Welcome to this special forum on Pertussis and Pneumococcal Disease from the 9th New Zealand Immunisation Conference and Pre-Conference Workshop 2015, which was hosted at WINTEC in Hamilton on 4-5 September 2015.

The review presents selected highlights from the meeting focusing on pertussis and pneumococcal disease and is intended as an education resource for health professionals involved in the prevention of vaccine-preventable diseases including paediatricians, GPs, nurses, midwives, and pharmacists.

DAY 1 CONCURRENT SESSION 1: ASPECTS OF PERTUSSIS IMMUNISATION
Chair: Asmitha Patchay

Influencing factors considered by women regarding the pertussis-containing (Tdap) vaccine during pregnancy

Linda Hill, Clinical Nurse Consultant, Plunket

New Zealand experienced a major epidemic of pertussis from September 2011 to January 2014. In response to the increased notifications, the Tdap vaccine was funded for pregnant women 28-38 weeks’ gestation.

This quantitative, retrospective, observational study was undertaken to explore the influencing factors that have the greatest impact on the decisions of women to accept or decline immunisation during pregnancy. The study utilised a self-administered survey, with the target population being all post-partum women in the Canterbury DHB region of New Zealand. The women were identified from birth notifications between June and October, 2013. The survey was mailed post-partum within 1-2 days of an infant birth so as not to influence maternal choices on vaccination during the pregnancy.

A total of 596 of 1883 women completed the survey resulting in a 31.6% response rate, which is a respectable response for a postal and self-reported survey. The mean age of respondents was 30-33 years, with lower representation from those aged <29 years. The ethnicity of respondents was primarily European. Of the 596 respondents, 441 (74.1%) received the vaccine during pregnancy, 154 (25.9%) were not vaccinated and one could not remember if she had received the vaccine.

The main influencing factors for women who accepted the Tdap vaccine during pregnancy were:

• Desire to protect their baby (96%).
• Health professional’s recommendation (84%).
• Awareness of the threat of pertussis in the community (50%).
• Awareness that the vaccine was available and funded (43%).

Conversely, for women who did not receive the Tdap vaccine during pregnancy the main influencing factors were:

• Being unaware of the availability of the vaccine (73%).
• Fear of side effects (68%).
• Doubt regarding vaccine effectiveness (56%).
All participants were also surveyed to identify whether the information on maternal immunisation that they received was encouraging or discouraging and to identify the source of the information. The majority of respondents reported receiving encouraging information from midwives (54.9%), followed by general practitioners (37.9%), and practice nurses (11.7%). Interestingly, GPs were reported as the largest source discouraging information (40.8%). Overall, though, the participants were largely not discouraged (37.8%). The survey did not ask for details of the discouraging information provided by healthcare professionals. Of the 441 women who were vaccinated, 7.9% had received discouraging information from a GP compared with 60.1% of the 154 women who were not vaccinated during their pregnancy (p<0.001). Of the women who did not receive the vaccine, 58% would have had the vaccine if it had been offered.

Based on these results, the recommended strategies to increase vaccine uptake in pregnancy are to raise awareness and increase promotion of maternal vaccination, establish a health target, provide GP education, add a GP funded visit (i.e. additional to current ante-natal primary care) to discuss maternal and infant immunisation or administer the vaccine, and to enable pharmacists and midwives to be able to administer funded vaccines.

**Take-home messages**
- Vaccine uptake is strongly associated with the recommendations of health professionals.
- An unequivocal positive recommendation for maternal Tdap immunisation from a health professional is a major factor influencing pregnant women and would likely improve the uptake of the vaccine.
- A sizeable proportion of health professionals are giving women negative or no information on vaccination during pregnancy and the reasons for this need to be explored.
- There is a need to raise awareness of maternal vaccination and improve access to it.

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**Use in Pregnancy (Category B1)**

Non-clinical data obtained with Boostrix® reveal no specific hazard for humans based on conventional studies of embryo-foetal development in rats and rabbits, and also of parturition and postnatal toxicity in rats (up to the end of the lactation period).

As with all inactivated vaccines, one does not expect harm to the foetus. However, adequate human data on use during pregnancy are not available. Therefore, Boostrix should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the foetus.

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**Pertussis mortality in Australia: implications on national policy**

*Dr Melina Georgousakis, Senior Research Officer, National Centre for Immunisation Research and Surveillance, Australia*

Changes over the long term in mortality due to pertussis have not been well studied in Australia. This retrospective study reviewed deaths attributable to pertussis captured over a 47-year period, by age, to inform policy on the control of pertussis.

National pertussis death data was obtained from two routine passive collection data sources:

1. Death certificate data where pertussis was coded as the underlying cause of death, which was obtained from the Australian Institute of Health and Welfare via the Australian Bureau of Statistics (ABS; 1967-2006).
2. Death as an outcome of notified cases, which was obtained from the National Notifiable Disease Surveillance System (NNDSS; 1993–2013).

The number and rate per million population for deaths recorded as being attributable to pertussis were analysed by time period and age group. Data from these two sources covered a 47-year time span (1967-2013), which included an overlap of 14 years (1993-2006) that was analysed for concordance of mortality data from the two passive data collection systems. Duplicate deaths were removed to provide a single consistent data set over the entire 14-year overlap period, which showed improving concordance between the two surveillance systems, especially in the latter half of the period.

During 1967-2013, a total of 86 deaths reported as being due to pertussis were identified, including 59 deaths from the ABS and 27 from the NNDSS. There were ten deaths captured in both surveillance systems during the 14-year overlap and removal of these duplicate deaths resulted in 76 actual deaths due to pertussis in total. The majority of deaths (80%, n=61) were in infants. There was a significant increase in the proportion of deaths recorded in infants aged <2 months, who are too young to be vaccinated, from 19% in 1967-1983 to 67% in 2004-2013 (p=0.001). In contrast, there was a disappearance of mortality in older age children, with the proportion of pertussis deaths in children aged 1 to <5 years decreasing from 19% (n=5) in 1967-1983 to 0% in the latest decade. No deaths were recorded in persons aged >70 years over the period 1967-1983; however, this age group accounted for 25% of deaths recorded during 2004-2013.

There were no changes in the infant and all-age pertussis mortality rates over the 47-year study period, particularly in the last 5 years where there has been increased detection of pertussis cases due to the introduction of PCR and increased testing. There has, however, been an apparent distribution change in the age that the deaths are occurring. There have been a number of changes in pertussis immunisation policy over this period aimed at protecting vulnerable age groups. In 2003, a single dose of pertussis vaccine was recommended for contacts of infants. More recent recommendations (2013) have been a booster dose in adults aged ≥65 years to address waning immunity and the introduction of maternal immunisation as an alternative to cocooning. In 2015, the 18-month booster dose was reintroduced to deal with the increased pertussis notifications in children prior to their 4-year booster dose and vaccination in the third-trimester of pregnancy was recommended due to strong evidence of the effectiveness of this measure in reducing pertussis in the youngest of infants.

**Take-home messages**
- The majority of pertussis deaths in Australia are occurring in the vulnerable age groups of infants aged <2 months and the elderly.
- The Australian Immunisation Handbook recommends pertussis vaccination to protect both of these vulnerable populations.

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Pertussis control strategies: a consistent approach for New Zealand

Diana Murfitt, Senior Advisor, Immunisation Team, Ministry of Health

The role of pertussis immunisation is to protect those most at risk. In the most recent pertussis outbreak in New Zealand, which peaked between August 2011 and December 2013, the highest notification rates were infants aged <1 year, with nearly half of those cases requiring hospitalisation. Māori and Pacific infants aged <1 year had the highest incidence rates and were more likely to be hospitalised. There were three notified deaths from pertussis: two infants too young to be immunised and another that had chronic co-morbidities. In 2013, PHARMAC funded pertussis immunisation of pregnant women between 28 and 38 weeks gestation as a part of an epidemic control strategy. Immunisation coverage at age 8 months has increased from 83% in June 2012 to 93% in 2015.

In April 2015, the Ministry of Health convened a strategy workshop, Pertussis Control Strategies: A Consistent Approach for New Zealand, to discuss pertussis disease control. The primary objective of the workshop was to devise strategies to minimise the impact of pertussis on infants aged >1 year. Focussing on the National Immunisation Schedule (NIS), the workshop discussions targeted five key areas: i) NIS timing and doses; ii) immunisation coverage, timeliness, and service delivery; iii) antenatal pertussis immunisation; iv) data surveillance and reporting; and v) methods of communication. The key workshop discussions included:

- The NIS should be reviewed regularly, especially with regard to the changing epidemiology of pertussis infection.
- The NIS is in line with international recommendations for the control of severe pertussis in childhood and no changes are required at this time, including:
  - The timing of the primary course, i.e. at 6 weeks, 3 months, and 5 months, is appropriate.
  - There is no evidence a toddler booster needs to introduced.
  - The booster dose timings at ages 4 and 11 years are appropriate.
  - There is no need to change to whole cell pertussis vaccine on the NIS.
- Effective cocooning strategies should require booster doses for all close contacts (caregivers as well as parents); antenatal immunisation appears to be superseding cocooning.
- Barriers to information and advice for Māori and Pacific peoples, and pregnant woman in particular, need to be removed.
- Importance of ensuring on-time delivery of not only the first vaccine dose but also the second dose in infants.
- Providers need to have courageous conversations with parents who are thinking of declining vaccination for themselves and their children.
- The National Immunisation Register (NIR) has to record ‘whole of life’ vaccinations and must be accessible to all immunisation providers.
- A review of the evidence on antenatal immunisation is required to ensure policies and systems maximise its implementation, promotion, and equity of coverage.
- In terms of the promotion of antenatal immunisation messages, women prefer to be informed via social media and SMS (i.e. text messages) rather than pamphlets.
- Consider funded GP visits in the first trimester and antenatal period and for general practice to place more emphasis on recalling pregnant women for pertussis immunisation.
- Healthcare professionals need high-quality detailed information so that they can have confidence when discussing the safety and efficacy of immunisation with pregnant women.
- Pregnant women need information that addresses their concerns around the safety of pertussis immunisation in pregnancy.
- Make better use of existing data to develop a more complete picture of pertussis control in New Zealand, including epidemiology, immunity, and vulnerable populations.

Take-home messages

- The Workshop concluded that the focus of pertussis control in New Zealand is still on protecting the most vulnerable.
- The current NIS is working well to prevent severe pertussis in childhood.
- The greatest disease burden is in infants aged <2 months, particularly among Māori and Pacific peoples and those living in deprived regions.
- Infants too young to be immunised are likely to benefit from antenatal immunisation.
- Greater effort is needed to communicate and educate the healthcare sector and parents to encourage antenatal immunisation and improve vaccine coverage and timeliness.

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Microbiology of otitis media and nasopharyngeal flora in children in the era of changing pneumococcal vaccination

Dr Emma Best, Paediatric Infectious Diseases Specialist, Starship Children's Hospital and Senior Lecturer, Department of Paediatrics, University of Auckland

OM is one of the most common infections in childhood, with 80% of children having experienced an episode of OM by their third birthday. It is also a recurrent infection as indicated by one-third of children having had >6 episodes of OM by age 7 years. It is not surprising then that OM is the most common reason for antibiotic prescriptions and ventilation tube (grommet) surgery in young children. The presence of bacteria in the nasopharyngeal passages is necessary for OM to occur and the three primary pathogens implicated are Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae.

New Zealand included PCV10 on its NIS for three years and the potential impact of this specific vaccine on OM incidence is of interest. Hence, the aim of this descriptive study was to characterise the microbiology of middle ear fluid and nasopharyngeal carriage in children during a period of changing PCV schedule by comparing a cohort vaccinated with PCV7 with a cohort that received PCV10.

Middle ear fluid and nasopharyngeal samples from children aged <3 years with recurrent OM were collected at the time of grommet surgery at three major New Zealand centres (two in Christchurch and one in Auckland) during May-November 2011 (phase 1; pre-PCV10 introduction cohort) and May-November 2014 (phase 2; post-PCV10 introduction cohort). Samples were also obtained from age-matched non-OM-prone comparison groups and the parents of all participating children completed a questionnaire on risk-factors for ear disease as well as providing a NP sample. Enrolment included 462 patients in phase 1 (325 children undergoing grommet surgery and 137 controls) and 473 patients in phase 2 (319 and 154, respectively). There were no significant differences between the groups at baseline. Children with ear disease were more likely to attend childcare, have a family history of glue ear, and use of antibiotics in the previous month.

In terms of the nasopharyngeal microbiology, children with a history of OM had a higher rate of carriage of any of the primary three pathogens than children with no history of ear disease. Children with ear disease were more likely to be carrying non-typeable H. influenzae and S. pneumoniae than the children without ear disease and the proportion of children carrying these in the nasopharynx did not change across time periods. In terms of the middle ear microbiology, whether determined by culture or PCR, non-typeable H. influenzae was the most commonly identified pathogen in middle ear fluid samples, followed by M. catarrhalis, and S. pneumoniae, which did not change across time periods. Non-typeable H. influenzae was also the dominant pathogen in nasopharyngeal samples and this did not change across time periods.

Prior to introduction of PCV10, 19F was the most prevalent S. pneumoniae serotype found in the nasopharynx from both cohorts whereas serotype 19A was the more commonly identified serotype in both middle ear fluid and nasopharyngeal samples after PCV10 introduction.

Impact of conjugate pneumococcal vaccines on otitis media-related hospitalisations in New Zealand

Helen Petousis-Harris, Senior Lecturer, Department of General Practice and Primary Health Care and Director of Research, Immunisation Advisory Centre, University of Auckland

S. pneumoniae is a common pathogen in cases of OM and ACP. New Zealand has a 5- to 10-fold higher rate of pneumonia than in the US, with Māori and Pacific children being disproportionately represented, and the rate of hospitalisations for lower respiratory tract infection having increased steadily over the period 2000-2012 in the poorest of children (aged 0- to 14-years). These observations suggest a high burden of pneumococcal disease in New Zealand, with a strong ethnicity and deprivation bias. Immunisation coverage does, however, appear to be closing the inequity gap.

Based on the hypothesis that the use of PCVs would have an impact on ACP- and OM-related hospitalisations, the aim of this study was to describe the burden of severe pneumococcal disease in New Zealand infants and children and to report on the impact of the PCV vaccination programme on rates of disease.

The population of interest was children aged <6 years born over an 8-year period (2006-2013) and who were included in the National Immunisation Register (NIR). Data was sourced from the National Health Index Database, NIR, National Minimal Dataset (NMDS; hospital events), and Notifiable Diseases Surveillance Database (EpiSurv). The effect of PCV7 and PCV10 on IPD-, ACP-, and OM-related hospitalisations was analysed using Poisson regression comparing vaccine time periods, i.e. pre-vaccine period up to 2008, the PCV7 period up to 2011, and PCV10 period up to 2014.

The study population involved 362,000 children. Since the introduction of PCV7 and PCV10, there has been an overall downward trend in hospitalisations for IPD, ACP and OM, but with dramatic reductions being seen in Māori and Pacific children. For example, there was a significant 70% decline in IPD hospitalisations among Māori and Pacifica children and a 40% decline in OM hospitalisations among Māori children. Substantial declines in hospitalisations were also seen in groups of greatest socioeconomic deprivation.

Overall, a protective effect of PCV10 against ACP- and OM-related hospitalisations was indicated by incidence rate ratios of 0.90 (95% CI 0.88-0.93) and 0.92 (95% CI 0.90-0.93), respectively. Using the indirect cohort method to consider vaccine impact on vaccine serotypes only, the vaccine effectiveness of PCV7 against vaccine serotypes was 89.8% (95% CI 77.9-95.3) but there were too few cases of PCV10 types for meaningful analysis.

Take-home messages

- PCV was associated with dramatic reductions in ethnic and socioeconomic disparities in the rates of IPD-, ACP- and OM-related hospitalisations in New Zealand children.
- Only PCV10 was associated with a protective effect on the incidence of ACP- and OM-related hospitalisations.
Does the current pertussis immunisation schedule provide sustained protection to New Zealand toddlers?

Dr Sarah Radke, Research Fellow, Research Fellow, Immunisation Advisory Centre, University of Auckland

A possible contributor to the recent resurgence in pertussis disease may be waning immunity following acellular pertussis vaccination. The Effectiveness of Pertussis Immunisation in Children (EPIC) study therefore addressed the question: does the current pertussis immunisation schedule provide sustained protection to New Zealand toddlers?

EPIC measured the effectiveness of vaccination against pertussis disease in New Zealand, as well as the duration of protection, following the primary 3-dose series of DTaP-IPV-HepB-Hib (Infanrix hexa) and the first booster dose of DTaP-IPV (Infanrix IPV) at age 4 years. Linking data from seven different data sets, a nested case-control study was used to estimate vaccine effectiveness both overall and stratified by age group (5-11 months, 1 year, 2 years and 3 years). Cases were identified as pertussis occurring between 2006 and 2013, including overnight hospitalisations and notifications to EpiSurv.

The study population was all children born during 2006-2013 enrolled in the NIR. Pertussis-related hospitalisation data were sourced from the NMDS and notifications data were sourced from EpiSurv (pertussis status confirmed, probable, or suspect). Immunisation status was provided by the NIR. Twenty controls per case were randomly sampled from the study population via random incidence-density sampling and matched on age and Hospital DHB of residence at the index date (date of hospitalisation or date of notification reported). The exposure of interest was the number of pertussis vaccine doses received prior to the index date.

Two supplemental methods for selecting controls were used to explore the suitability of the NIR as the source population for controls. Vaccine effectiveness was calculated using multivariable conditional logistic regression. Sex, ethnicity, and socioeconomic deprivation were examined as potential confounders. Sensitivity analyses were conducted to test the robustness of the study design.

There were 625 hospitalisations and 2025 non-hospitalised notifications for pertussis among children aged 6 weeks to <4 years in the study population. VE following two doses, i.e. age 3-4 months, was 78% (95% CI: 68-85) versus 89% (95% CI: 85-92) following three doses, i.e. age 5-11 months, and there was no decline in VE through to age <4 years (86%; 95% CI: 83-89). In children aged 4 to <8 years, VE was 92% (95% CI: 89-94) following the first booster dose at age 4 years with little subsequent decline in VE up to age 7 years (87%; 95% CI: 66-95). There were no substantial changes in VE estimates after adjusting for potential confounders.

Sensitivity analyses confirmed no change in VE and/or duration of protection with severe disease, when cases were limited to laboratory-confirmed pertussis, or with improved vaccine timeliness. In addition, sensitivity analysis supported the NIR as a valid source population for controls.

**Take-home messages**

- Moderate protection against pertussis is afforded after two doses of DTaP-IPV-HepB-Hib and good protection is afforded after three doses.
- There was no evidence of waning immunity following dose 3 (through to age 3 years) and dose 3 + 1 (through to age 7 years).
- The results were robust against severe disease.
- The current New Zealand immunisation schedule, which includes a three-dose primary course but no booster dose in the second year of life, is effective in providing sustained protection against pertussis hospitalisations and notifications in infants and toddlers.

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**POSTER PRESENTATION: POSTER 5**

**Review of 6-year post-licensure experience with the 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PCV10)**

Associate Professor Michael Nissen, Director of Scientific Affairs & Public Health, GSK Vaccines-AsiaPacific

PCV10 (Synflorix) was licensed in 2008 and has since been registered in >130 countries and included in national or regional vaccination programmes in >45 countries worldwide. The aim of this review was to assess the effectiveness of PCV10 against IPD, pneumonia, and OM in infants and young children since its licensure by analysing vaccine effectiveness data from large, randomised, double-blind trials in Finland (FinIP) and Latin America (COMPAS) and from post-marketing and surveillance studies in countries where PCV10 has been used, including Finland, Iceland, the Netherlands, Kenya, Brazil, Chile, Quebec, and New Zealand.

VE of 100% (95% CI: 83-100%) and of 100% (95% CI: 77-100%) against vaccine-type IPD (3+1 schedule) were reported in FinIP and COMPAS, respectively. This high level of VE against vaccine-type IPD demonstrated in clinical trials was confirmed by case control studies in Finland (VE of 98%; 95% CI: 72-100%), Brazil (84%; 95% CI: 66-92%), and Quebec (97%; 95% CI 84-99%). VE of 23% (95% CI: 9-36%) against WHO-defined consolidated CAP was reported in COMPAS. In FinIP, VE was 26% (95% CI: 3-43%) against pneumonia when clinically diagnosed in hospital and 47% (95% CI: 24-64%) with X-ray-confirmed consolidation. Furthermore, reductions in pneumonia hospitalisation and mortality rates in children aged 1-3 years after PCV10 introduction were demonstrated in post-marketing studies in Brazil, Finland, and Iceland. VE of 19% (95% CI: 4-31%) against clinically-diagnosed OM was reported in COMPAS while FinIP (3+1 schedule) reported VE of 8% (95% CI: -1-15%) against purchases of antimicrobials for OM. Three years after the introduction of PCV10 (3+1 schedule) in Brazil, OM outpatient visits for children aged <2 years have decreased by 45% (95% CI: 43-46%). In Iceland, OM-related hospital visits in a cohort of vaccine-eligible children aged <2 years decreased by 24% (95% CI: 15-33%) following introduction of PCV10 (2+1 schedule) compared with the pre-vaccine era.

PCV10 was introduced in New Zealand in October 2011 prior to which PCV7 (7vCRM; Prevenar™) had been used since July 2008 and the pre-PCV era being before 2008. Since the introduction of PCVs (3+1 schedule) in New Zealand, rates of overall IPD in children aged <2 years have decreased by >80%, with a 98% reduction in IPD due to PCV10 serotypes. There has been a 54% reduction in IPD hospitalisations among children aged ≤5 years since the introduction of PCV10 compared with the pre-PCV era (Table 1). Additionally, a 10% reduction in pneumonia-related and an 8% reduction in OM-related hospitalisations in children aged ≤5 years has been observed in New Zealand since the introduction of PCV10 compared with the pre-PCV era (Table 1).
Preventable infectious disease: strategies to protect our youngest infants

**Associate Professor Michael Nissen, Director of Scientific Affairs & Public Health, GSK Vaccines-AsiaPacific**

New Zealand has a good track record in the prevention of serious infectious disease in young children. There are, however, gaps in coverage with those who struggle to get vaccinated in time or those with other significant risk factors remaining vulnerable to serious diseases such as pertussis and pneumococcal disease.

**Pertussis**

The combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio and *H. influenzae* type b vaccine (DTaP-HepB-IPV/Hib), or the ‘six in one’ vaccine, that has been used in New Zealand since 2008, has been successful in contributing to the protection of children against vaccine-preventable diseases. For example, the use of DTaP-IPV-HepB/Hib and other vaccines has resulted in the near elimination of *H. influenzae* type b invasive disease and hepatitis B virus infection. Unfortunately, pertussis continues to circulate in the community with outbreaks occurring every 3-4 years, the most recent of which occurred in 2012.

New Zealand is not alone in this regard. A considerable number of pertussis cases are still reported annually (>5000 notifications according to the WHO) in many developed countries despite having well-developed primary immunisation programmes, irrespective of whether whole-cell or acellular vaccines are employed in those programmes, and despite achieving good immunisation coverage. These observations indicate that it is not sufficient to have an effective vaccine: an efficient delivery service, favourable public perception and acceptance of immunisation, and equitable access to immunisation are also required.

Whenever there is a pertussis outbreak, pertussis notifications and hospitalisation rates are highest in those aged <1 year, with hospitalisation rates being 45-fold higher than in other age groups, and the most recent outbreak having resulted in four infant deaths. Hence, pertussis is not controlled in New Zealand and continues to place a major burden on the public health system. Additionally, there are disparities in who is most affected by the continued presence of pertussis disease in New Zealand. Māori and Pacifica children, and those from areas of high deprivation, are disproportionately affected both between and during pertussis outbreaks, having the highest rates of hospitalisation compared with other ethnicities in the New Zealand population.

Clearly then, pertussis remains a problem despite good vaccine coverage. The following factors have been proposed as contributing to ongoing pertussis outbreaks:

- High reproductive capacity and therefore high communicability of *Bordetella pertussis*.
- Waning immunity following vaccination and natural infection.
- Suboptimal vaccine coverage, mainly poor uptake in older age groups.
- Suboptimal immunisation schedules.
- Vaccine switching in primary series.

Building an effective pertussis prevention strategy is a complex undertaking involving multiple factors, but probably the most important drivers of success are vaccine effectiveness as well as public and healthcare practitioner perceptions and acceptance of the vaccine. Access to the most vulnerable populations is also important in terms of timeliness of vaccination.

In terms of building a pertussis prevention strategy it makes sense to view pertussis as a whole of life disease with waning immunity following vaccination and natural infection partially underling the increasing incidence of pertussis in older age groups (Figure 1). Thus, adolescents, adults, and the elderly represent reservoirs of infection, potentially transmitting disease to unprotected infants who are at a greater risk of complications and even death. Therefore, the prevention strategy requires a strong, robust, and on-time infant immunisation programme followed by boosters in children prior to school entry and in adolescents prior to secondary school entry, vaccination of adults in the context of a cocooning strategy, and then boosting in elderly adults (Figure 1). Currently, maternal immunisation is being transitioned from a post-partum cocooning strategy to one of immunisation during pregnancy prior to delivery.

Regarding the composition of pertussis vaccines, pertactin, the highly immunogenic virulence factor of *Bordetella pertussis*, is an important component of an acellular pertussis vaccine. Head-to-head clinical studies have demonstrated that a five-component pertussis vaccine containing pertactin has greater VE than a two-component vaccines not containing pertactin. Furthermore, a Cochrane group review of six randomised double-blind clinical trials has also demonstrated that pertussis vaccines containing ≥3 pertussis components with pertactin, i.e. DTaP-IPV-HepB/Hib, have higher vaccine effectiveness than a one or two component vaccine containing no pertactin. The composition of DTaP-IPV-HepB/Hib is consistent with the position currently held by the UK Joint Committee on Vaccination and Immunisation (JCVI) that pertussis vaccines should contain no less than three pertussis components.

At the end of 2014, overall immunisation coverage at 6 months of age was 80% in New Zealand, with a narrowing of the gap between Māori/Pacifica children and European children occurring over the past year.

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**Take-home messages**

- Early childhood immunisation with PCV10 in different schedules, settings, and global populations has resulted in marked reductions in vaccine-type and overall IPD.
- Global data also indicate that PCV10 has been effective in preventing pneumonia and OM and in reducing antibiotic use in young children.
- In New Zealand, use of PCV10 has resulted in substantial reductions in OM and overall IPD.
- PCV10 vaccination in early childhood is effective against pneumococcal infections, highlighting the public health benefit of PCV10.

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**Table 1. Impact of PCV10 on pneumococcal disease in children aged ≤5 years and on OM in infants aged <1 year in New Zealand since its introduction in 2011.**

<table>
<thead>
<tr>
<th>Post- vs pre-vaccination</th>
<th>Endpoint (hospitalisations)</th>
<th>Incidence rate ratio (95% CI)</th>
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<tbody>
<tr>
<td>≤5 years</td>
<td>Overall IPD</td>
<td>0.46 (0.37, 0.58)</td>
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<tr>
<td>(Oct 2011– Dec 2013 vs Jan 2006– May 2008)</td>
<td>All-cause pneumonia</td>
<td>0.90 (0.86, 0.93)</td>
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<td></td>
<td>All-cause otitis media</td>
<td>0.92 (0.90, 0.95)</td>
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<tr>
<td>&lt;1 year</td>
<td>Otitis media</td>
<td>0.64 (0.44, 0.93)</td>
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<tr>
<td>(born Jul– Dec 2011, 3 doses of PCV10 vs 3 doses of 7vCRM)</td>
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Abbreviations: 7vCRM = 7-valent pneumococcal CRM19-conjugate vaccine; CI = confidence intervals; IPD = invasive pneumococcal disease.
Pertussis depicted as a whole of life disease together with pertussis prevention strategies throughout life. Until fully immunised, infants are at the highest risk of severe complications from pertussis and it is primarily parents and close family members who transmit pertussis to infants, with most newborn cases of pertussis coming from within the infected infant’s own family. This is why boosting in pre-schoolers and adolescents as well as parental protection is important in minimising intra-family transfer of pertussis to infants. Maternal immunisation appears to be the best means of preventing infant disease. It reduces transmission or provides direct protection to the foetus and new-born infant and reduces morbidity in mothers and children. Maternal immunisation, however, will not achieve community immunity unless combined with other immunisation strategies and may not always be accepted by a pregnant woman.

The primary rationale for pertussis vaccination during pregnancy is the passive transfer of maternal vaccine-induced antibody to the foetus before they are born and prior to their first vaccine dose at 2 months of age. It also boosts immunity in pregnant women making it unlikely they will transmit the disease to their infant. A US clinical study has demonstrated that levels of antibodies to pertussis antigens are significantly elevated in mothers vaccinated with a pertussis vaccine and their new-born infants compared with levels in mothers who were not vaccinated and their new-born infants. Comparative research has found maternal pertussis immunisation increasing from 1 to 18 countries in the last 24 months (as of November 2014).

Regarding the safety of maternal immunisation, no increased risk of adverse events (local and systemic reactions) among women who received a pertussis vaccine during pregnancy or their infants was revealed in a randomised placebo-controlled trial conducted in the US.\(^5\) In terms of pregnancy outcome, an observational study of approximately 20,000 women in the UK produced no evidence of an increased risk of adverse events related to pregnancy, including stillbirth, early neonatal death, and eclampsia. In women given pertussis vaccination during the third trimester.\(^7\) Closer to home, the New Zealand Pertussis Immunisation in Pregnancy Safety study of >30,000 exposures in >300 women who received a pertussis vaccine during pregnancy demonstrated a systemic events rate of <5% and that adverse pregnancy outcomes were no different or more frequent than general population pregnancy outcomes.\(^8\)

Use in Pregnancy (Category B1)
Non-clinical data obtained with Boostrix\(^\text{®}\) reveal no specific hazard for humans based on conventional studies of embryo-fetal development in rats and rabbits, and also of parturition and postnatal toxicity in rats (up to the end of the lactation period). As with all inactivated vaccines, one does not expect harm to the foetus. However, adequate human data on use during pregnancy are not available. Therefore, Boostrix should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the foetus.

Take-home messages
- DTaP-IPV-HepB/Hib is a cornerstone of the national immunisation programme.
- Despite having an effective vaccine, pertussis remains a significant public health problem in New Zealand.
- This is largely due to poor access in high-risk groups for pertussis disease: infants, Māori and Pacifica children, and those living in high deprivation areas.
- Current immunisation strategies to reduce pertussis in New Zealand communities include:
  - maternal vaccination
  - on-time infant vaccination
  - pre-school and adolescent boosters
  - opportunistic adult boosting including cocooning.
- Studies to date have shown maternal pertussis immunisation to be well tolerated with evidence of high effectiveness for protecting infants.
- The JCVI endorses the use of pertussis vaccines containing ≥3 pertussis components.

Pneumococcal disease
The New Zealand NIS for pneumococcal disease commenced in 2008 with use of PCV7 (Prevenar), then with PCV10 (Synflorix) from 2011, and now with PCV13 (Prevenar 13) since 2014, and has been very successful. It has resulted in a dramatic reduction in the number of cases of IPD in vaccinated children aged <5 years, including a 97% reduction of PCV10-type IPD cases.\(^9\) The large FinIP (Finland)\(^10\) and COMPAS (Latin America)\(^11\) randomised controlled clinical trials of PCV10 both demonstrated 100% efficacy against vaccine serotypes and 93% and 67% efficacy, respectively, against non-vaccine serotypes for IPD. Efficacy against non-vaccine serotypes was 44% in FinIP\(^12\) and 26% in COMPAS\(^11\) for pneumonia and 19% for OM in COMPAS.\(^11\) Studies that have evaluated the vaccine effectiveness of PCV10 versus post-introduction have shown vaccine effectiveness of 92% in Finland,\(^13\) 97% in Quebec,\(^14\) and 84% in Brazil\(^15\) against vaccine serotypes. Confidence in its effectiveness has resulted in PCV10 being licenced in 131 countries throughout the world and as of 2015 >40 countries have added PCV10 to their universal vaccination or high-risk programmes.
In New Zealand, pneumonia is a leading cause of lower respiratory tract infection hospital admissions in children aged <15 years, with admissions being highest in those aged 1-2 years, Māori and Pacifica children, and those living in the most deprived areas. The introduction of PCV10 in 2011 is associated with a reduction in ACP (incidence rate ratio: 0.88; 95% CI: 0.85-0.91), indicating that it has played a fundamental role in addressing the problem of ACP in New Zealand. PCV10 has also contributed to a reduction in disease burden in the most vulnerable populations. Since the start of the pneumococcal immunisation programme in 2006, the greatest decreases in ACP hospitalisations have been seen in Māori (41%) and Pacifica children (37%). OM is a major burden on the New Zealand healthcare system as evidenced by 5,000 hospital admissions and 83,000 GP consultations per year for children aged <5 years with OM. Moreover, Māori and Pacifica children are twice as likely to be hospitalised with OM complications and twice as likely to fail hearing checks as New Zealand European children when they start school. Preventing OM is therefore an important healthcare initiative. 

Non-typeable H. influenzae is the most common otopathogen identified in middle ear cultures of New Zealand children receiving grommets, followed by M. catarrhalis and S. pneumoniae. This data is consistent with global data implicating non-typeable H. influenzae and S. pneumoniae in the majority of cases of OM in children, which emphasises the importance of targeting these two pathogens in an OM prevention strategy.

Since the introduction of conjugated pneumococcal vaccines in New Zealand, there has been a significant (p<0.001) decrease in OM hospitalisations in children aged <5 years (in the period 2006-2013), with Māori achieving a 40% reduction OM hospitalisation. Much of this reduction is likely due to PCV10. Indeed, children vaccinated with PCV10 have been demonstrated to be significantly (p=0.037) less likely to be hospitalised for OM than children who received PCV7.

**Take-home messages**

- More than 40 countries are currently implementing PCV10 in universal or high-risk immunisation programmes in 2014/15.
- PCV10 has demonstrated clinical trial and real-world efficacy in preventing all types of pneumococcal disease, including IPD, pneumonia, and OM.
- PCV10 has shown significant impact on all types of pneumococcal disease in New Zealand, especially with respect to prevention of OM compared with previously used PCVs.

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**REFERENCES**


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**Boostrix®** (combined diphtheria-tetanus-acellular pertussis (dTpa or Tdap) vaccine) is available as an injection. A 0.5 mL dose contains not less than 2.5 LfU of diphtheria toxoid, not less than 5 LfU of tetanus toxoid, and three purified pneumococcal polysaccharide serotypes 4, 18C, and 19F adsorbed onto 0·5mg aluminium phosphate. Boostrix is government funded for 11 year olds as part of the national immunisation schedule, and for pregnant women between 28 and 38 weeks gestation (Category B1). It is also available as a private-purchase prescription medicine for booster vaccination against diphtheria, tetanus, and pertussis in individuals aged 4 years and older, when additional immunisation is required during pregnancy as there is no vaccine available for pregnant women. Alternatively a prescription for tetanus-diphtheria-acellular pertussis vaccine (Tdap) can be used in younger children. Boostrix should be used as a single dose during pregnancy, and no additional doses are recommended. The injection should be given only into a muscle and not intradermally. In general, a minimum of 4 weeks should be allowed between doses. Patients should be advised to seek medical advice if there is a history of allergy to any component of the vaccine. The injection should be given at the same site as any previous injections. Allergic reactions to previous doses are rare and most are mild. The usual reactions are local reactions such as pain, redness, or swelling at the injection site. Reactogenicity, with the exception of the inactivated poliovirus type 2 vaccine, for which inconsistent results have been observed across studies. Before prescribing Boostrix, Infanrix Hexa or Synflorix please review the full Data Sheet at www.medsafe.govt.nz. Boostrix, Infanrix Hexa and Synflorix are trade marks of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 880 500. TIPS 0800 317 061/1400 000 076.