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The further and future evolution of the New Zealand Immunisation Schedule

Stewart Reid

Abstract

MeNZB was introduced to control meningococcal disease in New Zealand in 2004 and routine use ceased in 2008. In that year, two new vaccines were added to the New Zealand Childhood Immunisation Schedule, pneumococcal and human papilloma virus, and two more, varicella and rotavirus, have been recommended but not funded. By comparison, in the 16 years prior to 2006 only one new vaccine was introduced, *Haemophilus influenzae* type B. Coverage is improving and is now around 90%, making timeliness an important target and supplementary strategies for controlling pertussis of greater importance. A personal view of each of these vaccines is provided in this article.

In 2006 an article on the evolution of the New Zealand Childhood Immunisation Schedule was published.[1] In that article, which covered from 1980 until 2006, there was a brief section on the future. Much has happened since then.

MeNZB has been and is now gone. Two new vaccines have been included on the Schedule, pneumococcal and human papilloma virus, and two more, varicella and rotavirus, recommended but not funded. By comparison, in the 16 years prior to 2006 only one new vaccine was introduced, *Haemophilus influenzae* type B. Coverage is improving and is now around 90%, making timeliness an important target and supplementary strategies for controlling pertussis of greater importance.

In this article I will provide my personal view on each of the above vaccines and the challenges they present, and describe how vaccines get onto the New Zealand Childhood Vaccination Schedule. I will make predictions about which vaccines may be included in the Schedule by the end of this decade and for comparison I present the 2006, 2008 and 2011 Schedules. For more detailed consideration of the diseases and vaccines available please consult the recently published Immunisation Handbook 2011.[2]

How do vaccines get on the Schedule?

There is no formalised process in New Zealand for vaccines to be included on the Immunisation Schedule, but there are nevertheless a number of hurdles to be crossed. The epidemiology of the target disease in New Zealand must be known and understood, and the impact of the disease must be of sufficient frequency and severity to justify vaccination.

The vaccine must have demonstrated that it prevents disease, has an acceptable safety profile and that it can be manufactured reliably, meeting licensure criteria as determined by the regulatory authority, Medsafe. Experience during the use of the vaccine in other countries will have been considered. How the vaccine will fit into the

Immunisation Schedule is important: are extra visits or extra injections required or, is there a suitable combination vaccine? There has to be a pharmacoeconomic evaluation indicating reasonable cost benefit.

In general an intervention can be considered highly cost-effective if it saves one quality adjusted life year (QALY) for less than the cost of the per capita GDP of the country, and cost effective if it saves one QALY for less than three times the cost of the per capita GDP.[3]

If the vaccine is to be introduced, effective surveillance has to be in place for the target disease, and for vaccine coverage and adverse events following vaccination. If a vaccine passes all these hurdles then the advisory committee is likely to recommend to the Ministry that it be included in the Immunisation Schedule.

The Ministry then has to consider the cost of the vaccine within the context of its total budget and the strategic direction for the immunisation programme and decide whether to make a recommendation to the Minister for funding. It will consider whether there will be a catch-up and, if so, this will substantially increase the first year cost.

The Ministry has to prepare all the necessary documentation for providers and vaccine recipients so that they are well informed. The Minister, if he or she agrees with the recommendation, has to persuade Government to provide the necessary funds. It is, quite appropriately, a process with many steps and no vaccine is included in the Schedule without careful consideration.

Meningococcal vaccination

Group B meningococcal vaccination—Between 1991 and 2008, New Zealand suffered an epidemic of group B meningococcal disease dominated by a single subtype. This subtype, characterised by its porA type, P1.7b4, was responsible for approximately 85% of invasive disease caused by Group B meningococci.[4]

The predominance of this single subtype meant that a tailor made vaccine had the prospect of controlling the bulk of group B meningococcal disease in New Zealand. Chiron Vaccines (now Novartis), in collaboration with the Norwegian Institute of Public Health, contracted with the New Zealand Government to produce an outer membrane protein vaccine against the New Zealand subtype.

MeNZB was studied in a series of trials conducted in New Zealand by the University of Auckland. Using a schedule of three doses of MeNZB™ with an interval of 6 weeks, it was demonstrated that for all age groups, except infants, at least 60% of vaccine recipients achieved a four fold rise in SBA titre,[5–8] the predetermined criteria for licensure. Infants, who received three doses concurrent with the routine immunisation schedule required a fourth dose at 10 months of age to achieve the predetermined criteria.[9]

Underpinning licensure was a comprehensive safety monitoring plan. This was required because 3300 doses were administered during the clinical trials, a rather small safety data set for a vaccine planned to be given to 1,000,000 New Zealanders aged 20 years and under.

The key features of the safety monitoring plan were the use of several data sources, including active hospital based monitoring for key events of interest, staggered delivery of vaccine with progress from one area to another occurring only after analysis of the available safety data and, most importantly, the creation of an independent safety monitoring board which assessed all safety data.[10]

Three important reasons resulted in the MeNZB™ vaccination campaign ceasing in 2008, though the vaccine remained available for high risk groups until 2011. Firstly, the incidence of group B meningococcal disease caused by the epidemic strain had fallen significantly.

Secondly, trial data indicated there was rapid antibody decay following vaccination, meaning protection would be short lived as circulating antibody rather than immune memory is required for protection from meningococcal disease.[11]

Thirdly the only group being vaccinated in 2008 was infants who required four doses to achieve a protective SBA response and the coverage for the fourth dose was low. A further reason was that pneumococcal vaccination was being introduced into the NZ Schedule and no data were available on the concurrent administration of MeNZB with pneumococcal conjugate vaccine.

A consideration of the efficacy of MeNZB is outside the scope of this article and is well covered elsewhere though it does seem likely that the vaccine contributed to the substantial decline in disease.[12,13]

The MeNZB™ vaccine campaign did, however, leave an important legacy. The safety monitoring strategy, which underpinned vaccine licensure, was dependent upon the creation of the National Immunisation Register which now provides accurate up-to-date information on childhood vaccine coverage throughout the country.

The future of group B meningococcal vaccines is uncertain. Generic group B vaccines based on a combination of outer membrane proteins and other proteins derived from studies of the meningococcal genome, are being studied in clinical trials. An article describing the current status of group B Meningococcal vaccines has been published recently.[14]

Conjugate group C meningococcal vaccination—This vaccine has been introduced into several countries, notably the UK and Australia but the incidence in New Zealand, when it was discussed in 2009, was not sufficiently high to merit its introduction. This may well have changed given recent outbreaks of group C meningococcal disease in New Zealand.

The vaccine presents some interesting possibilities for those deciding how it should be used. A modelling study indicated that the optimum schedule for conjugate MenC vaccination is a five-dose schedule with doses at 2, 4 and 12 months and 12 and 18 years of age. However this schedule was only marginally better than a two-dose schedule with doses at 12 months and 12 years,[15] and some countries, e.g. The Netherlands, have had excellent control of Group C meningococcal disease with a single dose at 14 months and a catch up for all aged 1 to 18 years.[16,17]

The vaccine strategy will depend on the epidemiology of the disease in New Zealand prior to the vaccine's introduction. If the epidemiology justifies vaccinating infants then two (or possibly three) doses will be offered in the first 6 months of life with a

booster dose in the second year; experience in the UK has established that a second year of life dose is required.[18] Currently the Immunisation Handbook recommends that this vaccine be offered to young adults entering hostel accommodation, particularly in their first year,[19] though this is not funded.

Conjugate pneumococcal vaccine

The decision to introduce a conjugate pneumococcal vaccine was very straightforward on scientific grounds. The incidence of invasive pneumococcal disease in New Zealand was high, particularly in children of Maori and Pacific ethnicity.[20]

The seven valent vaccine, Prevenar, containing serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, is highly efficacious in preventing invasive pneumococcal disease caused by the vaccine serotypes.[21] It also demonstrated modest efficacy against pneumonia and otitis media, though the prime reason for the introduction of conjugate pneumococcal vaccines is (and remains) the prevention of invasive pneumococcal disease.

Furthermore, data from the USA indicated a significant herd effect with two cases prevented in adults, predominately in those aged 65 and older, for every case of invasive disease prevented in child vaccine recipients.[22] This is probably because grandparents were less likely to be exposed to pneumococci by their vaccinated grandchildren.

In New Zealand the vaccine was introduced in June 2008 to all born from 1 January 2008. Surveillance data from 2004–2009 indicate a decline in invasive pneumococcal disease in those aged two and under during 2008 and 2009, in comparison to previous years. To date no reduction in the incidence of pneumococcal disease in elderly people has been observed.[23]

One of challenges of introducing pneumococcal vaccination was that it required a change to the *Haemophilus influenzae* type b (Hib) vaccine used. When the introduction of pneumococcal vaccine was being considered, there were three injections at each of the first three visits, DTaP-IPV, Hib-HepB and MeNZB.

To avoid adding a fourth injection, a change to the hexavalent vaccine, DTaP-IPV-HepB/Hib, was recommended, necessitating a change in Hib vaccine. All currently available Hib vaccines contain poly ribosyl ribitol phosphate (PRP), derived from the polysaccharide capsule of *H. influenzae* type b, conjugated to a carrier protein, which enhances the immune responses to the PRP.

A variety of carrier proteins have been used: an outer membrane protein (PRP-OMP) of *Neisseria meningitidis*, a mutant diphtheria toxin (Hb-OC) and tetanus toxoid (PRP-T). PRP-OMP, the Hib vaccine in the Hib-Hep combination, had been selected ahead of the other available conjugate Hib vaccines because it produced a particularly strong antibody response following the first vaccine dose, and thus provided protection more rapidly than the alternative Hib conjugate vaccines.[24] However the change, in 2008, to the hexavalent DTaP-IPV-Hep/Hib vaccine (Infanrix Hexa), meant that the Hib conjugate would be PRP-T, which stimulates a weak response after the first dose but does offer some protection after the second dose.[25] This meant that there was a difficult trade-off between either using the combination DTaP-IPV-Hep/Hib vaccine with a loss of early immunity against Hib, or giving four injections:

DtaP-IPV, Hib-HepB, pneumococcal vaccine and MeNZB™ at each of the first three visits.

In the end it was decided to use the combination vaccine and, as the use of MeNZB™ subsequently ceased, only two injections are given at each visit in the first 6 months. Despite the weak response to PRP after the first dose of Infanrix-Hexa the control of Hib disease has remained excellent since the change of Hib vaccine.

In 2011, to broaden protection against invasive pneumococcal disease, PCV7 was replaced by PCV10 which contains the same serotypes as Prevenar plus serotypes 1, 5 and 7F. PCV13, which contains the same serotypes as PCV10 plus additional serotypes 3, 6A and 19A, was considered but, on cost-effectiveness grounds, PCV10 was chosen. PCV13 is offered to high-risk children because it is important that those children receive the broadest protection.[26]

The main concern about using PCV10 is that it will not offer sufficient protection against invasive disease caused by serotype 19A which has increased in several countries, some of which have routine pneumocoocal vaccine and some of which do not. However immunogenicity data on PCV10 suggest that cross protection from serotype 19F may offer some protection against 19A.[27] Whether protection against 19A will be seen with widespread use is yet to be determined.

Very careful serotype surveillance of invasive pneumococcal disease is required; if the incidence of invasive disease caused by 19A increases significantly, a change in vaccine may be considered.

Conjugate pneumococcal vaccines offer some protection against otitis media caused by vaccine serotypes. Some of the serotypes in PCV10 are conjugated to an immunogenic protein from non typeable *Haemophilus influenzae* (NTHi). It is possible that this may provide some degree of protection against otitis media caused by NTHi.[28]

An additional possibility is to use a 2+1 schedule (two doses in the first 6 months and a booster dose in the second year of life) rather than a 3+1 schedule, as is done in some Scandinavian countries, Italy and the UK.

Immunogenicity studies suggest that a 2+1 schedule may be sufficient.[29] The main risk is a decline in antibody titre (and protection) prior to receipt of the dose in the second year of life, emphasising the importance of administering this dose on time.

Human papilloma virus (HPV) vaccine

The decision to recommend this vaccine was relatively straightforward. In clinical trials both HPV vaccines (Gardasil and Cervarix) demonstrated a high level of efficacy against persistent infection with vaccine HPV genotypes 16 and 18, and cellular changes caused by these genotypes. They have the potential to prevent the approximately 70% of cases of cervical cancer caused by genotypes 16 and 18. Gardasil, the vaccine currently used in New Zealand, also contains HPV genotypes 6 and 11, and has the potential to prevent 90% of genital warts.

Although injection site reactions occur and some adolescent girls faint following vaccination, which is an injection not a vaccine reaction, both vaccines have an excellent safety profile with serious adverse events being rare.[30] Trials of a higher

valency HPV vaccine with the potential to prevent approximately 90% of cervical cancer are ongoing.

This vaccine was introduced to the Immunisation Schedule in September 2008. There was a catch up for all females born from 1990 onwards, but now the main group of potential recipients is females aged 11 or 12.

It is disappointing that uptake of this vaccine has been relatively low, less than 50% for three doses in the eligible population, (Ministry of Health Data, October 2011). Reluctance to accept that girls are sexually active at a young age, concerns about duration of immunity, persistent anti vaccine publicity and opposition from Faith based groups underpin the low uptake.

Data from New Zealand clearly indicate that a significant percentage of girls (around 15%) had first sexual activity by age 12 or 13.[31,32] This argues very strongly for vaccinating at age 12 or possibly earlier, prior to the onset of sexual activity.

Data on the duration of protection are limited by the length of time the vaccine has been available. Current data indicate stable protection for 8.5 years for the HPV 16 monovalent vaccine[33] and it is expected that protection from HPV vaccines will be stable long term. There is additional reassurance for those aged 12 years or younger. Data indicate that the younger one is when vaccinated the higher the immune response. For example when the immune response in girls aged 9–15 is compared to that in women from age 16, the height of the antibody titre is approximately doubled in the younger group.[34]

More recent data indicate that 2 doses of either vaccine given at 0 and 6 months in 9-13-year-old girls produce a non inferior immune response to the standard three-dose schedule in 16–26 year old women.[35,36] As a result, Canada's British Columbia, for example, has introduced a two-dose, 0 and 6-month schedule for adolescent girls with the possibility of a third dose at 60 months.

In my view the decision to offer this vaccine to adolescent females is very straightforward and I anticipate that the acceptance rates will increase as confidence in the duration of protection increases, and evidence emerges of its protection against cervical cancer: more so if the number of vaccine doses required is reduced.

I anticipate that in a few years time as the vaccine price drops, and evidence of the protection against HPV-related cancers in other sites increases, it will become cost effective to offer it to young males as well. HPV vaccines are licensed for women to age 45. The peak age of HPV acquisition is much younger but the vaccine will protect older women against persistent infection by vaccine serotypes with which they are not already infected.

Varicella vaccine

Varicella vaccine has been recommended for introduction into the childhood schedule and a recent article has drawn attention to the case for its introduction.[37] Almost everyone gets chickenpox and even with a low complication rate there can be a large number of serious outcomes.

Immune compromised individuals, in whom chicken pox is more likely to be severe, remain at risk because of continued circulation of varicella virus. The number of

children hospitalised with varicella has quadrupled over the last 40 years.[38] Varicella vaccine has not been introduced for fiscal reasons and because it was thought that the greater priority was to increase overall coverage with already funded vaccines.

There are three interesting issues relating to this vaccine with regard to its introduction to the schedule and its use on the private market. Firstly, should the vacccine be administered as a one or two-dose schedule. Secondly, how should the first dose be administered, given that there are already three injections at the 15-month visit? Thirdly, in light of the US experience (see below), what is the duration of vaccine-induced immunity and will vaccinating children mean that we are creating a large number of young adults who become susceptible at an age when the disease is more severe?

In my view, a single dose is all that is required at present and this opinion is discussed in detail below. When varicella vaccine is introduced to the schedule, two doses at 15 months and 4 years should be offered from the start, with both doses being given at the same time as MMR. I would not recommend a catch up, meaning that the first children to receive a second dose would be those first immunised at 15 months, when they reach the age of 4.

Those who received a single dose at age 4 years would have their immunity boosted by regular exposure to wild varicella which would still be occurring, given the small percentage of the population that would be vaccinated in the first years after its introduction.

MMR, PCV and Hib vaccines are given at age 15 months and the addition of varicella vaccine would mean that four injections are necessary. However there are two licensed MMRV vaccines. Data from the USA indicate that there is an increased risk of febrile convulsions when MMRV is given compared with MMR and varicella vaccines given separately to children aged 12–23 months. The excess risk is one febrile convulsion for every 2000 children vaccinated.[39]

So, in the absence of a new formulation of MMRV which could eliminate this increased risk of febrile convulsions, there is a choice: four injections, an increase in febrile convulsions or an extra visit. There is no obvious answer and it may be necessary for the Ministry to commission focus group research among parents and vaccinators prior to the introduction of varicella vaccine, to determine the most acceptable strategy.

At present no MMRV vaccine is available in New Zealand. This means that, if varicella vaccine is being given privately, it would have to be as a single antigen varicella vaccine and, at parents' choice, it could be given at the 15-month visit with MMR, Hib and Pneumococcal conjugates.

Thirdly, the issue of duration of immunity is pertinent but it is necessary to consider the context in which immunisation against varicella is given.

The first context is that in which there is no national programme, the number of vaccinees is small and chickenpox continues to occur endemically: the current situation in New Zealand. In this situation those vaccinated will be regularly exposed to chickenpox and their immunity will be regularly boosted leading to secure long-term protection.

Data from Japan indicate that protection lasts for at least 20 years if chickenpox continues to circulate at high levels giving many opportunities for regular boosting of vaccine induced immunity.[40–42] Coverage in Japan, where the vaccine is "voluntary", was estimated to be around 20%. Antibody levels were higher at 20 years post-vaccination than at 10 years post-vaccination, confirming that boosting of immunity had occurred.[43,44]

The second context is that of a national programme when all children are offered routine varicella vaccination and the opportunity for boosting of immunity is significantly diminished. In the USA, following introduction of single-dose varicella vaccination in 1995, coverage for children aged 19 through 35 months had risen to 88% in 2005. These immunisation rates resulted in a 71% to 84% reduction in varicella cases, an 88% decrease in varicella-related hospitalisation and a 92 % decrease in varicella deaths in 1 to 4-year-old children when compared to the pre-vaccine era.[45] However, in the absence of regular boosting, following a single-dose 15–20% of children suffer breakthrough varicella, though it is a less severe illness than varicella in unimmunised children.

Put another way, vaccine effectiveness for a single dose is of the order of 80%–85% and, if a single dose strategy is retained, there are likely to be ongoing outbreaks of varicella. After a second dose in children the immune response is markedly enhanced with >99% of children attaining an immune response thought to provide protection and the height of the antibody titre is also significantly increased.

Estimated vaccine efficacy for two doses, over a 10-year period, for prevention of any varicella disease is 98%, with 100% efficacy for prevention of severe varicella. The likelihood of breakthrough varicella is reduced by a factor of 3.3.[45–47]

The USA commenced routine varicella immunisation 16 years ago and those vaccinated in the early years are now in their late teens. Any adverse change in disease epidemiology as a result of vaccination will be seen in the USA well in advance of New Zealand.

A vaccine against herpes zoster which provides approximately 60% protection when given to those age 60 years and older has been licensed in New Zealand but is not commercially available at present. It contains the came vaccine virus as varicella vaccine but at a titre increased approximately tenfold.[48]

Rotavirus vaccine

There are two rotavirus vaccines licensed in New Zealand; both are orally administered, meaning inclusion of either in the Schedule would not result in an increase in injections. Both are highly efficacious against severe rotavirus gastroenteritis, of which there is a significant burden, including hospitalisation, in New Zealand.[49–51]

Experience in other countries indicates that the efficacy seen in the clinical trials is also seen when the vaccines are in widespread use and there does appear to be a herd effect.[52,53] An increased risk of intussuception following receipt of these vaccines at the rate of 1–2/100,000 infants vaccinated has been observed.[54]

The barriers to the introduction of a rotavirus vaccine into the New Zealand Schedule, like that for varicella, are fiscal and because the greatest priority has been to increase overall vaccine coverage. The single cost benefit study indicates that the vaccine costs $46,000 per QALY saved. This is quite a high cost for New Zealand even though it is within the three times per capita GDP per QALY which WHO considers a cost-effective intervention.[55]

This figure does not take into account the work time lost by parents when their child suffers rotavirus gastroenteritis; between 2.3–7.5 days work are lost by parents when their child has an episode of sufficient severity to require a medical consultation.[56] And it is possible that the vaccine price would be less at tender than was assumed in the above cost benefit study, making the cost per QALY significantly less.

There is an additional important factor to consider: the potential of these vaccines to improve on-time coverage. Rotarix is administered in a two-dose schedule with doses separated by at least 4 weeks. The first dose should be given by 14 weeks and the last by 24. Rotateq is administered in a three-dose schedule with doses separated by at least 4 weeks. The first dose should be given by 12 weeks and the last by 32.

Data from National Centre for Immunisation Research and Surveillance in Australia indicate that the introduction of rotavirus vaccine has improved on-time (within 4 weeks of due date) coverage, and a similar improvement in New Zealand would be of considerable benefit, especially for the control of pertussis.[57]

Pertussis

To control pertussis well, the target has to be 95% vaccine coverage for three doses by six months. Currently about 60% of infants have the first three doses of vaccine administered within 4 weeks of the scheduled time (6 weeks, 3 and 5 months); there is plenty of room for improvement[58].

There is some encouragement however. It seems likely that the increase in vaccine coverage in the last few years to 90% has contributed to the much lower incidence of pertussis during the 2009–2010 epidemic compared to the previous epidemic in 2004–2006.[59] However ESR data from November 2011 with a substantial rise in incidence of pertussis indicate that the optimism in the above statement may be misplaced.[60]

Whilst the most important measure in Pertussis control is to improve on time coverage in infants and children additional strategies[61,62] are also important and as on time coverage increases they assume greater importance.

The aim of these additional strategies, vaccination of healthcare workers and childcare workers and cocoon immunisation around newborns, is to reduce the likelihood of children who are too young to be protected by vaccination from being exposed to pertussis. At least 8% of adults, who seek medical care for a cough illness of at least 5 days duration, will have pertussis.[63] Infants with pertussis are usually infected by a family member, most commonly the mother[64].

Thus it seems the theoretical case for cocoon vaccination around newborns is strong, though evidence supporting its efficacy currently is lacking. When pregnancy is diagnosed older siblings should be offered any overdue pertussis vaccine and adults in

the household and other significant adults likely to have contact should be offered a pertussis containing vaccine if one has not been received in the last 10 years.

The mother could be offered pertussis containing vaccine shortly after delivery, though US authorities have recently recommended that accellular pertussis vaccine may be given during the 2nd and 3rd trimesters of pregnancy.[65]

It seems to me that there is a strong case for healthcare workers who have contact with infants aged less than 6 months to receive a pertussis containing vaccine every 10 years. This would include at least paediatric, obstetric and primary care, including Emergency Department, staff.

The case for immunising childcare workers is less strong.[62] As stated in the Immunisation Handbook 2011 the recent receipt of a tetanus and diphtheria containing vaccine should not prevent the receipt of a pertussis containing vaccine, which in New Zealand will also contain tetanus and diphtheria toxoids.[66]

Another strategy which may be considered is neonatal vaccination with single antigen pertussis vaccine with the aim of protecting infants at an earlier age.[67,68]

Note pertussis-containing vaccines for adults (Tdap) are not currently funded beyond adolescence.

Conclusion

The vaccination schedule will continue to change and will include more vaccines in the future. However the antigen load of the vaccination programme is unlikely to be as great as it was when whole cell pertussis vaccine, with its approximately 3000 antigens, was included. The most important challenge for vaccination in new Zealand is, and will remain, obtaining high coverage with 95% of infants and children receiving the scheduled vaccines within 4 weeks of the due date.

I suggest that by the end of this decade the vaccination schedule will include some new vaccines and some changes in timing and number of doses. The key changes I predict are, the introduction of varicella and rotavirus vaccines, and the introduction of a meningococcal vaccine at least against group C disease. HPV vaccine will be given in a two-dose schedule to adolescent males and females.

Pneumococcal vaccine will be administered as a two-dose schedule in the first year of life with a booster dose after 12 months of age. I anticipate that MMR vaccine will be given at 12 instead of 15 months as presaged in the 2011 Immunisation Handbook[69] and, provided coverage of the first dose reaches 95%, no change in timing of the second dose will be required.

However it is important to remember that as Neils Bohr, the great Danish physicist, said “Prediction is very difficult, especially about the future”.

2006 SCHEDULE

	Dtap-IPV	Hib-Hep	Hep B	Hib	MMR	Tdap
6 weeks	X	X				
3 months	X	X				
5 months	X		X			
15 months				X	X	
4 years	X				X	
11 years						X

2008 and 2011 SCHEDULES

	DTaPIPV Hep/Hib	PCV	Hib	MMR	DtaP IPV	Tdap	HPV
6 weeks	X	X					
3 months	X	X					
5 months	X	X					
15 months		X	X	X			
4 years				X	X		
11 years						X	3X

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Author information: Stewart Reid, General Practitioner, Ropata Medical Centre, Lower Hutt—and Senior Lecturer, School of Population Health, University of Auckland

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Correspondence: Dr Stewart Reid. Email: Stewart_christine@mac.com

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