Australian Government

Department of Health

Australian Technical Advisory Group on Immunisation

Public consultation on changes to the recommended use of meningococcal and *Haemophilus influenzae* type B vaccines

The Australian Technical Advisory Group on Immunisation (ATAGI) is consulting with stakeholders on proposed changes to the meningococcal vaccination recommendations for inclusion in *The Australian Immunisation Handbook*, with an intention to submit the recommendations to the National Health and Medical Research Council (NHMRC) for its approval under section 14A of the *National Health and Medical Research Council Act 1992.*

This draft includes new recommendations and the rationale for the proposed changes.

You are invited to make a submission on the draft recommendations by 6 May 2018.

In particular, ATAGI is seeking comments on the following:

- Are there additional potential benefits, harms or unintended consequences which could arise from the proposed changes to the use of meningococcal vaccines, not already outlined, and how likely are they to occur?
- Are there additional clinical or implementation considerations which need to be outlined?

Should you require additional information please contact ATAGI Secretariat on atagi.secretariat@health.gov.au.

Summary

The Australian Technical Advisory Group on Immunisation (ATAGI), which advises the Australian Government on clinical recommendations for vaccinations, is proposing changes to the recommendations for use of meningococcal vaccines.

The proposed changes reflect the current best clinical practice to prevent invasive meningococcal disease and will be published in *The Australian Immunisation Handbook* online (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10-updates).

Meningococcal disease is a serious infection caused by meningococcal bacteria. In Australia, five subgroups (or serogroups) of meningococcal bacteria are found. ATAGI has been monitoring the epidemiology of meningococcal disease in Australia and observed that:

subgroup A	is currently extremely rare, but has historically been significant
subgroup B	has continued to be an important cause of disease for the last 10 years or more
subgroup C	was more common around 15 years ago, but was controlled through the introduction of a free meningococcal C vaccination on the National Immunisation Program since 2003
subgroup W	is a new strain which has become more common in Australia
subgroup Y	was previously rare, but is now also becoming more common

Several state and territory governments have introduced vaccination programs for adolescents, including through schools, particularly for protection against the emergence of meningococcal W and Y.

Given changes to the epidemiology of meningococcal disease and recognising the new programs available through states, ATAGI has reviewed the meningococcal chapter of *The Australian Immunisation Handbook*.

Rationale

The Therapeutic Goods Administration has recently registered:

- Trumenba for protection against meningococcal B;
- Menveo for use among infants for protection against meningococcal A, C, W and Y.

There is no single meningococcal vaccine in Australia which can protect against all 5 subgroups. Vaccines are available for protection against:

- meningococcal B – the meningococcal B vaccines: Trumenba and Bexsero
- meningococcal A, C, W and Y all at the same time – the meningococcal ACWY vaccines: Menactra, Menveo, Nimenrix
- meningococcal C only – NeisVacC (subgroup C alone) and Menitorix (combination that also protects against *Haemophilus influenzae* type b).

The review of the meningococcal chapter has prompted a review of the *Haemophilus influenzae* type B chapter recommendations, as meningococcal C vaccination on the National Immunisation Program is currently given as a combination vaccine with *Haemophilus influenzae* type B.

The vaccines are able to be used in different age groups and in different dosing schedules. A full list of vaccines and their details is provided in Attachment 1.

Recommendations

A ATAGI proposes all current recommendations in *The Australian Immunisation Handbook* are revoked with the exception of those relating to meningococcal B and meningococcal ACWY vaccination for people at occupational risk or travellers (refer to Attachment 2).

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with meningococcal B and meningococcal ACWY vaccines.
2. All children aged 2–23 months (<2 years) are recommended to receive meningococcal ACWY vaccines (according to an age-based dose schedule as shown in Table 1).
    - Children who commence the meningococcal ACWY vaccination schedule before 12 months of age should also receive a dose of meningococcal ACWY vaccine at 12 months of age (refer to Table 1).
3. For people aged ≥2 years, if more than one MenACWY vaccine brand is available, either Nimenrix or Menveo is preferred to Menactra.
4. Adolescents aged 15–19 years are recommended to receive a single dose of meningococcal ACWY vaccine.
5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.
6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive meningococcal ACWY vaccine (Table 1).
8. All Aboriginal and/or Torres Strait Islander infants and children aged 2 months to 4 years (<5 years) are recommended to receive meningococcal B vaccine (Table 2).
9. Infants aged 6–11 months with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1 below) are recommended to receive 3 doses of meningococcal ACWY vaccine (Table 1).

Table 1: Dose schedule recommendations for immunisation using MenACWY vaccines, by age and vaccine brand, and showing the number of doses required and minimum intervals

Age at commencement of vaccine course	MenACWY vaccine brand	Without any medical conditions associated with increased risk of meningococcal disease on List 1	With any specified medical conditions associated with increased risk of meningococcal disease on List 1
2*–5 months	Menveo	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age)	4 doses (8 weeks between doses; 4th dose at 12 months of age or 8 weeks after 3rd dose, whichever is later)
6–11 months	Menveo	2 doses (2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later)	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age or 8 weeks after 3rd dose, whichever is later)
12–23 months	Menveo	2 doses (8 weeks between doses)	2 doses[#] (8 weeks between doses)
	Nimenrix	1 dose	
≥2 years[†]	Menveo	1 dose	2 doses (8 weeks between doses)
	Nimenrix		
	Menactra		
Booster doses for all ages	Any brand	Not required	For those with ongoing increased risk for IMD who completed the primary series at: a) ≤6 years of age: 3 years after completion of primary immunisation schedule, then every 5 years thereafter b) ≥7 years of age: every 5 years after completion of the primary immunisation schedule

* First dose can be administered at as early as 6 weeks of age.

\# For those with specified medical conditions aged 12–23 months, 2 doses of either Menveo or Nimenrix are required.

† There is no registered upper age limit for use of Menveo®. Although both Menactra® and Nimenrix® are registered for use up to 55 years of age only, either of these brands can be given to people over 55 years of age, as per *The Australian Immunisation Handbook.*

Table 2: Dose schedule recommendations for immunisation using MenB vaccines, and showing number of doses required and minimum intervals

Age at commencement of vaccine course	MenB vaccine brand	Without any medical conditions associated with increased risk of meningococcal disease on List 1	With any specified medical conditions associated with increased meningococcal disease on List 1
6 weeks–5 months	Bexsero	4 doses (8 weeks between doses; 4th dose at 12 months)	4 doses (8 weeks between doses; 4th dose at 12 months or 8 weeks after 3rd dose, whichever is later)
6–11 months	Bexsero	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later)	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months or 8 weeks after 2nd dose, whichever is later)
12 months–9 years	Bexsero	2 doses (8 weeks between doses)	2 doses (8 weeks between doses)
≥10 years*	Bexsero	2 doses (8 weeks between doses)	2 doses (8 weeks between doses)
	Trumenba	2 doses (6 months between doses)	3 doses (At least 4 weeks between 1st and 2nd doses; 3rd dose at least 4 months after 2nd dose and at least 6 months after 1st dose)

* Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the primary vaccination course.

List 1: Specified medical conditions associated with increased risk of meningococcal disease

- defects in or deficiency of complement components, including factor H, factor D or properdin deficiency
- current or future treatment with eculizumab (a monoclonal antibody directed against complement component C5)
- functional or anatomical asplenia
- HIV infection, regardless of stage of disease or CD4+ count
- haematopoietic stem cell transplant

Note: This list is unchanged from the conditions specified in the current online chapter of *The Australian Immunisation Handbook*

C ATAGI proposes that the recommendation for the 4th dose of vaccine for protection against *Haemophilus influenzae* type B currently given at 12 months is revoked.

D ATAGI proposes the following changes to the use of *Haemophilus influenzae* type B vaccines in Australia:

- All children should receive a 4th dose of vaccine for protection against *Haemophilus influenzae* type B at 18 months of age.

Research evidence

Recommendations A and B 1-4

A ATAGI proposes all current recommendations in *The Australian Immunisation Handbook* are revoked with the exception of those relating to meningococcal B and meningococcal ACWY vaccination for people at occupational risk or travellers (refer to Attachment 2).

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

1. Anyone who wants to protect themselves against meningococcal disease can be vaccinated with meningococcal B and meningococcal ACWY vaccines.
2. All children aged 2–23 months (<2 years) are recommended to receive meningococcal ACWY vaccines (Table 1).
3. For people aged ≥2 years, if more than one MenACWY vaccine brand is available, either Nimenrix or Menveo is preferred to Menactra.
4. Adolescents aged 15–19 years are recommended to receive a single dose of meningococcal ACWY vaccine.

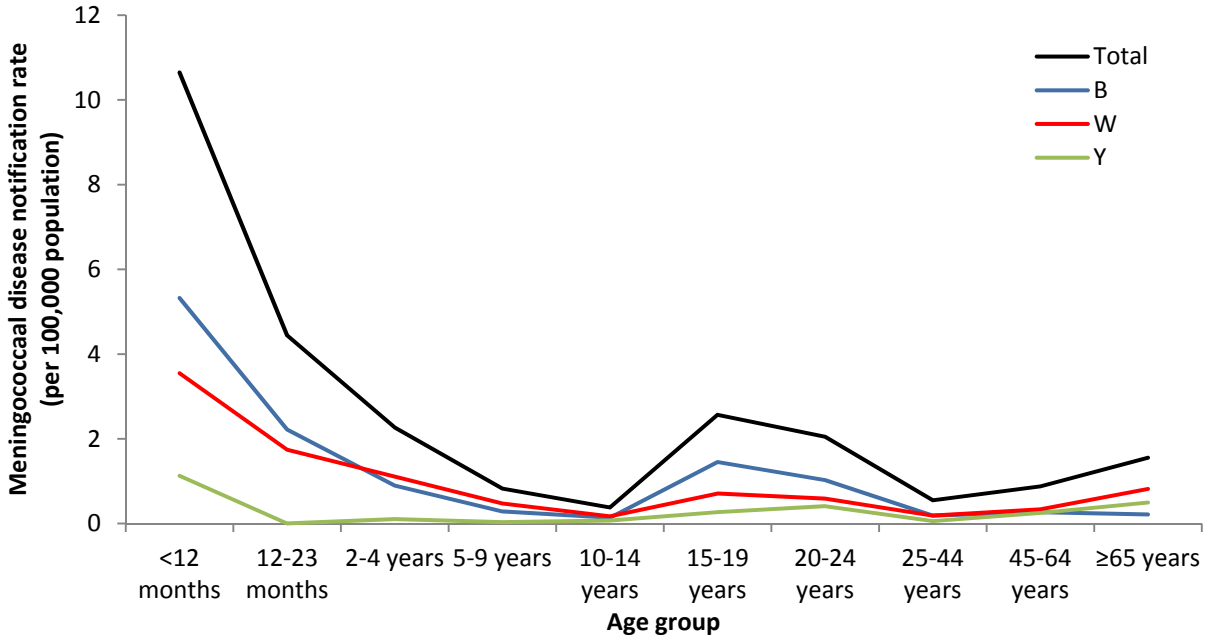
The meningococcal subgroups that cause meningococcal disease have been changing in the last few years. Since 2013, the occurrence of meningococcal W disease has been increasing rapidly. Many meningococcal W cases are caused by a strain (sequence type ST 11) associated with severe disease and a higher risk of death.[1]

A smaller yet steady rise in the occurrence of meningococcal Y disease has also been seen since 2016. Meningococcal B has historically caused the majority of meningococcal disease in Australia and it continues to cause around half of all reported cases of meningococcal disease.

Data from recent years show that young children aged <2 years have the highest rates of new cases reported. Among these young children, meningococcal disease occurs most often in infants between 3 and 5 months of age. Vaccination with meningococcal ACWY vaccine can prevent disease in this vulnerable age group. A high number of meningococcal disease cases also occur among adolescents aged 15–19 years (Figure 1).

People can carry the meningococcal bacteria in their throat and/or nose (i.e. ‘carriage’), with studies showing that adolescents and young adults have the highest carriage rates of meningococcal bacteria.[2] Vaccinating populations with high carriage rates is critical to achieve protection of the community more broadly (community or herd immunity).

Figure 1: Age-specific rates of meningococcal disease by subgroup and age group, Australia, 2016–2017*



*Data is for cases with a diagnosis date from 1 January 2016 onwards, as of 14 December 2017. Rates for 2017 have not been annualised. Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

Safety of meningococcal ACWY vaccines

Meningococcal ACWY vaccine safety has been shown in multiple clinical trials and large population studies (conducted in countries after the vaccines have become available) in people of different ages, from infants to adults.[3-18] The vast majority of reactions after vaccination are mild and resolve on their own. Meningococcal ACWY vaccines are safe for use in patients with human immunodeficiency virus (HIV) infection.[19,20]

Meningococcal ACWY vaccines can be safely administered at the same time as other routine vaccines provided to young children through the National Immunisation Program. Clinical trials in young children have included giving meningococcal ACWY vaccines with:

- diphtheria-tetanus-acellular pertussis (DTPa) combination vaccines (which included hepatitis B vaccine, inactivated polio vaccine [IPV] and/or *Haemophilus influenzae* type B vaccine),
- 7-valent pneumococcal conjugate vaccine (7vPCV) and 13-valent PCV (13vPCV),
- rotavirus vaccine,
- hepatitis A vaccine,
- measles-mumps-rubella (MMR) vaccine,
- measles-mumps-rubella-varicella (MMRV) vaccine and varicella vaccine.[5,11-14,21-23]

In adolescents, clinical trials have included giving meningococcal ACWY vaccines with:

- 4-valent and 9-valent human papillomavirus (HPV) vaccine,
- diphtheria-tetanus-acellular pertussis (dTpa) vaccine,
- combined hepatitis A and B vaccine and seasonal influenza vaccine.[24-28]

In most studies, the frequency of reactions following vaccination were similar regardless of whether the vaccines were given together or separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

Immune responses to meningococcal ACWY vaccines

The number and spacing of meningococcal vaccine doses vary by brand and the age the vaccination commences.

i) Children aged <2 years at commencement of vaccination

ATAGI proposes the following vaccination schedules in children aged <2 years (refer to Table 1 in Recommendations section above):

- 2–5 months: 3 doses of Menveo (ideally given at 2, 4 and 12 months of age)
- 6–11 months: 2 doses of Menveo (ideally given at 6 and 12 months of age)
- 12–23 months: a single dose of Nimenrix or 2 doses of Menveo (given at least 8 weeks apart)

As the highest rates of meningococcal disease occur very early in life, it is highly desirable to start vaccination as early as possible so that infants can develop an immune response early. Clinical trials have shown that Menveo is safe to use in children from 2 months of age.[10-13] When given in a 3-dose schedule at 2, 4 and 12 months of age, more than 99% of children in the clinical trial developed protection against meningococcal W and Y after the completion of the course.[13]

For children who commence vaccination at age 6 to <12 months, a 2-dose schedule with Menveo produces a good immune response. In one large study with over 1,600 participants, more than 96% of children given 2 doses of Menveo at age 7–9 months and 12 months developed protection against meningococcal C, W and Y.[14] Another smaller study showed that 100% of children who received Menveo at 6 and 12 months of age produced an immune response against meningococcal C, W and Y after the second dose.[16] In both studies, the response to meningococcal A was slightly lower (87-88%).

Although the vaccine is currently registered in a 2-dose schedule from 7 months onwards, data from these clinical trials showed that the immune response in children starting vaccination at 6 months of age was similar. The 6-months schedule point is well-established and accepted in Australia, with consistently high vaccine coverage.[29]

Two vaccines are available for children aged 12–23 months of age – Nimenrix and Menveo. Because of differences in the ingredients in the vaccines, there are differences in the level of immune response produced. However, both vaccines have been shown to produce good immune responses in children 1 month after vaccination when given in the appropriate schedule. There is no preference for one vaccine over the other.

Data from clinical studies have shown that 1 dose of Nimenrix produces a strong immune response in toddlers of this age, with over 97% of children developing an immune response against all four subgroups of meningococcal (A,C,W,Y).[5,6,22,23] With Menveo, 97% of children developed a protective immune response to all four subgroups of meningococcal after 2 doses.[10]

ii) Children aged ≥2 years, adolescents and adults at commencement of vaccination

ATAGI proposes the following vaccination schedule in children aged ≥2 years, adolescents and adults:

- a single dose of Nimenrix, Menveo or Menactra

There are three registered meningococcal ACWY vaccines available for people aged 2 years or older: Nimenrix, Menveo and Menactra. Each of these produces an immune response against the four meningococcal subgroups included in the vaccine when given as a single dose.[7,9,24,25,30-32]

In studies with adolescents, 67–100% of vaccine recipients developed an immune response to the vaccine.[3,9,24,25,30,31,33] Population data collected in the United States showed that the vaccine (Menactra) was 80-85% effective in preventing clinical infection in a population during the first year after vaccination.[34,35]

Because of differences in the ingredients in the vaccines, there are differences in the level of immune response produced by the three vaccines. It is not known whether these differences have an impact on a person's protection against meningococcal disease. The differences in immune response between Nimenrix and Menveo are very minor, so either vaccine may be given.

However, the level of antibody responses produced after a dose of Nimenrix or Menveo is modestly higher than that after a dose of Menactra, especially for meningococcal subgroups W and Y.[7,30,32] There is also some evidence showing that immunity decreases more quickly with Menactra than with Nimenrix or Menveo.[7,32,36]

Therefore, ATAGI proposes that either Nimenrix or Menveo be given over Menactra whenever possible. If Nimenrix or Menveo are unavailable, Menactra can be given as it will still provide adequate protection against meningococcal disease caused by subgroups A, C, W and Y, and is highly preferred to no vaccination.

Recommendation B5

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

5. Adolescents and young adults (aged 20–24 years) who live in close quarters (e.g. new military recruits and students living in residential accommodation) are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.

Adolescents and young adults have the highest rates of meningococcal carriage (i.e. presence of meningococcal bacteria in the upper respiratory tract without any signs or symptoms of infection) and are thought to play an important role in how the bacteria are transmitted in a community.[2] Living in close or prolonged contact with a person who is carrying meningococcal bacteria can increase the chances of the bacteria being passed between people.[37-39]

A clinical study of vaccination with Menveo in 18- to 24-year-old university students showed that there were reductions in meningococcal carriage among those who were vaccinated,[40] potentially reducing the chances of disease transmission.

As Australian data show that the risk of meningococcal disease caused by serogroup B is also high among adolescents and young adults aged 20–24 years (compared with other age groups) (refer to Figure 1 above), ATAGI is also proposing that the existing recommendation for meningococcal B vaccination (currently for ages 15–19 years as per *The Australian Immunisation Handbook*) be extended to also include those aged 20–24 years.

Recommendation B6

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

6. Adolescents and young adults (aged 20–24 years) who are current smokers are recommended to receive:
    a) a single dose of meningococcal ACWY vaccine.
    b) two doses of meningococcal B vaccine.

Smoking tobacco is known to increase the risk of carrying the meningococcal bacteria in the upper respiratory tract and of passing the bacteria to close contacts. Active smokers are at greater risk of meningococcal disease as they have high meningococcal carriage rates, which are approximately 1.5–2 times higher than those found in non-smokers.[41]

In a study of 14,000 teenagers aged 15–19 years, twice as many active smokers were carrying meningococcal bacteria compared with non-smokers, even after accounting for other risk factors known to impact carriage.[42] The risk of meningococcal carriage increases with heavier smoking[43] and studies have also shown adolescents in close contact to smokers are more likely to develop meningococcal disease.[42,44-46]

Recommendations B7-8

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

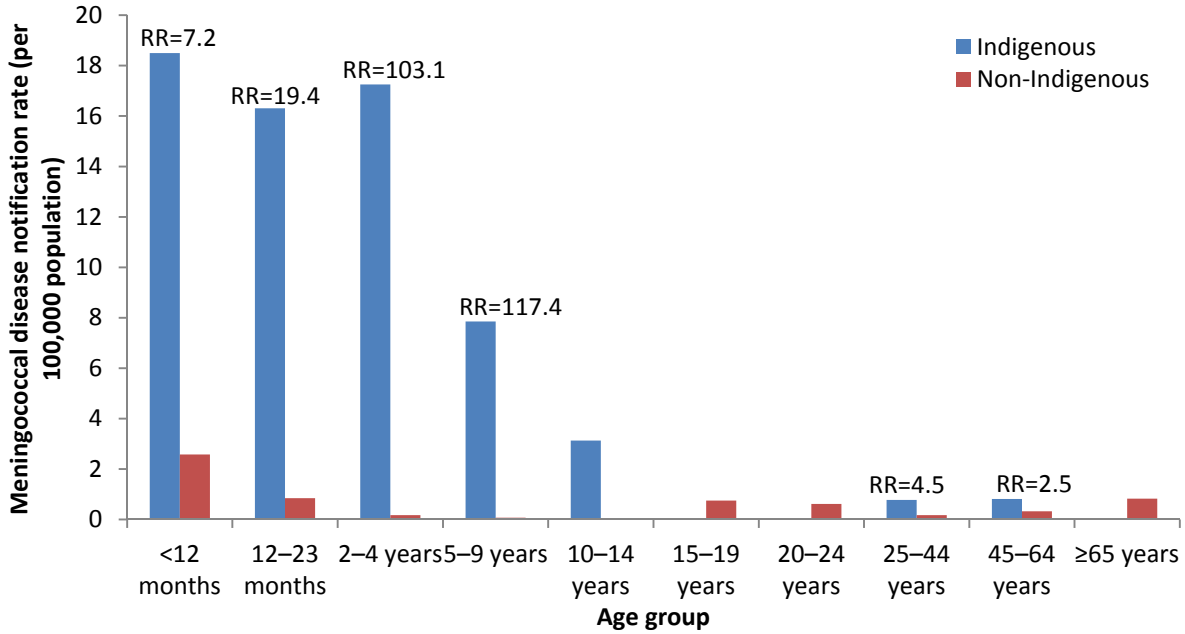
7. All Aboriginal and/or Torres Strait Islander persons aged 2 months to 19 years are recommended to receive meningococcal ACWY vaccine (Table 1).
8. All Aboriginal and/or Torres Strait Islander infants and children aged 2 months to 4 years (<5 years) are recommended to receive meningococcal B vaccine (Table 2).

Aboriginal and Torres Strait Islander Australians have much higher incidence rates of meningococcal disease compared to non-Indigenous Australians. This is particularly observed among children aged <15 years for the two most common meningococcal subgroups B and W.

During 2012–2017, the incidence rate of meningococcal disease caused by subgroup W was higher in Aboriginal and Torres Strait Islander children aged <5 years (3.10 versus 0.34 per 100,000; rate ratio=9.1).

More recently in 2016–2017, this disparity was even more striking, with meningococcal disease rates among Aboriginal and Torres Strait Islanders being greater than 100 times those observed among non-Indigenous Australians in certain age groups (refer to Figure 2). This has been partly due to the outbreak of serogroup W disease in Central Australia which particularly affected young Aboriginal and Torres Strait Islander people in remote communities.

Figure 2: Notification rates for meningococcal disease caused by serogroup W and rate ratio for Indigenous and non-Indigenous people, by age group, 2016–2017*

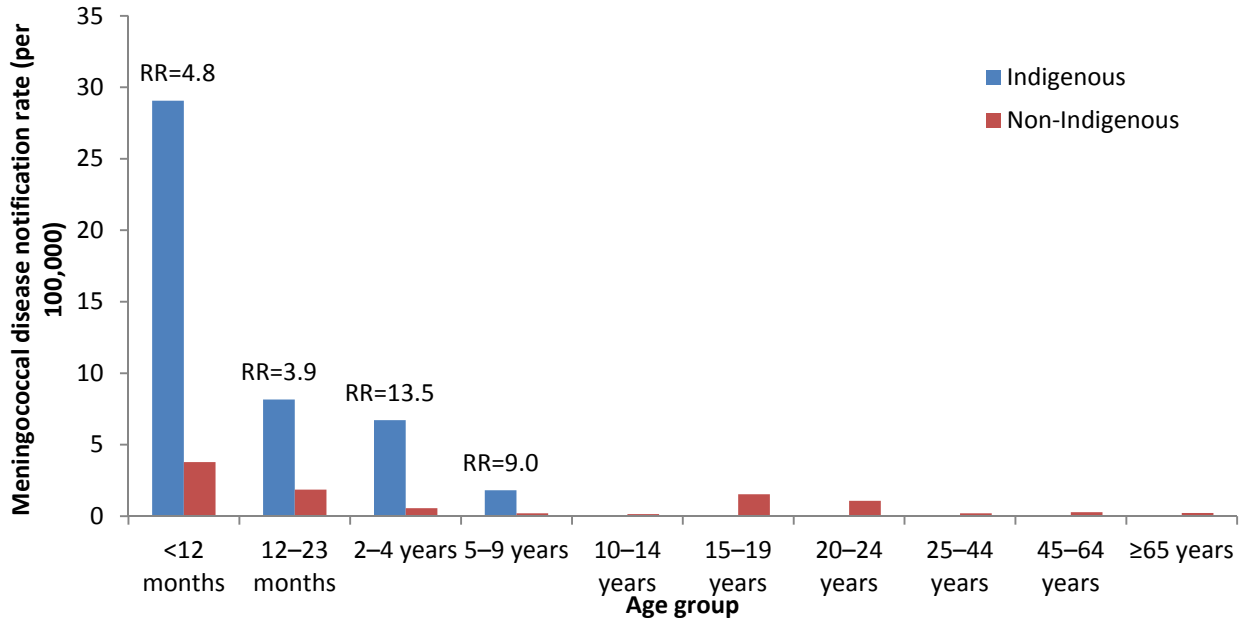


RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised.
Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

In 2016-17, there was a substantial disparity in the reported cases of meningococcal disease caused by subgroup B between Aboriginal and Torres Strait Islander people compared with non-Indigenous Australians, particularly among children aged <5 years old (refer to Figure 3).

This trend appears to be longstanding. Between 2006 and 2015, rates of meningococcal disease caused by subgroup B disease were reported as being 3.4 times and 3.8 times higher among Aboriginal and Torres Strait Islander infants aged <12 months and children aged 1–4 years, respectively, compared with non-Indigenous infants and children of the same age.[47]

Figure 3: Notification rates for meningococcal disease caused by serogroup B and rate ratio for Indigenous and non-Indigenous people, by age group, 2016–2017*



RR=rate ratio (Aboriginal and Torres Strait Islanders/non-Indigenous Australians). RR was not calculated where there were zero cases in one of the two population groups.
*Data shown is for notifications from 1 January 2016 to 14 December 2017. Rates for 2017 are not annualised. Source: Unpublished data from analysis of National Notifiable Diseases Surveillance System core data by NCIRS.

Recommendation B9

B ATAGI proposes the following changes to the use of meningococcal vaccines in Australia.

9. Infants aged 6–11 months with specified medical conditions associated with an increased risk of meningococcal disease (refer to List 1) are recommended to receive 3 doses of meningococcal ACWY vaccine (Table 1).

Clinical trials of Menveo in infants aged 6–11 months have only examined immune responses after 1 or 2 doses of the vaccine. No studies have examined immune response after 3 doses and no studies have been conducted in infants or young children with the specified medical conditions in List 1.

However, clinical studies of Menveo in young healthy infants starting vaccination at age 2 months show that immune responses were better after a 3rd dose (given 6 months of age) compared with immune responses after a 2nd dose (given at 4 months of age).[13]

While the differences in immunity are minor and likely to be unimportant in a healthy infant, ATAGI considers the higher risk of disease in an infant with a specified medical condition justifies the extra dose of vaccine. Studies with another meningococcal ACWY vaccine, Menactra, in older children and adolescents with HIV infection have shown that 2 doses, rather than 1, are required for an adequate immune response.[19,48]

Studies with meningococcal C vaccines have also shown that people with immunocompromising medical conditions have a lower immune response to vaccination and require additional doses.[49-53]

Extrapolating from these research findings, ATAGI considers a 3-dose course of Menveo (refer to Table 1 for dosing schedule) to be appropriate for infants commencing vaccination at age 6–11 months with a specified medical condition. The extra dose given to infants, compared with infants

without specified medical conditions, is similar to the schedule for older age groups, for whom an additional dose is currently recommended.

Recommendations C and D

C ATAGI proposes that the recommendation for the 4th dose of vaccine for protection against *Haemophilus influenzae* type B currently given at 12 months is revoked.

D ATAGI proposes the following changes to the use of *Haemophilus influenzae* type B vaccines in Australia:

- All children should receive a 4th dose of vaccine for protection against *Haemophilus influenzae* type B at 18 months of age.

A 4th dose of *Haemophilus influenzae* type B vaccine in the second year of life (in addition to the 3 doses given at 2, 4 and 6 months of age) is required to ensure long-term protection against *Haemophilus influenzae* type B disease and prevent cases of this disease later in childhood. A review of *Haemophilus influenzae* type B cases from 1996 to 2013 found that more than half were either unimmunised or partially vaccinated.[54]

Currently, a 4th dose is given at 12 months of age as a combined vaccine, Menitorix, which includes both *Haemophilus influenzae* type B and meningococcal C.

In January 2018, the Pharmaceutical Benefits Advisory Committee recommended the listing of Nimenrix on the NIP for infants 12 months of age.

The introduction of a meningococcal ACWY vaccine at 12 months of age means the meningococcal C component of Menitorix will no longer be required and the 4th dose of *Haemophilus influenzae* type B can be given in a monovalent formulation (i.e. containing only *Haemophilus influenzae* type B).

In addition, the Chief Executive Officer of the National Health and Medical Research Council agreed to amend a pneumococcal recommendation in the Australian Immunisation Handbook, proposed by ATAGI in late 2017, to move the 3rd dose of the infant pneumococcal vaccine from 6 months to 12 months.

The Pharmaceutical Benefits Advisory Committee is considering a submission to amend the infant pneumococcal schedule to align with the recommendations in the Australian Immunisation Handbook.

ATAGI has reviewed the epidemiology of all of the diseases with a vaccine scheduled at 12 months and proposes that the 4th dose of *Haemophilus influenzae* type B be moved to the 18-month schedule point.

Analysis of data on *Haemophilus influenzae* type B disease in Australia found that between 1993 and 2016, only 17 cases of invasive *Haemophilus influenzae* type B disease occurred in partially vaccinated children aged 6–23 months, with the majority (n=15/17) not having completed the initial 3-dose infant course (usually given at 2, 4 and 6 months of age).

In the United States, shifting the *Haemophilus influenzae* type B booster dose by 18 months in response to a vaccine supply shortage did not cause an increase in the incidence of invasive *Haemophilus influenzae* type B disease.[55]

On the basis of this information, ATAGI believes that moving the schedule point for the *Haemophilus influenzae* type B booster dose from age 12 months to 18 months is unlikely to result in more cases of *Haemophilus influenzae* type B in Australia.

Additional information to be included in *The Australian Immunisation Handbook*

Information on Trumenba, the newly registered alternative meningococcal B vaccine

Trumenba is a newly available alternative vaccine that provides protection against meningococcal disease caused by meningococcal subgroup B and is registered and suitable for use in people aged ≥10 years. Trumenba was licensed for use in Australia in September 2017 and has been supplied since early 2018. Clinical trials have shown that Trumenba is a safe and effective vaccine for use in adolescents and young adults. It can be used in a 2-dose or a 3-dose schedule depending on the patient's risk of meningococcal disease.[56,57]

People aged 11–18 years show good immune responses after receiving 2 doses of Trumenba 6 months apart and also after receiving 3 doses of Trumenba using a 0, 1–2-month and 6-month vaccination schedule.[56] A protective immune response was produced in 82–83% of participants after 3 doses given at 0, 1 and 6 months or 0, 2 and 6 months, and in 73.5% of participants after 2 doses given at 0 and 6 months. Several clinical trials in people aged 10–25 years have also shown that both 3-dose and 2-dose schedules are safe and can be administered with other vaccines.[56-60]

The recommended dosing schedule (3 doses or 2 doses) depends on the patient's level of risk of meningococcal disease. ATAGI proposes that adolescents without specific medical conditions, who have a lower risk of meningococcal disease, receive 2 doses of Trumenba. However, adolescents with a specified medical condition (refer to List 1) have a higher risk of meningococcal disease, so it is preferable that the 3-dose schedule of Trumenba is used.

There is no preference for the use of Trumemba or Bexsero for the prevention of meningococcal B disease. However, the vaccines should not be used interchangeably, that is, a person who has a first dose of one brand of meningococcal B vaccine should complete the course with the same brand.

Information on potential use of alternative meningococcal ACWY vaccines for infants if Menveo is not available

Currently, Menveo is the only meningococcal ACWY vaccine that is registered for use for infants (age <12 months) in Australia. In the possible event of a vaccine shortage of Menveo, Nimenrix can be used as an alternative for infants from age 6 weeks, and Menactra can be used as the other alternative from age 9 months. These age-based recommendations are consistent with age-groups approved for use by regulatory authorities in Europe (Nimenrix) and the United States (Menactra), based on clinical trial data which demonstrated adequate antibody responses and safety. This recommendation is a "Variation with Product Information" in Australia. In the event of shortages, further information on the dose schedule of alternative vaccines would be provided online at www.health.gov.au/immunisation.

Benefits/Harms

There are five key benefits from these proposed changes to the use of meningococcal vaccines:

1. Vaccination with meningococcal ACWY vaccine will provide protection to those age and population groups with the highest reported cases of meningococcal disease, particularly against disease caused by subgroups W and Y that have emerged and contributed significantly to total meningococcal disease cases in the past 2 years.
2. High uptake of meningococcal ACWY vaccine among adolescents has the potential to stop transmission of meningococcal bacteria in the community and provide community (herd) protection to the remainder of the population even if they are not vaccinated.

3. Vaccination of additional age groups among Aboriginal or Torres Strait Islander Australians with meningococcal ACWY and meningococcal B vaccines can address the large gap in the meningococcal disease burden compared with non-Indigenous Australians.
4. Additional vaccination recommendations to protect adolescents and young adults living in close quarters and those who are smokers can provide protection against the meningococcal subgroups that cause the majority of meningococcal disease in these high-risk individuals, and also stop transmission.
5. An additional dose of meningococcal ACWY vaccine given to infants aged 6–11 months with specified medical conditions diagnosed in infancy, who are most vulnerable to meningococcal disease, will provide them with additional protection against meningococcal disease, especially disease caused by subgroups W and Y.

There are potential concerns that may arise from the proposed changes to the use of meningococcal vaccines:

1. *Potential concern of 'schedule crowding'*

   Whilst ATAGI aims to minimise multiple visits for vaccinations scheduled at the same point ('schedule crowding'), ATAGI has a strong preference for avoiding adding new National Immunisation Program vaccination schedule points. Vaccination with meningococcal ACWY vaccine from infancy and shifting the 4th dose of *Haemophilus influenzae* type B vaccine will increase the number of vaccines administered at the 18-month schedule point. Non-Indigenous children without specified medical conditions will receive a maximum of 3 injections at both the 12- and 18-month schedule points. However, with the proposed changes, Aboriginal and Torres Strait Islander children living in four jurisdictions (Western Australia, South Australia, Northern Territory and North Queensland) will receive at least 4 injections at both the 12- and 18-month schedule points (because of the additional hepatitis A vaccine doses). In addition, children with various medical conditions (including but not limited to those in List 1) may require additional doses of other vaccines. This may impact acceptability for these population groups and may require additional visit(s) to receive all the recommended vaccines, which can affect compliance with the recommended schedule.

2. *Potential increased frequency and/or severity of adverse events due to a greater number of vaccinations being co-administered*

   Clinical trials have documented the general safety of meningococcal ACWY vaccines when given together with multiple routinely administered vaccines in both children aged <2 years and adolescents. In most studies, rates of adverse events when meningococcal ACWY and other vaccines were given together were similar to those when vaccines were given separately. In some studies, slight increases in mild reactions were observed when vaccines were given together.

3. *Potential for increased number of Hib cases occurring prior to the booster dose scheduled at 18 months of age.*

   Based on available Australian data and on the experience from a comparable situation in the United States, the postponement of the Hib dose from 12 months to 18 months is unlikely to lead to an increased number of Hib disease cases among children aged 12–18 months. In Australia, there has been a low number of Hib vaccine failures in the past two decades and a high population Hib vaccination coverage and community immunity. While an increase in Hib disease cases occurring among children aged 12–18 months who have received 3 primary doses of Hib-containing vaccine in infancy is not expected, there will be ongoing surveillance to detect any changes in the number of Hib cases in relation with age and vaccine-doses received.

Preference and values

The proposed changes to the use of meningococcal vaccines are in line with the best available clinical advice and with the ages for which the vaccines are currently registered. It is anticipated that use of the available meningococcal vaccines will result in additional protection for people most at risk and the wider community (including those who are not vaccinated) against meningococcal disease. This is considered consistent with societal expectations of the best use of vaccines in Australia, including vaccination use in the National Immunisation Program. Also, there has been substantial media interest in meningococcal vaccines following cases of meningococcal disease in young children and adolescents, and feedback from clinicians indicates a growing demand among parents for use of these vaccines especially for their young children. In 2017–2018, most states and territories initiated adolescent vaccination programs with meningococcal ACWY vaccine which were well-received, showing the importance of these vaccines in preventing this rare but serious condition.

Resources and other considerations

Product Information for Nimenrix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02123-1

Product Information for Menveo is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-02475-3

Product Information for Menactra is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-01448-1

Product Information for Bexsero is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02131-1

Product Information for Trumenba is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-PI-02674-1

Product Information for Hiberix is available at:

https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-05633-3

Practical information

Communication to providers will need to be made clear in *The Australian Immunisation Handbook* and other guidance to minimise confusion and ensure smooth implementation of these proposed changes in recommendations. In particular, the availability of three meningococcal ACWY vaccines and two meningococcal B vaccines, all registered in different schedules for different age groups, may cause confusion among immunisation providers. The shift in the schedule point for the 4th dose of *Haemophilus influenzae* type B from 12 to 18 months of age may cause further confusion in the initial stages of implementation of the revised vaccination schedule. Clear clinical advice, including fact sheets with answers to frequently asked questions, will need to be available for immunisation providers.

Glossary

Adverse event	An unwanted reaction usually following administration of a vaccine, which may or may not be caused by the vaccine. Adverse events may be at the site of injection or may be a general illness or a general allergic

	reaction.
Antibodies	A special protein produced by immune cells in response to antigens (foreign substances, bacteria, viruses or other microorganisms). Antibodies bind with antigens on microorganisms as one of the initial steps of the body's immune response against infection.
Carriage, or meningococcal carriage	The continual presence of bacteria (meningococci) in the upper respiratory tract, particularly the throat and/or nose, without causing disease to the host.
Carrier	A person who has carriage of bacteria, which are not currently causing disease or symptoms in that person, but which have the potential to be transmitted to others or to invade and cause disease in the individual.
Co-administration of vaccines	When two or more vaccines are administered at the same time (usually at different sites).
Conjugate vaccines	These are vaccines in which the vaccine antigen (the polysaccharides from the bacterial wall of meningococcal bacteria) has been joined or conjugated to a carrier protein to improve the immune response and immunological memory to the vaccine.
Herd protection	Herd protection, or herd immunity, is the protection of unvaccinated people indirectly, through a high vaccination rate in the rest of the population. The high level of vaccination and immunity in the population limits the number of people susceptible to infection and the ability for the infection to circulate.
Incidence or incidence rate	The number of, or rate of, new cases of a particular disease within a given period of time.
Immune response	The body's defence against a foreign object or infection, as shown in the case of a vaccine, by a rise in the level of antibodies above a threshold, or by an amount that is considered to provide protection against a particular disease.
Immunocompromising medical condition	A medical condition associated with a weakened immune system, either due to the condition or its treatment, which means that it is less able to fight off infection. People with these conditions are more vulnerable to infection and may have more severe disease than a healthy person.
Interchangeability of vaccines	This refers to the ability to use a different brand of vaccine against the same disease to complete a course of vaccination when more than one dose of vaccine is required.
Invasive disease (meningococcal or Hib)	Disease that results when bacteria (e.g. meningococcal or *Haemophilus influenzae* type B), which are usually harmlessly carried by the body, invade and cause clinical infection. The bacteria may infect the blood, spinal fluid or another part of the body that would normally be sterile (or germ-free). Invasive meningococcal disease most commonly causes meningitis and/or septicaemia (i.e. infection of the blood).

Monovalent vaccine	A vaccine against only one bacterium/virus that causes a disease or one variant subgroup of that bacterium/virus.
National Immunisation Program (NIP)	The National Immunisation Program was set up by the Commonwealth and state and territory governments to increase national immunisation coverage of important vaccines in Australia. The NIP provides free vaccines to eligible people to reduce the occurrence of diseases that can be prevented by vaccination.
Quadrivalent vaccine	A vaccine that targets four variant subgroups of a virus or bacterium that causes a disease.
Routinely administered vaccines	These are vaccines that are already included in the current NIP schedule and are to be given at specified schedule points.
Schedule point	These are time points or age milestones (e.g. 12 months of age) throughout a person's lifetime when a vaccine is scheduled to be given. The schedule points for vaccines have been selected to provide the best possible protection against diseases preventable by vaccination.
Serogroups	Serogroups are subgroups of certain bacteria distinguished by the presence of a common antigen. In the case of meningococcal bacteria, these antigens are the 'sugars' on their outer coating. The most common meningococcal serogroups that cause serious disease are A, B, C, W and Y.
Therapeutic Goods Administration (TGA) registration	Vaccines, like all medicines, are regulated by the TGA. They must be approved and registered for use by the TGA before they are available to the public in Australia. Before they are made available for use they are rigorously tested in human clinical trials to confirm that they are safe and that they stimulate protective immune responses. For a vaccine to be registered, the TGA reviews these data to ensure that the vaccine (or other medicine) works as it should and is safe to use.

References

1. Australian Government Department of Health. Invasive Meningococcal Disease National Surveillance Report 31 October 2017.2017. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/5FEABC4B495BDEC1CA25807D001327FA/$File/31-Oct-2017-IMD-Surveillance-report.pdf (Accessed 29 January 2018).
2. Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta analysis. *The Lancet Infectious Diseases* 2010;10:853-61.
3. Keyserling H, Papa T, Koranyi K, et al. Safety, immunogenicity and immune memory of a novel meningococcal (groups A, C, Y and W-135) polisaccharide diphtheria toxoid conjugate vaccine (MCV-4) in health adolescents. *Archives of Pediatrics and Adolescent Medicine* 2005;159:907-13.
4. Keyserling H, Pollard A, Detora L, Gilmet G. Experience with MCV-4 a meningococcal diphtheria toxoid conjugate vaccine against serogroups A, C, Y and W-135. *Expert Review of Vaccines* 2006;5:445-59.

5. Vesikari T, Karvonen A, Bianco V, Van der Wielen M, Miller J. Tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine is well tolerated and immunogenic when co-administered with measles-mumps-rubella-varicella vaccine during the second year of life: An open, randomized controlled trial. *Vaccine* 2011;29:4274-84.
6. Vesikari T, Forsten A, Boutriau D, et al. Randomized trial to assess the immunogenicity, safety and antibody persistence up to three years after a single dose of a tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine in toddlers. *Human Vaccines and Immunotherapeutics* 2012;8:1892-903.
7. Baxter R, Baine Y, Ensor K, et al. Immunogenicity and safety of an investigational quadrivalent meningococcal ACWY tetanus toxoid conjugate vaccine in healthy adolescents and young adults 10 to 25 years of age. *Pediatric Infectious Disease Journal* 2011;30:e41-8.
8. Perrett KP, Snape MD, Ford KJ, et al. Immunogenicity and immune memory of a nonadjuvanted quadrivalent meningococcal glycoconjugate vaccine in infants. *Pediatric Infectious Disease Journal* 2009;28:186-93.
9. Bermal N, Huang LM, Dubey AP, et al. Safety and immunogenicity of a tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine in adolescents and adults. *Human Vaccines* 2011;7:239-47.
10. Tregnaghi M, Lopez P, Stamboulian D, et al. Immunogenicity and safety of a quadrivalent meningococcal polysaccharide CRM conjugate vaccine in infants and toddlers. *International Journal of Infectious Diseases* 2014;26:22-30.
11. Klein NP, Reisinger KS, Johnston W, et al. Safety and immunogenicity of a novel quadrivalent meningococcal CRM-conjugate vaccine given concomitantly with routine vaccinations in infants. *Pediatric Infectious Disease Journal* 2012;31:64-71.
12. Nolan TM, Nissen MD, Naz A, et al. Immunogenicity and safety of a CRM-conjugated meningococcal ACWY vaccine administered concomitantly with routine vaccines starting at 2 months of age. *Human Vaccines and Immunotherapeutics* 2014;10:280-9.
13. Block SL, Shepard J, Garfield H, et al. Immunogenicity and Safety of a 3- and 4-dose Vaccination Series of a Meningococcal ACWY Conjugate Vaccine in Infants: Results of a Phase 3b, Randomized, Open-label Trial. *Pediatric Infectious Disease Journal* 2016;35:e48-59.
14. Klein NP, Shepard J, Bedell L, Odrljin T, Dull P. Immunogenicity and safety of a quadrivalent meningococcal conjugate vaccine administered concomitantly with measles, mumps, rubella, varicella vaccine in healthy toddlers. *Vaccine* 2012;30:3929-36.
15. Bona G, Castiglia P, Zoppi G, et al. Safety and immunogenicity of a CRM or TT conjugated meningococcal vaccine in healthy toddlers. *Vaccine* 2016;34:3363-70.
16. Halperin SA, Diaz-Mitoma F, Dull P, Anemona A, Ceddia F. Safety and immunogenicity of an investigational quadrivalent meningococcal conjugate vaccine after one or two doses given to infants and toddlers. *European Journal of Clinical Microbiology and Infectious Diseases* 2010;29:259-67.
17. Tseng HF, Sy LS, Ackerson BK, et al. Safety of quadrivalent meningococcal conjugate vaccine in 11- to 21-year-olds. *Pediatrics* 2017;139.
18. Reisinger KS, Baxter R, Block SL, et al. Quadrivalent meningococcal vaccination of adults: phase III comparison of an investigational conjugate vaccine, MenACWY-CRM, with the licensed vaccine, Menactra. *Clinical and Vaccine Immunology* 2009;16:1810-5.
19. Siberry GK, Warshaw MG, Williams PL, et al. Safety and immunogenicity of quadrivalent meningococcal conjugate vaccine in 2- to 10-year-old human immunodeficiency virus-infected children. *Pediatric Infectious Disease Journal* 2012;31:47-52.
20. Siberry GK, Williams PL, Lujan-Zilbermann J, et al. Phase I/II, open-label trial of safety and immunogenicity of meningococcal (groups A, C, Y, and W-135) polysaccharide diphtheria toxoid conjugate vaccine in human immunodeficiency virus-infected adolescents. *Pediatric Infectious Disease Journal* 2010;29:391-6.

21. Blanchard-Rohner G, Snape MD, Kelly DF, et al. The B-cell response to a primary and booster course of MenACWY-CRM197 vaccine administered at 2, 4 and 12 months of age. *Vaccine* 2013;31:2441-8.
22. Knuf M, Pantazi-Chatzikonstantinou A, Pfletschinger U, et al. An investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine co-administered with Infanrix hexa is immunogenic, with an acceptable safety profile in 12-23-month-old children. *Vaccine* 2011;29:4264-73.
23. Ruiz-Palacios GM, Huang LM, Lin TY, et al. Immunogenicity and safety of a booster dose of the 10-valent pneumococcal Haemophilus influenzae protein D conjugate vaccine coadministered with the tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine in toddlers: a randomized trial. *Pediatric Infectious Disease Journal* 2013;32:62-71.
24. Arguedas A, Soley C, Loaiza C, et al. Safety and immunogenicity of one dose of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, when administered to adolescents concomitantly or sequentially with Tdap and HPV vaccines. *Vaccine* 2010;28:3171-9.
25. Ostergaard L, Silfverdal SA, Berglund J, et al. A tetravalent meningococcal serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine is immunogenic and well-tolerated when co-administered with Twinrix in subjects aged 11-17 years: an open, randomised, controlled trial. *Vaccine* 2012;30:774-83.
26. Aplasca-De Los Reyes MR, Dimaano E, Macalalad N, et al. The investigational meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (ACWY-TT) and the seasonal influenza virus vaccine are immunogenic and well-tolerated when co-administered in adults. *Human Vaccines and Immunotherapeutics* 2012;8:881-7.
27. Schilling A, Parra MM, Gutierrez M, et al. Coadministration of a 9-valent human papillomavirus vaccine with meningococcal and Tdap vaccines. *Pediatrics* 2015;136:e563-72.
28. Reisinger KS, Block SL, Collins-Ogle M, et al. Safety, tolerability, and immunogenicity of Gardasil given concomitantly with Menactra and Adacel. *Pediatrics* 2010;125:1142-51.
29. National Centre for Immunisation Research and Surveillance. Annual Immunisation Coverage Report 2015.2017. Available from: http://www.ncirs.edu.au/assets/surveillance/coverage/Annual-Immunisation-Coverage-Report-2015.pdf (Accessed 28 August 2017).
30. Jackson LA, Baxter R, Reisinger K, et al. Phase III comparison of an investigational quadrivalent meningococcal conjugate vaccine with the licensed meningococcal ACWY conjugate vaccine in adolescents. *Clinical Infectious Diseases* 2009;49:e1-10.
31. Borja-Tabora C, Montalban C, Memish ZA, et al. Immune response, antibody persistence, and safety of a single dose of the quadrivalent meningococcal serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine in adolescents and adults: results of an open, randomised, controlled study. *BMC Infect Dis* 2013;13:116.
32. Baxter R, Baine Y, Kolhe D, et al. Five-year Antibody Persistence and Booster Response to a Single Dose of Meningococcal A, C, W and Y Tetanus Toxoid Conjugate Vaccine in Adolescents and Young Adults: An Open, Randomized Trial. *Pediatric Infectious Disease Journal* 2015;34:1236-43.
33. Jackson LA, Jacobson RM, Reisinger KS, et al. A randomized trial to determine the tolerability and immunogenicity of a quadrivalent meningococcal glycoconjugate vaccine in healthy adolescents. *Pediatric Infectious Disease Journal* 2009;28:86-91.
34. Macneil JR, Cohn AC, Zell ER, et al. Early estimate of the effectiveness of quadrivalent meningococcal conjugate vaccine. *Pediatric Infectious Disease Journal* 2011;30:451-5.
35. Macneil J, Cohn A, Anderson R, et al. The effectiveness of quadrivalent meningococcal conjugate vaccine (MenACWY-D) – a matched case-control study. International Pathogenic Neisseria Conference; 10–14 September 2012; Wurzburg, Germany2012.

36. Baxter R, Reisinger K, Block SL, et al. Antibody persistence and booster response of a quadrivalent meningococcal conjugate vaccine in adolescents. *Journal of Pediatrics* 2014;164:1409-15.
37. Bruce MG, Rosenstein NE, Capparella JM, et al. Risk factors for meningococcal disease in college students. *JAMA* 2001;286:688-93.
38. Bergman BP, Hayton JC, Green AD. Effectiveness of the meningococcal vaccination programme for British Armed Forces recruits. *Communicable Disease and Public Health* 2000;3:298-9.
39. Harrison LH, Dwyer DM, Maples CT, Billmann L. Risk of meningococcal infection in college students. *JAMA* 1999;281:1906-10.
40. Read RC, Chadwick DR, Faust SN, et al. Effect of a quadrivalent meningococcal ACWY glycoconjugate or a serogroup B meningococcal vaccine on meningococcal carriage: an observer-blind, phase 3 randomised clinical trial. *The Lancet* 2014;13:2121-31.
41. Soeters HM, Whaley M, Alexander-Scott N, et al. Meningococcal carriage evaluation in response to a serogroup B meningococcal disease outbreak and mass vaccination campaign at a college-Rhode Island, 2015–2016. *Clinical Infectious Diseases* 2017;64:1115-22.
42. MacLennan J, Kafatos G, Neal K, et al. Social behavior and meningococcal carriage in British teenagers. *Emerging Infectious Diseases* 2006;12:950-7.
43. Stuart JM, Cartwright KA, Robinson PM, Noah ND. Effect of smoking on meningococcal carriage. *The Lancet* 1989;2:723-5.
44. Fischer M, Hedberg K, Cardosi P, et al. Tobacco smoke as a risk factor for meningococcal disease. *Pediatric Infectious Disease Journal* 1997;16:979-83.
45. Coen PG, Tully J, Stuart JM, et al. Is it exposure to cigarette smoke or to smokers which increases the risk of meningococcal disease in teenagers? *International Journal of Epidemiology* 2006;35:330-6.
46. McCall BJ, Neill AS, Young MM. Risk factors for invasive meningococcal disease in southern Queensland, 2000–2001. *Internal Medicine Journal* 2004;34:464-8.
47. Archer BN, Chiu CK, Jayasinghe SH, et al. Epidemiology of invasive meningococcal B disease in Australia, 1999-2015: priority populations for vaccination. *Medical Journal of Australia* 2017;207:382-7.
48. Lujan-Zilbermann J, Warshaw MG, Williams PL, et al. Immunogenicity and safety of 1 vs 2 doses of quadrivalent meningococcal conjugate vaccine in youth infected with human immunodeficiency virus. *Journal of Pediatrics* 2012;161:676-81 e2.
49. Frota AC, Milagres LG, Harrison LH, et al. Immunogenicity and safety of meningococcal C conjugate vaccine in children and adolescents infected and uninfected with HIV in Rio de Janeiro, Brazil. *Pediatric Infectious Diseases Journal* 2015;34:e113-8.
50. Frota ACC, Harrison LH, Ferreira B, et al. Antibody persistence following meningococcal C conjugate vaccination in children and adolescents infected with human immunodeficiency virus. *J Pediatr (Rio J)* 2017;93:532-7.
51. Rezaei N, Aghamohammadi A, Siadat SD, et al. Serum bactericidal antibody response to serogroup C polysaccharide meningococcal vaccination in children with primary antibody deficiencies. *Vaccine* 2007;25:5308-14.
52. Bertolini DV, Costa LS, van der Heijden IM, Sato HK, Marques HH. Immunogenicity of a meningococcal serogroup C conjugate vaccine in HIV-infected children, adolescents, and young adults. *Vaccine* 2012;30:5482-6.
53. Balmer P, Falconer M, McDonald P, et al. Immune response to meningococcal serogroup C conjugate vaccine in asplenic individuals. *Infection and Immunity* 2004;72:332-7.
54. Menzies RI, Bremner KM, Wang H, Beard FH, McIntyre PB. Long-term trends in invasive Haemophilus influenzae type B disease among indigenous Australian children following use of PRP-OMP and PRP-T vaccines. *Pediatric Infectious Disease Journal* 2015;34:621-6.
55. Briere EC, Jackson M, Shah SG, et al. Haemophilus influenzae type b disease and vaccine booster dose deferral, United States, 1998-2009. *Pediatrics* 2012;130:414-20.

56. Vesikari T, Ostergaard L, Diez-Domingo J, et al. Meningococcal serogroup B bivalent rLP2086 vaccine elicits broad and robust serum bactericidal responses in healthy adolescents. *Journal of Pediatric Infectious Diseases Society* 2016;5:152-60.
57. Ostergaard L, Vesikari T, Absalon J, et al. A bivalent meningococcal B vaccine in adolescents and young adults. *New England Journal of Medicine* 2017;377:2349-62.
58. MacNeil JR, Rubin L, Folaranmi T, et al. Use of serogroup B meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. *Morbidity and Mortality Weekly Report* 2015;64:1171-6.
59. Patton ME, Stephens D, Moore K, MacNeil JR. Updated recommendations for use of MenB-FHbp serogroup B meningococcal vaccine – Advisory Committee on Immunization Practices, 2016. *Morbidity and Mortality Weekly Report* 2017;66:509-13.
60. Folaranmi T, Rubin L, Martin SW, Patel M, MacNeil JR. Use of serogroup B meningococcal vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2015. *Morbidity and Mortality Weekly Report* 2015;64:608-12.

Attachment 1: Meningococcal vaccine formulations and brands available for use in Australia and number of doses recommended by ATAGI for healthy individuals by age*

Vaccine	Formulation	Provides protection against serogroup	Currently registered age for its use	Number of doses recommended by ATAGI, according to age group*
Quadrivalent meningococcal conjugate vaccines (4vMenCV)				
Menveo	Quadrivalent CRM_{197} conjugate	A, C, W, Y	From 2 months†‡	2 to 5 months: • 2 primary doses and a booster 6 to 11 months: • 1 primary dose and a booster 12 to 23 months: • 2 primary doses From ≥2 years: • 1 primary dose
Nimenrix	Quadrivalent tetanus toxoid conjugate	A, C, W, Y	12 months to 55 years‡	• 1 primary dose
Menactra	Quadrivalent diphtheria toxoid conjugate	A, C, W, Y	2 to 55 years‡	• 1 primary dose
Multicomponent meningococcal B vaccines (MenBV)				
Bexsero	Recombinant multicomponent MenB	B	From 6 weeks§	6 weeks to 5 months: • 3 primary doses and a booster 6 months to 11 months: • 2 primary doses and a booster From 12 months: • 2 primary doses
Trumenba	Recombinant bivalent fHBP MenB	B	From 10 years§	• 2 primary doses
Meningococcal C conjugate vaccines (MenCCV)#				
Menitorix	Hib–MenC conjugate combination	C	From 6 weeks	Currently 1 dose at age 12 months. ATAGI recommends this dose to be replaced by a dose of meningococcal ACWY vaccine at 12 months and a dose of monovalent Hib vaccine at 18 months
NeisVac-C	Monovalent MenC conjugate	C	From 8 weeks	Currently ATAGI recommends 1 dose of meningococcal C vaccine at age 12 months, but monovalent meningococcal C vaccine is not currently used on the National Immunisation Program, as this dose is given in a combination vaccine with the Hib vaccine as Menitorix (refer to above)

* Dosing schedules are based upon ATAGI recommendations and may differ from the respective Product Information.

† The first dose of Menveo can be administered as early as 6 weeks of age.

‡There is no registered upper age limit for use of Menveo. Although both Menactra and Nimenrix are registered for use up to 55 years of age, either of these brands can be given to persons >55 years of age, as per *The Australian Immunisation Handbook.*

§ Bexsero and Trumenba are not interchangeable. The same vaccine should be used to complete the vaccination course.

Currently in the National Immunisation Program a dose of meningococcal C vaccine is given at age 12 months; this is different from the youngest age at which this vaccine can be given as stated in the Product Information.

Attachment 2: Recommendations for the use of meningococcal ACWY conjugate vaccine and meningococcal B vaccine by age group

Age group	Healthy people		Special risk groups*	Travellers†
	Aboriginal or Torres Strait Islanders	Non-Indigenous		
2§–23 months	MenB	MenB	MenB MenACWY	MenACWY
2–4 years		–	MenB MenACWY	MenACWY
5–14 years		–	MenB MenACWY	MenACWY
15–19 years	MenB	MenB	MenB# MenACWY	MenACWY
≥20 years	–	–	MenB MenACWY	MenACWY

* Includes those with a specified medical condition associated with increased risk of meningococcal disease (refer to List 1), laboratory personnel who are at occupational risk of exposure to *Neisseria meningitides*

\# Young adults living in close quarters (such as new military recruits and students living in residential accommodation) are recommended to receive MenB vaccine

† People (age ≥2 months) who are planning overseas travel to regions with an increased risk of exposure to meningococcal serogroups A, C, W, or Y disease.

§ First dose can be administered as early as 6 weeks of age.