrivalent meningococcal conjugate vaccine MenACWY-D (Menactra, Sanofi) contains 4 µg of each polysaccharide derived from the capsules of group A, C, W and Y *N. meningitidis* strains, each conjugated to diphtheria toxoid. Other components include sodium chloride and sodium phosphate.
- Recombinant meningococcal B vaccine, 4CMenB (Bexsero, GSK) contains four components from the group B meningococcus: three recombinant N. meningitidis group B surface proteins associated with bacterial adhesion and survival (*Neisseria* heparin binding antigen fusion protein, adhesin A protein, and factor H binding protein) plus detoxified outer membrane vesicles containing antigen as used in the MenNZB epidemic vaccine. Other components include aluminium hydroxide, sodium chloride, histidine and sucrose.

Other vaccines

A second quadrivalent meningococcal conjugate vaccine MenACWY-T (Nimenrix, Pfizer NZ Ltd) is registered and available in New Zealand for individuals from age 6 weeks. MenACWY-T contains 5 µg of each polysaccharide derived from the capsules of group A, C, W and Y *N. meningitidis* strains, conjugated to 44 µg of tetanus toxoid carrier protein. Other components and excipients include sodium chloride, trometamol and sucrose.

A two-component meningococcal group B recombinant vaccine (2CMenB; Trumenba, Pfizer Ltd) is licensed from 10 years of age, including in the US, Europe and Australia. It is not available in New Zealand.

Historic MeNZB vaccine

A strain-specific group B meningococcal vaccine (MeNZB, Chiron/Novartis) containing outer membrane vesicles derived from the epidemic strain B:4:P1.7b,4 (NZ 98/254) was developed for epidemic control in New Zealand and used between 2004 and 2008. The programme ceased in 2008 because of a decline in incidence of group B disease (see previous editions of the *Handbook)*.

Since the immune response to MenNZB was short-lived, previous recipients who wish to be protected against meningococcal B disease will need to be fully immunised with 4CMenB.

13.4.2 Efficacy and effectiveness

Meningococcal conjugate vaccines

Quadrivalent meningococcal conjugate vaccines

Clinical trial data use immunogenicity and bactericidal antibody titres as a proxy for efficacy. Effectiveness of conjugate meningococcal vaccination against laboratory-confirmed disease is difficult to assess due to the low incidence of cases, even during localised epidemics, such that data is limited around the effectiveness of the MenACWY vaccines. With the emergence of group W and Y strains, more countries have implemented mass campaigns and routine immunisation programmes to control outbreaks with MenACWY vaccines and can assess impact through disease incidence and carriage studies.

The overall effectiveness of a single dose of diphtheria conjugate quadrivalent meningococcal vaccine (MenACWY-D, Menactra) given at age 11–12 years was estimated to be 69 percent up to eight years post-vaccination (from 79 percent in year one to 61 percent up to eight years post-vaccination).[14] These findings cannot be extrapolated across all MenACWY vaccines due to differences in immunogenicity.

Following a mass vaccination campaign in children aged 9 months to 4 years in Chile with MenACWY (MenACWY-D or MenACWY-CRM, depending on age), there was a 92.3 percent reduction in group W disease and the case-fatality rate declined from 23 percent in 2012 to 0 percent in 2016 in children aged 1–4 years. However, there was no impact in infants aged under 12 months or adults aged 80 years or older.[15]

The MenACWY-D vaccine was poorly immunogenic in infants aged under 6 months,[16] and it is currently registered in New Zealand for individuals aged 9 months to 55 years.

The MenACWY-T vaccine (Nimenrix) is registered in New Zealand for individuals from aged 6 weeks. Clinical trials showed that the vaccine elicited bactericidal antibodies against all four groups from age 2 months with acceptable reactogenicity and safety profile.[17]

There is no published data on effectiveness in older adults.

Meningococcal group C conjugate vaccines

Meningococcal C conjugate vaccines were used successfully in national immunisation and mass vaccination programmes from 1999 in the UK, resulting in almost complete elimination of group C disease.[18] A targeted immunisation campaign during an epidemic in Salvador, Brazil demonstrated MenC vaccination to be 98 percent effective against group C disease in young children.[19] A booster dose in the second year of life was indicated in the UK for sustained protection.[20] The greatest impact from meningococcal immunisation campaigns was obtained through herd immunity and a reduction in transmission was observed across all age groups, including in unvaccinated adults, where catch-up programmes in adolescents were implemented.[21 22]

With the emergence of group W and now group Y meningococci, MenC has generally been replaced by MenACWY vaccines on national programmes in infants and adolescents.

Meningococcal group B recombinant vaccine

Three years after initiation of the introduction of 4CMenB to the national immunisation schedule in the UK, a 75 percent reduction in group B disease was reported in the vaccine-eligible age groups compared with a historical cohort.[23] With 88 percent coverage but a low number of cases (25), adjusted vaccine effectiveness for all group B strains was 59.1 percent (95% CI: -31.1–87.2) following two primary doses and one booster dose, with an estimated 277 cases prevented.[23] This research is ongoing.

Following 4CMenB vaccination of adolescents aged 15-16 years in South Australian schools, there was an overall reduction of 71 percent (95% CI 15-90; p=0.02) in group B meningococcal disease cases aged 16-19 years: five cases in 2017–2018 (predicted 9.9 [95% predicted interval 3.9-17.5]) and one case in 2018–2019 (predicted 10.9 [4.4–19.1]).[24]

As was observed during college outbreaks in the US,[25, 26] in South Australia where 4CMenB is administered in a school-based programme at age 15–18 years, 4CMenB had no effect on disease-causing meningococcal carriage suggesting that vaccination of adolescents is unlikely to generate herd immunity.[27] A 4CMenB vaccination campaign used during an isolated outbreak in a region of Québec, Canada outbreak demonstrated direct protection of 79 percent against outbreak strain group B disease and an overall impact of 86 percent in target groups with no herd effects.[28]

Cross-protection against meningococcal group W has been observed following vaccination of infants with 4CMenB in the UK. Among age-cohorts that were fully and partially eligible to receive 4CMenB, respectively, it was estimated that there were 69 percent (adjusted incidence rate ratio 0.31; 95% CI 0.2-0.67) and 52 percent (0.48; 0.28-0.81) fewer cases of group W disease than predicted in 2018/2019; this included direct and indirect protection over four years. An estimated 98 cases (95% CI 34-201) cases of group W disease were directly prevented in children aged under 5 years.[29] The researchers state that MenACWY conjugate vaccines would still be required for direct and indirect protection against those groups, since the degree of cross-protection is dependent on the expression of vaccine antigens on the meningococcal surface.[29]

There is limited data on its use in patients with chronic medical conditions and immunocompromised by medication or disease, such as HIV infection or hereditary immune system defects. In a phase 3 clinical trial, children aged 2–17 years showed good but reduced immunogenicity in those with immunocompromise.[30] Immunogenicity in children with asplenia and splenic dysfunction was similar to healthy children but reduced in children with complement deficiencies.[31]

The safety and efficacy of 4CMenB in adults above 50 years of age have not been established.

13.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. MenACWY-D, MenACWY-T and 4CMenB should be protected from light. Do not freeze.

Reconstitution

MenACWY-T (Nimenrix) must be reconstituted with the supplied diluent and used as soon as possible.

13.4.4 Dosage and administration

Quadrivalent meningococcal conjugate vaccines (MenACWY)

Each MenACWY dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Menactra (MenACWY-D)

MenACWY-D (Menactra) is registered in New Zealand for individuals aged 9 months to 55 years. See Table 13.5 for schedules for certain special groups.

- For children aged 9–23 months, two doses are given at least three months apart.
- For individuals aged 2–55 years, one dose is given.
- Booster doses may be indicated in some high-risk individuals

MenACWY-D can be concurrently administered with other vaccines in separate syringes and at separate sites,[32, 33, 34, 35] except for PCV13. MenACWY-D should preferably be administered at least four weeks after PCV13. This is because, when administered concurrently, there is possible blunting of the immune response to some of the pneumococcal serotypes.[36, 37] (see section 13.5.2 for recommendations in regard to high-risk children age under 12 months and section 4.3.3).

Nimenrix (MenACWY-T)

MenACWY-T (Nimenrix) is registered (not funded) in New Zealand for individuals from age 6 weeks.

- For infants aged under 12 months, two doses are given eight weeks apart, plus a booster from age 12 months at least six months after second dose.
- Healthy infants aged 6 months to under 12 months, who are not immunocompromised, can be given one dose instead of two primary doses, plus a booster from age 12 months, at least eight weeks later.
- For adults and children from age 12 months, one dose is given.
- Booster doses may be indicated in some individuals.

MenACWY-T can be concurrently administered with other vaccines in separate syringes and at separate sites; there is no data on concurrent administration of MenACWY-T and PCV13, however, interference is unlikely.

Meningococcal group C conjugate vaccine (MenC)

Each MenC (NeisVac-C) dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3). See Table 13.5 for schedules for at-risk individuals.

For infants aged under 9 months, two doses are given at least eight weeks apart, with the first dose given not earlier than age 6 weeks. One dose of MenACWY is recommended in the second year of life from age 12 months.

MenC can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

In view of the New Zealand epidemiology, a quadrivalent (MenACWY) vaccine would be preferable, to obtain broader meningococcal protection.

Meningococcal group B recombinant vaccine (4CMenB)

Each 4CMenB (Bexsero) dose is 0.5 ml, administered by intramuscular injection (see section 2.2.3).

- For infants aged 6 weeks to 11 months, two doses are given with a minimum of eight weeks between doses, with a booster given at least six months after the second dose, from age 12 months.
- For toddlers aged 12–23 months (at time of first dose) a primary course of two doses is given at least eight weeks apart. A booster dose is recommended from 12 to 23 months after dose two.
- For children aged from 2 years (at time of first dose) and adults, two doses are given at least eight weeks apart. (Note: the safety and efficacy in individuals aged over 50 years have not been established, but no safety concerns are expected.)

Generally, the need for booster doses from the age 2 years or older at the time of their first dose has not been established. A booster dose can be considered for individuals at continued risk of exposure to meningococcal disease. Booster doses are funded five-yearly for some high-risk individuals (see Table 13.5).

4CMenB can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

Note: 4CMenB elicits a robust immune response, sometimes with high fevers in some infants. Routine use of paracetamol with every dose of 4CMenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain. Some infants will still develop a fever and/or injection-site pain even though they have received paracetamol doses.

Prophylaxic paracetamol is recommended to be given 30 minutes prior to and six-hourly for up to 48 hours following vaccination for children aged under 2 years. For children and infants aged from 2 months, ibuprofen may be given as an alternative to paracetamol.

13.5 Recommended immunisation schedule

13.5.1 Individuals at increased risk

Meningococcal vaccines are not on the Schedule but are funded in special circumstances, as described in the shaded section of Table 13.4; Table 13.5 shows the recommended dosing schedules.

See sections 4.3, 4.4 and 4.5 for more information about vaccination of special groups, including recommended immunisation schedules for high-risk individuals with certain medical conditions.

The meningococcal vaccines are recommended (but not funded) for other individuals at risk, as described in non-shaded rows in Table 13.4.

Before travel

There are areas of the world where the risk of meningococcal disease is increased. Nevertheless, the risk to travellers to the developing world has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world, including in Europe and the Americas. Generally, countries outside of Africa experience smaller outbreaks, but case-fatality rates can be high.

The preferred vaccines (MenACWY and/or 4CMenB) for travel would be based on the epidemiology of the country. For website sources for information about meningococcal vaccines for travellers, see the WHO website (**who.int/travel-advice**). Quadrivalent meningococcal vaccine is a requirement for pilgrims to the Hajj.

Before moving into communal living situations

MenACWY-D is recommended and funded from age 13–25 years inclusively for individuals who will be living in communal accommodation within the next three months, or who are in their first year of living in communal accommodation (specifically, boarding school hostels, tertiary education halls of residence, military barracks or prisons) as they are likely to be at higher risk of acquiring meningococcal infection.

Table 13.4: Meningococcal vaccine recommendations

Note: **Funded circumstances are in the shaded rows**.

See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to the funding decisions.

Recommended and funded

MenC or MenACWY-D and 4CMenB are recommended and funded for:

- patients pre- or post-splenectomy or with functional or anatomical asplenia[a,b]
- patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited)
- patients who are pre- or post-solid organ transplant[b]
- HSCT (bone marrow transplant) patients[b]
- patients prior to planned immunosuppression[b,c]
- patients following immunosuppression[b,c]
- close contacts of meningococcal cases of any group[d]
- individuals who have previously had meningococcal disease of any group[d,e]

MenACWY-D is recommended and funded for:

- individuals aged 13–25 years inclusively who are entering within three months or are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks or prisons.

Recommended but not funded

Priority groups

MenACWY-D or MenACWY-T and 4CMenB are recommended, but not funded, for:

- individuals are laboratory workers regularly handling meningococcal cultures
- adolescents and young adults living in communal or overcrowded accommodation not covered by funded vaccine
- individuals who are travelling to high-risk countries (see **who.int/travel-advice**) or before the Hajj.

MenACWY-T is recommended but not funded for high-risk infants age under 9 months in place of MenC.

4CMenB is recommended but not funded for all the above high-risk groups.

Other groups

MenACWY and 4CMenB are recommended but not funded for all infants, young children, adolescents and young adults.

a. Pneumococcal, Hib, influenza and varicella vaccines are also recommended for individuals pre- or post-splenectomy or with functional asplenia. See section 4.3.4.

b. See section 4.3.4 for more information.

c. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d. For close contacts and individuals who have had previous meningococcal disease, given as per the routine dosage schedule (see section 13.4.4)

e. Regardless of time elapsed since disease. Vaccination can commence at any time from when the person is no longer acutely unwell.

Table 13.5: Recommended meningococcal vaccine schedule for high-risk individuals (funded)

Note: See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged 6 weeks to under 12 months	MenC (NeisVac-C) and MenACWY-D (Menactra)	If aged under 9 months, give 2 doses of MenC 8 weeks apart, followed by MenACWY-D[a] at ages 9 and 13 months. Administer one MenACWY-D booster dose after 3 years, then 5-yearly. (See alternative unfunded MenACWY-T (Nimenrix) option in • Table 13.6.) • If aged 9–11 months, give 2 doses of MenACWY-D[a] at least 3 months apart, followed by a booster dose after 3 years, then 5-yearly.
	4CMenB (Bexsero)	• Give 2 doses 8 weeks apart, plus booster given at least 6 months after second dose, from age 12 months and then 5-yearly[c].
Children aged 12 months to under 18 years	MenACWY-D (Menactra)	• If aged 12 months – under 7 years at diagnosis, give 2 doses of MenACWY-D[a] at least 3 months apart followed by a booster dose after 3 years, then 5-yearly. • If aged 7 years or older give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose 5-yearly.[a]
	4CMenB (Bexsero)	• For toddlers aged 12-23 months (at time of first dose), give 2 doses 8 weeks apart and a booster dose 12-23 months after second primary dose • From age of 2 years (at time of first dose), give 2 doses 8 weeks apart. • Give booster dose 5-yearly from age 2 years[c]
Adults aged 18 years and older	MenACWY-D (Menactra)	Give 2 doses 8 weeks apart, then 1 dose every 5 years.[a,b]
	4CMenB (Bexsero)	Give 2 doses 8 weeks apart, then booster 5 yearly.[c]
Individuals aged between 13 and 25 years, in certain communal living situations[d]	MenACWY-D (Menactra)	1 dose, no booster required

a. Give MenACWY-D at least 4 weeks before or after PCV13[36, 37] (see below).

b. MenACWY-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years. Likewise, 4CMenB is licenced to age 50 years but no safety concerns are expected when given to adults aged over 50 years.

c. 4CMenB booster funded for individuals pre- and post-splenectomy and for patients with functional or anatomic asplenia, HIV, complement deficiency (acquired or inherited), or pre- or post-solid organ transplant.

d. Funded for individuals aged 13–25 years inclusively who either: are entering within three months or who are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks or prisons.

There is a possibility of blunting of some PCV serotype antibody responses when MenACWY-D (Menactra) is given concurrently with the PCV13 series because both vaccines contain diphtheria-derived proteins as conjugates. The clinical significance of this blunting, observed in a clinical trial with PCV7,[37] is unknown and the affected serotypes (4, 6B, 18C) are currently rare in New Zealand. The benefits of achieving broad meningococcal protection as early as possible in immunocompromised infants outweigh the theoretical risk of modest reduction of some pneumococcal antibody levels, so MenACWY-D is recommended at 9 months rather than waiting until the PCV13 series is completed (see Table 4.5, Table 4.6 and Table 13.5). Note: two doses given at least three months apart are recommended as a primary series; ideally, each dose should be given at least four weeks before or after PCV13 to reduce this risk of interference, but PCV13 and MenACWY-D can be given together or at any interval for pragmatic reasons or if an accelerated schedule is required.

13.5.2 Recommendations for children and adolescents

In the absence of a universal programme, non-high-risk children and adolescents may be offered meningococcal vaccines, but these are not funded.

Table 13.6 suggests the most appropriate ages for this, reflecting the known ages of increased risk. The predominant meningococcal strains in New Zealand in childhood are B, W and C. With the current New Zealand epidemiology, neither MenACWY nor 4CMenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. For those who are likely to travel, the broadest protection is preferable because of the differing serotype patterns between countries.

Table 13.6: Recommended schedule for non-funded meningococcal vaccines in children and adolescents

Note: Vaccine immunity is not long-lasting. The suggested ages of vaccination are not expected to protect individuals through all of childhood but focused on protection during the ages of highest risk. This does not apply to epidemic situations.

Age at time of consultation	Vaccine options (trade name)	Number of doses
6 weeks to <12 months	4CMenB (Bexsero)	2 doses[a,b] plus a booster from age 12 months
	MenACWY-T (Nimenrix)	2 doses[a c] plus a booster from age 12 months
12 months to <5 years	4CMenB (Bexsero)	2 doses[a,b] plus a booster if aged 12–23 months at time of first dose
	MenACWY-D (Menactra) or	2 doses MenACWY-D[a,d] if aged 12-23 months or
	MenACWY-T (Nimenrix)	1 dose MenACWY-T if aged from 2 years
Early adolescence (12 to <16 years)[e]	4CMenB (Bexsero)	2 doses[a]
	MenACWY-D (Menactra) or MenACWY-T (Nimenrix)	1 dose plus a booster at age 16–18 years
Late adolescence ≥16 years[e]	4CMenB (Bexsero)	2 doses[a]
	MenACWY-D (Menactra) or MenACWY-T (Nimenrix)	1 dose, no booster required

a. Refer to section 13.4.4 for the intervals between doses.

b. Prophylaxis paracetamol (or ibuprofen as age-appropriate) is recommended for this age group, see section 13.7.3.

c. Infants aged from 6 months to ≤12 months who are not immunocompromised, can instead be given one dose plus booster from age 12 months at least two months later.

d. MenACWY-D should be administered at least four weeks after PCV13 (if used).

e. In particular, for individuals aged 13–25 years not eligible for funded vaccine, particularly living in crowded private homes, other hostels or student accommodation, or planning overseas travel.

13.5.3 Pregnancy and breastfeeding

There are no reports of any adverse effects among pregnant women who have been vaccinated during pregnancy.[36] The vaccine may be given to pregnant women if indicated.[36] Meningococcal vaccine may be given to breastfeeding women.

13.5.4 (Re)vaccination

Meningococcal conjugate vaccines, MenC (age under 2 years), MenACWY-D (from age 9 months) and 4CMenB are funded for vaccination or re-vaccination of eligible individuals, as follows. See also section 4.3.

Meningococcal conjugate vaccines, MenC (age under 2 years) and MenACWY-D (from age 9 months)

Up to three doses plus booster doses (as appropriate) are funded for individuals:

- pre- or post-splenectomy
- pre- or post-solid organ transplantation
- with functional asplenia
- with complement deficiency (acquired or inherited)
- who are HIV-positive.

Two doses are funded for individuals:

- post-haematopoietic stem cell transplantation
- prior to planned and following immunosuppression for longer than 28 days.

Recombinant meningococcal B vaccine, 4CMenB

- Age under 12 months – up to three doses plus booster after age 12 months and every five years (as appropriate)
- Age from 12 – 23 months – up to two doses plus booster given 12 to 23 months after second dose and every five years (as appropriate)
- Age from 2 years – up to two doses plus a booster every five years (as appropriate)

Funded for individuals:

- pre- or post-splenectomy
- pre- or post-solid organ transplantation
- with functional or anatomic asplenia
- with complement deficiency (acquired or inherited)
- who are HIV-positive
- post-haematopoietic stem cell transplantation
- prior to planned and following immunosuppression for longer than 28 days.

13.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

There are no specific contraindications for meningococcal vaccines, except for anaphylaxis to a previous dose or any component of the vaccine.

13.7 Potential responses and AEFIs

13.7.1 Quadrivalent meningococcal conjugate vaccine

Potential adverse reactions after meningococcal conjugate vaccines include localised pain, irritability, headache and fatigue.[17, 38] Fever is reported by 2–5 percent of adolescents who receive MenACWY-D.

The safety of two doses of MenACWY-D was assessed in a phase III trial of infants: dose one was administered at age 9 months and dose two was administered at age 12 months, with or without routine childhood vaccines.[37] The percentage of participants with solicited systemic reactions after MenACWY-D administration alone at age 12 months (60.6 percent) was lower than after the vaccination at age 9 months (68.2 percent), lower than the control groups at age 12 months (75.2–84.1 percent, depending upon the control vaccine) and lower than when MenACWY-D was administered concurrently with the routine childhood vaccines (68.3–73.2 percent).

The safety profile of MenACWY-T (Nimenrix) is very similar to other meningococcal conjugate vaccines.[17]

Guillain–Barré syndrome

There is no evidence of an association between meningococcal conjugate vaccines and GBS. An early report in the US of a suspected temporal association between MenACWY-D (Menactra) and GBS was followed by a large retrospective cohort study in the US that found no evidence of an increased risk of GBS following administration of MenACWY-D.[36, 39] If indicated, meningococcal conjugate vaccines may be administered to individuals with a history of GBS.[40]

13.7.2 Meningococcal group C conjugate vaccine

A Cochrane Review assessed the safety of MenC against group C disease.[41] MenC vaccines were shown to have an excellent safety profile in infants. The events more frequently reported in infants were fever (1–5 percent), irritability (38–67 percent), crying more than expected (1–13 percent), redness at the site of vaccination (6–97 percent), tenderness at the site of vaccination (11–13 percent) and swelling at the site of vaccination (6–42 percent). Anaphylaxis was reported at a rate of one per 500,000 doses distributed.[4]

13.7.3 Meningococcal B recombinant vaccine

There is an increased risk of fever and medically attended fever-related events, such as febrile seizures, associated with 4CMenB in some children age under 2 years.[4, 42, 43, 44, 45]

These events peaked at six hours post-vaccination and generally subsided by day 3. Prophylaxic paracetamol is recommended 30 minutes prior and six-hourly for up to 48 hours following vaccination for children aged under 2 years. Ibuprofen may be given as an alternative to paracetamol. Some infants will still develop a fever and/or injection-site pain even though they have received paracetamol doses.

In clinical trials, some infants and young children also experienced injection-site tenderness and irritability. Adolescents and adults may experience localised pain, nausea, myalgia, malaise, mild fever and headache.

13.8 Public health measures

> Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

The overall rate of secondary cases in untreated adults is around 1 per 300. Adults and children in close contact with primary cases of invasive meningococcal infection are recommended to receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Blood or cerebrospinal fluid culture is the main diagnostic method, but blood PCR may be useful if antibiotics are given without prior access to blood culture. It is recommended that in primary care 3–5 mL of blood should be taken in an ethylenediaminetetraacetic acid (EDTA) anticoagulant tube (usually with a purple top) prior to administration of antibiotics unless blood culture is available. This should accompany the patient to hospital.

13.8.1 Contacts

A contact is anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the seven days before onset of illness to 24 hours after onset of effective treatment.[46] Contacts at particular risk include:

- those sleeping at least one night in the same household, dormitory, military barrack or student hostel bunkroom (not residents of nursing or residential homes who sleep in separate rooms) as the case, or who have been in a seat adjacent to the case in a plane, bus or train for more than eight hours
- health care workers who have had intensive unprotected contact (not wearing a mask) with a case during intubation, resuscitation or close examination of the oropharynx
- exchange of upper respiratory tract secretions, including intimate kissing
- other contacts as determined by the medical officer of health on a case-by-case basis, such as children and staff attending an early childhood service.

Prophylaxis is not routinely recommended for health care personnel unless there has been intimate contact with oral secretions (eg, performing mouth-to-mouth resuscitation or suctioning of the case before antibiotic therapy has started).

13.8.2 Chemoprophylaxis for contacts

Recommended antibiotics

The recommended antibiotics are rifampicin, ceftriaxone or ciprofloxacin, preferably given within 24 hours of initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Rifampicin

The recommended dose of rifampicin is 10 mg/kg (maximum dose 600 mg) every 12 hours for two days. For infants aged under 4 weeks, the recommended dose is 5 mg/kg every 12 hours for two days.

Rifampicin should be avoided for pregnant or lactating women.

Ceftriaxone

A single dose of intramuscular ceftriaxone (125 mg for children aged under 12 years and 250 mg for older children and adults) has been found to have an efficacy equal to that of rifampicin in eradicating the meningococcal group A carrier state. Ceftriaxone is the drug of choice in a pregnant woman because rifampicin is not recommended later in pregnancy. Ceftriaxone may be reconstituted with lignocaine (according to the manufacturer's instructions) to reduce the pain of injection. A New Zealand study demonstrated that ceftriaxone and rifampicin were equivalent in terms of eliminating nasopharyngeal carriage of *N. meningitidis* group B.[47]

Do not use in infants under aged under 4 weeks.

Ciprofloxacin

Ciprofloxacin given as a single oral dose of 500 mg or 750 mg is also effective at eradicating carriage. This is the preferred prophylaxis for women on the oral contraceptive pill and for prophylaxis of large groups.[46]

Ciprofloxacin is not generally recommended for pregnant and lactating women or for children aged under 18 years.[48] Consult the manufacturer's data sheet for appropriate use and dosage of ciprofloxacin in children.

Use of meningococcal vaccines for close contacts

Close contacts of cases of any group (including group A, B, C, W or Y) meningococcal disease may be offered the appropriate meningococcal vaccine (see section 13.5).

See below for the use of the vaccines for the control of outbreaks, as initiated by the local public health service.

13.8.3 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, an immunisation programme may be recommended and funded for a defined population. The local medical officer of health will determine the necessary action in discussion with the Ministry of Health.

For more details on control measures, refer to the '*Neisseria meningitidis* invasive disease' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**).

13.9 Variations from the vaccine data sheets

The MenACWY-D data sheet states that the vaccine is indicated for use in individuals aged 9 months to 55 years. The Ministry of Health recommends that this vaccine can be used in adults aged over 55 years.[40]

The data sheet states that MenACWY-D should be given as a single dose for individuals aged 2 years and older. The Ministry of Health recommends that two doses are given to individuals at high risk of meningococcal disease (see Table 13.5 and section 4.3), with booster doses every five years. If the first MenACWY-D dose was given before age 7 years, give a booster after three years then five-yearly.[38]

A history of GBS is listed as a precaution in the MenACWY-D data sheet. However, there is no evidence of an association between meningococcal conjugate vaccines and GBS (see section 13.7.2). The Ministry of Health advises that, if indicated, MenACWY-D may be administered to individuals with a history of GBS.[40]

The MenC data sheet states that the first dose of vaccine is not be given earlier than age 8 weeks. However, the Ministry of Health recommends that MenC may be given from age 6 weeks to infants at high risk of meningococcal disease (see Table 13.4 and Table 13.5).

The 4CMenB data sheet states that the vaccine is indicated from age 2 months or older. However, the Ministry of Health recommends that 4CMenB can be given from age 6 weeks to infants at high risk of meningococcal disease (see Table 13.5). The datasheet states that infants who received their primary course from ages 6 to 11 months can receive a booster in the second year of life at least 2 months later. The Ministry recommends that all infants aged 11 months or less receive a booster dose at least 6 months after the primary doses, from the age of 12 months.

The data sheet recommends two doses of 4CMenB to be given eight weeks apart between ages 12 and 23 months and not less than one month apart from the age of 2 years. The Ministry of Health recommends two doses of 4CMenB be given at least eight weeks apart for those aged 12 months or older at the time of the first dose.

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14 Mumps

Key information

Mode of transmission	Airborne droplets or by direct contact with saliva or urine from an infected person.
Incubation period	About 16 to 18 days, ranging from 12 to 25 days.
Period of communicability	For contact tracing purposes, the recommended period of communicability is from 2 days before to 5 days after the onset of parotitis. The virus is also transmitted by asymptomatic infections.
Incidence and burden of disease	Outbreaks are continuing to occur in New Zealand.
Funded vaccine	MMR (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. For (re)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high-risk countries
Vaccine effectiveness	After one dose, MMR is 64–66 percent effective against laboratory-confirmed mumps and 83–88 percent after two vaccine doses.
Duration of protection	At least 10 years; protection is best achieved via herd immunity from high immunisation coverage.
Contraindication and precautions	MMR is contraindicated for anaphylaxis to neomycin, immunocompromise and in pregnancy. See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions. MMR may temporarily suppress tuberculin skin test reactivity.

Potential responses to vaccine	MMR is generally well tolerated. There can be mild salivary gland swelling after 10–14 days. If there is fever and rash 6–12 days after vaccination this is due to measles and rubella components. Alert parents of possible febrile seizure risk, particularly for those with a history of seizure.
Public health measures	Notify the local medical officer of health immediately on suspicion of wild-type measles. See section 14.8.3. Exclude cases for 5 days from onset of glandular swelling. Exclude susceptible contacts from 12 days after the first exposure to 25 days after last exposure to the infectious case.

14.1 Virology

Mumps is a paramyxovirus, genus *Rubulavirus*, with a single-stranded RNA genome. It is rapidly inactivated by heat, formalin, ether, chloroform and light.

14.2 Clinical features

Mumps is transmitted by airborne droplets or direct contact with infected respiratory tract secretions or urine. Humans are the only known host of the virus.

People with mumps are most infectious from two days before to five days after the onset of parotitis;[1] therefore, this is the recommended period of communicability for contact tracing purposes.[1] However, mumps virus has been isolated in saliva from seven days before to nine days after the onset of parotitis. Asymptomatic cases also can be infectious.[1]

Classic mumps, an acute viral illness, is characterised by fever, headache, and swelling and tenderness of one or more parotid (salivary) glands. Mumps starts as an upper respiratory tract infection that disseminates via plasma viremia to glandular tissue, kidneys and central nervous system. Some patients may experience involvement of other organs (eg, orchitis or meningitis) without salivary gland involvement. At least 30 percent of mumps infections in children are asymptomatic.[2]

The complications of symptomatic mumps include clinically evident aseptic meningitis in 5–10 percent (almost always without sequelae), orchitis (usually unilateral) in up to one-third of post-pubertal males, and oophoritis and mastitis in 5–30 percent of post-pubertal females. Sterility is exceedingly rare in males and unconfirmed in females.[2] Profound sudden onset unilateral nerve deafness occurs in 1 in 15,000–20,000 cases. Pancreatitis, neuritis, arthritis, myelitis, nephritis, thyroiditis and pericarditis may also occur.[3]

Encephalitis has been reported to occur at a frequency of between 1 in 400 and 1 in 6,000, the latter being a more realistic estimate. The case fatality rate for mumps encephalitis is 1.4 percent, while the overall mumps case fatality rate is reported as 1.8 per 10,000 cases. Mumps in the first trimester of pregnancy may increase the rate of spontaneous abortion, but there is no evidence that it causes fetal abnormalities.

14.3 Epidemiology

14.3.1 Global burden of disease

Prior to the introduction of immunisation, approximately 85 percent of adults had evidence of past mumps infection. Most infections in those aged under 2 years are subclinical, while those affected in adulthood are more likely to experience severe disease. The peak incidence was in late winter and spring.

More recently, there have been numerous reports of increasing numbers of mumps cases in the US, the UK and elsewhere, thought to be due to a waning of vaccine-induced immunity.[4] Many cases are reported in 18–30-year olds.[5] Outbreaks appear to occur mainly in those in crowded situations, such as university students and other close-knit communities, and have been associated with international travel.[6]

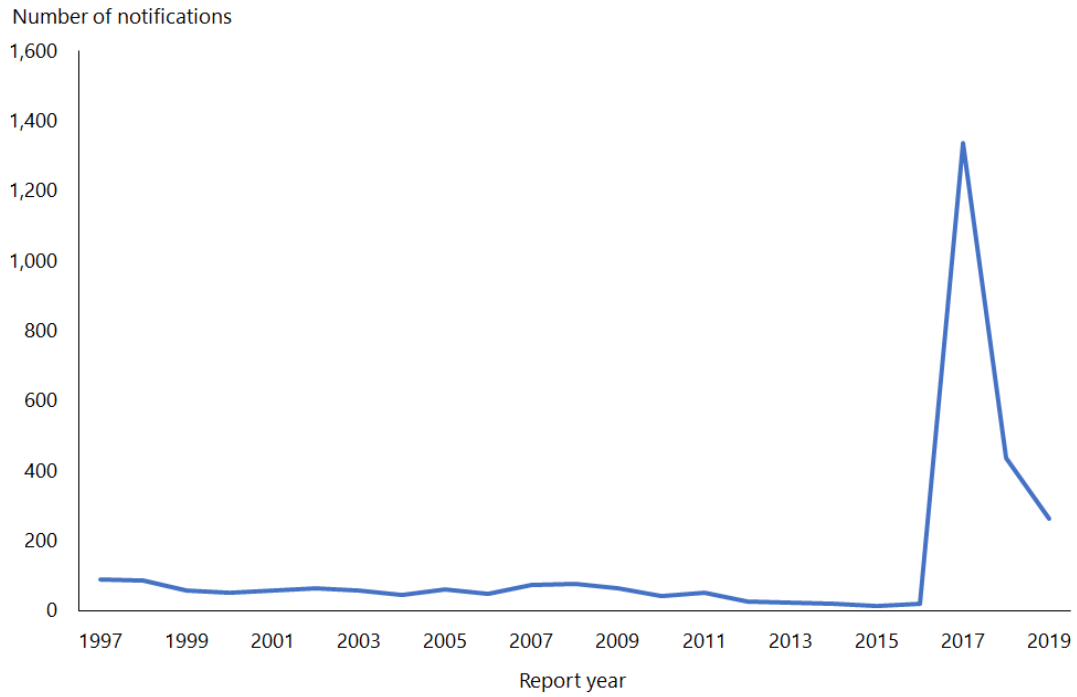
14.3.2 New Zealand epidemiology

Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12 to 15 months, with a second dose introduced in 1992 for children aged 11 years. A two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information). Prior to 2017, the last mumps epidemic had occurred in 1994. The current two-dose schedule was introduced in 2020 at age 12 months and 15 months.

People aged 12–29 years are at the greatest risk of catching mumps, as they are the group least likely to have been fully immunised as children. Those born in Fiji, Tonga, Kiribati, Nauru, Papua New Guinea, Solomon Islands, Tuvalu and Vanuatu as well as many mainland nations in Asia may not have been offered mumps immunisation as children.

From 1 January 2017 to 31 December 2019, 1,773 cases of mumps were notified (ESR, 8 June 2020). During 2019, the notification rate was 5.4 per 100,000 (264 cases) compared with 9.0 per 100,000 (435 cases) in 2018. In 2019, the highest notification rates were seen in young adults aged 15 to 29 years. Cases were predominantly in the Auckland region, with the highest notification rates in the Middle Eastern/Latin American/African (MELAA) ethnic group (19.9 per 100,000) and Pacific people (15.2 cases per 100,000; ESR, 8 June 2020).

Figure 14.1: Notified cases of mumps, 1997–2019



Source: ESR

Outbreaks continue to occur throughout New Zealand. For further details refer to the ESR surveillance reports for notifiable diseases (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

14.4 Vaccines

14.4.1 Available vaccines

Mumps vaccine is one of the components of the live attenuated MMR, considered in section 12.4 (and MMRV mentioned in section 22.4). There are no single antigen mumps vaccines available.

Funded vaccine

MMR vaccine funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella and Jeryl Lynn mumps. See section 12.4.1 for more information.

Other vaccines

M-M-R II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 12.4.1).

14.4.2 Efficacy and effectiveness

A 2012 Cochrane review of the safety and effectiveness of MMR estimated that a single dose of MMR was 69–81 percent effective in preventing clinical mumps. Effectiveness of MMR in preventing laboratory-confirmed mumps cases in children and adolescents was estimated to be between 64 and 66 percent for one dose and between 83 and 88 percent for two vaccine doses.[7]

A two-dose vaccination schedule and high immunisation coverage has been very successful in controlling disease. However, outbreaks can still occur in highly immunised populations, because two doses of vaccine are not 100 percent effective. Community coverage needs to be 85–90 percent by 2 years of age to prevent outbreaks from asymptomatic cases.[2] Declining vaccine-induced mumps immunity may also contribute to outbreaks.[4] Data from Finland shows that 20 years after the second MMR dose, immunity to mumps declined with just under 75 percent being seropositive.[8] The antibody avidity also decreased over time, by 24 percent for mumps.[9]

Two doses of MMR are required to ensure a high rate of seroprotection against mumps and induce antibody responses that persist for at least 10 years post-vaccination.[10, 11] However, waning in immunity has been observed in young adults and a third dose of MMR has been used safely and effectively during mumps outbreaks in highly immunised populations.[12, 13] Although the mumps vaccine is not quite as effective as measles and rubella vaccines, cases that have been vaccinated are significantly less likely to experience complications from disease such as orchitis, meningitis and hospitalisation.[14]

14.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

14.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

Co-administration with other vaccines

MMR can be given concurrently with other vaccines, by using separate syringes and giving the injections at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR available in New Zealand (Priorix and M-M-R II) may be used interchangeably for completion of a course.[15]

14.5 Recommended immunisation schedule

Table 14.1: Recommended MMR vaccination schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 12 months and 15 months
Catch-up[b] for children, adolescents and adults	2 doses: at least 4 weeks apart

a. If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 12 months (at least 4 weeks after previous dose) and 15 months.

b. MMR is funded for those who are susceptible to 1 or more of the 3 diseases.

14.5.1 Usual childhood schedule

Two doses of mumps-containing vaccine as MMR are recommended at age 12 months and 15 months (Table 14.1).

The second dose can be given as soon as four weeks after the first dose.

Children who receive MMR when aged under 12 months during an outbreak require two further doses administered after age 12 months. No opportunity should be missed to achieve immunity.

14.5.2 Catch-up

MMR is recommended and funded for children, adolescents and adults (born since 1 January 1969) who are known to be susceptible to one or more of the three diseases (two doses, four weeks apart). See sections 12.5.2 and 19.5.2.

14.5.3 Immunocompromise

Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). These individuals can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to the immunocompromised individual (see section 12.7.2).

See also in section 4.3.1.

(Re)vaccination following immunosuppression

MMR is funded for (re)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.3).

MMR is recommended for all HIV-positive children, whether they are symptomatic or asymptomatic, if their CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR if their CD4+ lymphocyte count is at least 200 cells/mm^3. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[16]

14.5.4 Pregnancy and breastfeeding

MMR is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.[16, 17] (see section 14.6.1).

After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccines recipients (see section A6.4.1). MMR can safely be given to breastfeeding women.

14.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

14.6.1 Contraindications

See section 12.6.1 for specific MMR contraindications.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[16, 17] However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.[18]

14.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication to MMR. See section 12.6.3 for more information, and section 12.6.2 for further precautions.

14.7 Potential responses and AEFIs

See sections 12.7 and 19.7.

14.8 Public health measures

It is a legal requirement that all cases of mumps be notified immediately on suspicion to the local medical officer of health.

14.8.1 Diagnosis

All suspected mumps cases should have diagnostic testing (eg, by buccal swab detection of wild-type mumps virus by PCR or culture) as there are other causes of parotitis other than the mumps virus. See the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual* for the specimens required for laboratory confirmation of mumps, or discuss these with the local laboratory (available at **health.govt.nz/publication/communicable-disease-control-manual**).

14.8.2 Susceptible contacts

A susceptible contact is anyone born after 1981 who has not had mumps infection or has not been fully vaccinated for their age.

All susceptible contacts should be offered MMR vaccinations. (All vaccinations given should be recorded on the NIR or the AIR, depending on the system rollout for the AIR.) There is no increased risk of adverse events after immunisation during the incubation period of mumps or if the recipient is already immune. Immunoglobulin is ineffective after exposure to mumps.

14.8.3 Exclusion and post-exposure prophylaxis

Cases

Exclude cases from tertiary education, school, sports, early childhood services or health care or other workplaces and from close contact with other susceptible people for five days from onset of parotitis.[1]

Susceptible contacts

Discuss exclusion of susceptible contacts with the local medical officer of health. Previously immunised (pre-exposure) contacts need not be excluded. Generally, unimmunised contacts who have no previous history of mumps infection should be advised not to attend early childhood services or school because of:

- the risk of catching the disease themselves
- the risk of passing on the disease, when asymptomatic or in the prodromal phase, to other susceptible children.

Health care settings or working or living with immunocompromised people

Advise exclusion of susceptible contacts in health care settings and for those working or living with immunocompromised people from 12 days after the first exposure to 25 days after last exposure to the infectious case.[1] Documented full immunisation with two MMR doses should be required in these situations.[1]

Other settings

Consider advising exclusion of susceptible contacts with no MMR doses from tertiary education, school, early childhood services or workplaces from 12 days after the first exposure to 25 days after last exposure to the infectious case, if there is a high risk of mumps transmission.[1] Exclusion is more important in secondary and tertiary education settings, as these settings are more conducive to outbreaks.[1]

All excluded contacts, in settings other than health care or in contact with immunocompromised people, can be readmitted immediately after they have received the first MMR dose.[1] Those who have a history of one dose of MMR vaccination should be offered their second vaccine dose and be allowed to remain in tertiary education, school, early childhood services or workplaces (except for health care workers or those working or living with immunocompromised people).[1]

For more details on control measures, refer to the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual* (available from **health.govt.nz/publication/communicable-disease-control-manual**).

Post-exposure prophylaxis

Passive immunisation is not effective. Active immunisation with MMR is not considered effective against incubating infection, but MMR should be offered to susceptible contacts for protection against future exposure.

14.9 Variations from the vaccine data sheet

See section 12.9 for variations from the MMR (Priorix) data sheet.

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15 Pertussis (whooping cough)

Key information

Mode of transmission	By aerosolised droplets.	
Incubation period	7–10 days (range 5–21 days).	
Period of communicability	For control purposes, in untreated cases the communicable stage lasts from the catarrhal stage to 3 weeks after the onset of paroxysmal cough. When treated communicability lasts approximately 2–5 days from the first dose.	
Incidence and burden of disease	Widespread outbreaks occur every 3–5 years. Infants aged under 12 months are at highest risk from pertussis, particularly those who have received fewer than two doses of vaccine and if the mother did not receive vaccine in pregnancy.	
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation)	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or special care baby units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	

Vaccine effectiveness	Vaccination in pregnancy is over 90 percent effective in preventing pertussis in infants up to age 3 months. A 3-dose primary course in infants has 84 percent efficacy against hospitalisation for pertussis.
Contraindications	Contraindicated where anaphylaxis to vaccine or vaccine components is proven.
Potential responses to vaccine	Extensive limb swelling occurs more commonly after increasing number of doses of DTaP. Affecting less than in 2 percent of children, this is typically painless and resolves spontaneously.

15.1 Bacteriology

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*, an exotoxin-producing gram-negative bacillus. The bacillus is fastidious (requires special techniques to grow in culture) and will often have decreased in numbers by the time the typical cough develops, making laboratory confirmation by culture difficult. The availability of sensitive and specific PCR and serological assays has improved laboratory confirmation of suspected *B. pertussis* infection (see section 15.8).

15.2 Clinical features

Pertussis is highly transmissible. It is one of the most infectious vaccine-preventable diseases in humans. The rate of transmission is several-fold greater than most respiratory pathogens, including influenza, such that in a non-immune population, approximately 5–17 secondary pertussis cases are expected from one case (see section 1.2.1).[1] Transmission occurs by aerosolised droplets, and the incubation period is 7–10 days (range 5–21 days).

There are three stages of typical pertussis infection:

1. Catarrhal stage – rhinorrhoea and irritating mild cough (typically lasting 7–10 days).
2. Paroxysmal stage – paroxysms (bursts) of coughing; in children, these may end in vomiting, cyanosis or apnoea and inspiratory gasp or whoop (1–6 weeks). Usually afebrile.
3. Convalescent stage – less persistent cough, gradual recovery (up to 10 weeks).

The communicable period lasts from the onset of symptoms to three weeks after the start of the paroxysmal stage.

Clinical presentation varies with age, immunisation status and previous infection. Pertussis must be considered in infants presenting with apnoea, since apnoea and/or cyanosis may precede paroxysmal cough.[2] In school-aged children, inspiratory whoop, post-tussive vomiting and the absence of wheezing and fever distinguish pertussis from other causes of coughing illnesses.[3, 4] Almost all pertussis infections in adolescents and adults occur in the context of previous infection and/or immunisation. Persistent cough for more than 14 days is the cardinal feature in adults.[4, 5, 6] Coughing is often paroxysmal and worsens at night, with the patient waking with a choking sensation, but post-tussive vomiting and whoop are infrequent.

Studies performed in several countries during both epidemic and non-epidemic periods have shown that between 12 and 37 percent of school-aged children, adolescents and adults with persistent cough (lasting 14 days or more) have evidence of recent *B. pertussis* infection.[3, 5, 7, 8, 9] A primary care-based study in New Zealand performed during the early phase of the 2011–2013 epidemic showed recent *B. pertussis* infection in 17 percent of children aged 5–16 years and 7 percent of adults aged 17–49 years presenting to primary care with a persistent cough of two or more weeks' duration.[10]

The disease is most often severe in infants in the first few months of life. One in six infants with pertussis sufficiently severe to require intensive care admission will either die or be left with brain or lung damage.[11] The most common complications of pertussis are secondary infections, such as otitis media and pneumonia, and the physical sequelae of paroxysmal coughing, (eg, petechiae and other haemorrhages within subconjunctiva, nasopharynx and central nervous system; pneumothorax; hernia; and urinary incontinence). At the peak of the paroxysmal phase, vomiting can lead to weight loss especially in infants and young children.

15.3 Epidemiology

The epidemiology of *B. pertussis* infection and pertussis disease differ. Infection occurs across the age spectrum, and repeated infection without disease is common.[12] The endemic circulation of *B. pertussis* in older children and adults provides a reservoir for spread of the infection and the development of severe disease in incompletely vaccinated infants. The high prevalence of subclinical infections in household contacts of pertussis cases indicates a significant role in disease transmission to young infants.[13, 14] As observed in Australia, seasonal peaks in incidence in children aged less than 5 years occurred 1–2 months later than for the general population, supporting the theory that older household members are sources of infection to younger children.[15]

15.3.1 Global burden of disease

Pertussis mortality and morbidity rates continue to be highest in the first year of life.[13] In the US during the 1940s pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.[16] Beyond age 3 years mortality rates have always been relatively low. In immunised populations virtually all deaths occur in the first two months of life, and deaths in toddlers and preschool-aged children have largely disappeared. Among infants, younger age, lack of immunisation, low socioeconomic status, premature gestation, low birthweight and female gender are associated with an increased risk of fatal pertussis.[17]

Pertussis mortality and morbidity is under-reported.[18, 19] It is estimated that there are three times more deaths due to pertussis than are reported in high-income countries.[18, 20, 21] The burden of pertussis in older adults is underestimated, particularly for those with chronic respiratory conditions, and increases with age.[22, 23] Infants continue to die from pertussis despite advances in intensive care.[11, 24, 25, 26]

Following the introduction of mass immunisation, countries with consistently high immunisation coverage rates have achieved consistently low pertussis incidence rates.[27] The most pronounced decrease in incidence was seen in those aged under 10 years. Although primarily associated with low immunisation coverage, in some instances higher pertussis incidence rates are due to lower or waning vaccine efficacy or less-than-optimal immunisation schedules.[28, 29, 30] The burden of severe disease, particularly since the introduction of acellular vaccines, is highest in infants and unvaccinated young children.[31] However, less severe pertussis cases are also seen in vaccinated children who are further away from the last DTaP and, in some countries, adolescents.[32, 33, 34] Infants too young to have received more than one dose of pertussis vaccine (age 3 months or less) have the highest rate of notification, hospitalisation and death.[35, 36]

Epidemic peaks of pertussis occur every 2–5 years without the consistent seasonal pattern that is typical of most respiratory infections, although evidence from Australia suggests increased incidence (by 15 percent compared with annual average) during spring to summer months.[15] Epidemics are frequently sustained over 18 months or more, during which there are dramatic increases in hospital admission rates. Lack of change in the pertussis epidemic cycle with mass immunisation suggests minimal impact on the circulation of *B. pertussis* in the population, unlike other epidemic vaccine-preventable diseases, such as measles.[12, 19, 37]

15.3.2 New Zealand epidemiology

Pertussis mortality in New Zealand

On average, zero to one deaths are associated with pertussis each year in New Zealand. During the 2011–2013 pertussis epidemic there were three deaths in children: two in infants aged under 6 weeks and one in an unimmunised pre-schooler.[38] No deaths from pertussis (as recorded in EpiSurv) occurred during the latest epidemic from October 2017 to May 2019.[38, 39]

Pertussis morbidity in New Zealand

Pertussis morbidity in New Zealand has usually been described using hospital discharge data. National passive surveillance data has been available since 1996, when pertussis became a notifiable disease.

Outbreaks continue to occur throughout New Zealand. For further details refer to the ESR surveillance reports for notifiable diseases (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

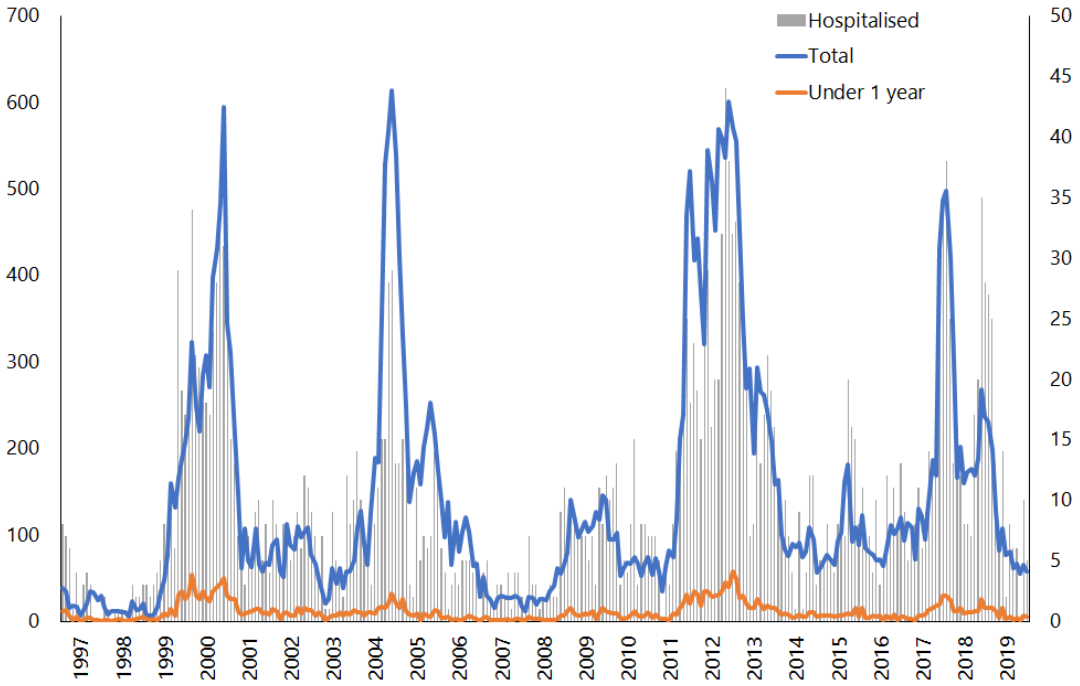
Pertussis morbidity in New Zealand as described by notification data

Four epidemics have occurred since pertussis became a notifiable disease, with an epidemic peak annual number of notified cases of 4,140 in 2000, 3,485 in 2004, 5,897 in 2012 and 2956 in 2018 (see Figure 15.1).

The most recent outbreak commenced in October 2017; by the end of May 2019, there were 4,697 cases notified (2,939 laboratory-confirmed).[39] During 2019, 1206 cases were notified, an overall notification rate of 24.5 cases per 100,000 population. Of these cases, 88 (7.3 percent, incidence 148 cases per 100,000) were aged under 1 year and half of these were hospitalised. The youngest infants were at highest risk of hospitalisation with 85 percent of cases age under 2 months, 80 percent age under 3 months and 66 percent aged under 6 months hospitalised (ESR, 8 June 2020). The next highest incidence rate occurred in children aged 1–4 years (68 per 100,000). Pacific and Māori infants had the highest notification rates (300 and 177 per 100,000 respectively), and in children aged 1–4 years, MELAA ethnic group had the highest notification rate (175 per 100,000) followed by European/Other (77 per 100,000).

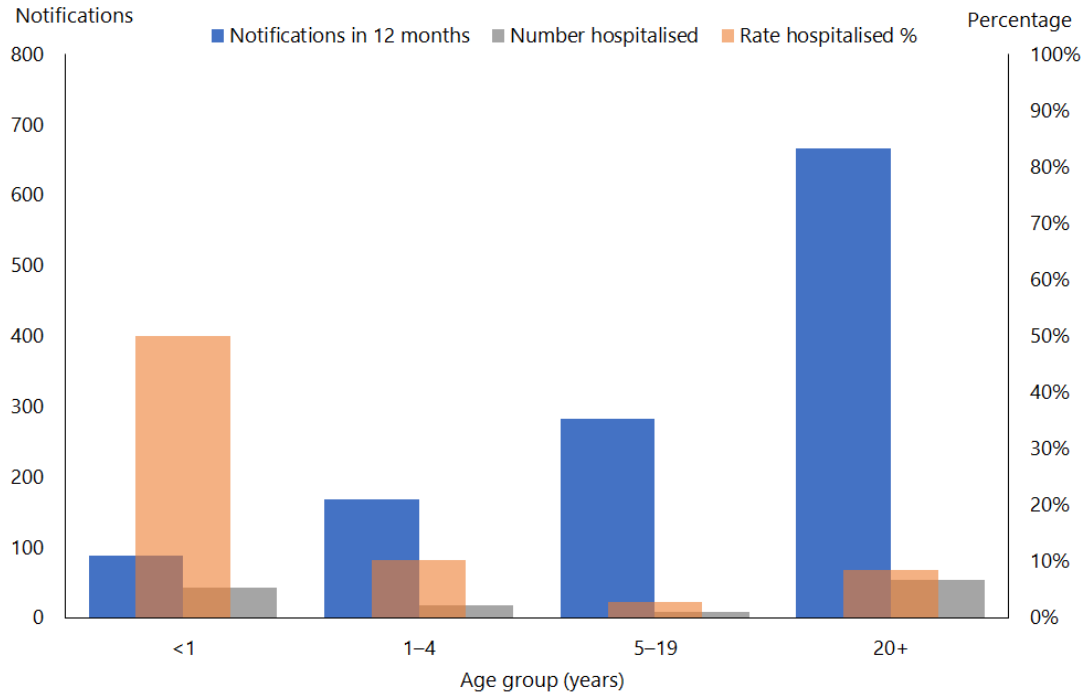
Figure 15.1: Pertussis notifications and hospitalisations, 1997–2019

Note: Includes confirmed, probable and suspect cases, and notifications still under investigation.



Since pertussis became notifiable, the annual proportion of notified cases aged 30 years or older has increased from 23 percent in 1997 to 48 percent in 2019 (ESR, 8 June 2020).[38] However, the highest proportion of hospitalised cases continues to be in infants. From 2010 to 2019 there were 1,544 notified cases in infants with 769 (53 percent) recorded as hospitalised (Figure 15.2).

Figure 15.2: Age distribution of notified and hospitalised pertussis cases, 2019



Source: ESR

Pertussis morbidity in New Zealand, as described by hospital discharge data

Infants aged under 1 year with pertussis are more likely (nearly 80 percent) to be admitted to hospital than older children and account for almost all the pertussis cases admitted to the paediatric intensive care unit.[40]

Hospitalisation rates for pertussis, as measured by ICD discharge diagnostic codes, provide a measure of severe pertussis disease. The discharge rate in the 2000s was lower than it was in the 1990s (2000s versus 1990s, relative risk 0.8 [95% CI: 0.7–0.8]). Despite this decrease, the infant hospitalisation rate for pertussis in New Zealand in the 2000s (at nearly 200 per 100,000) remained three times higher than contemporary rates in Australia (2001 infant rate: 56 per 100,000) and the US (2003 infant rate: 65 per 100,000).[41, 42, 43]

Pertussis hospital admission rates vary with ethnicity and household deprivation. From 2000–2014 the infant (under 1 year old) hospitalisation rates for pertussis fluctuated but were consistently higher for Pacific and Māori than European/Other prioritised ethnicities. Between 2010 and 2014, the hospitalisation rate was over 2.5 times higher for Pacific (4.4 per 1,000) and over 2 times higher for Māori (3.6 per 1,000) than it was for European/Other ethnicities (1.7 per 1,000).[44]

From 2010 to 2014 an infant living in a household in the most deprived quintile was at a five-fold increased risk of being hospitalised with pertussis compared with an infant in the least deprived quintile (4.0 versus 0.8 per 1,000).[44]

15.4 Vaccines

Whole-cell pertussis vaccine for routine use was introduced in 1960 and was replaced with acellular pertussis vaccine in 2000. The current schedule of three acellular pertussis-containing vaccines in the first year of life plus booster doses at ages 4 and 11 years has been in effect since 2006. See Appendix 1 for more information about the history of pertussis-containing vaccines in New Zealand.

15.4.1 Available vaccines

Funded pertussis vaccines

The acellular pertussis-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and Haemophilus influenzae type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a smaller adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine.

See section 6.4.1 for more details.

Other vaccines

Other acellular pertussis-containing vaccines registered (approved for use) and available (marketed) in New Zealand include:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

15.4.2 Efficacy and effectiveness

Immunogenicity

A review of published data on DTaP-IPV-HepB/Hib found it to be highly immunogenic in infants aged under 2 years for primary and booster vaccination.[45] In clinical studies there was a strong immune response against the vaccine antigens, which persisted for up to approximately six years after vaccination. A review of published clinical trial and post-marketing surveillance data supported the immunogenicity of DTaP-IPV-HepB/Hib across a range of schedules and when administered concurrently with other vaccines.[46]

Efficacy and effectiveness

Vaccination in pregnancy

Maternal vaccination, given more than seven days before delivery, was estimated to be 91 percent (95% CI: 88–94) effective against laboratory-confirmed pertussis in infants younger than 3 months of age[47] Protection of infants is achieved both by passive antibody transfer and reduced exposure to maternal disease.[48] Tdap given in pregnancy was shown to be 85 percent more effective than post-partum vaccination in preventing pertussis in infants younger than 8 weeks of age.[49]

Timing is important because protection is not as good if the mother is vaccinated less than two weeks prior to birth.[50] Vaccinating from 16 weeks' gestation allows time for passive transfer and accumulation of antibody in the fetus, such that by 40 weeks' gestation, infant antibody levels at birth are higher than those in the mother.[51] Giving maternal vaccination during the second trimester rather than later provides more preterm infants with pertussis protection.[52, 53]

See section 15.5.2 for information about maternal pertussis vaccine safety.

Direct protection

The acellular pertussis vaccines approved for use in New Zealand have been shown to provide around 81–85 percent efficacy (95% CI: 51–100) against confirmed pertussis after three infant doses, with follow-up studies suggesting sustained efficacy to age 6 years.[13, 54, 55] In a Swiss study, effectiveness against pertussis hospitalisation increased with each consecutive primary dose in infants from age 2.5 months to 2 years from 42.1 percent (95% CI: 11.3–62.6) after the first dose, 83.9 percent (70.2–92.1) after the second then 98.2 percent (96.1–99.3) to 100 percent (97.9–100) after the third and fourth doses.[56]

While effective, observational data from Australia found that acellular pertussis vaccines may be less effective than the best-performing whole-cell vaccines in preventing whooping cough.[57, 58] However, the quality of the whole cell vaccine varied between countries and a Canadian study found it to be less effective than the acellular vaccine.[59]

Age-appropriate pertussis vaccination in the US was shown to reduce the severity of symptoms and complications of the disease, including 60 percent reduction in the odds of severe disease (seizure, encephalopathy, pneumonia and/or hospitalisation) in children aged 7 months to 6 years, and 30 percent reduction in post-tussive vomiting in those aged 19 months to 64 years.[60]

Duration of protection

Protection against pertussis begins to wane within several years of completion of a three-dose primary and two-dose booster immunisation series. The US has a pertussis immunisation schedule that includes three doses of acellular vaccine during infancy and booster doses at 15 to 18 months and 4 to 6 years.[61] The risk of pertussis increases in the six years after receipt of the fifth dose of this series, indicating a waning in vaccine-induced immunity over this time interval.

A decline in effectiveness was seen in children more distant from the last DTaP dose, by 27 percent per year on average.[62] Waning effectiveness is more rapid following the adolescent booster at around 35 percent per year.[63] In children, vaccine was 80 percent (95% CI: 71–86) effective against pertussis from two weeks to a year following vaccination, 84 percent (77–89) after 1–3 years, declining to 62 percent (42–75) after 4–7 years and to 41 percent (0–66) at eight or more years after vaccination.[64] A meta-analysis estimated that only 10 percent of those vaccinated with five doses of DTaP would be immune to pertussis 8.5 years after their last DTaP dose.[65]

Antibodies to pertussis toxoid, filamentous hemagglutinin and pertactin have been shown to persist five years after receipt of Tdap (Boostrix) in a study of Australian adults aged 18 years and older.[66] However, the duration of protection is unknown.

15.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib should be stored in the dark.

> DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP-T pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

15.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap can be administered simultaneously (at separate sites) with other vaccines or IGs.

15.5 Recommended immunisation schedule

Table 15.1: Immunisation schedule for pertussis-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

15.5.1 Children

A primary course of pertussis vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 15.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

It is important to administer all vaccinations on time. Delays in receipt of infant immunisations significantly increase the risk of infants being hospitalised for severe pertussis.[67]

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2). The minimum interval between doses is four weeks. A booster dose should be given no earlier than six months after the primary series.

Catch-up immunisation

See Appendix 2 for detailed catch-up immunisation information.

- DTaP-IPV-HepB/Hib or DTaP-IPV may be used for primary immunisation and boosting of children aged under 10 years.
- Tdap may be used for primary immunisation and boosting of children aged 7 to under 18 years.

Tdap also may be given:

- as a single dose for vaccination of patients aged 65 years old
- as single dose for vaccination of patients aged 45 years old who have not had 4 previous tetanus doses
- for vaccination of previously unimmunised or partially immunised patients
- for vaccination prior to planned or revaccination following immunosuppression (see section 15.5.3)
- for boosting of patients with tetanus-prone wounds (see section 20.5.5).

15.5.2 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis.[47, 51] Post-partum maternal vaccination may reduce the risk of a mother infecting her baby but does not have the added benefit of providing the baby with passive antibodies (see section 15.4.2 for details of effectiveness).

Maternal Tdap vaccination has been shown to prevent pertussis disease or reduce severity of the disease and risk of pertussis-related death in very young infants.[68] There is no evidence that Tdap vaccination affects pregnancy outcomes[68, 69, 70] or causes harm to the fetus or neonate.[68, 71]

Tdap vaccines can be given to breastfeeding women, if not given during pregnancy.[72]

15.5.3 (Re)vaccination

Pertussis-containing vaccines are funded for vaccination or re-vaccination of eligible patients who have become immunocompromised, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

15.5.4 Recommended but not funded

Tdap is recommended but not funded, unless given as prophylaxis for a tetanus-prone wound, for protection against pertussis for:

- professions and students of professions in contact with infants (with a booster dose at least at 10-year intervals), for example, lead maternity carers and other health care personnel who work in neonatal units, other clinical settings (such as GPs and practice nurses) and early childhood education services staff (see Table 4.9). Infants with respiratory, cardiac, neurological or other co-morbid conditions are particularly at risk from pertussis.
- household contacts of newborns, including adult household and other close contacts (contacts aged under 18 years who are unimmunised or incompletely immunised for their age can receive funded pertussis vaccine; see Appendix 2 for catch-up schedules)
- regardless of maternal vaccination history, all caregivers of infants born at less than 32 weeks' gestation are recommended to receive a single dose of Tdap (see section 4.2.2)

- early childhood workers and students (with a booster dose at 10-year intervals), although the priority is to ensure all children attending childcare have received age-appropriate vaccination
- adults with a medical condition, not eligible for funded vaccine, who are at increased risk of severe consequences of pertussis (eg, those with chronic respiratory disease).

15.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

15.6.1 Contraindications

The only contraindication is an immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine, following a previous dose.

15.6.2 Precautions

A history of well-controlled seizures in the vaccine recipient or a family history of seizures (febrile or afebrile) or other neurologic disorder is not a contraindication to vaccination against pertussis.[50]

Vaccination for children with an unstable neurological disorder (eg, poorly controlled epilepsy or deteriorating neurological state) has previously been considered a precaution, but as these children may be high risk of severe pertussis complications, vaccination is recommended. Individual cases should be discussed with the specialist.[50]

15.7 Potential responses and AEFIs

Unless the specific contraindications and precautions outlined in section 15.6 above are present, practitioners should have no hesitation in advising the administration of acellular pertussis vaccine. Acellular pertussis vaccine has been used in New Zealand since 2000 and is significantly less reactogenic than the whole-cell pertussis vaccine.

15.7.1 DTaP-containing vaccines

DTaP-containing vaccines (eg, DTaP-IPV-HepB/Hib and DTaP-IPV) are generally well tolerated in children,[73] including preterm (24 to 36 weeks' gestation) and/or low birthweight (820–2,020 g) infants.[74, 75]

Local reactions commonly include pain, redness, swelling and induration at the injection site. Less common reactions include fretfulness, anorexia, vomiting, crying and slight to moderate fever. These local and systemic reactions usually occur within several hours of pertussis immunisation and spontaneously resolve within 48 hours without sequelae.[73]

Local reactions increase with age and additional doses of vaccine. The reaction may be due to some of the other vaccine components, such as aluminium. These reactions are usually minor and only last a day or so.

15.7.2 Tdap vaccine

The adult reduced-concentration Tdap (Boostrix) vaccines have been found to have no safety concerns in those aged 10–64 years and those aged over 65 years.[76, 77, 78, 79] Studies of Tdap in pregnant women have not identified any increased risk of adverse maternal, infant or fetal outcomes.[12, 71, 80, 81, 82]

Local reactions following immunisation of adolescents with Tdap are common but usually mild. They include pain (in 75 percent of recipients), swelling (21 percent) and redness (23 percent) at the injection site.[83] Potential systemic reactions following immunisation of adolescents with Tdap include fever >38°C (5 percent), headache (16 percent), fatigue (14 percent) and gastrointestinal symptoms (10 percent).[83]

15.7.3 Major adverse events associated with pertussis-containing vaccines

The incidence of major adverse events following primary pertussis immunisation is summarised in Table 15.2.

Table 15.2: Incidence of major adverse reactions following acellular pertussis vaccines (based on clinical trial data for DTaP vaccines)

Event following immunisation	Timing post-vaccination	Incidence per 100,000 doses
High fever >38°C	0–2 days	36
Persistent (>3 hours) inconsolable screaming	0–24 hours	44
Seizures	0–2 days	7
Hypotonic-hyporesponsive episode	0–2 days	0–47[a]
Anaphylaxis	0–1 hour	Very rare

a. Across clinical trials of multiple licensed DTaP formulations

Source: Edwards KM, Decker MD. 2018. Pertussis vaccines. In: Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th edition)*. Elsevier.

Parents should be alerted to the small but defined risk of extensive limb swelling to the injected thigh or upper arm, particularly following the fourth and fifth DTaP dose. This transient, usually painless and benign swelling occurs in 2–3 percent of children.[73] Resolution occurs without sequelae and it is not a contraindication for further pertussis vaccine doses.[72, 84]

Neither a hypotonic-hyporesponsive episode nor seizures are associated with long-term consequences for the child (see section 2.3.3).[85, 86, 87] Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.[88] It is safe to give acellular pertussis vaccine after a hypotonic-hyporesponsive episode has occurred following a previous dose.[89] A significant decrease of 60–67 percent in hypotonic-hyporesponsive episodes was observed in Canada following the switch from whole cell to acellular pertussis vaccines.[90]

15.8 Public health measures

15.8.1 Improving pertussis control

The goal of the pertussis immunisation programme is to protect those most at risk of developing severe disease; that is, infants in the first year of life. Two key strategies for reducing the burden of disease in infants are the administration of Tdap vaccination during pregnancy and on-time infant immunisation. Vaccination during pregnancy is recommended and funded for women from the second trimester, preferably from 16 weeks' gestation (see section 15.5.2). This is the most effective way to protect young infants. More complete and timely delivery of the current infant immunisation schedule would reduce the infant pertussis disease burden in older infants.[67] It is important that all children attending early childhood services are fully vaccinated for their age.

Data on the protective effects of indirect strategies is currently incomplete. 'Cocoon strategy' is the term used to describe the protection of infants by immunising those who are potential sources of *B. pertussis*.[91] Three identified target groups who have the most contact with young and vulnerable infants are (1) new mothers who have not had recent immunisation, family and close contacts of newborns; (2) health care workers; and (3) early childhood workers. Some protection may be provided to infants by cocoon immunisation of parents and other potential household contacts post-partum, may be pertinent in some circumstances where maternal vaccination did not occur, such as preterm birth, and infants in neonatal intensive care.[92]

Health care workers in particular are at increased risk of pertussis and can transmit pertussis to other health care workers and to patients.[93] Outbreaks in maternity wards, neonatal units and outpatient settings have been described.[94] Fatalities occur as a result of such nosocomial spread.[95]

Mass immunisation cannot be used to control an established community outbreak, although action to update age-appropriate vaccination in institutional settings (schools and early childhood services for staff and students) is appropriate. When an outbreak occurs, individual immunisation status should be checked, and any missing doses given. Vaccination in pregnancy is particularly important to protect the most vulnerable, young infants.

15.8.2 Notification

It is a legal requirement that all cases of pertussis be notified immediately on suspicion to the local medical officer of health.

A suspected pertussis case can be confirmed if a clinically compatible illness is laboratory-confirmed or is epidemiologically linked to a confirmed case. Because transmission is by aerosolised droplets, health care personnel looking after pertussis cases should be vaccinated and wear a mask.

15.8.3 Laboratory diagnosis of *Bordetella pertussis* infection

PCR is the most sensitive method for diagnosing *B. pertussis* infection. In general, *B. pertussis* can be identified by PCR from most upper respiratory tract samples, including throat swabs, for up to four to six weeks after symptom onset. Serology should only be done in consultation with the medical officer of health and the local microbiologist for public health purposes.

A negative test does not necessarily rule out pertussis: consider exposure, clinical compatibility, the test used and the timing of the test.

For further information about laboratory testing, refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

15.8.4 Antimicrobial treatment of case

A range of antibiotics are available for the treatment and prophylaxis of pertussis. Prompt treatment with macrolide antibiotics may reduce the severity and duration of clinical disease if started during the catarrhal phase. Antibiotics commenced after coughing paroxysms have begun have no effect on the clinical disease but do reduce the risk of spread of disease to others.[73, 96, 97] Antibiotics are of limited value if started after 21 days of illness, but should be considered where there are high-risk contacts (eg, young infants and pregnant women). Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual*[98] (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

To minimise transmission to newborn infants, it is recommended that pregnant women diagnosed with pertussis in the third trimester be treated with appropriate antibiotics (see Table 15.3), if within six weeks of cough onset.[99]

Macrolide use during pregnancy, lactation and in the neonatal period has been associated with 2–3 times increased risk of infantile pyloric stenosis (which affects 1–3 in 1,000 infants).[100, 101] The risk is lower when given during pregnancy and breastfeeding than when given to the infant during the neonatal period.[102] With erythromycin, the risk is highest when given within the first two weeks of life (relative risk 10.7; 95% CI: 5.2–21.9), and increased duration of treatment.[102, 103, 104] The risk is presumed to be lower with azithromycin, although there are case reports of infantile pyloric stenosis occurring when azithromycin has been used during pregnancy.

Parents should be informed of the risks of this complication and of the symptoms and signs of infantile hypertrophic pyloric stenosis. The infant should be monitored for this complication for four weeks after completion of treatment.[73, 105, 106]

Table 15.3: Recommended antimicrobial therapy and post-exposure prophylaxis for pertussis in infants, children, adolescents and adults

Azithromycin[a]		Trimethoprim-sulfamethoxazole[b]	
Age	**Recommended**	**Age**	**Recommended**
Younger than 4 weeks	Day 1: 10 mg/kg per day in a single daily dose Days 2–5: 5 mg/kg per day in a single daily dose	Under 2 months	Contraindicated (risk for kernicterus)
From age 1 month older, and children	Day 1: 10 mg/kg per day in a single daily dose (maximum 500 mg per day) Days 2–5: 5 mg/kg per day in a single daily dose (maximum 250 mg per day)	Aged 2 months or older	TMP, 8 mg/kg per day; SMX, 40 mg/kg/ day in 2 divided doses for 14 days
Adolescents and adults	Day 1: 500 mg as a single dose Days 2–5: 250 mg once daily	Adolescents and adults	TMP, 320 mg per day; SMX, 1,600 mg/day in 2 divided doses for 14 days

a. Preferred macrolide during pregnancy, lactation and in infants aged <1 month because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

b. TMP = trimethoprim; SMX = sulfamethoxazole. TMP-SMX can be used as an alternative agent to macrolides in patients aged ≥2 months who are allergic to macrolides, who cannot tolerate macrolides or who are infected with a rare macrolide-resistant strain of *Bordetella pertussis*.

Adapted from: Centers for Disease Control and Prevention. 2005. Recommended antimicrobial agents for treatment and post exposure prophylaxis of pertussis. *Morbidity and Mortality Weekly Report* 54(RR14): 1–16.

Exclusion

Exclude the case from school, early childhood services, other institutions or work until they have received at least two days of azithromycin (this lengthens to five days if other antibiotics, are used), or exclude them for three weeks from the date of onset of typical paroxysms of cough or until the end of the cough, whichever comes first.[98]

Children who have laboratory-confirmed pertussis should complete their immunisation series with all the scheduled doses recommended for their age.

15.8.5 Management of contacts

The local medical officer of health will advise on the management of contacts. For more details on control measures, see the latest version of the 'Pertussis' chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/pertussis**).

A contact can be defined as someone who has been in close proximity (within one metre)[105] of the index case for one hour or more during the case's infectious period. Contacts include household members, those who have stayed overnight in the same room, and those who have had face-to-face contact with the case.[98]

Those most at risk from pertussis and high-priority contacts for public health follow-up are:

- children aged under 12 months; particularly those whose mothers did not received Tdap in pregnancy or who have received fewer than two pertussis-containing vaccine doses by 14 days prior to exposure
- children and adults who live with, or spend time around a child including in health care and education settings
- unvaccinated pregnant women, especially in the last month of pregnancy
- individuals at risk of severe illness or complications (eg, with chronic respiratory conditions, congenital heart disease or immune deficiency).

As the evidence for the effectiveness of chemoprophylaxis of contacts is limited, antibiotics are currently only recommended for household or household-like settings where high-priority contacts as listed above reside – if prophylaxis is given, all members of the contact group should receive it. Health care workers are frequently exposed to *B. pertussis*. Although the greatest priority is given to protecting young infants and unimmunised children, there are well-documented examples of spread from staff to older adult patients. Pertussis in adults can be debilitating and can cause significant morbidity in those with respiratory disease.

Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/pertussis**).

Restriction

Any contacts, high priority or otherwise, should be advised to avoid attending early childhood services, school, work or community gatherings if they become symptomatic. It is important to clearly explain that symptoms in the early stages of pertussis are indistinguishable from minor respiratory tract infections, and pertussis is highly contagious.[98]

Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/pertussis**).

15.9 Variations from the vaccine data sheets

The DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets state that these vaccines are indicated for primary immunisation of infants and as a booster dose for children. The Ministry of Health recommends that DTaP-IPV-HepB/Hib and

DTaP-IPV vaccines may also be used for catch-up of the primary schedule in children aged under 10 years (see Appendix 2).

The data sheets for DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap (Boostrix) state that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within seven days following a vaccine dose. The Ministry of Health recommends that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components (see section 15.6.1). The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis (see section 15.6.2).

Tdap is not approved for use (registered) for primary immunisation. However, the Ministry of Health recommends that children aged from 7 years and adults may receive Tdap for catch-up of the primary schedule (see Appendix 2).

The Tdap data sheet states that the vaccine may be used during pregnancy when the possible advantages outweigh the possible risks for the fetus. However, the Ministry of Health recommends Tdap vaccine for all pregnant women from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth. It is funded when given any time in second or third trimester (see section 15.5.2).

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16 Pneumococcal disease

Key information

Mode of transmission	Contact with respiratory droplets.
Incubation period	Asymptomatic nasopharyngeal carriage is common. The incubation period is variable and may be as short as 1–3 days.
Incidence and burden of disease	Highest at extremes of age (<2 years and >75 years), Māori and Pacific people, those with multiple comorbidities and with immunocompromise.
Funded vaccines	All children aged under 5 years: PCV10 (Synflorix). Children and adults with eligible conditions: • PCV13 (Prevenar 13) • 23PPV (Pneumovax 23).
Dose, presentation and route	All vaccines: • 0.5 mL per dose • pre-filled syringe • intramuscular injection (23PPV also be given subcutaneously).
Funded vaccine indications and schedule	PCV10 at ages 6 weeks, 5 months and 12 months, and age-appropriate catch-up for children <5 years; or, PCV13 and 23PPV: • vaccination or re-vaccination at any age with eligible conditions • testing for primary immune deficiencies.
Vaccine efficacy	For pneumococcal conjugate vaccines: reductions in pneumococcal disease and carriage of vaccine serotypes in vaccinated populations, plus herd immunity effects reducing pneumococcal disease in other age groups; some increases in disease caused by non-vaccine serotypes.
Precautions and special considerations	Concomitant PCV13 and influenza vaccine may increase risk of fever and febrile convulsions in children aged 6 months to <5 years. 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines.

16.1 Bacteriology

Streptococcus pneumoniae is a gram-positive diplococcus. It is ubiquitous, and many individuals carry the organism asymptomatically in their upper respiratory tract.[1] There are over 90 identifiable serotypes of *S. pneumoniae*. Certain serotypes are more

invasive or more associated with antibiotic resistance, and dominant serotypes vary by age and geographical distribution.

See section 16.4.1 and Table 16.1 for a summary of the serotypes contained in the pneumococcal conjugate vaccines (PCV) and pneumococcal polysaccharide vaccine (PPV).

16.2 Clinical features

The human nasopharynx is the only natural reservoir of *S. pneumoniae*. Carriage rates in young children range from 21 percent in high-income settings to more than 90 percent in resource-limited countries.[1] Transmission of *S. pneumoniae* is by contact with respiratory droplets. Although nasopharyngeal colonisation precedes disease, most who are colonised do not develop disease. The nasopharynx is a source of spread between individuals, so reduced nasopharyngeal carriage of *S. pneumoniae* vaccine serotypes in vaccinated children decreases transmission to adults. Transmission of pneumococci and invasive potential is increased by concomitant viral upper respiratory tract infection, especially influenza. Invasive pneumococcal disease (IPD) is defined by isolation of *S. pneumoniae* from a usually sterile site, such as blood, pleural fluid or cerebrospinal fluid, and represents the most severe end of the disease spectrum. The most common clinical syndromes in IPD are bacteraemic pneumonia, non-localised bacteraemia and meningitis. Older adults generally have bacteraemic pneumonia, while young children may have any of the three, with meningitis being the most severe.

Pneumonia without bacteraemia is up to five times more common than bacteraemic pneumonia, especially in older adults, where it also has high mortality. Other non-invasive infections include acute otitis media (predominantly in children) and sinusitis (predominantly older children and adults). The period between colonisation with *S. pneumoniae* and infection is variable but may be as short as one to three days.

16.3 Epidemiology

16.3.1 Global burden of disease

Pneumococcal disease is a common cause of morbidity and mortality worldwide. Rates of disease and death are highest in low-income countries with the majority of deaths occurring in sub-Saharan Africa and Asia.[2] Along with the very old and very young, patients with underlying cardiorespiratory disease and congenital or acquired immunosuppression have the highest rates of disease.

Risk of disease increases with multiple comorbidities and lifestyle factors (this is described as risk-stacking, see section 16.5.4).[3] The risk of IPD in children and adults with two or more comorbid conditions can be as high as in those with a recognised 'high-risk' condition.[4] Lifestyle factors, such as passive smoking, environmental and workplace pollutions, smoking

and alcohol dependency, can increase the risk of severe pneumococcal disease, especially in those with chronic illnesses that predispose them to infection, such as asthma, diabetes, dementia and mental illness.[5, 6] Socioeconomic deprivation, homelessness and overcrowding have also been associated with increased risk of IPD.[7]

The WHO estimates that 300,000 (range 200–370,000) children aged under 5 years died from pneumococcal infections, representing around 5 percent of all-cause mortality in this age group, in 2015.[8] An additional 23,000 (15–40,000) deaths were estimated to occur in children co-infected with HIV. On average 75 percent of IPD and 83 percent of pneumococcal meningitis cases are aged under 2 years but the incidence and age distribution vary by country and socioeconomic status.[8] Importantly, at least one quarter of survivors of pneumococcal meningitis experience long-term sequalae such as hearing loss, seizures, mental and motor abnormalities.

In each geographical region globally, PCV10 and PCV13 were shown to cover more than 70 percent of the serotypes causing IPD under 5 years of age during 1980–2007 prior to PCV introduction (PCV10 range 70–94 percent and 74–88 percent for PCV13).[8]

16.3.2 Global epidemiology since the introduction of pneumococcal conjugate vaccines

Direct impact of PCV programmes on IPD in children

Reductions in IPD among target cohorts of children in high income countries have been similar for PCV10 and PCV7/13 in reported studies. Québec (PCV10 and 13) and Finland (PCV10) both used 2+1 schedules and observed 83 percent and 79 percent reductions in IPD in vaccine-eligible children, respectively.[9, 10] In England, using PCV7 then PCV13 in a 2+1 schedule, there was an estimated 5,000 (54 percent) fewer hospital admissions for bacteraemia, meningitis and pneumonia in children aged under 5 years over 12 years after the introduction of PCV7 and PCV13. The greatest reductions were seen in meningitis (by 71 percent) in children under 2 years age.[11]

Direct impact of vaccination on non-invasive pneumococcal disease

The impact of pneumococcal conjugate vaccination on the large burden of non-invasive pneumococcal disease has been clearly demonstrated internationally in countries that have introduced these vaccines, particularly through reductions in childhood hospitalisations due to pneumonia.[12, 13] Other impacts, such as on acute otitis media, are less clear and more difficult to measure accurately.[14] However, a systematic review found PCVs were associated with large reductions in risk of pneumococcal acute otitis media, but there was no evidence of benefit against all-cause otitis media in high-risk children over 1 year of age or older children with a history of respiratory illness.[15]

Herd immunity

The extent to which childhood PCV immunisation programmes provide indirect reductions in IPD among high-risk children and older adults varies between reports, settings and vaccine serotype (notably serotypes 3 and 19A). There is some good evidence for the indirect (herd) effects of infant PCV immunisation on vaccine serotype pneumococcal disease in the non-vaccinated population, especially in adults aged 65 years and older, and an all age-effect on non-bacteraemic pneumonia.[16] This includes data showing reductions in the rates of IPD due to PCV7 and, more recently, PCV13 serotypes in non-vaccinated groups in many countries (for both pneumonia and IPD in adults) in North America and Europe,[11, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26] Reductions in adult pneumococcal pneumonia have also been observed in Western Kenya following the introduction of PCV10 in children[27] and in Japanese community-dwelling older adults following the introduction of PCV13.[28] These herd effects are predominantly due to decreased nasopharyngeal carriage of vaccine types in immunised children lowering transmission to unimmunised older children and adults.

Although many countries have reported significant decreases in vaccine-type IPD among children and the wider population following the introduction of PCVs to the childhood schedules, IPD due to non-PCV serotypes has increased in some, particularly in older adults.[29, 30] Therefore, for direct protection against a broad range of serotypes 23PPV continues to be necessary for those at highest risk of IPD.

16.3.3 New Zealand epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months.[31, 32] In the pre-PCV era, incidence of IPD was highest in infants and the elderly, especially among Māori and Pacific peoples.[31, 33, 34, 35]

Isolates from cases of IPD are serotyped at ESR and detailed information by age group is regularly updated on the ESR Public Health Surveillance website (available at **surv.esr.cri.nz/surveillance/IPD.php**).

Incidence and mortality

In 2021, there were 468 notified IPD cases and the overall notification rate was 9.2 cases per 100,000 population (ESR, 3 May 2022). The highest rates of IPD were in adults aged 85 years and older (47.5 per 100,000) and in children aged under 1 year (46.0 per 100,000), followed by adults aged 75–84 years (24.3 per 100,000) and 65–74 years (17.8 per 100,000). The age-standardised rates of IPD were highest for the Pacific peoples (31.0 per 100,000, 64 cases) and Māori (26.5 per 100,000, 149 cases) ethnic groups. These rates were 4.9 and 4.2 times higher than the age-standardised rate for the European/Other ethnic group (6.3 per 100,000, 217 cases). The incidence of IPD was 12.5-fold higher for those living in areas with the highest levels of deprivation than those living in low deprivation areas across all age groups (60.9 vs 4.9 per 100,000). IPD was recorded as the primary cause of death for 16 cases in 2022, including 5 children aged under 5 years (the most since IPD became notifiable in late 2008). In 2021, the most reported risk factor in cases aged under 5 years were children who were born

premature (7.6 percent) and children who were immunocompromised (4.5 percent) (ESR, 3 May 2022).

New Zealand epidemiology since the introduction of PCV

PCV7 was introduced in June 2008, PCV10 in July 2011 and PCV13 in July 2014, PCV10 replaced PCV13 in July 2017 on the routine Schedule (see Appendix 1). As of July 2020, the number of primary doses of PCV10 were reduced to two (at age 6 weeks and 5 months) and the booster dose was brought forward from 15 months to 12 months in October 2020.

IPD incidence

There have been dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand since the introduction of PCV to the Schedule in 2008 (see Figure 16.1).

In children under 2 years of age, the total rate of IPD decreased by 74.3 percent since the introduction of PCV to the Schedule in late 2008: from 46.0 per 100,000 in 2009 to 11.8 per 100,000 in 2015. However, the rate has steadily increased since 2015 and in 2021 the rate of 35.7 per 100,000 was the highest since 2009.

There has also been a great reduction in PCV7 serotypes (see Figure 16.2), with few cases of PCV7 serotype IPD detected in children aged under 2 years since 2015 (ESR, 3 May 2022).

Similar reductions were seen for IPD caused by PCV10 serotypes under 2 years (see Figure 16.2). IPD incidence has decreased in children aged 2–4 years since 2009, for all-cause IPD (45.9 percent; Figure 16.1), however, since 2009 there have been only 2 years (2010 and 2016) in which the IPD rate for children aged 2-4 years exceeded the 2021 rate. Further, the rate of IPD due to PCV13 specific serotypes has been increasing since 2018 among children aged 2-4 years, though the rates are still low (Figure 16.2) (ESR, 3 May 2022).

In 2021, 41.0 percent of cases in adults aged 65 years and over were PCV13 serotypes, and 73.8 percent were due to 23PPV serotypes. Of these, 37.0 percent (50/135 cases) were due to serotype 19A, and 44.4 percent were due to 23PPV-non-PCV13 serotypes (ESR, 3 May 2022).

Figure 16.1: Rate per 100,000 of invasive pneumococcal disease by age group and year, 2009-2021

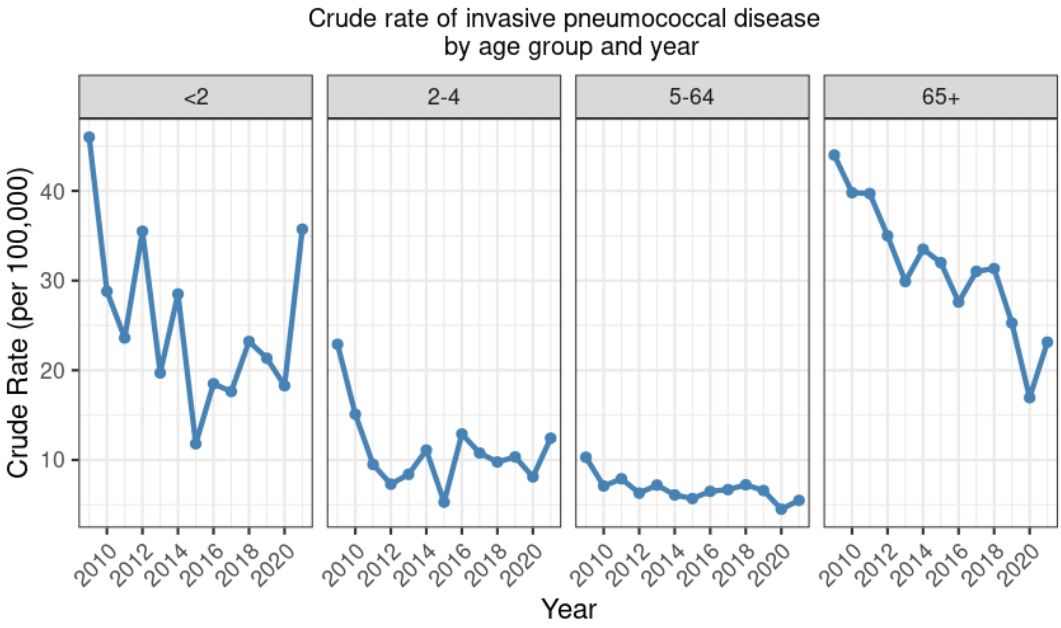
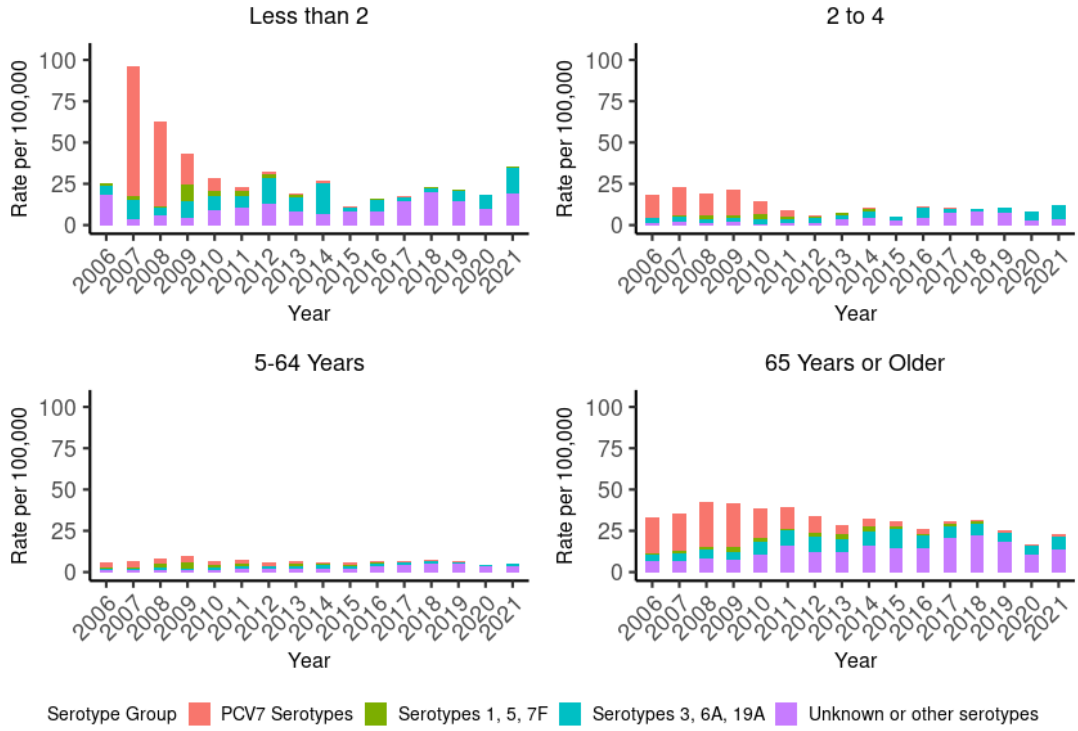


Figure 16.2: Rate per 100,000 population of invasive pneumococcal disease due to PCV7 serotypes, additional PCV10 types, additional PCV13 types and non-PCV types, by age group and year, 2006–2021



Notes:

PCV7 was introduced in 2008, PCV10 in 2011, PCV13 in 2014 and PCV10 reintroduced in 2017.

'PCV7 serotypes' are cases due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F); 'Serotypes 1, 5, 7F and 19A' are cases due to the additional serotypes covered by PCV10; 'Serotypes 3 and 6A' are cases due to the additional serotypes covered by PCV13; and 'Other serotypes' are all other culture-positive IPD cases.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Pneumococcal serotypes

Of the 468 IPD cases notified in 2021, 448 isolates were referred to ESR for serotyping. In children aged under 5 years, 49.2 percent (30/61) of cases were due to serotypes not covered by PCV, compared with 65.1 percent (136/209) and 57.9 percent (103/178) in the 5–64 years and 65 years and older age groups (ESR, 3 May 2022).

Serotype 19A was the most common serotype (32 cases) in 2021 among children under 5 years of age, increasing from 4 cases in 2017 to 18 cases in 2021 in children aged under 5 years. In adults aged 65 years or older, serotype 23B and 16F were the most prevalent non-vaccine serotypes (PCV13 or 23PPV) in 2021 (ESR, 3 May 2022).

Herd immunity

The addition of PCV to the New Zealand schedule in 2008 was followed by significant reductions in IPD due to PCV7 serotypes in age groups not eligible for routine infant immunisation (Figure 16.2). Since notification-based surveillance began in late 2008, the rate of IPD due to PCV7 serotypes in the 5–64-year age group decreased 96 percent from 3.8 per 100,000 to 0.2 per 100,000 in 2021, and the rate in cases aged 65 years and over decreased 94.3 percent from 26.6 to 1.5 per 100,000 (ESR, 3 May 2022). Though not as much of a decrease, the total rate of IPD in adults decreased by approximately 50 percent from 2009 to 2021 (rate for age 5–64 years: 10.3 to 5.5 per 100,000; age 65 years and over: 44.0 to 23.1 per 100,000

Impact of vaccination on non-invasive pneumococcal disease

While hospitalisations for respiratory infections in children aged 5 years and under have been increasing in New Zealand, hospitalisations for all-cause pneumonia have declined significantly since the implementation of the pneumococcal conjugate vaccine programme in 2008. The largest reductions in all-cause pneumonia hospitalisations between 2006 and 2015 were in Māori (a 12 percent reduction) and Pacific children (a 21 percent reduction) and those living in areas of high deprivation.[36] A 51 percent decline in otitis media hospitalisations was observed for Māori children aged under 6 years following PCV immunisation, compared with 8 percent decline in otitis media across all ethnicities.[36]

Antimicrobial resistance

Introduction of pneumococcal conjugate vaccination has reduced the circulation of resistant pneumococcal serotypes in the US,[37] but little change has been seen in New Zealand since PCV introduction. *S. pneumoniae* resistance to penicillin (14.1–23.5 percent) and cefotaxime resistance (0.4–2.1 percent) has varied year-to-year over the last decade with no significant trend.[38]

In 2020, PCV7 serotypes accounted for 7 percent of the penicillin-resistant isolates compared with 92.8 percent in 2006/07, but the prevalence of penicillin resistance

among serotype 19A isolates increased just over 4-fold from 15.8 percent in 2006/07 to 72.2 percent in 2020. The relative contribution of serotype 19A to penicillin-resistant invasive pneumococci had decreased, from a high of 52.1 percent in 2015 to 28.1 percent in 2019. However, in 2020, serotype 19A accounted for 44.8 percent of the penicillin-resistant isolates (ESR, 3 May 2022).

16.4 Vaccines

16.4.1 Available vaccines

There are two types of pneumococcal vaccine registered (approved for use) and available (marketed) in New Zealand for use against *S. pneumoniae*: pneumococcal conjugate vaccine (PCVs) with 10 or 13 serotypes and a plain polysaccharide pneumococcal vaccine (PPV) containing 23 serotypes. In PCV vaccines, the pneumococcal surface polysaccharide is coupled to a carrier protein that induces increased production of type-specific antibodies, particularly in children aged under 2 years, and immunological memory, enabling booster responses with subsequent doses (see section 1.4.3). Table 16.1 summarises the polysaccharide serotypes contained within each vaccine.

Table 16.1: Summary of pneumococcal vaccine serotype content

PCV7				4			6B				9V				14			18C		19F			23F	
PCV10	1			4	5		6B	7F			9V				14			18C		19F			23F	
PCV13	1		3	4	5	6A	6B	7F			9V				14			18C	19A	19F			23F	
23PPV	1	2	3	4	5		6B	7F	8	9N	9V	10A	11A	12F	14	15B	17F	18C	19A	19F	20	22F	23F	33F

Note: PCV10 contains serotype 6B and 19F, which elicit cross-reactive opsonophagocytic antibodies against serotype 6A and 19A, respectively, but at a lower level than PCV13.[8]

Funded vaccines

PCV10 (Synflorix, GSK)

Each 0.5mL dose of PCV10 contains:

- 1 µg of pneumococcal polysaccharide serotypes 1, 5, 6B, 7F, 9V, 14 and 23F and 3 µg of serotype 4, conjugated to a total of 9–16 µg of non-typeable *Haemophilus influenzae* (NTHi) protein D, 3 µg of serotype 18C conjugated to 5–10 µg of tetanus toxoid, and 3 µg of serotype 19F conjugated to 3–6 µg of diphtheria toxoid, adsorbed onto 0.5 mg of aluminium phosphate
- 4.3 mg of sodium chloride and water for injection. PCV10 contains no preservative.

PCV13 (Prevenar 13, Pfizer)

Each 0.5 mL dose of PCV13 contains:

- 2.2 µg of pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F, and 4.4 µg of serotype 6B, conjugated to non-toxic diphtheria CRM197 protein and adsorbed onto aluminium phosphate (0.565 mg)
- succinic acid, polysorbate 80, aluminium phosphate, phosphate, and sodium chloride in water for injection.

23PPV (Pneumovax 23, MSD)

Each 0.5 mL dose of 23PPV contains:

- 25 µg of each capsular polysaccharide antigen (serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F)
- sodium chloride, water for injection, and phenol (0.25 percent) added as a preservative.

16.4.2 Efficacy and effectiveness

10-valent pneumococcal conjugate vaccine

IPD

Two key randomised controlled trials have demonstrated the protective efficacy of PCV10 against pneumococcal disease.[39] The Finnish Invasive Pneumococcal disease (FinIP) study investigated a two- or three-dose infant series plus a toddler booster. Vaccine efficacy against vaccine-serotype IPD was 100 percent (95% CI: 83–100) for the 3+1 schedule and 92 percent (95% CI: 58–100) for the 2+1 schedule. Based on national hospital discharge register data, vaccine efficacy was 71 percent (95% CI: 52–83) for patient file-verified non-laboratory-confirmed IPD.[40, 41]

The Clinical Otitis Media and Pneumonia Study (COMPAS) showed PCV10 efficacy to be 100 percent (95% CI: 74.3–100) against vaccine-serotype IPD and 65 percent (95%

CI: 11.1–86.2) against any IPD.[42] In this study, approximately 24,000 infants received PCV10 or HepB at ages 2, 4 and 6 months with a booster at age 15–18 months as part of the phase III trial conducted in Latin America (Argentina, Colombia and Panama).

Two observational studies in Brazil examined effectiveness of PCV10 (as a 3+1 schedule) post-introduction in 2010. A matched case-control study of 316 cases of IPD and 1,219 neighbourhood age-matched controls showed adjusted vaccine effectiveness (VE) against vaccine-serotype IPD of 83.8 percent (95% CI: 65.9–92.3) for an age-appropriate PCV10 schedule.[43] A study based on data obtained from the Information System on Notifiable Diseases from 2007 to 2012 found two years after the introduction of routine PCV10 vaccinations that there was a decrease in pneumococcal meningitis morbidity and mortality in children aged under 2 years.[44]

Overall, the incidence of pneumococcal meningitis decreased by 50 percent from 3.7 per 100,000 population in 2007 to 1.84 per 100,000 in 2012. Mortality decreased by 69 percent from 1.3 to 0.4 per 100,000. The greatest impact of PCV10 vaccination was in infants aged 6–11 months, with a 73 percent reduction in pneumococcal meningitis incidence and an 85 percent reduction in mortality.[44]

Non-IPD pneumonia

The FinIP trial found vaccine effectiveness against all hospital-diagnosed pneumonia was 25.2 percent (95% CI: 2.6–42.6) for the 3+1 PCV10 schedule and 27.6 percent (95% CI: 5.5–44.6) for the 2+1 schedule.[39]

In Brazil, there was a significant decrease of 12.7 percent ($p<0.001$) in all-cause pneumonia hospitalisations of children aged under 4 years between the pre (2002–2009) and post-PCV10 (2011–2012) periods, in the absence of any reduction in non-respiratory-cause hospitalisations ($p=0.39$).[45] Active population-based surveillance studies in Central Brazil (across 17 paediatric hospitals) found around a 25 percent reduction in the rate of X-ray-confirmed pneumonia in children aged 2–23 months.[46] Five years after the introduction of PCV10 in Brazil, pneumonia hospitalisations significantly reduced, both in vaccine-targeted children (17.4–26.5 percent) and age groups not targeted for vaccination (11.1–27.1 percent for ages 10-49 years), but not in those aged 65 years or older.[47]

Otitis media

In the COMPAS trial, a post-hoc intent-to-treat analysis found that vaccine efficacy against bacteriologically-confirmed acute otitis media (AOM) was 19.0 percent (95% CI: 4.4–31.4; $p=0.007$), increasing to 55.7 percent (95% CI: 21.5–75.0) against pneumococcal AOM and 69.9 percent (29.8–87.1) against vaccine-serotype pneumococcal AOM.[42] Although PCV10 has been suggested to be protective against non-typeable *Haemophilus influenzae* (NTHi) confirmed-AOM,[42] following the introduction of PCV10 in New Zealand, no reduction in NTHi density in the nasopharyngeal or middle-ear microbiology in children with established ear disease was observed; NTHi remained the dominant pathogen for otitis media.[48, 49]

In a follow-up of the FinIP study, vaccine efficacy of PCV10 against all respiratory tract infections (RTIs) in children aged under 2 years was 12 percent (95% CI: 2–22), 23 percent (95% CI: 0–40) against RTIs with AOM, and 10 percent (95% CI: 0–19)

against RTIs without AOM. Most of these infections were caused by rhinovirus.[50] Despite low efficacy against any AOM (7–13 percent), the high incidence rate of AOM meant that related factors (antimicrobial prescriptions and tympanostomy tube placements) contributed to 95 percent of the reduction in total disease burden post PCV10, compared with 0.6 percent for laboratory-confirmed IPD.[51] Similarly in Iceland, PCV10 introduction was associated with a 5.8 percent (95% CI: 1.6–9.8) reduction in all-cause antimicrobial prescriptions and 21.8 percent (95% CI: 11.5–30.9) reduction in AOM-associated prescriptions in children up to 3 years of age.[52]

13-valent pneumococcal conjugate vaccine

Individuals at increased risk of IPD

Few studies have investigated the immunogenicity and effectiveness of PCV13 in individuals at increased risk of IPD. Studies using pneumococcal vaccines with similar but fewer antigens have demonstrated vaccine efficacy in individuals with immunocompromising conditions (eg, HIV, sickle cell disease), but the duration of protection against IPD remains unknown.[53] High IgG titres have been demonstrated following PCV13 vaccination of children with sickle cell disease,[54] HIV infection[55] and nephrotic syndrome.[56]

WHO recommends that children with medical conditions that reduce humoral immune response to vaccines, such as HIV, sickle cell disease and primary immune deficiencies, to have a 3+1 schedule of PCV13.[8] In children and adolescents with underlying medical conditions, such as type 1 diabetes, cancer, cystic fibrosis or asthma, the broader serotype protection provided by PCV13 can reduce nasopharyngeal carriage and the associated risk of IPD.[57, 58, 59, 60]

Use of pneumococcal conjugate vaccines in adults

PCV13 induces robust immune responses in adults,[61, 62, 63, 64] including elderly adults.[65] Although the antibody titres vary with serotype and between age groups, particularly for those aged over 65 years, the clinical significance of this variation is unclear.[62] PCV13 is at least as immunogenic as 23PPV in adults. Some studies suggest that 23PPV attenuates the immune response to subsequent doses of PCV13, not seen if PCV13 is given before 23PPV; PCV13 may augment the response to subsequent 23PPV vaccination.[65, 66, 67]

With respect to clinical outcomes, the Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA) was a large randomised placebo-controlled trial conducted in the Netherlands that assessed efficacy of PCV13 against pneumococcal community-acquired pneumonia (CAP) with and without IPD in adults aged 65 years and older. The efficacy of PCV13 against vaccine-type IPD was 75 percent (95% CI: 41.4–90.8) and 45.6 percent (95% CI: 21.8–62.5) against vaccine-type pneumococcal CAP; 45.0 percent (95% CI: 14.2–65.3) for both combined.[68] Although this study showed individual protection for vaccine-type CAP, there was no significant reduction in all-cause pneumonia.[68]

An important uncertainty is the extent of indirect protection in vaccine-type IPD cases stemming from childhood immunisation programmes, which varies between countries.

Where vaccine serotypes are sufficiently prevalent, PCV13 would provide some protection against all-cause CAP and lobular pneumonia.[69] Some of the non-PCV13 vaccine serotypes more likely to cause disease in adults are covered by 23PPV.

Data is limited for younger adults and specific at-risk adult populations.

23-valent vaccine pneumococcal polysaccharide

The polysaccharide vaccine (23PPV, Pneumovax 23) is made from the purified capsular polysaccharides of 23 serotypes of *S. pneumoniae*. It is available in New Zealand for adults and children from age 2 years. The 23 serotypes included in 23PPV (see Table 16.1) are responsible for about 90 percent or more of IPD in high-income countries.

See recent IPD surveillance reports from ESR for prevalence of serotypes covered by 23PPV in New Zealand (available at **surv.esr.cri.nz/surveillance/IPD.php**).

A meta-analysis of IPD in adults aged from 65 years in 10 European countries showed that incidence of PCV7 serotypes had declined by 77 percent and for additional PCV13 serotypes by 38 percent after 5 years of PCV13/PCV10 immunisation programmes. The incidence rate of 23PPV-non-PCV13 serotypes had increased by around 50 percent with these 11 serotypes causing 22–54 percent of IPD.[70] In 2016, more than two-thirds of IPD cases in adults age 65 years or older were 23PPV-non-PCV13 serotypes.[38]

The efficacy of 23PPV varies depending on whether immune-competent or immunocompromised patients are studied, and whether the end point is pneumococcal pneumonia or bacteraemia.

The limitations of the polysaccharide vaccine have been summarised as:

- reduced efficacy in high-risk individuals
- uncertain efficacy against pneumonia
- it is only suitable for children aged 2 years and older.
- waning protection 2.5 to 5 years after vaccination.

A 2017 meta-analysis from Germany found pooled VE for 23PPV against any serotype IPD of 45 percent (95% CI: 15–65), 59 percent (95% CI: 35–74) or 73 percent (95% CI: 10–92) across cohort, case-control or clinical trial data; and pooled VE against any serotype pneumococcal pneumonia of 48 percent (95% CI: 25–63) and 64 percent (95% CI: 35–80) in cohort studies and clinical trials.[71] For both outcomes, waning of protection was found between 2.5 years and 5 years of follow-up after 23PPV.[71] Other systematic reviews, with differing eligibility criteria, found lower pooled VE estimates against IPD or pneumococcal pneumonia for 23PPV.[72, 73, 74] A Japanese prospective study found 23PPV to have moderate but variable effectiveness against vaccine-type pneumococcal pneumonia in adults aged 65 years or older.[75] Hence, questions remain around the clinical effectiveness and intervals between repeat doses of 23PPV that provide continued protection.

16.4.3 Dosage and administration

The dose of PCV10, PCV13 and 23PPV is 0.5 mL, administered by intramuscular injection (see section 2.2.3). 23PPV can also be administered by subcutaneous injection (see section 2.2.3), but there is an increased likelihood of injection-site reactions.[76]

Co-administration with other vaccines

PCV10, PCV13 or 23PPV may be administered at the same time as other routine childhood vaccinations, in a separate syringe at a separate injection site (see section 2.2.7 for information about multiple injections at the same visit). The only exception is PCV13 with the quadrivalent meningococcal conjugate vaccine MenACWY-D, which should be given at least four weeks after PCV13. This is because, when these vaccines were administered concurrently during clinical trials, impairment of the antibody response to some of the pneumococcal serotypes (serotypes 4, 6B and 18C) was reported.[77, 78]

PCV13 has been associated with increased risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in children aged 6 months to under 5 years. Separation of the vaccines by two days can be offered but is not essential (see section 16.6.2). Systemic reactions have been noted in adults aged over 65 years.

16.4.4 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze.

16.5 Recommended immunisation schedule

16.5.1 Usual childhood schedule (PCV10)

PCV10 for children aged under 5 years

PCV10 (Synflorix) vaccine is funded for all children aged under 5 years. Two doses of PCV10 are given as the primary course, with a booster at age 12 months (Table 16.2). Children who started their immunisation course with PCV13 can complete it with PCV10.

Table 16.2: Usual childhood PCV10 (Synflorix) schedule

Age	Vaccine	Comment
6 weeks	PCV10	Primary series
5 months	PCV10	Primary series
12 months	PCV10	Booster

Where a previously unimmunised child aged under 5 years presents late for pneumococcal vaccination, the age-appropriate catch-up schedules in Appendix 2 should be followed.

16.5.2 Extended pneumococcal immunisation for high-risk groups

As part of the extended immunisation programme for high-risk groups, PCV13 and 23PPV are funded for eligible individuals, as shown in Table 16.3, Table 16.4 and Table 16.5. Because the recommended schedule depends on the age of the individual at diagnosis, the tables have been organised into age groups (under 5 years, 5–18 years and 18 years and older).

The PCV13 and 23PPV funding restrictions are as follows. See Table 16.3, Table 16.4 and Table 16.5 for the eligible conditions and dosing requirements.

PCV13

All high-risk infants are recommended to receive at least three doses of a PCV vaccine, with at least one dose after 12 months of age. Change from PCV10 to PCV13 as soon as the infant is diagnosed as being at high risk.

- Two doses of PCV13 are funded for high-risk children aged from 12 months and under 18 years who have previously received two or three doses of PCV10.
- Up to four doses of PCV13 are funded for vaccination or re-vaccination of high-risk children aged under 5 years.
- Up to four doses of PCV13 are funded for vaccination or re-vaccination of eligible individuals aged 5 years and older.

23PPV

- Up to three doses of 23PPV are funded for individuals with eligible conditions.
- Up to two doses of 23PPV are funded for high-risk children aged under 18 years.

See also section 16.5.3 '(Re)vaccination'. See sections 4.2 and 4.3 for more information about immunocompromised infants, children and adults, including additional vaccine recommendations and schedule tables for certain conditions.

Table 16.3: Extended pneumococcal immunisation for children aged under 5 years – funded PCV13 and 23PPV indications and schedules

See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to funding decisions.

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged under 5 years:

- prior to planned immunosuppressive therapy or radiotherapy, including prior to solid organ transplantation
- on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response)
- with primary immune deficiencies
- with HIV infection
- with renal failure or nephrotic syndrome
- who are immunosuppressed following organ transplantation (including HSCT)
- with cochlear implants or intracranial shunts
- with cerebrospinal fluid leaks
- who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation
- with cardiac disease, with cyanosis or failure
- with diabetes
- with Down syndrome
- who are pre-or post-splenectomy, or with functional asplenia.

Age at diagnosis	Vaccine	Recommended vaccine schedule
<12 months	PCV13	PCV13[a] at ages 6 weeks, 3, 5[b] and 12 months or an age-appropriate catch-up schedule. For those who have not been immunised at age 7–11 months – give 2 doses of PCV13 (8 weeks apart) and a further dose 8 weeks later, from age 12 months. For children aged 7–11 months who have completed a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) 8 weeks later, from age 12 months.
	23PPV	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.
12 months to <5 years	PCV13	For children who have not yet received any PCV13, give 2 doses of PCV13 at least 8 weeks apart.[c,d]
	23PPV	Give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

a. A three-dose primary series plus a booster dose of PCV13 replaces PCV10 on the usual Schedule.

b. Additional dose of PCV13 given at 3 months, differing from PCV10 Schedule.

c. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 5 years, wait at least 8 weeks before administering PCV13 (note: this timing differs in adults, see footnote in Table 16.5).

d. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

Table 16.4: Extended pneumococcal immunisation for children aged from 5 to under 18 years – funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged 5 to under 18 years:

- with HIV infection
- who are pre- or post-HSCT[a] or chemotherapy[a]
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants or intracranial shunts
- with cerebrospinal fluid leaks
- with primary immunodeficiency[d]

23PPV (Pneumovax 23) is also funded for children aged 5 to under 18 years:

- prior to planned immunosuppressive therapy or radiotherapy, including prior to solid organ transplantation
- on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response)
- with renal failure or nephrotic syndrome
- who are immunosuppressed following organ transplantation (including HSCT)
- who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation
- with cardiac disease, with cyanosis or failure
- with diabetes
- with Down syndrome

Age at diagnosis	Vaccine	Recommended vaccine schedule
5 years to <18 years	PCV13	For children who have not previously received PCV13 – give 1 dose of PCV13, even if fully vaccinated [b,c]
	23PPV	1 dose of 23PPV at least 8 weeks after the PCV13 dose. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

a. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

b. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.

c. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

d. See section 4.3.3 for children with Down syndrome.

Table 16.5: Extended pneumococcal immunisation for adults aged 18 years and older – funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for (re)vaccination of patients:

- with HIV infection
- who are pre- or post-HSCT[a] or chemotherapy[a]
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants, intracranial shunts[b] or cerebrospinal fluid leaks[b]
- with primary immunodeficiency.

Age at diagnosis	Vaccine	Recommended vaccine schedule
≥18 years	PCV13	Give one dose of PCV13[c]
	23PPV	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The first 23PPV dose is given at least 8 weeks after PCV13, the 2nd a minimum of 5 years later, and the 3rd dose at age ≥65 years.

a. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post HSCT or chemotherapy.

b. Only PCV13 is funded for these indications.

c. If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

16.5.3 (Re)vaccination

Up to an additional four doses of PCV13 and up to additional three doses of 23PPV are funded for vaccination or re-vaccination of high-risk individuals (as listed in Table 16.3, Table 16.4 and Table 16.5).

See also sections 4.3 and 4.6.

16.5.4 Recommended but not funded

Risk stacking

Two classifications of IPD risk are recognised: 'high-risk' conditions for which there is significant risk of IPD and 'at-risk' conditions, which on their own may not significantly increase risk, but when combined together or with lifestyle risk factors increase an individual's risk of IPD. This is described as 'risk stacking' – IPD incidence substantially increases with the accumulation of concurrent risk factors or conditions.[3, 4] The risk of pneumococcal infections in those with two or more at-risk conditions may be as high as the risk for those with a recognised high-risk condition.[79, 80, 81]

Recommendations

PCV13 and 23PPV are recommended but not funded for the following individuals:

- immune-competent adults (aged 18 years and older) at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic heart, renal, liver or pulmonary disease, diabetes or alcohol dependency)
- adults with cerebrospinal fluid leak
- immunocompromised adults at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin's disease)
- individuals of any age who have had one episode of IPD
- smokers.

For those individuals who choose to purchase PCV13 and 23PPV vaccines, providers may follow the age-appropriate schedules in Table 16.4 and Table 16.5.

Adults aged 65 years and older with no other risk factors

Give one dose of PCV13 followed at least eight weeks later with 23PPV (not funded).

16.5.5 Pregnancy and breastfeeding

Pneumococcal vaccines are not routinely recommended for pregnant women.

Women of childbearing age who are eligible for funded PCV13 and 23PPV should be vaccinated before a planned pregnancy or as soon as possible after delivery (see Table 16.5). Administration of these vaccines in pregnancy is unlikely to result in serious adverse effects and may be considered in individuals at the very high risk of IPD who were not vaccinated prior to pregnancy.[82]

PCV13 and 23PPV may be given to breastfeeding women.[82]

16.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

16.6.1 Contraindications

There are no specific contraindications to pneumococcal polysaccharide or conjugate vaccines apart from a severe reaction to a previous dose or known hypersensitivity to any components of either vaccine.

16.6.2 Precautions

Systemic reactions (chills, rash and myalgia) may occur when PCV13 and influenza vaccine are administered at the same time. PCV13 has been associated with a slightly higher risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in infants and young children, compared to when administered separately.[83] Febrile convulsion history is not a contraindication to PCV13 immunisation. If indicated, PCV13 and influenza vaccines may be given to a child aged under 5 years at the same visit.[82] Parents/guardians should be informed of the small risk of febrile convulsions, and separation of vaccines by two days can be offered. If the child has a history of febrile convulsions, separation of the vaccines is recommended.

23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines (see section 1.4.3).

16.7 Potential responses and AEFIs

16.7.1 Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccines have excellent safety profiles. A 2016 systematic review found that pneumococcal conjugate vaccines are considered safe for use in children, and serious adverse events are detected very rarely by post-marketing surveillance.[84]

PCV10

Pooled evaluation of data derived from several clinical trials found PCV10 to be very well tolerated and safe with a similar safety profile to other PCVs.[84] After primary immunisation of infants, mild to moderate irritability and injection-site redness were most commonly reported, occurring after 55 percent and 41 percent of all doses, respectively. Fever occurred in 30–35 percent of children, regardless of the dose. Injection-site pain increased with age, reported by more than 39 percent of younger children and 58 percent of the older subjects. Severe adverse events were exceptionally rare.

When PCV10 was co-administered with DTaP-containing vaccines, fever of 38°C or higher was reported after about one-third of primary or booster vaccine doses.[85] These are similar results to those seen following co-administration of PCV7 and DTaP-containing vaccines.[85]

PCV13

The most commonly reported adverse reactions are injection-site reactions, fever, irritability, decreased appetite and increased or decreased sleep.[86] An increase in injection-site reactions was reported in children older than 12 months compared to rates observed in infants during the primary series with PCV13.

No serious adverse events have been identified in adults or children, associated with underlying disease or immunocompromise.[87, 88, 89]

16.7.2 Pneumococcal polysaccharide vaccine

Local discomfort, erythema and induration lasting a couple of days are potential responses.[90] Local and systemic reactions, such as self-limiting mild fever, myalgia and decreased arm movement in injected limb, may occur after revaccination of adults, particularly when the second dose is given within five years of the first dose.[82]

16.8 Public health measures

> IPD is a notifiable condition, and if confirmed, the laboratory undertaking the testing must notify the local medical officer of health.

Local public health action is not expected in response to individual notifications of this disease. Passive surveillance for IPD and pneumococcal serotypes help to inform the immunisation schedule.

Antimicrobial prophylaxis is not indicated for close contacts of cases of IPD. For those at high risk of pneumococcal disease where response to vaccination may be poor, antimicrobial prophylaxis may be indicated. Discuss with an appropriate specialist.

For more details on control measures, refer to the '*Invasive pneumococcal disease*' chapter of the *Communicable Disease Control Manual (*available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

16.9 Variations from the vaccine data sheets

The PCV10 (Synflorix) vaccine data sheet recommends that infants and children who receive a first dose of PCV10 complete the full vaccination course with PCV10. The Ministry of Health recommends that those who started with PCV10 may complete with PCV13 if they are subsequently diagnosed with a PCV13-eligible condition (see section 16.5).

The PCV13 (Prevenar 13) data sheet states that there is no data on the interchangeability of PCV13 with other pneumococcal conjugate vaccines containing a protein carrier different from CRM197. The Ministry of Health recommends that those who started with PCV13 may complete with PCV10 (see section 16.5).

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17 Poliomyelitis

Key information

Mode of transmission	Faecal–oral route or by ingestion of pharyngeal secretions.
Incubation period	Paralytic disease usually 7–14 days, with a reported range of 3–35 days.
Period of communicability	Most infectious in the days immediately before and after the onset of any symptoms. Transmission is possible for as long as the virus is shed (can be years in immunocompromised individuals).
Incidence and burden of disease	Globally, endemic wild-type poliovirus 1 in Afghanistan and Pakistan. Circulating vaccine-derived poliovirus outbreaks continue. Wild-types 2 and 3 have been eradicated.
Funded vaccines	As inactivated polio vaccine (IPV), in combination with other antigens, or on its own: • DTaP-IPV-HepB/Hib (Infanrix-hexa) • DTaP-IPV (Infanrix-IPV) • IPV (IPOL).
Dose, presentation, route	All 0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial, the vaccine must be reconstituted prior to intramuscular injection. DTaP-IPV: pre-filled syringe, intramuscular injection. IPV: pre-filled syringe, intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Usual childhood schedule: • at age 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib (primary series) • at age 4 years: DTaP-IPV (booster). For non-immune adults, 3 doses of IPV 8 weeks apart (may be shortened to 4-week intervals). For (re)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV or IPV.
Vaccine efficacy	Greater than 90 percent.
Precautions and special considerations	Non-immune pregnant women may be immunised if they are travelling to a region where polio is endemic.
Public health measures	All suspected cases of poliomyelitis be notified immediately on suspicion.

17.1 Virology

Poliomyelitis (polio) is a highly transmissible infectious disease caused by poliovirus, a small, non-enveloped enterovirus of the family Picornaviridae. There are three serotypes of poliovirus (types 1, 2 and 3). Wild types 2 and 3 have now been eradicated, but vaccine-derived poliovirus continue to circulate in some countries.

17.2 Clinical features

Poliovirus is transmitted by the faecal–oral route or by ingestion of pharyngeal secretions. The incubation period for poliomyelitis is commonly 7–14 days for paralytic disease, with a reported range of 3–35 days. The risk of transmission of infection is greatest shortly before to shortly after the onset of symptoms. The virus persists in the pharynx for approximately one week, and in the faeces for three to six weeks or longer, particularly in immunocompromised individuals, where cases have been reported shedding for many years.

The virus is highly neurotropic and its primary effect occurs in the neurones of the spinal anterior horn or the motor ganglia of the brain stem. in Up to 95 percent of infections are clinically inapparent; clinical cases range in severity from a non-paralytic fever to viral meningitis and acute flaccid paralysis.

Symptoms include fever; headache; gastrointestinal disturbances; malaise; stiffness of the neck and back; and pain in the limbs, back and neck, with or without paralysis. In children who develop paralysis, the illness may be biphasic with the initial phase of one to three days' duration being indistinguishable from that of other viral infections. The patient appears to recover, only to be struck down abruptly two to five days later with meningism, followed by paralysis. In adults and adolescents, the illness usually presents with a gradual onset of paralysis and pain without the early symptoms.

Infected asymptomatic people will shed the virus in their stool and may spread the infection to others. Infection rates may be as high as 100 percent in households where there are non-immune young children.

Paralysis may occur in 0.1–2 percent of infected individuals. It is more common in adults, occurring in up to 1 in 75 cases of infection. Case fatalities from paralytic polio vary from 2–5 percent among children and up to 15–30 percent for adults, increasing to 25–75 percent with bulbar involvement.

Post-polio syndrome may occur some 30–40 years after poliomyelitis. The cause is unknown but is probably related to the ageing or death of nerves and muscles that were compensating for the original damage. Patients experience muscle pain and exacerbation of existing muscle weakness. The risk of developing post-polio syndrome is greater in women than in men, and the risk increases with time from the episode of acute polio.

17.3 Epidemiology

17.3.1 Global burden of disease

In the pre-vaccination era, cases of poliomyelitis occurred sporadically with epidemics in high-income countries in temperate zones. In tropical countries, where the virus still circulates, there is no seasonal pattern.

Classically, poliomyelitis is a disease of young children and adolescents. In countries where polio was endemic, most children acquired antibodies to all three subtypes by age 5 years and most paralytic disease occurred in children aged under 3 years. However, with improvements in living standards a greater number of cases have occurred at an older age, particularly in early adult life, with an associated higher frequency of paralytic disease.

In the 30 years since the Global Polio Eradication Initiative began, an estimated 18 million cases of paralytic poliomyelitis have been prevented, and out of 125 countries, two have ongoing transmission of wild-type 1 disease (Afghanistan and Pakistan).[1] No wild-type disease has been detected in Nigeria since 2016, and the WHO hopes to declare Africa wild poliovirus free in 2020.[2] Although wild-type 2 and 3 polio have been eradicated, there was a dramatic increase in polio cases during 2019, primarily due to outbreaks in Pakistan which spread across its borders to Afghanistan and Iran.[1] Disruption of immunisation programmes and poor sanitary conditions has enabled polio to spread, and in some countries, there are pockets of children unable to be accessed for vaccination due to conflict.

The risk of international spread of poliovirus was declared as a Public Health Emergency of International Concern in May 2014. Further to wild-type 1 disease, the incidence of circulating vaccine-derived poliovirus types (cVDPV) within under-vaccinated populations is of significant international concern, particularly in Africa and South-East Asia (China, Malaysia, Philippines and Indonesia).[3] For up-to-date surveillance information and countries at risk of potential international spread of polioviruses, see the 'Polio Now' section of the Global Polio Eradication Initiative website (**polioeradication.org/polio-today/polio-now**).

There was a synchronised global switch to bivalent oral polio vaccine (bOPV) in 2016 in countries with circulating polio once the wild-type 2 disease was declared eradicated. In these countries, OPV is used together with inactivated poliovirus vaccine (IPV). Many countries without circulating virus have discontinued OPV and provide only IPV to eliminate the risk vaccine-associated paralytic poliomyelitis (VAPP). However, shortages of IPV supply led to delays in this switch and mixed schedules have continued. A revised Polio Eradication & Endgame Strategic Plan 2019–2023 has been developed by the Global Polio Eradication Initiative.[4] Its goal is 'the complete eradication and containment of all polioviruses'. Vaccination will continue worldwide until all polio has been eradicated.[1]

17.3.2 New Zealand epidemiology

Since 1962 only six polio cases have been reported. Four of these cases were laboratory confirmed as VAPP and two were classified as probable VAPP.[5] The last case of VAPP was reported in 1999.[6] No cases have been reported since IPV replaced OPV in 2002.

The New Zealand Paediatric Surveillance Unit carries out active surveillance of acute flaccid paralysis (AFP). In 2019 there were nine notifications: all were reviewed by the New Zealand National Certification Committee for the Eradication of Polio and all were classified as non-polio (ESR, 8 June 2020).

The risk of importing wild-type or neurovirulent oral vaccine-derived (cVDPV) strains means that maintaining high IPV coverage in New Zealand is essential.

For further details, refer to the ESR annual notifiable disease reports (available at **surv.esr.cri.nz/surveillance/IPD.php**).

17.4 Vaccines

New Zealand switched from OPV to IPV in 2002 (see Appendix 1).

17.4.1 Available vaccines

Funded polio vaccines

The polio-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 6.4.1 for more information)
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (see section 6.4.1 for more information)
- IPV (IPOL, Sanofi): contains three strains of poliovirus (40D antigen units of the Mahoney, 8D antigen units of the MEF-1 and 32D antigen units of the Saukett strains), inactivated by formaldehyde and containing phenoxyethanol as a preservative; trace amounts of neomycin, streptomycin, polymyxin B, polysorbate 80 and bovine serum albumin may be present.

Other vaccine

Adacel Polio (Sanofi) is a Tdap-IPV vaccines registered (approved for use) and available (marketed) in New Zealand.

17.4.2 Efficacy and effectiveness

See also section 15.4.2 for information about DTaP-IPV-HepB/Hib vaccine.

Immunogenicity and efficacy

IPV induces good systemic immune responses to protect against paralytic polio, but does not induce adequate intestinal neutralising antibody to interrupt faecal-oral transmission in regions with circulating polioviruses and with poor sanitation.[7]

Virtually all infants (99–100 percent) will seroconvert against all three strains after three doses of IPV vaccine, and more than 95 percent will seroconvert after two doses.[8] The efficacy of IPV is greater than 90 percent and immunity is expected to be long lasting.[9] Although antibody may decline over time in some individuals, there is no evidence that this leads to increased susceptibility to poliomyelitis.[10]

The combined IPV-containing vaccines induce immune responses against polioviruses superior to IPV stand-alone vaccines. This is due to the effect of the aluminium adjuvant present in these combination vaccines.[9]

Although immunocompetent adults previously immunised with OPV are expected to have lifelong protection against paralytic disease,[10] a study in Australia found that adolescents and young adults who were primed only with OPV had lower levels of serum neutralising antibody than the younger cohorts who had received OPV and at least one dose of IPV.[11] This data suggests that immunity provided by OPV primary schedule can be boosted by IPV to maintain individual immunity.

17.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib vaccine should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

17.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

The dose of IPV (IPOL) is 0.5 mL, administered by subcutaneous injection.

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and IPV may be given at the same time as inactivated or live attenuated vaccines, at separate sites and in separate syringes.

17.5 Recommended immunisation schedule

Table 17.1: Immunisation schedule for IPV-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster

17.5.1 Usual childhood schedule

A primary course of poliomyelitis vaccine is given as DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, followed by a booster dose given as DTaP-IPV at age 4 years (see Table 17.1).

17.5.2 Unimmunised adults and children

For partially immunised or previously unimmunised individuals, a primary immunisation course consists of three doses of IPV-containing vaccine (funded). The recommended interval is eight weeks between doses, but the minimum interval can be as short as four weeks for catch-up of children or adults (see Appendix 2).[12]

If a course of vaccine is interrupted, it may be resumed without repeating prior doses. A booster may be given if 10 years have elapsed since the last dose and exposure is possible (eg, in the case of a traveller to an area where the virus circulates; this is not funded).

If a child who began a course of OPV in another country moves to New Zealand, they can switch to IPV to complete the final doses. A further dose of IPV should be administered even if they have completed a full OPV (OPV or bOPV) course.

Note: All immunocompromised individuals and their household contacts may receive IPV. OPV was contraindicated in the immunocompromised because of the risk of VAPP. There is no risk of VAPP with IPV.

17.5.3 Pregnancy and breastfeeding

No adverse effects on the fetus have been reported following administration of IPV during pregnancy, but immunisation should not be carried out during the first or second trimester unless there are compelling reasons to do so, such as planned travel to an endemic area. However, bear in mind that pregnant women are particularly susceptible to paralytic polio.

If a previously unvaccinated pregnant woman is travelling to a country where polio is occurring, two doses should be administered four weeks apart prior to departure. If departure cannot be delayed allowing a four-week gap, give two doses at the maximum possible interval, though protection cannot be guaranteed. If the available interval is less than two weeks, a single dose is recommended, with further doses given on arrival where possible.

IPV may be given to breastfeeding women.

17.5.4 (Re)vaccination

Polio-containing vaccines are funded for (re)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

IPV (IPOL)

IPV is funded for patients following immunosuppression.

17.5.5 Recommendations for other groups

Booster doses of IPV are recommended (but not funded) for:

- all travellers to areas or countries where poliomyelitis remains endemic or with cVDPV (see section 17.3.1), who should receive a pre-travel polio booster
  - Under the Public Health Emergency of International Concern (PHEIC) regarding polio, proof of polio vaccination is required on **departure** from certain countries. See Global Polio Eradication Initiative website for the current country list: **polioeradication.org/polio-today/polio-now/public-health-emergency-status**
  - Evidence of polio vaccination (a booster dose of IPV given 4 weeks to 12 months prior to exit from these countries) must be recorded on an International Certificate of Vaccination and Prophylaxis (ICVP).
  - An adult polio booster is recommended also for those travelling to countries that have cVDPV-2 only.[1]
- health care workers in direct contact with a case of poliomyelitis
- individuals at particular risk of exposure (eg, laboratory workers routinely handling faecal specimens from persons recently arriving from high-risk countries, which may contain wild or vaccine-derived polioviruses); a booster dose of IPV is recommended every 10 years.

All the above should have completed a primary course of polio vaccines. See Table 4.9 for those for whom IPV is particularly recommended. Where there is uncertainty about previous immunisation, a full course of IPV is recommended (see Appendix 2). There is no evidence for the need for routine boosters, but they are recommended to reduce any possible risk from waning immunity in situations of increased risk of exposure.

17.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

17.6.1 Contraindications

IPV-containing vaccines are contraindicated if there is a history of an anaphylactic reaction to a previous dose or to any of the vaccine components.

See also section 15.6 for information about DTaP-IPV-HepB/Hib vaccine.

17.6.2 Precautions

Pregnancy is a precaution for IPV-containing vaccination, but may be given to women who clearly need it. See section 17.5.3.

17.7 Potential responses and AEFIs

See also section 15.7 for information about DTaP-IPV-HepB/Hib and DTaP-IPV vaccines.

17.7.1 Potential responses

A small proportion of individuals experience mild local symptoms following IPV. Injection-site erythema is seen in 1–2 percent of infants, induration in 3–11 percent and pain in 14–29 percent. Similar local reactions are seen with combination vaccines.[9] There is no poliovirus excretion following IPV.

17.7.2 AEFIs

Serious adverse events are very rare following administration of the IPV currently manufactured.[8] See section 15.6 for information about DTaP-IPV-HepB/Hib vaccine.

17.8 Public health measures

It is a legal requirement that all suspected cases of poliomyelitis be notified immediately on suspicion to the local medical officer of health.

Collect two faecal specimens 24 hours apart, 0–14 days after the onset of paralysis and send to the national poliovirus reference laboratory at ESR.

Contact the polio reference laboratory for specific advice on the specimens required, and on packing and transporting the specimens (see also the 'Single human source specimen form', available on the ESR website: **www.esr.cri.nz/our-services/testing/test-request-forms/**).

All cases of acute flaccid paralysis must be investigated as suspected poliomyelitis. All clinicians caring for any person aged under 15 years with AFP must notify the case to the local medical officer of health and report the case to the New Zealand Paediatric Surveillance Unit. If in a hospital, all cases of AFP should also be discussed with a local microbiologist and infection control service.

Case investigation and surveillance for AFP will continue in New Zealand to monitor the successful eradication of polio.[13] The New Zealand Paediatric Surveillance Unit is based at the University of Otago and is responsible for sending case investigation and follow-up forms to clinicians to continue to monitor that New Zealand has eradicated polio and to provide information to the WHO.

Any case of poliomyelitis in New Zealand constitutes a Public Health Emergency of International Concern, and the Director of Public Health at the Ministry of Health should be contacted urgently. The *National Poliomyelitis Response Plan for New Zealand (Updated 2019)* outlines the actual response and is published on the Ministry of Health website (**health.govt.nz**).[13]

Although wild-type polio has been eradicated in the WHO Western Pacific Region, circulating vaccine-derived poliovirus has been notified within the region (Indonesia, Philippines, China). New Zealand continues to need high levels of IPV coverage because of the small risk that polio may be imported from regions where poliovirus remains in circulation (see section 17.3.1).

For more details on control measures, refer to the 'Poliomyelitis' chapter of the *Communicable Disease Control Manual*[14] (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

17.9 Variations from the vaccine data sheets

See section 15.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets.

The IPV (IPOL) data sheet recommends three doses of vaccine administered at eight-week intervals.[15] The Ministry of Health recommends that this schedule may be shortened to four-week intervals for catch-up (see Appendix 2).

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18 Rotavirus

Key information

Mode of transmission	Faecal–oral route through close personal contact and fomites.
Incubation period	1–3 days.
Period of communicability	During symptoms and until approximately 8 days after onset of symptoms. Up to 30 days after onset of symptoms in immunocompromised patients.
Burden of disease	All children during infancy or early childhood. Severe disease occurs most often in children aged 3 months to 2 years.
Funded vaccine	Oral live attenuated monovalent rotavirus: RV1 (Rotarix).
Dose, presentation, route	1.5 mL per dose. Oral suspension in an oral applicator, Administered orally.
Funded vaccine indications and schedule	2 doses for infants, at ages 6 weeks and 3 months. For catch-up schedules, the first dose should be given before age 15 weeks (latest is 14 weeks and 6 days), and the 2nd dose should be given before age 25 weeks (latest is 24 weeks and 6 days).
Vaccine effectiveness	Highly effective against severe rotavirus diarrhoea; some evidence for efficacy against all-cause diarrhoea and herd protection.
Contraindications	Previous intussusception and with conditions that predispose the infant to intussusception. Severe combined immune deficiency.
Precautions and special considerations	Infants living in households with immunocompromised persons or pregnant women should still be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household contacts. Immunosuppressed infants including those on immunosuppressive therapy (other than SCID, where it is contraindicated). Infants born to mothers on immunosuppressive biologic agents (see section 18.6.2).
Potential responses to vaccine	A possible, very small risk for intussusception; the benefits of immunisation considerably outweigh this potential risk.

18.1 Virology

The rotaviruses are segmented, double-stranded RNA viruses of the family Reoviridae.[1] They are classified according to two surface proteins on the outer capsid: VP4 protease cleaved 'P' protein and VP7, the 'G' glycoprotein, which allows a binary classification system. The G and P proteins are immunological targets for neutralising antibodies protecting against disease and re-infection.[2] While more than 60 G and P combinations have been found in humans, there are only five strains (P[8]G1, P[4]G2, P[8]G3, P[8]G4, and P[8]G9) that are associated with 80–90 percent of the global burden of disease in children.[3] For simplicity, these strains are commonly referred to by their G serotype as G1, G2, G3, G4 and G9.

18.2 Clinical features

Rotavirus infects almost all children during infancy or early childhood. Transmission occurs through the faecal–oral route through close personal contact and through fomites. Aerosol transmission has been hypothesised but remains unproven.[1]

The incubation period is one to three days, after which illness can begin abruptly, with fever and vomiting often preceding the onset of diarrhoea.[1, 4] Up to one-third of children will develop a fever of greater than 39°C.[5, 6] The illness lasts from three to eight days.

Children with rotavirus are infectious while they have symptoms and until approximately eight days after the onset of symptoms. Immunocompromised patients may be infectious for up to 30 days after the onset of symptoms.[7] Large quantities of rotavirus are shed in the stool, and only a few virions are required to cause infection in a susceptible host.[8]

Rotavirus infection in the first three months of life is frequently mild or asymptomatic. This is possibly due to passive protection from maternally acquired antibodies, being breastfed and the intestinal cell structure of newborn infants.[1, 9]

The burden of severe dehydrating gastroenteritis caused by rotavirus occurs predominantly in infants and children aged 3 months to 2 years.[3]

The clinical spectrum ranges from asymptomatic infection to an acute severe illness with frequent and large-volume diarrhoea and vomiting, leading to dehydration, electrolyte disturbance and their sequelae. The illness spectrum from rotavirus is more severe than from other common causes of diarrhoea in children.[1]

18.3 Epidemiology

18.3.1 Global burden of disease

Rotavirus gastroenteritis is a significant cause of infant diarrhoea worldwide, both in high- and low-income countries. Virtually all children are infected by age 5 years.[1] Each year rotavirus causes the death of approximately 200,000 to 450,000 children aged under 5 years worldwide[10, 11] and results in 2.4 million paediatric hospital admissions.[12] Virtually all of the deaths occur in low-income countries. Prior to the introduction of licensed rotavirus vaccines in high-income countries, more than 220,000 children were hospitalised with rotavirus gastroenteritis every year.[13, 14]

Rates of rotavirus illness in children before the introduction of vaccine were similar in high- and low-income countries, indicating that good hygiene and clean water supplies are unlikely to have a significant impact on disease prevention. As a result, immunisation is the primary public health measure for the reduction of rotavirus disease burden.[1]

In countries with a temperate climate, rotavirus epidemics occur every winter and spring. Factors associated with an increased risk of severe rotavirus gastroenteritis include age under 2 years, low birthweight, premature gestation, lack of breastfeeding, socioeconomic disadvantage, malnutrition and impaired immunity.[1, 15, 16, 17, 18] Rotavirus gastroenteritis is not, however, more severe in HIV-infected children, although viral shedding may be longer.[3]

Rotavirus is an important cause of hospital-acquired infection[19] and can also cause disease in adults, especially those caring for children[20] and those living in aged-care facilities. During outbreaks in early childhood settings, rotavirus has been isolated from telephone receivers, drinking fountains, water-play tables and toilet handles.[21] Outbreaks in elderly populations may be linked to waning immunity, institutional crowding or both.

Children and adults can be infected with rotavirus several times in their lives. After a single natural infection during infancy, approximately one-third are protected against subsequent rotavirus infection, more than three-quarters are protected against subsequent rotavirus gastroenteritis and 85–90 percent are protected against severe rotavirus gastroenteritis.[22] The proportion with protection against both infection and symptomatic rotavirus gastroenteritis increases with successive episodes.[22]

These observations serve as the biological basis for rotavirus vaccines, whereby live attenuated strains can induce cumulative protective immunity similar to that following natural infection by wild-type rotaviruses. Although the immune mechanism and correlates of protection against rotavirus infection are incompletely understood, it is likely that both mucosal and serum antibodies are associated with protection against rotavirus infection and disease.[23]

Since the introduction of the vaccine in other high-income countries, there have been reductions in all-cause and rotavirus gastroenteritis in age groups not eligible for the vaccine, suggesting herd immunity effects as a result of rotavirus vaccines[3, 24, 25] (see 'Herd immunity in the post-licensure period' in section 18.4.2).

18.3.2 New Zealand epidemiology

Rotavirus vaccine was introduced in July 2014, as a three-dose schedule to infants at ages 6 weeks, 3 months and 5 months, using the RV5 vaccine (RotaTeq) (see Appendix 1).

At present rotavirus is not a notifiable disease, so there is no national surveillance data available. National hospital discharge rates, community and hospital laboratory data plus a sentinel hospital-based surveillance system have been used to monitor rotavirus disease since vaccine introduction. The sentinel hospital-based rotavirus surveillance was introduced in December 2014 at Kidz First Children's Hospital in Counties Manukau DHB and extended to Wellington, Hutt and Christchurch Hospitals in April 2016.

For detailed information about rotavirus surveillance and rotavirus infections in New Zealand, see the ESR website (**surv.esr.cri.nz/surveillance/Rotavirus.php**).

Pre-vaccine epidemiology

Prior to the introduction of vaccine, by the age of 5 years, it is estimated 1 in 5 children had sought medical advice for rotavirus gastroenteritis and 1 in 43 children had been hospitalised.[13]

From 2010 to 2014, the average annual national hospitalisation rate for rotavirus in children aged under 5 years was 215.4 per 100,000.[26] The highest hospitalisation rates for children aged under 5 years were in those from the Middle Eastern/Latin American/African ethnic group, followed by Pacific and Māori ethnic groups. Hospitalisation rates in children aged under 5 years who reside in the most deprived NZDep2013 quintiles (quintiles 4 and 5) were significantly higher than those who reside in the least deprived quintile. There is a seasonal peak for rotavirus hospitalisations, usually occurring around September each year.

Post-vaccine epidemiology

The introduction of rotavirus vaccination in Australia resulted in a 70 percent decrease in rotavirus hospitalisations in the two and a half years post-vaccine introduction.[27]

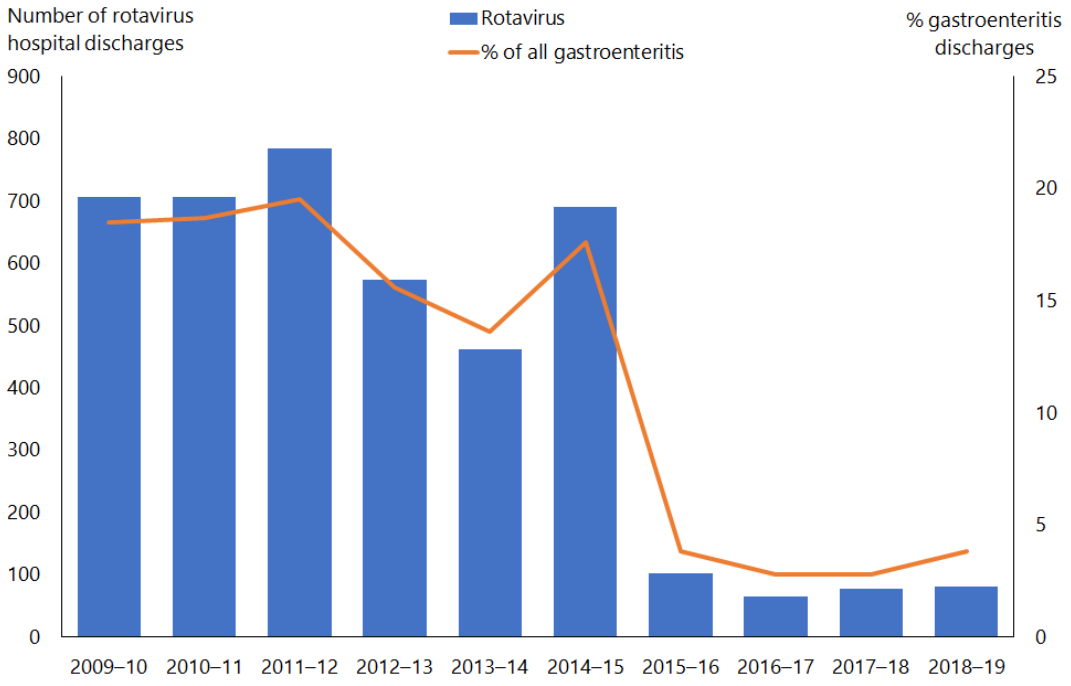
A similar decline has been noted in New Zealand in the first year post-vaccine introduction, where rotavirus hospitalisation rates for children aged under 5 years declined by 85 percent in 2015 compared with the previous five-year average (2010–2014)[26] (Figure 18.1). The vaccine has been effective in decreasing the most severe rotavirus disease. Hospitalisation rates decreased for all ethnic groups and levels of socioeconomic deprivation. Community laboratory data also supports the large decrease in rotavirus infections in the community.

Although only children aged under 1 year were eligible for rotavirus vaccination, hospital discharge rates decreased in all children aged under 5 years in 2015[26] (Figure 18.2). Older children are more likely to have been exposed to rotavirus already, and are less likely to benefit from vaccination.

Hospital discharges for rotavirus ranged from 510 to 822 cases per year in the four years prior to vaccine introduction (2010–2013).[26] There were 99 hospital discharges for rotavirus in children aged under 5 years in New Zealand in 2015, compared with 770 in 2014. This reduction in rotavirus hospitalisations of children aged under 5 years was maintained to 2019, with 80 cases hospitalised in the year to June 2019.

There was a 93.6 percent decrease in rotavirus outbreaks (three outbreaks reported in 2015 compared with 47 in 2014) after the introduction of vaccine in New Zealand.[26] This demonstrates that universal rotavirus vaccination is an effective public health intervention.

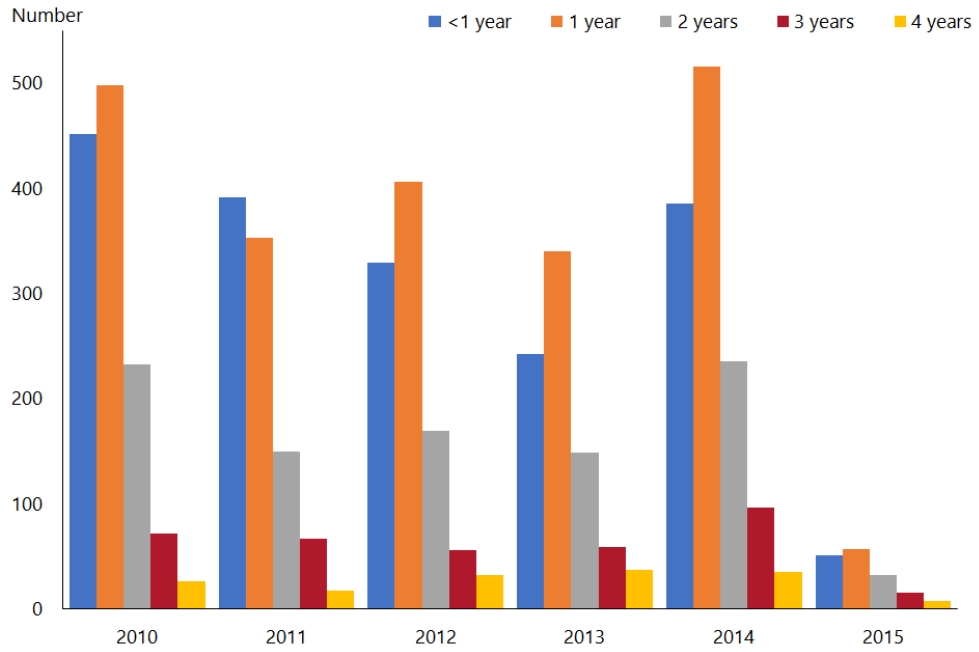
Figure 18.1: Rotavirus hospital discharges and as a percentage of all gastroenteritis discharges for children aged under 5 years, all New Zealand, June 2009–June 2019



Note: Rotavirus vaccine introduced in July 2014.

Source: Ministry of Health.

Figure 18.2: Rotavirus hospital discharge rates for children aged under 5 years by age and year, all New Zealand, 2010–2015



Source: ESR

18.4 Vaccines

18.4.1 Available vaccines

The types of virus assessed for use as rotavirus vaccines have included live attenuated virus, both human and animal strains of the virus, and human–animal reassortant viruses. Two rotavirus vaccines have been used in New Zealand. Both are orally administered live attenuated vaccines and have been extensively evaluated.[28, 29] The live attenuated vaccine viruses replicate in the intestinal mucosa and are shed in the stools of vaccine recipients.[28, 30, 31]

Funded vaccine

RV1 (Rotarix, GSK) is a live attenuated monovalent human G1P1A[8] strain rotavirus vaccine. It protects against non-G1 serotypes (these include G2P[4], G3P[8], G8P[4], G9P[8] and G12P[6]) on the basis of other shared epitopes. Each 1.5 mL dose contains:

- at least 106 CCID50 (cell culture infective dose 50 percent) of the RIX 4414 strain of human rotavirus
- other components and residuals, including sucrose, disodium adipate and culture medium.

18.4.2 Efficacy and effectiveness

Prevention of disease

A 2012 Cochrane review[32] of the efficacy of rotavirus vaccines for the prevention of rotavirus diarrhoea assessed 41 trials which met the inclusion criteria, involving 186,263 enrolled participants. Of these, 29 trials assessed the monovalent vaccine (RV1; Rotarix) and 12 trials assessed the pentavalent vaccine (RV5; RotaTeq).

For the first two years of life in countries with low mortality rates, both vaccines prevented over 80 percent of cases of severe rotavirus diarrhoea (Table 18.1). Both vaccines impact severe all-cause diarrhoea (moderate to low quality of evidence). See also Figure 18.1 and Figure 18.2 above, which show a reduction in rotavirus hospitalisations in New Zealand children aged under 5 years after rotavirus vaccine was introduced in 2014.

Table 18.1: Cochrane review: percentage of severe rotavirus and all-cause diarrhoea cases prevented in children by RV1 and RV5, compared to placebo (low mortality rate countries)

Vaccine	Percentage of cases prevented	Risk ratio (95% confidence interval)	Number of participants (number of trials)	Quality of evidence
Severe rotavirus diarrhoea: infants aged under 1 year				
RV1	86	0.14 (0.07–0.26)	40,631 (6)	High
RV5	87	0.13 (0.04–0.45)	2,344 (3)	Moderate
Severe rotavirus diarrhoea: children aged under 2 years				
RV1	85	0.15 (0.12–0.2)	32,854 (8)	High
RV5	82	0.18 (0.07–0.5)	3,190 (3)	Moderate
Severe all-cause diarrhoea: infants aged under 1 year				
RV1	40	0.60 (0.5–0.72)	17,867 (1)	Moderate
RV5	72	0.28 (0.16–0.48)	1,029 (1)	Low
Severe all-cause diarrhoea: children aged under 2 years				
RV1	37	0.63 (0.56–0.71)	39,091 (2)	Moderate
RV5	96	0.04 (0.00–0.70)	5,916 (1)	Low

Adapted from: Soares-Weiser K, MacLehose H, Bergman H, et al. 2012. Vaccines for preventing rotavirus diarrhoea: vaccines in use. *Cochrane Database of Systematic Reviews* Issue 11, Art. No. CD008521. DOI: 10.1002/14651858.CD008521.pub3 (accessed 24 June 2020).

Effectiveness

In pre-marketing clinical trials, rotavirus vaccination prevented 42–58 percent of all-cause hospital admissions for acute gastroenteritis, suggesting it is responsible for more gastroenteritis than is detected by routine testing.[28, 33, 34]

Post-licensure surveillance studies have demonstrated large reductions in rotavirus-positive stool isolates from children with gastroenteritis (US)[35] and in diarrhoea-related deaths (Mexico).[36, 37] Summarised, post-licensure vaccine effectiveness studies in high-income countries have shown an 89–100 percent reduction in emergency department visits or hospitalisation; a 74–90 percent decline in hospitalisations for rotavirus gastroenteritis in children aged under 2 years; and a 29–50 percent decline in 'all-cause' acute gastroenteritis hospitalisations for children aged under 5 years.[38]

A protective association between rotavirus vaccine and childhood seizures has been reported in the US[39] and Australia.[40] In US children, a full course of rotavirus vaccination was associated with an 18–21 percent reduction in the risk of seizure requiring hospitalisation or emergency department care in the year following vaccination, compared with unvaccinated children.[39] In the Australian state of Queensland, rotavirus vaccine was 35.8 percent effective at preventing emergency department presentation for febrile seizures and 38.0 percent effective at preventing subsequent hospitalisation in children up to two years following vaccination.[40]

Herd immunity in the post-licensure period

Since the beginning of the post-licensure period, over 80 countries have introduced the rotavirus vaccine into their national immunisation programmes.[41] There has been substantial though somewhat variable efficacy data to show a decline in rotavirus infections in the different country environments. In the US, there was a 73 percent reduction in rotavirus infections among infants from 2003 to 2014.[42] The effectiveness tends to wane with age, and rotavirus 'seasons' appear to be longer in the post-licensure period.[42]

While a decline has occurred in rotavirus infection alone, there has also been a reduction in all-cause diarrhoeal illnesses.[41] Furthermore, the protective effect of the vaccine has surpassed the expected level of vaccine efficacy and coverage, resulting in a herd protection. Therefore, the immunised proportion of the population is causing a reduction of infection in the unimmunised portion of the community.[43]

Duration of protection

Prior to the introduction of rotavirus vaccines in Europe, extension studies of the pivotal phase III RV5 trial showed protection lasting up to three years from the last vaccine dose.[44] The duration of protection provided by rotavirus vaccines is difficult to measure because of the herd immunity effect that occurs after the vaccine is implemented. Some studies indicate waning immunity after the first year of life, particularly in low-income countries.[45, 46] In a large multicentre study in the US, both RV1 and RV5 vaccines were found to provide lasting and broadly heterologous protection against infection. Vaccine effectiveness persisted to the seventh year of life for RV5 and through the third year of life for RV1.[47] Note that the differences in duration are because RV1 was licensed in the US approximately two years later than RV5, affecting vaccination coverage and corresponding study power for older age groups for RV1 analyses.[47]

Partial vaccination

Studies in partially vaccinated infants (ie, those who had not completed the three-dose course of RV5 or the two-dose course of RV1) found that protection against rotavirus gastroenteritis ranged from 51–55 percent in low- and middle-income countries, and from 69–93 percent in high-income countries.[48]

Cross-protection

Rotavirus vaccine strains vary considerably, and multiple wild-type strains can occur at the same time. In high-income countries, both vaccines appear to provide some cross-protection against non-vaccine serotypes.[49, 50] Vaccine protection against newly emerging genotypes is not well known, and national surveillance of circulating rotavirus types post-vaccination is necessary.[51]

18.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store in the dark at +2°C to +8°C. Do not freeze.

18.4.4 Dosage and administration

The dose of RV1 (Rotarix) is 1.5 mL, administered orally (for administration instructions see section A7.2.4 of this *Handbook* or the vaccine data sheet, available at **medsafe.govt.nz**). Do not inject RV1.

Two doses are given, at ages 6 weeks and 3 months. See section 18.5 below for more information.

Co-administration with other vaccines

Rotavirus vaccines can be administered at the same time as other scheduled vaccines. Note that no time interval is required between administration of rotavirus and BCG vaccines; the two live vaccines likely to be administered to infants aged under 6 months.

If the dose is regurgitated or vomited

If the dose of rotavirus vaccine is regurgitated or vomited during or after administration, a repeat dose *should not be given*.[52] The second dose should be administered as per the schedule. Receptor binding of vaccine is instantaneous, making repeat dosing unnecessary.

If the first dose is immediately spat out then a single repeat dose could be given.

18.5 Recommended immunisation schedule

RV1 is recommended and funded for all infants. See section 18.5.2 for RV1 age limit information.

Immunisation is especially encouraged for those who will be attending early childhood education services or where there is an immunocompromised individual living in the household.

Infants who have already had rotavirus gastroenteritis should still receive the full course of immunisation. Initial rotavirus infection only provides partial protection against subsequent infection.[1, 22]

18.5.1 Routine schedule

Two RV1 doses are given orally, at ages 6 weeks and 3 months.

Table 18.2: The infant RV1 (Rotarix) schedule

Dose	Usual scheduled age	Recommended age limits for dosing
Dose 1	6 weeks	6–14 weeks[a]
Dose 2[b]	3 months	10–24 weeks[c]

a. The upper age limit for receipt of the first dose of RV1 is immediately prior to turning 15 weeks old (14 weeks and 6 days).

b. The minimum interval between doses 1 and 2 is 4 weeks.

c. The upper age limit for receipt of the second dose of RV1 is immediately prior to turning 25 weeks old (24 weeks and 6 days).

18.5.2 Catch-up schedules

The first dose of RV1 should be given before age 15 weeks (ie, 14 weeks and 6 days), and the second dose administered at least four weeks later (see Table 18.2). An infant who has not had the first dose before age 15 weeks will not be able to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the second dose should be given, but both doses should be given before age 25 weeks (ie, the latest is 24 weeks and 6 days).[1] Rotavirus vaccine is not intended for use in older children, adolescents or adults.

The age limits for initiating and completing the vaccine series are recommended because there is insufficient safety data on the use of these vaccines outside this age range. If a partially vaccinated infant reaches age 25 weeks before the second dose is given, the first dose already given will offer them partial protection against disease.

The severity of rotavirus infection decreases with age, so a cost–benefit analysis for vaccinating older children is a low priority and has not been done.

18.5.3 Preterm infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm infants and infants with low birthweight, including those still in hospital (see below). Rotavirus vaccine can be given to preterm infants born who are receiving corticosteroids. (See also 4.2.1 for more immunisation recommendations for preterm infants.)

18.5.4 Hospitalised infants

Rotavirus vaccine should be given on time to any infant admitted to a general hospital ward (where other patients are not high risk). If standard infection control precautions are maintained, there is no risk of transmission of vaccine strain rotavirus when rotavirus vaccine is administered to hospitalised infants, including hospitalised preterm infants and those in neonatal units.[53, 54] (See also section 4.2 for more information about infants with special immunisation recommendations.)

18.5.5 Pregnancy and breastfeeding

There is no concern caused by vaccine exposure during pregnancy. There is no restriction for breastfeeding before or after vaccination of the infant (see 'Shedding' in section 18.6.2).

18.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

18.6.1 Contraindications

Rotavirus vaccine should not be given to infants with:

- a history of a severe (anaphylactic) allergic reaction after a previous dose or to a vaccine component
- a history of intussusception or an uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant to intussusceptions (see section 18.7.1).
- severe combined immunodeficiency (SCID).[55]

18.6.2 Precautions

Rotavirus vaccine can be administered to infants with a mild illness, including gastroenteritis and upper respiratory tract infections. Infants with moderate to severe gastroenteritis should not be vaccinated until symptoms resolve.

There is very little safety data on infants with predisposing conditions such as metabolic disorders and chronic gastrointestinal diseases (Hirschsprung's, malabsorption syndromes or short gut syndromes). Since there is a greater risk of serious wild-type rotavirus disease, the benefits outweigh the risk, and vaccination is encouraged.[52]

Infants who have received antibody-containing blood products and are the appropriate age should be vaccinated. Rotavirus vaccine and antibody-containing blood products can be administered simultaneously.[52] There is a theoretical risk of interference in the immune response to the vaccine; therefore the interval between vaccination and receipt of blood products should ideally be as long as possible within the age limits of the vaccine schedule.

Administration of RV1 in immunosuppressed infants, including infants on immunosuppressive therapy, should be based on careful consideration of potential benefits and risks.

Infants born to mothers on immunosuppressive therapies

There is limited data on rotavirus vaccination safety when given to infants born to mothers receiving immunosuppressive therapy during pregnancy.[19, 36, 56] Although in most cases it is likely to be safe, caution is required. The level of circulating wild-type rotavirus is currently very low in New Zealand; therefore, the risk of gastroenteritis following rotavirus vaccination in this cohort of infants may be greater than the risk of acquiring the disease. The decision to administer rotavirus vaccine to infants born to mothers who received immunosuppressive agents (biologic agents) during pregnancy should be determined case by case.

If an infant turns 15 weeks of age before the first rotavirus vaccine dose can be administered, they will not be able to receive any rotavirus vaccine doses.

See section 4.3.7 and Table 4.2 for a list of the highly immunosuppressive medications with long half-lives that require a prolonged delay before vaccination (for up to one year in those being treated). These include monoclonal antibody (mab) agents that readily cross the placenta.

Each case should be assessed on a risk–benefit basis and with specialist advice.

Shedding

Since rotavirus vaccine virus replicates in the gastrointestinal tract, it can be shed in stools – especially after the first dose.[57] Shedding is also more likely in immunocompromised patients (eg, children with HIV). The vaccine virus could then be transmitted to unvaccinated populations; a feature that is generally beneficial as it promotes herd immunity.

Infants living in households with immunocompromised individuals should be vaccinated. So far there are no safety concerns, but there is also no data to confirm the safety of these vaccines for immunocompromised patients. Infants living in households

with pregnant women should also be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household contacts.[52, 53]

18.7 Potential responses and AEFIs

The 2012 Cochrane review[32] described in section 18.4.2 also reviewed the safety of RV1 and RV5 vaccines. No significant difference was found between children receiving RV1 or RV5 and placebo in the number of serious adverse events, particularly intussusception (see below). No statistical differences were observed for fever, diarrhoea and vomiting between cases and placebo groups. There was no significant difference between cases and placebos in the number of adverse events leading to discontinuation of the schedule.

In 2010 porcine circovirus or porcine circovirus DNA was detected in both rotavirus vaccines. However, there is no evidence that this virus is a safety risk or causes illness in humans.[52]

18.7.1 Intussusception

Intussusception is a cause of an acute abdomen when one part of the intestine telescopes into another part of the intestine; the mechanism by which these events occur remains uncertain. In 1999 an oral human–rhesus rotavirus quadrivalent vaccine (RotaShield) was licensed in the US and on the infant schedule but was withdrawn later that year after reports of an association with intussusception (a risk of approximately one case in 5,000–10,000 vaccine recipients).

No increased risk of intussusception was detected in the large phase III pre-licensure clinical trials of RV1 (Rotarix) and RV5 (RotaTeq), despite this being a specifically monitored adverse event. However, post-marketing surveillance of both rotavirus vaccines indicates the possibility of an increased risk of intussusception shortly after the first dose of rotavirus vaccination. Evidence from Australia[58] indicates that after the first dose, RV1 had a relative incidence (relative risk) of 6.8 (95% CI: 2.4–19.0, $p<0.001$) and 3.5 (95% CI: 1.3–8.9, $p=0.01$) for the periods of 1–7 days and 8–21 days after vaccination, respectively. For RV5, the relative incidence was 9.9 (95% CI: 3.7–26.4, $p<0.001$) and 6.3 (95% CI: 2.8–14.4, $p<0.001$) for the same time periods.

There was also some elevated risk of intussusception 1 to 7 days after the second dose of both vaccines. The relative incidence for RV1 was 2.8 (95% CI: 1.1–7.3, $p=0.03$) and for RV5 was 2.8 (95% CI: 1.2–6.8, $p=0.02$). There was no evidence of increased risk of intussusception following a third dose of RV5.[58] The increased risk of intussusception following rotavirus vaccination is estimated at approximately 6 additional cases of intussusception among every 100,000 infants vaccinated (approximately 1 in 15,500 vaccine recipientss), or 14 additional cases per year in Australia.[58]

Studies in the post-licensure period continue to show small increases in risk for both RV1 and RV5 and primarily within seven days of the first dose of vaccine.[59, 60] Recent safety data has continued to emphasise the clear and dramatic benefit of vaccination over the very low risk of vaccine-associated intussusception.[41] For example, a self-controlled case-series study estimated that the RV1 programme in England caused 21 intussusception admissions annually and prevented 25,000 gastrointestinal infection admissions with a clear risk–benefit ratio.[61]

While there appears to be an increased relative risk of intussusception, the condition remains rare, and this risk is outweighed by the benefits of rotavirus vaccination in preventing rotavirus infections; there was an estimated 70 percent reduction in hospitalisations in young children after the vaccine's introduction to the Australian schedule.[62] It is uncertain whether rotavirus vaccine administration affects the overall incidence of intussusception: US data suggests no increased overall rate in infants despite a small cluster effect.[63] Both the WHO[64] and the Australian Technical Advisory Group on Immunisation[62] continue to recommend the use of rotavirus vaccine for infants.

Although the risk of intussusception after rotavirus immunisation is very small, it is recommended that parents seek medical advice and health care professionals are attentive if the baby develops intermittent crying or screaming episodes, pulling their knees towards their chest and vomiting, or pink- or red-coloured jelly-like stools.

A recent study has described the epidemiology of intussusception in New Zealand children aged 0–36 months (794 cases) for a 16-year period before the introduction of routine rotavirus vaccination.[65] This study will provide a valuable baseline to determine if the introduction of the vaccine has significant effects on intussusception rates in the New Zealand population.

18.8 Public health measures

Prevention of spread is by contact precautions, including careful handwashing. In an early childhood service setting where there has been a child known to have had a rotavirus infection, the surfaces should be washed with sodium hypochlorite (bleach) and water. Disinfectants inactivate rotavirus and may help to prevent disease transmission resulting from contact with environmental surfaces.[52]

For more details on control measures, refer to the 'Acute gastroenteritis' chapter of the *Communicable Disease Control Manual*[7] (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

18.9 Variations from the vaccine data sheet

The RV1 (Rotarix) vaccine data sheet states that if an infant vomits or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit. The Ministry of Health does not recommend repeating the dose (see section 18.4.4).[52]

The RV1 data sheet recommends postponing the administration of the vaccine in infants suffering from diarrhoea or vomiting. The Ministry of Health recommends vaccinating infants with mild gastroenteritis, and to wait until symptoms have resolved for infants with moderate to severe gastroenteritis (see section 18.6.2).

The RV1 data sheet states that the vaccine should not be administered to subjects with any chronic gastrointestinal disease. The Ministry of Health recommends instead that pre-existing chronic gastrointestinal disease is not a contraindication to rotavirus vaccination, with the exception of those conditions that may predispose the infant to intussusceptions (see sections 18.6.1 and 18.7.1).[53]

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19 Rubella

Key information

Mode of transmission	By contact with infected nasopharyngeal secretions. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine.
Incubation period	14–23 days, usually 16–18 days. Up to 50 percent of rubella infections are subclinical.
Period of communicability	7 days before until 7 days after the onset of the rash. Infants with CRS may be infectious for months.
Incidence and burden of disease	Endemic rubella was verified as eliminated in 2017. One imported case of rubella was notified in 2018. Cases continue in other regions, including China.
Funded vaccine	MMR is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. For (re)vaccination following immunosuppression, if the individual is immunocompetent enough to safely receive the vaccine.
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high-risk countries.
Vaccine efficacy/ effectiveness	Highly effective, 2 doses are anticipated to provide lifelong protection. Protection is best achieved through herd immunity from high immunisation coverage.
Contraindication	MMR is contraindicated for those with anaphylaxis to neomycin, immunocompromise and in pregnancy. See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions.

Precautions and special considerations	All pregnant women and women planning pregnancy should have their immunisation history checked. A woman is immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least 4 weeks apart and given after age 12 months, regardless of serology. Pregnant non-immune women should avoid contact with known cases of rubella and should receive MMR after delivery.
Potential response to vaccine	MMR is generally well tolerated. Temporary joint pain 2–4 weeks after vaccination due to rubella component of the vaccine is more common in adults than children. See section 12.7. Alert parents of possible febrile seizure risk, particularly for those with a history of seizure.
Public health measures	All suspected cases must be notified immediately on suspicion.

19.1 Virology

Rubella is an enveloped RNA virus from the family Togaviridae and the genus *Rubivirus*. It is less stable than measles virus and can be inactivated by solvents, trypsin, formalin, extremes of heat and pH, and light.[1]

19.2 Clinical features

> The purpose of the rubella immunisation programme is to prevent congenital rubella syndrome (CRS).

Rubella infection during pregnancy can result in fetal infection, causing CRS in a high proportion of cases. Rubella infection in the first 12 weeks of pregnancy results in fetal damage in up to 85 percent of infants, and multiple defects are common. The risk of damage declines to 50 percent by about 16 weeks' gestation and 25 percent by the end of the second trimester.[2] Fetal abnormalities are rare from infection in the third trimester of pregnancy.

Infants born with CRS may have cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow. Some infected infants may appear normal at birth, but have nerve deafness, oesophageal and eye defects, and diabetes detected later.[3] CRS is one of the few known causes of autism.[2]

Clinical features of rubella in children and adults include a transient erythematous rash and lymphadenopathy without respiratory symptoms. Arthritis or arthralgia is relatively common and a classic feature of infection in adults. While usually a mild childhood illness, rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs with a prevalence of approximately 1 in 6,000 cases

and may result in residual neurological damage or, occasionally, death. Thrombocytopenia rarely occurs.

Clinical diagnosis is unreliable because the symptoms are often fleeting and can be mimicked by other viruses. In particular, the rash is not diagnostic of rubella. Up to 50 percent of rubella infections are subclinical or asymptomatic. Asymptomatic cases are also able to transmit the virus. A history of rubella should therefore never be accepted as proof of immunity without laboratory confirmation.[3]

Transmission of rubella is through direct or indirect contact with infected nasopharyngeal secretions and droplets. The incubation period is usually 16–18 days (range 14–23 days) and infectivity is between seven days before and seven days after the onset of the rash. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine for months after birth and should be considered infectious until they are aged 12 months.

Although the vaccine virus is excreted after vaccination, mostly from the pharynx, transmission to susceptible contacts has not been demonstrated (see section 12.7.2). Therefore, a recently immunised contact is not a risk to a pregnant woman.

The frequency of complications and consequences of rubella infection are best described from the 1963/1964 US outbreak, involving 12.5 million cases of rubella and 30,000 infants damaged by intrauterine rubella, an incidence rate of 1 per 100 pregnancies (see Table 19.1).

Table 19.1: Estimated morbidity and mortality associated with the 1963/64 US rubella epidemic

Total number of cases of rubella:	**12,500,000**
Complications of rubella	**Risk per case**
Arthritis or arthralgia	13 per 1,000
Encephalitis	17 per 100,000
Neonatal deaths	17 per 100,000
Complications caused by congenital rubella syndrome (CRS)	**Numbers of cases (% of CRS cases)**
Total number with CRS	20,000
Deaf children	8,055 (40%)
Deaf–blind children	3,580 (18%)
Mentally disabled children	1,790 (9%)

Adapted from: Reef SE, Plotkin S. 2018. Rubella vaccines. In: Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th Edition*). Philadelphia, US: Elsevier. Table 53.7.

Rubella infection can occur (very rarely) in individuals with either naturally acquired or vaccine-induced antibody.[3] Rare cases of CRS have been reported after reinfection during pregnancy.[3]

As with measles, public health measures of accurately diagnosing potential cases of rubella with notification and contact tracing are critical (see section 19.8).

19.3 Epidemiology

19.3.1 Global burden of disease

Humans are the only source of rubella infection. Infection is often asymptomatic. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among 5–9-year-old children, and 80–90 percent of adults were immune to rubella. Extensive outbreaks of rubella occurred every six to nine years, in which many children were affected by CRS. Immunisation against rubella, introduced to prevent the occurrence of CRS, has resulted in a very significant reduction in infection, especially once vaccination was introduced to boys and girls.

The Global Vaccine Action Plan set a specific target to eliminate measles and rubella by 2020 and to reduce the incidence of CRS from 100,000 cases per year. The number of notified rubella cases fell from over 670,000 in 2000 to just over 22,000 in 2016. However, from January to September 2019, nearly 40,000 cases were reported: 92 percent of those cases were in China and 7 percent in Japan.[4]

Although rubella elimination has been verified in 81 countries, less than 70 percent of infants across 168 countries worldwide were immunised against rubella by the end of 2018.[5]

19.3.2 New Zealand epidemiology

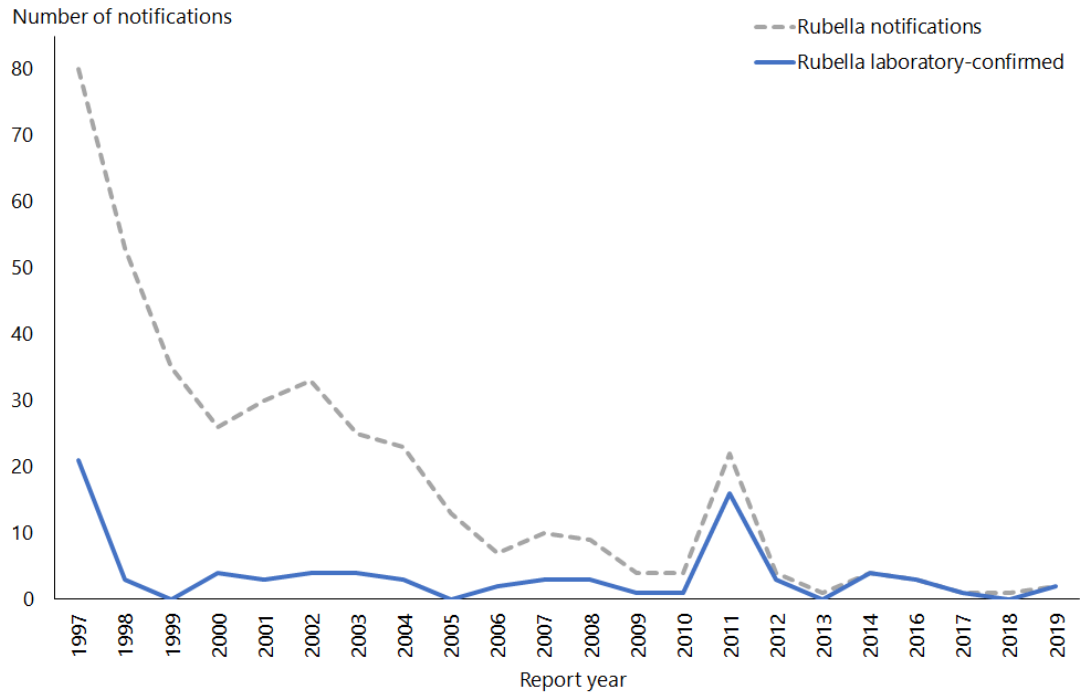
Rubella immunisation was introduced in 1970 (see Appendix 1), and rubella has been a notifiable disease since 1996. The last large rubella outbreak in 1995–1996 mostly involved young adult males, who would not have been offered immunisation. This emphasises the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.

Two cases of rubella were notified in 2019, in a male and a female both aged 30–39 years.

Rubella was verified as eliminated from New Zealand in October 2017. There have been no reported cases of CRS in New Zealand since 1998.

For further information, see the ESR's notifiable disease reports (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

Figure 19.1: Rubella notifications and laboratory-confirmed cases by year, 1997–2019



Source: ESR

19.4 Vaccines

19.4.1 Available vaccines

Rubella vaccine is one of the components of the live attenuated MMR vaccine (see section 12.4.1) (and also MMRV vaccine mentioned in section 22.4.1).

Funded vaccine

MMR funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella and Jeryl Lynn mumps. (See section 12.4.1 for more information.)

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 12.4.1).

19.4.2 Efficacy and effectiveness

The rubella vaccine has been shown to be 90–97 percent effective in an outbreak after a single dose, and this is likely to be higher with a two-dose schedule. One dose of rubella vaccine at 12 months or older induces an antibody response in at least 95 percent of recipients. Studies have found no evidence of waning of protection over decades of follow-up.[3] In more than 90 percent of recipients, antibodies persisted for at least 16 years; other studies have reported persistence up to 21 years.[3] A few recipients fail to produce antibodies following immunisation, and a small number of individuals lose antibodies, whether they are derived from natural infection or the vaccine. As part of a follow-up of those who received MMR in Finland, it was shown that while antibodies wane over time, immunity to rubella remained secure 20 years after the second dose of MMR.[6]

19.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

19.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

Co-administration with other vaccines

MMR can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR (Priorix and MMR II) may be used interchangeably for completion of a course.[1]

19.5 Recommended immunisation schedule

To prevent all cases of CRS, rubella must not circulate in the community. Achieving at least 95 percent coverage of two doses of MMR prevents the circulation of rubella (which is much less infectious than measles). As in other high-income countries, New Zealand's primary strategy for preventing and maintaining elimination of rubella is to vaccinate both boys and girls (Table 19.2).

Historically, a targeted individual protection approach was used in which only 11-year-old girls were immunised with one dose of rubella vaccine. Even with high coverage, there remained women of childbearing age who were susceptible to rubella due to failure to be vaccinated or vaccine failure and cases of CRS continued to occur albeit at a reduced rate. Rubella remained in circulation in New Zealand because children aged under 11 years and males were not vaccinated.

Table 19.2: Recommended MMR vaccination schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 12 months and 15 months
Catch-up[b] for children adolescents and adults	2 doses: at least 4 weeks apart

a. If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 12 months (at least 4 weeks after previous dose) and 15 months.

b. MMR is funded for those who are susceptible to 1 or more of the 3 diseases. See sections 19.5.2 and 19.5.3.

19.5.1 Usual childhood schedule

Two doses of rubella vaccine as MMR are recommended at age 12 months and 15 months. Over 95 percent of individuals will become immune to rubella after one dose.[2] The second dose is not a booster. Two doses are recommended because nearly all the 2–5 percent not protected by the first dose will be protected by the second. The second dose of vaccine can be given as soon as four weeks after the first dose. (See below for the recommendations for other groups.)

Children who receive MMR vaccination during an outbreak (of measles, mumps or rubella) when aged under 12 months require two further doses administered at age 12 months and 15 months. No opportunity should be missed to achieve immunity, if not contraindicated.

19.5.2 Catch-up

Any individual born on or after 1 January 1969 (see section 12.5.2) who does not have two documented doses of MMR, given at least four weeks apart with the first dose given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded).

Even if the individual has previously received single-antigen measles vaccine, up to two doses of MMR (ie, additional doses of measles vaccine) may be given to these individuals to ensure rubella and mumps protection. There are no significant adverse effects from further vaccinating individuals who are already immune to measles, mumps and/or rubella, and no reliance can be placed on a prior clinical history of rubella infection.

Immigrants to New Zealand

The vaccination status of immigrants should be checked as a priority group: particularly, those born overseas (especially in Asia, the Pacific Islands, sub-Saharan Africa and South America) who entered New Zealand after the age of routine vaccination.

Anyone who does not have two documented doses of MMR, given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded if eligible). Some countries provide a rubella-containing vaccine before the age of 12 months; these children may require extra MMR doses to be fully immunised.

Occupational risk

Visitors to countries with circulating rubella virus, including those travelling for work or humanitarian purposes, are at highest risk of importing disease. It is recommended to be fully immunised prior to departure from New Zealand. During an outbreak, health care workers and those working with infants in day care facilities are at high risk of transmitting disease to pregnant women and their infants. MMR is funded for all New Zealand residents born since 1 January 1969 if they have not previously had two documented doses of MMR.

19.5.3 Pregnancy and breastfeeding

Women planning pregnancy

It is particularly important to ensure that women of child-bearing age are immune to rubella.[1] Women who are planning pregnancy should have their immunisation history checked for having received two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months. Non-immune women may receive MMR before pregnancy, but pregnancy should be avoided for four weeks after the last MMR vaccination.[7, 8]

As seen with recent measles and mumps outbreaks, community immunity in the 15–29 years age group is low due to historically poor MMR vaccination coverage during the 1990s and early 2000s; there is a cohort of women of child-bearing age potentially susceptible to rubella.

Pregnant women

MMR is contraindicated during pregnancy.

> All pregnant women should have their immunisation history checked. A pregnant woman is considered immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months, *regardless of serology*. As soon as possible following delivery, as appropriate, give one or two doses of MMR four weeks apart to women who are not immune (funded).

Serological testing for immunity to rubella is not usually performed in New Zealand except as part of routine antenatal care. Improved documentation and effective surveillance showing the rarity of CRS when there is high immunisation coverage has led to some countries, such as England, discontinuing routine antenatal rubella screening.[9] Also, the screening tests used for rubella serology can potentially give inaccurate results and may cause unnecessary stress for women.[9]

In general, it should be remembered that the great majority of New Zealand-born individuals who received all scheduled childhood vaccines will be immune to rubella. Although the chance of being exposed in New Zealand to an infectious case is becoming increasingly rare, rubella remains endemic in some countries, and the risk remains to those who are unimmunised when travelling overseas or through an imported case. (If exposure during pregnancy does occur, see the guidelines in section 19.8.3.)

After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccine recipients (see section A6.4.1).

Breastfeeding

There is no risk to the mother or child in giving MMR to breastfeeding women.[3]

19.5.4 Immunocompromise

MMR is contraindicated in immunocompromised children (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised, including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to the immunocompromised individual. See section 12.7.2.

MMR is funded for (re)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialists (see 'HIV infection' in section 4.3.3).

MMR is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if their CD4+ lymphocyte percentage is 15 percent or greater. It is recommended that asymptomatic children who are not severely immunocompromised receive MMR from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR if the CD4+ lymphocyte count is 200 cells/mm^3 or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[7]

19.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

19.6.1 Contraindications

See section 12.6.1 for specific MMR contraindications.

The general contraindications that apply to all immunisations are relevant to MMR.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[2, 3] However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.[3]

19.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication for MMR. See section 12.6.3 for more information, and section 12.6.2 for further precautions.

19.7 Potential responses and AEFIs

See also section 12.7.

19.7.1 Potential responses

A fever of 39.4°C or more occurs in 5–15 percent of children 6 to 12 days after immunisation and generally lasts 1 to 2 days.[7] A rash may also occur in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others, unless the rash is caused by a different concurrent illness.[7] The majority of these events are coincidental and not caused by the vaccine.[10] Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

Joint symptoms may be reported in 0.5 percent of young children and 10–25 percent of post-pubertal women.[2] Symptoms begin one to three weeks after immunisation and are usually transient. The prevalence of joint symptoms following rubella immunisation is lower than occurs with natural infection at a corresponding age.[2]

It was previously thought that the rubella vaccine might lead to long-term arthritis. A 2012 Institute of Medicine review concluded that the evidence was inadequate to accept or reject a causal relationship between MMR and chronic arthritis in women.[11]

19.7.2 AEFIs

ITP and, rarely, neurological disturbances have been reported (see section 12.7.2).

19.8 Public health measures

Rubella (including CRS) is a notifiable disease, and suspected cases should be notified by the clinician on suspicion to the local medical officer of health. Accurate diagnosis requires laboratory confirmation.

The preferred method of diagnosis is by PCR or culture; see the 'Rubella' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**). Serology may be useful but can be hard to interpret if the person has received rubella vaccine in the past.

The local medical officer of health will arrange contact tracing and alert the contacts or the public of potential exposure, particularly of pregnant women.

19.8.1 Exclusion of cases of rubella infection

Parents/guardians should be advised that children with suspected rubella should be excluded from early childhood services or school until fully recovered and for seven days after the appearance of the rash. Children with CRS should be considered infectious until they are aged 12 months. Adults should be excluded from work until fully recovered and for seven days after the appearance of the rash.

19.8.2 Management of non-pregnant contacts

The local medical officer of health will advise on contact management. Check the immunisation status of all close contacts.

Rubella-containing vaccine does not provide protection if given after exposure to rubella. However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection. Human normal immunoglobulin does not prevent rubella infection after exposure and should not be used for that purpose.[12]

19.8.3 Management of pregnant contacts

It is critical to accurately document the rubella status of all people who may have rubella and potentially exposed a pregnant woman to the virus. Such people will have travelled overseas or had contact with an infected returned traveller. As described in section 19.3.2, rubella virus does not circulate in New Zealand. Rubella infection in the first half of pregnancy is potentially devastating, and every possible exposure of a pregnant woman should be discussed with the local medical officer of health, obstetrician and microbiologist or infectious diseases physician.

Pregnant contacts with confirmed immunity can be reassured that the likelihood of rubella infection is remote.[13] This applies if:

- she has received at least two documented doses of rubella-containing vaccine, or
- a previous antibody screening test has detected a protective level of antibodies, and this has been documented, or
- one dose of vaccine followed by a rubella antibody screening test showing a protective level of antibodies has been documented.[13]

Coordinated care and management

Coordinated care and management are essential (Table 19.3). An obstetrician (or a maternal fetal medicine specialist) and an infectious diseases specialist/microbiologist should be consulted when the diagnosis of possible rubella infection in a pregnant woman is first considered. The clinical picture and all test results should be discussed by all involved in the care of the woman, to enable an accurate interpretation of the serological results before advising the woman about the risk to her fetus and options regarding the continuation of pregnancy.

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, **and who have been exposed to rubella in the first half of pregnancy**, must be investigated serologically irrespective of immunisation history or history of previous clinical rubella. Serum should be obtained as soon as possible, with the clinical details included on the request form. The laboratory should be asked to store an aliquot of serum for later testing in tandem with a follow-up sample. These results must be interpreted in conjunction with the time since exposure, to determine whether acute infection has occurred.

It is essential to discuss testing with the local clinical microbiologist before taking samples, to ensure that the right samples are obtained, and the best tests performed expeditiously. All requests to laboratories must state the:

- duration of pregnancy and last menstrual period
- date of exposure to possible rubella
- date of blood specimen
- name of the index case who is thought to have rubella.

The use of IG is not recommended for post-exposure prophylaxis of rubella in early pregnancy or any other circumstance. However, IG may be considered if termination of the pregnancy is not an option, but termination must be discussed when maternal infection is confirmed. Although IG has been shown to reduce clinically apparent infection in the mother, there is no guarantee that fetal infection will be prevented.

> It is a legal requirement that all cases of CRS and rubella be notified immediately on suspicion to the local medical officer of health.

For more details on control measures, refer to the 'Rubella' chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/publication/communicable-disease-control-manual**).

Table 19.3: Suggested roles of health professionals

	Lead maternity carer	Medical officer of health	GP	Obstetrician/ infectious diseases specialist/ maternal fetal medicine specialist
Check rubella status in every pregnancy (2 documented doses of rubella-containing vaccine)	✓			
Investigate initial suspected rubella case and trace contacts		✓		
Coordinate care of exposed non-immune pregnant woman		✓	✓	
Review clinical and laboratory results, and discuss options with the pregnant woman if rubella is confirmed				✓
AFTER delivery – vaccinate any woman who is not immune	✓		✓	

19.9 Variations from the vaccine data sheet

See section 12.9 for variations from the MMR (Priorix) data sheet.

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20 Tetanus

Key information

Mode of transmission	Environmental exposure to the bacillus, usually through contaminated wounds. The disease is not directly transmitted from person to person.	
Incubation period	Between 3 and 21 days, commonly about 10 days; may vary from 1 day to several months.	
Period of communicability	A person with tetanus is not infectious to others.	
Incidence and burden of disease	Older individuals, usually women, who are less likely to have received a primary series of tetanus vaccine; and in unvaccinated children.	
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	Intramuscular injection. 0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation) for pertussis protection	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or specialist baby care units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth for pertussis protection	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	
	For boosting of patients with tetanus-prone wounds	Tdap
Post-exposure prophylaxis	If an injury is tetanus prone *and* there is any doubt about previous tetanus immunisation, the individual must be given tetanus immunoglobulin (TIG) and a 3-dose primary immunisation course. (see section 20.5.6).	

20.1 Bacteriology

Tetanus is caused by the action of tetanus toxin released by *Clostridium tetani*, a spore-forming gram-positive, motile, anaerobic bacillus. The most common source of environmental exposure to *C. tetani* spores and bacilli is soil. However, soil is not the only reservoir of the organism. Animals, both herbivores and omnivores, can carry *C. tetani* bacilli and spores in their intestines, and the organism is readily disseminated in their faeces. Once introduced into the relatively anaerobic conditions found in wound tissue, they germinate and produce toxin.

Tetanus spores or bacilli can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. Contaminated wounds, especially wounds with devitalised tissue and deep-puncture trauma, are at greatest risk.

20.2 Clinical features

The clinical diagnosis of tetanus is characterised by muscular rigidity and very painful contraction spasms. When severe, it is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus). The patient suffering from tetanus remains alert unless they become severely hypoxic.

The *C. tetani* toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking the release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between 3 and 21 days, commonly about 10 days, but it has been reported to vary from one day to several months. The bacteria need an anaerobic environment in which to grow, and this is often found in damaged and necrotic tissue, although the inoculation site may appear insignificant. Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food. Reflex muscle spasms usually occur within one to four days of the initial symptoms, the interval being called the onset period. The shorter the incubation and onset periods, the more severe the disease. Even with modern intensive care, tetanus mortality is about 10 percent overall, and much higher in older people.

Neonatal tetanus, from infection of the umbilical stump, is the commonest form of the disease in some low-income countries, particularly where births take place at home without adequate sterile procedures and antenatal screening and immunisation programmes are disrupted.[1]

A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Protective immunity can only be conferred by vaccination with tetanus toxoid and not through exposure to the natural pathogen or suffering tetanus. See section 20.5.2.

20.3 Epidemiology

20.3.1 Global burden of disease

Tetanus infection continues to occur globally but is rare in high income countries. The estimated total number of tetanus cases (including neonatal cases) globally fell from more than 110,000 in 1980 to 15,000 in 2018.[2] The highest numbers of cases were in India, Uganda and other sub-Saharan African countries.[2] Tetanus in males in some sub-Saharan countries has been associated with voluntary circumcision aimed at reducing the risk of HIV infection.[3]

There were 1,803 neonatal tetanus cases reported worldwide in 2018, two-thirds of which were in Africa, and all the cases of tetanus reported in Afghanistan, Chad and Yemen were neonatal.[4] Maternal and neonatal tetanus is described as a silent killer, since many cases are unreported.[5] Worldwide, all countries are committed to 'elimination' of maternal and neonatal tetanus; that is, a reduction of neonatal tetanus incidence to below one case per 1,000 live births per year in every district.[1] However, this goal has not yet been reached in 14 countries.

The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. Global immunisation coverage for DTP is around 86 percent and 129 countries have reached at least 90 percent coverage for three doses of the DTP vaccine. In 2018, an estimated 19.4 million children aged under 1 year did not receive DTP. Of these, 13.5 million lack access to vaccination service and live in the poorest most fragile or conflicted states, and 60 percent live in 10 countries: Nigeria, India, Pakistan, Indonesia, Ethiopia, Philippines, Brazil, Angola and Vietnam.[6]

20.3.2 New Zealand epidemiology

No cases of tetanus were notified during 2017-2019. There were 33 tetanus cases notified between 1997 and 2017.[7] There were four cases in unvaccinated children (aged under 10 years), 14 cases in unvaccinated adults and three cases in vaccinated adults (the time since vaccination is not known). Two females aged 70 years or older died (one was not vaccinated and the vaccination status of the other was unknown).[8]

For further information, see to the ESR's notifiable disease reports (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

20.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent *C. tetani* growing in a contaminated wound. The tetanus vaccine is prepared from cell-free toxin treated with formaldehyde to produce a toxoid. The toxoid is adsorbed onto an aluminium salt adjuvant to improve immunogenicity.

20.4.1 Available vaccines

Funded vaccines

Tetanus vaccine as a single antigen is no longer available in New Zealand. It is only available in combination with other vaccines.

The tetanus toxoid-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and Haemophilus influenzae type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a lower adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine.

See section 6.4.1 for more detailed vaccine information.

Other vaccines

Other tetanus toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

20.4.2 Efficacy and effectiveness

Efficacy and effectiveness

Tetanus toxoid vaccine administered to pregnant women can prevent tetanus in their newborns (neonatal tetanus). Subsequent field assessments of the efficacy of two or more tetanus toxoid doses using data collected during neonatal tetanus mortality surveys demonstrated effectiveness of 70–100 percent.

A systematic review and meta-analysis concluded that immunisation of pregnant or childbearing-age women with two or more doses of tetanus toxoid reduces neonatal tetanus mortality by 94 percent (95% CI: 80–98).[9]

Tetanus in adults is too rare for vaccine efficacy to be tested in a clinical trial. However, the effectiveness of tetanus vaccine was clearly demonstrated in World War II, when only 12 cases of tetanus occurred among the 2.7 million wounded US army personnel (0.44 per 100,000), compared to 70 cases out of 520,000 wounded in World War I (13.4 per 100,000).[9] Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case-fatality.

Duration of protection

Serological studies show that the three-dose primary series of a tetanus vaccine given in infancy plus a booster during the second year of life, provide 3–5 years of protection against tetanus. WHO recommends six doses of tetanus-containing vaccine before age 18 years to induce immunity that lasts for much of adulthood.[1] It is recommended that adults receive at least one booster dose, particularly where fewer than six doses have been given in childhood.

Over the last two decades, there has been a significant increase in the proportion of the adult population with protective antitoxin levels by mid-life.[10] One mathematical model estimated protection to last for at least 30 years in most adults after vaccination.[11] But as age increases, by every 10 years there is an associated 50 percent reduction in antitoxin levels.[12, 13] Even if documented as fully immunised, older adults are likely to have had fewer tetanus doses in their lifetime than adults younger than 30 years.[14] Protection against the effects of tetanus toxin may be insufficient in adults who have not been adequately primed, and those aged over 65 years are at particularly increased risk of tetanus.[10]

A single dose of tetanus toxoid produces a rapid anamnestic response.[15, 16, 17, 18] To ensure that there is adequate antitoxin to neutralise tetanus toxin in the case of a tetanus-prone injury, a booster dose is advised if it has been longer than 10 years since the last tetanus vaccine dose. The extent of wound contamination and delays in seeking medical assistance can result in high levels of tetanus toxin being released. (See also sections 6.4.2 and 15.4.2.)

20.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and Tdap should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

20.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap is 0.5 mL administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap can be administered simultaneously (at separate sites) with other vaccines or IGs.

20.5 Recommended immunisation schedule

Table 20.1: Immunisation schedule for tetanus-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

20.5.1 Usual childhood schedule

A primary course of tetanus vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 20.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

20.5.2 Catch-up immunisation for individuals aged 10 years and older

For adults and children who present with a tetanus-prone wound, boosters are recommended in accordance with the guidelines in the following sections and Table 20.2.

See Appendix 2 for detailed catch-up immunisation information.

Tdap may be used for primary immunisation of children aged 7 to under 18 years. Tdap can be given for vaccination of previously unimmunised or partially immunised adult patients.

Prior clinical tetanus does not usually confer immunity, and immunisation is required. In 1995, a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after the first episode of tetanus.[19]

Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults, no minimum interval between Td and Tdap is required,[20, 21, 22] unless Tdap is being given as part of a primary immunisation course.

20.5.3 Booster doses for adolescents and adults

Adults are recommended to have their tetanus immunisation status assessed at ages 45 and 65 years, and given either a booster dose of tetanus toxoid-containing vaccine if more than 10 years has elapsed since the previous dose, or a primary course, if there is any doubt about the adequacy of previous tetanus immunisation (uncertain or no history of a prior primary course). Protection against tetanus is expected to last at least 20 years following a booster dose after the primary series.

Tdap is recommended and funded:

- as a booster dose to all adolescents at school year 7 or age 11 years
- as a single dose for vaccination of individuals aged 65 years old
- as a single dose for catch-up vaccination of individuals aged 45 years old who have not had four previous tetanus doses.

These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures. Offer a booster dose of Tdap for someone travelling overseas if it has been more than 10 years since the last dose (unfunded) (see section 6.5.3).

The administration of tetanus and diphtheria (Tdap) boosters given at ages 45 and 65 years, is also funded.

See Table 4.9 for occupational groups specifically recommended Tdap (not funded) vaccination due to risk of tetanus or pertussis.

20.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide pertussis protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis (see section 15.5.2).[23]

Tdap vaccine may also be given to pregnant women when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound (see section 20.5.5).[23, 24]

Tdap can be given to breastfeeding women.[24]

20.5.5 (Re)vaccination

Tetanus toxoid-containing vaccines are funded for (re)vaccination of eligible patients as follows, including prior to planned immunosuppression regimes or following immunosuppression. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis

- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

20.5.6 Prevention of tetanus following injury

Following injury, it is essential that all wounds be adequately cleaned and devitalised tissue removed to reduce the level of contamination and tetanus toxin release. Further treatment depends on the circumstances of each case.

If the injury is considered to be tetanus-prone and there is any doubt about the adequacy of previous tetanus immunisation, the individual must have tetanus immunoglobulin (TIG) and commence or complete the recommended primary course of three doses of a tetanus toxoid-containing vaccine (depending on age and other antigens required: DTaP-containing vaccine or Tdap).

The definition of a tetanus-prone injury is not straightforward, because tetanus can occur after apparently trivial injury, such as from a rose thorn, or with no history of injury. However, there are certain types of wounds likely to favour the growth of tetanus organisms. These include:

- compound fractures
- bite wounds
- deep, penetrating wounds
- wounds containing foreign bodies (especially wood splinters)
- wounds complicated by pyogenic (pus-forming) infections
- wounds with extensive tissue damage (eg, crush injuries, avulsions, contusions or burns)
- wounds associated with vascular insufficiency (eg, leg or foot ulcers in the elderly)
- any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than four hours)

- re-implantation of an avulsed tooth – in this case, minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful re-implantation.

General measures for the treatment of tetanus-prone wounds

Wounds or injuries should be classified as tetanus-prone or non-tetanus-prone as follows (see Table 20.2):

- non-tetanus-prone wounds – clean, minor wounds that are less than six hours old, non-penetrating and with negligible tissue damage
- tetanus-prone wounds – all wounds that may be contaminated or infected, and are penetrating, more than six hours old and with tissue damage.

Immunised individuals respond rapidly to a booster injection of tetanus toxoid-containing vaccine, even after a prolonged interval. Tetanus toxoid-containing vaccine and TIG should be given at the same time, but into different limbs and using separate syringes.

See also the IMAC factsheet *Guidelines for the management of tetanus-prone wounds* (available at **immune.org.nz/resources/written-resources**).

Table 20.2: Guide to tetanus prophylaxis in wound management

History of tetanus vaccination[a]	Time since last dose	Type of wound	Tdap[b]	TIG[c]
≥3 doses	<5 years	Tetanus-prone wounds	No	No
≥3 doses	>5 years	Clean minor wounds	No	No
≥3 doses	>5 years	Tetanus-prone wounds	Booster dose[d]	No
≥3 doses	>10 years	Clean minor wounds	Booster dose[d]	No
<3 doses or uncertain		Clean minor wounds	Complete the course[e]	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course[e]	Yes

a. People who have experienced Arthus-type hypersensitivity reactions (see 20.7.2) after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

b. See Appendix 2 for catch-up schedules for previously unimmunised children. DTaP-containing vaccine may be used in children aged under 10 years.

c. TIG = tetanus immunoglobulin. The recommended dose is 250 IU given by IM injection as soon as practicable after injury. If more than 24 hours has elapsed, 500 IU is recommended. A dose of TIG can be given for up to 3 weeks after injury.

d. If appropriate, this may count as the booster dose at age 45 or 65 years.

e. To complete the 3-dose primary immunisation course, give 1–3 doses at not less than 4-weekly intervals.

Tetanus immunoglobulin availability and storage

Tetanus immunoglobulin (TIG) is issued in ampoules, each containing 250 IU of human tetanus antitoxin. (Ampoules of 2,000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2°C to +8°C. They must never be frozen. TIG is given intramuscularly.

TIG dose

The recommended dose to prevent tetanus is 250 IU of TIG for recent injuries, but this should be increased to 500 IU if more than 24 hours has elapsed since injury, or if there is a risk of heavy contamination or following burns. A dose of TIG can be given for up to 3 weeks after injury.

There is no need to test the patient's sensitivity before administering TIG, but caution is necessary if the patient is known to suffer complete immunoglobulin A (IgA) deficiency. In this situation, specialist help should be sought (see section 4.3).

Patients with impaired immunity who suffer a tetanus-prone wound may have failed to respond to prior vaccination and may therefore require TIG.

TIG can be given in pregnancy if clinically indicated. Whilst the safety of TIG for use in pregnancy has not been established in controlled clinical trials, no known risk to the fetus has been associated with use in pregnancy.

20.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

20.6.1 Contraindications

Immunisation with Tdap or another tetanus toxoid-containing vaccine should not be repeated in individuals who have had previous severe hypersensitivity reactions to the vaccine or a vaccine component. Most cases of hypersensitivity have been reported in individuals who have had an excessive number of booster injections outside the guidelines noted above.

20.6.2 Precautions

Protection against the risk of tetanus is paramount if the wound is thought to be tetanus-prone. Immunisation should not be postponed because the patient has a minor infection.

People who have experienced Arthus-type hypersensitivity reactions (see section 20.7.2) after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor. Arthus-type reactions are rare in children and did not occur during the clinical trial of Tdap vaccines.[25]

Guillain–Barré Syndrome within six weeks of a tetanus toxoid-containing vaccine weeks is a precaution to receiving a further dose (see section 20.7.2).[22]

See section 15.6.2 for precautions to pertussis-containing vaccines, including DTaP-IPV-HepB/Hib.

20.7 Potential responses and AEFIs

See also sections 6.7 and 15.7 for potential responses and AEFIs to DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap vaccines.

20.7.1 Potential responses

Tetanus toxoid combination vaccines have not been associated with any safety concerns. Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle.[26] Mild discomfort or pain at the injection site persisting for up to a few days is common.[24]

Tdap has a safety profile similar to Td and is generally well tolerated.[27, 28]

20.7.2 AEFIs

The 1994 US Institute of Medicine review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy (brachial neuritis) at a rate of 0.5–1 per 100,000 doses within four weeks of immunisation.[29] Occurrence of brachial neuritis following vaccination does not preclude the future use of a tetanus-toxoid containing vaccine in the same person.[22]

Severe local reactions (including large injection-site swelling) called Arthus reactions, immune-complex mediated hypersensitivity reactions that were associated with older tetanus and diphtheria toxoid-containing vaccines. Historical data on multiple doses of Td and tetanus toxoid vaccines indicate that hypersensitivity was associated with very high levels of pre-existing antibody.[9, 30]

No increased risk of GBS has been observed with use of tetanus toxoid-containing vaccines, and therefore a history of GBS is not a contraindication to receiving a tetanus toxoid-containing vaccine. However, out of prudence, it is recommended that having GBS within six weeks of a tetanus toxoid-containing vaccine is a precaution to receiving a further dose.[9, 30]

20.8 Public health measures

All cases of tetanus must be notified immediately on suspicion to the local medical officer of health, who should be provided with as accurate an immunisation history as possible.

See section 20.5.6 'Prevention of tetanus following injury'. See also the 'Tetanus' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**).

20.9 Variations from the vaccine data sheets

Tdap vaccine is not approved for use (registered) for primary immunisation. However, adults aged over 18 years may receive Tdap (funded) for catch-up of the primary schedule (see Appendix 2).

See section 15.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

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21 Tuberculosis

Key information

Mode of transmission	Inhalation of airborne droplets produced by people with pulmonary or laryngeal tuberculosis (TB). People with latent TB infection and non-pulmonary TB disease are not infectious.
Incubation period	Between 2 and 10 weeks from infection to primary lesion or significant tuberculin skin test (Mantoux) reaction.
Period of communicability	May be years with untreated pulmonary TB. See the *Guidelines for Tuberculosis Control in New Zealand 2019* (or current edition) – see section 21.5.3.
Burden of disease	Disseminated and meningeal TB are more common in very young children. The immunocompromised individuals, particularly HIV-infected, are more at risk of disease and complications. In New Zealand, TB incidence is highest in those born in high prevalence countries.
Funded vaccine	Bacillus Calmette-Guérin (BCG) Vaccine SSI.
Dose, presentation and route	Vaccine can only be administered intradermally by an authorised vaccinator with BCG endorsement. Live attenuated vaccine, which must be reconstituted.
Funded vaccine indications and recommended schedule	Neonatal BCG vaccine should be offered to infants at increased risk of TB, as defined in section 21.5.2. (See section 21.5.2 for countries with a TB rate ≥40 per 100,000.)
Contraindications	Individuals with primary or secondary immunocompromise, including: • receiving immunosuppressive treatment • malignant conditions of the reticulo-endothelial system (eg, lymphoma, leukaemia) • HIV-positive or potentially HIV-positive individuals • infants of mothers who received biologic immunosuppressive agents during pregnancy • other individuals in whom immunocompromise is known or suspected (see section 21.6.1). Individuals with generalised infected skin conditions.
Potential responses	A local reaction develops in 90–95% of those vaccinated with BCG, which may scar within 3 months. A minor degree of adenitis is normal, not a complication. Suppurative adenitis may take months to resolve; usually no treatment is required.
Public health measures	All cases of active TB must be notified to the local medical officer of health.

21.1 Bacteriology

Human TB is caused by infection with *Mycobacterium tuberculosis* or *Mycobacterium bovis*.

21.2 Clinical features

M. tuberculosis or *M. bovis* infection most commonly causes disease in the lungs, but any part of the body can be affected.

The initial infection with *M. tuberculosis* usually goes unnoticed. Early infections can be cleared, progress rapidly to primary TB, or be contained in a latent phase (LTBI): see Figure 21.1.

Primary TB occurs most commonly in young children aged under 5 years, individuals with immunocompromise and those infected by particularly transmissible isolates of TB.

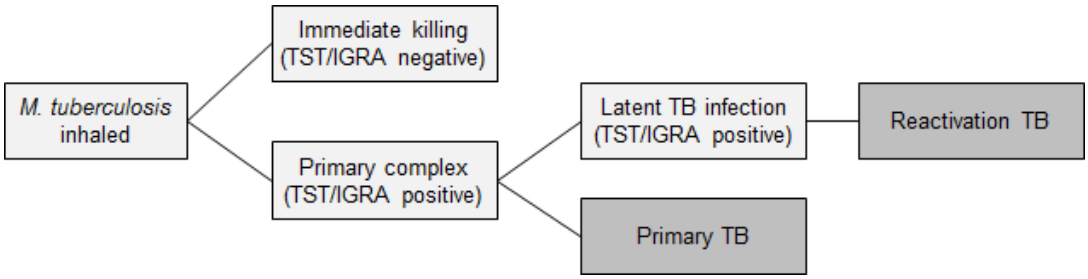
Latent TB infection has no symptoms and is diagnosed by a positive tuberculin skin test or interferon gamma release assay after the exclusion of active TB. Latent infection progressing to active TB is also called reactivation TB.

The lifetime risk for infected people progressing from this latent phase to active TB disease may be as high as 20 percent, but this risk is strongly affected by infecting dose, the age of the person, the presence of healed lesions on chest X-ray and immunocompromise.[1, 2]

The time from infection to clinical manifestations of primary TB varies, from one to six months after infection. Reactivation TB can occur at any time thereafter, even decades after infection. The most common site of infection is the lung (pulmonary TB), where TB infection classically causes an asymmetrical pulmonary infiltrate. The 'classic' TB pathology of caseation, cavity formation and fibrosis occurs late and in a minority of cases. Young children with active TB disease may be asymptomatic or present with symptoms of fever, lassitude and failure to thrive. Older children and adults with active TB disease may present with symptoms of anorexia, fatigue, weight loss, chills, night sweats, cough, haemoptysis and chest pain.

Any organ can be affected by extrapulmonary TB, causing meningitis, pleurisy, pericarditis, bone or joint infection, renal infection, gastrointestinal tract infection, peritonitis or lymphadenitis, or disseminating via the bloodstream and affecting multiple organs (disseminated TB). Disseminated and meningeal TB are more common in very young children. Immunocompromise, like HIV, is associated with higher rates of disseminated TB and less specific clinical features.[3]

Figure 21.1: Stages in the natural history of tuberculosis



Key: TST = tuberculin skin test; IGRA = interferon gamma release assay; TB = tuberculosis.

21.3 Epidemiology

21.3.1 Global epidemiology

Worldwide, the incidence rate of TB is slowly falling by about 1.5 percent per year, but TB remains a major global health problem. Much of the TB burden exists in 30 high-burden countries, spread mainly in poor, crowded and poorly ventilated settings. Between 2015 to 2000 the cumulative reduction in TB incidence per 100,000 population as 11 percent, just over half of the 2020 milestone for the End TB strategy.[4] Globally, as of 2018, an estimated 1.7 billion people are infected with *M. tuberculosis* of which 5–15 percent will develop active TB during their lifetime.[5] WHO estimates there were 10.4 million new TB cases in 2016 and TB remained the top cause of infectious disease mortality with 1.7 million deaths.[5] Of those cases, an estimated 1.9 million cases were linked to undernourishment and 1 million to HIV, 0.8 million to smoking and 0.8 million to diabetes. There has been an increasing burden of multidrug-resistant TB (defined as resistance to at least isoniazid and rifampicin) with an estimated 600,000 new cases of multidrug-resistant TB in 2016.[5]

In low-burden countries, such as New Zealand, the peak age for TB is in older adults, reflecting their exposure to TB in the past when incidence was higher. In high-burden countries TB is most common in children and young adults. The risk of TB in people who emigrate from high-burden countries is proportionate to the incidence in their country of origin.[6]

21.3.2 New Zealand epidemiology

For detailed TB information, see the *Tuberculosis in New Zealand: Annual Report*, available at **surv.esr.cri.nz/surveillance/AnnualTBReports.php**.

Notification rates and risk factors

TB remains one of the most common notifiable infectious diseases in New Zealand. Cases of TB declined substantially between 1980 and 2007, but they have remained relatively stable since then.[7]

In 2019, there were 323 notifications for TB (notification rate of 6.6 per 100,000; ESR, 8 June 2020 at a similar rate to 2018 (6.4 per 100,00).[7, 8] Notification rates were highest in those aged 20–29 years (12.2 per 100,000) and 30–39 years (10.6 per 100,000), with slightly higher rates in males than females.

Asian ethnic groups had the highest notification rate in 2019 (35.7 per 100,000, 206 cases), followed by Middle Eastern/Latin American/African (30.7 per 100,000, 17 cases) and Pacific peoples (15.5 per 100,000, 49 cases). Of the 306 new TB cases with risk factors recorded in 2019, 251 were born overseas (ESR, 8 June 2020). The highest disease rate was among those born in Southern and Central Asia (129 per 100,000), followed by those born in South-East Asia (57 per 100,000), the Pacific Islands (23 per 100,000). The most reported country of birth in SE Asia was Philippines (64 percent).

The notification rate was considerably lower for Māori (3.8 per 100,000, 29 cases) and European/Other (0.6 per 100,000, 20 cases) groups (ESR, 8 June 2020). There is substantial regional variation in TB notification rates: the highest rates are in the Auckland and Wellington regions; this is associated with immigration.

Of the 81 percent of cases in 2019 with date of arrival recorded, the median interval between arrival and the TB notification ranged from 0 to 65 years (mean 8 years and median 5 years) (ESR, 8 June 2020).

One child under 5 years of age was notified with TB in 2019 (ESR, 8 June 2020). The child was born in New Zealand and not vaccinated.

Multidrug-resistant TB

Multidrug-resistant TB is rare but does occur in New Zealand. Over 10 years (2009–2018), a total of 36 cases were multidrug resistant (annual average rate of 2 percent).[8] All these cases were born and assumed to have acquired the infection overseas; 83 percent were born in an Asian country.

21.4 Vaccine

Note: Depending on world supply, BCG vaccine may not be available in New Zealand.

BCG vaccine types vary widely, with different strains. The incidence of side-effects with BCG vaccination differs between strains that are considered more reactogenic (ie, those that elicit stronger immune responses in animal models) and strains that are considered less reactogenic.[9] The more reactogenic strains have also been associated with a higher rate of lymphadenitis and osteitis, especially among neonates. Reducing the vaccination dosage for the more reactogenic strains also reduces the incidence of lymphadenitis.

21.4.1 Licensed vaccine

BCG Vaccine SSI (Seqirus (NZ) Ltd) is a live attenuated vaccine, containing the less reactogenic Danish 1331 strain of *M. bovis*. The 0.1 mL dose for children aged 12 months and older contains 2–8 × 10^5 colony-forming units of *M. bovis*, and the 0.05 mL dose for infants contains 1–4 × 10^5 colony-forming units. Other components and residuals include sodium glutamate, magnesium sulphate heptahydrate, dipotassium phosphate, citric acid, L-asparagine monohydrate, ferric ammonium citrate and glycerol.

21.4.2 Efficacy and effectiveness

The exact immune response elicited by BCG vaccination and the mechanism of action in the host are still not well understood. There is no reliable established laboratory correlate for immunity to *M. tuberculosis*,[10] though this remains an active area of study.[11]

BCG protection is partial and varies according to the age at which vaccination is administered and the disease phenotype in question. A meta-analysis of randomised controlled trials showed neonatal BCG had 59 percent efficacy against pulmonary TB (95% CI: 0.42–0.71) and 90 percent efficacy against meningeal TB (95% CI: 0.23–0.99).[12] Studies conducted since the advent of interferon gamma release assays suggest BCG may also be effective against *M. tuberculosis* infection. A meta-analysis has estimated BCG effectiveness against *M. tuberculosis* infection at 20 percent, though different methods in the included studies each had a wide range of estimates.[13] Thus, the principal role of BCG in New Zealand is to protect young children who are at greatest risk of disease, particularly miliary and meningeal disease.[9] BCG is less effective in adults and older children, particularly if they already have latent infection.

As BCG has been propagated *in vitro* for over 40 years, there are now several strains being manufactured.[14] Immunological responses vary considerably across vaccine strains, but the data to date cannot differentiate which strains, if any, are overall more effective.[15, 16]

In low-income countries, a birth dose of BCG significantly reduces overall infant mortality.[17, 18]

BCG has had little effect in reducing the population rate and transmission of TB,[19] so there are no herd immunity effects. Duration of protection is unknown, possibly 10 to 15 years, but it may be much longer in some populations.[9]

There have been a number of different approaches to using BCG in the control of TB in middle- and high-income countries.[20] For example, the US has not had a BCG programme, whereas New Zealand (see Appendix 1) and the UK had programmes until 1990 and 2005, respectively. The WHO recommends that countries with low rates of active TB, such as New Zealand, target BCG vaccination at children who are at significantly increased risk of TB exposure through household contact.[5] New Zealand

(see section 21.5) and the UK now only offer BCG vaccine to high-risk individuals. A study from the Netherlands suggests that around 9,000 children from countries with rates greater than 50 per 100,000 population would have to be given BCG to prevent a severe case.[21]

The current recommendation to use neonatal BCG vaccination in populations with high rates of active TB is part of a control and treatment programme for TB in New Zealand, which includes active contact tracing and treatment of latent TB infection.

There are large international efforts working to improve BCG vaccines and develop new, more effective vaccines.[22]

21.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store in the dark at +2°C to +8°C. Do not freeze.

There are variances in strain potency between brands of BCG vaccine so vaccinators should always follow the instructions in the vaccine data sheet (available on **www.medsafe.govt.nz**).

BCG vaccine requires reconstitution before administration. It is presented as freeze-dried vaccine in a multi-dose vial with diluent in a separate vial. The diluent must be added to the freeze-dried vaccine vial and mixed gently (do not shake vigorously). Protect the vial from light. Leave the reconstituted vaccine to stand for one minute until it forms an opalescent liquid. Reconstituted vaccine should be stored at 4°C, protected from sunlight and used within four hours.

21.4.4 Dosage and administration

Only authorised vaccinators with BCG endorsement can administer BCG vaccine (see A3.6).

Administer a dose of:

- 0.05 mL to infants aged under 12 months
- 0.1 mL to children aged 12 months or older.

The vaccine is administered by intradermal injection over the point of insertion of the left deltoid muscle (see sections 2.2.3 and 2.2.4).

No follow-up tuberculin skin testing is required.

Repeat BCG vaccination is not recommended.

BCG immunisation given in other countries

BCG is one of the vaccines that are part of the WHO Expanded Programme on Immunization. It is given at birth in most low-income countries.

The following Pacific Island countries[23] recommend BCG vaccination at birth: Cook Islands, Fiji, Kiribati, Nauru, Niue, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu and Vanuatu.

Usually BCG vaccine is administered in the left deltoid area, but other sites of administration have also (although uncommonly) been used, such as the right deltoid. Revaccination with BCG is not recommended by the WHO.[5]

Co-administration with other vaccines

BCG can be given simultaneously with any other vaccine. However, it must be administered into a separate site in a separate syringe. Because of the risk of local lymphadenitis, no further vaccinations should be given into the arm used for BCG for at least three months. If not given concurrently, BCG should be given at least four weeks after MMR or VV. Note that no time interval is required between administration of BCG and rotavirus vaccines.

HBIG (given at birth to babies of mothers with chronic HBV infection) or human normal immunoglobulin is thought not to reduce the effectiveness of BCG immunisation, which principally acts through cell-mediated immunity.

21.5 Recommended immunisation schedule

21.5.1 Tuberculin skin testing (Mantoux) before BCG vaccination

Tuberculin skin testing is not needed if BCG is given before age 6 months unless a history of contact with a known or possible case of TB is obtained. Although the tuberculin skin test is usually positive in the year following BCG vaccination, at least 50 percent of children will be negative beyond that time, so tuberculin skin testing still has utility for diagnosing TB infection.

Children who have missed vaccination at birth may be vaccinated at any time up to age 5 years. If the child is 6 months or older, they should have a pre-vaccination tuberculin skin test to detect whether they have already been infected: vaccination only to being given if the child is uninfected.

21.5.2 BCG eligibility criteria

TB is more common in migrants or families of migrants from high-incidence countries. However, anyone who is pregnant should have a discussion with their lead maternity carer about the risk of TB for their baby.

Neonatal BCG is recommended and funded for infants at increased risk of TB, as defined in Table 21.1.

Table 21.1: Neonatal BCG eligibility criteria

Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:
• will be living in a house or family/whānau with a person with either current TB or a history of TB
• have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥40 per 100,000*
• during their first five years will be living for three months or longer in a country with a TB rate ≥40 per 100,000.*

* For TB incidence rates in specific countries see **https://worldhealthorg.shinyapps.io/tb_profiles/**.

The WHO Global Tuberculosis 2021 report showed that the highest burden for TB was seen in 30 countries. For more detail see **https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2021**.

As a general indication, the following global areas have TB rates ≥40 per 100,000:

- most of Africa
- much of South America
- Russia and the former Soviet states
- the Indian subcontinent
- Eastern Mediterranean
- China (including Hong Kong) and Taiwan
- South-East Asia
- some parts of the Pacific (Kiribati and Papua New Guinea have consistently high rates).

For TB incidence rates in specific countries see
https://worldhealthorg.shinyapps.io/tb_profiles/

Neonates at risk should be identified antenatally by lead maternity care providers and antenatal referral made to the neonatal BCG service. Health care providers can also identify and refer neonates at risk. Immunisation is desirable before infants leave

hospital. If this does not happen, immunisation should be arranged through the local medical officer of health.

Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.[24] Babies born after this or with low birthweight appear to produce an adequate response, based on tuberculin skin test responses.[25, 26, 27]

If the baby has not been vaccinated before leaving hospital, and if there is a history of *current* TB in a relative who has had contact with the baby, *do not vaccinate immediately*. Withhold vaccination, conduct tuberculin skin testing, seek paediatric advice and vaccinate only after the possibility of infection in the baby has been excluded. Vaccination may not protect the baby who is incubating disease and may prevent the tuberculin test from assisting with the diagnosis of disease.

A parent's/guardian's request should not be accepted as an indication for immunisation. Parents/guardians seeking vaccination of children who do not meet the above criteria should be referred to the local medical officer of health to discuss the risks and benefits of immunisation before a final decision is made.

BCG vaccine information for parents

Information about the BCG vaccine is available in English and other languages from the HealthEd website (**healthed.govt.nz**). This includes information for parents on why the vaccine is recommended, what to expect and how to care for the vaccination site.

21.5.3 Children aged under 5 years at high TB risk

Repeat BCG vaccination is not recommended. Vaccination for overseas travel is not available in New Zealand.

Funded BCG may be offered to children aged under 5 years if they are tuberculin skin test- or interferon gamma-release assay negative and are at increased risk of TB because they:

- will be living in a house or family/whānau with a person with either current TB or a history of TB or
- have one or both parents, household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥40 per 100,000* or
- during their first five years will be living for three months or longer in a country with a TB rate ≥40 per 100,000*.

* For TB incidence rates in specific countries see **https://worldhealthorg.shinyapps.io/tb_profiles/**

Refer to the *Guidelines for Tuberculosis Control in New Zealand 2019*[28] (available at **health.govt.nz/publication/guidelines-tuberculosis-control-new-zealand-2019**).

21.5.4 Pregnancy and breastfeeding

BCG vaccine is not recommended for when someone is pregnant or breastfeeding.

21.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

21.6.1 Contraindications

BCG vaccine should not be given to individuals:

- known to be hypersensitive to any component of the vaccine
- receiving corticosteroids or other immunosuppressive treatment, including radiotherapy (see section 4.3)
- suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system
- in whom immunocompromise is known or suspected, such as individuals with hypogammaglobulinaemia – primary immune deficiencies in children are often not detected until after the first few weeks of life (ie, after BCG vaccine is given), so a family history of immune deficiency should be sought and, if present, discussed with a paediatrician before vaccination
- known to be infected with HIV, including neonates where the mother's HIV status is unknown – maternal HIV infection should be excluded prior to neonatal vaccination; testing should have been offered as part of the National Antenatal HIV Screening Programme, and infants born to HIV-infected mothers should be under the care of a paediatrician
- with generalised infected skin conditions.

Infants born to those who received immunomodulatory biologic agents during pregnancy must not be vaccinated with a BCG vaccine until they are identified as being immunocompetent. See section 4.3.6 and Table 4.2 for a list of the highly immunosuppressive medications with long half-lives that require a prolonged delay before vaccination (for up to one year in those being treated). These include monoclonal antibody (mab) agents that readily cross the placenta. Each case should be assessed with specialist advice.

21.6.2 Precautions

- BCG vaccine should be avoided in those who are pregnant (this is a counsel of caution, as no harmful effects to the fetus have been observed following accidental immunisation of the mother during pregnancy).
- In the case of eczema, an immunisation site should be chosen that is free of skin lesions.
- Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.[24]
- Avoid or defer immunisation in a child born with a condition that may require immunosuppressive therapy in future.
- Before BCG vaccination is scheduled for neonates (up to 4 weeks of age), a normal metabolic/immune deficiency (Guthrie test) result needs to have been confirmed, specifically for severe combined immunodeficiency (SCID).

21.7 Potential responses and AEFIs

21.7.1 Potential responses

Following the BCG injection, a white weal should appear. This should subside in approximately 30 minutes. The site requires no swabbing or dressing.

A local reaction develops in 90–95 percent of people vaccinated with BCG, which may include shallow ulceration, followed by healing and scar formation within three months. To ensure appropriate healing, encourage parents/caregivers to keep the injection site clean and dry, to allow sore to scab and to avoid ointments and scratching. A minor degree of adenitis developing in the weeks following immunisation should be regarded as normal, not a complication. It may take months to resolve. Suppurative adenitis may also take months to resolve; usually no treatment is required.

21.7.2 AEFIs

AEFIs with BCG vary with age and vaccine strain and are summarised in Table 21.2.

Table 21.2: Age-specific estimated risks for complications after administration of BCG vaccine

Complication	Incidence per 1 million vaccinations	
	Age <1 year	Age 1–20 years
Local subcutaneous abscess; regional lymphadenopathy	387	25
Musculoskeletal lesions	0.39–0.89	0.06
Multiple lymphadenitis; non-fatal disseminated lesions	0.31–0.39	0.36
Fatal disseminated lesions	0.19–1.56	0.06–0.72

Reprinted with permission of the International Union Against Tuberculosis and Lung Disease. Copyright © The Union. Lotte A, Wasz-Hockert O, Poisson N, et al. 1988. Second IUATLD study on complications induced by intradermal BCG-vaccination. *Bulletin of the International Union against Tuberculosis and Lung Disease* 63: 47–59.

The risk of BCG adverse reactions depends on many factors, including strain type, route of administration and the underlying immune state of the patient. Severe injection-site reactions, large ulcers and abscesses can occur in individuals who are tuberculin positive. Special care is needed both in interpreting initial tuberculin skin results and in delivering the BCG vaccine.

Rarely, osteitis and osteomyelitis, lupoid and other types of skin disorders, and neurological disorders have been reported following BCG vaccination. Although rare, disseminated BCG disease is the most severe BCG vaccine complication occurring in immunocompromised people, such as children with primary immune deficiency. This needs rapid and aggressive treatment and has a high mortality.

Keloid scars at the injection-site, although not uncommon, are largely avoidable. Some sites are more prone to keloid formation than others and vaccinators should adhere to the site recommended (mid-upper arm). Most experience has been with the upper arm site, and it is known that the risk of keloid formation increases greatly if the injection is given higher than the insertion of the deltoid muscle into the humerus.

Every effort should be made to recover and identify the causative organism from any lesions that constitute a serious complication.

Most local and regional adenopathy resulting from BCG vaccination will resolve spontaneously, and there is rarely a need for medical or surgical intervention. Treatment recommendations for local abscess formation and suppurative lymphadenitis remain controversial.[29] If suppurative adenitis reactions persist for longer than three months, seek specialist opinion. However, anyone presenting with more widespread or distant disease needs referral to a specialist.

Abscesses and more serious complications should be reported to CARM (see 'AEFI reporting process – notifying CARM' in section 1.6.3), and also reported to the local medical officer of health in the interests of quality control of the BCG vaccination technique.

21.8 Public health measures

It is a legal requirement that all cases of active TB be notified to the local medical officer of health. While there is no legal requirement to notify cases of latent TB infection that are being treated, for surveillance purposes and with the patient's consent they should be reported to the local medical officer of health.

Under the Health (Protection) Amendment Act 2016, the medical officer of health is given wide powers to investigate and control all TB cases and their contacts, while DHBs are required to make provision for the treatment and supervision of patients and their contacts.

The primary purpose of neonatal BCG vaccination is to protect child case contacts from TB disease and its most devastating consequences. Screening of certain risk groups and case contact management are other elements of TB control in New Zealand. These programmes do not obviate the need for BCG vaccination, as screening coverage is partial and contact tracing may not occur in time to prevent illness in child contacts. The local medical officer of health can advise on local TB control policies, including issues in BCG immunisation.

Both TB infection and BCG immunisation lead to the development of a cellular immune response, which can be detected by measuring dermal induration after the injection of tuberculin-purified protein derivative (eg, via the tuberculin skin test). A positive response to a tuberculin skin test may be an indication of current infection, previous natural infection or prior BCG immunisation. However, the false positive effect after vaccination will wane, rapidly in all individuals who receive the vaccine in the neonatal period and more slowly in those who are vaccinated at an older age such as during the primary-school years.[30]

In vitro tests have been developed to measure the release of interferon-gamma from host lymphocytes in response to well-defined antigens. The antigens used are not present in BCG strains of *M. bovis* or most non-tuberculous mycobacteria. Interferon gamma release assay has the advantage of greater specificity and convenience, but it is more expensive.[31]

For more information, refer to the 'Tuberculosis' page of the Ministry of Health website (**health.govt.nz/our-work/diseases-and-conditions/tuberculosis**) and the 'Tuberculosis' chapter of the *Communicable Disease Control Manual* (available at **health.govt.nz/publication/communicable-disease-control-manual**).

21.9 Variations from the vaccine data sheet

The data sheet states that BCG vaccine should not be given to infants born to HIV-positive mothers. The Ministry of Health recommends that BCG may be given to HIV-negative infants born to HIV-positive mothers – providing that the infant is confirmed to be HIV negative by appropriately-timed PCR tests before the vaccine is given.[32, 33] Seek specialist advice.

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22 Varicella (chickenpox)

Key information

Mode of transmission	Airborne droplets from, or contact with, vesicular lesions or possibly respiratory secretions.
Incubation period	Usually 14–16 days (range 10–21 days).
Period of communicability	From 2 days before onset of the rash until all lesions have crusted.
Incidence and burden of disease	Without immunisation, most people have infection during childhood. Groups at risk of severe complications include pregnant women and their unborn babies, and immunocompromised individuals.
Funded vaccine	VV (Varivax) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	1 dose is funded for: • children at age 15 months; or • previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history). Up to 2 doses are funded for certain special groups and their household contacts if non-immune to varicella.
Recommended	Susceptible children and adults who are not eligible by age for funded vaccine.
Vaccine effectiveness	One dose confers approximately 99% protection against severe disease and 80% protection against varicella disease of any severity. Breakthrough disease is usually mild. Herd immunity has been documented.
Contraindications	Pregnancy Certain immune deficiency and immunocompromised states Known anaphylaxis to neomycin, gelatin or other vaccine components Active untreated TB (see section 22.6)
Potential responses to vaccine	Generally mild and self-limiting, and include local reactions, fever and mild papulo-vesicular rash in normal healthy individuals.

Post-exposure prophylaxis	VV may be used for post-exposure prophylaxis for immune-competent people if given within 5 days of exposure. Zoster immunoglobulin (ZIG) is most effective if given as soon as possible after exposure but may be given up to 10 days post-exposure (see section 22.8.2).

22.1 Virology

Varicella (chickenpox) is a highly infectious disease caused by human herpes virus type 3 (varicella zoster virus or VZV). Reactivation of latent VZV results in herpes zoster (zoster; shingles), a disease with considerable morbidity (see chapter 23).

22.2 Clinical features

Varicella is one of the most infectious diseases known (along with pertussis and measles). Transmission occurs via airborne droplets from, or contact with, vesicular lesions and possibly respiratory tract secretions. The incubation period is usually 14–16 days (range 10–21 days but can be longer in immunocompromised individuals and those who have received ZIG), and cases are infectious from two days before the onset of the rash until all the lesions have crusted. A maculopapular rash, which becomes vesicular, appears in crops over several days, first on the face and scalp, later spreading to the trunk and then the limbs. Vesicles, ranging in number from few to many hundred, dry and crust after three to four days. A hallmark of the rash is lesions in varying stages of development. Lesions on mucosal surfaces (mouth, vagina) can cause considerable distress. The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

In most children, varicella is a mild disease but complications requiring hospitalisation and fatalities do occur. Secondary bacterial skin infections are common. Serious complications include central nervous system involvement (encephalitis, cerebellar ataxia, stroke), pneumonia, secondary invasive bacterial infections, and even death. Adults are 25 times more likely to develop severe disease than children, with pneumonia being the most common complication, often requiring mechanical ventilation. VZV pneumonia carries an overall mortality rate of 10–30 percent.

Maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 22.4), whereas disease very late in pregnancy (from five days before to two days after delivery) may cause severe neonatal varicella infection. Pregnant women who contract varicella have an estimated 10–20 percent risk of developing VZV pneumonia.

Others vulnerable to both VZV and zoster are those who are immunocompromised, such as people taking immunosuppressive medications (eg, cancer treatment or organ transplant patients) and those with HIV infection. Varicella can be a fatal disease in immunocompromised individuals.

VZV infection is followed by the production of VZV-specific T-cell mediated immunity, necessary to maintain the latency of VZV in the ganglia and prevent reactivation as zoster. The immune response is boosted by subclinical reactivation of latent virus. The incidence of zoster increases with age as VZV-specific T cell-mediated immunity declines (see chapter 23).

22.3 Epidemiology

22.3.1 Global burden of disease

In temperate climates, winter-spring epidemics occur with peak incidence in preschool and early primary school ages (1–9 years). Around 90 percent of individuals have been infected by adolescence and fewer than 5 percent of adults are susceptible. The annual number of infections therefore approximates the birth cohort.[1, 2]

Transmission of the virus is less efficient in tropical climates. Adolescent and adult immigrants to New Zealand from such countries are more likely to be susceptible, placing them at risk of contracting chickenpox in their new environment. Being older, they are more likely to suffer severe disease.

The long incubation and high transmissibility of VZV conspire to maximise disruption to families: by the time the rash occurs a child will have been infectious for two days; any susceptible household contacts will then become unwell just as the first child recovers. This results not only in morbidity but also in financial consequences for parents missing work.

Crude hospitalisation admission rates in high-income countries range from around 2–6 per 100,000 population-year. Most of these admissions are children, consistent with the high incidence of varicella in children. Crude mortality rates ranged from 0.3–0.5 per million population-year with overall case fatality ratios of around 2–4 per 100,000 cases. Almost 90 percent of varicella hospital admissions occur in otherwise healthy and immunocompetent individuals.[1, 2]

VV has been introduced into childhood immunisation programmes overseas, including the US from 1995 and Australia from 2005, resulting in dramatic reductions in varicella morbidity, hospitalisations and mortality.[3, 4, 5] By 2005 in the US, vaccine coverage was approximately 90 percent and varicella incidence had declined by more than 90 percent. Herd immunity was observed outside of age groups targeted for vaccination.[1]

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in zoster in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of zoster to the childhood VZV vaccine programme.[6, 7] Studies from the UK and Canada reported increases in zoster not

associated with a vaccination programme, and some US data showed zoster rates were increasing prior to the initiation of their varicella vaccination programme.[8, 9]

22.3.2 New Zealand epidemiology

Varicella is not a notifiable disease, so data is limited for uncomplicated varicella, but the epidemiology is likely to be as described above for temperate climates. With increasing participation in early childhood services, a greater proportion of infections may now be occurring in preschool-aged children. It is expected that zoster numbers will rise in New Zealand as the population ages.

Prospective nationwide surveillance of varicella in New Zealand children, conducted from November 2011 to October 2013, found that the incidence of varicella-related hospitalisation was 8.3 per 100,000 children per year – although this is likely to be a significant underestimate.[10] Māori and Pacific children were disproportionately affected, with an almost three- and four-fold increase in the relative risk of hospitalisation for varicella or its complications, respectively. Of the hospitalised children, 9 percent required ICU admission and most of them were previously healthy. Almost one-third of hospitalised children had multiple complications from varicella, and those with neurological complications were more likely to have ongoing problems at discharge.

A retrospective survey of admissions to the paediatric intensive care unit at Auckland's Starship Children's Hospital during 2001–2011 found 26 children admitted for varicella or its secondary complications.[11] The main admission reasons were neurological (38.5 percent) and secondary bacterial sepsis or shock (26.9 percent). Four children died (15 percent), three of whom were immunocompromised. A further eight children (31 percent) had ongoing disability at discharge, most having had no prior medical condition.

Based on overseas rates, it is estimated that up to one case of congenital varicella syndrome may be expected in New Zealand each year, although few have been reported.

In 2017, adults (aged 20 years and older) accounted for 25 percent of varicella-related hospital admissions;[12] approximately one person per year dies from VZV infection, and most VZV-related deaths occur in adults.[13]

22.4 Vaccines

22.4.1 Available vaccines

There are two live attenuated monovalent VVs registered (approved for use) and available (marketed) in New Zealand. Two quadrivalent live attenuated MMRV vaccines are registered but not currently available in New Zealand.

Funded vaccine

Monovalent VV (Varivax, MSD) contains not less than 1,350 PFU of the varicella-zoster virus (Oka/Merck strain). Other components and residuals include sucrose, gelatin, urea, sodium chloride, monosodium L-glutamate, potassium chloride, MRC-5 cells, neomycin and bovine calf serum.

Other vaccines

Monovalent VV

Varilrix, (GSK): each 0.5 mL dose contains no less than $10^{3.3}$ PFU (plaque-forming units) of the varicella virus (VZV Oka strain). Other components and residuals include amino acids, lactose, neomycin sulphate and polyalcohols (mannitol and sorbitol). See section 22.5.2 for eligible infants aged 9–11 months available from hospitals.

Quadrivalent MMRV – not currently available in New Zealand

- Priorix-Tetra (GSK) contains the Schwarz measles, RIT 4385 mumps, Wistar RA 27/3 rubella and varicella (Oka/Merck VZV) virus strains.
- ProQuad (MSD) contains Enders' attenuated Edmonston (Moraten) measles virus strain, Wistar RA 27/3 rubella virus, Jeryl Lynn mumps virus and live varicella virus vaccines (Oka/Merck VZV)

See also section 12.4.1 for more information about MMR vaccines.

22.4.2 Efficacy and effectiveness

Single-dose varicella vaccination programmes have had a dramatic impact on the incidence of VZV infections,[14, 15, 16] hospitalisations[3, 4, 17] and serious outcomes,[5] particularly when high coverage rates are achieved. Indirect effects are also apparent. A 2014 systematic review of varicella vaccines found that a single dose of VV is moderately effective for preventing any severity of varicella (approximately 80 percent) in immune-competent individuals, highly effective for preventing moderate-severe disease (approximately 95 percent) and highly effective in preventing severe disease only (approximately 99 percent).[18] However, single-dose programmes are associated with outbreaks even among highly vaccinated groups.[19, 20]

The use of a second dose during outbreaks has been an effective strategy to prevent further cases. Catch-ups for non-immunised groups without a previous history of varicella are also important. There is a significant reduction in breakthrough disease when two doses are given. After a second dose in children the immune response is markedly enhanced, with over 99 percent of children attaining an immune response thought to provide protection, and the geometric mean antibody titre is also significantly increased.

Over a 10-year period the estimated vaccine efficacy of two doses for prevention of any varicella disease is 98 percent (compared to 94 percent for a single dose), with 100 percent efficacy for the prevention of severe varicella. The likelihood of breakthrough varicella is reduced by a factor of 3.3.[21, 22] Because of this data, in 2006 the US authorities recommended a two-dose strategy for varicella prevention, with the first dose at age 12–15 months and the second at age 4–6 years, as for MMR.[19, 21] A Hong Kong study recommended reducing the time between doses, to age 12 months and 18 months, to reduce breakthrough cases and outbreaks in preschools.[23]

The antigenic components of MMRV vaccines are non-inferior compared with simultaneous administration of MMR and VV,[24, 25] for both the first and second doses.

Herd immunity

In regions where universal varicella vaccination programmes have been implemented, significant declines in varicella cases and hospitalisation have been observed. These programmes also reduce circulating VZV and provide protection through herd immunity for those who are unable to be immunised, such as infants and immunocompromised individuals.

In the US, the annual average age-adjusted mortality rate for varicella was 0.05 per million population during 2008–2011, an 87 percent reduction from the pre-vaccine years.[26] In Canada between 2000 and 2007, a single dose of VV was introduced to the immunisation schedules of different provinces at 12 months of age; most provinces also included catch-ups for susceptible children at preschool or school. An ecological study of varicella-related hospitalisations in Canada between 1990 and 2010 found that hospitalisation rates decreased in all age groups, including infants and those aged 20–39 years.[27] Similar herd effects were seen in Germany, with declines in varicella cases and hospitalisations in infants and adolescents who were not eligible for VV.[28]

Duration of immunity

Varicella vaccination provides long-term but probably not lifelong immunity against VZV, in contrast to VZV natural infection. The duration of protection after a single dose of vaccine is difficult to study – especially if wild-type varicella continues to circulate liberally in the community, providing natural boosting and prolonging the duration of protection.[18] Many countries that initially introduced a single-dose vaccination programme have subsequently changed to a two-dose programme as the epidemiology of the disease has changed over time.

22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

VV requires reconstitution before administration.

Varivax is presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, although the diluent may be stored at room temperature (to a maximum of 25°C). Reconstituted vaccine should be used immediately, if possible, and discarded if reconstituted vaccine is not used within 150 minutes (2½ hours) at room temperature. Do not freeze reconstituted vaccine.[29]

22.4.4 Dosage and administration

The dose of monovalent VV is 0.5 mL, administered by intramuscular or subcutaneous injection in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

Monovalent VV can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (eg, MMR, BCG) by at least four weeks.

22.5 Recommended immunisation schedule

Recommendations for VV are summarised in Table 22.1 and discussed below.

VV is recommended to be administered with the second MMR dose and Hib-PRP at age 15 months. VV can be used for a second (unfunded) dose or first dose after age 4 years, as appropriate for those not in eligible special groups.

Table 22.1: Varicella vaccine recommendations and schedule

Funded individuals are shown in shaded boxes. See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to funding decisions.

Recommended and funded
1 dose of VV for: • children at age 15 months; or • previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.
2 doses of VV, at least 6 weeks apart, for the following special groups[a] • non-immune patients: – with chronic liver disease who may in future be candidates for transplantation[b] – with deteriorating renal function before transplantation[b,c] – prior to solid organ transplant – prior to any planned immunosuppression[d] – for post-exposure prophylaxis of immune-competent in-patients • patients at least 2 years after bone marrow transplantation, on the advice of their specialist • patients at least 6 months after completion of chemotherapy, on the advice of their specialist • HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression, on the advice of an HIV specialist • patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella • household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella • household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.
Recommended, not funded
1 dose for all susceptible healthy children aged under 13 years who do not meet the eligibility criteria for the funded dose. 2 doses, at least 6 weeks apart, for all susceptible adolescents and adults.

a. See chapter 4 'Immunisation of special groups' for more information.

b. See Table 4.4 for an accelerated immunisation schedule for infants in whom liver or kidney transplant is likely.

c. Check Starship Children's Hospital guidelines for children with chronic kidney disease, dialysis and renal transplant, (available at **www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd**).

d. Note that immunosuppression due to steroid or other immunosuppressive therapy must be for a treatment period of greater than 28 days.

22.5.1 Usual childhood schedule

From 1 July 2020, one dose of VV (Varivax) is funded for children at age 15 months. A second VV dose is not currently funded but may be purchased for those who wish to reduce the risk of breakthrough disease.

A catch-up dose of VV is funded for previously unvaccinated children turning 11 years old who have not previously had a varicella infection (as determined by clinical history). This dose aims to protect those who have not become immune to varicella before adolescence, as disease in adolescents and adults can be more severe.

22.5.2 Special groups

Two doses of VV (Varivax), at least six weeks apart, are recommended and funded for the special groups listed in Table 22.1 above. Since Varivax is not licenced for infants under 12 months of age, Varilrix continues to be available from hospitals only for infants with certain medical conditions aged 9–11 months of age requiring an accelerated immunisation schedule (see Table 4.4).

Immunocompromised (including immunosuppressed) individuals

The vaccine should not be given to immunocompromised individuals except under the direction and care of a specialist, following a suitable protocol[19] (see section 4.3).

Some clinical trials of the original vaccine formulations were conducted in immunocompromised children (with leukaemia in remission or with HIV infection on antiretroviral treatment). One study found that half the vaccinated children receiving maintenance chemotherapy developed a rash up to one month after vaccination (40 percent of these required acyclovir treatment), compared with 5 percent of those no longer on chemotherapy.[30] Despite this, the study concluded that the vaccine, Varivax, was safe, immunogenic and effective in these children.[30, 31]

The combination MMRV vaccine should not be used in immunocompromised individuals.

Varicella immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with impaired humoral immunity may be immunised (see section 22.6.1 for further contraindications). Seek specialist advice.

Household contacts of immunocompromised individuals

Immunocompromised individuals are at highest risk of severe varicella and zoster infections.

Where such individuals cannot be vaccinated, it is important to vaccinate the non-immune household members and other close contacts (funded for household contacts) to provide 'ring-fence' protection (see sections 4.2, 4.3 and 22.7.1).

22.5.3 Recommended but not funded

A single dose of VV is recommended for susceptible children who do not meet the eligibility criteria for funded vaccine (Table 22.1). A second dose may also be purchased for those who wish to reduce the risk of breakthrough disease.

VV in a two-dose schedule is recommended but not funded for the following groups:[19]

- adults and adolescents who were born and resided in tropical countries, if they have no history of varicella infection
- susceptible adults and adolescents (ie, those who have no prior history of chickenpox)
- susceptible individuals who live or work in environments where transmission of VZV is likely (see Table 4.9 for occupational groups)
- susceptible non-pregnant women of childbearing age
- susceptible international travellers[19]
- health care workers (see below)
- susceptible individuals who have been exposed to varicella (see section 22.8.3).

See section 22.8.1 for information about assessing susceptibility.

Health care workers

All health care workers should be immunised with VV if they are susceptible to varicella (not funded), particularly those within obstetric, paediatric and neonatal units, and those caring for immunocompromised children and adults. When a health care worker has a good history of prior varicella infection, no blood test is required.[32] If there is not a good history of varicella infection, a blood test to assess susceptibility will be necessary, as many individuals with no clinical history of varicella are immune (see section 22.8).

If a health care worker who has clinical contact with patients develops a rash as a result of the vaccine (around 5 percent), they must be excluded from contact with immunocompromised or other at-risk patients and allocated other duties, or excluded from their place of work, for the duration of the rash.

22.5.4 Pregnancy and breastfeeding

Varicella vaccines are contraindicated in pregnant women. Pregnancy should be avoided for at least four weeks after vaccination.[33] The vaccine's safety for the fetus has not yet been demonstrated, although no congenital defects have been described following inadvertent administration to pregnant women.

A pregnant woman in the household is not a contraindication for immunisation of a child, and the vaccine can be administered to non-immune mothers who are breastfeeding.

22.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

22.6.1 Contraindications

Varicella vaccines are contraindicated for the following people:

- individuals with primary or acquired T-cell immune deficiency states – consult the child's paediatrician for advice[33]
- individuals with blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.
- individuals on high-dose steroids for more than two weeks (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20mg per day if their weight is over 10 kg)
- individuals are receiving or who have recently received chemotherapy (consult with specialist)
- individuals with a family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.
- individuals with a history of an anaphylactic reaction to a prior dose of VV or any component of the vaccine, including neomycin and gelatin.
- individuals with active untreated TB
- pregnant women – women should avoid pregnancy for at least four weeks after vaccination[33] (see section 22.5.4).

22.6.2 Precautions

Because of the association between Reye syndrome, natural varicella infection and salicylates, the vaccine manufacturers advise against the use of salicylates for six weeks after VV is given. There has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution,[33] and physicians need to weigh the theoretical risk of Reye syndrome from the vaccine against the known risk from varicella disease in children receiving long-term salicylate therapy. Children on low-dose aspirin following cardiac surgery would be more at risk of thrombosis from stopping their aspirin[34] than from the theoretical risk of Reye's with VV.

If tuberculin testing has to be done, it should be carried out before or simultaneously with vaccination because it has been reported that live viral vaccines may cause a temporary depression (anergy) of tuberculin skin sensitivity.[35] As this anergy may last up to a maximum of six weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

On the advice of their specialist, VV may be administered to:

- patients at least two years after bone marrow transplantation
- patients at least six months after completion of chemotherapy
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression.

For suggested intervals between receipt of human normal immunoglobulin or other blood products and VV, see Table A6.1 in Appendix 6.

Antiviral medications with anti-VZV activity, such as acyclovir, valaciclovir and famciclovir, can interfere with the replication of the VZV strain in VV. It is recommended that antiviral medication be stopped at least 24 hours before vaccination and recommenced at least 14 days after vaccination.

22.7 Potential responses and AEFIs

22.7.1 Potential responses

A 2013 systematic review of varicella vaccines found that mild adverse events were the most frequently reported AEFIs.[36] This includes injection-site reactions such as pain, swelling and redness, which occurred in up to 28 percent of recipients. There was no increased risk of cerebellar ataxia, encephalitis or ischaemic stroke following vaccination. Post-marketing surveillance in the US found the rate of AEFIs to be 30 per 100,000 doses of VV, and the rate of serious AEFIs was less than 4 per 100,000 doses. Fever has been reported in 15 percent of healthy children following VV and 10 percent of adults.[33, 37]

Post-VV rash

In approximately 1–3 percent of immunised children, a localised rash develops, and in an additional 3–5 percent a generalised varicella-like rash develops.[33] These rashes typically consist of two to five lesions and may be maculopapular rather than vesicular; lesions usually appear 5–26 days after immunisation. Not all rashes can be attributable to the vaccine;[33] some may be due to exposure to wild-type virus, prior to vaccination.

Transmission of vaccine virus to contacts of vaccinated individuals

In healthy vaccine recipients, transmission of vaccine virus to contacts is exceedingly rare, documented in nine immunised people and resulting in 11 secondary cases. The documented risk exists only if the immunised person develops a rash.[33] Err on the side of caution and isolate the vaccine recipient if they are a household contact of an immunocompromised individual and a post-immunisation rash occurs. If an immunocompromised individual inadvertently comes in contact with a vaccine recipient who has a varicella-like rash, the administration of zoster immunoglobulin (ZIG) and/or acyclovir should be considered (see below).[33] Intravenous acyclovir may be required if symptoms develop.

22.7.2 AEFIs

Vaccine virus shingles

The Oka strain of VZV used in the available vaccines can establish latent ganglionic infection in vaccine recipients and later reactivate to produce clinical zoster (shingles). The risk of zoster is lower, and the clinical severity milder, in immunocompentent vaccine recipients than in naturally infected children. A cohort study in children with acute lymphoblastic leukaemia (who have a high rate of zoster in childhood) showed that vaccine recipients had less than one-fifth the zoster rate of their naturally infected counterparts.[30, 38] Some zoster lesions in vaccine recipients have been shown to contain wild-type virus, likely acquired prior to vaccination.[33]

Febrile seizures with MMRV vaccine

MMRV vaccines are not currently available in New Zealand. Compared with the use of MMR and VV at the same visit, use of MMRV vaccine requires one fewer injection but is associated with a higher risk of fever and febrile seizures 5 to 12 days after the first dose among children aged 12–23 months (approximately one extra febrile seizure for every 2,300–2,600 MMRV vaccine doses).[39]

After the second dose, there are no differences in incidence of fever, rash or febrile seizures among recipients of MMRV vaccine compared with recipients of MMR and VV.[39] There is no evidence of an association with increased febrile seizures when MMRV is given to toddlers as a second dose of MMR.[40] For example, in Australia, the first dose of MMR is given at 12 months and the second dose is given as MMRV at 18 months.

22.8 Public health measures

At present, VZV is not a notifiable disease in New Zealand.

22.8.1 Susceptibility

In general, a positive history of chickenpox can be taken as indicating immunity, provided there has not been an intervening bone marrow transplant or other immunosuppressive therapy. Recall of varicella or characteristic rash is reliable evidence of immunity. In people with no history or recall of the rash, 70–90 percent are found to be immune.[33] Consult with the local laboratory about the availability and interpretation of varicella serology.

22.8.2 Post-exposure prophylaxis with zoster immunoglobulin

Zoster immunoglobulin (ZIG) is a high-titre immunoglobulin available from the New Zealand Blood Service for passive immunisation of varicella in high-risk individuals. It is most effective if given within 96 hours after exposure, but may be have some efficacy if given up to 10 days post-exposure.[39, 41, 42, 43] ZIG should be given intramuscularly.[43] Intravenous immunoglobulin (IVIG) can be given when ZIG is unavailable.
For further information, see Starship Child Health guidelines (available at **starship.org.nz/guidelines/zoster-immunoglobulin**).

The decision whether to offer ZIG depends on:[43]

- the likelihood that the exposed person is susceptible to varicella
- the probability that a given exposure to varicella will result in infection
- the likelihood that complications would develop if the person exposed is infected.

Contact (exposure) can be classified as follows:[43]

- household contact – infection is very likely to occur in a susceptible individual living with an infected contact
- playmate contact – more than one hour of play indoors with infected individual
- newborn infant contact – when the mother of a newborn infant develops chickenpox (but not shingles) from seven days before to seven days after delivery
- hospital contact – individuals in the same two-bed room or have face-to-face contact for longer than five minutes.

Provided exposure has occurred and susceptibility is likely, **ZIG is recommended for**:

- pregnant non-immune women (see section 22.8.6 below and discuss with an infectious diseases physician)
- newborn infants whose mother had onset of chickenpox (but not shingles) within seven days before or after delivery (see section 22.8.6)
- hospitalised premature infants whose mothers have no history of chickenpox, or who were born at less than 28 weeks' gestation, or with birthweight less than 1,000 g, irrespective of maternal history
- immunocompromised individuals – discuss the use of ZIG with their specialists, as appropriate.

Dosage of ZIG

ZIG prepared by CSL Behring in Melbourne, derived from human plasma donated in New Zealand, is available in single vials containing 200 IU varicella-zoster antibody. The actual volume in the vial is stated on the label. The recommended dose is based on body weight and is shown in Table 22.2 below. ZIG should be given intramuscularly, not intravenously.[43]

Table 22.2: Dose of ZIG based on body weight

Weight of patient (kg)	Dose (IU)	Number of vials
0–10	125	1
10.1–20	250	2
20.1–30	375	2
30.1–40	500	3
over 40	600	3

Source: CSL Behring. 2018. *Zoster Immunoglobulin-VF New Zealand Data Sheet*. URL: **www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins** (accessed 17 February 2020).

If ZIG is not available, IVIG can be used. The titre of anti-varicella antibody will vary between lots, and the blood transfusion centre haematologist needs to be contacted to confirm the appropriate dose when IVIG is used.

22.8.3 Post-exposure vaccination and outbreak control

VV may be used for post-exposure prophylaxis of susceptible individuals aged 9 months or older, if there are no contraindications to vaccine use[33] – see Table 22.3. Data from the US and Japan from household, hospital and community settings indicates that VV is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure.

Table 22.3: Post-exposure varicella vaccination recommendations

Note: **Funded individuals are shown in the shaded rows below**. See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to the funding decisions.

	Schedule
Immune-competent hospital in-patients who are susceptible to varicella, from age 9 months[a,b]	First dose within 3 days of exposure (up to a maximum of 5 days) Second dose at least 6 weeks later
Susceptible individuals aged from 9 months – who are not eligible for age-appropriate funded vaccine[b,c,d]	Give 1 dose within 3 days of exposure (up to a maximum of 5 days) A second dose can be given at least 6 weeks later

a. Varilrix is available from hospitals for infants aged 9 months to under 12 months.

b. The funded 15-month VV dose can be given from 12 months of age for post-exposure prophylaxis

c. VV can be purchased for individuals who are not eligible to receive funded VV, including infants aged 9 months to under 12 months who do not have an eligible condition listed in Table 21.1.

d. Children who were under age 12 months when they received VV for post-exposure prophylaxis will still be eligible for the age 15-month dose. Ensure there are at least 6 weeks between doses.

VV may not prevent disease in all cases because some individuals may have been exposed to the same source as the index case.[33] If exposure to varicella does not result in infection, post-exposure vaccination should induce protection against subsequent exposure. If the exposure results in infection, no evidence indicates that administration of VV during the pre-symptomatic or prodromal stage of illness increases the risk for AEFIs. Note that although this method of immunisation may be successful, it is not necessarily reliable. Immunisation before exposure is therefore recommended as the preferred method of preventing outbreaks.

22.8.4 In-hospital exposure

In the event of an exposure:

- susceptible staff should be excluded from contact with high-risk patients from day 8 to day 21 after exposure to varicella (or shingles in an immunocompromised patient)
- hospital staff who have no history of chickenpox and who will be in contact with pregnant women or high-risk patients should be tested for varicella zoster antibodies; vaccination is recommended for those who are not immune or whose serostatus cannot be promptly determined.

Two doses of VV are funded for post-exposure prophylaxis of immune-competent in-patients who are susceptible to varicella (see section 22.8.3).

22.8.5 Exclusion from school or early childhood education services

Parents/guardians should be advised that:

- infected children should be excluded from early childhood education services or school until fully recovered, or all lesions have crusted. Lesions from mild breakthrough disease in immunised children may not crust but these children should be excluded until no new lesions appear for 24 hours[33]
- immune-deficient children should be excluded from early childhood education services or school until three weeks after the last documented case.

22.8.6 Care of pregnant women after exposure

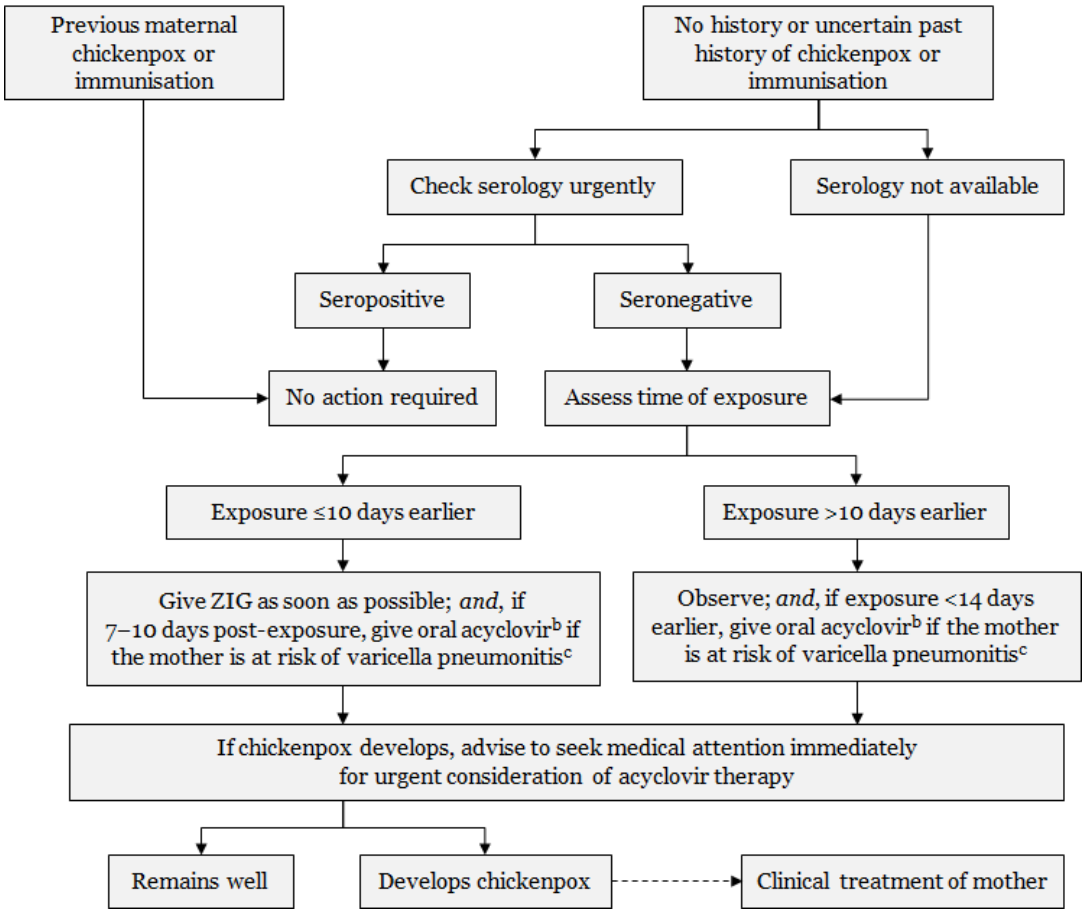
Pregnant women are at higher risk of severe complications from varicella. If an immune-competent pregnant woman with no history of varicella or vaccination is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed (Figure 22.1). If there is no evidence of immunity, two possible courses of action are available: either administer ZIG, or await the onset of symptoms and as soon as possible commence the administration of acyclovir, which is effective in this

situation and now regarded as safe in pregnancy. Discuss the clinical circumstances with an infectious diseases physician before deciding on which course of action is best.

Intravenous acyclovir is recommended for the pregnant woman with severe complications of varicella. ZIG given to a pregnant woman within five days of delivery may not protect the fetus/neonate: the neonate should receive ZIG on delivery and may need treatment with acyclovir (Figure 22.2).

Figure 22.1: Management of pregnant women exposed to varicella or zoster

Every effort should be made to confirm the diagnosis in the suspected positive contact and assess significance of exposure.[a] Exposure or symptoms in the final two weeks of pregnancy should always be discussed with a specialist.



a. Exposure to varicella or zoster for which ZIG is indicated for susceptible persons includes: living in the same household as a person with active chickenpox or herpes zoster; face-to-face contact with a case of chickenpox for at least 5 minutes; close contact (eg, touching, hugging) with a person with active zoster.

b. Efficacy of acyclovir for post-exposure prophylaxis has not been tested in controlled trials. Dose is 800 mg orally, 5 times per day for 7 days.

c. The mother is at risk of pneumonitis if she is in the second half of pregnancy; has underlying lung disease; is immunocompromised; or is a smoker.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

Pregnant women exposed to VZV should be counselled about the risks of congenital varicella syndrome (CVS), a rare but devastating disorder that can occur following varicella zoster infection during pregnancy (see Table 22.4). The risk of CVS is greatest in the first 20 weeks of pregnancy. Large case studies suggest that the rate of CVS is 0.4 percent when maternal infection occurs up to week 12 of pregnancy, and 2 percent from weeks 13 to 20.

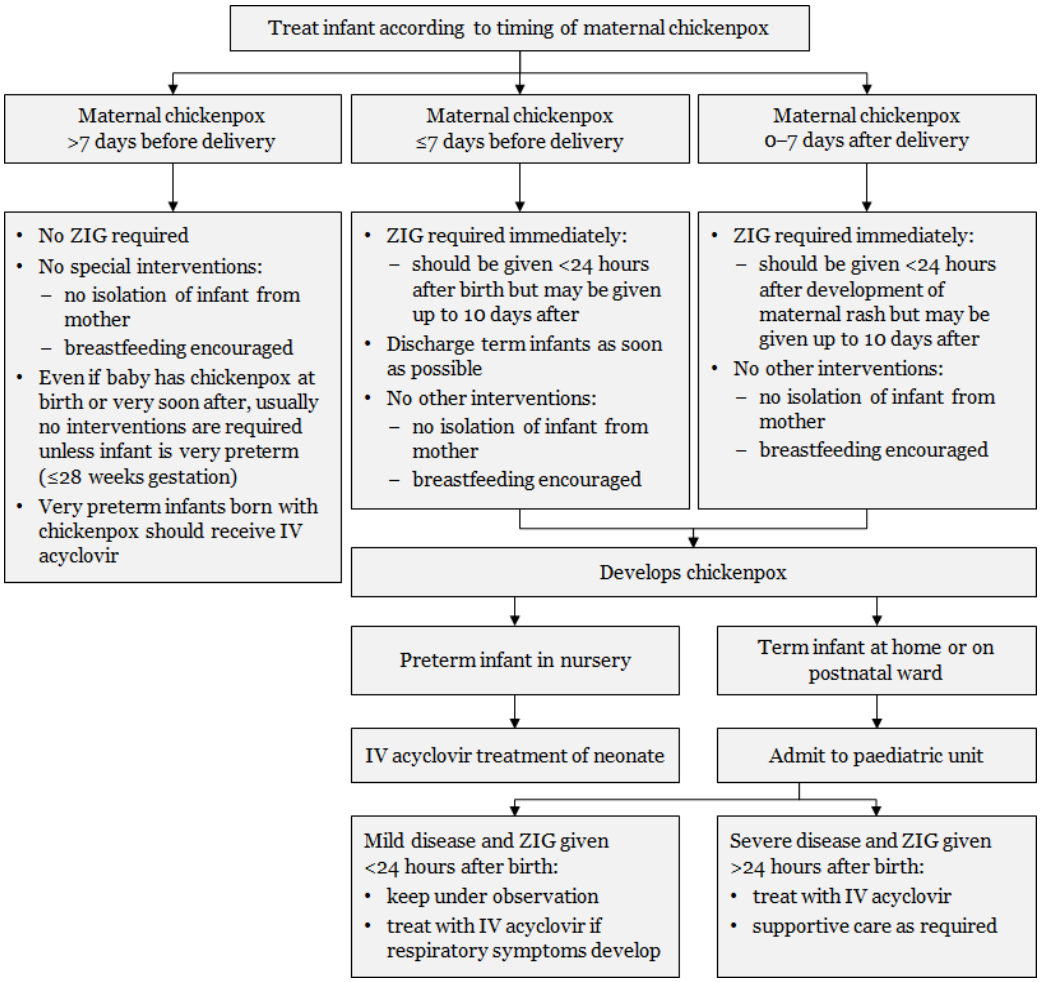
There is no single diagnostic test available for CVS. Regular fetal ultrasound for developmental anomalies is recommended. VZV fetal serology is unhelpful but amniocentesis may be considered; negative VZV PCR may be reassuring.

Table 22.4: Sequelae of congenital varicella

Sequelae	Frequency
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birthweight	50%
Cortical atrophy, severe developmental delay	46%
Poor sphincter control	32%
Early death	29%

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

Figure 22.2: Management of infants from mothers with perinatal varicella or zoster



Notes:

a. Transplacentally acquired VZV is high risk and severity is reduced by ZIG.

b. ZIG is not always effective in preventing severe disease.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

22.9 Variations from the vaccine data sheet

The VV (Varivax) data sheet recommends that children aged 12 months to 12 years receive a second dose administered at least three months after the first to ensure optimal protection against varicella.[29] The Ministry of Health instead recommends a single dose of VV for healthy children at 15 months or 11 years of age (see section 22.5.1) and two doses for individuals with a special groups condition given 6 weeks apart (see section 22.5.2).

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23 Zoster (herpes zoster/shingles)

Key information

Mode of transmission	Zoster is a reactivation of the varicella-zoster virus in someone who has previously had varicella disease (most often as chickenpox). Direct contact with zoster vesicles has a low risk of causing varicella in non-immune individuals – can be prevented by covering the rash. There is potential for aerosol transmission from some immunocompromised cases with viraemia.
Period of communicability	Until lesions have crusted.
Incidence and burden of disease	Increasing incidence with age; lifetime risk about 1 in 3. For those aged over 85 years, the risk is 1 in 2. Complications include post-herpetic neuralgia and herpes zoster ophthalmicus.
Funded vaccine	Recombinant zoster vaccine – rZV; Shingrix • approved for use for all adults aged 50 years and over • for adults aged 18 years or over at increased risk of zoster due to immunocompromise.
Dose, presentation, route	• 0.5 ml per reconstituted dose • vial of vaccine powder and vial of suspension for one dose. The vaccine must be reconstituted prior to injection. • Intramuscular injection only
Funded vaccine indications and recommended schedule	Two doses of rZV are funded for individuals at age 65 years.
Recommended, not funded	• for use from age 50 years, including those aged 66 years and older, due to older age and comorbidity • for individuals aged 18 years or older with increased risk of zoster due to immunocompromise.
Vaccine efficacy/ effectiveness	rZV showed efficacy against both zoster and post herpetic neuralgia of over 90 percent in participants aged over 50 years and over 70 years, including those with comorbidities, maintained at 84 percent for at least 7 years.
Contraindications	For contraindications and precautions see section 23.6.1. Use in pregnancy is limited and not routinely recommended.

23.1 Virology

Varicella-zoster virus (VZV) is a DNA virus from the herpesvirus family. The virus is usually acquired in childhood and primary infection with VZV causes varicella disease (chickenpox). Herpes zoster (zoster), or 'shingles', is a clinical syndrome caused reactivation of latent VZV, which resides in the dorsal root or trigeminal nerve ganglia after primary infection. VZV is usually acquired in childhood, but it is often many decades before the virus reactivates, at times when cellular immunity is compromised and is unable to maintain suppression of the virus.

23.2 Clinical features

Herpes zoster (shingles) occurs when the cell-mediated immune response is impaired and unable to maintain suppression of latent varicella-zoster virus reactivation (see chapter 22). Zoster occurs only by loss of suppression and reactivation of the patient's own virus – which is often acquired in childhood; it is not acquired from other patients with zoster or varicella.[1]

VZV, present at low levels in lesions of zoster rash, is transmissible via direct contact with fluid in the rash vesicles to VZV-naïve or other susceptible individuals (causing chickenpox). Episodes of zoster in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals. Covering the rash can reduce this risk of transmission.

Zoster presents clinically as a unilateral vesicular rash, which in most cases is in a dermatomal distribution. The dermatomal distribution of the rash is the key diagnostic feature. In 70–80 percent of zoster cases in older adults, prodromal pain and/or itching occurs three to four days before the appearance of the rash.[2] In the majority of patients, zoster is an acute and self-limiting disease, with the rash lasting 10–15 days. However, complications can occur, especially with increasing age.

Although most zoster cases occur in adults aged 40 years or older, it may be seen less commonly in infants and children. In those aged under 2 years may reflect *in utero* chickenpox, with the greatest risk arising following exposure between 25 and 36 weeks' gestation, and reactivation in early life. Infants who get varicella at a young age have a higher change of having zoster before the age 20 years.

A common complication of zoster is post-herpetic neuralgia (PHN), a chronic, often debilitating pain condition that can last several months or even years. A systematic review of the incidence and complications of zoster found that the risk of developing post-herpetic neuralgia ranges between 5 percent and about 30 percent (depending on the type of study design, age distribution of the study populations and definition).[3] The risk rises with age, and it is uncommon in healthy children and young people.

Herpes zoster ophthalmicus (HZO) is another complication of zoster, which occurs when VZV reactivation affects the ophthalmic branch of the trigeminal nerve. HZO can

occur with or without eye involvement, and can result in prolonged or permanent pain, facial scarring and loss of vision. About 10 percent of zoster patients develop HZO, if that dermatome is affected, and the risk is similar across all age groups.[3]

The incidence of zoster is highest in immunocompromised individuals,[4, 5] including:

- following HSCT
- solid organ transplants[6]
- haematological malignancy[7]
- immunomodulatory treatments and immune-mediated inflammatory diseases including treatments for
  - rheumatoid arthritis[8]
  - systemic lupus erythematosus
  - inflammatory bowel disease
  - cancer
- those living with HIV infection.[9]

Up to 10 percent of children treated for a malignant neoplasm may develop zoster. In immunocompromised patients, extensive viraemia in the absence of a vigorous immune response can result in a disseminated form of zoster that includes severe multi-organ disease.[2, 10] There is an increased risk of airborne transmission of VZV for immunocompromised individuals with viraemia.

Other factors associated with an increased risk of developing zoster include splenectomy, chronic pancreatitis, chronic kidney disease, chronic inflammatory skin disease,[11] anxiety and depression,[12, 13] sleep disorders[14] and type 1 and type 2 diabetes,[15, 16, 17] chronic obstructive pulmonary disease and adult asthma.[18] Environmental factors such as exposure to high ambient temperature, UV radiation[19, 20] and high altitudes[21] have also been proposed as potential triggers. There is some evidence that a family (sibling or parent) history of zoster is also a potential risk factor in elderly individuals.[22] Incidence of zoster is higher in women than men.[4]

23.3 Epidemiology

23.3.1 Global burden of disease

Zoster is a sporadic disease occurring as a reactivation of the VZV in individuals who have previously had chickenpox. Approximately one in three people will develop zoster during their lifetime with the incidence rising as cell-mediated immunity to VZV declines with age;[23] 50 percent of those aged 85 years or over will suffer zoster.[24, 25] A systematic review documented an incidence rate between 3 and 5 per 1,000 person-years in North America, Europe and Asia-Pacific.[3] The incidence rate was about 6–8 per 1,000 person-years at age 60 years and 8–12 per 1,000 person-years at age 80 years.

Recurrence is greater in females than males (about 7 percent after eight years compared with 4 percent for males), and in those who are immunocompromised. Third

episodes are rare. In those who have zoster at a younger age (45–54 years) the time from the first episode to recurrence is shorter than for those who are aged over 55 years (mean time 2 years [IQR 1.0–2.3] vs 3 years [1.4–4.2], respectively).[26]

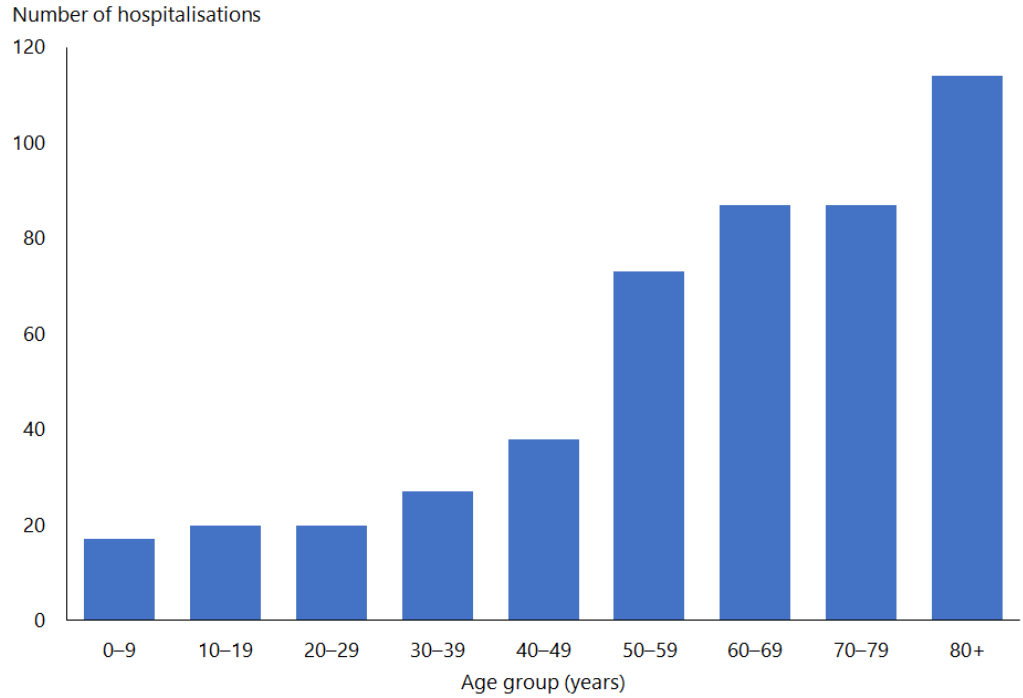
VZV is present in lesions of zoster and is transmissible via direct contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immunocompromised individuals with disseminated zoster. Episodes of zoster in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals.

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in zoster in older adults. However, several studies that have investigated this issue, observed an increase in zoster prior to VV programme introductions and have been unable to attribute any increase in incidence of zoster to childhood VV programmes.[11, 12, 13, 14] Such increases have been observed in countries both with and without childhood varicella immunisation.

23.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2018/2019 are shown in Figure 23.1, with around 60 percent occurring in adults aged 60 years and older. Hospitalisations are predicted to account for only a very small proportion of the overall zoster cases as most are managed in primary care. Interrogation of general practice electronic records found the incidence of zoster in New Zealand to be similar (approximately 5 per 100,000 patient-years rising to 12.8 per 100,000 in those aged 80–90 years) to the global incidence estimates described in section 23.3.1.[27] In 2018/2019, there were 483 hospitalisations associated with herpes zoster.

Figure 23.1: Hospitalisations with herpes zoster as primary diagnosis by age group, 2018/2019



Source: Ministry of Health.

23.4 Vaccine

23.4.1 Available vaccines

Funded vaccine

The funded vaccine is an adjuvanted recombinant subunit zoster vaccine (Shingrix, GSK) containing recombinant VZV glycoprotein E and a proprietary AS01$_B$ adjuvant system that is designed to specifically boost T-cell immunity against VZV.[28]

Each 0.5 ml dose contains:

- 50 µg of recombinant VZV glycoprotein E
- AS01$_B$ liposome-based adjuvant containing two immunostimulants: 50 µg of *Quillaja saponaria* (soapbark tree) saponin fraction 21 (QS-21) with 50 µg detoxified lipopolysaccharide fraction, 3-O-desacyl-4'-monophosphoryl lipid A (MPL), from *Salmonella minnesota*.
- It also contains dioleoylphosphatidylcholine, cholesterol, sodium chloride, dibasic sodium phosphate, monobasic potassium phosphate and water.

Other vaccines

A live attenuated varicella-zoster virus vaccine (Zostavax, MSD) is approved for use from the age of 50 years and used as part of the Schedule at age 65 years from 2018 to August 2022. It is no longer available in New Zealand. This higher titre formulation of the varicella vaccine is designed to protect against zoster in those already immune to varicella.[29] By mimicking the immune response seen following a zoster episode and boosting cell-mediated immunity in older adults, the incidence and severity of zoster is reduced. Efficacy against zoster is around 60 percent in adults aged from 50 years and 67 percent against post-herpetic neuralgia in clinical trial settings.[29] Vaccine effectiveness in adults aged 70–79 years in the UK was estimated to be 64 percent (95% CI: 60–80) against zoster and 81 percent (95% CI: 61–91) against PHN. Vaccine effectiveness was lower in those who had a history of zoster (47 percent; 95% CI: 31–58).[30] Clinical effectiveness declined beyond five years post-vaccination.[31] The use of this live vaccine was limited due to a risk of disseminated VZV infection in severely immunocompromised individuals.

23.4.2 Efficacy and effectiveness

Efficacy in adults aged 50 years and over

Two phase III clinical trials (ZOE-50 and ZOE-70) demonstrated vaccine efficacy of over 90 percent in adults aged from 50 years and aged over 70 years, and those with medical conditions that increase their risk of zoster.[32, 33, 34, 35, 36] Pooled data gave vaccine efficacy of 91 percent (95% CI 87–95 percent) against the incidence of zoster overall, and 91 percent (86–98 percent) against post-herpetic neuralgia across all age groups. No decline in efficacy was observed with increasing age; in those aged over 80 years efficacy was 91 percent (80–97 percent) against zoster.[37]

Immunogenicity of rZV was shown to be similar in adults aged 65 or over who have previously received live zoster vaccine compared with those who were live ZV naïve. A strong humoral and polyfunctional cell-mediated immune response was shown to persist for at least 1 year after dose 2 of rZV.[38]

Post-hoc analysis, long term follow-up of trial participants found rZV efficacy against zoster plateaued after four to six years and was sustained overall at 84 percent for at least seven years post-vaccination, including in individuals aged 70 years and over and people with pre-existing medical conditions.[33, 37]

Effectiveness in adults aged 50 years and over

Most effectiveness studies of recombinant ZV have been conducted in the US, as of July 2022. One study involving 1.74 million people found the vaccine effectiveness of two doses of rZV against zoster overall was 85.5 percent (95% CI 83.5–87.3 percent), 86.8 percent (84.6–88.7 percent) in those aged 50 to 79 years and 80.3% (75.4–84.3 percent) for those aged 80 years and over. In those who received live ZV within 5 years, vaccine effectiveness of recombinant ZV was 84.8 percent (75.3–90.7 percent) compared with unvaccinated people. Adjusted effectiveness of two doses rZV against herpes zoster ophthalmicus was 89.1 percent (82.9–93.0 percent).[39] Another real-world study found that administering the second dose beyond six months after the first dose

did not impair effectiveness in community-dwelling adults aged over 65 years (approximately 1.5 million participants received one dose and 1.0 million received two doses, compared with 15.6 million unvaccinated controls).[40] One dose was 59.5 percent (57.4–61.4 percent) effective for up to six months and 43.5 percent (37.9–48.7 percent) after six months; whereas, two doses were 70.0 (68.4–71.5 percent) effective for up to six months after the second dose, and effectiveness was maintained beyond six months.[40]

Severely immunocompromised adults

Good immunogenicity was also shown in immunocompromised participants, including those aged from 18 years with solid organ transplants, solid organ tumours, haematopoietic stem cell transplants or living with HIV infection.[41, 42, 43, 44, 45] In HSCT recipients, efficacy of 72 percent (39–88%) was shown in those aged 18–49 years and 67 percent (53–78 percent) in those aged 50 or older with 21 months follow-up; in those aged from 18 years with haematological malignancies, efficacy was estimated at 87.2 percent (44.3–98.6 percent) up to 13 months post vaccination.[42]

23.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

The recombinant rZV (Shingrix) must be reconstituted before use with supplied diluent. Once reconstituted, if not used promptly, can be store in a refrigerator (+2°C to +8°C) for up to 6 hours. Do not freeze. Protect from light.

23.4.4 Dosage and administration

Two doses of 0.5 ml are administered intramuscularly from two to six months apart.

This recombinant zoster vaccine can be given safely to individuals who are immunocompromised and/or receiving immunosuppressive agents. If a shortened schedule is required, the second dose can be given optimally at two months after the first dose.

Serological testing for previous VZV infection is not necessary prior to administration of this rZV to individuals with immunocompromise.

Individuals who are receiving antiviral medications, such as acyclovir, can be given rZV at any time without discontinuing their treatment. This vaccine does not contain live VZV.

Co-administration with other vaccines

Recombinant ZV (rZV) can be co-administered with most vaccines, including seasonal influenza vaccine, COVID-19 vaccines (mRNA-CV), 23PPV and Tdap. Due to limited experience at this time, it is recommended to allow three days spacing between rZV and the COVID-19 vaccine, rCV (Nuvaxovid) or the adjuvanted influenza vaccine (Fluad Quad), due to theoretical risk of two adjuvants increasing reactogenicity.

23.5 Recommended immunisation schedule

Table 23.1: Herpes zoster vaccine (rZV) recommendations

Note: Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of rZV. **Funded individuals are shown in the shaded row**. See the Pharmaceutical Schedule (**pharmac.govt.nz**) for any changes to funding decisions.

Recommended and funded
2 doses of recombinant rZV at age 65 years[a]

For consideration, but not funded

Two doses of recombinant rZV are recommended but not funded for all individuals aged from 50 years, including those aged over 66 years; and for individuals aged from 18 years who are at increased risk of zoster[5, 6, 9, 46, 47] including:

- prior to planned, receiving[b] or post immunosuppressive therapy
- with HIV infection
- with end-stage kidney disease (CKD stages 4–5)
- prior to or post solid organ transplantation
- prior to or post HSCT
- with immune-mediated inflammatory disease receiving immunomodulatory agents (eg, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis).

Other conditions that can increase risk of zoster in older adults include: [11, 13, 15]

- diabetes
- chronic obstructive pulmonary disease
- chronic inflammatory skin diseases
- splenectomy
- chronic pancreatitis
- psychiatric disorders, including depression and anxiety
- sleep disorders.

a. The second dose is funded at age 66 years if the first dose was given at age 65 years.

b. Ideally, vaccinate prior to planned immunosuppression. If rZV is given during treatment regimen, take timing of treatment and level of immunosuppression into consideration when timing vaccinations. If a shortened schedule is required, the second doses can be given optimally at two months after the first dose.

23.5.1 Other considerations

Recommended not funded

Adjuvanted recombinant zoster vaccine (rZV; Shingrix) is approved for use in New Zealand for all individuals aged 50 years or older (including those aged 66 years and over not eligible to funded vaccine).

It is also available (unfunded) for individuals aged 18 years and older at increased risk of zoster, particularly those who are at increased risk of zoster due to comorbidities[4, 7, 46] such as those who are immunocompromised due to an existing illness and/or its treatment or prior to planned immunosuppression. This includes individuals due to receive or following solid organ transplant, chemotherapy or systemic radiotherapy, and individuals with IMIDs (autoimmune disease) or living with HIV infection (see Table 23.1).

This vaccine can be given safely to individuals who are immunocompromised and/or receiving immunosuppressive agents. It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointments for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.7). If a shortened schedule is required, the second doses can be given optimally at two months after the first dose.

Individuals with a history of zoster (shingles)

Individuals with a history of zoster episodes can be given rZV. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis.[46] In addition, the risk of a repeat episode of zoster has been estimated at approximately 5 percent in immunocompetent individuals.[26, 46] The incidence of recurrence is higher in women than men, in people who are immunosuppressed, and in younger people, aged 45–64 years compared with those aged over 65 years at the time of the first episode.[26]

There are no recognised safety concerns in giving zoster vaccines to people with prior history of zoster.[48, 49] The length of time following an episode of zoster after which it may be beneficial to vaccinate has not been established.[50] Recombinant ZV is recommended to be given from 12 months after zoster has resolved from which time the rate of recurrence is increased.[26, 50] This timing may be shortened to at least three months for the use of rZV individuals who are immunocompromised with the highest risk of zoster recurrence.

Individuals with a history of zoster vaccination

The optimal time for administration of recombinant zoster vaccine following live ZV vaccination is not yet established.[50] Effectiveness of live ZV wanes significantly within three to five years of vaccination in adults aged 60 or older.[38] Individuals who previously received live ZV (Zostavax) can receive two doses of recombinant ZV (funded only at aged 65 years). Spacing of at least 12 months after live zoster vaccine is recommended but timing may be shortened to at least three months for the use of rZV in individuals who are immunocompromised with an increased risk of zoster recurrence or prior to planned immunosuppression.

Household contacts of immunocompromised individuals

See also 'Household contacts' in section 4.3.1 for general recommendations for vaccination of household contacts of immunocompromised individuals. Household contacts aged 50 years or over (funded at age 65 years) are recommended to receive two doses of rZV to reduce the risk contact with a zoster rash and the fluid in the vesicles being a source of VZV infection to immunocompromised individuals.

23.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

23.6.1 Contraindications

Recombinant rZV (Shingrix) is contraindicated to individuals with a history of hypersensitivity to a previous dose or to any component of the vaccine.

23.6.2 Precautions

There is limited data on the use of rZV in human pregnancy however, since it is a non-live vaccine, there are no theoretical safety concerns should it be inadvertently administered during pregnancy.

23.7 Potential responses and AEFIs

23.7.1 Potential responses

During clinical trials, rZV was generally well tolerated. The most commonly responses were injection-site pain, myalgia and fatigue; other responses included headache, shivering, fever and gastrointestinal symptoms. These were mild to moderate and lasting for one to three days post vaccination, with higher incidence in those aged under 70 years than in the older age groups.[35] Adverse events were also more frequently reported in younger age groups (ages 18 to 49 years compared with those aged over 50 years). In clinical studies in those aged 50 years and over, a higher incidence of fever and shivering was reported when rZV was co-administered with 23PPV.[51]

23.7.2 AEFIs

Injection-site reactions (eg redness or swelling) were more common after vaccination with rZV than live ZV according to a meta-analysis of clinical trial data (risk difference of 30 percent; 95% CI 2 to 51 percent). There was no statistical difference between serious adverse events or study withdrawal due to adverse events.[52] No safety concerns in immunocompromised populations were associated with rZV across six clinical trials; most adverse events reported were consistent with the underlying diseases or treatments and similar between vaccinated and placebo controls.[53] A post-market surveillance study in adults aged 65 years or over observed a slightly increased risk of Guillain-Barré syndrome (estimated three excess cases per million doses) during 42 days following vaccination with rZV.[51]

23.8 Variations from the vaccine data sheet

None.

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Appendix 1: The history of immunisation in New Zealand

This appendix details the history of immunisation in New Zealand. Section A1.1 is a summary of when each vaccine was introduced to the National Immunisation Schedule (the Schedule). This summary includes vaccines which were initially introduced as targeted programmes for a defined population and were then added to the Schedule, and those vaccines which were introduced to the Schedule and then changed to targeted programmes. Section A1.2 shows the historical immunisation schedules for New Zealand. Section A1.3 provides detailed information about the history of the Schedule[1, 2, 3] – this information was previously contained within the disease chapters of earlier editions of the *Handbook*.

A1.1 History of the Schedule – summary tables

Table A1.1: Summary of when each vaccine was introduced to New Zealand

Vaccine	Year the vaccine was introduced, plus comments	
Diphtheria	1926	Became available in New Zealand for selected schools and orphanages.
	1941	Offered routinely to children aged under 7 years. See DTwP for more information.
Tetanus	1940–1955	Tetanus toxoid became available as a voluntary vaccination. See DTwP for more information.
Pertussis	1945	Introduced by the Department of Health – given on request.
	1953	Combined pertussis-diphtheria vaccine became available, although usage was restricted. See DTwP for more information.
BCG	1948	Initially introduced for nurses, then later extended to all adolescents.
	1963	Adolescent BCG programme was discontinued in the South Island. Phased out in the North Island by 1990.
	1976	Neonatal BCG was introduced initially in high-risk districts, and then variably implemented throughout New Zealand.
	1990	Neonatal BCG was given for high-risk groups only. This continues in 2020.
Salk poliomyelitis (IPV)	1956	Became available; initially 8–9-year-olds were targeted, then 5–10-year-olds, then 11–15-year-olds.
	1960	Offered to all those aged 6 months to 21 years.
	2002	IPV replaced OPV on the Schedule, either as IPV or combined with the DTaP vaccine. See Hib for more information.
	2014	IPV became available for (re)vaccination following immunosuppression (see also DTaP).

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
DTwP (diphtheria, tetanus, whole-cell pertussis)	1958	DTwP became available and the first Schedule commences.
	1960	DTwP was supplied to medical practitioners free of charge. See Hib for more information.
Sabin poliomyelitis (OPV)	1961	Initially introduced for children aged under 12 months, administered by the Department of Health.
	1962	In April 95% of all school children received 2 doses; in September it was offered to all adults and adolescents (administered by the Department of Health).
	1967	From April GPs were able to administer OPV along with DTwP at ages 3, 4, 5 and 18 months.
	2002	Sabin OPV was replaced by Salk-derived IPV on the Schedule, as DTaP-IPV at ages 6 weeks, 3 and 5 months, and at 4 years, and as IPV at age 11 years. See Hib for more information.
Measles	1969	Introduced for children aged 10 months to 5 years and those aged under 10 years at special risk. Due to adverse reactions, the measles programme was suspended in late 1969 until the Edmonston B strain vaccine became available in February 1970.
	1974	The recommended age changed to age 12 months.
	1981	The recommended age changed to age 12–15 months.
	1990	Measles, mumps and rubella (MMR) vaccine was introduced to the Schedule for all infants at age 12–15 months, replacing monovalent measles vaccine. See MMR for more information.
Rubella	1970	Introduced to the Schedule for all children at age 4 years.
	1979	Low uptake at age 4 years, especially by boys, spurred a change to a vaccination for girls at age 11 years (year 7/form 1).
	1990	MMR was introduced to the Schedule for all infants at age 12–15 months. See MMR for more information.
Hepatitis B	1985	Plasma-derived vaccine was introduced for newborn babies born to HBeAg-positive mothers.
	1987	Extended to newborns of HBsAg-positive mothers and newborns in high-risk districts (eg, Northland, South Auckland, Rotorua, Napier, Gisborne).
	1988	In February 1988 it was introduced to the Schedule for all infants (catch-up programmes for preschoolers are implemented during 1988).
	1989	In December 1989 recombinant HepB replaced the plasma-derived vaccine.
	1990	Funded hepatitis B immunisation was extended to all children aged under 16 years (catch-up school programmes were also implemented).
	1996	The third HepB dose was brought forward from 12–15 months to age 5 months. See Hib for more information.
	2014	HepB vaccine became available to individuals at high risk of hepatitis B or its complications (see also DTaP).
	2015	Funding extended to include other high-risk conditions.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Measles, mumps and rubella (MMR)	1990	Introduced to the Schedule for all infants at age 12–15 months.
	1992	A second dose was introduced for 11-year-old (school year 7/form 1) boys and girls.
	2001	The second dose of MMR was changed from age 11 years to age 4 years. A school-based catch-up programme was offered for all 5–10-year-olds.
	2014	The 2-dose schedule at ages 15 months and 4 years continues. MMR became available for (re)vaccination following immunosuppression.
	2020	In October 2020, the recommended age for MMR dose one changed to 12 months with dose 2 recommended at 15 months.
Haemophilus influenzae type b (Hib-PRP)	1994	Hib-PRP vaccine was introduced to the Schedule as DTwPH (replacing DTwP) at ages 6 weeks, 3 months and 5 months, and as monovalent Hib at age 18 months. All children aged under 5 years were offered vaccination against Hib.
	1996	Given as DTwPH at ages 6 weeks, 3 months and 5 months, with a booster at age 15 months.
	2000	Given as Hib-HepB at ages 6 weeks and 3 months, and as DTaP/Hib at age 15 months.
	2006	Given as Hib-HepB at ages 6 weeks and 3 months, and as monovalent Hib at age 15 months. Monovalent Hib-PRP became available to older children and adults pre- or post-splenectomy.
	2008	Given as DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, and as monovalent Hib-PRP at age 15 months. This schedule continues in 2020.
	2014	Monovalent Hib-PRP became available for additional high-risk conditions (see also DTaP).
Td (Tetanus-diphtheria)	1994	Introduced to the Schedule, replacing tetanus toxoid. See Tdap for more information.
	2002	Adult Td boosters are introduced at ages 45 and 65 years.
	2014	Td became available for (re)vaccination following immunosuppression.
	2020	Adult Td replaced with Tdap at ages 45 years (if not had previously had 4 doses of Td) and 65 years.
Influenza	1997	Introduced to the Schedule for adults aged 65 years and older.
	1999	Introduced to the Schedule for those aged under 65 years with certain medical conditions.
	2010	Pregnant women became eligible to receive the funded vaccine.
	2013	Children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness became eligible to receive the funded vaccine.
	2015	Funding extended to include other high-risk conditions.
Acellular pertussis (DTaP)	1999	Introduced for infants/children aged under 7 years who have a previous reaction to the whole-cell pertussis in DTwPH.
	2000	In August, DTaP was introduced for all infants to replace whole cell pertussis vaccine at ages 6 weeks, 3 months and 5 months (see also Hib).
	2014	DTaP-IPV-HepB/Hib and DTaP-IPV became available for (re)vaccination of children with certain high-risk conditions.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Meningococcal B (MeNZB)	2004–2008	MeNZB was used as an epidemic control vaccine between 2004 and 2008. It was offered in a three-dose schedule to all aged under 20 years. The vaccination programme ceased in 2008 following a decline in the incidence of group B disease and because the immune response to the vaccine was short-lived. The vaccine remained available until March 2011 for some high-risk individuals. (See the 2011 edition of the *Handbook* for more information.)
(4CMenB)	2021	Funded for eligible high-risk groups from 1 July 2021.
Adult-dose acellular pertussis (Tdap)	2006	Introduced to the Schedule at age 11 years, combined with IPV as Tdap-IPV, but changed to Tdap only in 2008. This schedule continues in 2017.
	2013	Pregnant women from 28 to 38 weeks' gestation became eligible for the funded vaccine (under the outbreak policy).
	2014	Tdap became available for (re)vaccination of children following immunosuppression.
	2015	Tdap became available for (re)vaccination of patients with certain high-risk conditions. Pregnant women from 28 to 38 weeks' gestation become eligible for the funded vaccine for every pregnancy.
	2019	Tdap eligibility for pregnant women extended to include when given in second or third trimester every pregnancy. It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester.
	2020	Adult Td replaced with Tdap at ages 45 years (if the individual had not previously had 4 doses of tetanus vaccine) and 65 years.
Pneumococcal conjugate vaccine (PCV)	2006	Introduced as PCV7 for high-risk children.
	2008	Introduced to the Schedule in June as PCV7 at ages 6 weeks, 3 months, 5 months and 15 months.
	2011	PCV10 replaced PCV7 on the Schedule. PCV13 replaced PCV7 for high-risk children.
	2014	PCV13 replaced PCV10 on the Schedule.
	2015	PCV13 became available for patients of any age with certain high-risk conditions.
	2017	PCV10 replaced PCV13 on the Schedule. PCV13 continues for high-risk individuals.
	2020	PCV10 recommended as a 2-dose primary schedule plus booster dose given at 6 weeks, 5 months and 12 months. PCV13 remained at 3-dose schedule plus booster for high risk infants (ie given at ages 6 weeks, 3, 5 and 12 months)
Human papillomavirus vaccine (HPV)	2008	HPV4 was introduced to the Schedule at age 12 years, for females only. There was a catch-up programme for females born from 1990.
	2013	HPV4 was made available in hospitals for transplant patients, and for boys and men under 26 years with confirmed HIV infection.
	2014	Lower age limit for vaccine eligibility changed to age 9 years. Routine immunisation continued for girls aged 12 years, plus a targeted programme for high-risk individuals. Individuals aged under 26 years with HIV infection became eligible for HPV4.
	2015	Funding extended to include other high-risk conditions.
	2017	Funding extended to include all males and females aged 26 years and under. HPV9 replaced HPV4.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Rotavirus	2014	RV5 vaccine was introduced to the Schedule at ages 6 weeks, 3 months and 5 months.
	2017	RV1 replaced RV5, at ages 6 weeks and 3 months.
Varicella (VV)	2014	Two doses of VV were introduced for high-risk individuals.
	2017	One dose of VV was introduced onto the Schedule for children at age 15 months (born on or after 1 April 2016), with a catch-up for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.
Herpes zoster (ZV)	2018	From 1 April, ZV was introduced onto the Schedule as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (until 31 December 2021).
COVID-19 vaccines mRNA-CV ChAd-CV	2021	Available to all in New Zealand from February 2021, initially given as part of a prioritised rollout from age 16 years. Age groups widened to 12–17 year-olds from September 2021 and 5-11 year-olds in January 2022. Alternative vaccines, ChAd-CV and rCV from age 18 years available from December 2021 and March 2022, respectively.

A1.2 Previous national immunisation schedules

Table A1.2: October 2020 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	RV1	Hib-PRP	MMR	VV	DTaP-IPV	Tdap	HPV9	Influenza	ZV
Pregnancy								•		•	
6 weeks	•	•	•								
3 months	•		•								
5 months	•	•									
12 months		•			•						
15 months				•	•	•					
4 years							•				
11 or 12 years								•	•		
45 years								•			
65 years								•		•	•

Table A1.3: April 2018 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	RV1	Hib-PRP	MMR	VV	DTaP-IPV	Tdap	HPV9	Td	Influenza	ZV
Pregnancy								●			●	
6 weeks	●	●	●									
3 months	●	●	●									
5 months	●	●										
15 months		●		●	●	●						
4 years					●		●					
11 or 12 years								●	●			
45 years										●		
65 years										●	●	●

Table A1.4: July 2017 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	RV1	Hib-PRP	MMR	VV	DTaP-IPV	Tdap	HPV9	Td	Influenza
Pregnancy								●			●
6 weeks	●	●	●								
3 months	●	●	●								
5 months	●	●									
15 months		●		●	●	●					
4 years					●		●				
11 or 12 years								●	●		
45 years										●	
65 years										●	●

Table A1.5: July 2014 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV13	RV5	Hib-PRP	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●	●							
3 months	●	●	●							
5 months	●	●	●							
15 months		●		●	●					
4 years					●	●				
11 years							●			
12 years (girls only)								● ×3 doses		
45 years									●	
65 years									●	●

Table A1.6: July 2011 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	Hib-PRP	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●							
3 months	●	●							
5 months	●	●							
15 months		●	●	●					
4 years				●	●				
11 years						●			
12 years (girls only)							● × 3 doses		
45 years								●	
65 years								●	●

Table A1.7: June 2008 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV7	Hib-PRP	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●							
3 months	●	●							
5 months	●	●							
15 months		●	●	●					
4 years				●	●				
11 years						●			
12 years (girls only)							● × 3 doses		
45 years								●	
65 years								●	●

Table A1.8: February 2006 immunisation schedule

	DTaP-IPV	Hib-HepB	Hib-PRP	Tdap-IPV	MMR	MeNZB	Td	Influenza
6 weeks	●	●				●		
3 months	●	●				●		
5 months	●	●				●		
10 months						●		
15 months			●		●			
4 years	●				●			
11 years				●				
45 years							●	
65 years							●	●

Table A1.9: February 2002 immunisation schedule

	DTaP-IPV	Hib-HepB	HepB	DTaP/Hib	Polio (IPV)	MMR	Td	Influenza
6 weeks	●	●						
3 months	●	●						
5 months	●		●					
15 months				●		●		
4 years	●					●		
11 years					●[a]		●	
45 years							●[b]	
65 years							●[b]	●

a. For those children who had not received a fourth dose of polio vaccine.

b. With the introduction of Td at ages 45 and 65 years, 10-yearly boosters were no longer recommended.

Table A1.10: January 2001 immunisation schedule

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza
6 weeks	●	●			●			
3 months	●	●			●			
5 months	●		●		●			
15 months				●		●		
4–5 years					●	●[a]		
11 years					●[b]		●	
65 years								●

a. MMR was also offered to children aged 5–10 years in a school catch-up programme.

b. For those children who had not received a fourth dose of polio vaccine.

Table A1.11: August 2000 immunisation schedule

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza*
6 weeks	●	●			●			
3 months	●	●			●			
5 months	●		●		●			
15 months				●		●		
11 years					●	●	●	
65 years								●

* Influenza vaccine was introduced for adults aged 65 years and older in 1997 and in 1999 for individuals aged 6 months and older at increased risk of influenza complications.

Table A1.12: 1996 immunisation schedule

	DTwPH	HepB	Polio (OPV)	MMR	Td
6 weeks	●	●	●		
3 months	●	●	●		
5 months	●	●	●		
15 months	●			●	
11 years			●	●	●

Table A1.13: 1994 immunisation schedule

	DTwPH	HepB[a]	Polio (OPV)	MMR[b]	DT	Hib	Td
6 weeks	●	●					
3 months	●	●	●				
5 months	●		●				
12–15 months		●		●			
18 months			●		●	●[c]	
5 years			●				
11 years				●			
15 years							●[d]

a. Hepatitis B was introduced for all neonates, with catch-up for children aged under 5 years in 1988. In 1990 free immunisation was extended to all children aged under 16 years.

b. MMR was introduced at 12–15 months in 1990 and at age 11 years in 1992.

c. A single dose of Hib was also offered to all children aged under 5 years.

d. 10-yearly boosters of Td were recommended.

Table A1.14: 1984 immunisation schedule

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
6 weeks	●					
3 months	●	●				
5 months	●	●				
12–15 months			●*			
18 months		●		●		
5 years		●				
11 years (girls only)					●	
15 years						●

* Measles vaccine administered at age 12 months was changed to age 12–15 months in 1981.

Table A1.15: 1980 immunisation schedule

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
3 months	●	●				
5 months	●	●				

12 months			●[a]			
18 months		●		●		
5 years		●				
11 years (girls only)					●[b]	
15 years						●

a. Measles vaccine administered at age 10 months was changed to age 12 months in 1974.

b. Rubella vaccine was introduced in 1979.

Table A1.16: 1971 immunisation schedule

	DTwP	Polio	Measles	DT	Rubella	Tetanus
3 months	●	●				
5 months	●	●				
10 months			●[a]			
18 months		●		●		
4 years					●[b]	
5 years				●		
15 years						●

a. Measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk.

b. Rubella vaccine was introduced in 1970 for children at age 4 years, along with a school-based programme for children aged 5–9 years.

Table A1.17: 1967 immunisation schedule

	DTwP	Polio[a]	DT
3 months	●	●	
4 months	●	●	
5 months	●	●	
18 months		●	●[b]
5 years			●

a. Between 1961 and 1967 polio vaccine was administered by the Department of Health.

b. The DT booster at age 18 months was introduced in 1964.

Table A1.18: 1961 immunisation schedule

	DTwP	DT
3 months	●	
4 months	●	
5 months	●	
5 years		●

A1.3 History of the Schedule: background information

Note that the following information describes the vaccines which have been, or currently are, on the National Immunisation Schedule. Vaccines which are used for targeted programmes only (ie, hepatitis A, meningococcal) are not discussed. Information about the Meningococcal B Immunisation Programme (an epidemic programme between 2004–2006) can be found in earlier editions of the *Handbook*.

A1.3.1 Diphtheria-containing vaccines

During the 1920s the Department of Health, at the instigation of individual school medical officers or medical officers of health, began delivering diphtheria immunisations in a few selected schools and orphanages, but there was no national policy. By 1941 diphtheria immunisation was offered routinely to children aged under 7 years through the School Medical Service and the Plunket Society.

From 1960 the Department of Health programme was delivered by GPs using three doses of non-adsorbed triple vaccine (diphtheria, tetanus and whole-cell pertussis vaccine, DTwP) at ages 3, 4 and 5 months, and a dose of double (diphtheria and tetanus, DT) vaccine before school entry at age 5 years. (For the history of the Schedule's diphtheria toxoid-containing vaccine history after 1960, see A1.3.13 'Tetanus-containing vaccines').

A1.3.2 Hib-containing vaccines

Haemophilus influenzae type b (Hib) vaccine was added to the Schedule in January 1994, which meant that diphtheria, tetanus, whole-cell pertussis and Hib (DTwPH) vaccine replaced the diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine given at ages 6 weeks, 3 months and 5 months. A monovalent Hib vaccine was given at age 18 months, and a catch-up programme of a single dose of monovalent Hib vaccine was recommended for all children aged under 5 years (ie, those born from January 1989).

From February 1996 the fourth dose was changed to age 15 months and given as DTwPH to reduce the two immunisation events in the second year to one at age 15 months.

DTwPH led to a more than 90 percent reduction in the number of invasive Hib cases in those aged under 5 years but resulted in an increase in the percentage of Hib cases occurring in those aged under 6 months, some of whom had received age-appropriate vaccination. When a supply issue resulted in a change of vaccine in 2000, the opportunity was taken to change to PRP-OMP (polyribosylribitol phosphate outer membrane protein, as Comvax, Hib-HepB combination), which offers substantial protection after a single dose.

This vaccine was used until 2008, when a hexavalent vaccine containing PRP-T Hib component was introduced. This vaccine induces a minimal first-dose response, with some protection after the second dose. It was acknowledged that there was a risk that the change would result in an increase in cases aged under 6 months, but this risk was outweighed by the benefit of reducing the number of injections at each of the first three visits and the reduction in IPD with the introduction of pneumococcal conjugate vaccine (PCV7).

The Hib component of Infanrix-hexa, PRP-T, requires a primary course of three doses with a booster dose at age 15 months, though some protection is induced after the second dose.

In 2006, Hib-PRP-T was funded for older children and adults pre- or post-splenectomy. In 2014 funding was extended to include other high-risk conditions.

A1.3.3 Hepatitis B-containing vaccines

HepB was added to the Schedule gradually, starting in September 1985, when it was offered to newborn babies of HBeAg-positive mothers. Three 10 µg doses of plasma-derived vaccine were given, as recommended by the manufacturer. In March, 1987 the immunisation programme was extended to newborns of all HBsAg-positive mothers and to children born in certain high-risk districts (Northland, Takapuna, Auckland, South Auckland, Rotorua, Napier and Gisborne).

In 1988 a universal infant vaccination programme was introduced using four low doses (2 µg) of the plasma-derived vaccine H-B-Vax. A catch-up campaign for all preschoolers was undertaken in 1989, and household and sexual contacts of HBsAg-positive women identified during antenatal screening were also entitled to free immunisation.

In December 1988 H-B-Vax was replaced by a recombinant vaccine, Engerix-B. This was given at the manufacturer's recommended dose (10 µg) at 6 weeks, 3 months and 15 months of age. Babies of carrier mothers also received a dose of vaccine, plus HBIG at birth. From February 1990 free hepatitis B immunisation was extended to all children aged under 16 years.

In February 1996 the third dose of HepB was brought forward from 15 to 5 months of age to give early protection to infants and to complete the HepB schedule in the first year of life, in the expectation that this would improve vaccine uptake. This schedule continues in 2020, with 10 µg given at ages 6 weeks, 3 months and 5 months as DTaP-IPV-HepB/Hib (Infanrix-hexa). For infants born to HBsAg-positive mothers, an additional dose of HepB plus HBIG is given at birth.

In 2014, HepB was made available to individuals at high risk of hepatitis B disease or its complications. In 2015, funding was extended to include other high-risk conditions.

A1.3.4 HPV vaccines

Human papillomavirus (HPV) vaccination, using Gardasil, a quadrivalent vaccine containing virus-like particles (VLPs) derived from HPV types 16, 18, 6 and 11 (HPV4), began in New Zealand on 1 September 2008 and was initially offered only to females born in 1990 and 1991. In 2009 the programme was extended to females born from 1992 onwards. In 2009 and 2010, HPV immunisation was offered through most participating schools to females in school years 8–13.

From 2011 the HPV immunisation was only offered in participating schools to females in school year 8. HPV immunisation was also available through family doctors, local health centres and most Family Planning clinics for females who did not attend a participating school or who did not want to have it at school. In 2013 HPV vaccine was funded (for delivery in hospitals only) for other groups at risk of HPV-related disease; from 2014, high-risk groups have also been able to access HPV vaccine in primary care. In 2015, funding was extended to include other high-risk conditions.

Males became eligible for HPV vaccine in 2017, with funding extended to include all males and females aged 26 years and under. The nine-valent HPV vaccine (HPV9, Gardasil 9) replaced HPV4, and a two-dose schedule was recommended for immunocompetent children aged 9–14 years.

A1.3.5 Influenza vaccines

Funded influenza immunisation was introduced in 1997 for people aged 65 years and older. From 1999 the vaccine became funded for younger people (aged from 6 months to 64 years) who were at increased risk of influenza complications. In 2010 funded vaccine was extended to pregnant women, and in 2013 to children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness. In 2015, funding was extended to include other high-risk conditions. In 2018, quadrivalent influenza vaccine replaced the previously used trivalent vaccine.

A1.3.6 Measles-containing vaccines

The measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk. In 1974 the recommended age for measles vaccine was changed from 10 months to 12 months, and in 1981 it was changed to age 12–15 months. These changes attempted to achieve a balance between too early immunisation, where the vaccine is neutralised by maternally acquired antibody, and the requirement to protect the very young during an epidemic.

MMR (measles, mumps and rubella) vaccine was introduced in 1990 to be given at age 12–15 months in place of the measles vaccine. The dose at age 11 years was introduced in 1992. In 1996 the timing of the first dose of MMR was changed to age 15 months, to be given at the same time as the booster dose of diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b (DTwPH) vaccine.

At the start of the 1997 epidemic, the measles immunisation campaign, using MMR, targeted all children aged under 10 years. During the campaign, the recommended time for the first dose was brought forward to age 12 months, and in Auckland a dose was recommended for children aged 6–11 months, to be repeated at age 15 months.

The national coverage achieved in the campaign is not known, but estimates for the school-aged population range from 55 percent for Auckland to 85 percent for the Wellington region.

In 2001 the Schedule was changed to give the first dose of MMR at age 15 months and the second dose at 4 years. There was a school catch-up programme for the second MMR dose for children aged 5–10 years. This schedule of two doses of MMR at 15 months and 4 years continued.

Vaccine-derived maternal antibody levels, which protect young infants, are lower and wane earlier than the antibody levels derived from natural infection. It is likely that in due course the age of the first dose of measles-containing vaccine will be changed to age 12 months.

In 2014, MMR became available for (re)vaccination following immunosuppression (upon specialist advice).

In 2020, the Schedule changed to recommend the first dose of MMR be given at 12 months and the second dose at 15 months.

A1.3.7 Mumps-containing vaccines

Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12–15 months. (See section A1.3.6.)

A1.3.8 Pertussis-containing vaccines

A monovalent pertussis vaccine was introduced by the Department of Health in 1945, and from 1953 it was also available combined with the diphtheria and tetanus vaccine. Routine childhood immunisation began in 1960 using the plain (ie, no adjuvant, not adsorbed) diphtheria, tetanus and whole-cell pertussis (DTwP) triple vaccine. Three doses were given, at ages 3, 4 and 5 months.

In 1971 the policy was altered to two doses of adsorbed triple vaccine given at ages 3 and 5 months. It was believed efficacy would be unaltered and the risk of serious reactions would be reduced. Following this schedule change, there was a progressive increase in hospitalisation rates in 1974, 1978 and 1982. Review of the increase in hospitalisations led to the addition, in 1984, of a third dose of DTwP, given at age 6 weeks, to provide earlier protection. From 1994 whole-cell pertussis vaccine was administered as a quadrivalent vaccine with diphtheria and tetanus toxoids and conjugate *Haemophilus influenzae* type b (diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b – DTwPH).

A fourth dose of pertussis vaccine was added in 1996 (as DTwPH vaccine), given at age 15 months, with the goals of increasing protection in young children and reducing risk of transmission to younger siblings.

Acellular pertussis vaccine was introduced in August 2000, and diphtheria, tetanus and acellular pertussis (DTaP) and DTaP/Hib replaced the whole-cell pertussis vaccines. In February 2002 the vaccine given at ages 6 weeks, 3 months and 5 months was changed to DTaP with inactivated polio vaccine (DTaP-IPV), and a booster dose of DTaP-IPV was introduced and given at age 4 years to protect children during the early school years and to decrease transmission of the infection to younger children.

In 2006 the timing of the booster components of the pertussis schedule was changed to extend vaccine-induced protection into adolescence. Following the three doses of a pertussis-containing vaccine in the first year of life, booster doses are given at ages 4 and 11 years. Since March 2008 the acellular pertussis vaccine has been delivered as DTaP-IPV-HepB/Hib for the primary immunisation series, scheduled at ages 6 weeks, 3 months and 5 months; as DTaP-IPV at age 4 years; and as Tdap at age 11 years. In comparison with DTaP, Tdap contains smaller doses of tetanus and diphtheria toxoids and the pertussis antigens.

Since January 2013 pregnant women have been eligible for a booster dose of Tdap vaccine. Initially, this was under the outbreak policy and became part of high-risk funded vaccine criteria in July 2015. In 2014, pertussis-containing vaccines (as DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap) became available for (re)vaccination of children with certain high-risk conditions. This was extended to high-risk adults (as Tdap) in 2015. In 2019 eligibility for pregnant women was extended to include when given any time in their second or third trimester, with a recommendation it be given from 16 weeks' gestation every pregnancy, preferably in the second trimester.

In 2020, Tdap replaced Td for adult vaccinations at age 45 years and 65 years. Tdap is only offered at age 45 years for those who had not previously had four tetanus containing vaccinations.

A1.3.9 Pneumococcal vaccines

The 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar 7) and the 23-valent pneumococcal polysaccharide vaccine (23PPV, Pneumovax 23) were introduced in 2006 for high-risk individuals. PCV7 became part of the Schedule in June 2008, with four doses recommended at ages 6 weeks, 3 months, 5 months and 15 months.

In July 2011, the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix) replaced PCV7 and the 13-valent pneumococcal conjugate vaccine (PCV13, Prevenar 13) was introduced for some high-risk children. PCV13 replaced PCV10 on the Schedule in July 2014. In 2015, PCV13 became available for adults with certain high-risk conditions.

PCV10 replaced PCV13 on the usual childhood schedule in July 2017, with PCV13 and 23PPV continuing for high-risk individuals.

In July 2020, the PCV10 schedule changed to a two-dose primary plus booster given at 6 weeks, 5 months and 12 months. The PCV13 remained at a three-dose primary series plus booster for high risk individuals, ie given at 6 weeks, 3 months, 5 months and 12 months.

A1.3.10 Poliomyelitis-containing vaccines

Limited supplies of the Salk vaccine (inactivated polio vaccine, IPV) became available in 1956, and immunisation initially targeted 8- and 9-year-old children. As supplies improved, immunisation was extended to include all 5–10-year-olds, then children aged 11–15 years, with approximately 80 percent coverage. By 1960 immunisation was offered to everyone between 6 months and 21 years of age (with three doses of vaccine).

The Sabin vaccine (oral polio vaccine, OPV) was introduced in August 1961, initially for children up to age 12 months; eight months later it was made available to all school children. On completion of this programme in September 1962 the vaccine was offered to adolescents and adults.

In 1967 OPV was given with diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine at ages 3, 4, 5 and 18 months. The deletion of the DTwP dose at age 4 months in 1971 meant the OPV dose at age 4 months was also removed. An extra dose of polio vaccine was added at age 5 years in 1980, based on serological data, which showed decreased immunity to poliovirus types 1 and 3 in school entrants.

In 1996, as part of the Schedule changes, the third dose of the primary series was moved back to the first year of life, with OPV given at ages 6 weeks, 3 months and 5 months. The booster dose was moved to age 11 years, to be given at the same time as the MMR and adult tetanus and diphtheria (Td) vaccines. In 2001 the Schedule was changed to give the fourth dose of OPV at age 4 years, at the same time as the second dose of MMR. Students aged 5–10 years in 2001 who did not receive the fourth dose of polio vaccine at age 4 years were offered a dose at age 11 years.

IPV replaced OPV in 2002 and was included in three doses of DTaP-IPV in the first year of life, with a booster at age 4 years. Those children who had not received four doses of polio vaccine were offered IPV with Tdap, as Tdap-IPV (Boostrix-IPV) at age 11 years in 2006 and 2007. From 2008, Tdap has been offered at age 11 years, as all children should now have received four doses of polio vaccine by age 4 years.

Combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio vaccine and *Haemophilus influenzae* type b vaccine (DTaP-IPV-HepB/Hib, Infanrix-hexa) replaced DTaP-IPV (Infanrix-IPV) and Hib-HepB (Comvax) on the Schedule in March 2008.

In 2014, IPV vaccine became available for (re)vaccination following immunosuppression.

A1.3.11 Rotavirus vaccines

The three-dose pentavalent rotavirus vaccine (RV5, RotaTeq) was introduced to the Schedule in 2014, for infants at ages 6 weeks, 3 months and 5 months. In 2017, the two-dose monovalent vaccine (RV1, Rotarix) replaced RV5 on the Schedule, for infants at ages 6 weeks and 3 months.

A1.3.12 Rubella-containing vaccines

Immunisation with an attenuated rubella vaccine (Cendehill strain) was first offered to all 4-year-old New Zealand children in 1970, the rationale being to prevent transmission of the wild virus in 5–9-year-old children, who were the main sufferers from clinical disease. At the same time, the Department of Health delivered a school-based programme, which succeeded in immunising 95 percent of children aged 5–9 years. The acceptance rate of the preschool entry dose of rubella was only about 40 percent, and many practitioners did not feel it was appropriate to immunise males.

In 1979 the immunisation policy for rubella was altered to offer the vaccine to girls aged 11 years, in school year 7 (form 1). The aim was to immunise females before they attained childbearing age. In 1990 MMR was introduced at age 12–15 months for all children, and rubella vaccine continued to be offered to girls in school year 7. Since 1992 two doses of rubella vaccine – as measles, mumps and rubella (MMR) vaccine – have been offered to all children, the first dose in the second year of life and the second dose at age 11 years. This was changed in 2001, maintaining the first dose of MMR at age 15 months and changing the second to age 4 years. The aim of this strategy was to prevent rubella epidemics, reduce the background incidence of rubella and continue to protect women before childbearing, therefore eventually eliminating CRS.

In 2001 there was an MMR school catch-up programme throughout the country for all children aged 5–10 years who would no longer receive an MMR dose in school year 7. The rubella schedule continued as two doses of MMR offered at ages 15 months and 4 years.

In 2014, MMR became available for (re)vaccination following immunosuppression (upon specialist advice).

In 2020, the Schedule changed to recommend the first dose of MMR be given at 12 months and the second dose at 15 months (see section A1.3.6).

A1.3.13 Tetanus-containing vaccines

The history of tetanus vaccine use prior to the 1960 introduction of diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine is not well recorded, but tetanus vaccine was widely used in World War II and subsequently by the armed forces. In New Zealand, universal infant immunisation with tetanus toxoid began in 1960 with the use of three doses of triple vaccine. Anyone born before 1960 is less likely to have received a

primary series, unless they were in the armed forces. Older women appear to be at particular risk.

The first scheduled vaccine used for infants (from 1960) was the DTwP vaccine, with three doses at monthly intervals at ages 3, 4 and 5 months, and a diphtheria and tetanus (DT) booster before school entry (at age 5 years). A DT booster at age 18 months was added in 1964, primarily to enhance protection against tetanus. There was a change to a more immunogenic adsorbed vaccine in 1971, and the dose given at age 4 months was dropped.

In 1980 the dose of DT given at age 5 years was replaced by the monovalent tetanus toxoid given at age 15 years, as part of a move from 10-yearly to 20-yearly boosters for tetanus. It was considered that more frequent boosters were unnecessary and the cause of significant local reactions. There was a return to a three-dose primary series of DTwP (by the addition of a 6-weeks-of-age vaccination) in 1984 because two doses had been inadequate to control pertussis. In 1996 the booster of Td, which had been changed from tetanus toxoid in 1994 (see below), and previously given at age 15 years, was changed to age 11 years.

In 2002 the primary schedule for tetanus, given in combination vaccines at ages 6 weeks, 3 months and 5 months, followed by a dose at 15 months, was changed when a further dose was introduced at age 4 years. The Td given at age 11 years continued.

Since 2006 the childhood schedule for tetanus has been given in combination vaccines at ages 6 weeks, 3 months, 5 months (DTaP-IPV-HepB/Hib), 4 years (DTaP-IPV) and 11 years (Tdap).

Td replaced the tetanus toxoid vaccine in 1994, and 10-yearly boosters were recommended. The change was recommended to maintain the adult population's immunity to diphtheria, in response to outbreaks overseas affecting adults and the absence of natural boosting because the disease had become rare. Since 2002 adult boosters have been recommended at ages 45 and 65 years (instead of 10-yearly) as a pragmatic attempt to increase coverage in the adult population.

In 2014, Td became available for (re)vaccination following immunosuppression.

In 2020, Td was discontinued and replaced with Tdap for wound prophylaxis and adult booster doses. A Tdap dose is offered at 45 years, for adults who had not previously received four doses of a tetanus-containing vaccine, and at age 65 years.

A1.3.14 BCG vaccines

BCG immunisation was first introduced to New Zealand in 1948 and later extended to all adolescents. BCG immunisation of neonates was introduced in 1976, initially in districts with high rates of active TB.

Universal screening and vaccination of 13-year-olds was discontinued in the South Island in 1963, was phased out in regions of the North Island in the 1980s, and had ceased by 1990. It was stopped because TB had declined to a point at which the

advantages of universal vaccination were outweighed by the disadvantages (cost, side-effects and reduced diagnostic value of the Mantoux test). BCG vaccine is now only available to neonates and children aged under 5 years at high risk of TB.

A1.3.15 Varicella vaccines

In 2014 two doses of varicella vaccine (VV, Varilrix) were introduced for individuals at high risk of varicella infection. In 2017 one dose of VV was introduced to the Schedule at age 15 months (for children who were born on or after 1 April 2016). One catch-up VV dose was introduced for previously unvaccinated children turning 11 years old on or after 1 July 2017 who had not previously had a varicella infection.

A1.3.16 Herpes zoster vaccines

ZV was introduced onto the Schedule on 1 April 2018, as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (the catch-up programme ceases on 31 December 2021).

Appendix 2: Planning immunisation catch-ups

It is essential that vaccinators have a sound understanding of the number of antigens and the most effective spacing of doses required for a primary course and subsequent boosters in order to assess an individual's immunisation requirements. The principles described below will help vaccinators in this process.

Section A2.2 discusses catch-up requirements for children aged under 18 years, and section A2.3 discusses the requirements for adults.

Plan and document your complete catch-up schedule in the patient notes and recall system to ensure continuity of care.

For assistance with planning catch-up schedules, contact your immunisation coordinator, call the IMAC freephone line on 0800 IMMUNE/0800 466 863, or discuss with an experienced colleague.

A2.1 Eligibility for publicly funded vaccines

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services, including National Immunisation Schedule vaccines, in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded health and disability services.

However, regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines.

A2.2 Planning catch-ups for infants, children and adolescents aged under 18 years

When planning a catch-up schedule, start by focusing on the antigens already received and the additional antigens required, not the vaccine combinations available or trade names. There is no need to think in terms of events missed (eg, the 6-week, 3-month,

5-month, 12-month or 15-month vaccination events). It is important to note the age of the child when the antigens were received.

Although catch-up tables are provided in this appendix, children may not fit these unless they are completely unvaccinated, or there is no documented history and they are assumed to be unvaccinated. Trying to fit a child's vaccine requirements to a table can result in too many or not enough antigens being administered.

Use the following principles to establish what antigens the infant, child or adolescent requires.

A2.2.1 Principles of catch-up for infants and children aged under 10 years

1. If the immunisation status of a child is uncertain or unknown, plan the catch-up schedule assuming the vaccines have not been given.
2. Administer catch-up immunisations as per the New Zealand Schedule, not an overseas immunisation schedule.
3. The best approach is to ascertain the antigens required for the child's current age, subtract any already given and then develop the individual's catch-up schedule.
4. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given at the same visit, and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.
5. If the schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given. Exceptions to this principle are the following vaccines given to children aged under 12 months: MMR or measles-containing vaccine (see point 9 below), Hib vaccine (see point 10), PCV (see point 11), and varicella vaccine (see point 12).
6. If a child infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit.
7. For infants and children aged under 10 years, use DTaP-IPV-HepB/Hib or DTaP-IPV for primary immunisation. Tdap may be used as an alternative for primary immunisation of children aged 7 to under 18 years (note that Tdap (Boostrix) is not registered for primary immunisation, but there is no evidence of safety concerns).
8. The first dose of rotavirus vaccine (RV1, Rotarix) should be given before age 15 weeks (ie, the latest age is 14 weeks and 6 days), and the second dose administered a minimum of four weeks later. An infant who has not had the first dose before age 15 weeks will not be eligible to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the remaining

dose should be given, but both doses should be given before age 25 weeks (ie, by age 24 weeks and 6 days).

9. From 1 October 2020, the first dose of MMR is scheduled at 12 months and the second dose of MMR at 15 months, or at least four weeks after the first MMR. MMR or any single-antigen measles vaccine given before age 12 months is not counted as part of the two-dose MMR schedule.

10. A single dose of Hib-PRP-T is required for all children aged 12 months to under 5 years regardless of the number of doses given in their first year. Children who receive catch-up DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib vaccine as this is covered by the combination vaccine. Healthy children aged 5 years and older do not need Hib-PRP-T.

11. For healthy infants commencing PCV10 vaccination under 12 months of age, a primary course is two doses with a minimum of eight weeks between doses. A booster dose is given eight weeks after the completion of the primary course. It may be given after at least four weeks if that coincides with the 12-month immunisation event, to get them back on to schedule. Unimmunised healthy children aged 12 months to under 5 years require two PCV doses at least eight weeks apart. If a child did not complete their primary course when under 12 months of age, do not count the doses given prior to 12 months when determining the number of PCV10 catch-up doses required. Healthy children aged 5 years and older do not need PCV. See chapter 16 'Pneumococcal disease' for PCV13 schedules for high-risk children.

12. One dose of varicella vaccine is funded at 15 months for children who were born on or after 1 April 2016. A child who has received a non-funded varicella vaccine prior to 12 months is still eligible to receive the 15-month funded vaccine. A child who has had varicella disease does not require the varicella vaccine.

13. Remember to check whether the infant/child has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').

14. Once the child has received the appropriate vaccines for their age, they should continue with the Schedule as usual.

Table A2.1: Minimum number of antigens required, by age at time of presentation, for infants and children aged <10 years

<12 months	12 months to <5 years	5 years to <10 years
3 DTaP[a]	3 or 4 DTaP[a]	4 DTaP[a]
3 IPV[a e]	3 or 4 IPV[a,e]	3 or 4 IPV[e]
3 HepB[b]	3 HepB[b]	3 HepB[b]
3 Hib-PRP-T	1 Hib-PRP-T[f]	2 MMR
2 PCV10[c]	2 PCV10[c]	
2 RV[d]	2 MMR[g]	
	1 VV[h]	

a. Use DTaP-IPV-HepB/Hib (or DTaP-IPV) for the 3-dose primary series (at a minimum of 4-weekly intervals), then continue with the usual childhood schedule with a booster dose of DTaP-IPV given at age 4 years. If the child commences immunisation at age 4 years or older, give the booster dose at least

6 months after the 3rd dose of the primary series. A fourth DTP given earlier than 3 years of age on an overseas schedule is not counted as the 4 year dose.

b. If the child received HepB at birth, they require a total of 4 HepB doses. Children born to HBsAg-positive mothers require serological testing at age 9 months – see section 9.5.2.

c. For healthy infants commencing PCV10 vaccination under 12 months of age, a primary course is 2 doses with a minimum of 8 weeks between doses. A booster dose is given 8 weeks after the completion of the primary course. It may be given after at least four weeks if that coincides with the 12-month event, to get them back on to schedule. For healthy children aged 12 months to under 5 years who are commencing immunisation or with an incomplete course, 2 doses of PCV10 at least 8 weeks apart. (See chapter 16 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

d. The first dose of rotavirus vaccine should be given before age 15 weeks (ie, the latest is 14 weeks and 6 days) and the second dose given a minimum of 4 weeks later. Both doses must be given before age 25 weeks (ie, the latest is 24 weeks and 6 days). Where the first dose is inadvertently given at age 15 weeks or older, the second dose should be given, but both doses must be given before age 25 weeks (ie, latest age 24 weeks and 6 days).

e. A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals) for children aged under 10 years, but 4 doses may be given when combination vaccines are used (eg, DTaP-IPV-HepB/Hib or DTaP-IPV). For all infants and children who have had OPV (ie, either OPV or bOPV) a further dose of IPV should be administered even if they have completed a full OPV/bOPV course.

f. A single dose of Hib-PRP is required for all children from age 12 months to under 5 years, regardless of the number of doses given before age 12 months. Children who receive catch-up DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP vaccine as this is covered by the combination vaccine.

g. Children commencing immunisation at age 12 months or older require 1 dose of MMR, then continue the usual childhood schedule with a second dose of MMR given at age 15 months, or at least 4 weeks after the first MMR dose.

h. One dose of varicella vaccine is funded for children at 15 months born on or after 1 April 2016. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the funded 15-month varicella vaccine. A child who has had varicella disease does not require the varicella vaccine.

A2.2.2 Principles of catch-up for children and adolescents aged 10 to under 18 years

1. The best approach is to ascertain the antigens required for current age, subtract any already given and then develop the individual's catch-up schedule.

2. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given at the same visit and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.

3. If the Schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given.

4. If the immunisation status of an individual is uncertain or unknown, plan the catch-up schedule assuming the vaccine has not been given.

5. If an individual infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit. MMR should be recommended at the first visit.

6. For individuals aged 10 years to under 18 years, Tdap is recommended and funded for primary and booster immunisation. While Tdap is not approved for use

(registered) as a primary course, no safety concerns are expected when using Tdap for primary immunisation in individuals aged 10 to under 18 years.

7. For individuals aged 11–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using Engerix B 20 µg, with the second dose given four to six months after the first.

8. A two-dose schedule of HPV at least 6–12 months apart is recommended for individuals who receive their first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose. Individuals who start their HPV schedule from age 15 years and older receive three doses of HPV at 0, 2 and 6 months. If required, a shortened schedule of three doses can be given with a minimum of four weeks between doses one and two, and the third dose given at least 12 weeks after dose two. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. See Table A2.9 for HPV catch-up schedules.

9. One dose of varicella vaccine is funded for children born on or after 1 July 2006, from age 11 years, who have not previously had varicella vaccination or infection. The appropriate varicella schedule for those ages 13 years or older when starting is two doses with a minimum of a four-week gap; however, only one dose is currently funded for those born on or after 1 July 2006.

10. Remember to also check whether the individual has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').

11. Once the individual has received the appropriate vaccines for their age, they should continue with the Schedule as usual.

Table A2.2: Minimum number of antigens required by individuals aged 10 to under 18 years at the time of presentation

10 years to <18 years
4 Tdap[a]
3 IPV[b]
3 HepB for children aged 10 to <18 years; or alternatively 2 HepB doses for children aged 11–15 years[c]
2 MMR
2 HPV[d, e, f] for those aged 11–14 years, or 3 HPV[d, g] for those aged 15 years and older
1 VV[h]

a. If aged 10 years to under 18 years, use Tdap for the primary series and the booster dose, with a minimum interval of 6 months between doses 3 and 4 (the primary series and the booster dose).

b. A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals).

c. If aged 10 years to under 18 years, 3 doses of HepB are required. An alternative 2-dose schedule may be used for children aged 11–15 years with the second dose given 4–6 months after the first.

d. Individuals who started with HPV4 may complete their remaining doses with HPV9.

e. For those aged 11–14 years, the second HPV dose is preferably given at least 6 months after the first. If the second dose is given earlier than 5 months after the first, a third HPV dose is recommended and funded — give the third dose at least 5 months after the first dose.

f. A two-dose schedule of HPV at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose.

g. For those aged 15 years and older, give a 3-dose HPV course at 0, 2 and 6 months. If a shortened schedule is required for these older individuals, the three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.

h. One dose of varicella vaccine is funded for children born on or after 1 July 2006, who have not previously had varicella vaccination or infection.

A2.2.3 National Immunisation Schedule catch-up guides for infants, children and adolescents aged under 18 years

Note: the following tables are guides only, and the principles described in sections A2.2.1 and A2.2.2 should be followed. The vaccinator must subtract any previous doses given. It is important to note the age at which the antigens have been given.

Table A2.3: Age at presentation: 3–6 months

Note: Subtract previous doses given.

Dose	Vaccines		
First dose*	DTaP-IPV-HepB/Hib	PCV[a]	RV[b]
4 weeks later	DTaP-IPV-HepB/Hib		RV[b]
4 weeks later	DTaP-IPV-HepB/Hib	PCV[a]	
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.			

a. See chapter 16 'Pneumococcal disease' for PCV13 schedules for high risk children.

b. Only eligible for RV if the first dose is given before age 15 weeks (ie, 14 weeks and 6 days). The second dose must be given before age 25 weeks (ie, 24 weeks and 6 days).

Table A2.4: Age at presentation: 7–11 months

Note: Subtract previous doses given.

Dose	Vaccines	
First dose	DTaP-IPV-HepB/Hib	PCV*
4 weeks later	DTaP-IPV-HepB/Hib	
4 weeks later	DTaP-IPV-HepB/Hib	PCV
Once the infant has received the appropriate vaccines for their age, continue with the Schedule as usual.		

* See chapter 16 'Pneumococcal disease' for PCV13 schedules for high-risk children.

Table A2.5: Age at presentation: 12–23 months

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	DTaP-IPV-HepB/Hib[a]	PCV[b]	MMR[c]	VV[d]
4 weeks later	DTaP-IPV-HepB/Hib[e]		MMR[c]	
4 weeks later or at age 15 months, whichever is applicable	DTaP-IPV-HepB/Hib[e]	PCV[b]		
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.				

a. One dose of Hib-PRP is required from age 12 months to under 5 years regardless of previous doses. Children who receive DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP as this is covered by the combination vaccine.

b. Healthy children commencing immunisation at age 12–23 months require 2 PCV doses, with a minimum interval of 8 weeks between doses. If the child did not complete a primary course of PCV when under 12 months of age, do not count the previously given doses when determining the number of PCV catch-up doses required. If the child completed a primary course of PCV before age 12 months, give a booster dose from 12 months of age, at least 4 weeks after the completion of the primary course. (See chapter 16 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

c. The first dose of MMR is scheduled at age 12 months, with a second dose given at 15 months or at least 4 weeks after the first dose.

d. One dose of varicella vaccine is funded for children born on or after 1 April 2016 at 15 months. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the 15-month varicella vaccine.

e. Parents/guardians should be informed that their child will receive extra doses of Hib but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

Table A2.6: Age at presentation: 2 years to under 5 years

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	DTaP-IPV-HepB/Hib[a]	PCV[b]	MMR	VV[c]
4 weeks later	DTaP-IPV-HepB/Hib[d]		MMR[e]	
4 weeks later	DTaP-IPV-HepB/Hib[d]	PCV[b]		
6 months later	DTaP-IPV[f]			
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.				

a. One dose of Hib-PRP is required from age 12 months to under 5 years regardless of previous doses. Children who receive DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP as this is covered by the combination vaccine.

b. A healthy child who presents at age 2 years to under 5 years: if previously unvaccinated, requires 2 PCV doses at least 8 weeks apart. If they completed a primary PCV course before age 12 months, give 1 PCV dose. If they started but did not complete a primary PCV course before age 12 months, give 2 PCV doses at least 8 weeks apart (this is the exception to the principle of counting previous doses given). (See chapter 16 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

c. One dose of varicella vaccine is funded for children who were born on or after 1 April 2016. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the 15-month varicella vaccine.

d. Parents/guardians should be informed that their child will receive extra doses of Hib, but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

e. Administer the second MMR dose a minimum of 4 weeks after the first dose.

f. Administer DTaP-IPV at age 4 years, a minimum of 6 months after the third DTaP-IPV-HepB/Hib dose. If the child is aged 4 years or older at presentation, administer DTaP-IPV a minimum of 6 months after the third DTaP-IPV-HepB/Hib dose. A fourth DTP given earlier than 3 years of age overseas is not counted as the 4-year dose.

Table A2.7: Age at presentation: 5 years to under 10 years

Note: Subtract previous doses given.

Dose	Vaccines	
First dose	DTaP-IPV-HepB/Hib[a,b]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,b,c]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,b,c]	
6 months later	DTaP-IPV[c]	
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.		

a. Healthy children aged 5 years and older do not need Hib-PRP. However, DTaP-IPV-HepB/Hib should be offered to reduce the number of injections at each visit. Parents/guardians should be informed that their child will receive extra doses of Hib-PRP but there are no safety concerns with these extra doses.

b. If the parents/guardians prefer, vaccinators may administer DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

c. If a child turns 10 years old before completing their catch-up programme, they should continue on the 10 years to under 18 years catch-up schedule (see Table A2.8).

Table A2.8: Age at presentation: 10 years to under 18 years – excluding HPV

Note: Subtract previous doses given.

Dose	Vaccines				
First dose	Tdap[a]	IPV[b]	HepB[c]	MMR	
4 weeks later	Tdap[a]	IPV[b]	HepB	MMR	
4 weeks later	Tdap[a]	IPV[b]	HepB		
6 months later, or at age 11 years	Tdap				
At age ≥11 years					VV[d]

a. Use Tdap for the primary series and the booster dose, with a 6-month interval between the completion of the primary series and the booster (doses 3 and 4).

b. A minimum of 3 IPV doses are required for the primary series (at a minimum of 4-weekly intervals).

c. If aged 10 years to under 18 years, 3 doses of HepB are required. An alternative 2-dose schedule of HepB may be used for children aged 11–15 years with the second dose given 4–6 months after the first.

d. One dose of varicella vaccine is funded for children born on or after 1 July 2006, who have not previously had varicella vaccination or infection.

Table A2.9: Age at presentation: 11 years to under 18 years – HPV only

Note: Subtract previous doses given.

Dose	Vaccine
Age 11–14 years[a,b] at presentation	
First dose	HPV
6–12 months later[c,d]	HPV
Age 15 years or older[b,e] at presentation	
First dose	HPV
2 months later	HPV
4 months later	HPV

a. Although the usual schedule is at age 11 or 12 years (school year 7 or 8), HPV vaccine may be given from age 9 years.

b. Individuals who started with HPV4 may complete their remaining doses with HPV9.

c. For those aged 11–14 years, the second dose is preferably given at least 6 months after the first. However, if the second dose is given less than 5 months after the first, a third HPV dose is recommended and funded — give the third dose at least 5 months after the first dose.

d. A two-dose schedule at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose.

e. If a shortened schedule is required for those aged 15 years or older, three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.

A2.3 Immunisation catch-up for eligible adults aged 18 years and older

When seen at general practice or by vaccination providers, adults should be checked to see that they have received protection against the following diseases and have received a primary immunisation course as in Table A2.10 below. Adults are eligible for age-appropriate catch-up immunisations if they are New Zealand residents, citizens, former refugees or hold a visa which makes them eligible for health care in New Zealand.

1. If the requisite number of doses have not been received, catch-up vaccination is recommended. There is flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines may be given at the same visit and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.

2. Do not repeat prior doses regardless of how long ago the previous doses were given.

3. Adults should be reminded of the necessity for age-appropriate boosters for tetanus, diphtheria and pertussis at 45 years of age if they have not previously received four tetanus vaccines in their lifetime, and for all adults at 65 years of age.

4. Pertussis (Tdap; given from 16 weeks' gestation) and influenza vaccines are recommended and funded in every pregnancy. A single dose of unfunded Tdap

and influenza vaccines may be considered for adults requesting pertussis and influenza protection, especially for those in close contact with young babies.

5. Women of childbearing age should know whether they are immune to rubella, and are considered immune if have two documented doses of MMR after 12 months of age. If the patient does not have documented evidence of immunity (see section 12.8.3), two doses of funded MMR should be offered four weeks apart (MMR cannot be given in pregnancy and pregnancy should be avoided for four weeks following vaccination). If they have received one documented dose of MMR, a second dose should be administered.

6. Previously unvaccinated males and females aged 15 years to 26 years inclusive may receive three doses of HPV vaccine. Those who started with HPV4 may complete their remaining doses with HPV9. Those who were aged under 27 years when they commenced but did not complete HPV vaccination are funded to complete the three-dose course even if they are aged 27 years or older when they complete it. Non-residents who were under the age of 18 years when they commenced HPV vaccination are funded to complete the course, even if they are aged 18 years or older when they complete it.

7. Two doses of rZV are funded for adults aged 65 years. The second dose is funded and can be given if the individual turns 66 years after their first dose. There is no catch-up programme currently.

8. Check whether the individual has any additional immunisation requirements, such as specific health conditions or occupational risk (see chapter 4 'Immunisation of special groups').

Table A2.10: Primary immunisation requirements for adults

Antigens and number of doses required
3 Tdap[a]
3 polio (IPV)[b]
2 MMR[c]
3 HPV[d,e] (aged 26 years and under)

a. A primary course of 3 doses of Tdap vaccines (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults. At age 45 years, the Tdap is recommended for those adults who have not previously received four tetanus containing vaccines in their lifetime, and for all adults at age 65 years.

b. A primary course of 3 polio (IPV) doses (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults.

c. Two doses of MMR (given a minimum of 4 weeks apart) are recommended and funded for unimmunised adults who are susceptible to any one of the three diseases. Those born in New Zealand before 1969 are considered immune to measles and those born prior to 1980 are considered to be immune to mumps.

d. HPV9 vaccine is recommended and funded for individuals aged up to 26 years inclusive. Give the 3-dose course at 0, 2 and 6 months. If a shortened schedule is required, the 3 doses can be given with a minimum of 4 weeks between the doses one and two, and third dose given at least 12 weeks after dose two.

e. Those who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are aged 27 years or older when they complete it. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

1. Dow D ,Mansoor O. New Zealand immunisation schedule history. *New Zealand Medical Journal*, 1996. 109: : p. 209–12.
2. Reid S. Evolution of the New Zealand childhood immunisation schedule from 1980: A personal view. *New Zealand Medical Journal*, 2006. 119(1236): p. 73–83.
3. Reid S. The further and future evolution of the New Zealand Immunisation Schedule. *New Zealand Medical Journal*, 2012. 125(1354): p. 86–99.

Appendix 3: Immunisation standards for vaccinators and guidelines for organisations offering immunisation services

A3.1 Purpose

The 'Immunisation standards for vaccinators' (see section A3.3) are quality levels all vaccinators should achieve to ensure they can competently deliver safe and effective immunisation services.

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' (see section A3.4) apply to all vaccinators, including those delivering National Immunisation Schedule vaccines, vaccines on an authorised programme or privately purchased vaccines including travel vaccines.

The Schedule aims to protect children and adults against 16 serious vaccine-preventable diseases and offers publicly funded immunisation to individuals at risk of COVID-19, hepatitis A, influenza, varicella, TB, meningococcal and/or pneumococcal disease.

Note: The term 'vaccinator' used throughout these standards applies to *any* health professional offering a vaccinator service, including registered nurse vaccinators, authorised vaccinators, pharmacist vaccinators, GPs and midwives. For the purposes of this appendix the term pharmacist vaccinator refers to both registered pharmacist and registered intern pharmacist who have met the educational and clinical requirements: although the scope of vaccines they can administer is different, the process they undergo to gain vaccinator status is the same. These standards apply to fully authorised, pharmacist and provisional vaccinators. For COVID-19 vaccinators (working under supervision), see section A4.3.

A3.2 Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996

It is expected that all organisations and providers offering immunisation services practise in accordance with the Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996. The Regulations establish the rights of consumers and the obligations and duties of providers to comply with the Code of Rights made pursuant to the Health and Disability Commissioner Act 1994.

The obligation under the Regulations is to take 'reasonable actions in the circumstances to give effect to the rights and comply with the duties' in the Code of Rights. The Code of Rights is as follows.

- Right 1: Right to be treated with respect
- Right 2: Right to freedom from discrimination, coercion, harassment and exploitation
- Right 3: Right to dignity and independence
- Right 4: Right to services of an appropriate standard
- Right 5: Right to effective communication
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent
- Right 8: Right to support
- Right 9: Rights in respect of teaching or research
- Right 10: Right to complain

For more detailed information on the Code of Health and Disability Services Consumers' Rights, refer to the Health and Disability Commissioner's website (**hdc.org.nz**).

A3.3 Immunisation standards for vaccinators

These standards apply to fully authorised, pharmacist and provisional vaccinators. For COVID-19 vaccinators (working under supervision), see section A4.3.

Standard 1: The vaccinator is competent in all aspects of the immunisation technique and has the appropriate knowledge and skills for the task

Required characteristics of the vaccinator

1.1 The vaccinator completes an appropriate training programme approved by the Ministry of Health. If a vaccinator is working as a fully authorised vaccinator, pharmacist or provisional vaccinator, they will also have undertaken a clinical assessment and vaccinate in accordance with their Scope of Practice (see A3.6).

1.2 Vaccinators are required to have a summary[1] of their immunisation practice over the past 12 months.

1.3 The vaccinator remains current with developments in immunisation theory, practice, cultural competency, and policy. At least every two years the vaccinator is required to retrain having completed a vaccinator update course that meets the current *Vaccinator Update Course Standards* (published by IMAC) and have evidence of completion. See authorisation requirements outlined in A3.6.

1.4 The vaccinator maintains linkages with other providers associated with immunisation delivery; for example, immunisation coordinators, outreach immunisation providers, Māori and Pacific health providers, and their local DHB NIR team.

1.5 Vaccinators are recommended to carry indemnity insurance for their personal/professional protection.

Standard 2: The vaccinator obtains informed consent to immunise

Required characteristics of the vaccinator

2.1 The vaccinator is able to assess the knowledge of the individual/ parent/guardian regarding vaccine-preventable diseases and the process of immunity, and has the knowledge of the relevant diseases and vaccines to be able to provide evidence-based information to enable individuals/parent/guardian to make an informed choice and give informed consent.

2.2 The vaccinator communicates in a form, language and culturally appropriate way that enables the individual/parent/guardian to understand the information provided. Communication should be supported by evidence-based health information material (see section 2.1.2).

2.3 The vaccinator allows time to answer questions and obtains feedback indicating that the individual/parent/guardian understands which vaccine is being recommended and why.

2.4 The vaccinator informs the individual/parent/guardian about the NIR/AIR, including information on the use and disclosure of the information held on the NIR/AIR, how the information is stored, and that all vaccinations given will be recorded on the NIR or AIR (if applicable) unless the individual/parent/guardian chooses to opt off the NIR. If an individual/parent/guardian chooses to opt off the NIR, this process must be explained to them.

2.5 Consent does not need to be given in writing (except for school-based immunisation programmes and BCG vaccination), but the vaccinator must document in the clinical notes a summary of the discussion and note that verbal consent was obtained.

2.6 The vaccinator obtains consent for each immunisation episode and documents that the individual/parent/guardian has been made aware of the benefits and risks of the disease and the vaccine in order to make an informed choice about

[1] The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy, etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc).

immunisation and the immunisation programme, including the NIR (see section 2.3.5).

2.7 If the individual/parent/guardian declines to be immunised/to immunise their child, the vaccinator provides information about keeping themselves and others healthy. The individual/parent/guardian should be advised that they can reconsider their decision at any time, and the declined immunisation will be offered again by their health provider.

Standard 3: The vaccinator provides safe immunisation

Required characteristics of the vaccinator and immunisation setting

3.1 The venue provides privacy and is appropriate for the individual/parent/guardian/whānau. Facilities are available for assessment and management of adverse events, including anaphylaxis (see section 2.3.3).

3.2 If the venue is a non-clinical setting (eg, in a home, workplace, marae or school) then a minimum of two immunisation team members must be present for vaccination; one of whom must be an authorised vaccinator or pharmacist vaccinator, the other must be a competent adult who is able to call for emergency support and has a current basic life support certificate.

3.3 The vaccinator can manage AEFIs, including anaphylaxis, ensures that they have onsite access to the minimum set of emergency equipment (see Table 2.12 in chapter 2), and has a contingency plan for seeking emergency assistance.

3.4 Because of the potential for anaphylactic reactions, vaccine recipient (with their parents/guardians if applicable) are required to remain under observation for a minimum of 20 minutes after immunisation.

3.5 The vaccinator ensures continuity of the cold chain and adheres to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* and the practice/clinic cold chain management policy. The vaccinator ensures the practice/clinic achieves Cold Chain Accreditation.[1]

3.6 Before vaccinating, the vaccinator undertakes an appropriate clinical assessment (pre-vaccination screen) (see section 2.1.3).

3.7 The vaccinator uses clean techniques in the preparation and administration of all vaccines (see section 2.1 and Appendix 7), visually checks the vaccine, checks expiry date, prepares vaccine as appropriate and uses vaccines within the recommended period after preparation.

3.8 The vaccinator provides verbal and written information that is evidence based and follows best practice principles about care after immunisation (see sections 2.1.2 and 2.3.1).

[1] Refer to the National Immunisation Programme cold chain management (available at **www.health.govt.nz/our-work/preventative-health-wellness/immunisation/national-immunisation-programme-cold-chain-management**).

Standard 4: The vaccinator documents information on the vaccine(s) administered, and maintains patient confidentiality

Required characteristics of the vaccinator

4.1 The vaccinator has had training in the correct use of their PMS, the SBVS, the NIR or AIR manual forms to enable them to correctly enter an individual's information on the NIR or AIR (if applicable) and to claim an immunisation benefit (if applicable).

4.2 The vaccinator documents the individual's personal details, including NHI number, name, date of birth, ethnicity, address, contact telephone number, next of kin details and primary health care provider (if the vaccinator is not the usual primary health care provider).

4.3 Having chosen the appropriate immunisation schedule, the vaccinator documents the following details:

- consent obtained
- date vaccine administered
- vaccine type and number in the series
- batch number and expiry date
- injection site (eg, 'right deltoid' not 'upper arm')
- needle length
- that the patient was observed for 20 minutes post-vaccination
- if the vaccine was given by a non-standard route (the reasons must be documented)
- the immunisation event in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
- the date for the next immunisation in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
- advice and resources given.

4.4 The vaccinator ensures the immunisation information is sent to the NIR (ie, electronically or manually) where applicable, unless the individual/parent/guardian has opted off the collection of their/their child's immunisation information on the NIR.

4.5 The vaccinator ensures the immunisation certificate (see Appendix 5) is accurately completed following the 15-month and 4-year immunisation events.

4.6 If the practice/clinic is not the usual primary health care provider, then the individual's primary health care provider is informed by the vaccinator or by NIR notification within five working days of giving the vaccine, unless the individual declines for this to occur.

4.7 All clinical documentation is appropriately managed and stored to maintain confidentiality, and is made available to the individual/parent/guardian on request.

Standard 5: The vaccinator administers all vaccine doses for which the vaccine recipient is due at each visit and only follows true contraindications

Required characteristics of the vaccinator

5.1 The vaccinator adheres to the National Immunisation Schedule or approved immunisation programme and delivers all the immunisations recommended for that visit, unless the individual/parent/guardian does not consent to this.

5.2 When catch-up immunisation is required, this is planned with the minimum number of visits/injections and in conjunction with the individual/parent/guardian.

5.3 A dose of vaccine is deferred or avoided only when contraindicated or the individual/parent/guardian has chosen to defer/avoid it. The reason for deferral or avoidance must be documented (see section 2.1.4 and the specific disease chapters).

Standard 6: The vaccinator reports AEFIs promptly, accurately and completely

Required characteristics of the vaccinator

6.1 All serious or unexpected AEFIs are reported by the vaccinator to the Medical Assessor, CARM (see section 1.6.3 for the adverse event reporting process) and to the individual's primary health care provider (if the vaccinator is another person). If the individual/parent/guardian does not consent to being identified, the report should be made without personal identification.

6.2 The vaccinator informs the individual/parent/guardian that if an adverse event occurs, they can also report it to CARM.

6.3 When a CARM report is received, and further doses of the vaccine have been contraindicated, the vaccinator advises the local DHB NIR Administrator so that an appropriate AEFI code is recorded in the individual's NIR record.

6.4 The vaccinator seeks specialist (eg, GP, paediatrician, infectious diseases physician or medical officer of health) opinion if uncertain about the safety of further doses, and referral is made to secondary care if required.

6.5 The vaccinator ensures the adverse event, and any subsequent decisions relating to the event, are effectively communicated to the individual/parent/guardian and clearly documented in the child's *Well Child Tamariki Ora My Health Book* (if applicable) and in the patient records, and appropriate follow-up is carried out.

A3.4 Guidelines for organisations storing vaccines and/or offering immunisation services

These guidelines apply to all organisations that store vaccines and/or offer immunisation services, including (but not limited to) general practices, public health units, community pharmacies, travel clinics, occupational health clinics, emergency medical services, research units and hospital wards/clinics/departments/pharmacies.

The organisation that employs vaccinators to offer immunisation services has links to primary health care and to Well Child Tamariki Ora providers

Required characteristics

Immunisation is not delivered in isolation, but as an integrated part of primary health care services, including Well Child Tamariki Ora for children.

If possible, at the time of immunisation, the organisation undertakes other health promotion and/or disease prevention activities as applicable, such as the Well Child National Schedule or Care Plus.

Immunisation events, childhood and adult, are well communicated to other health services linked to the individual (eg, primary health care, outreach immunisation services, pharmacies, occupational health).

The organisation achieves high immunisation coverage of its population

Required characteristics

The organisation has an effective, secure, NHI-based system for recording and reporting immunisations and identifying individuals requiring immunisation.

Respecting the individual's/parent's/guardian's rights to make an informed choice, the organisation takes all steps to ensure that an individual's immunisation schedule commences on time and that subsequent events are administered on the due date.

The organisation has electronic linkage to the NIR or AIR for registration and immunisation event notification, and the NIR or AIR is used to assist with follow-up. If electronic linking is not available, manual processes must be used.

The organisation has a robust reminder (pre-call) system which encourages the delivery of on-time immunisation and timely follow-up for overdue immunisation.

The organisation has an effective communication strategy to target high-needs population groups.

Attendance at the practice/organisation is used as an opportunity to remind individuals/parents/guardians of the importance of immunisation and, if appropriate, to check and offer to bring up to date the individual's immunisation status.

Those who do not respond to recall and who have not declined to take part are referred to the outreach immunisation service, as per local protocol.

The organisation supports vaccinators and NIR administrators

Required characteristics

The organisation has comprehensive immunisation-related policies based on best practice, informed consent, the vaccination process and management of adverse events.

The organisation uses a pharmaceutical refrigerator to store vaccines, has a vaccine cold chain policy in place and meets the requirements outlined in the *National Standard for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*[1] for all areas within the organisation storing vaccines.

The organisation provides training and support workers (eg, kaiāwhina, community health workers) for vaccinators working in the community.

The organisation supports the need for vaccinators to have access to ongoing education and training on all aspects of immunisation at least every two years and when there are changes to the Schedule.

The organisation provides initial and ongoing training and support specific to the NIR, PMS, and/or the SBVS (if applicable).

The service is readily available, with no barriers to access

Required characteristics

No fee is charged to the individual/guardian for the immunisations that are on the Schedule or high-risk programmes (or for completing the child's immunisation certificate). Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive funded Schedule vaccines, and providers may claim the immunisation benefit for these children. Non-residents who were under age 18 years when they commenced HPV vaccination in New Zealand are currently funded to complete the course, even if they are aged 18 years or older when they complete it. Further information on eligibility can be found on the Ministry of Health website (**www.health.govt.nz/eligibility**).

Immunisations are provided to both enrolled and casual patients, at all times when the organisation or service is open.

[1] Refer to the National Immunisation Programme cold chain management (available at **www.health.govt.nz/our-work/preventative-health-wellness/immunisation/national-immunisation-programme-cold-chain-management**).

A person's immunisation status is checked at each visit to the service.

The organisation is culturally appropriate (ie, all health workers are assessed as culturally competent, reflect the populations they serve and offer a range of health information resources[1] in different languages).

A3.5 Recommended resources

Ministry of Health (health.govt.nz/our-work/preventative-health-wellness/immunisation)

- The current Immunisation Handbook
- National Immunisation Register Privacy Policy
- The current National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 2nd Edition (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**)
- Cold Chain Management Policy Template
- Cold Chain Accreditation Provider Self-Assessment Form
- Cold Chain Accreditation Provider Reviewer Form
- Kōrero Mārama: Health Literacy and Māori – Results from the 2006 Adult Literacy and Life Skills Survey, February 2010 (**www.health.govt.nz/system/files/documents/publications/korero-marama.pdf**)
- Whakamaua: Māori Health Action Plan 2020–2025, July 2020 (**www.health.govt.nz/publication/whakamaua-maori-health-action-plan-2020-2025**)

A3.6 Relevant legislation and regulations

See **www.legislation.govt.nz**.

- Health (Immunisation) Regulations 1995
- Medicines Act 1981
- Medicines Regulations 1984
- Health (Infectious and Notifiable Diseases) Regulations 1966, Amendment No. 2, regulation 44A
- Health Act 1956, section 22F
- Health Information Privacy Code 1994

[1] Ministry of Health immunisation resources are available in English and a variety of languages from the HealthEd website (**healthed.govt.nz**) or from the local health education authorised provider.

- Health and Disability Commissioner Act 1994: Code of Health and Disability Services Consumers' Rights 1996 (see **hdc.org.nz**)
- Health Practitioners Competence Assurance Act 2003
- Privacy Act 1993
- Care of Children Act 2004
- Accident Compensation Act 2001
- Health and Safety at Work Act 2015
- Resource Management Act 1991
- Primary Maternity Services Notice 2007 (see **www.health.govt.nz**) pursuant to section 88 of the New Zealand Public Health and Disability Act 2000

Immunisation Advisory Centre (immune.org.nz)

- Vaccinator Foundation Course Standards
- Vaccinator Update Course Standards

Appendix 4: Authorisation and criteria of vaccinators

This section provides details around the authorisation of vaccinators. There are three main categories of authorisation: fully authorised, provisionally authorised and supervised vaccinators. Pharmacists can vaccinate, having met certain criteria, as either fully authorised or provisionally authorised vaccinators. See Table A4.1 (Full authorisation), Table A4.2 (Pharmacist vaccinators), Table A4.3 (Provisional vaccinators), and0 Table A4.4 and Table A4.5 (supervised vaccinators) for details of the criteria and authorisation of each group. All vaccinators are required to meet resuscitation requirements as given in section A4.4.

A4.1 Protocols for full authorisation of vaccinators and pharmacist vaccinators

A4.1.1 Authority for fully authorised vaccinators[1] and pharmacist vaccinators

A person may be authorised under regulation 44A(2) of the Medicines Regulations 1984 by the Director-General of Health or the National Medical Officer of Health to administer a vaccine for the purposes of an approved immunisation programme.[2] Regulation 44A(2) stipulates that the person seeking approval must apply in writing to the Director-General or a medical officer of health and provide documentary evidence that they:

- can carry out basic emergency techniques including resuscitation and the treatment of anaphylaxis
- have knowledge of the safe and effective handling of immunisation products and equipment
- can demonstrate clinical interpersonal skills
- have knowledge of the relevant diseases and vaccines to be able to explain the vaccination to the individual, parent or guardian who is to consent to the vaccination on behalf of the individual, to ensure that the individual or parent or guardian of the individual can give informed consent to the vaccination.

The usual protocol requires fully authorised vaccinator applications to be submitted to a medical officer of health in the applicant's local region. Authorisation given under Regulation 44A(2) is valid for a period of two years from the date of authorisation and is subject to such conditions as the Director-General or the National Medical Officer of

1 Fully authorised vaccinators were previously called 'authorised independent vaccinators'.

2 See the Ministry of Health document *Definition of an Approved Immunisation Programme* (available for download from **www.health.govt.nz/our-work/preventative-health-wellness/immunisation**).

Health thinks fit. During the early stages of the COVID-19 response, the Director of Public Health, in their capacity as a National Medical Officer of Health, authorised all authorised vaccinators and provisional authorised vaccinators to provide National Immunisation Schedule and funded vaccinations (as noted in their authorisation) for those at increased risk of vaccine-preventable disease (as identified in this Immunisation Handbook). This meant they did not need to apply for authorisation in different PHU areas.

Successful applicants will be authorised to administer either all or specific vaccines depending on the training they have completed (see Table A4.1). Details of the training they must complete is set out in section A4.1.2.

Table A4.1: Fully authorised vaccinators

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups[a]	Sites for injection	Authority to obtain informed consent
Fully authorised vaccinator	Director-General or Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Health professionals with current annual practicing certificate[b]	Vaccines on the National Immunisation Schedule and any other vaccines part of an approved immunisation programme (approved by the Director-General or Medical Officer of Health)	All ages	Vastus lateralis Deltoid	Yes

a. Restrictions may apply depending on scope of authorisation, vaccine reclassification and/or DHB funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.
b. Practitioners without a New Zealand practicing certificate may be unable to get indemnity insurance.

Authority for pharmacist vaccinators

A number of vaccines have been reclassified by the Medicines Classification Committee from prescription medicines to prescription medicine except when administered by pharmacists or registered intern pharmacists who have successfully completed the *Vaccinator Foundation Course* (or any equivalent training course approved by the Ministry of Health, but excluding vaccinators who have completed the *Provisional Vaccinator Foundation Course*) and who comply with the immunisation standards of the Ministry of Health.

The reclassification means that pharmacists and pharmacist interns can administer specific vaccines once they have: successfully completed a Ministry of Health-approved VFC (including the open-book assessment); and are complying with the immunisation standards as described in Appendix 3 of this Handbook. Pharmacist and intern pharmacist vaccinators are expected to be aware of which vaccines have been reclassified for their scope (see Table A4.2).

Due to these classifications, pharmacist vaccinators are not required to apply to a medical officer of health for authorised vaccinator status to be able to administer vaccines that have been reclassified. However, the expectation is they notify Pharmaceutical Society of New Zealand (PSNZ) when they have completed the requirements specified above, including the course completion date (see Completion of authorisation).

Like all vaccinators, pharmacists and pharmacist interns must attend an approved vaccinator update every two years to be able to continue to administer vaccines. The training required for pharmacists and intern pharmacists is detailed in section A4.1.3.

Table A4.2: Pharmacist vaccinators

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups[a]	Sites for injection	Authority to obtain informed consent
Pharmacist vaccinator	Enabled to vaccinate pursuant to the Medicines Regulations classifications on completion of full vaccinator training. It is then recommended that they inform the Pharmaceutical Society of New Zealand to be added to the vaccinator database.	Registered Pharmacists	Influenza	Ages 3 years and over	Deltoid only	Yes
			MMR	All ages		
			COVID-19[b]	All ages		
			HPV	Ages 9 years and over		
			Meningococcal	Ages 16 years and over		
			Tdap	Ages 18 years and over. Pregnant women aged 13 years and over		
			Zoster	Ages 50 years and over		
Intern Pharmacist Vaccinators	Enabled to vaccinate pursuant to the Medicines Regulations classifications on completion of full vaccinator training. It is then recommended that they inform the Pharmaceutical Society of New Zealand to be added to the vaccinator database.	Registered Pharmacist interns	Influenza	Ages 3 years and over	Deltoid only	Yes
			MMR	All ages		
			COVID-19[b]	All ages		
			HPV	Ages 9 years and over		

Provisional pharmacist vaccinator[c] MMR, Influenza and COVID 19	Director-General or Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Registered Pharmacists and Pharmacist interns	Influenza MMR COVID-19[b,c]	Ages 3 years and over Ages 16 and over Age groups covered in the Ministry approved COVID-19 training	Deltoid only	Yes

a. Restrictions may apply depending on scope of authorisation, vaccine reclassification and/or DHB funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.
b. Upon completion of appropriate COVID-19 vaccine education course.
c. See section A4.2.

A4.1.2 Process for full authorisation for vaccinators and pharmacist vaccinators

Assessment requirements

To become a fully authorised vaccinator or pharmacist/intern pharmacist vaccinator, all applicants must first meet the following Ministry of Health requirements.

1. Demonstrate that within the preceding 24 months they have attended, completed and passed a Vaccine Foundation Course (VFC) and have received the associated certificate. The VFC must meet the current *Vaccinator Foundation Course Standards* (published by IMAC) and the course should consist of:
    a. a minimum of 16 hours' educational input
    b. a written open-book assessment (minimum one-hour duration), which may be oral at the facilitator's discretion.
2. Undergo an independent clinical assessment by an immunisation coordinator or an approved assessor (as agreed by the Medical Officer of Health).[1] Information about the practice environment, including cold chain and emergency management processes, will be collected at the time of the clinical assessment.
3. Have evidence that they hold a current practising certificate from their registration authority (eg, Nursing Council of New Zealand, Pharmacy Council of New Zealand).
4. Have a current cardiopulmonary resuscitation (CPR) certificate (see section A4.4 for details).

[1] If it has been more than 12 months but less than 24 months since the applicant completed a full VFC, they should complete an online update prior to the clinical assessment.

Completion of authorisation

Fully authorised vaccinator applicants

Authorised vaccinator applicants[1] who have successfully completed their clinical assessment will then need to apply for authorisation under Regulation 44A(2) by submitting an application, including the documentation described above, to a medical officer of health. Generally, this will be their local Medical Officer of Health but in some instances this authorisation may be given by a national Medical Officer of Health.

Pharmacist vaccinator applicants

Pharmacists and intern pharmacists who have met the assessment requirements detailed above and should notify the Pharmaceutical Society (PSNZ) by an email containing the following information:

1. full name
2. membership number
3. name of the pharmacy or pharmacies which vaccinations will be provided from, or if the pharmacist is a locum
4. date of the course (or update course)
5. date of their clinical assessment.

Copies of the vaccination certificate or resuscitation certificates are not required. Emails should be sent to **p.society@psnz.org.nz** and need to include 'pharmacist vaccinator' in the subject line.

For audit purposes, it is recommended that all pharmacist vaccinators keep a copy of the record of their vaccinator training and other relevant documentation in a file at their current place of work.

A4.1.3 Process for renewal of vaccinator status for fully authorised vaccinators and pharmacist vaccinators

Authorisation of fully authorised vaccinators is valid for two years from the date of the authorisation approval letter from the Medical Officer of Health. To maintain status as an authorised vaccinator, authorisation must be renewed two yearly. To be authorised, the vaccinator must meet the requirements specified below.

To renew their vaccinator status, vaccinators are required to:

1. during the past two years or within a month of expiry of status, have completed a vaccinator update course that meets the current *Vaccinator Update Course Standards*[2]

[1] Fully authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes.

[2] Authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes.

2. have a summary of their immunisation practice over the past 12 months. The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc)
3. have evidence of a current practising certificate
4. have evidence of a current CPR certificate (see section A4.4 for details).

Fully authorised vaccinators

To continue vaccinating, fully authorised vaccinators need to apply for renewal of their authorisation to their local Medical Officer of Health and submit all relevant documentation (ie, immunisation update, CPR certificates and immunisation summary), prior to the expiry of their authorised vaccinator status.

Pharmacist vaccinators and intern pharmacist vaccinators

Prior to the expiry of their pharmacist vaccinator status, pharmacist vaccinators should notify PSNZ when they have completed the Ministry of Health requirements specified above.

A4.1.4 Process when fully authorised vaccinator status has not been maintained or has not been achieved

If it is less than five years since the vaccinator attended and completed an approved vaccinator course

When a vaccinator has not achieved or maintained their vaccinator status, they must:

1. have a clinical assessment by an immunisation coordinator or approved assessor within the past three months (only required if vaccinator status expired more than a month earlier)
2. have completed a vaccinator update course that meets the current *Vaccinator Update Course Standards* in the last two years
3. have a summary of their immunisation practice over the past 12 months or intended area of practice. The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy, etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person)
4. have evidence of a current practising certificate
5. have evidence of a current CPR certificate (see section A4.4 for details).

If it is five or more years since the applicant completed an approved vaccinator training and they have not achieved or maintained their vaccinator status

If it is more than five years since the applicant completed their initial VFC or approved vaccinator update, they will be required to attend and pass another VFC. This is because there will have been significant developments in vaccination delivery in the intervening interval.

See section A4.1.2 Process for full authorisation for vaccinators and pharmacist vaccinators.

A4.1.5 Process when a vaccinator is new to the health district in which they intend to practise

If a fully authorised vaccinator wishes to practise in another health district and/or public health area, they must advise the local Medical Officer of Health and send through a copy of their current authorisation.

Pharmacist and intern pharmacist vaccinators are required to advise the local immunisation coordinator of their intention to set up a new pharmacist vaccinator service; this is to ensure that the coordinator is aware of which pharmacies require three-yearly spatial logging of the refrigerator. Where a vaccination service is already being offered this is not required.

A4.1.6 Additional endorsement process for BCG vaccinators

All BCG vaccinators are fully authorised vaccinators with BCG endorsement. They are authorised by the local Medical Officer of Health as described below.

New BCG vaccinators and gazetted BCG vaccinators seeking regional BCG endorsement

To be endorsed as a BCG vaccinator, the applicant needs to:

1. complete an approved VFC
2. be nominated by their employer to become a BCG vaccinator
3. successfully complete a Ministry of Health-approved online BCG vaccination course
4. complete under clinical supervision a minimum of five BCG vaccinations (using a standing order or prescription)
5. successfully complete a BCG clinical assessment by an approved BCG assessor
6. apply to the Medical Officer of Health for BCG endorsement approval, providing documented evidence of these requirements.

If a BCG vaccinator needs to administer additional Schedule vaccines, they will need to undertake a clinical assessment appropriate for the age group they will be vaccinating. Standing orders or prescriptions are required for the clinical assessment process.

For more information, see the Ministry of Health webpage *BCG vaccine and vaccinator endorsement* (available at **www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-programme-decisions/bcg-vaccine-and-vaccinator-endorsement**).

Process for two-yearly renewal of BCG vaccinator status

To renew BCG endorsement, vaccinators must apply to their local Medical Officer of Health prior to the expiry date and provide documented evidence that they:

1. are a current authorised vaccinator, and
2. have completed an online vaccination course that includes an update on BCG.
3. A BCG vaccinator who also holds full authorisation will need to complete a standard vaccinator update course, in addition the BCG update.

Note: BCG vaccinators must complete a *BCG Vaccinator Update* course every two years. This online course is available as part of IMAC education (available at **immune.org.nz/health-professionals/education**).

A4.2 Protocols for provisional authorised vaccinators and provisional pharmacist vaccinators

In April 2020, as part of the New Zealand COVID-19 response, a pathway to provisional authorisation for vaccinators (PAV) was developed. This pathway is a short-term measure alongside the *Provisional Vaccinator Foundation Course* available from IMAC. This pathway was extended into 2022.

A4.2.1 Authority for provisional authorised vaccinators and provision authorised pharmacist vaccinators

Provisional authorised vaccinators and provisional authorised pharmacist vaccinators, like fully authorised vaccinators, are authorised under regulation 44A(2). Regulation 44A(2) stipulates that the person seeking approval must apply in writing to the Director-General or the national Medical Officer of Health and provide documentary evidence that they:

1. can carry out basic emergency techniques, resuscitation, and the treatment of anaphylaxis
2. have knowledge of the safe and effective handling of immunisation products and equipment

3. can demonstrate clinical interpersonal skills
4. have knowledge of the relevant diseases and vaccines to be able to explain the vaccination to the individual, parent or guardian of the individual who is to consent to the vaccination on behalf of the individual, to ensure that the individual or parent or guardian of the individual can give informed consent to the vaccination.

Provisional authorised vaccinators and provisional authorised pharmacist vaccinators are only able to be authorised to administer influenza, MMR and COVID-19 vaccines (these are the only vaccines covered by the *Provisional Vaccination Foundation Course* and the *COVID-19 Vaccine Education Course* that these vaccinators complete). See Table A4.3.

Table A4.3: Provisional authorised vaccinators

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups[a]	Sites for injection	Authority to obtain informed consent
Provisional Vaccinator MMR, Influenza and COVID 19	Director-General or national Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Health professionals with current annual practicing certificate[b]	Influenza	Ages 3 years and over	Deltoid only	Yes
			MMR	Ages 3 years and over		
			COVID-19	Age groups covered in the Ministry approved COVID-19 training[c]		
Provisional pharmacist vaccinator MMR, Influenza and COVID 19	Director-General or national Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Registered Pharmacists and Pharmacist interns	Influenza	Ages 3 years and over		
			MMR	Ages 16 and over		
			COVID-19c	Age groups covered in the Ministry approved COVID-19 training		

a. Restrictions may apply depending on scope of authorisation, vaccine reclassification and/or DHB funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.
b. Practitioners without a New Zealand practicing certificate may be unable to get indemnity insurance.
c. Upon completion of appropriate COVID-19 vaccine education course.

A4.2.2 Process for provisional authorised vaccinators

To achieve provisional authorised vaccinator or provisional authorised pharmacist vaccinator status, Ministry of Health requires vaccinators to:

1. complete the online *Provisional Vaccinator Foundation Course* (including learning assessment and webinar)
2. successfully complete a peer assessment of clinical practice
3. hold a current *New Zealand Annual Practising Certificate*
4. final year students completing a degree within a relevant field of study to provide proof of enrolment and student identification
5. have evidence of current CPR certificate (see section A4.4 for details)
6. submitted a completed application for authorisation as a provisional authorised vaccinator to the Ministry of Health
7. on receipt of written authorisation from a medical officer of health, provisional authorised vaccinators send copy of authorisation and peer assessment to the local immunisation coordinator.

Provisional authorised vaccinators who wish to continue to vaccinate after expiration of their authorisation will be required to transition to become a fully authorised vaccinator or pharmacist vaccinator. A bridging course will be made available in 2022 from IMAC. Those who want to be approved as full authorised vaccinators or pharmacist vaccinators before this bridging course is available will be required to complete a full VFC. More information is available from the IMAC education website (**immune.org.nz/health-professionals/education**).

A4.3 Protocols for Vaccinating Health Workers (working under supervision)

In May 2022 a new vaccinating health worker (VHW) role was created under section 44AA of the Medicines Regulations 1984.

Authority for already approved COVID-19 vaccinators (working under supervision) (CVWUS) will expire on 1 June 2023 (see Table A4.4). This workforce can only administer mRNA-CV (30 µg). To expand the capacity of this workforce, CVWUS vaccinators are encouraged to become authorised vaccinating health workers (VHS), as shown in Table A4.5. The training required for supervised vaccinating health workers is detailed in section A4.3.2.

Table A4.4: COVID-19 Vaccinator working under supervision (CVWUS)

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4). Anaphylaxis training is part of the IMAC course for CVWUS and VHW.

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups	Sites for injection	Authority to obtain informed consent
COVID-19 Vaccinator working under supervision (CVWUS)	Director-General or Medical Officer of Health (under reg 44AB of the Medicines Regulations 1984)	Person working under clinical supervision and direction of a suitably qualified health practitioner	COVID-19 (mRNA vaccines) only[a]	Age 12 years and over	Deltoid only	**No**

a. Upon completion of appropriate COVID-19 vaccine education course. Note this course is no longer available and vaccinators are encouraged to complete VHW education to extend their scope.

Table A4.5: Vaccinating health workers (VHW)

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4). Anaphylaxis training is part of the IMAC course for CVWUS and VHW.

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups	Sites for injection	Authority to obtain informed consent
Vaccinating Health Worker: Stage one	Director-General or National Medical Officer of Health (under reg 44AA of the Medicines Regulations 1984)	Person working under clinical supervision and direction of a suitably qualified health practitioner	mRNA-CV (30 µg)[a]	Ages 12 years and over	Deltoid only	**No**
			Influenza, administration only[a]	Ages 12 years and over		
			Tdap, administration only[b]	Ages 11 years and over		
			HPV9, administration only[b]	Ages 11 years and over		

Continued overleaf

Vaccinating Health Worker: Stage two	Director-General or National Medical Officer of Health (under reg 44AA of the Medicines Regulations 1984)	Person working under clinical supervision and direction of a suitably qualified health practitioner	mRNA-CV (30 µg), administer[a,c]	Ages 12 years and over	Deltoid only	**No**
			mRNA-CV (10 µg) administer[a,c]	Ages 5 to 11 years		
			Influenza, prepare and administer [a,c,d]	Ages 5 years and over		
			Tdap, prepare and administer[b,c,d]	Ages 11 years and over		
			HPV, prepare and administer [b,c,d]	Ages 11 years and over		
			MMR, prepare and administer [c,d]	Ages 5 years and over		
			Prepare mRNA-CV multidose vials[c,d]			

a. Upon completion of appropriate Stage One education course plus influenza and COVID-19 vaccine specific course.
b. Upon completion of appropriate Stage One education course plus Tdap/HPV9 vaccine education course.
c. Upon completion of appropriate Stage Two vaccine education course.
d. Upon completion of appropriate vaccine preparation course.

A4.3.1 Authority for vaccinating health workers (working under supervision)

A person may be authorised by the Director-General of Health or a National Medical Officer of Health to prepare and administer a vaccine without a prescription. An authorised vaccinating health worker must, at all times while performing the tasks authorised under regulation 44AA, work under the clinical supervision and direction of a suitably qualified health practitioner.

Regulation 44AA(3) stipulates that the person must apply to the Director-General of Health or a National Medical Officer of Health and provide documentary evidence that they:

1. have successfully completed training as approved by the Director-General
2. can carry out basic emergency techniques, including resuscitation and the treatment of anaphylaxis and
3. have knowledge of the safe handling of immunisation products and equipment.

A4.3.2 Process for authorisation for vaccinating health worker

The VHW role is authorised in stages.

- Stage One vaccinators can administer specific vaccines to a limited age range:
  - mRNA-CV (30 µg) and influenza vaccine to those aged 12 and over
  - and/or Tdap and HPV9 to those aged 11 and over.
- Stage Two vaccinators can prepare and administer influenza and MMR vaccine, and administer prepared mRNA-CV (10 µg) to children from age 5 years. There is an optional extension of training to allow them to prepare multidose vials of mRNA-CV.

Further detail is provided at **health.govt.nz/our-work/preventative-health-wellness/immunisation/vaccinating-workforce**.

Stage One

Vaccinating Health Workers are not required to be registered health care professionals, but to complete Stage One authorisation they are required to apply to the Ministry of Health and provide the following evidence:

1. course completion certificates for Vaccinating Health Worker Stage 1 eLearning course, plus vaccines specific course(s)
2. completed practical assessment from the IMAC Training and Competency Workbook
3. a current CPR certificate in basic life support (anaphylaxis management is covered through Ministry-approved IMAC training for all vaccinators)
4. a completed and signed Vaccinating Health Worker Stage 1 authorisation application form.

Once authorisation is accepted a letter will be issued stipulating which vaccines they can administer under supervision.

Stage Two

For further authorisation as a Stage Two Vaccinating health worker, all applicants must meet the following Ministry of Health requirements for stage two. Stage Two Vaccinating Health Workers may prepare and administer certain vaccines to children aged from 5 years under the clinical supervision and direction of a qualified health professional. Option of extending skills by completing mRNA-CV multidose vial preparation. Separate training and authorisation process.

To be granted Vaccinating Health Worker Stage 2 status, all applicants are required to apply to the Ministry of Health and provide the following evidence:

1. Letter showing VHW authorisation Stage One all four authorised vaccines.
2. Completion of core in-house training for stage one*
3. Evidence of at least 25 vaccination events
4. Vaccinating Health Worker Stage 2 eLearning course completion certificate,

5. completed Practical assessment from the IMAC Training and Competency Workbook
6. A current CPR certificate in basic life support (anaphylaxis management is covered through Ministry-approved training for all vaccinators)
7. A completed and signed Vaccinating Health Worker Stage 2 authorisation application form

A4.3.3 Process for renewal of vaccinator status for vaccinating health workers

Authorisation of a vaccinating health worker (VHW) is valid for two years from the date of the authorisation from the National Medical Officer of Health. To maintain status as an authorised VHW, authorisation must be renewed two yearly and the vaccinator must meet the requirements specified below.

To renew their vaccinator status, vaccinators are required:

1. during the past two years or within a month of expiry date on authorisation letter, have completed a vaccinating health worker update course that meets the current *Vaccinator Update Course Standards*[1]
2. to provide a summary of their immunisation practice over the past 12 months. The summary should include type of immunisation practice as a vaccinator (eg, general practice, pharmacy etc); and other responsibilities related to immunisation (eg, cold chain-designated person, etc)
3. to have evidence of a current CPR certificate (see section A4.4 for details).
4. to submit this evidence to receive updated authorisation letter.

A4.4 Resuscitation requirements for all vaccinators

All vaccinators, by virtue of their occupation, need to be able to resuscitate patients and therefore need to achieve and maintain the following resuscitation skills:

1. infant, child and adult CPR, including mouth-to-mouth, mouth-to-mask and the management of choking
2. administration of IM adrenaline for treatment of anaphylaxis
3. use of an automated external defibrillator
4. one- and two-person bag valve mask ventilation and mouth-to-mask technique.

Resuscitation training for vaccinators should cover the specific skills outlined above. The use of oxygen, sizing of airways, insertion of intravenous lines and the preparation of emergency medications (except for intramuscular adrenaline) are not skills specifically required of a vaccinator.

[1] Authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes.

All vaccinators must maintain their current resuscitation certification, typically, this is required every two years. (Note: employer protocols may require this more frequently.)

All vaccinators, except COVID-19 vaccinators (working under supervision) and vaccinating health workers, need to be able to administer intramuscular adrenaline in the event of an anaphylactic reaction to an immunisation event (see section 2.3.3).

COVID-19 vaccinators (CVWUS) and vaccinating health workers must be aware of the signs of anaphylaxis and have the knowledge to treat it but are not expected to administer adrenaline in practice.

All vaccinators must meet the emergency equipment and management requirements, regardless of the immunisation setting (eg, in general practice and in non-clinical settings, such as homes, schools, rest homes, workplaces and pharmacies), as listed in section 2.3.3.

All vaccinators are expected to keep up to date with any guidance changes, including infection control and requirements for PPE.

A4.5 Local immunisation programmes

Medical Officers of Health may approve additional vaccinations (funded or unfunded) for authorised vaccinators to administer either as part of the standard authorisation process or as part of a local immunisation programme. Public health units (PHU) need to maintain a register of the authorised vaccinators in their region. Temporary authorised vaccinators can be added to approved local immunisation programmes by Medical Officers of Health.

During the early stages of the COVID-19 response all authorised vaccinators and temporary authorised vaccinators were approved to provide National Immunisation Schedule and funded vaccinations for those at increased risk of vaccine-preventable disease by the Director of Public Health, in their capacity as national Medical Officer of Health. This means they did not need to apply for authorisation in different PHU areas.

A4.6 Minimum staff and equipment requirements for vaccination services

All vaccinators providing immunisation services need to have a minimum of two people present, one of whom must be an authorised vaccinator or pharmacist vaccinator; the other must be a competent adult who is able to call for emergency support and has a basic life support certificate.

Vaccinating health workers and COVID-19 vaccinators working under supervision must work at all times under clinical supervision and direction of a suitably qualified health practitioner.

The following check list contains the emergency equipment that is required when vaccinating offsite.

	Check list of Emergency Equipment required for off-site vaccinations	Office use only
1.	Equipment The following should be available: • Emergency kit containing: – adrenaline 1:1000 (minimum of 3 ampoules) – syringes (1 mL), 25 mm needles for IM injection (minimum of six) – adrenaline IM dose chart (ideally laminated) – cotton wool balls, gauze • cell-phone or phone access • sharps box • bag valve mask resuscitator (eg, Ambu bag) suitable for the population being vaccinated • pen and paper for emergency use • appropriately sized syringes and needles for specific vaccine programme • cotton wool balls, gauze, surgical tape or plasters • vaccines • cold chain equipment as required by the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition) (see link in note below)[a] • data logger with a probe, external display and alarm[1] • vomit bowl • tissues • gloves • appropriate surface cleaner • approved biohazard bag	Yes / No
		Continued overleaf
2.	Optional additional emergency equipment • an oxygen cylinder, flow meter, tubing and paediatric/adult masks • airways – infant through to adult • blood pressure monitoring equipment • thermometer • Intravenous cannula and administration sets: • intravenous fluids • hydrocortisone for injection • saline flush	Yes / No

a. Consider using a secondary back-up device in case the data logger gets damaged. See the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Appendix 5: Immunisation certificate

A5.1 Introduction

The Health (Immunisation) Regulations 1995 require parents/guardians of children born from 1 January 1995 to show their child's immunisation certificate when these children start at an early childhood service and on entry to primary school (school year 1). The immunisation certificate shows whether a child is fully immunised or not. Information must be recorded at age 15 months when the early childhood vaccinations are complete, and after the immunisations at age 4 years. For those parents/guardians who decline to have their child vaccinated, the immunisation certificate may be completed at any time, but the completed immunisation certificate must still be shown when the child starts at an early childhood service or primary school.

A5.2 Parent/guardian responsibilities

Parents or guardians can choose whether to vaccinate their child, but they must show the immunisation certificate when their child starts at an early childhood service and on school entry, regardless of the child's immunisation status.

A5.3 Vaccinator responsibilities

When completing and signing the immunisation certificate, vaccinators should be confident that a child is fully vaccinated. The primary concern is the child's protection. If the previous vaccination history is uncertain and parents/guardians do not wish their child to be vaccinated, the child should be certified as 'not fully immunised'. Children who have not received the necessary doses of a vaccine or have no evidence of laboratory-proven disease should be recorded as 'not fully immunised'.

The immunisation certificate is included in the *Well Child Tamariki Ora My Health Book*. This book also contains the record of the child's vaccinations. Vaccinators should ensure they record vaccination and other relevant health information in this book. This becomes particularly important if the child sees different health professionals. If the child's book is lost, it should be replaced. Copies of the *Well Child Tamariki Ora My Health Book* and immunisation certificate pads can be obtained from the authorised provider of health education materials, usually the local public health service, or ordered from the HealthEd website (**www.healthed.govt.nz**).

A5.4 Early childhood services and school responsibilities

All early childhood services and primary schools, including kōhanga reo, independent schools and kura kaupapa Māori, must keep an immunisation register for children born from 1 January 1995. The register is a tool to help reduce the spread of vaccine-preventable diseases in early childhood services and schools, as well as in the wider community. Registers are available from the authorised provider of health education materials or from the HealthEd website (**www.healthed.govt.nz/**).

The early childhood service or school has the responsibility to:

- advise the child's parent/guardian that an immunisation certificate is required
- ensure the parent or guardian is asked to provide the immunisation certificate
- record the information from the immunisation certificate (or the fact that it was not shown) on the register
- advise the parent/guardian that a GP, practice nurse or public health nurse can help them to get an immunisation certificate if they do not have one.

Appendix 6: Passive immunisation

A6.1 Introduction

Passive immunisation involves administering pre-formed antibody as human immunoglobulin to a recipient who is thought to have either no natural immunity to one or more infections, or who has impaired antibody production. CSL Behring Australia is the primary manufacturer of immunoglobulin products for the New Zealand Blood Service (NZBS). These products are prepared by fractionating large pools of plasma collected from blood donors.

The immunoglobulin products available in New Zealand are usually derived from voluntary, unpaid New Zealand donors who are in good health and who do not have any conditions identifiable by the standard questionnaire that all blood donors complete or by the mandatory testing for HIV/AIDS, hepatitis B, hepatitis C and syphilis on each donation. Blood donations are only used if the tests show no evidence that these infections are present. Similar screening standards apply to the manufacture of other specialist immunoglobulin products which are obtained from an overseas sources. Some of these commercial products may be derived from remunerated, voluntary donors.

A6.2 Preparations available in New Zealand

Immunoglobulin products available in New Zealand include human normal immunoglobulin for intramuscular (IM) use, specific immunoglobulins for intramuscular use, human normal immunoglobulin for intravenous use (IVIG) and human normal immunoglobulin for subcutaneous use (SCIG). All these products have an excellent safety record in both Australia and New Zealand.

A6.2.1 Human normal immunoglobulin for intramuscular use

Human normal immunoglobulin for intramuscular use (available as Normal Immunoglobulin-VF) is a sterile, preservative-free, pasteurised solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. At least 98 percent of the protein comprises immunoglobulins, mainly immunoglobulin G (IgG). Normal Immunoglobulin-VF is intended for IM injection and is available in 5 mL preservative-free vials. It is prepared by Cohn cold ethanol fractionation of human plasma. The manufacturing process involves specific viral removal steps to reduce the possibility of virus transmission, and includes pasteurisation for viral inactivation and nanofiltration for virus removal.

A6.2.2 Specific immunoglobulin for intramuscular use

Specific human immunoglobulin preparations for IM use are available, including those for tetanus, hepatitis B, varicella zoster and anti-D. These are manufactured from plasma pools containing donations from individuals known to have high levels of the appropriate antibody. These preparations are available in single vials containing the specific antibody. The volume of the product will be determined by the potency for the appropriate antibody. In unusual circumstances, when supplies of specific immunoglobulin products manufactured from New Zealand plasma are not available, commercial products from alternative donor sources may be supplied by NZBS.

RIG is imported from a commercial source and is held at NZBS sites in Auckland, Christchurch and Wellington. The product is not registered as a medicine in New Zealand. It may be accessed and supplied under section 29 of the Medicines Act 1981 after discussion with an NZBS medical officer.

A6.2.3 Human normal immunoglobulin for intravenous use

The current human normal immunoglobulins for intravenous use in New Zealand are Intragam P and Privigen. Intragam P is produced by CSL Behring Australia and Privigen is produced by CSL Behring in the US. The latter commercial product has been introduced as stocks of IVIG from New Zealand plasma have not been sufficient to meet overall clinical requests for IVIG.

Intragam P is a sterile, preservative-free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. The solution has a pH of 4.25. Isotonicity is achieved by the addition of maltose. At least 98 percent of the protein has the electrophoretic mobility of IgG. At least 90 percent of the protein is IgG monomer and dimer. Intragam P contains only trace amounts of immunoglobulin A (IgA) (nominally <0.025 mg/mL). Intragam P is available in 50 mL and 200 mL vials.

Intragam P and Privigen are produced by chromatographic fractionation of large pools of human plasma obtained from voluntary blood donors. The protein has not been chemically or enzymatically modified. The manufacturing process contains special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and incubation at low pH.

Note: In New Zealand, Intragam P is used to provide intravenous (high-dose) tetanus immunoglobulin. Because the level of immunoglobulin in each batch varies and this indication is not included in the product registration, consultation with an NZBS medical officer is required prior to issuing a prescription.[1]

Privigen is a sterile, preservative-free 10 percent solution containing 10 g/100 mL of normal immunoglobulin; it is available in 50 mL, 100 mL and 200 mL vials. The solution has a pH of approximately 4.8, has a low sodium content, contains 250 mmol/L of proline, a non-essential amino acid, as a stabiliser and is approximately isotonic. It contains no carbohydrate stabiliser.

Privigen is made by cold ethanol fractionation, octanoic acid fractionation and anion exchange chromatography of large pools of human plasma obtained from blood donors in Europe and the US. The distribution of IgG subclasses in Privigen is similar to that in plasma; only trace amount of IgA are present, typically <0.025 mg/mL. The protein has not been enzymatically modified. The manufacturing process involves special steps to reduce the possibility of virus transmission including pasteurisation (heating to 60°C for 10 hours) and nanofiltration.

A6.2.4 Human normal immunoglobulin for subcutaneous use

Human normal immunoglobulin for subcutaneous use (Evogam) is produced by CSL Behring, Australia, from NZBS New Zealand-sourced plasma. It is a sterile solution containing 16 g per 100 mL of human immunoglobulin with a purity of at least 98 percent immunoglobulin G (IgG). At least 85 percent consists of monomers and dimers (typically >90 percent), and less than 10 percent of the IgG is aggregates. The distribution of the IgG subclasses closely resembles that found in normal human plasma.

The pH value of the solution is 6.6. It contains 2.25 g/100 mL of glycine as a stabiliser. It does not contain a carbohydrate stabiliser (eg, sucrose, maltose) and contains no preservative. Evogam contains only trace amounts of IgA, typically <0.025 mg/mL.

Evogam is produced by chromatographic fractionation of large pools of human plasma obtained from New Zealand's voluntary blood donors. The manufacturing process involves special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and nanofiltration.

A6.2.5 Accessing immunoglobulin or contacting NZBS for advice

NZBS operates a 24-hour on-call service for medical advice and access to these products. Details of the medical officer on call can be obtained from any DHB hospital blood bank in New Zealand.

Product can be requested using the NZBS request form. This can be accessed online (**www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Information-for-Health-Professionals/Request-forms**), by contacting your local blood bank or writing to:

New Zealand Blood Service
Private Bag 92071
Victoria Street West
Auckland 1142

email: **info@nzblood.co.nz**
telephone (during normal office hours): 09 523 5744.

A6.3 Indications for use

A6.3.1 Passive immunisation

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a medical officer at NZBS. Copies of the product data sheet are available on the NZBS website (**www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins**).

Normal Immunoglobulin-VF is available for passive immunisation (pre- or post-exposure prophylaxis) against measles (see section 12.8.2) and hepatitis A (see section 8.8) where active vaccination is not appropriate or is contraindicated. It is not recommended for the prevention of rubella or mumps. Guidance on the use of specific preparations is provided in other sections of this *Handbook*: for pre- or post-exposure prophylaxis against hepatitis B (section 9.5.2 and section 9.8.1), tetanus (section 20.5.5) and varicella zoster (section 22.8.2).

A6.3.2 Management of primary and acquired immune deficiency

Recurrent infections can occur in individuals who have low or absent levels of circulating immunoglobulins – so-called humoral immune deficiency. This can arise as a congenital disorder, or it can be acquired as a consequence of a number of diseases. Humoral immune deficiency can exist alone or as part of a wider immune deficiency syndrome. Immunoglobulin products can be used to prevent recurrent infections in these patients.

Until recently, IVIG was the product of choice for managing these patients. A subcutaneous IgG product (Evogam) is also now available, which can be infused by patients at home. This avoids the need for outpatient or day-case admission for infusion of IVIG and is preferred by some patients. The subcutaneous preparation is not suitable for use in prophylaxis against hepatitis A or measles infection.

For replacement therapy in antibody deficiency disorders, monthly administration of IVIG is given, usually at a dosage of 0.2 to 0.6 g/kg of body weight.[2] Subcutaneous product is administered one to two times per week, with the overall monthly dosage similar to that of IVIG. For both types of product, the dosage and frequency of infusion should be based on the effectiveness in the individual patient. In general, however, the aim of treatment should be to maintain the serum IgG at or above a level of 5 g/L.

A6.4 Storage and administration

Immunoglobulin products must be stored at +2°C to +8°C and must not be frozen. They should also be protected from light. If the product appears turbid or contains sediment, it must not be used. Always check and observe the manufacturer's expiry date before injecting the product. The product does not contain an antimicrobial preservative and must be used immediately after opening the vial; any unused portions should be discarded. Information on the batch number and dose injected must be kept in the recipient's records.

The intramuscular and subcutaneous forms of normal immunoglobulin should be brought to room temperature before use. They *must not* be given intravenously because of the possible reactions discussed in section A6.7.[2]

The intramuscular product, Normal Immunoglobulin-VF, should be given slowly by deep IM injection, using a needle of appropriate gauge and length. If a large volume (more than 5 mL) is required, administration in divided doses at different sites is recommended.

The subcutaneous product, Evogam, is normally given using an infusion pump. Information on infusion rates is provided in the medicine's data sheet.

A6.4.1 Interactions with other drugs

Immunoglobulin should not be mixed with other pharmaceutical products, except as indicated by the manufacturer.

Passively acquired antibody can interfere with the response to live attenuated virus vaccines. Live virus vaccines should be given at least three weeks before, or deferred for up to 11 months after, doses of human normal immunoglobulin or other blood products. The interval will be determined by the blood product and dose received (see Table A6.1).

Table A6.1: Suggested intervals between immunoglobulin and blood product administration or blood transfusion and MMR or varicella vaccination

Product or indication	Route	Dose	Interval (months)[a]
Tetanus immunoglobulin (250 IU/vial)	IM	250 IU if <24h 500 IU if >24h or gross contamination or burns	3
Hepatitis A prophylaxis (with human normal immunoglobulin)			
• Contact and short-term travel (<3 months prophylaxis)	IM	0.03 mL/kg	3
• International travel (>3 months)[b], other requirement for long-term prophylaxis – repeated 6-monthly	IM	0.06 mL/kg	3
Hepatitis B immunoglobulin (a different low-volume product is provided for neonatal use)	IM	Adults 400 IU Neonates 100 IU	3
Rabies immunoglobulin	IM	20 IU/kg	4
Varicella prophylaxis (with zoster immunoglobulin, 200 IU/vial)	IM	125 IU/10 kg (max 625 IU) 0–10 kg: 1 vial 10.1–30 kg: 2 vials >30 kg: 3 vials	5
Measles prophylaxis (with human normal immunoglobulin)			
• immunocompromised contact	IM	0.6 mL/kg	6
Blood transfusion:			
• washed red blood cells	IV	10 mL/kg	0
• red blood cells resuspended, adenine saline added	IV	10 mL/kg	3
• whole blood, allogeneic	IV	10 mL/kg	6
• platelets in PAS	IV	1 unit	5
• plasma	IV	10 mL/kg	7
Cytomegalovirus immunoglobulin[c]	IV	Contact NZBS MO to discuss product and dose	6
Replacement (or therapy) of immune deficiencies (with IVIG)	IV	0.3–0.4 g/kg occasionally higher	8
IVIG therapy for autoimmune or inflammatory disorders, including idiopathic thrombocytopenic purpura and Kawasaki's disease	IV	0.4 g/kg 1–1.5 g/kg 1.6–2 g/kg	8 10 11
Rh (D) immunoglobulin (anti-D)	IM	na	0
Monoclonal antibody (as palivizumab)[d] to respiratory syncytial virus	IM	15 mg/kg	0
Berinert, Riastap and Biosate[e]	IV	na	0

Key: IM = intramuscular; IU = international units; IV = intravenous; IVIG = intravenous immunoglobulin; NZBS MO = New Zealand Blood Service medical officer; PAS = platelet additive solution; RBCs = red blood cells; na = not applicable.

Notes

a. Unvaccinated persons might not be protected fully against measles during the entire recommended interval, and additional doses of immunoglobulin or measles vaccine might be indicated after measles exposure.

b. Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.

c. Cytomegalovirus immunoglobulin is not available in New Zealand. Contact NZBS MO to discuss access to an alternative product.

d. Palivizumab contains antibody only to respiratory syncytial virus and does not interfere with the immune response to live or inactivated vaccines. For further information, see Starship guidelines **starship.org.nz/guidelines/palivizumab-synagis-r-immunisation-for-respiratory-syncytial-virus-rsv**

e. Other fractionated blood products may contain traces of immunoglobulin. Contact a transfusion medicine specialist to discuss potential impact on vaccination.

Adapted from: Centers for Disease Control and Prevention. 2011. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report* 60(RR2): 1–61. Table 5. Deferral interval for vaccination after blood components and products calculated from NZBS data.

Note: These intervals do not apply to BCG vaccines and rotavirus vaccines in infants, nor to zoster vaccine for individuals ≥50 years of age, the efficacy of which is unaffected by the presence of passive immunoglobulin.

Inactivated vaccines may be administered concurrently with passive antibody (although in separate syringes) to induce active immunity, as is done for some tetanus-prone wounds and for babies born to HBsAg-positive mothers.

A6.4.2 Passive transfer of antibodies and interference with serological testing

Serological testing after the administration of immunoglobulin may detect transfused antibodies for several months after administration. Serological testing for any infection after immunoglobulin should therefore be discussed with an expert.

A6.5 Duration of effect

- The estimated half-life of **intramuscular** human normal immunoglobulin is 27 ± 7 days (mean ± standard deviation [SD]).[2] The duration of effect is linked to the initial dosage.
- The estimated half-life of **intravenous** human normal immunoglobulin is 40 ± 8 days (mean ± SD).[2]
- The estimated half-life of **subcutaneous** human normal immunoglobulin is 55 days (range 14–165 days).[2]

A6.6 Contraindications and precautions

A6.6.1 Contraindications

> Immunoglobulin products intended for subcutaneous and intramuscular injection must not be administered intravenously because of the potential for anaphylactic reactions.

Health professionals should check the package insert for the immunoglobulin product to be administered.

Skin tests should not be conducted with immunoglobulin preparations. Intradermal injection of any concentrated immunoglobulin product may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Allergic responses to normal immunoglobulin given in the prescribed IM route are extremely rare, but may occur in those with complete immunoglobulin A (IgA) deficiency in whom anti-IgA is present.

Intramuscular injection of immunoglobulin products should be avoided in patients with a low platelet count or with any coagulation disorder that would contraindicate IM injections. In these circumstances, the injection may be given subcutaneously, with a lightly applied pressure pad if prone to bruising; for example, if thrombocytopenia or von Willebrand disease is present.[1]

A6.6.2 Precautions

Injections of Normal Immunoglobulin-VF must be IM, and care should be taken to draw back on the plunger of the syringe before injection to be certain that the needle is not in a blood vessel (see section 2.2.3).

As with any injection, there is a risk of anaphylaxis. Adrenaline and other means of treating acute reactions should therefore be immediately available (see section 2.3.3).

A6.7 Potential responses and adverse events following passive immunisation

Clinicians in New Zealand are requested to notify all adverse reactions arising from, or in association with, the use of blood products. Reactions to any immunoglobulin product should be reported on a form obtainable from NZBS or any local DHB hospital blood bank.

Local tenderness, erythema and muscle stiffness occasionally occur at the site of injection and may persist for several hours after intramuscular injection. An occasional recipient may react more strongly, with a low-grade fever. Systemic reactions, including nausea, urticaria and generalised hypersensitivity reactions, may occur.[1, 2]

Reactions to IVIG tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. However, delayed reactions can occur, and include nausea, vomiting, chest pains, rigors, dizziness and aching legs. Systemic and local reactions are more common in those being treated for hypogammaglobulinaemia than in those with normal gammaglobulin levels who are being treated with immunoglobulin preparations for autoimmune conditions.

Occasional reports exist of renal failure following infusion of IVIG. These largely relate to sucrose-containing products. Intragam P and Privigen, the IVIG products available in New Zealand, do not contain sucrose, but patients should be adequately hydrated prior to their administration. Renal function should be monitored in patients considered to be at increased risk.

Aseptic meningitis has been reported following treatment with IVIG. This may present up to two days following treatment. Anaphylactic reactions, although rare, have been reported following injection of immunoglobulin products, although anaphylaxis is more likely to occur following intravenous infusion. Other significant adverse events that have been observed in New Zealand and are mostly associated with large or ongoing treatment with high-dose IVIG or SCIG include: haemolysis, rashes, febrile events, pain or hypotension.

Immunoglobulin products may interfere with the immune response to live virus vaccines. In general, live vaccines should be given at least three weeks before or up to 11 months after the immunoglobulin preparation (see Table A6.1). This does not apply to the yellow fever vaccine, because New Zealand blood donors are very unlikely to have antibodies to this virus. For travellers abroad, the necessary interval may not be possible. No evidence of adverse interaction with rotavirus vaccine has been reported.

See section 1.6.3 for further information about adverse events and reporting.

References

1. NZ Blood. 2016. *Transfusion Medicine Handbook Third Edition, 2016: A guide to the clinical use of blood components, blood products and blood transfusion procedures in New Zealand* (ed.), Epsom, Auckland: New Zealand Blood Service. URL: **https://www.nzblood.co.nz/assets/Transfusion-Medicine/PDFs/111G122.pdf** (accessed 3 July 2020)
2. NZ Blood. 2017 *Immunoglobulins: CSL Product Data Sheets*. New Zealand Blood Service; 2017 [updated 07 March 2017]; URL: **https://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins**. (accessed 3 July 2020)

Appendix 7: Vaccine presentation, preparation, disposal, and needle-stick recommendations

A7.1 Presentation of vaccines

Most of the vaccines in current use are supplied in prefilled syringes or vials. The exceptions to this are the rotavirus vaccine, which is supplied as a syringe-style oral applicator, and the BCG vaccine, which is supplied as a multi-dose vial.

A vial is a glass container with a rubber seal on the top, protected by a metal or plastic cap until it is ready for use. Assume the rubber seal is latex unless stated 'latex-free'. Vials contain either liquid or powder (freeze-dried or pellet/cake) preparations.

Vaccines should not be mixed in the same syringe, unless the manufacturer's data sheet specifically states it is permitted (eg, the DTaP-IPV-HepB vaccine is mixed with the Hib-PRP pellet for the Infanrix-hexa vaccine).

A7.2 Preparation and administration of vaccines

To minimise the risk of spread of infection and needle-stick injury, vaccinators should observe standard occupational health and safety guidelines.

- Ensure proper hygiene is maintained (ie, regularly wash hands for at least 20 seconds and dry them for 20 seconds, or regularly use an alcohol-based hand rub if hands are not visibly soiled).
- Prepare the appropriate injection equipment for the vaccines to be administered (see section 2.2).
- Ensure the refrigerator temperature is within the required range of +2°C to +8°C before removing the vaccines (refer to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*, available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).
- Ensure the correct vaccine is taken from the refrigerator and that it is within the expiry date.

- Vaccines should only be drawn up after informed consent has been obtained and the vaccine requirements determined. This should include an NIR or AIR status query (if applicable) if there is uncertainty about previous doses. Any vaccines drawn up and not used should be discarded unless otherwise stated.

Vaccines in vials require one needle to draw the vaccine into the syringe, and then a new needle to administer the vaccine. The passage of needles through rubber seals causes blunting, resulting in increased tissue trauma if that needle is used to administer the injection. Also, a new needle prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions. Do not expel the air contained in the new needle – it is sterile and minute in quantity (see chapter 2, Table 2.7). These recommendations differ for COVID-19 vaccine (see section 5.4.5 for specific information about mRNA-CV).

A7.2.1 Preparing vaccines supplied as a liquid preparation

- Where applicable, remove the detachable portion of the label from the vial or syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the vial: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being drawn up.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.
- With the vial upright, insert the tip of the needle through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.2 Preparing vaccines supplied as powder/pellet vaccines

Some vaccines are presented as a prefilled syringe and freeze-dried (lyophilised) combination vaccines where:

- the pellet or powder preparation is reconstituted with the diluent (vial or prefilled syringe) supplied by the manufacturer (eg, MMR or Hib-PRP-T), or
- the pellet or powder preparation is reconstituted with a prefilled syringe containing vaccine (eg, DTaP-IPV-HepB/Hib).

The method for reconstituting the vaccine varies depending upon whether vials or prefilled syringes are used, as follows.

Reconstituting vaccines where the diluent is in a vial

- Where applicable, remove the detachable portion of the label from the diluent and/or vaccine (powder/pellet) vials and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both vaccine and diluent.
- Inspect the vaccine (powder/pellet) and diluent vials for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the diluent vial, taking care not to touch the rubber seal.
- With the diluent vial upright, insert the needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume of diluent into the syringe.
- Flip the plastic cap off the powder/pellet vial, and slowly, to avoid frothing, empty the contents of the syringe (diluent) into the powder/pellet vial, using the vial entry technique mentioned above.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution, the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

Reconstituting vaccines where the vaccine or diluent is in a prefilled syringe

- Where applicable, remove the detachable portion of the label from the prefilled syringe and/or vaccine (powder/pellet) vial and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both the prefilled syringe and the vaccine (powder/pellet) vial.
- Inspect the prefilled syringe and vaccine (powder/pellet) vial for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the powder/pellet vial, and with the vial upright, insert the prefilled syringe needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.

- Slowly, to avoid frothing, empty the contents of the prefilled syringe into the vial.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution, the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour or presentation does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.3 Preparing vaccines supplied as prefilled syringes

- Where applicable, remove the detachable portion of the label from the prefilled syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the syringe: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being administered.
- Do not expel air if the needle is fixed (eg, with an influenza vaccine). This prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions.
- When the needle is not fixed, attach an appropriate administration needle. Do not expel the air.
- Administer the vaccine.
- Dispose of the used syringe and needle into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.4 Preparing the rotavirus vaccine

The rotavirus vaccine is administered orally. It is available as a syringe-type applicator with a plunger stopper.

- Remove the detachable portion of the label (which includes the batch number but not the expiry date) and place it on (or with) the appropriate documentation. Note the expiry date.

- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Remove the protective tip cap from the oral applicator.
- Administer the entire contents of the oral applicator into the infant's mouth, towards the inner cheek.
- Discard the empty applicator and cap into the sharps container.

For more information, refer to the manufacturer's data sheet (available on the Medsafe website, **medsafe.govt.nz**).

A7.2.5 Preparing vaccines supplied as multi-dose vials[1]

Note: These processes differ for the COVID-19 vaccine (see section 5.4.5 for specific information about mRNA-CV).

- The vial should be marked with the date and time of opening and the vaccinator's initials.
- Shake the vial before use and before drawing up subsequent vaccine doses.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- To ensure optimal vial dosage and minimal vaccine wastage, use a 1 mL syringe.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.
- Inspect the rubber seal. If there is any doubt about the integrity of the seal (eg, the vial leaks when turned upside down), do not use.
- Ideally, draw up all doses of the vaccine at the same time; this allows the drawing-up needle to remain in the vial and avoids the need for alcohol swabbing (of the rubber seal).
- Alcohol swabs should be used with caution. There is an increased risk of alcohol contamination when the swabbed rubber seal is repeatedly pierced. If an alcohol swab is used, allow 30 seconds for the alcohol to completely dry before inserting the needle into the rubber seal.
- Use each vial in one session of vaccinating and discard the vial four hours after first opening (or follow the manufacturer's instructions), even if the vaccine has not been used.

[1] Sources: WHO. 2014. *WHO Policy Statement: Multi-dose Vial Policy (MDVP) – Handling of multi-dose vaccine vials after opening.* Geneva: World Health Organisation URL: **https://apps.who.int/iris/bitstream/handle/10665/135972/WHO_IVB_14.07_eng.pdf** (accessed 06 May 2022); the Australian Technical Advisory Group on Immunisation and the National Centre for Immunisation Research and Surveillance.

A7.3 Disposal of needles, syringes and vaccine vials

Note: For information about returning vaccines for destruction (such as in the event of a cold chain excursion or failure), see the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*, available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**.

- Do not separate needles from syringes or recap needles, unless a recapping device is used.
- All needles plus empty or partly used vials, syringes, dosing tubes and caps should be discarded into the sharps container for crush incineration.

A7.3.1 Sharps containers

- Sharps containers should be made of rigid, leak- and puncture-proof material. They must be fitted with a carrying handle and have an opening that is wide enough to allow disposable materials to be dropped into the container with one hand while still preventing removal of the contents.
- Sharps containers should be situated out of children's reach and available in every area where vaccinations take place.
- Sharps containers should be filled only to the indicated line, then sealed and given to an approved hazardous waste disposal person for incineration (as per the Resource Management Act 1991).

A7.3.2 Spillages

- In the event of blood or vaccine splashes on the skin, thoroughly wash the area under cold running water, then wash with soap and water or the hand wash that vaccinators have available.
- In the event of spills on work surfaces, put on gloves and treat the spill by wiping the area with a disposable pad soaked in 0.5 percent hypochlorite (household bleach diluted 1 to 9 parts water). Repeat with the hypochlorite solution and a fresh pad, then clean up with water or a commercial detergent. Alternatively, granular hypochlorite can be used for liquid spills, by applying sufficient granules to absorb the spilt fluid and then cleaning up after 10 minutes' contact time. Carefully seal all contaminated material in an approved biohazard bag for incineration by an approved hazardous waste disposal person.
- Contaminated linen is adequately treated by a routine hot wash cycle (60–70°C) using an ordinary bleach concentration.

A7.3.3 Recommendations following a needle-stick injury

In the event of a needle-stick injury, follow the guidelines below.

- The vaccinator should stop what they are doing and attend to the injury.
- Wounds and skin sites should be washed with soap and water. There is no evidence that encouraging bleeding or applying antiseptic reduces the risk of infection, but these actions are not contraindicated.
- The injury should be immediately reported to the medical advisor or employer, who should consider what immediate action is advisable.
- When the needle-stick injury involves exposure to an individual's blood, serological testing of that source individual should be sought and undertaken as soon as possible.
- Blood should be withdrawn from the affected vaccinator within a few days after the injury and counselling arranged. Testing for hepatitis B, hepatitis C and HIV serology should be undertaken.
- Depending on the infection status of the individual and the immune status of the injured vaccinator, it may be appropriate to start anti-HIV medications within the next few hours or to administer HBIG within the next few days.
- The blood-borne viruses of main concern in needle-stick injuries are hepatitis B, hepatitis C and HIV. All vaccinators should be immunised against hepatitis B and their antibody status known. Currently in New Zealand most HIV-infected individuals (or their parents/guardians) are likely to know their status at the time of immunisation, so HIV testing in case of needle-stick injuries is not routinely advocated. If there is a possibility that the individual could be HIV infected, the informed consent of the individual/parent/guardian is required before blood is drawn for testing.
- Blood-borne virus exposures after vaccination are rarely of high risk: because of the small needle size there is seldom visible blood, and there is a low risk of blood-borne viruses in the community.

For more information, see also section 9.5.7 for serological testing guidelines for hepatitis B, the *Starship Clinical Guidelines for Community Needle-stick Injuries* (available at **https://www.starship.org.nz/guidelines/community-needlestick-injuries/**) (for needle-stick injuries from needles discarded in the community) or your local DHB guidelines (if available).

Appendix 8: Websites and other online resources

A8.1 New Zealand-based websites

Ministry of Health

health.govt.nz
The official website for the Ministry of Health.

Immunisation

www.health.govt.nz/your-health/healthy-living/immunisation and www.health.govt.nz/our-work/preventative-health-wellness/immunisation
Ministry of Health information about immunisation in New Zealand, including vaccination laws and practices, information for parents/guardians, young people and health professionals about the vaccines and the disease they protect against, immunisation coverage, and links to other reputable national and international websites. Electronic versions of the *Handbook* (pdf, html and ebook) are also available.

COVID-19 vaccines

www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines
Ministry of Health information about getting a COVID-19 vaccine, the safety and approval process, types of vaccine and the vaccine rollout plan, including updates for the health sector.

Pregnancy and kids

www.health.govt.nz/your-health/pregnancy-and-kids
Ministry of Health information for parents, guardians and whānau about pregnancy, labour and birth, and caring for children during their first five years.

Pharmaceutical Management Agency (PHARMAC)

pharmac.govt.nz
Information about the medicines (including vaccines) and related products which are funded on the Pharmaceutical Schedule for use in the community and public hospitals. Electronic versions of the Pharmaceutical Schedule and updates (pdf and html) are published on the PHARMAC website (**pharmac.govt.nz/tools-resources/pharmaceutical-schedule** and **schedule.pharmac.govt.nz/ScheduleOnline.php**).

Medsafe – New Zealand Medicines and Medical Devices Safety Authority

medsafe.govt.nz
Information on the regulation of medicines and medical devices in New Zealand and the safe use of medicines, including medicine data sheets for health professionals and consumer medicine information for consumers.

Institute of Environmental Science and Research Ltd (ESR)

esr.cri.nz
A source of New Zealand infectious disease epidemiology, including regular surveillance reports for a number of diseases (**surv.esr.cri.nz**).

HealthEd

healthed.govt.nz
A source of public health education resources, including immunisation and communicable diseases, for health professionals and the public. Resources can be viewed, downloaded and/or ordered from this site.

Immunisation Advisory Centre (IMAC)

immune.org.nz
Information for parents and clinicians, including newsletters for providers of immunisation services in New Zealand.

covid.immune.org.nz
Information for the COVID-19 vaccine workforce, about the COVID-19 vaccination programme and to support the COVID-19 vaccination education programme.

KidsHealth

kidshealth.org.nz
A joint initiative between the Paediatric Society of New Zealand Inc and the Starship Foundation. The KidsHealth website provides accurate and reliable information about children's health for New Zealand parents and caregivers, the wider family and whānau, and health professionals working with parents.

Health Promotion Agency (HPA)

www.hpa.org.nz
The HPA works closely with the Ministry of Health to deliver immunisation messages to the general public.

A8.2 International websites

World Health Organization (WHO)

www.who.int/teams/immunization-vaccines-and-biologicals
Sources of statistics, graphs and maps for immunisation profiles, by country. Useful for the practitioner planning vaccination of an immigrant child based on the current Schedule.

The Global Health Observatory
www.who.int/data/gho
Provides access to a range of data sets and dashboards, including immunisation data and vaccine-preventable disease, including the **Immunization dashboard**.

Centers for Disease Control and Prevention (CDC)

cdc.gov/vaccines/
This site includes sections on the vaccines recommended (in the US) by age and for specific groups of people, and also includes safety factsheets for individual vaccines.

Immunize.org (formerly Immunization Action Coalition)

immunize.org
Educational information for both clinicians and parents. This site includes an 'Unprotected people stories' section and has its own search facility.

Healthychildren.org – American Academy of Pediatrics

www.healthychildren.org
Information for parents and clinicians, which includes colourful (and graphic) pictures (**www.healthychildren.org/immunizations**). Useful articles include 'Why immunize your child?' and 'Vaccine safety: examine the evidence'.

Institute for Vaccine Safety

www.vaccinesafety.edu
Information on the safety of recommended vaccines and current vaccine issues in the media. Based at Johns Hopkins University, Baltimore, USA.

The Vaccine Page

www.vaccines.org
The latest information and news about vaccines for adults, parents, practitioners and researchers. This site also has links to journals and other vaccine-related sites.

National Centre for Immunisation Research & Surveillance (NCIRS)

www.ncirs.org.au
An Australian-based research organisation that provides independent expert advice on all aspects of vaccine-preventable diseases, vaccine safety, communication and social and other issues related to immunisation.

Sharing Knowledge About Immunisation (SKAI)

ncirs.org.au/our-work/sharing-knowledge-about-immunisation
An Australian website containing a package of communication strategies and tools to assist in conversations between health providers and families around immunisation. It includes an e-learning module for health providers and a website with information accessible by parents (**talkingaboutimmunisation.org.au/**) to help inform consent.

A8.3 Influenza-related websites

National Influenza Immunisation Programme

influenza.org.nz
Influenza immunisation programme for health professionals. Information for consumers is available on the Ministry of Health website.

Ministry of Health – Pandemic planning and response

health.govt.nz/our-work/emergency-management/pandemic-planning-and-response
Pandemic planning and response information, including the current pandemic influenza alert status and pandemic plans, policies and other guidance for the health sector.

FluTracking

https://info.flutracking.net/
Online surveillance system used to detect the potential spread of influenza, influenza-like respiratory illnesses and COVID-19 within Australia and New Zealand.

Institute of Environmental Science and Research Ltd

Virological surveillance

www.surv.esr.cri.nz/virology/virology.php
Weekly, monthly and annual influenza surveillance reports.

WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia

www.influenzacentre.org
Part of the WHO's Global Influenza Surveillance and Response System. The Centre analyses influenza viruses currently circulating in the human population in different countries around the world.

WHO – Global Influenza Programme

www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/
Information on national influenza centres and vaccine manufacturers around the world, as well as global surveillance data and links to reports of the *Weekly Epidemiological Record*. It also includes the WHO's geographical information system for monitoring global influenza activity. Recent activity is featured in a series of animated maps and news reports, and listings of participating centres, influenza vaccine manufacturers and related websites are provided and shared through FluNet and FluID.

CDC – Influenza (Flu)

www.cdc.gov/flu/index.htm
Information for the public and health professionals on influenza viruses, vaccines, and antiviral agents, and on the clinical features and natural history of human influenza.

A8.4 Travel-related websites

Ministry of Health – Travelling

www.health.govt.nz/your-health/healthy-living/travelling
Information to help travellers manage risk and stay well. Includes links to other New Zealand-based travel websites.

Ministry of Foreign Affairs and Trade – Safe Travel

safetravel.govt.nz
Official advice for New Zealanders living and travelling overseas.

WHO – International travel and health

who.int/travel-advice
Immunisation and disease information for travellers.

CDC – Travellers' health

wwwnc.cdc.gov/travel

US-based information for travellers and health professionals, including updates on national and international disease outbreaks.

Fit for travel

fitfortravel.nhs.uk
Travel health information for people travelling abroad from the UK, including updates on national and international disease outbreaks.

Funded vaccines for special groups

As described in chapter 4, certain vaccines may be given in addition to or instead of the routine Schedule vaccines as part of an extended immunisation programme for special groups.

Vaccine	Individuals eligible for funded vaccine
Hib	Post-HSCT or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant (SOT), pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens. Testing for primary immune deficiency.
Hep A	Transplant patients. Children with chronic liver disease. Close contacts of hepatitis A cases.
HepB and HBIG	HepB and HBIG at birth for babies of mothers with chronic HBV infection. HepB for: household or sexual contacts of HBsAg-positive patients; children <18 years who have not achieved positive serology and who require additional vaccination; HIV- or hepatitis C-positive patients; following non-consensual sexual intercourse; following immunosuppression; SOT; post-HSCT; following needle-stick injury; dialysis and liver or kidney transplant.
HPV	Individuals aged 9–26 years: with confirmed HIV infection; transplant (including stem cell) patients; post-chemotherapy.
Influenza	Pregnant women. Individuals aged 6 months to <65 years with certain medical conditions.
MMR	For (re-)vaccination following immunosuppression.
MenC, MenACWY-D and 4CMenB	Pre- or post-splenectomy or with functional asplenia; with HIV, complement deficiency (acquired or inherited) or pre- or post-SOT; close contacts of meningococcal cases; prior meningococcal disease (any group); HSCT patients; prior to planned immunosuppression; following immunosuppression.
Pertussis-containing vaccine	Tdap for pregnant women, recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth. (Funded when given any time in second or third trimester.) Tdap is funded for parents or primary caregivers of infants admitted to a Neonatal Intensive Care Unit or Specialist Care Baby Unit for more than 3 days. Tdap, DTaP-IPV-HepB/Hib or DTaP-IPV for (re-)vaccination: post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-SOT, renal dialysis and other severely immunosuppressive regimens.
PCV13 and 23PPV	Children and adults with eligible conditions. PCV13 and 23PPV for testing for primary immune deficiency.
IPV	For (re-)vaccination following immunosuppression.
Tdap	For (re-)vaccination following immunosuppression; boosting of patients with tetanus-prone wounds; testing for primary immune deficiency.
BCG	Infants and children <5 years at increased risk of TB.
Varicella	Non-immune patients: with chronic liver disease who may need a transplant in the future; with deteriorating renal function before transplant; prior to SOT; prior to elective immunosuppression; for post-exposure prophylaxis of immune-competent in-patients. Patients at least 2 years after bone marrow transplant or at least 6 months after completion of chemotherapy, on advice of their specialist. HIV-positive patients with mild or moderate immunosuppression who are non-immune to varicella, on advice of their specialist. Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella. Household contacts of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella. Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.

For details by vaccine and special groups, see the most current IMAC factsheet '*Funded vaccines for special groups*' (available at **www.immune.org.nz/resources/written-resources**).

Also, see the Pharmaceutical Schedule (**pharmac.govt.nz**) for the number of funded doses and any changes to the funding decisions.

Anaphylaxis response/management

CALL FOR HELP – send for professional assistance (ambulance, doctor).
Never leave the individual alone.

ASSESS FOR ANAPHYLAXIS (see Table 2.10 for full details)

Airway and breathing
Noisy breathing due to airways obstruction; or respiratory arrest

Circulation/shock
Tachycardia; hypotension; dysrhythmias; circulatory arrest

Skin changes
Red, raised and itchy rash; swollen eyes and face; generalised rash

If cardiac arrest – commence age appropriate CPR and life support measures

LAY THE PATIENT DOWN (do not allow them to stand)
If they have breathing difficulties, elevate the head and chest.

ADMINISTER ADRENALINE by deep IM injection into outer thigh

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 ml.

For those under 10 kg or if weight is not known, use the following guidelines:

Age	Dose
under 2 years	0.1 mL
2–4 years	0.2 mL
5–11 years	0.3 mL
12 years and over	0.5 mL
Adult	0.5 mL

You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15-minute intervals, while waiting for assistance.

ADMINISTER OXYGEN, if available, at high flow rates when there is respiratory distress, stridor or wheeze.

IF HYPOTENSIVE, ELEVATE LEGS.

RECORD VITAL SIGNS every 5–10 minutes. All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

ADMIT TO HOSPITAL – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

Note: Only medical practitioners should administer IV adrenaline.

National Immunisation Schedule

Antigen(s)	DTaP-IPV-HepB/Hib	PCV10	RV1	MMR	Hib	VV	DTaP-IPV	Tdap	HPV9	Influenza	rZV
Brand name	**Infanrix-hexa**	**Synflorix**	**Rotarix**	**Priorix**	**Hiberix**	**Varilrix**	**Infanrix-IPV**	**Boostrix**	**Gardasil 9**	**Afluria Quad**	**Shingrix**
Pregnancy								Tdap		Influenza	
6 weeks	DTaP-IPV-HepB/Hib	PCV10	RV1								
3 months	DTaP-IPV-HepB/Hib		RV1								
5 months	DTaP-IPV-HepB/Hib	PCV10									
12 months		PCV10		MMR							
15 months				MMR	Hib	VV					
4 years							DTaP-IPV				
11 or 12 years								Tdap	HPV9 (2 doses)		
45 years								Tdap			
65 years								Tdap		Influenza (annually)	rZV (2 doses)

Key:

D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; PCV10 = 10-valent pneumococcal conjugate vaccine; RV1 = rotavirus vaccine (monovalent); MMR = measles, mumps and rubella; VV = varicella vaccine; d = adult diphtheria; ap = adult acellular pertussis; HPV9 = human papillomavirus (9 serotypes); rZV = herpes zoster vaccine.

All individuals aged from 5 years are eligible to receive two doses of a COVID-19 vaccine. Additional doses and booster doses are also available to different groups.