# Child Deaths from Vaccine Preventable Infectious Diseases, NSW 2005–2014

**Prepared by**
**National Centre for Immunisation Research and Surveillance**
**2016**

# Contents

## Authors

This report was prepared by Anastasia Phillips, Frank Beard, Kristine Macartney and Peter McIntyre from the National Centre for Immunisation Research and Surveillance. Gemma Saravanos and Jocelyn Chan contributed to the literature review, data collection and analysis.

## Acknowledgements

This review was commissioned by the NSW Child Death Review Team (CDRT) who provided medical records for the cases. Health Protection NSW provided data from the Notifiable Conditions Information Management System (NCIMS). Stephanie Knox, NCIRS, provided assistance with data analysis; Catherine King and Edward Jacyna, NCIRS, provided assistance with literature review.

**ISBN: 978-1-925569-01-8**

## List of figures



## List of tables

## Abbreviations used in this document

| | |
|---|---|
| 7vPCV | 7-valent pneumococcal conjugate vaccine |
| 13vPCV | 13-valent pneumococcal conjugate vaccine |
| ACIR | Australian Childhood Immunisation Register |
| BDM | Registry of Births, Deaths and Marriages |
| CDR | Child Death Register |
| CDRT | Child death review team (NSW) |
| COD | Cause of death |
| ICD-10-AM | International classification of diseases, 10th revision, modified for Australia |
| IPD | Invasive pneumococcal disease |
| NCIRS | National Centre for Immunisation Research and Surveillance |
| NCIMS | Notifiable Conditions Information Management System |
| NIP | National Immunisation Program |
| NSW | New South Wales |
| PBS | Pharmaceutical Benefits Scheme |
| PBAC | Pharmaceutical Benefits Advisory Committee |
| VPD | Vaccine preventable disease |

# 1. Executive Summary

## 1.1 Aims

This report was commissioned by the New South Wales (NSW) Child Death Review Team (CDRT) to:

- Describe child deaths in NSW from diseases for which a vaccine is currently available in Australia, over the period 2005 to 2014; and
- Provide recommendations to improve prevention of child deaths due to vaccine-preventable diseases.

## 1.2 Background

Immunisation has been successful in dramatically reducing the number of childhood deaths from infectious diseases in Australia. The current National Immunisation Program (NIP) provides funded vaccination to protect against 16 infectious diseases. Most of these vaccines are available for all children, although a small number of vaccines or doses are funded for specific high-risk groups. Other vaccines are available for private purchase in Australia.

While child deaths due to vaccine preventable diseases (VPDs) are now rare in Australia, small numbers of deaths due to pneumococcal disease, meningococcal disease, pertussis, influenza and varicella have been reported in recent years. Although vaccines are provided through the NIP for these diseases, deaths can occur due to disease subtypes not included in current vaccines (for example pneumococcal or meningococcal subtypes), among infants too young to be vaccinated or in unvaccinated older children. Children with some underlying medical conditions are more likely to be affected by severe disease and may have inadequate immune responses to vaccines.

## 1.3 Methods

For the purposes of this review, a *disease of interest* was defined as a disease caused by a pathogen (virus or bacterium) for which a vaccine is currently provided by the NIP. Cases were identified from the Child Death Register (CDR), which is a database of all child deaths in NSW maintained by the CDRT under the *Community Services (Complaints, Review and Monitoring) Act 1993*. In order to validate this data source, cases were also identified from the Notifiable Conditions Information Management System (NCIMS). NCIMS is maintained by the Communicable Diseases Branch, Health Protection NSW, and captures notification of VPDs by laboratories and doctors in NSW under the *NSW Public Health Act 2010.* Data from the two sources were matched to determine how many cases were identified in both databases versus one only. Data was requested for deaths among children resident in NSW occurring in neighbouring states.

For each case of the disease of interest identified, all available records were reviewed including medical records, post-mortem examinations, laboratory results and coronial findings. To ascertain whether death was due to the disease of interest, cases were classified as confirmed, probable or uncertain depending on the strength of evidence for the disease and cause of death. Cases considered as confirmed or probable were

then further classified according to whether the death was considered preventable through vaccination. Deaths were considered preventable, potentially preventable or not preventable depending on the disease subtype, age and medical conditions of the child, and the availability of the relevant vaccine and recommendations for its use prior to the time of the child's death.

## 1.4 Results

Of 788 cases in the CDR, 55 cases were assessed as likely to be due to a disease of interest. Thirty-five cases were successfully matched to an NCIMS record and a further 18 cases were identified from NCIMS only. Of the resulting 73 cases, 54 were classified as confirmed or probable.

Among all 54 confirmed and probable cases, the highest number of deaths was in infants under six months of age, with male children overrepresented. While most deaths occurred in major cities, the highest per capita mortality rate was in inner regional areas. Meningococcal disease deaths tended to occur more in children residing in regions of greater disadvantage, whereas influenza deaths tended to occur more in children residing in less disadvantaged regions. Two thirds of confirmed and probable deaths were in previously healthy children, not known to have an underlying high-risk medical condition. One third had medical conditions affecting the lungs, heart or brain, or impaired immune function, that put them at increased risk of severe disease, which was significantly more than expected from the community prevalence of these conditions.

Twenty-three deaths were considered preventable or potentially preventable by vaccination, with influenza and meningococcal disease the most common causes of preventable or potentially preventable deaths. Five preventable or potentially preventable influenza deaths occurred in children with high-risk medical conditions, and seven in children without documented high-risk conditions. Two further influenza deaths in children at high risk were not considered preventable as an influenza vaccine against the applicable subtype was not available; one non-preventable influenza death occurred in a child too young to be vaccinated. In addition, for three infants for whom a cause of death could not be determined at post-mortem, there was evidence of influenza by laboratory testing. Of twelve meningococcal deaths identified, five were considered preventable or potentially preventable. Overall, eight were due to meningococcal subtype B, for which a vaccine was not available until 2014. Only one death occurred in 2014. Two of the three cases of meningicocal subtype C occurred in children eligible for the catch-up program with this vaccine in 2003.

Thirty deaths were considered not preventable through immunisation, predominantly because the subtype was not covered by the vaccine, the relevant vaccine was not available prior to the time of the child's death, or the child was too young to be eligible for vaccination. Nine deaths were in children too young to be vaccinated (infants aged two months of age or less). Although not preventable through immunisation of the child, pertussis and influenza deaths (four cases) may have been preventable through immunisation of the mother during pregnancy. Three of these infants died of pertussis prior to the NSW government-funded program to vaccinate pregnant women, which commenced in 2015. Vaccination of pregnant women aims to protect infants in the early months through the transfer of maternal vaccine-acquired antibodies, and also by reducing the chance that the mother will develop pertussis infection and pass it on to her infant. Of 16 deaths from pneumococcal disease, 11 were not considered to be preventable or potentially preventable, including seven due to subtypes not covered by the vaccine at the time of the child's death. In addition, one death caused by a vaccine strain occurred in a fully vaccinated child.

Identification of some cases from the CDR was limited by lack of information about the specific type of the pathogen causing some disease syndromes, for example whether a case of pneumonia was due to a vaccine preventable pathogen. The use of NCIMS, which contains data on disease types, increased the identification of cases for this review.

## 1.5 Conclusions and recommendations

Deaths in children from potentially preventable infectious diseases continue to occur in NSW, particularly in young infants. This review makes the following recommendations:

1. Immunisation of children at high risk is recommended and provided free under the NIP:

    - General and specialist practitioners who care for children with medical conditions or compromised immune systems placing them at increased risk of influenza, invasive pneumooccal disease, meningococcal disease or Haemophilus influenzae type b disease should put mechanisms in place to ensure that additional vaccines specifically recommended in the Australian Immunisation Handbook are received.

        - General and specialist practitioners providing care for children with predisposing medical conditions should ensure responsibilities for immunisation are clear.

        - Examples of relevant mechanisms may include flags in hospital electronic records, amendments to medical practice software to issue alerts to general practitioners, configuration of immunisation registers to issue alerts to parents and providers, and routine provision of information to parents.

2. Vaccines against influenza and meningococcal B disease are recommended for all Australian children although not provided free of charge in 2016:

    - Parents wishing to reduce their child's risk of influenza and meningococcal B should discuss this with their general practitioner or other immunisation provider.

    - General practitioners and other immunisation providers should ensure that they are aware of the recommendations on influenza vaccination in the Australian Immunisation Handbook, including that influenza vaccination is recommended for infants and children aged from six months to less than five years due to the increased risk of hospitalisation and death in this group.

    - General practitioners and other immunisation providers should ensure that they are aware of the recommendations on meningococcal B vaccination in the Australian Immunisation Handbook, including that meningococcal B vaccination is recommended for infants and young children, particularly those aged <2 years, due to their higher risk of serogroup B meningococcal disease.

3. Immunisation of contacts is recommended for children at high risk of influenza, pertussis and varicella:

    - General practitioners and specialists who care for infants aged under 6 months should be aware of the recommendation in the Australian Immunisation Handbook for pertussis vaccination of household contacts and carers of these infants, and should promote immunisation to these groups, particularly if vaccination has not been received in pregnancy.

    - General practitioners and specialists who care for children at high risk of influenza (particularly those with a high-risk medical condition) should be aware of the recommendations in the Australian Immunisation Handbook to vaccinate household contacts and carers of these children and should actively promote immunisation to these groups.

    - Facilities that provide health care or child care services for children who are at high risk of influenza or infants at risk of pertussis should take steps to provide comprehensive occupational immunisation programs for their workers as per the recommendations in the Australian Immunisation Handbook.

    - Specialists who care for children at risk of severe varicella infection should be aware of the recommendation in the Australian Immunisation Handbook to ensure household contacts without a history of varicella receive two doses of varicella vaccine and actively promote immunisation to this group.

4. Immunisation against pertussis and influenza is recommended during pregnancy and provided free in NSW:

    - Health practitioners providing antenatal care should be aware that pertussis and influenza vaccine is provided free for pregnant women in NSW and that detailed information about this program can be obtained from the NSW Health website.[1,2]

    - Pertussis and influenza vaccination during pregancy should be promoted and encouraged by general practitioners, obstetricians and midwives to reduce the risk of disease in young infants.

5. Children should receive vaccines for which they are eligible under immunisation catch up programs:

    - Immunisation providers should ensure children receive all vaccines for which they are eligible under funded immunisation catch-up programs, for example through the use of electronic alerts or flags on medical records.

    - Catch-up programs should be widely promoted to parents when new immunisation programs commence.

6. Travel immunisation should be provided as recommended:

    - General practitioners should be aware of recommendations on vaccination for international travel in the Australian Immunisation Handbook that are relevant to children, including hepatitis A and BCG vaccines, and these should be actively promoted to parents.

7. Data collections on child deaths in NSW should be enhanced and cross-checked between sources:

    - The CDRT should implement measures to improve identification and coding in the CDR of specific pathogens and isolation sites associated with VPDs to facilitate review of child deaths from infectious diseases in NSW.

    - The CDRT and Health Protection NSW should engage in regular communication and cross-checking regarding child deaths from VPDs.

    - The CDRT and Health Protection NSW should work with NSW Health Pathology in regard to standard protocols for testing for and notification of infectious diseases identified following a child's death.

# 2. Background

The NSW Child Death Review Team (CDRT) was established under the *Community Services (Complaints, Review and Monitoring) Act 1993* with a mandate to prevent and reduce child deaths in New South Wales (NSW). Within this role, the CDRT have commissioned the National Centre for Immunisation Research and Surveillance (NCIRS) to complete a report on child deaths in NSW from 2005 to 2014, focussing on recommendations to prevent or reduce deaths from vaccine preventable diseases (VPDs).

## 2.1 Aims

This report aims to:

- Describe child deaths in NSW, from diseases for which a vaccine is currently available in Australia, over the period 2005 to 2014; and
- Provide recommendations to improve prevention of child deaths due to vaccine-preventable diseases.

## 2.2 Immunisation in Australia

There has been a significant decline in the absolute number of deaths due to a range of vaccine-preventable diseases in Australia, compared with relevant pre-vaccination baselines, despite substantial increases in the Australian population.[3] Although smallpox, plague and typhoid vaccines were used in the 1800s, the first vaccination programs at state level commenced in the 1930s with diphtheria vaccine.[4] The first immunisation schedule adopted at national level commenced in 1975.[4] The Immunise Australia 'Seven Point Plan' was launched in 1997, to address low coverage for recommended childhood vaccines (estimated to be 53% for "fully immunised" among children under 6 years). The plan, which included incentive payments for parents and general practitioners, monitoring of immunisation targets through the Australian Childhood Immunisation Register (ACIR), and the introduction of school entry requirements, drove increases in the proportion of children fully immunised at 6 years at the national level to around 93%. [5]

The current nationally funded childhood schedule (Appendix A), known as the National Immunisation Program (NIP), protects against 16 infectious diseases. Most vaccines are funded for all children, although a small number of additional vaccines or additional doses are funded for specific high-risk groups. During the period of this review, nationally funded immunisation programs were introduced against pneumococcal disease, hepatitis A, rotavirus, varicella and influenza (Table 1).

**Table 1 Nationally funded immunisation programs for children, by disease and year of funding[4,6]**

| Disease | Funded group | Vaccine recommended or local programs | National childhood vaccination funded |
|---|---|---|---|
| **Measles** | All children | 1969 | 1975 |
| **Mumps** | | 1981 | 1983 |
| **Rubella** | | 1969 | 1971[1] |
| **Polio** | | 1956 | 1975 |
| **Diphtheria** | | 1932 | 1975 |
| **Tetanus** | | 1953 | 1975 |
| **Pertussis** | | 1942 | 1975 |
| **Haemophilus influenzae type b** | | 1993 | 1993 |
| **Hepatitis B** | | 1980s | 2000 |
| **Meningococcal type C** | | 2003 | 2003 |
| **Varicella** | | 2003 | 2005 |
| **Rotavirus** | | 2006 | 2007 |
| **Pneumococcal disease** | At-risk medical conditions and Aboriginal and Torres Strait Islander children2 | 2001 | 2001 |
| | All children | 2003 | 2005 |
| **Hepatitis A** | Aboriginal and Torres Strait Islander children 12-24 months in (NT, QLD, SA and WA) | 2005 | 2005 |
| **Human Papillomavirus** | Females | 2007 | 2007 |
| | Males | 2011 | 2013 |
| **Influenza** | Children 6 months or older medically at risk for severe influenza3 | Pre-1991 | 2010 |
| | Aboriginal and Torres Strait Islanders 15 years and over | 2008 | |
| | Aboriginal and Torres Strait Islander children 6 months to 5 years | 2013 | 2015 |

[1] School based program (funded for young children in 1989)

[2] These groups have an additional vaccine dose funded under the NIP in addition to the three-dose course available to all children

[3] Subsidised under the PBS pre-2010

In addition to vaccines included in the nationally funded program, some vaccines registered for use in Australia are available only through private purchase (Table 2). The *Australian Immunisation Handbook* provides recommendations about the use of these vaccines.[7]

**Table 2 Vaccines recommended for specific groups in the Australian Immunisation Handbook, not NIP funded[6,7]**

| Disease | Current handbook recommendation for children | Year recommended |
|---|---|---|
| **Meningococcal type A, C, W and Y** | At risk individuals (including high-risk medical conditions and travel) | 1991 |
| **Hepatitis A** | Travellers to endemic areas aged one year and over | 2000 |
| **Influenza** | All children 6 months to 5 years | 2013 |
| **Meningococcal type B** | Infants and young children, particularly ages less than 2 years, and adolescents 15-19 years | 2014 |
| **Varicella** | Second dose | 2008 |
| **Tuberculosis** | Aboriginal and Torres Strait Islander neonates in some regions; travellers | |
| **Japanese encephalitis** | Travellers, residents of outer Torres Strait Islands | 1994 |
| **Cholera** | Travellers at risk, aged 2 years and over | |
| **Typhoid** | Travellers aged 6 years and over | |
| **Yellow fever** | Travellers aged 9 months and over | |
| **Q fever** | Adolescents 15 years and over at risk of infection from animals | 1989 |
| **Rabies** | Travel, bat handling | |

## 2.3 Child deaths from vaccine preventable diseases

While child deaths due to VPDs are rare in Australia, some deaths do occur. Table 3 summarises deaths in children less than five years of age reported in various VPD surveillance reports prepared by the NCIRS. Reported deaths are based on data obtained from both the National Mortality Database held by the Australian Institute of Health and Welfare (AIHW), which is in turn derived from death certificate data coded by the Australian Bureau of Statistics; and the National Notifiable Diseases Surveillance System (NNDSS).[3,8-13] While these data provide background to the national picture of vaccine preventable deaths and allow historical comparison, reported deaths are not subject to individual review and death certificates are known to under-report certain diseases.[14]

**Table 3 Child deaths (< 5 years of age) due to vaccine preventable diseases (death certificate (AIHW) and notification (NNDSS) data)*, Australia [3,8-13]**

| | 1993-1997 | 1998-2000 | 2001-2002 | 2003-2005 | 2005-2007 | 2008-2011 |
|---|---|---|---|---|---|---|
| **Diphtheria** | 0 | 0 | 0 | 0 | 0 | 0 |
| **Invasive Haemophilus influenzae[1] disease** | 13 | 1 | 1 | 1 | 1[5] | 1 |
| **Influenza** | NR | 12 | 3 | 5 | 6[6] | 3 |
| **Measles** | 2 | 0 | 0 | 0 | 0 | 0 |
| **Invasive Meningococcal disease[2]** | NR | 33 | 26 | 12 | 15[6] | 15 |
| **Pertussis** | 9 | 1 | 5 | 1[4] | 1[5] | 8 |
| **Pneumococcal septicaemia, meningitis and pneumonia[2,3]** | 25 | 17 | 8 | 13 | 6[5] | 23 |
| **Poliomyelitis** | 0 | 0 | 0 | 0 | 0 | 0 |
| **Rotavirus** | NR | NR | NR | 0 | 0 | 0 |
| **Tetanus** | 0 | 0 | 0 | 0 | 0 | 0 |
| **Varicella** | 8 | 1 | 1 | 3 | 1[5] | 1 |

*The data source documenting the highest number of deaths for each disease is reported; NR: not reported
[1] Deaths are reported for any deaths identified as *Haemophilus* meningitis, not specifically type b. Deaths from acute epiglottis were also identified prior to 2003.
[2] Deaths are reported regardless of whether the disease was caused by a type contained in the vaccine.
[3] Deaths due to pneumococcal pneumonia were not included from 1993-1998
[4] 2003-4 data; [5] 2005-6 data; [6] 2006-7 data

### 2.3.1 Influenza

Influenza causes epidemics of illness each winter, with symptoms in children including cough, fatigue, muscle aches and high fever. Although symptoms in young children may be non- specific, infection may be complicated by middle ear infections, pneumonia and febrile seizures.[9] Children with high-risk medical conditions are more likely to suffer severe disease.[15] However, rates of hospitalisation are high in healthy children under five years of age [7,9,16-18] and deaths occur.[19]

Influenza vaccine is recommended annually for anyone aged six months or older who wishes to reduce the likelihood of becoming ill with influenza. The vaccine available in each year is matched as closely as possible to the subtypes predicted to cause disease in that year. The Australian Immunisation Handbook highlights the increased risk of severe disease and hospitalisation in children less than five years of age. Population groups at higher risk of severe disease (all persons with heart and lung disease, neurological conditions, immune system compromise and Down Syndrome and pregnant women) have been funded for influenza vaccine since 2010 and all Aboriginal and Torres Strait Islander Children (hereafter referred to as Indigenous) since 2015.[6,7]. Influenza vaccine is not funded under the NIP for all children, but in Western Australia, has been funded by that state for children aged 6 months to 5 years since 2008.[20]

Nationally, a background rate of one to six influenza deaths, with an average of 2.6 deaths, per year was reported for children under five years of age between 1997 and 2005.[21] In 2005-6, there were five deaths in children under five, and two in children aged 5 to 14 years.[3] During the 2007 influenza season, 7 deaths in children under five were reported.[21] During the 2009 influenza season (often referred to as the H1N1 2009 pandemic), when a large proportion of the population was infected, 11 children were reported to have died due to influenza.[22]

### 2.3.2 Pneumococcal disease

*Streptococcus pneumoniae* (pneumococcus) causes a diverse range of diseases, from middle ear infection to pneumonia, septicaemia and meningitis. Invasive pneumococcal disease (IPD), defined as isolation of *Streptococcus pneumoniae* from the blood or another sterile site, has a reported mortality of around 1%.[23] Pneumococcal disease can be caused by ninety different serotypes (strains or subtypes), but a small number of strains cause a large proportion of IPD in most populations; pneumococcal vaccines to date have covered serotypes causing the majority of disease in the United States at the time they were developed.[24]

There are two different types of pneumococcal vaccine – pneumococcal conjugate vaccine (PCV) and pneumococcal polysaccharide vaccine (PPV). Unlike polysaccharide vaccines, conjugate vaccines are able to induce immune responses in children under the age of 2 years and to set-up the immune system to respond to later exposure to pneumococcal serotypes included in the vaccine.[6,7] The serotypes included in PCVs increased from seven serotypes (7vPCV) in 2001 to 13 serotypes (13vPCV) in 2011 (Table 4). In 2001, 7vPCV was funded under the NIP for medically at-risk and Indigenous children, extended to all children in 2005 and replaced by 13vPCV in 2011. Following introduction of 7vPCV, the overall rate of IPD has substantially declined in Australia, even after accounting for increases in some types not contained in the vaccine, a phenomenon known as 'serotype replacement'. [25]

The polysaccharide vaccine (23vPPV) contains 23 serotypes. It was funded as a booster dose at 12 months of age for children with certain high risk medical conditions from 2001 to 2005, and for 4 to 5 year olds from 2004. Indigenous children in some states (not NSW) had a dose of 23vPPV at 18 to 24 months of age funded under the NIP from 2001 to 2011.[26]

**Table 4 Vaccine for pneumococcal disease and serotypes covered[24]**

| Vaccine | Availability | Serotypes |
|---|---|---|
| **23vPPV** | 2001 | 1 2 3 4 5 6B 7F 8 9N 9V 10A 11A 12F 14 15B 17F 18C 19A 19F 20 22F 23F 33F |
| **7vPCV** | 2001[1]<br>2005[2] | 4 6B 9V 14 18C 19F 23F |
| **13vPCV** | 2011 | 1 3 4 5 6A 6B 7F 9V 14 18C 19A 19F 23F |

[1]Indigenous children and medically at-risk children

[2]All children

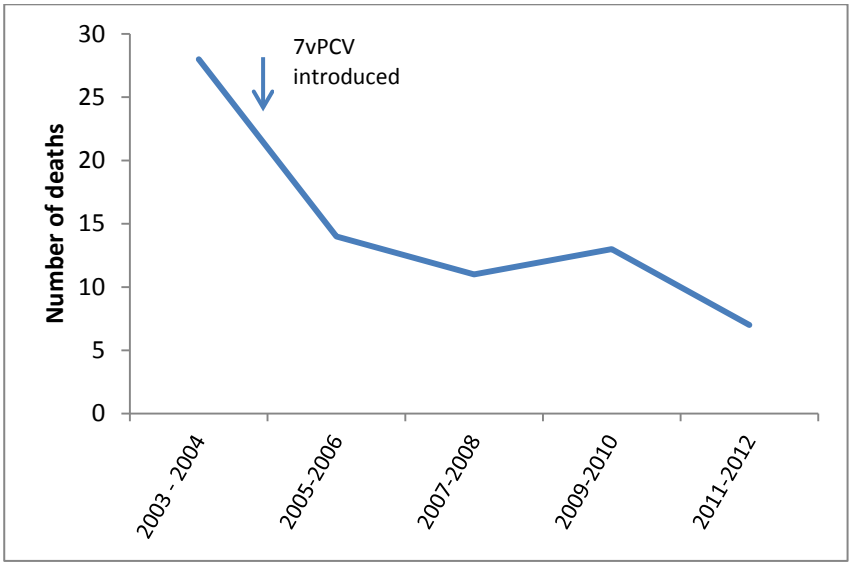
Deaths from IPD in Australian children aged less than five between 2005 and 2012 are shown in table 5.

**Table 5 IPD deaths in children less than 5 years, Australia (Data from Invasive Pneumococcal Disease surveillance program) [27-35]**

| Year | 2003 - 2004 | 2005-2006 | 2007-2008 | 2009-2010 | 2011-2012 | 2013 |
|---|---|---|---|---|---|---|
| **Vaccine availability** | Pre universal vaccine | 7vPCV | | | | 13vPCV |
| **Deaths** | 28 | 14 | 11 | 13 | 7 | * |

*Data not yet available

**Figure 1 IPD deaths in children less than 5 years, Australia, 2003-2012**




### 2.3.3 Pertussis (whooping cough)

Pertussis is a bacterial infection caused by *Bordetella pertussis*; typical clinical symptoms are respiratory infection characterised by paroxysmal cough. Infants who have received less than 2 vaccine doses are at greatest risk of severe disease, with complications including pneumonia, apnoea (stopping breathing for periods of time), seizures, encephalitis (inflammation of the brain) and death.[36]

State-based vaccination programs for pertussis commenced in the 1940s[4], and even prior to national programs using the combined diphtheria-tetanus-pertussis (DTP) vaccine in 1954, had resulted in substantial decreases in pertussis deaths.[3] The first of three infant doses of vaccine is given at 6 to 8 weeks of age. [37] The current acellular vaccine, given as combination with other infant vaccines, has been used since 1999. It provides good protection against severe illness but lesser protection against mild illness; importantly, immunity declines within 2 years following the initial vaccine doses given at 2, 4 and 6 month of ages. Three to 4 year old siblings are well known to be a source of infection for younger siblings who are too young to be immunised. [37-39] In 2015, vaccination of pregnant women against pertussis (maternal vaccination) was recommended in the Australian Immunisation Handbook and funded in all states and territories, with the aim of protecting babies less than 3 months of age through the transfer of vaccine-derived antibodies from their mother.[7,40]

Pertussis is the most commonly notified vaccine preventable disease in Australia,[39] with epidemics every three to four years. This high rate of notification is in part due to our easy access to diagnostic tests and the requirement for positive results to be notified to the laboratory. Between 2006 and 2012, 10 of 11 notified pertussis deaths in Australia were in infants less than 2 months of age, [39] and between 2004 and 2013, eight of twelve identified pertussis deaths were in infants less than 2 months of age.[41]

### 2.3.4 Meningococcal disease

Meningococcal disease is a bacterial infection caused by *Neisseria meningitidis*, which can result in septicaemia (blood poisoning) or meningitis. It has a high case fatality rate (which varies by age and subtype but can be as high as 10-15%), despite advances in treatment. [23] Disease is caused by a range of different subtypes (serogroups) of the meningococcal bacteria, with five serogroups (A, B, C, W and Y) causing most disease worldwide.[7] Since the success of the immunisation program for meningococcal C, introduced from 2003, most cases in Australia are now due to meningococcal type B disease (80% overall in 2014, with a higher proportion in children under the age of 10).[42]

A conjugate vaccine against meningococcal type C has been included in the NIP at 12 months of age since 2003.[3] In August 2013, a new vaccine effective against meningococcal type b became available in Australia. In 2014, it was recommended in the Australian Immunisation Handbook for infants and young children, particularly those aged <24 months, for adolescents aged 15-19 years, and those with high-risk medical conditions; however, the vaccine is not funded under the NIP. [43] Conjugate vaccines that include types A, W and Y in addition to C are available and recommended for those with high-risk medical conditions and travellers to high risk areas.[7]

Meningococcal disease can occur in any age group, but children less than 5 years of age and adolescents 15-19 years have the highest incidence. [44] In Australia, 15 deaths in children under five years were reported between 2005 and 2007,and 15 between 2008 to 2011. There were also deaths in older children aged 5 to 14 years (two 2005-7 and one in 2008-11) and in adolescents and young adults aged 15 to 24 years (three in 2005-7 and nine in 2008-11).[3,10] The mortality rate per million population was in infants under one year.[3,10]

### 2.3.5 Measles

Measles is a highly infectious disease with symptoms including cough, fever and rash. Complications can include pneumonia and encephalitis.[45] A single dose of measles vaccination was funded in the 1970s, with two doses funded since 1993. Two doses of measles vaccination are currently given at 12 and 18 months under the NIP.[7]

Deaths from measles encephalitis in Australia occurred at an average of 3.3 per year between 1979 and 1985, decreasing to two deaths per year 1986-1992.[46] Elimination of locally circulating measles was declared in Australia in 2014, but cases acquired overseas may cause outbreaks in Australia, mostly among people who are not vaccinated.[3,45,47] The last measles death in Australia was recorded in 1995,[3,45] and no deaths were reported during an outbreak of 168 cases in Sydney in 2012.[47]

### 2.3.6 Mumps

Mumps is a viral infection with symptoms ranging from mild cold-like symptoms to fever, fatigue and facial swelling. It can be complicated by meningitis, encephalitis and testicular swelling, with death resulting from 1.5% of encephalitis cases.[48] Mumps vaccination has been funded under the NIP since 1983, initially as mumps-rubella vaccine and since 1988 as MMR.[4] While outbreaks of mumps do occur in Australia, only adult deaths were reported from 2001 to 2006 in Australia, [3,8,9] and no deaths were reported from 2008 to 2011.[10,49]

### 2.3.7 Rubella

Rubella infection is generally mild and complications are rare. The main concern is infection in pregnant women, which can cause birth defects (congenital rubella syndrome).[7,49] Childhood vaccination has been funded under the NIP since 1989.[4] No deaths were recorded in death certificates in Australia from 2001 to 2006 [3,8,9] or from 2008 to 2011.[10,49]

### 2.3.8 Varicella (chickenpox)

Varicella infection can vary from mild to severe, with complications including secondary bacterial skin infection, pneumonia, or encephalitis. Risk factors for severe varicella include older and younger ages, and impaired immune function (immunocompromised). From US studies, the case-fatality rate is reported as 2.6 per 100,000 cases. [23]

Varicella vaccine was registered for use in Australia in 2002 and in 2005 a single dose of varicella vaccine at 18 months of age was funded under the NIP. Varicella vaccine has been given in a combined measles, mumps, rubella and varicella (MMRV) vaccine since 2013. It is a live vaccine so is unable to be given to children who have significant immune system problems.[7] Prior to 2005, studies reported between 5 and 8 deaths per year in Australia, most occurring under five years of age.[50,51] One death was reported nationally in children under 5 years of age in each of 2005-7 and 2008-11, compared to three between 2003 and 2004.[3] Among four Australian childrens' hospitals, no deaths were identified in any hospital between 2007 and 2010, compared to two from one hospital between 1999 and 2001.[52].

### 2.3.9 Haemophilus influenzae

*Haemophilus influenzae* type b (Hib) is a bacterial infection that may cause meningitis, epiglottitis (swelling in the respiratory tract) and pneumonia, among other conditions.[53] Hib meningitis has a high case-fatality rate and risk of long term complications. [7] While most cases of severe disease are caused by subtype b, other types (A,C,E,F) and occasionally non-typeable *Haemophilus influenzae* (NTHI) can cause severe disease, although NTHI in particular is more likely to cause respiratory infection or milder diseases such as middle ear infections.[7]

Infant Hib vaccination was introduced to the NIP in 1993 and is only effective against this type.[7] Prior to the vaccination program, it was estimated that up to 19 child Hib deaths occurred per year in Australia.[54] Following the introduction of the program, eight Hib deaths were reported nationally in children under five between 1993 and 1996, with two of these being Indigenous children. Five of these deaths occurred in the second half of 1993, with one each subsequent year until 1996.[55] Between 1993 and 2007, the

NNDSS reported five Hib deaths and was one infant death from Hib reported between 2005 and 2007 in an Indigenous infant.[3]

### 2.3.10 Rotavirus

Rotavirus causes gastroenteritis, predominantly in infants and young children. The disease can range from mild to severe diarrhoea with fever, dehydration and death. The case-fatality rate is estimated to be approximately 1 in 200,000 cases of rotavirus gastroenteritis in developed countries like Australia. [23]

There has been a substantial decrease in severe rotavirus disease since the vaccine was introduced in 2007.[56] Prior to 2007, one study reported 13 rotavirus deaths in all ages between 1990 and 2002 (approximately one death per year), with most occurring in infants under one year of age. There were three deaths reported overall between 2001 and 2007,[3] and from 2008-2011, there was one death reported in a child under five years of age in Australia.[10]

### 2.3.11 Tetanus

Tetanus is caused by a toxin produced by the bacterium *Clostridium tetani*, which leads to painful generalised spasms which are often fatal through effects on the respiratory system. Tetanus vaccines were introduced in 1939, included in state immunisation programs since 1953 and funded under the NIP since 1975.[7] Tetanus occurs at very low rates in Australia, mostly following injury in adults over the age of 70 years who are not fully vaccinated or have not had booster vaccinations.[3] Tetanus deaths were reported only in adults in between 2001 and 2007.[3,8,9] Tetanus among newborns has effectively been eliminated in developed countries like Australia but is a significant problem in developing countries.[7]

### 2.3.12 Diphtheria

Diphtheria is a bacterial disease causing either respiratory or skin infection, with heart and neurological complications.[57] Disease is usually caused by the strain of the *Corynebacterium diphtheriae* bacteria that carries a toxin, although may occur from non-toxin containing strains in some circumstances.[57] Vaccination has been available since the 1930s.[7] Previously the most common cause of infectious death in Australia, vaccination programs have virtually eliminated diphtheria,[57] although cases may be acquired from overseas.[3] No deaths in Australia were reported from 1996 to 2005,[3] however one death occurred in 2011 in an unvaccinated adult who acquired the disease from someone who had returned from overseas.[57]

### 2.3.13 Poliomyelitis

Paralytic polio occurs as a complication of infection with poliovirus.[7] Mass vaccination with polio vaccine has occurred since the 1950s in Australia, with the last locally acquired case in 1972. Australia was declared free of polio in 2000.[3,7] Cases may be acquired overseas with the last case imported into Australia in 2007.[3,58] No deaths were reported from 1986 to 2005.[3]

### 2.3.14 Hepatitis

A number of hepatitis viruses cause liver disease, and vaccination is available for two types - Hepatitis A and B.

### Hepatitis A

Hepatitis A virus often causes no symptoms or mild disease in children, while adults are more likely to have symptoms. Typically initial fever is followed by nausea, vomiting and liver impairment with jaundice; severe liver disease associated with liver failure occurs uncommonly. It is transmitted from contaminated food or water, or person to person.[7]

Hepatitis A vaccination has been funded for Indigenous children, who are at increased risk of severe disease, since 2005. It is also available but not funded for travellers to high risk countries.[7] Although cases and outbreaks may occur in Australia,[59] the disease has been declining in recent years.[3] It is considered the most common and potentially preventable disease of international travellers.[60] Hepatitis A deaths were reported only in Australian adults between 2005 and 2007.[3] One death was reported in an Indigenous child aged under five between 2000 and 2002.[61]

### Hepatitis B

Hepatitis B is transmitted via blood or body fluids, and can be transmitted from mother to child around the time of birth. Infection in infants and children is usually without symptoms, but death can occur in adulthood following chronic infection, due to liver damage and cancer.[7] Groups at higher risk of infection and chronic disease include Aboriginal and Torres Strait Islander people and some migrant groups.[7] Vaccination has been recommended for high risk groups since 1987 and funded for all newborns since 2000.[4] Hepatitis B deaths were reported only in Australian adults between 2005 and 2007.[3]

#### 2.3.15 Human Papillomavirus

Infection with human papillomavirus (HPV) may cause a range of cancers, including cancer of the cervix. While vaccination is given as part of the adolescent immunisation program, the impact of this disease is experienced in adulthood.[62]

# 3. Methods

For the purposes of this review, a disease of interest was defined as a disease caused by a pathogen (virus or bacteria) for which a vaccine is currently available on the NIP. Diseases were included regardless of whether the vaccine covered that specific subtype of disease (Table 6). We excluded HPV because this causes disease in adulthood.

**Table 6 Diseases of interest**

| Diseases of interest | | |
|---|---|---|
| *Haemophilus influenzae* | Meningococcal disease | Rotavirus |
| Diphtheria | Mumps | Rubella |
| Hepatitis A & B | Pertussis | Tetanus |
| Influenza | Pneumococcal disease | Varicella |
| Measles | Poliomyelitis | |

## 3.1 Case identification

### 3.1.1 Databases

We identified deaths due to diseases of interest through the NSW Child Death Register (CDR), maintained by the Child Death Review Team (CDRT). The CDR records all deaths in NSW among children less than 18 years of age, with cause of death coded based on a combination of death certificates and coroner's reports using International Statistical Classification of Diseases and Related Health Problems (ICD) system, 10th revision, modified for Australia (ICD-10-AM).

In order to validate the data available on the CDR and determine how many cases were not identified from the CDR data alone, we also identified deaths due to the diseases of interest from the Notifiable Conditions Information Management System (NCIMS), which is the state-based version of NNDSS. NCIMS is maintained by the Communicable Diseases Branch, Health Protection NSW, and captures notification of vaccine preventable diseases by laboratories and doctors in NSW under the *NSW Public Health Act 2010*. Case definitions for each disease are described here: http://www.health.nsw.gov.au/Infectious/controlguideline/Pages/default.aspx

CDR data was provided by the CDRT (for the NSW Ombudsman) to allow completion of this report under their mandate to prevent and reduce child deaths in NSW, as outlined in the *Community Services (Complaints, Review and Monitoring) Act 1993*. NCIMS data access was approved and data released to the NSW Ombudsman by Health Protection NSW.

### 3.1.2 CDR data

From all infectious causes of death in the CDR (2005 to 2014), we identified cases of diseases of interest using CDRT-applied ICD-10-AM coding for cause of death (COD) and associated COD (ACOD) codes. The following ICD-10-AM codes were of particular interest: diphtheria (A36), *Haemophilus* disease (G00.0 – *Haemophilus* meningitis, J14 – *Haemophilus* pneumonia, A41.3 - *Haemophilus* sepsis, J05.1 - Epiglottitis), hepatitis A (B15), hepatitis B (B16), influenza (J10, J11), measles (B05), meningococcal disease (A39), mumps (B26), pertussis (A37), pneumococcal disease (G00.1 –pneumococcal meningitis, A40.3 – pneumococcal septicaemia, and J13 pneumococcal pneumonia), acute poliomyelitis (A80), rotavirus (A0.80), rubella (B06, P350), tetanus (A34, A35), varicella zoster virus infection (B01 – chickenpox, B02 – shingles). We also identified cases based on any mention of the diseases of interest in the Registry of Births, Death and Marriages (BDM) COD (coded from death certificates) or coroner's report COD fields or notes.

#### CDR assessment process

Cases in the CDR were assessed as being either a) *highly likely* or b) *moderately likely* to be associated with a disease of interest if the disease was mentioned in any field in the CDR Dataset, either by ICD code or text (Appendix B). Cases were assessed as c) *possible* or *d) unlikely* to be associated with the disease of interest if any field identified a clinical syndrome known to be associated with the disease of interest, without identifying the specific disease. Syndromes of interest are listed in Appendix B. Full case notes were only obtained for cases that were assessed as *highly* or *moderately likely* to be associated with the

disease of interest. Cases assessed as *possible* or *unlikely* to be associated with the disease of interest were not reviewed further.

### 3.1.3 NCIMS data

From NCIMS, we identified notified cases of child deaths under the age of 15 years due to diseases of interest between 2005 and 2014. Data were extracted if the disease was listed in the 'notifiable condition' field and a death was also recorded. To compare NCIMS and CDR data, cases identified through the CDR were matched to cases in NCIMS using dates of birth and last name, or date of birth and death. A manual review of other personal identifiers was then conducted to ensure that the matched case was in fact the same individual child.

### 3.1.4 Interstate data

The Child Death Review Team requested data on deaths of children from NSW from neighbouring jurisdictions in Queensland, the Australian Capital Territory and Victoria. This was to account for the possibility that children may have travelled interstate before their death, and that those living close to state borders may have been transferred to a hospital in another state.

## 3.2 Data extraction

For each of the cases identified for further review either through the CDR or NCIMS, the CDRT provided medical records, post-mortem examinations and coronial findings if available. Some laboratory results were also recorded on NCIMS. A standard set of information was collected on case demographics (age, sex, Indigenous status, and residential postcode), clinical presentation and history (medical comorbidities, vaccination status, clinical presentation and management) and laboratory results.

## 3.3 Case definition

Cases of each disease of interest identified from each database were classified as *confirmed, probable* or *uncertain* depending on the strength of evidence for the disease and cause of death (Table 7). Two authors (JC and AP) reviewed available medical documentation in order to classify the likelihood that the death was attributable to a disease of interest according the case definitions. Complex cases were reviewed by an expert panel (KM, PM and FB).

**Table 7 Case definitions for deaths due to diseases of interest**

| | Laboratory & Epidemiological evidence | | Clinical & Post-mortem evidence |
|---|---|---|---|
| Confirmed | Laboratory definitive evidence[1] of pathogen[2] of interest from a clinical specimen | AND | Post-mortem or clinical evidence of severe disease consistent with the disease of interest |
| Probable | Laboratory suggestive evidence of pathogen of interest from a clinical specimen<br>OR<br>Laboratory evidence of a pathogen of interest from a post-mortem specimen[3]<br>OR<br>Epidemiological[4] link to a case of disease of interest | AND | Post-mortem or clinical evidence of severe disease consistent with the disease of interest |
| Uncertain | Laboratory evidence (clinical or post-mortem specimen) of a pathogen[2] of interest<br>OR<br>epidemiological link to a case of disease of interest | AND | *Absence* of post-mortem or clinical evidence of severe disease consistent with the disease of interest |
| Not a case | No laboratory evidence of pathogen of interest | | |

[1] Laboratory evidence is consistent with National notifiable diseases case definitions, where available

[2] A pathogen of interest refers to the bacteria or virus that causes the disease on interest and is detectable in the laboratory

[3] Expert panel reviewed cases where second pathogen was identified at post-mortem examination but was unlikely to be clinically relevant. Where two organisms of interest were identified with consistent clinical or post-mortem findings (e.g. S.pneumoniae and H.influenzae) the case was ascribed a probable status.

[4] Epidemiological evidence refers to a contact with another known case of the disease in an appropriate timeframe, consistent with national notifiable diseases case definitions

Post-mortem samples were considered relevant although lesser evidence of infection with the pathogen of interest. In the presence of relevant clinical or post-mortem findings, these cases were given a probable classification and therefore included with confirmed cases in the initial analysis.

## 3.4 Descriptive analysis

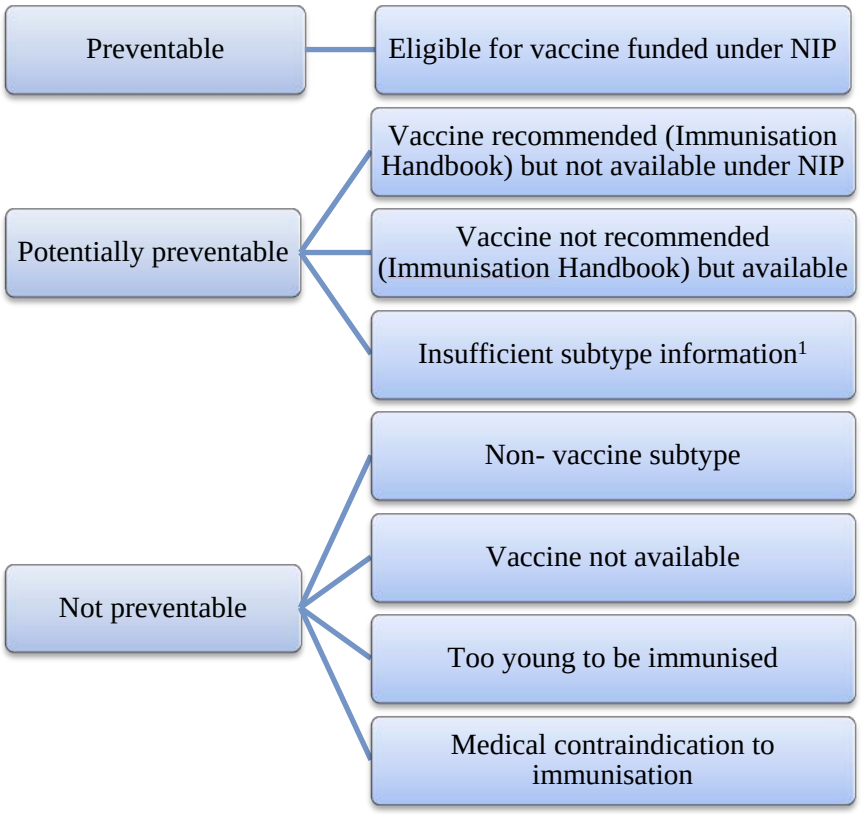
All confirmed and probable cases due to the diseases of interest were included in the initial analysis. Further analyses focused on preventable and potentially preventable deaths only. Data were analysed using STATA (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) and Microsoft Excel (2010). Death rates were presented as annual average rates per 100,000 child population.

Postcode data were linked to the Socio-Economic Indexes for Areas (SEIFA) and Australian Standard Geographic Classification (ASGC) Remoteness Structure data provided by the Australian Bureau of Statistics (ABS) in order to describe deaths by socioeconomic status and remoteness. Population data by remoteness was obtained from the Centre for Epidemiology and Evidence, NSW Ministry of Health.[63]

## 3.5 Assessment of preventable deaths

Confirmed and probable cases were classified as preventable through vaccination according to the framework below (Figure 2).

**Figure 2 Framework for prevention by vaccination**




1 Where the pathogen of interest has not been further subtyped by the laboratory, it is not possible to know whether the subtype is in the vaccine

# 4. Results

## 4.1 Cases identified

Of 788 cases in the CDRT Infectious Disease dataset, 55 cases were assessed as highly or moderately likely to be due to a disease of interest. Thirty five cases were successfully matched to an NCIMS record. A further 18 cases were identified from NCIMS only (Table 8 and Figure 3). A total of 73 cases were included.

**Figure 3 Cases identified**

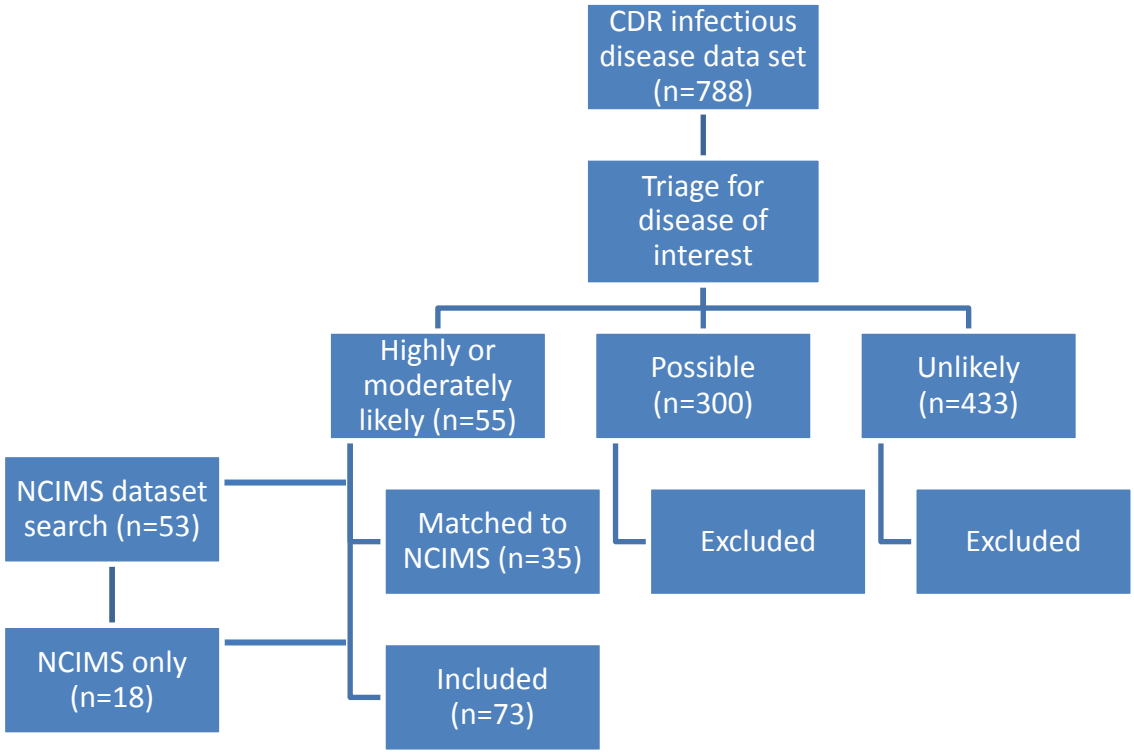



**Table 8 Sources of cases**

| Source | Number | Per cent |
|---|---|---|
| **Both** | 35 | 48.0 |
| **CDRT only** | 20 | 27.4 |
| **NCIMS only** | 18 | 24.7 |

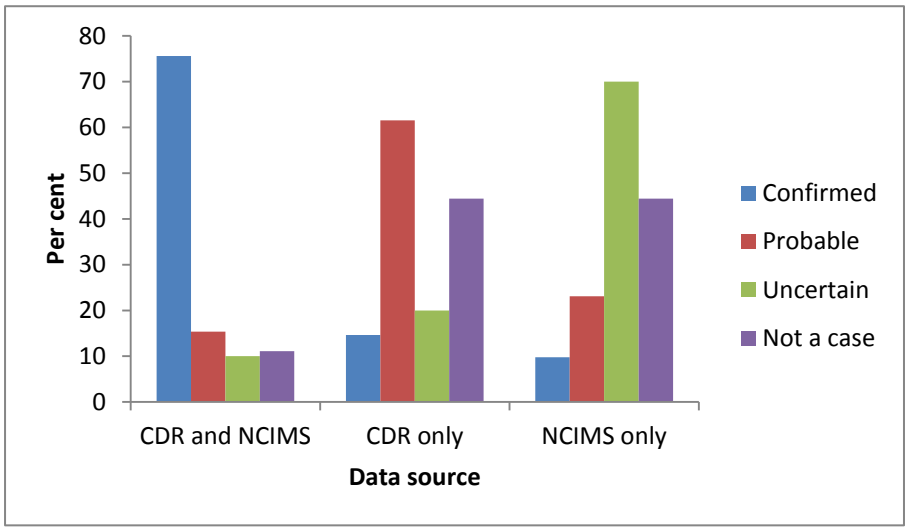
Of the 73 included cases of diseases of interest, 54 were classified as confirmed or probable based on the case definition (Table 9).

**Table 9 Classification of cases**

| Classification | Number | Per cent |
|---|---|---|
| Confirmed | 41 | 56.2 |
| Probable | 13 | 17.8 |
| Uncertain | 10 | 13.7 |
| Not a case | 9 | 12.3 |
| Total | 73 | 100.0 |

Confirmed cases were more likely to have been identified from both data sources, while uncertain cases were more likely to have been identified from NCIMS only. The CDR database identified a high proportion of probable cases (Figure 4).

**Figure 4 Data source by case classification (per cent of classification)**




Of the 18 cases identified by NCIMS only, seven were classified as confirmed or probable. This included two cases who had died in Queensland so were not recorded in the NSW CDR. Two pneumococcal cases identified from NCIMS and classified as probable were not in the original CDR database. Two cases were triaged as possible or unlikely in the initial CDR review but later classified as confirmed or probable. One of these was originally assessed as possible based on an ICD code of bacterial meningitis and was classified on review of medical records to be a confirmed case of pneumococcal meningitis. The other was assessed as unlikely based on an ICD code of birth asphyxia and was later classified as a probable case of neonatal pneumococcal disease. One case was identified from NCIMS only but was matched to re-extracted CDR data showing deaths in 2014 as not all deaths were registered at the time of initial data extraction.

Of the cases identified by the CDR only, 14 were classified as confirmed or probable. Most of these were not recorded on NCIMS as the cases did not meet the criteria for notification under the *Public Health Act 2010*, such as *S. pneumoniae* isolated from a non-sterile site, or *Haemophilus influenzae* not further typed. Two were deaths from varicella, which is not notifiable in NSW. Two influenza cases and one hepatitis A case were not notified to NCIMS, although laboratory reporting of all detections of these pathogens should be routine.

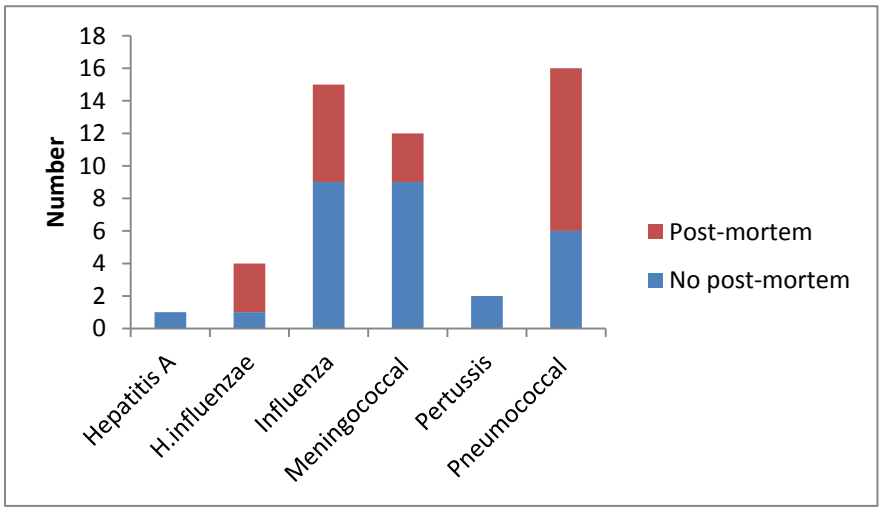
We identified NSW residents who died in neighbouring states. Two cases of pertussis identified from Queensland were captured in NCIMS with sufficient information provided by the Queensland Family and Child Commission and NCIMS to allow inclusion in the review. For 13 infectious disease deaths in Victoria among children who usually reside in NSW, only ICD-10 codes were provided with no further information. Three of these ICD-10 codes were among the codes used to identify cases in the NSW CDR data (two cases coded as meningococcal disease and one as influenza with pneumonia). We were unable to access more detailed information on these cases and so they were not included. From the ACT, no deaths were triaged as highly or moderately likely to have been caused by a disease of interest.

## 4.2 All confirmed and probable cases of diseases of interest

### 4.2.1 Post mortem

Of the 52 cases with information on whether a post-mortem had been conducted, 22 had a post mortem performed (42%) (Figure 5). Children with high-risk medical conditions were less likely to have a post mortem performed. Of 18 children with high-risk conditions, 6 had a post-mortem (33%), while of 34 children without documented high-risk conditions, 16 had a post-mortem (47%).

**Figure 5 Number of death where post-mortem performed, confirmed and probable cases, 2005-2014**




### 4.2.2 Child deaths by Indigenous status, sex and county of birth

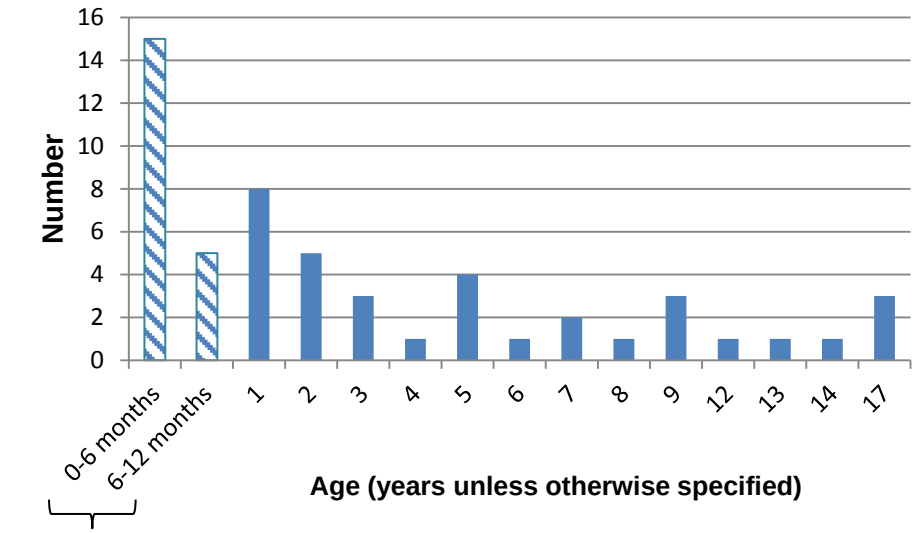
Among all 54 confirmed and probable cases, male children were overrepresented. Deaths among Indigenous children identified accounted for 5.6%, similar to the proportion of Indigenous children residing in NSW (5.5%)[64] (Table 10). However, Indigenous status may not have been adequately identified.

**Table 10 Demographic information**

| | Number | Percentage |
|---|---|---|
| Indigenous | 3/53 | 6% |
| Male | 39/54 | 72% |
| English speaking family | 48/52 | 89% |

The number of deaths was highest in infants under six months of age. The death rate was 2.1 per 100 000 infants under 12 months (Figure 6) and 0.33 per 100 000 children overall.

**Figure 6 Deaths by age, confirmed and probable cases, 2005-2014**




### 4.2.3 Median age at death, by disease

The average age of death due to *H.influenzae*, meningococcal disease and pertussis was under 12 months of age, while the average age of pneumococcal deaths was 16 months. Influenza deaths had a median age of seven years (Table 11).

**Table 11 Median age at time of death by disease, confirmed and probable cases, 2005-2014**

| Disease* | Observations | Median age (years) | Median age (months) |
|---|---|---|---|
| ***H.influenzae*** | 4 | | 6 |
| **Influenza** | 15 | 7 | |
| **Meningococcal** | 12 | | 9 |
| **Pertussis** | 4 | | 2 |
| **Pneumococcal** | 16 | | 16 |
| **Varicella** | 2 | 11.5 | |

* Median age for diseases with only one case are not reported.

### 4.2.4 Deaths over time

Over time, the rate of death due to meningococcal disease appeared to decrease, while the rate of deaths due to influenza appeared to increase (Figures 7 and 8). The increase in influenza deaths may be partly attributable to increased testing following the 2009 H1N1 pandemic season.

**Figure 7 Overall rate and number of child deaths, confirmed and probable cases 2005-2014 (number of cases shown labelled for each year)**

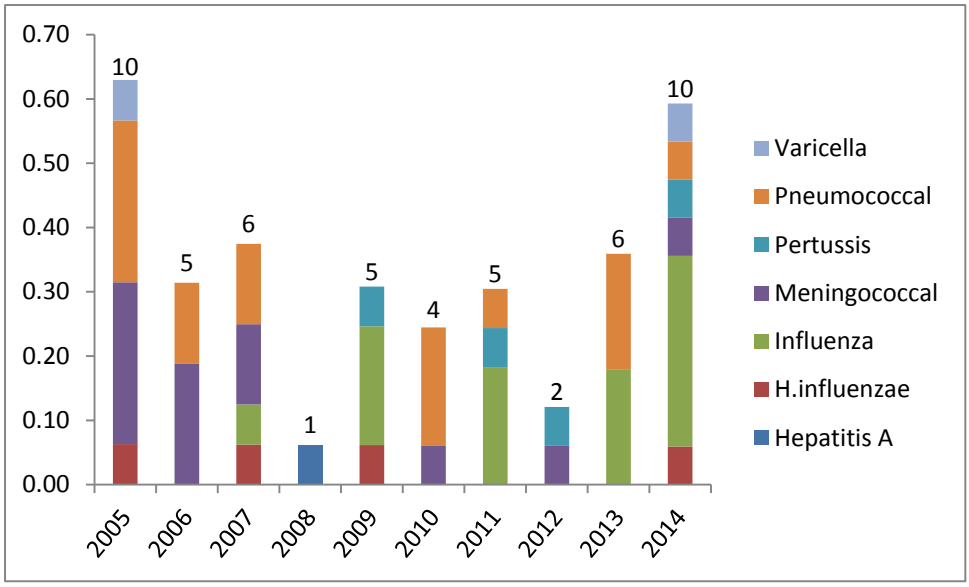
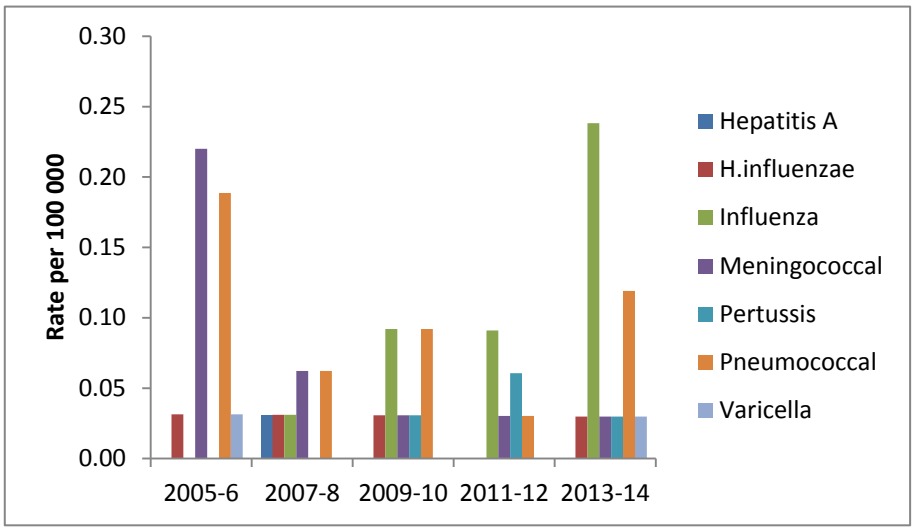


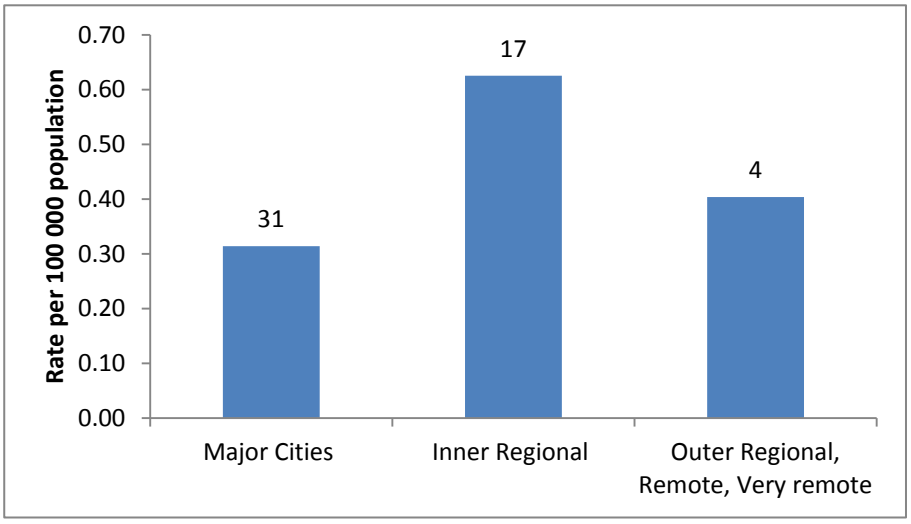

**Figure 8 Rate of child deaths by disease, confirmed and probable cases, 2005-2014**




### 4.2.5 Child deaths by remoteness

While most deaths (n=31) occurred in major cities, the highest rate of death was in inner regional areas (Figure 9). Because of small numbers, deaths in outer regional, remote and very remote areas were combined. There were no deaths in children from very remote areas.

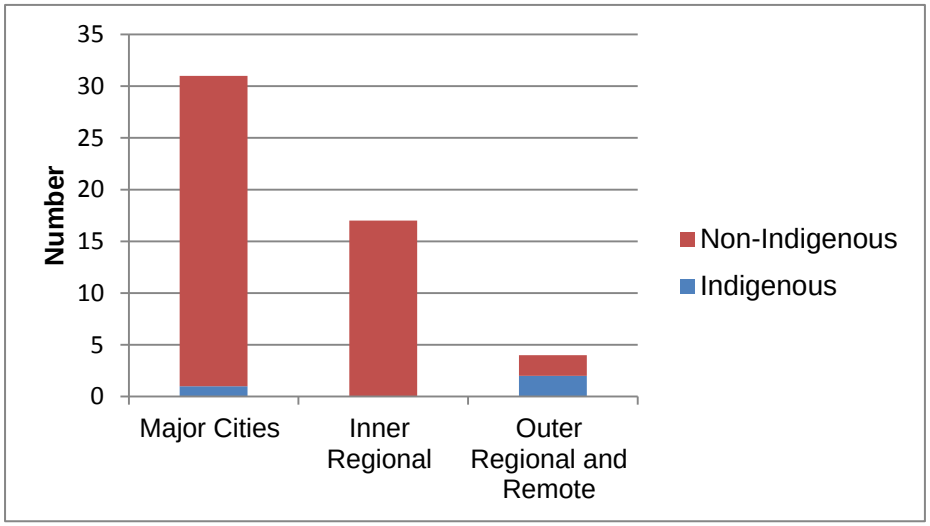
**Figure 9 Deaths per 100,000 population by remoteness, confirmed and probable cases, 2005-2014 (number of cases shown labelled for each region)***




* Population data were only available for age 0 to 14. Given that only 3 of 53 cases were aged over 14 years (5.7%), this data may slightly overestimate rates. Population data for 2014 are population projections based on data from the NSW Department of Planning and Infrastructure (SAPHaRI). Centre for Epidemiology and Evidence, NSW Ministry of Health.

Of the four outer regional and remote deaths, half were in Indigenous children, both of whom died from meningococcal B disease, and one was a visiting Pacific Islander child (Figure 10). During the 2011 census, 17% of children aged up to 14 living in outer regional, remote and very remote areas were Indigenous.[65]

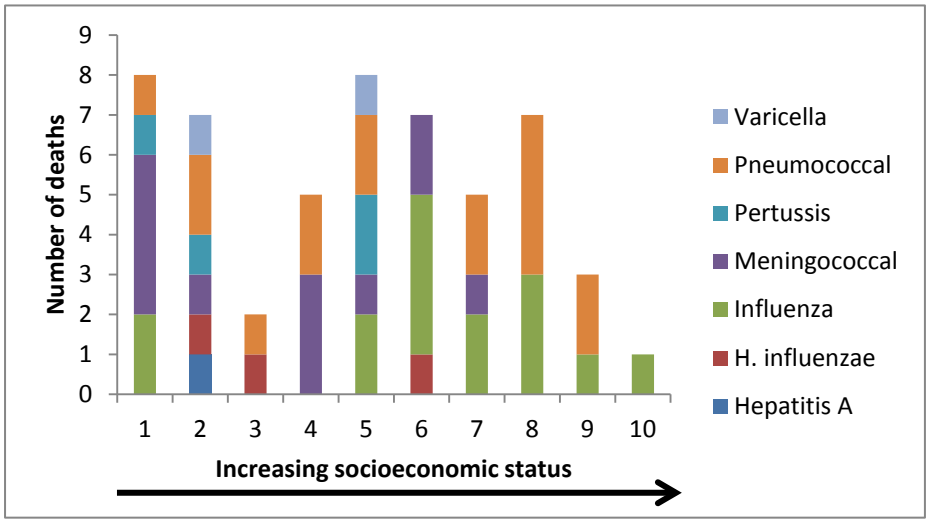
**Figure 10 Deaths by remoteness and Indigenous status, confirmed and probable cases, 2005-2014**




### 4.2.6 Child deaths by level of disadvantage

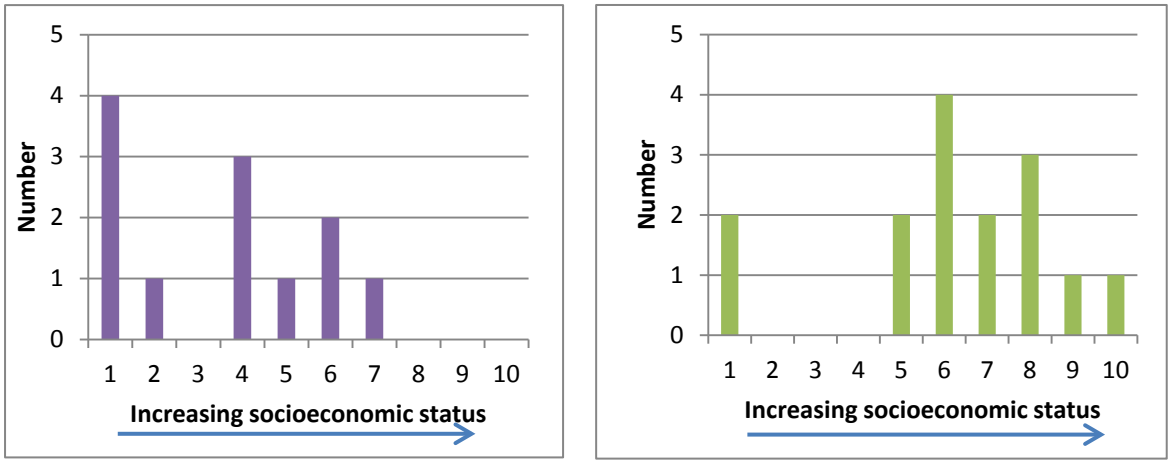
Child deaths were analysed by level of socioeconomic disadvantage using SEFIA deciles based on postcode of residence, where 1 represents the most disadvantaged areas and 10 represents the areas of greatest social advantage (Figure 11).

**Figure 11 Number of child deaths by level of disadvantage and disease, confirmed and probable cases, 2005-2014**




Meningococcal deaths tended to occur more in children residing in more disadvantaged regions, whereas influenza deaths tended to occur more in children residing in less disadvantaged regions (Figures 12 a. and b.).

**Figure 12 a. Number of child deaths from meningococcal disease by level of disadvantage; b. Number of child deaths from influenza by level of disadvantage**




### 4.2.7 High risk medical conditions

Two thirds of confirmed and probable deaths were in children without a documented high-risk medical condition. One third (n=18) had medical conditions that put them at increased risk of severe disease (Table 12). For 12 of these children, their high-risk medical conditions meant that they were eligible for NIP funded vaccine or additional vaccine doses for the disease of interest, although not all children died from strains that were covered in the relevant vaccine. All children who died from influenza were eligible for the vaccine due to their medical conditions and all children who died from pneumococcal disease were eligible for

additional vaccine doses. Some children were eligible for vaccines based on their age rather than their medical condition (Table 12).

All children with conditions of the brain had both seizures and cerebral palsy; three also had scoliosis and two had microcephaly. Of eight children with impaired immune function, two who died from pneumococcal disease just before two years of age were born without a spleen, but this had not been diagnosed before death. Four children were on immune suppressive treatment and two had medical conditions that suppressed the immune system.

**Table 12 High-risk medical conditions, by disease**

| Disease | Lung | Heart | Brain | Impaired immune function |
|---|---|---|---|---|
| **Influenza** | 1 | | 4 | 2 |
| **H. influenzae** | | | 1[1] | |
| **Pneumococcal** | | 2 | | 3 |
| **Meningococcal** | | 1[2] | | 1[3] |
| **Varicella** | | | | 2[4] |
| **Pertussis** | | 1[5] | | |

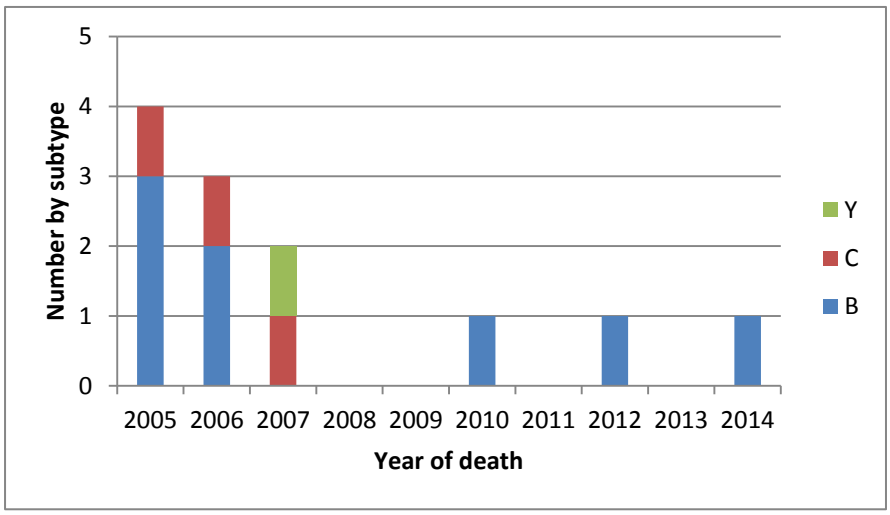
[1] All children are eligible for *H.influenzae* type b vaccine, but this *H.influenzae* type was unknown and the child was too young to be vaccinated
[2] Recommended but unfunded for meningococcal B vaccine on basis of age, not medical condition
[3] Funded for meningococcal C vaccine catch up program based on age, not medical condition
[4] Not recommended to be vaccinated due to immune compromise
[5] Funded under NIP for vaccination based on age not medical condition

## 4.3 Disease subtypes

### 4.3.1 Meningococcal disease

Most meningococcal deaths were due to meningococcal B disease, in keeping with the prevalence of serotype B meningococcal disease in NSW. Three meningococcal C deaths occurred in the early years of the review following introduction of the meningococcal C immunisation program (Figure 13).

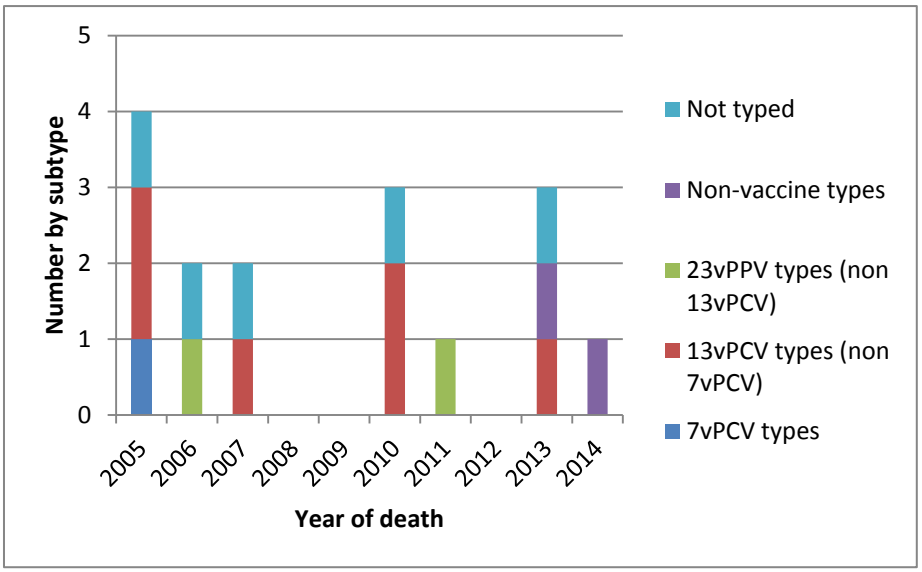
**Figure 13 Meningococcal disease subtype by year**




### 4.3.2 Pneumococcal disease

Pneumococcal disease subtype also varied by year (Figure 14). Most deaths were due to non-vaccine serotypes. One death from 19A occurred after the introduction of 13vPCV and one death occurred due to type 9V, present in the 7vPCV, six months after this vaccine was introduced.

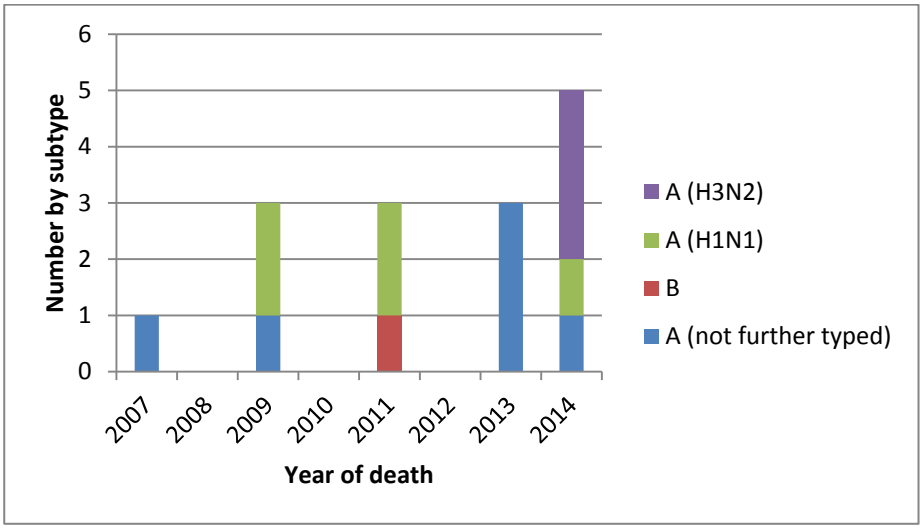
**Figure 14 Pneumococcal disease subtypes by year**



### 4.3.3 Influenza

Influenza deaths were predominantly due to Influenza A (Figure 15).

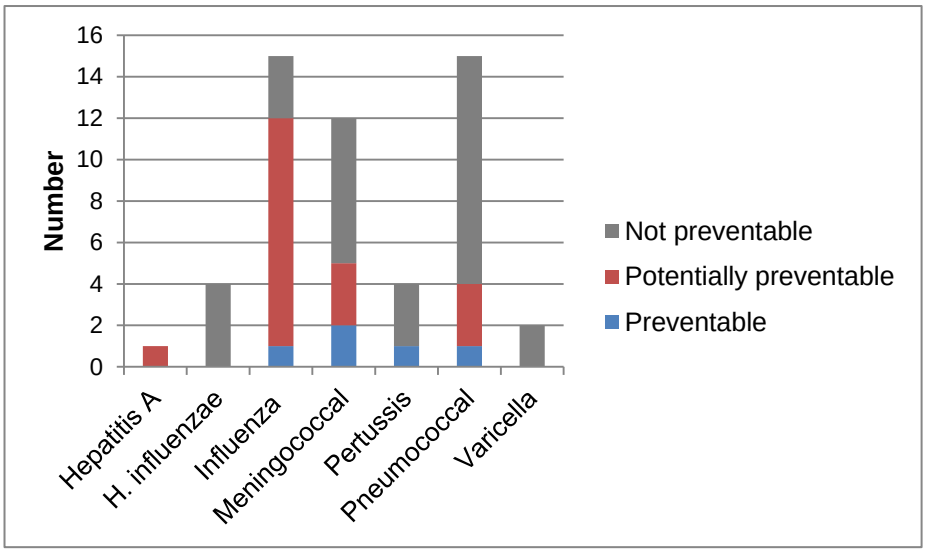
**Figure 15 Influenza subtypes by year**




## 4.4 Preventable and potentially preventable deaths

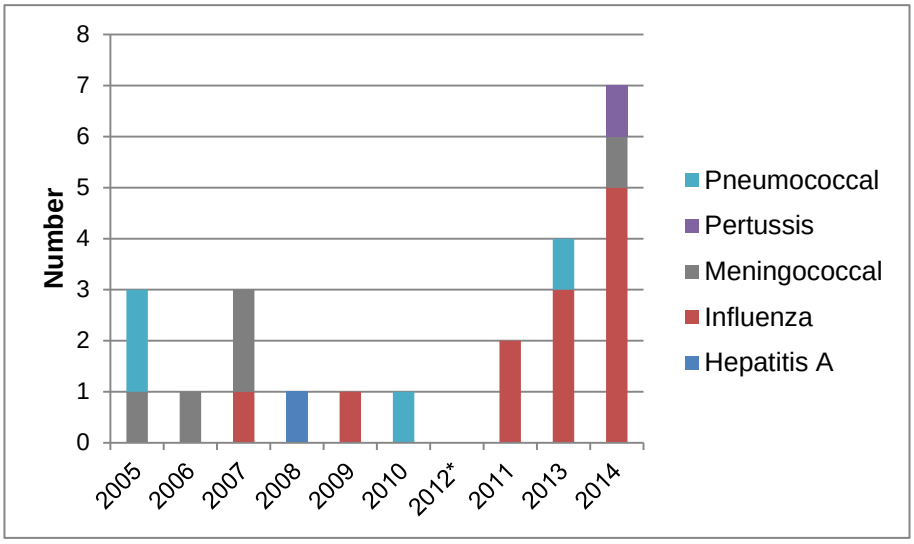
There was one death from pneumococcal disease in a fully vaccinated child, which was considered a vaccine failure that was not preventable by vaccination. Of all confirmed and probable deaths, the number of deaths considered preventable by vaccination is shown in Figure 16.

**Figure 16 Number of deaths of confirmed and probable cases considered preventable by vaccination 2005-2014**




Twenty-three deaths were considered preventable or potentially preventable by vaccination. The distribution of these deaths over the review period is shown in Figure 17.

**Figure 17 Preventable and potentially preventable deaths, 2005 – 2014***




*Eleven of twelve influenza cases were positive clinical samples; one was a post-mortem sample

### 4.4.1 Preventable deaths

Five deaths occurred in children eligible under the NIP for the relevant vaccine and were considered preventable under the framework in Figure 2. These included two meningococcal deaths (aged 5 and 17 years), one pneumococcal death (aged 14 months), one influenza death (aged 12 years) and one pertussis death (aged 8 months). These children were either unvaccinated (n=3) or had unknown vaccination status (n=2). Overall, three cases were eligible for vaccination through catch-up programs, including both meningococcal cases who were eligible for the meningococcal C catch up from 2003 and one case who was eligible for pneumococcal vaccine catch up. One influenza death occurred in a child with a high risk medical condition eligible for influenza vaccination. While parental views on immunisation are not always recorded, objection to immunisation was formally documented in one case.

### 4.4.2 Potentially preventable deaths

A further 18 deaths were considered potentially preventable as defined by the framework (Figure 2). For four deaths from influenza A, there was no additional subtyping so it was not possible to confirm whether the subtype was the same as the vaccine type. These deaths occurred in children aged five and over with high risk medical conditions and unknown vaccination status. Four had cerebral palsy along with other conditions. Among children without documented high risk medical conditions, five influenza deaths occurred in children aged between two and five years and two occurred in children over the age of five. Influenza deaths appeared to increase over the last few years of the study period, but this could be partially due to increased testing following the 2009 H1N1 pandemic season.

Two deaths occurred due to untyped *Streptococcus pneumoniae* (pneumococcal disease), one in a vaccinated but immunocompromised child. One hepatitis A death occurred following travel to a country for which vaccination was recommended. Three meningococcal deaths occurred: one type B after meningococcal B vaccine was available, and type Y and C when vaccines covering these subtypes were available but not recommended.

### 4.4.3 Non preventable deaths

Thirty deaths were considered not preventable through immunisation (Table 13). Two deaths from varicella were in children unable to be vaccinated due to impaired immune function, although it is unknown whether their family members were vaccinated. Seven deaths from pneumococcal disease occurred due to subtypes not covered by the 7vPCV then available. This included two deaths from non-vaccine serotypes and three deaths (before 2011) from serotypes in the 13vPCV but not the 7vPCV. Two deaths occurred due to strains in the 23vPPV in children with high-risk medical conditions. Two deaths from H1N1 influenza occurred in 2009 prior to the availability of the specific vaccine; both children were over the age of five but had high risk medical conditions so would have been eligible for the vaccine under the NIP.

Deaths from untyped *H.influenzae* were not considered preventable due to the low likelihood that the infecting strain was type b (Hib). The six meningococcal deaths were due to meningococcal B disease and occurred before the meningococcal B vaccine was available. Five of these six deaths were in infants under 12 months of age. Nine deaths were in children too young to be vaccinated (infants aged two months of age or less) (Table 12). Although not preventable through immunisation of the child, pertussis and influenza deaths may have been preventable through immunisation of the mother during pregnancy.

**Table 13 Reasons children could not be vaccinated for the disease of interest**

| | H.influenzae | Influenza | Meningococcal | Pertussis | Pneumococcal | Varicella |
|---|---|---|---|---|---|---|
| **Medical exemption** | | | | | | 2 |
| **Non-vaccine serotype** | | 2[1] | | | 7[3] | |
| **Too young** | | 1[4] | 1 | 3[4] | 4 | |
| **Vaccine not available** | 4 | | 6[2] | | | |

[1] These deaths would now be preventable as the H1N1 pandemic strain is now included in the vaccine
[2] All of these deaths were from meningococcal B, for which a vaccine is now available
[3] Three of these deaths would now be preventable through 13vPCV vaccination
[4] These deaths may be preventable through maternal immunisation

## 4.5 Deaths in cases classified as uncertain

The deaths described as preventable and not preventable above were a subset of cases classified as confirmed or probable. In cases classified as uncertain according to the case definition in Table 7, seven were coded as possible influenza and three as possible pneumococcal disease. Of the influenza cases, three were in three month old infants where the post mortem could not determine a clear cause of death but influenza was detected in respiratory swabs taken post-mortem. Four older children had other underlying causes of death likely to be primary, including bacterial infection (two cases), epilepsy and injury.

One of the pneumococcal cases was a three month old infant with a positive post-mortem lung culture sample but no evidence of pneumonia or meningitis. The two other pneumococcal cases had also sustained significant injury prior to death which was considered likely to be the primary cause of death, with pneumococcal disease a potential contributing cause

## 4.6 Deaths in children classified as non-cases

Nine cases were identified from the databases but then excluded as cases. These included cases with no laboratory evidence of the pathogen of interest. One death due to gastroenteritis with dehydration did not have any laboratory evidence to confirm the pathogen so it was not possible to determine whether this was due to rotavirus.

# 5. Discussion

## 5.1 Diseases causing the most deaths

### 5.1.1 Influenza

A large proportion of preventable and potentially preventable deaths were due to influenza. Five deaths occurred in children aged five and over with high-risk medical conditions who were eligible for funded vaccination. In addition, two children with high-risk medical conditions died from the H1N1 pandemic strain of influenza in 2009 prior to the specific vaccine becoming available (these deaths were considered not preventable as the vaccine was not available).

While influenza vaccination is recommended and funded under the NIP for children with high-risk medical conditions, who are at greater risk of severe disease and death,[7,66] studies have found low vaccine coverage in this group of around 40%.[15,67] The Australian Paediatric Surveillance Unit reported no vaccinated children among high-risk cases admitted with severe disease during September 2007.[68] One survey reported the main reason children did not receive the vaccine is that parents were not aware it was needed, although some did not get around to it or were advised not to have it. Of those children with high-risk medical conditions who were vaccinated, the most important factor was advice from a medical practitioner.[67]

Seven influenza deaths in our review occurred in children with no documented high-risk medical conditions, five of whom were between six months and five years of age. Studies of influenza hospitalisation have shown high rates of admission, including to intensive care, in previously healthy young children.[16,17,19,69] A study of influenza deaths during the 2009 H1N1 pandemic showed that, in Australia and overseas, a high proportion of children under 10 years did not have high-risk medical conditions.[70] One US study reported that children without high-risk medical conditions were more likely to die from influenza before hospital admission or within three days of symptom onset, compared to those with high-risk medical conditions.[66] Of all confirmed and probable cases of influenza in our review, four died before arrival at hospital; all of these cases were under five years of age and had no documented high-risk conditions.

While influenza vaccination is currently recommended in Australia for children under five years of age, it is not funded under the NIP, except for children with high risk medical conditions.[7] Coverage is known to be low outside WA (where it is funded), and in one NSW study was reported to be 14%.[15] None of 12 healthy children hospitalised with severe influenza nationally in September 2007 was vaccinated.[68] While the funded influenza vaccination program in Western Australia led to coverage of 40% in children under five in 2008 and 2009, this dropped to around 5% following an increase in adverse reactions to a specific brand of

influenza vaccine in 2010.[20] This vaccine brand is no longer recommended in young children.[71] The high proportion of healthy children among those suffering severe complications of influenza has led to calls for the vaccine to be funded for children under five.[17]

One influenza death occurred in a child under six months of age who was too young to be vaccinated. In addition, among cases where it was 'uncertain' (as per the case definition in Table 7) whether death was due to influenza, three deaths occurred in previously healthy infants under six months of age. At post-mortem examination, a cause of death for these three infants was not able to be determined, although all had laboratory evidence of influenza. These kinds of sudden deaths in infancy are thought to be due to many contributing causes. Although signs of infection are often found at autopsy in these cases, minor respiratory infection in infants are common and in many cases infection is not considered to be the only factor contributing to death.[72-74] The CDRT has completed a review of sudden unexplained death in infancy and is considering the process for investigation of these deaths in NSW.

These infants would have been too young to be vaccinated because the influenza vaccine cannot be given under 6 months of age. However, they may have been protected by immunisation of their mother during pregnancy (maternal vaccination) with antibody transfer and reduced influenza-related hospitalisation well documented among infants born to such mothers.[7] Influenza vaccination is currently recommended for pregnant women, both to reduce severe disease during pregnancy and to protect infants for six months after birth, and has been nationally funded since 2010.[6,7] Vaccination is also recommended for people who may transmit influenza infection to high risk groups, including household contacts, healthcare workers and childcare workers.[7]

### 5.1.2 Meningococcal disease

We identified 12 deaths from meningococcal disease which was consistent with the NSW VPD reports, based on NCIMS data, which are available for 2009 to 2013.[75-79] This is substantially less than the 26 deaths identified in NSW in children less than 15 years between 2000 and 2007; [80] the reduction in deaths is attributable to the meningococcal C vaccination program.[42]

Most cases of meningococcal disease in Australia are now caused by subtype B[42] and a vaccine is now available and recommended for young children, particularly those aged <24 months, adolescents aged 15-19 years, and those with specific high-risk medical conditions.[7] In our review, one case of meningococcal B disease was potentially preventable, as it occurred after the vaccine was available and recommended in Australia. Another six were not considered preventable as the vaccine was not available at that time and one additional case occurred in a child too young to be vaccinated. While the vaccine is currently available for private purchase, it has not been funded under the NIP because of uncertainties about the effectiveness of the vaccine when delivered as part of an immunisation program, particularly with regard to long-term protection and cost-effectiveness.[81]

While meningococcal disease is now rarely caused by subtype C, two deaths in our review occurred in children eligible for the catch-up program after the introduction of the meningococcal C vaccination program. Catch-up programs are offered when an immunisation program is first introduced, and offered to children outside the targeted age group. Coverage has been noted to be low in catch-up programs for other vaccines.[82-84]

### 5.1.3 Pertussis

One death in an eight month old, unvaccinated infant was considered preventable. Three infant pertussis deaths were not considered preventable at the time of death, as the infants were too young to be vaccinated. The two deaths occurring in 2011 and 2012 were also captured in the NSW vaccine preventable diseases reports.[75,76] Various strategies are recommended to reduce the risk of pertussis in young infants, including vaccination of close contacts to reduce exposure of the infant to pertussis (known as cocooning) and maternal vaccination.[39]

Vaccination of close contacts including household contacts and carers, healthcare workers and childcare workers is recommended in the Australian Immunisation Handbook.[7] Maternal vaccination leads to the transfer of antibodies to the newborn, providing protection in the early months before vaccination, and also reduces the chance that the mother will contact pertussis and pass it on to her infant.[7] It is considered the best strategy for protecting vulnerable infants from infection.[40] Maternal pertussis immunisation was recommended in the Australian Immunisation Handbook in April 2015 and subsequently provided free of charge by all states and territories, but was not funded nationally through the NIP.[7,40]

### 5.1.4 Pneumococcal disease

We reported 16 pneumococcal deaths, consistent with those reported in NSW Vaccine Preventable Disease reports based on NCIMS data for 2009 to 2013.[75-79] One death occurred in a fully vaccinated child, caused by a vaccine strain. This is a case of vaccine failure, which can occur as a result of an ineffective immune response.[7] This case was also reported in the NSW vaccine preventable disease report.[77] One death was considered preventable as it occurred due to strain 9V, which is present in the 7vPCV vaccine. The child was eligible for a catch-up program which commenced six months prior to the child's death. Four cases occurred in infants too young to be vaccinated.

Seven deaths were due to subtypes not present in the vaccine that was available at that time. Two deaths in our review were due to subtypes not present in any pneumococcal vaccine. Three deaths, occurring between 2007 and 2010, were due to subtypes (19A and 3) not present in the 7vPCV (available from 2005) that were later included in the 13vPCV vaccine, which was only available from 2011. An increase in IPD due to certain non-vaccine subtypes, particularly 19A, following introduction on 7vPCV is well documented as a serotype replacement phenomenon.[25] Despite this increase, the overall number of cases and deaths due to pneumococcal disease dramatically reduced since the introduction of the vaccine. In NSW, 27 children under five died from pneumococcal disease between 1998 and 2004, with only 3 deaths between 2005 and 2010.[85]

Two deaths in our review were due to subtypes (22F and 33F) that were not present in either 7vPCV or 13vPCV, but were present in the 23vPPV. For children with high-risk medical conditions, the 23vPPV was funded as a booster dose at 12 months of age from 2001 to 2005, and at 4 to 5 years of age from 2003. A booster dose was funded for Indigenous children in some states (not NSW) from 2001 to 2011.[26] Both deaths in our review occurred after 2005 and were in children under five years who had high-risk medical conditions, although in one case this condition was not diagnosed until after death. In one case the child was also Indigenous.

## 5.2 Risk factors

Fifteen of the 54 confirmed and probable cases occurred in infants under six months of age, reflecting both those too young to be vaccinated (10 infants), and the increase risk of severe infectious disease in that age group. Males were disproportionately affected, and other studies have shown that male sex is a risk factor for infant infectious disease deaths.[86] One third of deaths occurred in children with medical conditions known to increase the risk of severe disease.[7] However, it is concerning that two thirds occurred in children with no known high-risk medical conditions.

Deaths from meningococcal disease tended to occur in children residing in more disadvantaged regions. An association was shown between socio-economic status (including low education and income) and hospitalisation for infectious diseases in pre-school children in Denmark, despite universal health care and social benefits available in that country.[87] This association may be due to increased exposure to infection (for example, through crowding), decreased resistance to infection (for example, due to parental smoking) or access to care in groups with lower socioeconomic status.[87-89]

## 5.3 Data completeness

Review of deaths from any data source is limited by whether cases have been tested and diagnosed within the health system. Deaths may occur due to complications of an initial infection, and these complications may be diagnosed and recorded as the cause of death. Laboratory testing may not always be required at the time the patient receives care, and infections may not always be detected in the laboratory.[14]

Various data sources are available in Australia to examine deaths, but all have limitations.[3] We used two separate data sources for our review: the CDR (through the NSW Ombudsman) and NCIMS (through Health Protection NSW).

The CDRT applied ICD codes based on information gained from death certificates (from BDM), coroner's reports and other records. Classification of deaths using ICD coding is known to provide limited information.[14] Although we identified information from additional fields, specific infectious disease or laboratory data was not always available. Due to the large number of cases in the original CDR database, we assessed cases and included only those most likely to be due to diseases caused by a pathogen of interest. This assessment system only captured deaths where a specific pathogen was mentioned and excluded cases where a disease syndrome such as pneumonia or sepsis was identified without specific reference to the relevant pathogen. As a result, we may have underestimated of the number of deaths from the database. Collection of specific pathogen information in CDR fields would improve case ascertainment.

The use of NCIMS data to match information for the CDR cases and identify additional cases improved our ascertainment of relevant deaths over this period. Cases on NCIMS are classified using standardised case definitions based on laboratory, clinical and epidemiological criteria and allow for the accurate identification of vaccine preventable diseases caused by specific pathogens. Although this addresses a major limitation of the CDR database, recording of death in NCIMS is inconsistent. We noted that our cases were consistent with those reported in NSW vaccine preventable disease reports, which provides confidence that cases were adequately captured.[75-79] Confirmed cases were more likely to have been identified from both sources, suggesting that use of two sources increase the accuracy of case identification.

# 6. Conclusion

Deaths in children from potentially preventable infectious diseases continue to occur in NSW, particularly in young infants. There is scope to prevent further severe disease and death, particularly from influenza, meningococcal B and pertussis. In particular, it is important that clinicians are aware of recommendations for influenza and pneumococcal vaccination for high-risk children as well as maternal influenza and pertussis immunisation programs. These findings demonstrate that review of child deaths is important to inform future policy and practice.

# 7. Recommendations

1. Immunisation of children at high risk is recommended and provided free under the NIP:

    - General and specialist practitioners who care for children with medical conditions or compromised immune systems placing them at increased risk of influenza, invasive pneumooccal disease, meningococcal disease or Haemophilus influenzae type b disease should put mechanisms in place to ensure that additional vaccines specifically recommended in the Australian Immunisation Handbook are received.

        - General and specialist practitioners providing care for children with predisposing medical conditions should ensure responsibilities for immunisation are clear.
        - Examples of relevant mechanisms may include flags in hospital electronic records, amendments to medical practice software to issue alerts to general practitioners, configuration of immunisation registers to issue alerts to parents and providers, and routine provision of information to parents.

2. Vaccines against influenza and meningococcal B disease are recommended for all Australian children although not provided free of charge in 2016:

    - Parents wishing to reduce their child's risk of influenza and meningococcal B should discuss this with their general practitioner or other immunisation provider.

    - General practitioners and other immunisation providers should ensure that they are aware of the recommendations on influenza vaccination in the Australian Immunisation Handbook, including that influenza vaccination is recommended for infants and children aged from six months to less than five years due to the increased risk of hospitalisation and death in this group.

    - General practitioners and other immunisation providers should ensure that they are aware of the recommendations on meningococcal B vaccination in the Australian Immunisation Handbook, including that meningococcal B vaccination is recommended for infants and young children, particularly those aged <2 years, due to their higher risk of serogroup B meningococcal disease.

3. Immunisation of contacts is recommended for children at high risk of influenza, pertussis and varicella:

- General practitioners and specialists who care for infants aged under 6 months should be aware of the recommendation in the Australian Immunisation Handbook for pertussis vaccination of household contacts and carers of these infants, and should promote immunisation to these groups, particularly if vaccination has not been received in pregnancy.

- General practitioners and specialists who care for children at high risk of influenza (particularly those with a high-risk medical condition) should be aware of the recommendations in the Australian Immunisation Handbook to vaccinate household contacts and carers of these children and should actively promote immunisation to these groups.

- Facilities that provide health care or child care services for children who are at high risk influenza or infants at risk of pertussis should take steps to provide comprehensive occupational immunisation programs for their workers as per the recommendations in the Australian Immunisation Handbook.

- Specialists who care for children at risk of severe varicella infection should be aware of the recommendation in the Australian Immunisation Handbook to ensure household contacts without a history of varicella receive two doses of varicella vaccine and actively promote immunisation to this group.

**4.** Immunisation against pertussis and influenza is recommended during pregnancy and provided free in NSW:

- Health practitioners providing antenatal care should be aware that pertussis and influenza vaccine is provided free for pregnant women in NSW and that detailed information about this program can be obtained from the NSW Health website.[1,2]

- Pertussis and influenza vaccination during pregancy should be promoted and encouraged by general practitioners, obstetricians and midwives to reduce the risk of disease in young infants.

**5.** Children should receive vaccines for which they are eligible under immunisation catch up programs:

- Immunisation providers should ensure children receive all vaccines for which they are eligible under funded immunisation catch-up programs, for example through the use of electronic alerts or flags on medical records.

- Catch-up programs should be widely promoted to parents when new immunisation programs commence.

**6.** Travel immunisation should be provided as recommended:

- General practitioners should be aware of recommendations on vaccination for international travel in the Australian Immunisation Handbook that are relevant to children, including hepatitis A and BCG vaccines, and these should be actively promoted to parents.

**7.** Data collections on child deaths in NSW should be enhanced and cross-checked between sources:

- The CDRT should implement measures to improve identification and coding in the CDR of specific pathogens and isolation sites associated with VPDs to facilitate review of child deaths from infectious diseases in NSW.
- The CDRT and Health Protection NSW should engage in regular communication and cross-checking regarding child deaths from VPDs.
- The CDRT and Health Protection NSW should work with NSW Health Pathology in regard to standard protocols for testing for and notification of infectious diseases identified following a child's death.

# 8. References


1. NSW Health. Pregnant Women – Protect Your Newborn From Whooping Cough. Sydney: 2016. Available from: http://www.health.nsw.gov.au/immunisation/pages/wc-newborns.aspx (Accessed 29 July).

2. NSW Health. Information for antenatal care providers. Sydney: 2016. Available from: http://www.health.nsw.gov.au/Infectious/Influenza/Pages/hp_pregnancy_advice.aspx (Accessed 29 July).

3. Chiu C, Dey A, Wang H, et al. Vaccine preventable diseases in Australia, 2005 to 2007. *Commun Dis Intell Q Rep* 2010;34 Supp:S1-167.

4. Gidding H, Burgess M, Kempe A. A short history of vaccination in Australia. *Med J Aust* 2001;174:37-40.

5. Ward K, Hull BP, Leask J. Financial incentives for childhood immunisation - a unique but changing Australian initiative. *Med J Aust* 2013;198:590-2.

6. NCIRS. History of vaccination in Australia. Westmead: NCIRS; 2016. Available from: http://www.ncirs.edu.au/index.php/provider-resources/vaccination-history/ (Accessed 20 June).

7. Australian Technical Advisory Group on Immunisation. *The Australian Immunisation Handbook 10th edition 2013*. Canberra: Australian Government Department of Health; 2015.

8. Brotherton J, McIntyre P, Puech M, et al. Vaccine preventable diseases and vaccination coverage in Australia 2001 to 2002. *Commun Dis Intell Q Rep* 2004;28 Suppl 2:vii-S116.

9. Brotherton J, Wang H, Schaffer A, et al. Vaccine preventable diseases and vaccination coverage in Australia, 2003 to 2005. *Commun Dis Intell Q Rep* 2007;31 Suppl:S1-152.

10. Dey A, Knox S, Wang H, Beard FH, McIntyre PB. Summary of National Surveillance Data on Vaccine Preventable Diseases in Australia, 2008-2011. *Commun Dis Intell Q Rep* 2016;40 Suppl:S1-s70.

11. McIntyre P, Gidding H, Gilmour R, et al. Vaccine preventable diseases and vaccination coverage in Australia, 1999 to 2000. *Commun Dis Intell* 2002;Suppl:i-xi, 1-111.

12. Naidu L, Chiu C, Habig A, et al. Vaccine preventable diseases and vaccination coverage in Aboriginal and Torres Strait Islander people, Australia 2006-2010. *Commun Dis Intell Q Rep* 2013;37 Suppl:S1-95.

13. McIntyre P, Amin J, Gidding H, et al. Vaccine preventable diseases and vaccination coverage in Australia, 1993-1998. *Commun Dis Intell Q Rep* 2000;24:276-97.

14. Muscatello DJ, Amin J, MacIntyre CR, et al. Inaccurate ascertainment of morbidity and mortality due to influenza in administrative databases: a population-based record linkage study. *PLoS One* 2014;9:e98446.

15. Newcombe J, Kaur R, Wood N, et al. Prevalence and determinants of influenza vaccine coverage at tertiary pediatric hospitals. *Vaccine* 2014;32:6364-8.

16. D'Onise K, Raupach JC. The burden of influenza in healthy children in South Australia. *Med J Aust* 2008;188:510-3.

17. Khandaker G, Zurynski Y, Ridley G, et al. Clinical epidemiology and predictors of outcome in children hospitalised with influenza A(H1N1)pdm09 in 2009: a prospective national study. *Influenza Other Respir Viruses* 2014;8:636-45.

18. Poehling KA, Edwards KM, Weinberg GA, et al. The Underrecognized Burden of Influenza in Young Children. *N Eng J Med* 2006;355:31-40.

19. Milne B, Williams S, May M, et al. Infl uenza A associated morbidity and mortality in a Paediatric Intensive Care Unit. *Commun Dis Intell* 2004;28:504-9.

20. Blyth CC, Jacoby P, Effler PV, et al. Effectiveness of trivalent flu vaccine in healthy young children. *Pediatrics* 2014;133:e1218-25.

21. Owen R, Barr IG, Pengilley A, et al. Annual report of the National Influenza Surveillance Scheme, 2007. *Commun Dis Intell Q Rep* 2008;32:208-26.

22. Isaacs D. Lessons from swine flu: Pandemic, panic and/or pandemonium? *J Paediatr Child Health* 2010;46:623-6.

23. Plotkin S, Orenstein W, Offit P. *Vaccines 6th Edition*: Saunders; 2012.

24. Fitzgerald T, Massey P, Islam F. Changes in invasive pneumococcal disease serotypes in a regional area of Australia following three years of 7vPCV introduction. *Western Pac Surveill Response* 2012;3:33-8.

25. Williams SR, Mernagh PJ, Lee MH, Tan JT. Changing epidemiology of invasive pneumococcal disease in Australian children after introduction of a 7-valent pneumococcal conjugate vaccine. *Med J Aust* 2011;194:116-20.

26. National Centre for Immunisation Research & Surveillance. NCIRS vaccination history tables. 2015. Available from: http://ncirs.edu.au/immunisation/history/ (Accessed 5 June).

27. Bareja C, Toms C, Lodo K, De Kluyver R. Invasive pneumococcal disease in Australia, 2009 and 2010. *Communicable Diseases Intelligence* 2015;39:265-79.

28. Barry C, Krause VL, Cook HM, Menzies RI. Invasive pneumococcal disease in Australia 2007 and 2008. *Commun Dis Intell Q Rep* 2012;36:E151-65.

29. De Kluyver R. Invasive Pneumococcal Disease in Australia 2011 and 2012. Canberra: Department of Health,; 2015.

30. Roche P, Krause V, Cook H, et al. Invasive pneumococcal disease in Australia, 2005. *Commun Dis Intell Q Rep* 2007;31:86-100.

31. Roche PW, Krause V, Cook H, et al. Invasive pneumococcal disease in Australia, 2006. *Commun Dis Intell Q Rep* 2008;32:18-30.

32. Roche PW, Krause VL, Bartlett M, et al. Invasive pneumococcal disease in Australia, 2004. *Commun Dis Intell Q Rep* 2006;30:80-92.

33. Roche P, Krause V, Andrews R, et al. Invasive pneumococcal disease in Australia, 2002. *Commun Dis Intell Q Rep* 2003;27:466-77.

34. Roche P, Krause V, Bartlett M, et al. Invasive pneumococcal disease in Australia, 2003. *Commun Dis Intell Q Rep* 2004;28:441-54.

35. Roche P, Krause V. Invasive pneumococcal disease in Australia, 2001. *Commun Dis Intell Q Rep* 2002;26:505-19.

36. Wood N, Quinn H, Mc IP, Elliott EJ. Pertussis in infants: Preventing deaths and hospitalisations in the very young. *J Paediatr Child Health* 2008;44:161-5.

37. Chuk L, Lambert S, May M, et al. Pertusis in infants: How to protect the vulnerable? *Communicable Diseases Intelligence* 2008;32:440-56.

38. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J* 2005;24:S58-61.

39. Pillsbury A, Quinn H, Mc IP. Australian vaccine preventable diseases epidemiology review series: Pertussis, 2006-2012. *Communicable Diseases Intelligence* 2014;38:179-94.

40. Beard FH. Pertussis immunisation in pregnancy: a summary of funded Australian state and territory programs. *Commun Dis Intell Q Rep* 2015;39:E329-36.

41. Georgousakis M, Wang H, Quinn H, McIntyre P. Pertussis mortality in Australia – what has changed? *Manuscript submitted to Medical Journal of Australia* 2015.

42. Lahra M, Enriquez R. Annual Report of the Australian Meningococcal Surveillance Programme, 2014. Canberra: Deaprtment of Health 2015.

43. Australian Technical Advisory Group on Immunisation. Advice for immunisation providers regarding the use of Bexsero. Canberra:2015.

44. Simpkins D, Wood N, Jelfs J, et al. Modern trends in mortality from meningococcal disease in Australia. *Pediatr Infect Dis J* 2009;28:1119-20.

45. Chiew M, Dey A, Martin N, et al. Australian vaccine preventable disease epidemiological review series: measles 2000-2011. *Commun Dis Intell Q Rep* 2015;39:E1-9.

46. Huppatz C, Kelly P, Levi C, et al. Encephalitis in Australia, 1979-2006: Trends and aetiologies. *Commun Dis Intell* 2009;33:192-7.

47. Najjar Z, Hope K, Clark P, et al. Sustained outbreak of measles in New South Wales, 2012: risks for measles elimination in Australia. *Western Pacific Surveillance Response* 2014;5.

48. Hviid A, Rubin S, Muhlemann K. Mumps. *Lancet* 2008;371:932-44.

49. Chan J, Dey A, Wang H, Martin N, Beard F. Australian vaccine preventable disease epidemiological review series: rubella 2008-2012. *Commun Dis Intell Q Rep* 2015;39:E19-26.

50. Chant KG, Sullivan EA, Burgess MA, et al. Varicella-zoster virus infection in Australia. *Australian and New Zealand Journal of Public Health* 1998;22:413-8.

51. Macartney K, Burgess M. Varicella Vaccination in Australia and New Zealand. *JID* 2008;197:S191-5.

52. Marshall HS, McIntyre P, Richmond P, et al. Changes in patterns of hospitalized children with varicella and of associated varicella genotypes after introduction of varicella vaccine in Australia. *Pediatr Infect Dis J* 2013;32:530-7.

53. Gilbert G, Johnson P, Clements D. Clinical manifestations and outcome of Haemophilus influenzae type b disease. *J Paediatr Child Health* 1995;31:99-104.

54. Harris A, Hendrie D, Bower C, et al. The burden of Haemophilus influenzae type b disease in Australia and an economic appraisal of the vaccine PRP-OMP. *Med J Aust* 1994;160:483-8.

55. Herceg A. The decline of Haemophilus influenzae type b disease in Australia. *Communicable Diseases Intelligence* 1997;21:173-6.

56. Dey A, Wang H, Menzies R, Macartney K. Changes in hospitalisations for acute gastroenteritis in Australia after the national rotavirus vaccination program. *Med J Aust* 2012;197.

57. Adler N, Mahony A, Friedman N. Diphtheria: forgotten, but not gone. *Intern Med J* 2013;43:206-10.

58. Stewardson AJ, Roberts JA, Beckett CL, et al. Imported case of poliomyelitis, Melbourne, Australia, 2007. *Emerg Infect Dis* 2009;15:63-5.

59. Donnan EJ, Fielding JE, Gregory JE, et al. A multistate outbreak of hepatitis A associated with semidried tomatoes in Australia, 2009. *CID*;54:775-81.

60. Khuroo M. Viral hepatitis in international travellers: risks and prevention. *Int J Antimicrob Agents* 2003;21:143-52.

61. Naidu L, Chiu C, Habig A, et al. Vaccine preventable diseases and vaccination coverage in Aboriginal and Torres Strait Islander people, Australia 2006-2010. *Commun Dis Intell Q Rep* 2008;37 Suppl:S1-95.

62. NCIRS. Evaluation of the National Human Papillomavirus Vaccination Program. Canberra: Department of Health.; 2014.

63. Centre for Epidemiology and Evidence. Health Statistics NSW. Sydney. Available from: www.healthstats.nsw.gov.au.

64. Australian Bureau of Statistics. Table generated 12 May 2016 using Australian Demographic Statistics, Estimates of Aboriginal and Torres Strait Islander Australians, Jun 2011, NSW, cat. no. 3238055001DO006_201107, data cube: SuperTABLE. 2013. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3238.0.55.001June%202011?OpenDocument

65. Australian Bureau of Statistics. Estimates of Aboriginal and Torres Strait Islander Australians, Jun 2011. Canberra: 2013. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3238.0.55.001 (Accessed 20 May).

66. Wong K, Jain S, Blanton L, et al. Influenza-Associated Pediatric Deaths in the United States, 2004–2012. *Paediatrics* 2013;132:796-804.

67. Hale K. Survey of influenza immunisation uptake in high-risk children. *J Paediatr Child Health* 2006;42:321-.

68. Zurynski Y, Lester-Smith D, Festa M, et al. Enhanced surveillance for serious complications of influenza in children: role of the Australian Paediatric Surveillance Unit. *Communicable Diseases Intelligence* 2008;32:71-6.

69. Lester-Smith D, Zurynski Y, Booy R, et al. The burden of childhood influenza in a tertiary paediatric setting. *Communicable Diseases Intelligence* 2009;33:209-15.

70. Vaillant L, La Ruche G, Tarantola A, Barboza P. Epidemiology of fatal cases assocaited with pandemic H1N1 influenza 2009. *Eurosurv* 2009;33:pii=19309.

71. TGA. Flu vaccine: 2016 seasonal influenza vaccines for use in children. Canberra: Department of Health.; 2016. Available from: https://www.tga.gov.au/alert/flu-vaccine-2016-seasonal-influenza-vaccines-use-children (Accessed 20 June).

72. Mitchell E. What is the mechanism of SIDS? Clues from epidemiology. *Dev Psychobiol* 2009;51:215-22.

73. Vege A, Ole Rognum T. Sudden infant death syndrome, infection and inflammatory responses. *FEMS Immunol Med Microbiol* 2004;42:3-10.

74. Blood-Siegfried J. The role of infection and inflammation in sudden infant death syndrome. *Immunopharmacology and Immunotoxicology* 2009;31:516-23.

75. Rosewell A, Spokes PJ, Gilmore R. NSW Annual Vaccine-Preventable Disease Report, 2011. *NSW Public Health Bulletin* 2012;23:171-8.

76. Rosewell A, Spokes PJ, Gilmore R. New South Wales annual vaccine preventable disease report, 2012. *Western Pacific Surveillance Response* 2014;5.

77. Rosewell A, Spokes PJ, Gilmore R. NSW vaccine preventable diseases report, 2013. *Western Pacific Surveillance Response* 2015;6.

78. Spokes PJ, Gilmore R. NSW Annual Vaccine-Preventable Disease Report, 2009. *NSW Public Health Bulletin* 2010;21:197-209.

79. Spokes PJ, Gilmore R. NSW Annual vaccine preventable diseases report, 2010. *NSW Public Health Bulletin* 2011;22:171-8.

80. Gibson A, Jorm L, Mc IP. Using linked birth, notification, hospital and mortality data to examine false-positive meningococcal disease reporting and adjust disease incidence estimates for children in New South Wales, Australia. *Epidemiol Infect* 2015:1-10.

81. PBS. Multicomponent meningococcal group b vaccine (4cmenb); 0.5 mL suspension for injection pre-filled syringe; Bexsero®: Public summary July 2015 PBAC meeting. Canberra: Department of Health.; 2015. Available from: http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2015-07/mulit-component-meningococcal-group-b-vaccine-psd-july-2015.

82. Ward K, Dey A, Hull B, et al. Evaluation of Australia's varicella vaccination program for children and adolescents. *Vaccine* 2013;31:1413-9.

83. Hull BP, Dey A, Menzies RI, Brotherton JM, McIntyre PB. Immunisation coverage annual report, 2011. *Commun Dis Intell Q Rep* 2013;37:E291-312.

84. Hull BP, Dey A, Menzies RI, Brotherton JM, McIntyre PB. Immunisation coverage, 2012. *Commun Dis Intell Q Rep* 2014;38:E208-31.

85. Lowbridge C, McIntyre PB, Gilmour R, et al. Long term population impact of seven-valent pneumococcal conjugate vaccine with a "3+0" schedule-How do "2+1" and "3+1" schedules compare? *Vaccine* 2015;33:3234-41.

86. Person MK, Esposito DH, Holman RC, Mehal JM, Stoll BJ. Risk factors for infectious disease death among infants in the United States. *Pediatr Infect Dis J* 2014;33:e280-5.

87. Biering-Sorensen S, Sondergaard G, Vitting Andersen K, Andersen AM, Mortensen LH. Time trends in socio-economic factors and risk of hospitalisation with infectious diseases in pre-school children 1985-2004: a Danish register-based study. *Paediatr Perinat Epidemiol* 2011;26:226-35.

88. Goldacre MJ, Wotton CJ, Maisonneuve JJ. Maternal and perinatal factors associated with subsequent meningococcal, Haemophilus or enteroviral meningitis in children: database study. *Epidemiol Infect* 2014;142:371-8.

89. Murray RL, Britton J, Leonardi-Bee J. Second hand smoke exposure and the risk of invasive meningococcal disease in children: systematic review and meta-analysis. *BMC Public Health* 2012;12:1062.

## A. Appendix: National Immunisation Schedule

Australian Government
Department of Health

# National Immunisation Program Schedule

**From February 2016**

| Child programs | |
|---|---|
| **Age** | **Vaccine** |
| **Birth** | • Hepatitis B (hepB)[a] |
| **2 months** | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)<br>• Pneumococcal conjugate (13vPCV)<br>• Rotavirus |
| **4 months** | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)<br>• Pneumococcal conjugate (13vPCV)<br>• Rotavirus |
| **6 months** | • Hepatitis B, diphtheria, tetanus, acellular pertussis (whooping cough), *Haemophilus influenzae* type b, inactivated poliomyelitis (polio) (hepB-DTPa-Hib-IPV)<br>• Pneumococcal conjugate (13vPCV)<br>• Rotavirus[b] |
| **12 months** | • *Haemophilus influenzae* type b and meningococcal C (Hib-MenC)<br>• Measles, mumps and rubella (MMR) |
| **18 months** | • Diptheria, tetanus, pertussis (whooping cough) (DTPa)<br>• Measles, mumps, rubella and varicella (chickenpox) (MMRV) |
| **4 years** | • Diphtheria, tetanus, acellular pertussis (whooping cough) and inactivated poliomyelitis (polio) (DTPa-IPV)<br>• Measles, mumps and rubella (MMR) (to be given only if MMRV vaccine was not given at 18 months) |
| **School programs** | |
| **10–15 years** (contact your State or Territory Health Department for details) | • Varicella (chickenpox)[c]<br>• Human papillomavirus (HPV)[d]<br>• Diphtheria, tetanus and acellular pertussis (whooping cough) (dTpa) |
| **At-risk groups** | |
| **Aboriginal and Torres Strait Islanders** | |
| **12–18 months** (in high risk areas)[e] | • Pneumococcal conjugate (13vPCV) |
| **12–24 months** (in high risk areas)[f] | • Hepatitis A |
| **6 months to less than 5 years** | • Influenza (flu) |
| **15 years and over** | • Influenza (flu)<br>• Pneumococcal polysaccharide (23vPPV) (medically at risk) |
| **50 years and over** | • Pneumococcal polysaccharide (23vPPV) |
| **Other at-risk groups** | |
| **6 months and over** (people with medical conditions placing them at risk of serious complications of influenza) | • Influenza (flu) |
| **12 months** (medically at risk)[e] | • Pneumococcal conjugate (13vPCV) |
| **4 years** (medically at risk)[e] | • Pneumococcal polysaccharide (23vPPV) |
| **Pregnant women** (at any stage of pregnancy) | • Influenza (flu) |
| **65 years and over** | • Influenza (flu)<br>• Pneumococcal polysaccharide (23vPPV) |

* Please refer to reverse for footnotes

IMMUNISATION

### Footnotes to the National Immunisation Program (NIP) Schedule

a. Hepatitis B vaccine: should be given to all infants as soon as practicable after birth. The greatest benefit is if given within 24 hours, and must be given within 7 days.

b. Rotavirus vaccine: third dose of vaccine is dependent on vaccine brand used. Contact your State or Territory Health Department for details.

c. Varicella vaccine: contact your State or Territory Health Department for details on the school grade eligible for vaccination.

d. HPV vaccine: is for all adolescents aged between 12 and 13 years. Contact your State or Territory Health Department for details on the school grade eligible for vaccination.

e. Pneumococcal vaccine:
   i. Medically at risk children require a fourth dose of 13vPCV at 12 months of age and a booster dose of 23vPPV at 4 years of age.
   ii. Aboriginal and Torres Strait Islander children require a fourth dose of pneumococcal vaccine (13vPCV) at 12-18 months of age for children living in high risk areas (Queensland, Northern Territory, Western Australia and South Australia). Contact your State or Territory Health Department for details.

f. Hepatitis A vaccine: two doses of Hepatitis A vaccine for Aboriginal and Torres Strait Islander children living in high risk areas (Queensland, Northern Territory, Western Australia and South Australia). Contact your State or Territory Health Department for details.

## Further information

Further information and immunisation resources are available from the Immunise Australia Program website at **www.immunise.health.gov.au** or by contacting the infoline on **1800 671 811.**

You should contact your State or Territory Health Department for further information on the program specific to your State or Territory:

| State/Territory | Contact Number |
|---|---|
| Australian Capital Territory | (02) 6205 2300 |
| New South Wales | 1300 066 055 |
| Northern Territory | (08) 8922 8044 |
| Queensland | 13 HEALTH (13 4325 84) |
| South Australia | 1300 232 272 |
| Tasmania | 1800 671 738 |
| Victoria | 1300 882 008 |
| Western Australia | (08) 9321 1312 |

IMMUNISE AUSTRALIA PROGRAM

**A joint Australian, State and Territory Government initiative**

**www.immunise.health.gov.au**

All information in this publication is correct as at February 2016

11178 February 2016

## B. **Appendix:** Infectious Diseases CDRT Data Assessment Protocol

***What is the likelihood that the case is associated with a disease of interest?***

1. ***Highly Likely***
2. ***Moderately Likely***
3. ***Possible***
4. ***Unlikely***

1. ***Highly Likely***

   i. [1]Any field on the Infectious Disease CDRT dataset names a specific disease of interest or pathogen or interest

2. ***Moderately Likely***

   ii. As above but further clinical review is required to confirm that it is a disease of interest

3. ***Possible***

   iii. Any field names a [2]syndrome of interest without identifying a causative agent AND the individual is > 2 months of age

4. ***Unlikely***

   iv. Any field names a [2]syndrome of interest without identifying a causative agent AND the individual is < 2 months of age

   v. A disease of interest does not appear in any field and if a syndrome of interest is present, a cause is identified

*[1]**any field** incorporates the following: International Classification of Disease (ICD) Chapter Description, BDM cause of death (COD), additional cause of death (ACOD), Coroner COD and Case Notes*

*[2]**syndrome of interest*** refers to a collection of syndromes that may be associated with a VPD and includes (but is not limited to) the following;

| Syndrome | Potential VPD |
|---|---|
| **1.** gastroenteritis | rotavirus |
| **2.** pneumonia, bronchopneumonia, respiratory tract infection, bronchitis, bronchiolitis | influenza, pneumococcal, meningococcal, varicella, Hib, measles, pertussis, varicella, diphtheria |
| **3.** meningitis | pneumococcal, meningococcal, varicella, Hib, polio |
| **4.** encephalitis | pertussis, measles, mumps, rubella, varicella, polio |
| **5.** septicaemia, sepsis | pneumococcal, meningococcal, Hib, varicella |
| **6.** myocarditis, endocarditis | influenza, mumps, viral hepatitis, varicella, streptococci, meningococci, rubella, diphtheria |
| **7.** enterovirus | polio |