Varicella Vaccination in New Zealand: NHC Assessment 2012

In 2014 the National Health Committee (NHC) received a request for a copy of the NHC’s assessment report on varicella (chicken pox) vaccination. This report was part of early assessment work the NHC undertook in both varicella and rotavirus vaccination in 2011/12, before responsibility for the management and purchasing of vaccines (including considering any changes to the National Immunisation Schedule) transferred from the Ministry of Health to New Zealand’s Pharmaceutical management Agency (PHARMAC). The NHC provided PHARMAC copies of the vaccine assessment reports and recommendations papers in 2013 and formal NHC recommendations on this work were never provided to the Minister of Health. Following the principal of open disclosure the Committee has decided to release the package of NHC vaccination assessments and recommendations on their website (www.nhc.health.govt.nz).
Table of Contents

List of Tables ................................................................................................................................. 4
Executive Summary ......................................................................................................................... 5
Policy Question ............................................................................................................................... 6
  Who initiated or commissioned the report? ................................................................. 6
  Why is an assessment needed right now? ................................................................. 6
  Which decision is it going to support? ................................................................. 6
  Who represents the primary target audience for the report? ........................................ 7
Background ................................................................................................................................... 7
  Condition & target group ............................................................................................. 7
    Nature of the health problem or disease ........................................................... 7
    Epidemiology and burden of the disease ......................................................... 9
    Treatments for the disease & current practice ............................................. 10
  Technology status ......................................................................................................... 11
    Intervention type ..................................................................................................... 11
    Requirements for its use ....................................................................................... 11
    Current technology status ................................................................................... 12
Research Questions .................................................................................................................... 13
  Clinical safety & effectiveness ............................................................................... 13
  Value for money ........................................................................................................ 13
  Societal & ethical considerations .......................................................................... 14
  Feasibility of adoption in the health system .......................................................... 14
    Policy congruence .................................................................................................. 14
    Organisational issues ............................................................................................ 14
    Legal considerations ............................................................................................... 14
    Budget impact ......................................................................................................... 14
Methodology ............................................................................................................................... 15
  Narrative literature review ....................................................................................... 15
  Internet ............................................................................................................................. 16
  Ministry of Health knowledge systems .................................................................. 16
  Summary of latest New Zealand evaluation report .............................................. 16
Results & Discussion .................................................................................................................. 17
  Clinical safety & effectiveness ............................................................................... 17
    What is the clinical safety and efficacy of vaccines for varicella in children aged
    0-5 years? ................................................................................................................. 17
    Safety ........................................................................................................................... 17
Effectiveness........................................................................................................18
Outstanding uncertainty ..................................................................................20
Value for money..................................................................................................21
What costs were included? .............................................................................22
What non-financial benefits are expected? ...................................................23
What is the cost-effectiveness of adding the varicella vaccine to the existing
childhood immunisation schedule in New Zealand as a separate shot at 15
months and 4 years (Option 1), relative to a counterfactual scenario where the
varicella vaccine is not available at all (Option 2)? .......................................24
Would the vaccine be more cost-effective if it were targeted to different
population groups? If so, which groups? ......................................................27
Does reducing the number of doses affect the cost-effectiveness of the vaccine?28
Societal & ethical considerations ....................................................................28
  Acceptability .................................................................................................29
  Equity & Ethics ..............................................................................................31
  Psychological considerations .........................................................................33
Feasibility of adoption in the health system ....................................................33
  Policy congruence ..........................................................................................34
  Organisational issues .....................................................................................34
  Legal issues .....................................................................................................37
  Budget impact ..................................................................................................37
  Funding ............................................................................................................41
Conclusion ..........................................................................................................42
Options ..............................................................................................................42
Glossary of Terms .............................................................................................45
References ..........................................................................................................48
Appendix 1: Immunisation Programme ............................................................54
Appendix 2: HTA repositories searched ...........................................................55
Appendix 3: Search strategies ..........................................................................58
List of Tables

Table 1: Summary of the different quality of life weights for varicella in the literature... 8
Table 2: Registration status of NZ Varicella Vaccines ................................................................. 17
Table 3: Costs included in the economic evaluation of universal varicella vaccination .......................................................... 22

Table 4: Estimated annual costs of delivering a universal varicella vaccination programme with 100% uptake. ................................................................. 38
Table 5: Strengths and weakness of different options for publicly funding varicella vaccination in New Zealand ................................................................. 43
Executive Summary

Aim/Objective

The Immunisation Technical Forum has recommended that MMR + Varicella vaccination be publicly funded for children at 15 months, and that MMRV be funded at 4 years of age. To support advice to the Minister in September 2012 on whether or not to add the vaccine to the Schedule in 2014, this report examines the evidence for and against its inclusion across the National Health Committee’s five domains for assessment: Clinical, societal, ethical, economic and financial.

Method

The policy question, background and research questions have been developed according to best-practice methods for Health Technology Assessment (HTA). In order to answer the research questions in each domain a systematic search of the scientific literature published after 2009 and reports held by HTA agencies and repositories was undertaken. Abstracts were sifted through and categorised on the basis of their content into four domains and relevant papers were used to provide a narrative summary of the issues relevant to each domain. No formal critical appraisal of studies was undertaken. The use of Ministry of Health knowledge systems and targeted internet searches was also used to obtain context-specific information to address questions in the ‘societal & ethical’ and ‘feasibility of adoption’ domains.

Results & Discussion

Evidence suggests that all single-antigen vaccines currently available for varicella are clinically safe and effective for most children aged 0-5 years. Universal vaccination (2 doses) for varicella is cost-saving from a societal perspective, but not from a health payer’s perspective. The cost-effectiveness of vaccination will change depending on what it is compared against – it is more cost-effective than a universal rotavirus vaccination programme for infants, but may not be more cost-effective than increasing the coverage of existing vaccines on the schedule. The acceptability of the vaccine to the New Zealand public is uncertain and there are ethical and equity issues around the decision to vaccinate or not which require further exploration, particularly given the potential for universal varicella vaccination of children to increase the incidence of herpes zoster in adults. While it would be feasible to adopt a universal varicella vaccination programme in New Zealand, this may jeopardise other policy initiatives aimed at increasing overall vaccination coverage, and a systematic evaluation of the impact of the vaccination programme would require the set-up of a surveillance system; requiring the addition of varicella and herpes zoster to the list of mandatory notifiable diseases contained in part 2 of schedule 1 of the Health Act 1956.

Conclusion

The decision to publicly fund the universal vaccination of children aged 15 months and 4 years is complex and hinges on a number of uncertainties, which may, depending on the level of risk decision-makers are comfortable with, require further research and analysis. There are a number of alternative options to ‘universal vaccination’, which may be preferable depending on the priorities of decision-makers.

---

1 Note that to ease analysis and include the decision criteria, in the report these domains are covered under the headings of Clinical safety & effectiveness, Societal & ethical, Value for Money (ie ‘Economic) and Feasibility of adoption within the system (includes financial).
Policy Question
The goal of this assessment is to answer the policy question: Should the Ministry of Health fund the universal vaccination of children for varicella zoster virus (ie, chicken pox)? It follows a recommendation by the Immunisation Technical Forum (ITF) that MMR\(^2\) + Varicella (separate vaccines) vaccination be publicly funded for children at 15 months, and that MMRV (combined vaccine) be funded at 4 years of age. No preference for either the Merck Sharp & Dohme (MSD) or GlaxoSmithKline (GSK) vaccines was expressed by the ITF.

Who initiated or commissioned the report?
The Ministry of Health’s (‘the Ministry’) Immunisation team in the Sector Capability & Implementation business unit have commissioned the National Health Committee (‘the NHC’) to assess the addition of the varicella vaccine to the National Immunisation Schedule (‘the Schedule’) following a clinical recommendation by the ITF.

A brief overview of the Ministry of Health’s immunisation programme and the role of ITF and the Immunisation team are provided in Appendix 1 (page 54).

Why is an assessment needed right now?
The ITF, appointed by the Director-General of Health, reviews the Schedule every three years and makes recommendations on the use of current vaccines and new vaccines (or new combinations of vaccines) to be added to the Schedule. The ITF bases its advice on technical evidence on effectiveness of new vaccines, epidemiology, availability of new types of vaccines and sector capability. Historically, a full assessment of a vaccine has not been undertaken, and the other domains (such as value for money, societal & ethical, and feasibility of adoption in the system) have only been considered on an ad-hoc basis.

A full assessment of the addition of varicella to the vaccine schedule is needed now because the:

1. Immunisation team needs to show it is taking account of value for money in vaccines prioritisation
2. NHC wants to signal its intent to work in the area of vaccines in the future.

The most recent cost-effectiveness analysis of varicella immunisation in New Zealand was conducted in 1999 and was a cost-benefit analysis, based on a single dose of the vaccine, rather than a cost-utility analysis based on two doses (ie, it did not include quality of life or quality adjusted life years (QALYs) (Scuffham et al 1999). In order for the cost-effectiveness of the introduction of this vaccine to reflect current clinical recommendations and be comparable with previous evaluations conducted by PHARMAC and future evaluations conducted by the NHC, a cost-utility analysis is required. As cost-utility analyses comprise a core part of HTAs, this proposal was identified as a suitable learning project to be used in the development of the NHC’s HTA processes and products.

Which decision is it going to support?
The assessment will support advice to the Minister on a budget bid in September 2012 on whether or not to add the varicella vaccine to the Schedule at its next revision in 2014.

---

\(^2\) MMR stands for Measles, Mumps and Rubella
Who represents the primary target audience for the report?

The primary audience for this report are political decision-makers. However, as a policy review of the management of vaccines in New Zealand is currently underway, it is unclear whether the review will affect the audience for the report or when the audience for the report will be known. Until this is clarified, the assessment will proceed on the basis that the audience comprises: the Immunisation team, National Health Committee Board, and the Minister of Health.

Background

The first part of this background section describes the condition and target group the intervention is expected to influence and the epidemiology and burden of the disease in the New Zealand population. Following this introduction, all the available treatments for the disease are outlined, and the effectiveness of current practice is discussed. The second part of this background section looks at the intervention that is proposed, including the requirements of its use and its current regulatory status and uptake in New Zealand.

Condition & target group

Nature of the health problem or disease

What are the mechanisms of disease?

Varicella-zoster virus (VZV) causes two distinct clinical entities: varicella (chickenpox) and herpes zoster (shingles) (Whitley 2011b). Chickenpox is a contagious infection of childhood characterized by rash. The reactivation of latent VZV, most common after the age of 60, presents as a herpes zoster and is incredibly painful (Whitley 2011b). Varicella is one of the most infectious diseases known (along with pertussis and measles). Transmission of varicella occurs via airborne droplets, or contact with infected respiratory tract secretions or vesicular lesions. Humans are the only reservoir of the disease (Whitley 2011b).

Is there any variation in pathogenicity?

Three different genotypes have been recognized with a different geographic distribution, but they belong to the same serotype (Loparev et al 2004) in (2006). No difference in virulence or transmissibility between strains of these different genotypes has been reported.

Are there interactions with other pathogens?

Bacterial superinfections of the skin, lungs and bones are complications of a varicella infection. In particular, severe invasive group A streptococcal infections are associated with varicella infection (Laupland et al 2000).

What is the course and prognosis of the condition?

The incubation period of varicella is 10-21 days (usually 14-16 days). A red area on the skin, covered with small merged bumps (maculopapular), that become small, fluid filled cavities (vesicular), appears on the face and scalp (Ministry of Health 2011a). This later spreads to the trunk and abdomen and eventually to the limbs. The vesicles dry and crust after three to four days, but may be followed by further lesions. A wide variation in the number of lesions is possible, ranging from a few to many hundred, but there are lesions at all states.

In the immunocompetent child, varicella is usually a benign illness associated with weariness and with body temperatures of 37.8°–39.4°C (100°–103°F) of 3–5 days' duration. Lesions can be found in the mouth and at times in the vagina, where they can be the cause of
considerable distress. The rash is itchy and is usually associated with mild fever, malaise, anorexia and listlessness (Ministry of Health 2011a). Immunocompromised patients—both children and adults, particularly those with leukaemia—have lesions (often with a hemorrhagic base) that are more numerous and take longer to heal than those of immunocompetent patients. Immunocompromised individuals are also at greater risk for visceral complications, which occur in 30–50% of cases and are fatal 15% of the time in the absence of antiviral therapy (Whitley 2011b).

What is the infectiveness of various stages of infection?
VZV is highly contagious, both by aerosols and direct contact with lesions of varicella and, to a lesser extent, zoster. In temperate climates the mean age of VZV-infection is lower than in (sub-) tropical climates (Boot et al 2006).

What are the consequences?
Following infection with varicella, most children return to good health and are protected from future infection. However, there are a number of complications of varicella along with the possibility of reactivation of the virus in adulthood (herpes zoster). The most common complication is secondary bacterial superinfection of the skin, which is usually caused by Streptococcus pyogenes or Staphylococcus aureus, including strains that are methicillin-resistant. Skin infection results from tearing of lesions after scratching (Whitley 2011b). Other complications include varicella pneumonia (more common in adolescents and adults), acute cerebella ataxia (more common in infants and children, and almost always self-limited), and, rarely, encephalitis, with permanent neurological disability or fatal outcome. Transverse myelitis, thrombocytopenia and rarely, involvement of the viscera and joints may also occur (Ministry of Health 2011a).

The consequences of the disease may be more serious in adults, particularly pregnant women, and the risk of severe disease is greatly increased in neonates and immune-suppressed individuals.

There is also potential for the virus to be re-activated in adults. Herpes zoster (shingles) results from reactivation of the latent varicella virus infection. The majority of cases of zoster occur in adults aged 40 years or older. Herpes zoster occurs more commonly in immune-suppressed individuals (Ministry of Health 2011a). The factors responsible for the reactivation of VZV are not known. In children, reactivation is usually benign; in adults, it can be debilitating because of pain and has been associated with loss of taste, blindness and ipsilateral facial palsy (Whitley 2011b).

What is the quality of life following infection?
The quality adjusted life year (QALY) is a summary measure of health gain that takes into account not only length of life but also quality of life. When QALYs are calculated, the number of life years over which an individual will experience a particular condition is combined with the quality of life during those years. Quality of life in the calculation of QALYs is measured on a 0 to 1 scale where 0 is equated to ‘being dead’ and 1 is ‘full/normal health’. Values between 0 and 1 are known as ‘health state utilities’. Essentially reflecting different degrees of impairment across different dimensions of health, these utilities can be interpreted as judgements of how ‘good’ or ‘bad’ different conditions are.

For example, in Table 1 Smith & Roberts (2000) in Boot et al (2006) note that adults who have been hospitalised for varicella have a quality of life of 0.40, compared with children with varicella who experienced less of a drop in quality of life, with a value of 0.76 (Boot et al 2006). The table below also illustrates the variability of the available estimates of the impact of varicella on the quality of life of different groups.

Table 1: Summary of the different quality of life weights for varicella in the literature
Quality of life following infection | Quality of life lost | Description | Source |
--- | --- | --- | --- |
0.40 | 0.60 | Adults with varicella during hospitalisation | Smith & Roberts (2000) in Boot et al (2006). |
0.50 | 0.50 | Adults with varicella during hospitalisation | Paul et al (1995) in Boot et al (2006). |
0.65 | 0.35 | Adults with varicella receiving acyclovir³ | Sackett & Torrance (1978) in Boot et al (2006). |
0.76 | 0.24 | Children with varicella | Brisson & Edmunds (2004) in (Boot et al 2006) |
0.80 | 0.20 | Adults with varicella without complications | Sackett & Torrance (1978) in Boot et al (2006) |
0.85 | 0.15 | Adults with varicella not receiving acyclovir | Sackett & Torrance (1978) in Boot et al (2006) |

Source: (Rosevear and Urlich 2012b)

### Epidemiology and burden of the disease

#### How many people are affected?

The epidemiology of this infection appears to be similar in all developed countries with temperate climates. Epidemics occur each winter/spring with some variability annually (Ministry of Health 2011a). Over 97% of each birth cohort is infected with varicella by the age of 40. Approximately 3% of each cohort are infected in infancy, and a further 8-9% are infected annually, so that by age 14 less than 10% remain susceptible (Ministry of Health 2011a). Most infections are symptomatic, but there is evidence that asymptomatic infections also occur in some countries (Boot et al 2006).

In New Zealand, there is not reliable surveillance data on the incidence of varicella in the population, or the proportion of symptomatic versus asymptomatic infections (Ministry of Health 2011a). However, it is estimated that each year there are approximately 50,000 chickenpox infections, of which 150-200 result in hospitalisation, and 1-2 cases result in long-term disability or death (Ministry of Health 2008). Mortality in normal healthy children is less than 2 per 100,000 cases, but this increases up to 15 fold in adults (Ministry of Health 2008).

Based on the information above, and assuming a total population of 4,409,000⁴ (Statistics New Zealand 2009), in 2011 the estimated incidence of varicella was 1,134 per 100,000 of the population, the incidence of hospitalisation for varicella will be 5 per 100,000 of the population.

---

³ One of the most commonly used antiviral drugs; it is primarily used for the treatment of herpes simplex virus infections, as well as in the treatment of varicella zoster (chickenpox) and herpes zoster (shingles).

⁴ Statistics New Zealand: Series 1: Assuming low fertility, high mortality and long-run annual net migration of 5,000.
population, and the mortality rate will be less than 0.05 per 100,000. It has been estimated that in 2008/09, hospitalisations for chickenpox cost the public health system approximately $0.8 million; driven largely by the hospitalisation of children under 5 years of age.

Who is affected?
The average age of infection is seven years. As transmission of the virus is less efficient in tropical climates, adolescent and adult immigrants to New Zealand from these countries are more susceptible, placing them at risk of contracting the disease in their new environment. Being older, their experience of the disease may be more severe (Ministry of Health 2011a). There is also evidence those individuals with immune-suppression and pregnant women who are at greater risk of severe disease if they have not been infected with it previously.

Treatments for the disease & current practice
Medical management of chickenpox in the immunologically normal host is directed toward the prevention of avoidable complications. Secondary bacterial infection of the skin can be avoided by meticulous skin care, particularly with close cropping of fingernails. Itching can be decreased with topical dressings or the administration of anti-itching drugs. Administration of aspirin to children with chickenpox should be avoided because of the association of aspirin derivatives with the development of Reye’s syndrome (Whitley 2011a).

Acyclovir (800 mg by mouth five times daily), valacyclovir (1 g three times daily), or famciclovir (250 mg three times daily) for 5–7 days is recommended for adolescents and adults with chickenpox of 24 h duration. Likewise, acyclovir therapy may be of benefit to children <12 years of age if initiated early in the disease (<24 h) at a dose of 20 mg/kg every 6 h.

Three methods are currently used to prevent infections from varicella:
First, a live attenuated varicella vaccine (Oka) is recommended for all children >1 year of age (up to 12 years of age) who have not had chickenpox and for adults known to be seronegative for VZV (Whitley 2011a).

A second approach is to administer varicella-zoster immune globulin (VZIG) to individuals who are susceptible, are at high risk for developing complications of varicella, and have had a significant exposure (Whitley 2011a).

Lastly, antiviral therapy can be given as prophylaxis to individuals at high risk who are ineligible for vaccine or who are beyond the 96-h window after direct contact. While the initial studies have used acyclovir, similar benefit can be anticipated with either valacyclovir or famciclovir. Therapy is instituted 7 days after intense exposure. At this time, the host is midway into the incubation period. This approach significantly decreases disease severity, if not totally preventing disease (Whitley 2011a).

How effective are current preventive measures?
The clinical importance of the treatment of varicella with antiviral treatment (ie, with acyclovir) in otherwise healthy children remains uncertain. While it appears to be effective in reducing the number of days with fever and the maximum number of lesions among otherwise healthy children with chickenpox, results are less convincing with respect to the number of days to no new lesions and relief of itchiness (Klassen and Hartling 2005). Vaccination is the best way

to prevent infection with varicella—the virus that causes chickenpox—both in an individual and in the community (CDC 2007).

**Technology status**

**Intervention type**
An attenuated (live) VZV (Oka strain), developed in Japan was found suitable as a vaccine for the prevention of varicella (Ministry of Health 2011a). The vaccine is available in the form of a lyophilised powder for reconstitution with the supplied diluent, administered by subcutaneous injection in the deltoid area. The vaccine works by stimulating the immune system of an individual to develop adaptive immunity to the varicella zoster virus.

*What is the protection afforded by the vaccine?*
Post-licensure, vaccine-effectiveness studies of one dose of the single-antigen varicella vaccine have shown high levels of protection (70%-90%) against any form of varicella disease and more than 90% protection against severe disease. In the randomized clinical trial of one versus two doses of single-antigen varicella vaccine administered 3 months apart, the estimated vaccine efficacy of two doses was 98%, which was significantly higher than after one dose. The two-dose regimen was 100% efficacious against severe varicella. If a vaccinated person does get varicella, it is usually a very mild case with fewer lesions (usually less than 50, which are frequently not vesicular), mild or no fever, and a quicker recovery. Persons with rash, however, are infectious (CDC 2007).

**Requirements for its use**
Vaccines are prescription medicines, so they can only be administered by medical practitioners, registered midwives, designated prescribers (including registered nurses), and people authorised to administer the medicine in accordance with a standing order.

The vaccine needs to be stored in a refrigerator at +2°C to +8°C, while the diluent can be stored at room temperature. The reconstituted vaccine must be used immediately. The two manufacturers of the vaccine recommend one dose for children aged 9 months to 12 years and two 0.5 ml doses given 4 to 8 weeks apart for those aged 13 years and older. The vaccine can be administered concurrently with other vaccines in a separate syringe at a different site. The optimal vaccination schedule for varicella would be as a single-shot fourth injection for infants at the 15 month visit and then as a four-fold MMRV combination vaccination at 4 years. If not administered concurrently, the vaccine must be separated from other live vaccines by at least four weeks. While only two doses of the vaccine are currently recommended, ongoing studies and surveillance will determine the need for and, if appropriate, the timing of additional doses in the future (CDC 2007).

As transmission continues to decline, decreasing circulation of wild virus will increase the likelihood that unexposed and unvaccinated children will enter adolescence and adulthood without immunity. The Centers for Disease Control and Prevention (CDC) therefore note that it is increasingly important to offer vaccination to all susceptible adolescents and adults as well as children.

Successful implementation of vaccines is associated with the public’s perception of the disease burden the vaccine aims to prevent. There is some evidence that in some countries the public’s perception of the burden of varicella is low, and that this may influence acceptance of the vaccine (Boot et al 2006).
Current technology status

The United States, Australia, Germany, and Canada have all adopted recommendations to routinely immunize children for chickenpox while other countries, such as the United Kingdom, have targeted recommendations for the vaccine.

In New Zealand, as noted in the Immunisation Handbook 2011 (Ministry of Health 2011a), the varicella vaccine is recommended, but not currently publicly funded, for:

- Susceptible adults and adolescents with no prior history of infection, particularly those
  - born and residing in tropical countries
  - who live or work in environments where transmission of the virus is likely (eg, early childhood services etc)
  - who live and work in environments where transmission can occur (eg, college students, inmates and staff)
  - non-pregnant women of childbearing age
  - international travellers
  - healthcare workers
  - post exposure.

- Children undergoing solid organ transplant, including those with
  - chronic liver disease who may be future candidates for transplantation
  - deteriorating renal function

- Children with HIV infection CDC stage N1 or A1

Currently Varilrix (GSK) and Varivax (MSD) (both based on the Oka strain) are approved for use and are available for distribution in New Zealand (Ministry of Health 2011a). Two quadrivalent measles, mumps, rubella and varicella vaccines (MMRV) are approved for use and are also available for distribution in New Zealand (Priorix-Tetra-GSK and ProQuad - MSD).

The main supplier of the varicella vaccine in New Zealand is GlaxoSmithKline (Varilrix; 90% market share), with a comparatively smaller share of the market held by Merck Sharp & Dohme (Varivax). The number of people privately purchasing Varilrix vaccine has increased by 84% since 2010, from 5,532 to 10,201 doses. The increase in uptake over the last 18 months has been attributed to medical education, advertising, consumer support material such as brochures and a website. Previously this vaccine was not promoted.

The Varivax brand of vaccine sold less than 1,000 doses in 2010. However, as with Varilrix, the sales of Varivax also increased by half between 2009 and 2010. The wholesale price for both vaccines is $50 per dose, excluding GST. It is estimated that the price currently paid by consumers range from $70 to $130 once the practice charge is taken into account. Based on the 2011 sales data for Varilrix and assuming a 1-dose regime, 16% of the New Zealand children are being vaccinated. Assuming a 2-dose regime, approximately 8.3% of children are vaccinated. The actual percentage of coverage will be between these two figures because while 2 doses are recommended for children, they often are prescribed just 1 dose. ProQuad, the MSD branded quadrivalent MMRV vaccine has never been introduced in New Zealand.
Zealand due to a global shortage of supply. The GSK quadrivalent MMRV vaccine is registered in New Zealand but is not currently available for private purchase.

**Research Questions**

These research question/s outlined below have been formulated with reference to the policy question and in terms of the domains for assessment7. Various assessment frameworks specific to vaccines have been developed and the questions under each of the domains below have been formulated with reference to a selection of these (Boot et al 2006) in addition to those detailed in the Busse et al’s (2002) paper detailing ‘best practice’ for undertaking Health Technology Assessments (HTAs).

**Clinical safety & effectiveness**

What is the clinical safety and efficacy of vaccines for varicella in children aged 0-5 years?

What is the mortality and morbidity directly related to the use of the vaccine?

What is the morbidity/disability directly related to the use of the vaccine?

What is the overall change in condition-specific mortality?

What is the overall change in morbidity/disability/disease-free interval?

What is the change in quality-/disability-adjusted-life-years (QALYs/DALYs)?

**Value for money**

In this domain of the Health Technology Assessment the cost-effectiveness and value for money from adding the vaccine to the New Zealand immunisation schedule is addressed. It looks at what are the costs and changes in cost compared to current practice using the appropriate form of economic evaluation (cost-effectiveness8, cost-utility, cost-benefit, cost minimisation etc).

The objective of this domain is to determine whether the recommendation of the Immunisation Technical Forum (ITF), for the addition of varicella vaccination to the immunisation schedule, is cost-effective from both a health payer’s and societal perspective. The specific question to be addressed is thus:

What is the cost-effectiveness of adding the varicella vaccine to the existing childhood immunisation schedule as a separate shot at 15 months and 4 years (Option 1), relative to a counterfactual scenario where the varicella vaccine is not available at all (Option 2)? The costs of vaccination and illness should be considered from a health payer’s perspective and a societal perspective.

Other questions, for consideration are:

- How does reducing the number of doses affect the cost-effectiveness of the vaccine?
- Would the vaccine be more cost-effective if it were targeted to different population groups? If so, which groups?
- What is the potential impact of an increase in Herpes Zoster virus on the cost-effectiveness of vaccinating for varicella?

---


8 For a quick explanation of what cost-effectiveness is and how the analysis is done, check out the briefing by Phillips Phillips C. 2009. What is cost-effectiveness? www.whatisseries.co.uk.
• Do caregivers associate their children getting varicella with a significant loss of income?
• Do employers believe the productivity of their business is significantly affected by caregivers taking sick days to care for children with varicella?

Societal & ethical considerations
What proportion of the target population will accept the vaccine, or has already been vaccinated? (Acceptability)
Will reduced pathogen transmission lead to enhanced vulnerability of specific sub-populations (eg, to Herpes zoster/shingles)? (Ethics)
Are the benefits of vaccination, or costs of not vaccinating, experienced disproportionately by different groups and if so, which ones? (Equity)
Are there any psychological issues associated with varicella or the vaccine?

Feasibility of adoption in the health system
What additional health sector factors would need to be addressed to ensure successful implementation of the proposed vaccination programme in New Zealand?

Policy congruence
How does the addition of this vaccine fit with other policy and practices in immunisation and the wider health sector?

Organisational issues
How would the addition of the vaccine fit with the existing Immunisation Schedule?
How would universal vaccination affect the use of other health services (ie, GP visits, hospitalisations, pharmaceutical consumption etc)?
What are the health workforce implications of introducing universal vaccination for varicella?

Legal considerations
Are there any legal considerations around continuing not to vaccinate, or around the decision to vaccinate?

Budget impact
What impact would the introduction of universal vaccination have on the available budget for vaccines and the total budget of Vote: Health?
Is the universal public funding of varicella vaccination affordable and sustainable?
How difficult would it be to disinvest in this vaccination programme in the future?
Methodology

Health Technology Assessment is a multidisciplinary field of policy analysis that studies the medical, economic, social and ethical implications of development, diffusion and use of health technology. It usually involves systematic reviews of the literature, epidemiological and financial analysis of administrative health data, economic evaluation and budget impact analysis, and public and health sector engagement. It aims to answer a specific set of research questions across domains in order to answer an overall policy question around investment. This section of the report describes the methods used in the assessment of the addition of varicella vaccine to the immunisation schedule.

The latest review of the clinical safety & effectiveness, and cost-effectiveness, of introducing varicella immunisation in New Zealand were published in 2011 (Ministry of Health) and 1999 (Scuffham et al), respectively. The review of the vaccine’s clinical safety & effectiveness was undertaken by the Immunisation Technical Forum (ITF) and published in the Ministry of Health’s Immunisation Handbook 2011. No formal systematic review or clinical appraisal of the clinical evidence was undertaken as part of this review. The cost-effectiveness analysis of introducing the vaccine was determined through a pure cost-benefit analysis based on a single dose of the vaccine delivered at 15 months of age alongside the vaccines for measles mumps and rubella (MMR) and diphtheria, tetanus, pertussis and haemophilus influenzae type b (DTPH) and published in 1999 (Scuffham et al 1999).

Significant developments in the clinical efficacy of the vaccine, and the requirement for the evaluation results to be comparable with evaluations conducted by PHARMAC, and to take into account not only clinical and economic factors, but also social, ethical and financial, have necessitated an updated and broader assessment of varicella vaccination. This assessment achieves this in a number of ways: Firstly, through reviewing the literature from 2009 onwards; secondly, targeted searches of the internet, thirdly, use of the Ministry of Health’s existing knowledge systems (national collections and Health Report database), and finally, through summarising the findings of a recent evaluation report commissioned by the Ministry of Health’s immunisation team.

Narrative literature review

On the 16 September 2011 the Ministry of Health reference librarians searched the sites of key Health Technology Assessment (HTA) agencies and repositories using the following search terms: Varicella, Herpes Zoster, VZV vaccination. A full list of the repositories and agencies searched is attached in Appendix 2. No time or language constraints were used. Publications that focussed solely on herpes zoster were excluded. Three publications were retrieved from this search, the first was a systematic review and recommendations report published by the Canadian Taskforce on Preventive Health Care (CTPHC) in 2000, the second was the Economics of Childhood Immunisations in Canada: Data Book published in 2007 by the Institute of Health Economics Canada, and the third was a cost-utility analysis of vaccination in Belgium against chickenpox in children and against herpes zoster in the elderly published by the Belgian Health Care Knowledge Centre in 2010.

Following this initial search of HTA agencies and repositories, Ovid MEDLINE® and Cochrane Library were searched for scientific journal papers published between 1 January 2009 and 2 November 2011. The search terms used were: cost-effectiveness, cost-benefit, cost-utility, economic evaluation, economic model, decision analysis, varicella vaccination, chicken pox vaccination, herpes zoster. Results were limited to either systematic reviews OR studies based in the United States, Europe, Canada, Australia, or New Zealand. No language limits were applied. A subsequent search of EMBASE for papers published between 1 January 2009 and 16 November 2011, using the same inclusion and exclusion
criteria was also undertaken. The reference lists of identified publications were not searched. The full search strategy is provided in Appendix 3.

In addition to papers identified in this search, three papers included in the Ministry of Health’s tender for the economic evaluation were also retrieved (Boot et al 2006; Macartney and Burgess 2008; Scuffham et al 1999).

Abstracts were sifted through and categorised, on the basis of their content, into one of four domains: Economic, Clinical, Social & Ethical, and Feasibility of adoption within the system. All abstracts were included (regardless of position on evidence hierarchy) but only the full text of relevant studies where further detail was required were retrieved. No formal critical appraisal of studies was undertaken. Abstracts and full papers retrieved were used to create a narrative summary of the issues relevant to each domain and answer the specific research questions.

Internet

If, after producing the narrative summaries for each domain the key research questions had not been addressed, further targeted searches using Google and Google scholar were undertaken. This strategy was used primarily to identify context-specific information required to answer questions in the ‘societal and ethical’ and ‘feasibility of adoption within the system’ domains and included New Zealand-specific information on immunisation coverage, as well as an investigation of other vaccines on the horizon.

Ministry of Health knowledge systems

The Ministry of Health’s filing cabinets were used to obtain contextual information, particularly around the amount of money spent on promoting new vaccines. Data collected by Medsafe on adverse reactions to the varicella vaccines currently available in New Zealand was also reviewed.

Summary of latest New Zealand evaluation report

As of 2005, the recommended number of doses of the varicella vaccine changed from one to two. It has also become more important for decision-makers to prioritise new investments against others, and value all consequences, regardless of whether a monetary value can be attached to them. These changes have meant that the initial New Zealand-based evaluation of the vaccine by Scuffham et al 2009 which was based on a single dose, and provided only a cost-benefit analysis, needed to be updated to include the new two dose regime and a cost-utility analysis.

In June 2011 the Ministry of Health put out a request for tender (RFT) for an economic assessment of the introduction of the varicella vaccine into the national immunisation schedule as a two dose programme. A literature search regarding the diseases and vaccines and an appraisal of the evidence was not expected of the contractor. Estimates of vaccine effectiveness were based on the Immunisation Technical Forum’s assessment of the literature, and were to be taken from the Immunisation Handbook 2011. The cost-effectiveness of the programme was to be determined via a cost-utility analysis consistent with PHARMAC’s analytical guidelines. A member of the NHC executive and PHARMAC were part of the steering panel for the contract. The results from the analysis were provided to the Ministry of Health as a report on 20 January 2012 (Rosevear and Urlich 2012b). The report was critically appraised using the checklist for economic evaluations constructed by Drummond et al (2005), and the results of the evaluation and findings from the critical appraisal are presented in section 0 alongside those of other cost effectiveness analyses identified in the initial literature search described in section 0. The report by Rosevear and Urlich is used to provide contextualised answers to the research questions posed in the ‘value for money’ domain.
### Results & Discussion

The results from each of the processes described above are presented below under the headings of clinical safety & effectiveness, value for money, societal & ethical, and feasibility of adoption within the system.

#### Clinical safety & effectiveness

Evidence suggests that all the vaccines currently available for varicella are clinically safe and effective for most children aged 0-5 years. Internationally, it is evident that countries that have introduced vaccination for varicella have seen declines in the number of cases, hospitalisations and deaths associated with the disease. However, there is evidence that the quadrivalent MMRV vaccine may be less safe for children aged 15 months than the single-antigen vaccine, and that the universal vaccination for varicella may increase the incidence of herpes zoster in the unvaccinated population in the short to medium term.

**What is the clinical safety and efficacy of vaccines for varicella in children aged 0-5 years?**

To ensure that the evidence around the safety and efficacy of the vaccines available has not changed since the Immunisation Technical Forum (ITF) recommendation, this section of the report provides a narrative review of the experience with the vaccine to date and highlights the main issues of interest.

#### Safety

Both the two quadrivalent mumps, rubella and varicella vaccines (MMRV) (*Priorix-Tetra* (GSK), *ProQuad* (MSD)), and the two single-antigen varicella vaccines (*Varilrix*-GSK & *Varivax*-MSD) have been approved for use by Medsafe and have consent for distribution in New Zealand (Table 2). Medsafe’s approval of the vaccines indicates that all brands of varicella vaccine have met the required thresholds for safety & efficacy.

**Table 2: Registration status of NZ Varicella Vaccines**

<table>
<thead>
<tr>
<th>Brand</th>
<th>Registration situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varilrix Vaccine (GSK)</td>
<td>Consent given</td>
</tr>
<tr>
<td></td>
<td>Approval date: 12/9/1996</td>
</tr>
<tr>
<td>Varivax(MSD)</td>
<td>Consent given</td>
</tr>
<tr>
<td></td>
<td>Approval date: 3/6/1999</td>
</tr>
<tr>
<td>Priorix-Tetra (GSK)</td>
<td>Not marketed</td>
</tr>
<tr>
<td></td>
<td>Approval date: 15/3/2007</td>
</tr>
<tr>
<td></td>
<td>Notification date: 25/8/2011</td>
</tr>
<tr>
<td>ProQuad (MSD)</td>
<td>Consent given</td>
</tr>
<tr>
<td></td>
<td>Approval date: 6/12/2007</td>
</tr>
</tbody>
</table>


While there are instances of morbidity directly related to the use of both the single-antigen and combined MMRV vaccines, there do not appear to be any deaths. Experience internationally, suggests the following adverse reactions are possible: local reactions, febrile seizures (MMRV), fever and mild papulovesicular rash (Ministry of Health 2011a). Five-year results of the European Varicella Zoster Virus Identification Programme continue to confirm that Oka/Merck vaccine is generally well tolerated (Goulleret et al 2010).
adverse reactions database contains few events reported to be associated with varicella vaccination; as with any vaccine there are a number of reports of vaccine failure.

Varicella vaccine is contraindicated for:

- individuals with primary or acquired T-cell immune deficiency states – consult the child’s paediatrician for advice
- children on high-dose steroids (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20 mg per day if their weight is over 10 kg)
- children on salicylates, because of the association between Reye syndrome, natural varicella infection and salicylates – the vaccine manufacturers advise against the use of salicylates for six weeks after varicella vaccine is given; there has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution, and physicians need to weigh the theoretical risk from the vaccine against the known risk of varicella disease in children receiving long-term salicylate therapy
- individuals with known systemic hypersensitivity to neomycin
- women during pregnancy – women should be advised to avoid pregnancy for three months after vaccination, because the vaccine’s safety for the fetus has not yet been demonstrated.

(Ministry of Health 2011a p329-330)

Co-administration

The Immunisation Technical Forum (ITF) has recommended that the varicella vaccine be administered at 15 months and 4 years of age. This means it will be administered at the same time as PCV10, MMR and Hib at 15 months of age and alongside MMR and DTaP-IPV at 4 years of age. For the vaccine to fit with the existing schedule, evidence that the vaccine can be co-administered with these vaccines is essential. The ITF have advised that the administration of the single-antigen varicella vaccination alongside existing immunisations at 15 months and that administration of varicella + MMR, or replacement with MMRV for the second dose at 4 years is safe (Ministry of Health 2011a). However, the handbook does not comment on whether there is evidence supporting the administration of MMRV or MMR + V alongside DTaP-IPV. However, the Canadian National Advisory Committee on Immunisation (NACI) notes that varicella vaccine may be administered during the same visit but at a separate injection site as DTaP-IPV-Hib vaccines (PHAC 2007). If not given during the same visit as other live virus vaccines (e.g., MMR), administration of the two live vaccines should be separated by at least 4 weeks.

Other vaccines where coadministration with MMRV has shown to be effective include: Tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine is well tolerated and immunogenic when co-administered with MMRV vaccine during the second year of life (RCT) (Vesikari et al 2011). PHiD-CV and MMRV vaccine can be coadministered without compromising the safety and immunogenicity profiles of either vaccine (Vesikari et al 2010).

Effectiveness

In addition to the clinical efficacy and immunogenicity data that supported their licensure, subsequent studies of the 1 and 2 dose programmes overseas continue to provide evidence of the vaccine’s effectiveness in non-trial conditions. A review of 17 studies (case control, cohort (outbreak), and house contact) by the Centers for Disease Control and Prevention (CDC) found that on average, one dose protected against 81% of varicella cases, while 2 doses protected against 98% of varicella cases (CDC 2011b). The CDC have also noted

\[9\] Pers comm. – Manager, Clinical Risk Assessment at Medsafe (Email dated: 1 February 2012)
that one dose protects against 97% of moderate and severe disease combined, and 100% of severe disease\textsuperscript{10} (CDC 2011b).

\textit{United States}

In 1999, the Advisory Committee on Immunisation Practices (ACIP) recommended the vaccination of children aged 12-18 months with a single dose of the varicella vaccine. In 2005, ACIP adopted new recommendations – advising that an additional dose be added at 4-6 years to prevent break-through cases (Marin et al 2007).

Since the implementation of the single-dose varicella vaccination program in 1995, varicella-related hospitalization numbers and rates declined significantly (Lopez et al 2011; Shah et al 2010). Similarly, it has been argued that the impressive decline in varicella deaths can be directly attributed to the successful implementation of the single-dose vaccination programme (Marin et al 2011).

\textit{Australia}

The varicella vaccine was licensed in Australia in 1999 and a single dose of the vaccine has been publicly funded for children aged 18 months since 2005, with a catch-up program for children aged 10-13 years who have not received varicella vaccine or who have not had the disease (Department of Health and Ageing 2011). A second dose is recommended for, but not publicly funded for, parents/caregivers that wish to minimise the risk of break-through varicella in children (NHMRC 2008).

Between 2000 to 2007, varicella hospitalisation rates declined by 7% each year, predominantly in children under five (12%) and a similar decline was observed in community data (Carville et al 2010). There also appears to have been a reduction of congenital varicella and a significant reduction of neonatal varicella in Australia following the introduction of universal varicella vaccination (Khandaker et al 2011).

\textit{Canada}

In Canada the vaccination (single dose) of children aged 12-18 months has been routine since 1997 (PHAC 2007). Unlike the United States, Canada does not currently have as a goal the elimination of varicella and their National Advisory Committee on Immunisation (NACI) continue to recommend a single-dose vaccine strategy for children\textsuperscript{11}.

An Edmonton-based study estimated that direct medical costs averted from vaccination were $102,717 (909 cases) in 2004 (Jacobs et al 2006 in IHE 2007).

\textit{Germany}

In 2004, the German Standing Committee on Vaccination (STIKO) recommended routine varicella vaccination for all children 11-18 months with the aim of reducing varicella associated morbidity and the reduction of the burden of disease. In July 2009, STIKO decided to follow the change of licensure and recommended a second dose of the varicella vaccine (Wiese-Posselt and Hellenbrand 2010). Descriptive analysis of sentinel data provided evidence of a reduction in the number of cases in four consecutive seasons following the introduction of the vaccination programme. The decrease was greatest in 0-4 year-olds, but the trend was seen in all age groups. In the three years after the general recommendation of varicella vaccination the annual number of hospitalised varicella cases steadily declined from 1,751 in 2005 to 1,269 in 2007 (Siedler and Arndt 2010). The decline

\textsuperscript{10} Severe varicella is defined here as greater than 500 lesions or a complication requiring a physician visit., and the disease severity scale used in clinical trials.

\textsuperscript{11} NACI recommends two doses for adults and adolescents ≥ 13 years of age.
in number of hospitalised cases per 100,000 population was largest in the age group 1-4 years old (from >20 hospitalised varicella cases per 100,000 population in 1994-2004 to 10 in 2007) and in infants (>30 in 1994-2004 to 21 in 2007).

**Single antigen varicella vaccine vs MMRV**

At the time of its licensure (2005), the use of MMRV vaccine was preferred for both the first and second doses over separate injections of equivalent component vaccines (MMR vaccine and varicella vaccine). However, on the basis of preliminary data from two studies conducted post licensure that suggested an increased risk for febrile seizures following vaccination with MMRV compared to MMR+V among children aged 12-23 months (Jacobsen et al 2009), the United States Advisory Committee on Immunization Practices (ACIP) updated its recommendations. Now both the ACIP and the Centers for Disease Control and Prevention (CDC) recommend the use of MMR + V in children aged 12-47 months for the first dose and MMRV for children >48 months (Marin et al 2010). The ITF in New Zealand has made the same recommendation (Ministry of Health 2011a).

A randomized comparative study suggests that MMRV vaccine is an immunogenic and safe substitute for a second dose of MMR vaccine in young children (Gillet et al 2009). It has also been noted that the MMRV vaccine is well tolerated and highly immunogenic when administered either subcutaneously or intramuscularly to children in the second year of life (Knuf et al 2010). A further study has also shown that two doses of MMRV vaccine administered in the second year of life elicited adequate immunogenicity and were well-tolerated whether administered with a dose interval of 4 weeks or 12 months (Rumke et al 2011).

Currently, only certain European countries (Germany, Israel, Latvia, Luxembourg) (World Health Organization 2011b) and the United States (Marin et al 2007) have included MMRV on their vaccination schedule. MMRV is not currently available in Australia (NHMRC 2008) or Canada (PHAC 2007).

**Outstanding uncertainty**

However, despite existing evidence on clinical safety and efficacy, from both randomised controlled trials and observational studies, uncertainty remains around whether there is a significant difference in clinical safety & efficacy between different vaccine brands, and the impact of varicella vaccination on herpes zoster in the future (Brisson et al 2010; Carville et al 2010; Civen et al 2009).

**Vaccine brands**

While Spackova et al (2010) attempted to compare vaccine efficacy and risk of varicella breakthrough in different vaccine brands, concluding that the one dose effectiveness of Varivax was 86% (95%CI:56-96), while the Varilrix one was 56% (95%CI: 29-72), the quality of the study has been challenged by GlaxoSmithKline (Marchetti and Cuccia 2010). The systematic review commissioned from the NZGG should clarify whether any other studies exist, whether they are suitable quality, and/or whether a meta-analysis of existing studies could provide this information. However, an initial search provides little evidence that one brand of vaccine is preferred over another, and the Immunisation Technical Forum in New Zealand expressed no preference for either the MSD or GSK vaccines (Ministry of Health 2011b).

While the United States uses only the MSD-branded vaccines (Varivax and ProQuad ) (Marin et al 2007), both brands of the single-antigen vaccine (Varivax and Varilix) are marketed in Canada (PHAC 2007), Germany (Wiese-Posselt and Hellenbrand 2010), and Australia (NHMRC 2008). Neither brand of the MMRV vaccine is currently available in Canada or Canada.
Australia, and the only brand of MMRV vaccine available in Germany is Priorix-Tetra (GSK) (Wiese-Posselt and Hellenbrand 2010).

Herpes zoster (HZ)
In most countries, baseline incidence of HZ prior to the introduction of the varicella vaccine is not well described, and it is unclear whether introduction of the varicella vaccination program has altered the epidemiology of herpes zoster and what impact this might have on the quality of life of the population as a whole.

Varicella vaccination might alter the risk for HZ at the level of both the individual and the population (i.e., herd immunity). At the individual level, most studies suggest that the risk of HZ following a single dose varicella vaccination is lower than the risk following wild-type varicella infection (Marin et al 2007). However, it has been suggested that varicella vaccination could change the risk of HZ at the population level. With the development of herd immunity and reduction in the likelihood of exposure, the varicella vaccination program prevents wild-type VZV infection among vaccine recipients and non-vaccine recipients, eliminating the risk of wild-type HZ in these groups. Given that exposure of persons with latent wild-type VZV infection to persons with varicella is thought to boost specific immunity, thereby controlling reactivation of VZV and the development of HZ, concern has been expressed that by providing fewer opportunities for varicella exposure among persons with previous wild-type varicella infection, a reduction in the likelihood of exposure might increase the risk for HZ (Marin et al 2007).

Models based on this assumption have suggested that childhood vaccination for varicella is expected to increase the incidence of herpes zoster for more than 40 years after introduction of the programme (van Hoek et al 2011b). It has also been suggested that while the increase in zoster incidence can be partly offset by vaccination of the elderly, the effectiveness of this combined strategy is limited, as much of the increase occurs in those adults too young to be vaccinated. The potential of this scenario, to some extent depends on the level of coverage, whereby intermediate levels (70% and 60% for first and second dose coverage respectively) is expected to lead to an increase in adult varicella, while high coverage (90%-80%) is less likely to lead to an increase (van Hoek et al 2011b).

While many studies analysing hospitalisation discharge and general practice data have found that the incidence of herpes zoster in the population following vaccination is increasing (Carville et al 2010; Nelson et al 2010; Patel et al 2008), there continues to be insufficient evidence to attribute the increase directly to the varicella vaccine programme (Alain et al 2009; Carville et al 2010; Donahue et al 2010; Harpaz and Yawn 2009; Jardine et al 2011; Leung et al 2011).

The uncertainty around the impact of varicella vaccination on herpes zoster is the main reason the United Kingdom has not commenced a programme of universal varicella vaccination (National Health Service 2010).

Value for money
The objective of this domain is to determine whether the recommendation of the Immunisation Technical Forum (ITF), for the addition of varicella vaccination to the immunisation schedule, is cost-effective from both a health sector and societal perspective. To address this, the section summarises and critically appraises the economic evaluation undertaken at the request of the Ministry’s Immunisation team by Rosevear & Ulrich (2012b), and places it in the context of other studies investigating the cost-effectiveness of varicella vaccination. The evaluation question was:

“What is the cost-effectiveness of adding the varicella vaccine to the existing childhood immunisation schedule as a separate shot at 15 months and 4 years (Option 1),
relative to a counterfactual scenario where the varicella vaccine is not available at all (Option 2)?"

The impact of an increase in herpes zoster and decrease in the number of doses (one dose versus two) on the cost-effectiveness of universal vaccination, as well as a targeted rather than universal programme of vaccination, are also briefly discussed.

What costs were included?
Rosevear & Ulrich (2012b) determined that each year, varicella cost the New Zealand economy approximately $29 million through lost productivity as a result of parental time spent caring for sick children instead of working, and loss of future earnings through death (Table 3). In addition to lost productivity, the annual medical costs incurred were estimated to be around $3.0 million, bringing the overall cost of varicella to around $32 million. The cost of varicella increases by 25% when the costs of herpes zoster (caused by reactivation of the varicella virus in adults) are taken into account, bringing the combined cost of herpes zoster and varicella to around $39 million. Rosevear & Ulrich (2012b pgs 44-45) suggest that, if their assumptions are correct, spending $6.1 million on a universal varicella vaccination programme for infants could save $1.8 million in medical costs (50% of total medical costs for varicella) and $24 million in lost productivity (84% of total productivity costs due to varicella).

Table 3: Costs included in the economic evaluation of universal varicella vaccination

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost (NZ$2011)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccination Programme</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ wholesale vaccine cost (excl. GST + excl. freight) with volume discount of 85%</td>
<td>$42.50 ($=50.00 × 0.85)</td>
<td>Limited information survey of medical centres</td>
</tr>
<tr>
<td>Administration cost based on 15 min time to administer, $32/hour for nurse and 50% practice overhead costs; $12=0.25×$32×1.5</td>
<td>$12.00</td>
<td>Vaccination nurse</td>
</tr>
<tr>
<td>Ministry procurement costs (5% of the cost of the vaccine)</td>
<td>$2.13 (=$42.50 × 0.05)</td>
<td>Estimate</td>
</tr>
<tr>
<td><strong>Total cost of programme</strong></td>
<td>$56.63</td>
<td>Assumes 100% uptake</td>
</tr>
<tr>
<td><strong>Productivity costs</strong></td>
<td>Average per case</td>
<td>Per year</td>
</tr>
<tr>
<td>Lost productivity due to caregiver taking care of sick child with varicella (2.2)</td>
<td>$463.00</td>
<td>$27,780,000.00</td>
</tr>
</tbody>
</table>

---

12 Assumes 60,000 cases of varicella per annum
13 Based on 60,000 cases of varicella
14 If only 91% uptake of first dose and 98% uptake of second dose following first dose, this total may reduce to $6,122,156.04 (($56.63 × 54,600) +($56.63 × 53,508))
days×$26.30/hr×8hrs)

| Lost future productivity due to mortality from varicella | $17.00 | $1,020,000.00 | Estimate |
| Total productivity costs for varicella | $480.00 | $28,800,000.00 | Estimate |
| Lost productivity due to adult case of herpes zoster | $766.00 | $10,417,600.00 | Estimate |
| Total productivity costs from varicella & herpes zoster | $1,246.00 | $39,217,600.00 |

<table>
<thead>
<tr>
<th>Medical costs</th>
<th>Average per case</th>
<th>Per year</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP visit due to varicella</td>
<td>$10.00</td>
<td>$600,000.00</td>
<td>Assumes 12,000 (20%) cases go at $50 per visit.</td>
</tr>
<tr>
<td>Pharmaceuticals for varicella</td>
<td>$13.37</td>
<td>$802,200.00</td>
<td>Community pharmacist</td>
</tr>
<tr>
<td>Emergency department for varicella</td>
<td>$17.00</td>
<td>$1,020,000.00</td>
<td>(Boot et al 2006) and analysis.</td>
</tr>
<tr>
<td>Hospitalisation for varicella</td>
<td>$10.36</td>
<td>$621,600.00</td>
<td>Assumes 0.54% cases, at $1927.</td>
</tr>
<tr>
<td>Total medical costs for varicella</td>
<td>$50.73</td>
<td>$3,043,800.00</td>
<td></td>
</tr>
<tr>
<td>GP visit due to herpes zoster</td>
<td>$70.00</td>
<td>$952,000.00</td>
<td>Assumes 1.4 visits (Gauthier et al 2009) per case at $50 per visit.</td>
</tr>
<tr>
<td>Pharmaceuticals for herpes zoster</td>
<td>$42.00</td>
<td>$571,200.00</td>
<td>Community pharmacist.</td>
</tr>
<tr>
<td>Outpatient for herpes zoster</td>
<td>$14.00</td>
<td>$190,400.00</td>
<td>(Gauthier et al 2009)</td>
</tr>
<tr>
<td>Hospitalisation for herpes zoster</td>
<td>$154.00</td>
<td>$2,094,400.00</td>
<td>(Boot et al 2006) and analysis.</td>
</tr>
<tr>
<td>Total medical costs for herpes zoster</td>
<td>$280.00</td>
<td>$3,808,000.00</td>
<td></td>
</tr>
<tr>
<td>Total medical costs from varicella &amp; herpes zoster</td>
<td>$330.73</td>
<td>$6,851,800.00</td>
<td></td>
</tr>
</tbody>
</table>

Source: Summarised and cost per year column calculated from Rosevear & Urlich (2012b).

### What non-financial benefits are expected?

In addition to a reduction in the medical and productivity costs associated with varicella, the annual number of varicella cases is anticipated to decrease by 86% (from 60,000 to 8,198), and the number of cases requiring general practice and hospital care is expected to decrease by 86% (from 12,000 to 1,640) and 90% (from 315 to 30), respectively (Rosevear 2015).

15 Assuming approximately 13,600 cases per year (average incidence of 340 cases per 100,000 (Rosevear & Urlich 2012 p18). Therefore, in a population of approximately 4 million would be 40*340=13,600). In the actual model, however, it looks like they have assumed 15,000 cases per year on the assumption that 25% of varicella cases (60,000) lead to herpes zoster, but no reference is provided for this.
What is the cost-effectiveness of adding the varicella vaccine to the existing childhood immunisation schedule in New Zealand as a separate shot at 15 months and 4 years (Option 1), relative to a counterfactual scenario where the varicella vaccine is not available at all (Option 2)?

The economic assessment commissioned by the immunisation team to address this question looked at three scenarios from both a societal and health payer’s perspective via a cost-benefit and cost-utility analysis, respectively (Rosevear and Urlich 2012b). In all scenarios vaccination was cost-saving from a societal perspective (ie, when the costs of lost productivity from parental work absenteeism were included). However, this was not the case for any of the scenarios where cost effectiveness was examined from a health payer’s perspective; under each scenario vaccination would cost more to the health system than it would save.

Different disease scenarios were used to illustrate the uncertainty around the influence of varicella vaccination on the incidence of herpes zoster:

1. The first scenario assumed that vaccination only protected against varicella. Under this scenario, vaccination would cost the health system $16,000 for every QALY gained and save society $3.90 for every $1.00 invested.

2. The second scenario assumed that vaccination protected against both varicella and herpes zoster in the vaccinee. Under this scenario, vaccination would cost $9,000 for every QALY gained and would save society $4.30 for every $1.00 invested.

3. The third scenario assumed that vaccination protected against both varicella and herpes zoster in the vaccinee, but increased herpes zoster in the unvaccinated population by 20%. Under this scenario, vaccination would cost $13,000 for every QALY gained and would save society $4.10 for every $1.00 invested.

Scenario 2 is treated as the ‘base-case scenario’ by the author due to the greater certainty around the supporting evidence relative to the other scenarios. The cost-per QALY under this scenario declined with decreased vaccine cost and when one dose was considered instead of two. If the cost of delivering the vaccine declined from $57 to $25, and there was no increase in herpes zoster in the unvaccinated population, universal vaccination for varicella would become cost saving from a health payer’s perspective, as well as a societal perspective. However, a switch from 2 doses to 1 dose, while having the potential to decrease the cost per QALY from $9,000 to $2,000, was still not cost saving from a health payer’s perspective (Rosevear and Urlich 2012b).

Unless an intervention is clearly cost saving, whether an intervention is cost effective or not is a subjective judgement often made via comparisons to previous or competing investments. While in the UK health economists inferred from previous recommendations that NICE had a threshold of £20,000-£30,000 per QALY for new investments, the use of thresholds to indicate whether an intervention is ‘cost effective’ is problematic (NICE 2009), particularly in New Zealand. This is because thresholds inadequately account for opportunity cost and affordability, and are incompatible with budgets and maximising health gains (Metcalfe and Grocott 2010).

In New Zealand, pharmaceutical investments can only be considered ‘cost-effective’ when prioritised against other proposals at the time, and threshold levels must inevitably vary with available funds and PHARMAC’s other 8 criteria, thus thresholds cannot be inferred and
calculated for New Zealand (Metcalfe and Grocott 2010). In spite of this, the author of the economic assessment report for varicella uses a table referred to by Metcalfe and Grocott (2010) as incorrect, to infer a threshold of $15,000(NZ) per QALY and comment that the cost-utility value of varicella vaccination in all three scenarios, despite not being cost saving to the health system, is cost effective for the health system when compared with historical PHARMAC purchasing. As thresholds cannot be determined on the basis of historical PHARMAC purchasing, the author’s conclusion that it varicella vaccination is cost-effective on this basis is misleading.

What is the potential impact of an increase in Herpes Zoster virus on the cost-effectiveness of vaccinating for varicella?

Overall, Rosevear and Urlich (2012b) argue that if decision-makers are only going to consider the savings accrued by the health system and Vote: Health, then further analysis is required to more accurately measure the impact of herpes zoster on the vaccinated and unvaccinated populations. In contrast, if decision-makers plan to consider savings accrued through both increased productivity (i.e., reduced work absenteeism), in addition to the reduced use of health care, they can be confident in the ‘cost saving’ results from the analysis. While not explicitly detailed in the report, the reason we can have confidence in the analysis from a societal perspective, but not from a health payer’s perspective, is presumably because any costs incurred by the health system through increases in herpes zoster will still be offset by the productivity savings. In contrast, when productivity savings are excluded, the additional health service costs due to herpes zoster are less likely to be offset by savings.

Critical appraisal of assessment

A critical appraisal of the evaluation by Rosevear and Urlich (2012b) was undertaken using Drummond’s checklist for appraising economic evaluations (Drummond et al 2005). The results of this appraisal showed that the evaluation performed well against six of the ten criteria.

The assessment:

1. posed a well-defined question in answerable form and stated the perspective of the analysis
2. provided a comprehensive description of competing alternatives
3. measured costs and consequences accurately in appropriate physical units. However, rather than using the same analytical technique for both perspectives (i.e., cost-benefit analysis OR cost-utility analysis), the author chose to use a cost-benefit analysis for the societal perspective and a cost-utility analysis for the health payer’s perspective.
4. adjusted all costs and consequences for differential timing using the standard 3.5% discount rate. However, while a lifetime horizon was suggested in the tender, the timeframe and analytic horizon was not clearly stated and the report did not comment on the time interval between vaccination and realisation of health effect – though it was suggested to be 50+ years.
5. performed an incremental analysis of costs and consequences of alternatives
6. allowed for uncertainty in the estimates of costs and consequences through the use of sensitivity analysis

However, the study did not perform well on:

7. establishing the effectiveness of the vaccine programme – effectiveness data was not summarized through a systematic overview of clinical studies as this was excluded from the tender, and the search strategy and rules the author used for inclusion and exclusion were not outlined.
8. Identifying all important and relevant costs and consequences for each alternative—while the analysis included all costs relevant to a societal perspective, it did not include all costs relevant to a health payer's perspective. In particular, initial set-up costs of the vaccination programme, including promotion and education, were not included, and neither were the initial or ongoing costs of an associated surveillance programme. This is important given that the cost of the vaccine itself represents only a small percentage of the total cost of delivering it to the public\(^{16}\). Thus, 5% of the vaccine cost for administration is probably a considerable underestimate.

9. Valuing costs and consequences credibly—whether some of the hospitalisation parameters costs for a single District Health Board in 2003 were inflated to 2011 values instead of using the proper costing methodology appropriate for the National Minimum Dataset (NMDS) for hospital discharges. Similarly, when compared with recent coverage data for immunisations at 18 months and 5 years (80% and 77%, respectively)\(^{17}\), the coverage rates assumed in the model were optimistic—with 91% for the first dose, and 98% for the second\(^{18}\). While these were reported to be coverage rates achieved for polio, when the reference for this was followed up, the coverage rates for polio at age 2 were a lot lower: 92.1%, 90.4% and 88.5%, for doses 1, 2 and 3 respectively (Ministry of Health 2005 pgs 23 & 63).

10. The inclusion of all issues of concern to users in the presentation and discussion of the study results—while an overall index or ratio of costs to consequences was provided, they were interpreted in a mechanistic fashion. Total annual costs of the vaccination programme were not mentioned (instead they were left for the reader to calculate) and there were a number of misleading statements that suggested the type of analysis (cost-utility vs cost-effectiveness) determined whether vaccination was ‘cost saving’ (as opposed to the inclusion or exclusion of productivity costs). While results were compared with those of others who have investigated the same question, few allowances were made for potential differences in study methodology, and the use of an inappropriate threshold to suggest cost-effectiveness was used. The study did not discuss the generalizability of results to other settings and patient/client groups and did not discuss issues of implementation, however it is recognised that this was beyond the scope of the tender.

Taking these limitations into account, and the uncertainty around the impact of varicella vaccination on herpes zoster, the cost-effectiveness of universal varicella vaccination may be overestimated in Rosevear and Urlich (2012b).

**How does the assessment compare to others previously conducted in New Zealand and internationally?**

The findings from the assessment discussed above are comparable to a previous New Zealand study, and are similar to some of the simulation studies published overseas. In most studies, universal vaccination for varicella is more cost-effective from a societal perspective than a health payer's perspective, and all have noted that if the vaccine were to increase incidence of herpes zoster, cost-effectiveness estimates would decrease.

The cost-benefit analysis undertaken by Scuffham et al in (1999) looked at the cost-effectiveness of adding a single dose of the varicella vaccine to the New Zealand immunisation schedule compared with making the vaccine available on a user pays basis.

\(^{16}\) Health Report number: 20100423.

\(^{17}\) Coverage rates for 18 months and 5 years were chosen in the absence of specific coverage rates at 15 months and 4 years.

This study found over a 30 year period, assuming 80% coverage, 95% effectiveness, and no effect on herpes zoster, that universal vaccination of children at 15 months was cost saving from a societal perspective (every dollar invested returned $2.79), but not from a health payer’s perspective (every dollar invested returned $0.67). When compared with scenario 1 (vaccine only affects varicella not herpes zoster), the evaluation by Rosevear and Urlich (2012b), found that $3.90 was returned to society for every dollar invested.

Studies conducted in France (Littlewood et al 2009), Netherlands (Boot et al 2006) and Canada (Brisson and Edmunds 2002) have also shown varicella vaccination to be cost-saving from a societal but not a health payer’s perspective. These findings contrast with a systematic review of studies published between 1966 and 1998 which found net cost savings from both a societal and health payer’s perspective for routine varicella vaccination programs directed at children aged 15 months (Skull and Wang 2000).

Scuffham et al (1999) and Brisson & Edmunds (2002) only briefly alluded to the possibility that increases in herpes zoster, as a result of vaccination, may reduce cost-effectiveness. However, Bilcke et al (2010) investigated this possibility using a dynamic modelling strategy for varicella in Belgium and concluded that if the exogenous boosting hypothesis was confirmed, then vaccinating children would not be cost effective for many decades after vaccination due to herpes zoster. This finding is supported by other studies by van Hoek et al (van Hoek et al 2011a; van Hoek et al 2011b) which have explicitly noted that “policy makers should be aware of the potential negative benefits in the first 30-50 years after introduction of a childhood varicella vaccine, which can only be partly mitigated by the introduction of a herpes zoster vaccine”.

Would the vaccine be more cost-effective if it were targeted to different population groups? If so, which groups?

Targeting the public funding of vaccination for varicella is likely to increase the cost-effectiveness of vaccination from a health payer’s perspective, but decrease the cost-effectiveness from a societal perspective. Determining whether targeted vaccination in New Zealand would be cost-saving (not just ‘cost-effective’) from a health payer’s perspective would require additional analysis.

A Swiss study (Banz et al 2009) compared universal childhood vaccination of toddlers aged 1-2 years with targeted vaccination of 11-15 year olds with a negative or uncertain history for chickenpox. From a societal perspective, the study found that universal vaccination resulted in a benefit cost ratio of 1.29, a net saving of $1.29 for every $1.00 spent on the programme. However, from a health payer’s perspective the model predicted a net cost of $0.30. In Spain, Plans-Rubi and Huang (2009) investigated the cost-effectiveness of targeting vaccination through prior screening for antibodies versus universal vaccination. Based on their results and the prevalence of protected individuals observed in the population (p) in serological surveys, the least costly immunisation strategy was screening prior to vaccination in the case for varicella, but vaccination without screening for hepatitis B, measles and tetanus at all ages and for hepatitis A in adolescents (since p < p).

These studies are comparable to those summarised in a 2000 systematic review by Skull & Wang (2000), in which serotesting of children aged 9-12 years, with an uncertain history of varicella, followed by vaccination of those negative for VZV was the most cost-effective approach. Likewise, serotesting regardless of history was also found to be the most cost-effective strategy for adolescents, adults and health care workers.

These studies suggest that targeting vaccination to specific groups may be more cost-effective from a health payer’s perspective than universal vaccination. However, from a societal perspective, a targeted approach is likely to be less cost-effective. This is because the majority of savings from a universal vaccination program come from reductions in productivity loss due to parents taking time off work to care for children with mild cases of
varicella. Targeting vaccination to individual groups at risk of severe varicella (eg, adults with an uncertain history, close contacts of immune compromised individuals unable to receive the vaccine), will mean that mild cases among children will continue, and parents will still need to take time off work to care for them. It is also unclear whether a targeted vaccination program would be cost-saving to health payer’s compared with the status quo (some private funding), or no vaccination. Further modelling is required to assess this.

**Does reducing the number of doses affect the cost-effectiveness of the vaccine?**

A two dose programme of the varicella vaccine is now recommended to reduce the proportion of breakthrough cases. While the majority of evidence suggests that two doses is more clinically effective than one (Gao et al 2010; Nguyen et al 2010; Shapiro et al 2011; Tafuri et al 2010), the cost-effectiveness and ‘real world’ impact of the second dose is disputed and thus far out of the United States, Germany, Canada, and Australia, only the United States and Germany have a two-dose vaccination program.

In an outbreak of varicella in elementary school children with two-dose varicella vaccine recipients, the vaccine effectiveness of 1 and 2 doses were similar (Gould et al 2009). Likewise, while the reported varicella incidence has declined in some places following implementation of routine 2-dose varicella vaccination, most studies are recommending continued surveillance to determine the full impact (Kattan et al 2011).

Brisson et al (2010) modelled the potential impact of 1-dose versus 2-dose varicella vaccination programs on varicella and zoster incidence, using Canada as an example. Assuming 90% coverage, they found that 1-dose vaccination reduced varicella and zoster cases by 64% and 5% respectively, over 80 years and that adding a second dose reduced varicella and zoster cases by a further 22% and 6%, respectively. However, they argue that the incremental benefit of the second dose is highly dependent on the effectiveness of the first dose and its impact on herpes zoster. Because of its greater efficacy at preventing varicella, the addition of a second dose may have the detrimental short-term effect of increasing zoster incidence even though in the long-term, zoster incidence is predicted to decline more significantly under a 2-dose strategy as there will be a lower proportion of individuals with a history of VZV infection.

The first study assessing the cost-effectiveness of combined varicella and zoster vaccination options and comparing these to alternative programmes, was published by van Hoek et al (2011a). This study concluded that the optimum vaccination strategy for varicella would be a two-dose policy with vaccination of the elderly. However, they cautioned that vaccination would not be deemed cost-effective from a health payer’s perspective for many years after implementation (ie, more than 100 years), and for 30-50 years it is likely to result in significant extra health care expenditure.

In New Zealand, the study by Rosevear and Urlich (2012b), which was summarised in section 0, a single dose of the varicella vaccine was shown to be more cost effective than two doses, but was still not cost-saving from a health payer’s perspective. Furthermore, this was based on a scenario that did not factor in the possible impact of universal vaccination on herpes zoster.

Reducing the number of doses of the varicella vaccine has the potential to increase the cost-effectiveness of a universal vaccination program in New Zealand, but from a clinical perspective, would still result in break-through cases of the disease.

**Societal & ethical considerations**

While the cost-effectiveness of an intervention can be assessed from both a ‘societal’ and ‘health payer’s’ perspective, there are societal and ethical considerations which cannot be incorporated into an economic model. This section of the assessment looks at some of
these considerations, which include: the acceptability of the intervention, the equitable
distribution of benefits and costs, and any ethical issues associated with the decision to
vaccinate or not. Overall, there is insufficient evidence to say whether health practitioners
and individuals would support a universal vaccination programme in New Zealand. However,
given the coverage rates for existing vaccines on the schedule, the usually benign impact of
varicella, and the uncertainty surrounding the impact of vaccination on herpes zoster, it is
possible that a universal varicella vaccination programme may not be seen as a high priority
at a societal level.

Acceptability

What proportion of the target population will accept the vaccine, or has already been
vaccinated?

Perceptions and acceptability of varicella vaccination in a population are important indicators
of the coverage levels achieved, and thus the likelihood the programme will achieve its
desired outcome. Perceptions and acceptability of vaccination are influenced by a number of
factors including: the opinions of health practitioners, availability of public funding, and
information on, or previous experience of, the disease and vaccine. Experiences overseas
may be able to provide some indication of the expected acceptability of varicella vaccination
(and therefore coverage) in New Zealand and how this might change over time.

Health practitioner support

Evidence to date suggests that recommendations from health practitioners to vaccinate for
varicella affects uptake by caregivers. However, while vaccination for varicella receives
moderately high support from health practitioners overseas, few actively recommend it to
their patients. Further evidence on the extent to which findings may be similar in New
Zealand is required.

In Australia, it was found that GPs who always provided information about varicella were
more likely to have parents accept their advice about varicella vaccine (62.7%) than those
who never provide information (40%) (Marshall, Ryan et al. 2009). This is supported by
similar findings in Bavaria, Germany, whereby recommendations supporting the varicella
vaccine by paediatricians was the main independent factor associated with parental
acceptance (Streng et al 2010).

A cross-sectional survey of primary health care professionals from two health departments of
the Valencia Community (Spain), found that the systematic inclusion of the varicella vaccine
was supported by 53% of health care professionals (Tuells et al 2009). In Italy, a group of
public health officers and gynaecologists were requested to express their opinion on whether
immunisation for HPV in girls older than 12 years, rotavirus, and varicella with combined
MMR vaccine should be included in the National Immunization Plan. Overall, 77.9% agreed
that MMRV should be introduced, compared with 83.5% for HPV and 52.4% for rotavirus
(Marchetti and Morelli 2009). In this instance, varicella was preferred over rotavirus, but not
over HPV in girls older than 12 years. The public health priority, the burden of disease, the
economic and financial issues determined the priority placed on different vaccines.

The Bavarian study also indicated that in 2006, initially only 48% of patients reported that the
paediatrician had recommended the vaccine, and while in 2008 this had increased to 60%,
additional programmes targeting paediatricians’ and parents’ acceptance were still needed to
achieve the WHO defined goal of at least 85% coverage (Streng et al 2010). Similar trends
were observed in a Spanish and Australian study. In Spain, only 66% of nurses and doctors
reported always informing patients about vaccines (Tuells et al 2009) and in the Australian
study, where 89% of GPs considered varicella was an important disease to prevent, only

Full text of this article is in the process of being interloaned by the library.
25% of GPs always discussed the non-funded varicella immunisation with parents at the time of a routine immunisation (Marshall et al 2009).

**Public funding & information on disease and vaccine**

A case control study set in Wisconsin, United States, found that the varicella vaccine was the most often refused vaccine by exempt\(^{20}\) children (49%), followed by Hepatitis B (30%) (Salmon et al 2009). The most common reason for claiming exemptions was ‘the vaccine might cause harm (57%).’ This finding is similar to that of Smith et al (2010), which found that among parents who intentionally delayed vaccination, 44.8% did so because of concerns around vaccine safety or efficacy. This study also found that parents that delayed due to vaccine safety and efficacy were significantly more likely to seek additional information about their decision from the Internet, and less likely to seek information from a doctor. A comparative study of parents’ attitudes towards varicella vaccination acceptance in France and Germany support the findings of others, whereby the main reason for parental reluctance was ‘fear of complications due to vaccinations’. The most convincing arguments for parents who were initially reluctant were ‘information on the potential seriousness of the disease’ and ‘availability of an effective, well-tolerated vaccine’ (Allaert et al 2009). In Australia, the main reason reported for parental refusal of varicella vaccine was due to the cost and the perception that varicella is a mild disease (Marshall et al 2009).

These studies emphasise the importance of better methods for communicating vaccine safety information (such as educational materials) and the importance of studies to explore vaccine safety concerns.

**Perceived seriousness**

While in Australia the main reason for refusing varicella vaccination was due to the perception that it was a mild illness (Marshall et al 2009), a UK study suggests that varicella is perceived as a serious disease. A recent multicentre qualitative interview study in the United Kingdom explored parental experiences and perceptions of childhood varicella and parental attitudes towards a universal vaccination programme (Lee et al 2011). The survey found that while some parents of children with varicella were concerned about scarring (14%) and fever (4.8%), the majority of parents had no concerns at all (69%) (Lee et al 2011). However, most parents viewed the condition as serious (61.5%) and while only 26% of parents prior to the interview were aware of the varicella vaccine, most (67.3%) said they would be in favour of a universal vaccination programme in the UK (Lee et al 2011).

**Coverage rates achieved overseas**

The coverage rate achieved in countries which have implemented a universal varicella vaccination programme can be used as a good indication of what proportion of the target population might initially accept the vaccine in New Zealand and how this might change over time. In most instances, coverage starts off relatively low, and takes a number of years to reach the recommended levels of over 85% (Streng et al 2010).

In the United States routine varicella vaccination has been recommended since 1995. National varicella vaccination coverage (1 or more doses) of children 19-35 months in 1997 was approximately 26% and it was not until around 2002 that coverage rates of approximately 80% were achieved, and not until 2007 that 90% coverage was reached (CDC 2011a). Varicella vaccination coverage also remains lower than that for measles.

These initial low coverage estimates for the varicella vaccine have also been observed in Germany and Australia. Following the recommendation for routine varicella vaccination in 2004 in Germany, the proportion of children under 2 years that had been vaccinated with either 1 or 2 doses increased from 34% in 2004 to 51% in 2005 (Reuss et al 2010). In Australia, varicella vaccine coverage of children has been increasing steadily since 2005.

----

\(^{20}\) Children are referred to as ‘exempt’ when their caregiver chooses not to get their child vaccinated.
from around 70% in 2006, to just over 80% in 2009 (Hull et al 2011). However, varicella remains the only vaccine with coverage lower than 90% (Hull et al 2011).

Information from manufacturers suggests that currently, less than 0.09% of the New Zealand population is already receiving the varicella vaccine. This is unsurprising given that while the vaccination is recommended for particular groups, it is not publicly funded (Ministry of Health 2011a), and only one of the manufacturers has recently started advertising. If the vaccination were to be given at the same time as MMR at 15 months and 4 years then it might be plausible that vaccination for varicella would achieve similar levels of coverage to MMR, particularly at age 4 where the ITF have recommended the replacement of MMR with MMRV. In 2010, the coverage for the first dose of a measles containing vaccine in Australia was 94%, while the second dose was 88% (World Health Organization 2011a). In 2010 the coverage for the first dose of MMR vaccine in New Zealand was 91%, while information on the second dose was unavailable (World Health Organization 2011a).

However, if the acceptability of a varicella vaccine in New Zealand is low, combining varicella with MMR (in MMRV), may affect uptake of MMR (Bilcke et al 2010) due to fears surrounding the risk of febrile seizures (discussed further in section 0).

**Equity & Ethics**

*Will reduced pathogen transmission lead to enhanced vulnerability of specific sub-populations?*

Given that exposure of persons with latent wild-type varicella zoster virus (WTVZV) infection to persons with varicella is thought to boost specific immunity, thereby controlling reactivation of WTVZV and the development of herpes zoster (HZ), concern has been expressed that by providing fewer opportunities for varicella exposure among persons with previous wild-type varicella infection, a reduction in the likelihood of exposure might increase the risk for HZ (Marin et al 2007). If this increase were to occur, it would be experienced disproportionately by unvaccinated adults. In this way, a decrease in the incidence of the relatively benign disease varicella in childhood, may result in an increase, at least in the short term, of the more serious (and costly), herpes zoster (van Hoek et al 2011a).

It has been suggested that WTVZV early in childhood protects against the development of asthma and atopic dermatitis (Silverberg et al 2010). If this was the case, then universal varicella vaccination may have the unintended consequence of increasing rates of asthma and atopic dermatitis. Given that Pacific and Maori populations are at an increased risk of these conditions, varicella vaccination might enhance the vulnerability of these populations. However, this is the only study retrieved in the systematic search that reports this connection, suggesting that a critical appraisal of the study, and further research would be necessary before this association was certain.

*Are the benefits and costs of vaccination, or benefits and costs of not vaccinating, experienced disproportionately by different groups and if so, which ones?*

The benefits and costs of vaccination are experienced disproportionately by different population groups.

**Benefits of vaccination**

Most countries, including New Zealand report that vaccination rates generally vary by geography, ethnicity, and socio-economic status, and this is likely to be true for varicella vaccination in New Zealand.

There is variation in varicella vaccine coverage by ethnicity and socioeconomic status in the United States (CDC, 2009). The United States National Immunisation Survey continues to show that low vaccination coverage is associated with low household income (Smith et al
2009; Smith et al 2011), higher percentage of black children, and high levels of housing stress (>30% income for rent or mortgage and certain inadequate housing characteristics) (Smith et al 2011).

In New Zealand, overall immunisation coverage rates for children aged 18 months between October 2010 and October 2011 was 80%, with lower uptake among Maori (71%) and higher uptake among Asian (91%) than among Pacific (80%) and European population groups (both 84%) (Ministry of Health 2011c). There is also evidence that immunisation coverage varies by socio-economic deprivation in New Zealand, with 85% coverage in the least deprived areas, and 75% in most deprived areas (Ministry of Health 2011c)\(^{21}\). This suggests that while universal funding of vaccination for varicella will make it more financially accessible to these populations, Maori and those in the most deprived areas and least populated areas (Silhol et al 2010) may still be less likely than others to experience the benefits.

There is also some evidence from the United States suggesting that due to genetic variation, some ethnic groups (eg, African American children) may be less likely to develop herpes zoster following reactivation of the varicella virus. This might mean that the impact of varicella vaccination on reducing herpes zoster in these groups may not be as significant as among other ethnic groups who do not have protective genes (eg, white children) (Tseng et al 2010). It is unclear to what extent this might also apply in New Zealand.

**Costs of not vaccinating**

It has been argued that the costs of not universally vaccinating for varicella may currently be disproportionately experienced by individuals for whom the vaccine is contraindicated (identified on page 329 of the Immunisation Handbook (2011a)), but who would benefit from those around them being vaccinated. These include organ and bone marrow transplant recipients, as well as other immune-suppressed patients on chemotherpay and rheumatologic agents (Walls and Wilson 2010). These groups cannot be immunised themselves, but could be protected by immunising those around them (Walls and Wilson 2010). However, the argument in support of a universal vaccination programme over a targeted programme is not as strong with respect to non-immune adults from tropical climates such as Indostan, Southeast Asia, South America, and the Caribbean are also susceptible (Ayres et al 2010; Valerio et al 2009). A universal vaccination programme instead of a programme which specifically targeted them is not be as important as it is for those that cannot receive the vaccine themselves.

**Is there potential for the vaccine to be targeted to specific groups?**

Rather than the universal vaccination of children at 15 months and 4 years, it may be possible to publicly fund the vaccination of certain groups. For instance, publicly funded vaccination could be advertised and available for the vulnerable groups identified in the Immunisation Handbook (ie, adults without a previous history of infection) and individuals residing closest to immune-compromised individuals for whom the vaccine is contraindicated (as suggested by Walls & Willson (2010). Targeted use of the vaccine in this way currently occurs in the United Kingdom, where only health care workers and people in close contact with someone who has a weakened immune system are vaccinated for varicella (National Health Service 2010). Targeting to specific or at risk groups also occurs in Israel, Brazil and Argentina (World Health Organization 2011b).

However, targeted rather than universal vaccination may be problematic, not just because of the relative increased risk faced by immune-compromised individuals, but also due to poor recall of previous varicella infection in the population. Perella et al (2009) found that self-reported varicella history varied according to age, and that reported history was no longer

highly predictive of seropositivity among cohorts born since 1994. The conclusion was that universal varicella vaccination, regardless of history, for children born after 1994 should be considered.

In contrast to the general population, positive past history of varicella in health care workers has been shown to be a good predictor of previous exposure to varicella, with 99% of individuals declaring to have experienced the disease, being immune (Garcia-Basteiro et al 2011). In instances where there is uncertainty around immunity, screening is appropriate (Plans-Rubi and Huang 2009), and there are a variety of commercial assays for varicella zoster available, with at least one reporting sensitivity greater than 70% (high sensitivity is preferable to prevent inappropriate and expensive treatment) (Chris Maple et al 2009).

**Psychological considerations**

*Are there any psychological issues associated with varicella or the vaccine?*

There are already a number of vaccines and shots on the immunisation schedule for children aged 2 years and under and psychologically, the addition of another, may not be received well by either parents or children. Adding the varicella vaccine to the schedule at 15 months and 4 years would increase the number of shots children receive before the age of 2 to over 16, and an even greater number of vaccines.

In 2006, the Immunisation Awareness Society noted that prior to the addition of the pneumococcal vaccine, babies between birth and two years received 25 vaccines for eleven different diseases and the addition of the pneumococcal vaccine would bring this to 29 vaccines for twelve diseases by the age of 15 months22. If varicella were added to the immunisation schedule, the number of vaccines received by the age of 15 months would increase to 30, for 13 different diseases.

A study set in Wisconsin, United States, reported that 25% of parents of vaccinated children thought that children got more immunisations than was good for them and 34% expressed concern that children’s immune systems could be weakened by too many immunisations (Salmon et al 2009).

The Immunisation Technical Forum noted that their view on the vaccines offered at the 15 month visit might change following focus groups with parents regarding their views on vaccine preference, specifically with respect to the use of the single antigen vaccine compared with MMRV (Ministry of Health 2011b).

**Feasibility of adoption in the health system**

In addition to clinical safety and efficacy, cost-effectiveness, and acceptability to the New Zealand population, a universal vaccination programme for varicella needs to be feasible to adopt in the New Zealand health system. This section of the report looks at how a universal varicella vaccination programme would fit with current policies and practices in the immunisation and wider health sector, including the use of other health services, and additional demands on the health workforce. It also examines any legal issues associated with vaccinating or not, and the impact of a vaccination programme on the Vote:Health Budget which includes a discussion of competing priorities in this space. Following the budget impact analysis, a brief discussion of how such a service might be funded is provided.

---

22 http://www.scoop.co.nz/stories/GE0605/S00060.htm
Policy congruence

*How does the addition of this vaccine fit with other policy and practices in immunisation and the wider health sector?*

The Immunisation Technical Forum (ITF) initially recommended that the varicella vaccine be added to the National Immunisation Schedule in 2006. However, in “March 2010 the Ministry of Health agreed with the Minister not to seek funding for the introduction of varicella and rotavirus vaccines until immunisation for two-year-olds was closer to the target of 95%” (Ministry of Health 2011b).

Since 2009 the Immunisation Health Target required District Health Boards to ensure that: 85% of two-year-olds be fully immunised by July 2010, 90% by July 2011 and 95% by July 2012. During this time the actual coverage achieved in this age group was: 86% (Jul09-10) and 89% (Jul10-11). While coverage has improved, the target was not met, raising the question of whether increasing coverage for existing vaccines on the schedule should continue to receive higher priority than rolling out a new one – particularly given coverage among Maori, and areas of high deprivation (deciles -9 &10) remain lower than overall (86% and 88%, respectively). The current coverage of children aged 18 months and 5 years (the recommended age for varicella vaccination) also remains lower than total coverage, at 80% and 77%, respectively, and this may drop as a result of the new immunisation target introduced in 2012, which switches the focus from children up to the age of two, to children eight months and under.

Preliminary analysis of data collected from December 2007 to May 2008 from 24 diverse New Zealand General Practices suggests that low coverage may be due to the Immunisation Benefit Subsidy funding being inadequate remuneration to support service delivery at the practice level (Immunisation Advisory Centre 2012).

Depending on whether the subsidy has changed since 2007/08, this finding might also support prioritising funding to improve current vaccination coverage, rather than funding a new vaccine. In New Zealand, anecdotal evidence suggests that currently outreach immunisation services costs between $250 and $1000 per hard to reach child.

Organisational issues

*How would the addition of the vaccine fit with the existing Immunisation Schedule?*

The recommended delivery of the varicella vaccine at 15 months and 4 years of age would fit well with the existing immunisation schedule. At 15 months the ITF have said that the vaccine can be given alongside PCV10, MMR and Hib, but did not explicitly mention


25 Coverage rates for 18 months and 5 years were chosen in the absence of specific coverage rates at 15 months and 4 years.

26 Health Report number: 20111273

27 GM Planning & Funding and Chief Planning & Funding Officer, Waikato & Auckland District Health Boards, respectively.

28 10-valent Pneumococcal Conjugate vaccine

29 Haemophilus influenzae type b vaccine
DTaP-IPV (at 4 years) (Ministry of Health 2011a). However, clinical trials have shown that MMRV and DTaP can be given together at 4 years (Marin et al 2007 p13). However, it is unclear whether DTaP-IPV, which is on the schedule, can be given alongside MMRV, particularly as in 2007 the Advisory Committee on Immunization Practices (ACIP) noted that data was absent or limited for the concomitant use of MMRV vaccine with inactivate polio (Marin et al 2007). ACIP also noted that data was absent or limited for the concomitant use of MMRV vaccine with pneumococcal conjugate, influenza, and hepatitis A vaccines. However, unless any of these are given as ‘catch up’ doses at the same time as the varicella vaccine is scheduled to be given, this may not matter because at present they are not scheduled to be delivered concurrently.

How would universal vaccination affect the use of other health services (ie, GP visits, hospitalisations, pharmaceutical consumption etc)?

Vaccination for varicella is anticipated to reduce the use of health services to an extent. However, as varicella is a relatively mild disease, the overall impact on health services of vaccination may be negligible. The mild nature of this disease, which rarely requires hospitalisation, is the main reason vaccination is cost saving from a societal perspective, but not from a health payer’s perspective.

Depending on assumptions around how universal vaccination affects herpes zoster, there is a possibility that health sector use related to herpes zoster might increase, in at least the short term.

What are the health workforce implications of introducing universal vaccination for varicella?

The primary healthcare workforce, specifically general practice, will be the main section of the health workforce affected by the introduction of a universal varicella vaccine, in terms of both the time spent on delivery and reporting requirements.

The immunisation process delivery activities are undertaken mainly by practice nurses (90%), who spend around 12% of their total nursing time on delivering immunisation activities (Immunisation Advisory Centre 2012).

Data collected from December 2007 to May 2008 from 24 diverse New Zealand General Practices suggests that the immunisation process routinely takes around 24 minutes (median time) with a range from 18 – 29 minutes (Immunisation Advisory Centre 2012). The longest time commitment is the informed consent process (mean of 4.5 minutes), followed by administering the vaccine (mean of 3.5 minutes) and documentation (mean of 3.4 minutes). The widest variability is the length of time spent in checking registrations. This may be due to a range in practice experience and ability as well as ongoing technical issues around access and use of the National Immunisation Register to check immunisation status.

Furthermore, to meet monitoring requirements and the national immunisation target, a requirement to report the incidence of varicella and herpes zoster to a national surveillance system, and chasing up unvaccinated children may further increase the burden on these groups.

What additional health system factors would need to be addressed to ensure successful implementation of the proposed vaccination programme in New Zealand?

The successful implementation of the varicella vaccination programme in New Zealand depends on being able to achieve sufficient coverage and to monitor and respond, if necessary, to increases in the incidence of herpes zoster and waning immunity. For this to

30 Diptheria-Tetanus-acellular Pertussis
31 Diptheria-Tetanus-acellular Pertussis-Inactivated Polio vaccine
occur the factors that affect coverage need to be addressed by the health system and a surveillance system may need to be set up.

**Sufficient coverage**

For the benefits of varicella vaccination to be realised in New Zealand, sufficient uptake of the vaccine is necessary. The analysis to determine whether vaccination would be cost-effective assumed a coverage rate of 91% at both 15 months and 4 years, this is over 11% higher than the coverage currently experience by these age groups. As discussed in section 0, uptake depends on the perceptions of the public, which are largely influenced by information. The support of clinicians for the vaccine and active promotion of the safety and benefits to both the public and health sector will therefore be crucial, along with a particular focus on ‘hard to reach’ groups like Maori and areas of high socio-economic deprivation. Further progress in timely vaccination may also be achieved by improving health care providers’ reminder/recall systems, implementing educational interventions that address barriers to vaccination (Smith et al 2009).

**Surveillance**

Due to the uncertainty around the impact of varicella vaccination on herpes zoster, and to monitor waning immunity, ongoing surveillance of varicella and herpes zoster incidence in populations implementing universal vaccination is necessary.

In the United States, the CDC has set up a Varicella Active Surveillance Project to obtain population-based incidence rates for varicella and herpes zoster diseases in a community with established high varicella vaccination coverage rates and to evaluate the impact of current and future varicella vaccination practices and policies. As break-through varicella is characteristically mild, with fewer lesions that frequently do not progress to a vesicular stage, laboratory diagnosis and the need to develop new diagnostic approaches that rely on alternative patient samples, has grown increasingly important, particularly in outbreak settings (Schmid and Jumaan 2010).

Germany has also set up a similar sentinel surveillance programme for monitoring varicella and herpes zoster as the United States (Siedler and Arndt 2010). However, in other countries, evaluation of the varicella vaccination programme relies on analyses of existing administrative health data. The experience overseas suggests that prior to vaccination, good data on the incidence of the disease, and relative immunity of the population prior to implementing the programme is important. Likewise, addressing the complexities in monitoring VZV-related diseases, requires a very sensitive and well validated surveillance system, and some capacity for laboratory testing to differentiate between wild-type and break through cases of varicella.

In Canada surveillance systems are currently inadequate to assess the impact of varicella immunisation in Canada (PHAC 2007). Varicella cases are under-reported, and herpes zoster is not a reportable disease in most jurisdictions. Varicella-related hospitalizations in children are captured through the IMPACT system, which has provided baseline data from before the introduction of provincial and territorial immunisation programs. Virus identification from clinical specimens (e.g., vesicle scraping) by laboratory methods in order to differentiate wild-type from vaccine-derived VZV should be considered when:

a) a severe post-vaccination rash occurs,

b) vaccine-modified varicella requires admission to hospital,

c) herpes zoster occurs in a previously immunized (especially immunocompromised) individual,

32 http://www.cdc.gov/vaccines/stats-surv/vasp/default.htm
d) a varicella-like illness occurs in an immunized health care worker with subsequent spread in the health care setting and

e) a varicella-like illness develops in a pregnant or immunocompromised contact of a vaccinee with a varicella-like rash.

To differentiate vaccine-derived from wild-type varicella virus polymerase chain reaction (PCR) testing is required (PHAC 2007).

While New Zealand does have a system for the mandatory notification of certain diseases, varicella and herpes zoster are not currently on the list. This means, either they will need to be added to the list, a separate sentinel surveillance system will need to be set up, regular screening for immunity in the population may need to be undertaken, or we will be in the same position as other countries – relying on administrative collections and not having a clear estimate of incidence and prevalence at baseline in order to monitor change. Surveillance is discussed further in the section exploring legal issues.

Herpes zoster vaccine

One response to address concerns that varicella vaccination may increase the incidence of HZ is to consider publicly funding the herpes zoster vaccine for adults aged 65-75 years until the varicella vaccinated cohort reach this age (at which time HZ vaccine would no longer be necessary) (van Hoek et al 2011a). However, this will obviously have additional financial implications, and given the uncertainty around supply due to manufacturing problems, many countries have postponed decisions around publicly funding the herpes zoster vaccine (Heywood and Macartney 2011).

Legal issues

Are there any legal considerations around continuing not to vaccinate, or around the decision to vaccinate?

Continuing not to vaccinate for varicella will not have any legal implications. However, depending on how surveillance of the incidence of varicella and/or herpes zoster were to be undertaken, and whether they were to become ‘mandatory’ to notify, an amendment to schedule 1 of the Health Act 1956 may be required. While, varicella zoster infection is currently listed in Part 2 of schedule 1, as an ‘other infectious disease’, it is not currently a ‘notifiable disease’ that requires notification to either the Medical Officer of Health or local health authority. Similarly, Herpes Zoster infection is not currently listed in the schedule at all.

Budget impact

What impact would the introduction of universal vaccination have on the available budget for vaccines and the total budget of Vote: Health?

There has been a sharp increase in spending on vaccines by the Ministry of Health over the last five years due to the addition of new vaccines such as Gardasil (for Cervical Cancer) and Prevenar (for pneumococcal disease)33. Annual spending has increased from around $20-$40 million (2006/07) to $60-$80 million since 2008. Furthermore, this budget is just for the purchase of the vaccines and represents only a small percentage of the total cost of delivering the vaccines to the public. This expenditure does not include development or implementation costs. For example, the total costs for MeNZB were over $220 million, but the cost of purchasing the vaccine itself was only $75.4 million over six years.

33 Health Report number: 20100423
The total estimated annual costs of delivering the two doses of the varicella vaccine to an entire birth cohort of approximately 60,000 is $9,680,400 (Table 4). However, this estimate assumes 100% uptake, when it is more likely that only 80% (48,000) take up the first dose and 77% (46,200) will take up the second. Thus, the overall annual cost may be closer to $7,128,114\(^{34}\). Assuming that the wholesale price of MMR and MMRV are also $50.00 per dose, the overall cost of vaccination could be reduced with the substitution of the second dose of the MMR vaccine with MMRV. If this were the case, an annual universal vaccination programme with single antigen varicella at 15 months and MMRV at 4 years may reduce by half, to approximately $3,632,160\(^{35}\). Assuming a budget for $60 million, the cost of the varicella vaccine (excluding promotion and surveillance), would comprise approximately 6% of the total available budget for vaccines.

Table 4: Estimated annual costs of delivering a universal varicella vaccination programme with 100% uptake.

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost per dose</th>
<th>Cost per person</th>
<th>Cost per cohort</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella vaccine (wholesale – excl GST &amp; freight)</td>
<td>$50.00</td>
<td>$100.00</td>
<td>$6,000,000.00</td>
<td>Manufacturers (2012)</td>
</tr>
<tr>
<td>Administration/delivery costs (2007/08)</td>
<td>$25.67</td>
<td>$51.34</td>
<td>$3,080,400.00</td>
<td>(Immunisation Advisory Centre 2012)</td>
</tr>
<tr>
<td>Surveillance and service audit, and research and evaluation(^{36})</td>
<td>n/a</td>
<td>n/a</td>
<td>$500,000.00</td>
<td>Health Report number: 20110143</td>
</tr>
<tr>
<td>Promotion &amp; advertising(^{37})</td>
<td>n/a</td>
<td>n/a</td>
<td>$100,000.00</td>
<td>Health Report number: 20110143</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$75.67</strong></td>
<td><strong>$151.34</strong></td>
<td><strong>$9,680,400.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

Note: In 2010-11 the Ministry of Health paid a vaccination benefit of $18.80 for each visit (pers comm. Mishra Suryaprakash, Immunisation Team, SCI) and Rosevear and Urlich (2012) used an estimate of $12.00 (see section 0).

In addition to the annual costs of delivering the vaccine, in the first year of the vaccination programme, substantial costs may be incurred through media advertising, distribution of information to GPs, and health promotion activities. Annually, the Ministry of Health spends between $891,095 (2010/2011) and $1,811,056 (2009/2010) on promoting immunisation\(^{38}\). While estimates of the cost of promoting specific vaccines were unavailable, in 2009 it was estimated that initial promotion of a varicella vaccine in New Zealand might cost around $100,000 (Scuffham 1999), which is $138,361.17 in 2011 dollars\(^{39}\). Other sources suggest

\[34 = (48,000 \times \$75.67) + (46,200 \times \$75.67)\]

\[35 = (48,000 \times \$75.67)\]

\[36\] This is based on an estimate for the rheumatic fever programme. More accurate data should be located.

\[37\] This is based on an estimate for the rheumatic fever programme. More accurate data should be located.

\[38\] Health Report number: 20111006

that these initial costs may be higher, and that there will also be ongoing promotion costs of at least $100,000 per year (Health Report number 20110143).

The delivery and the promotion of the vaccine will not be the only costs associated with a universal varicella vaccination programme. As mentioned in section 0, ongoing surveillance of the incidence of varicella and herpes zoster will be required which is estimated to cost around $500,000 per annum.

The overall budget impact of implementing a universal vaccination programme for varicella will therefore be approximately $9,680,400.00 annually. However, further work to confirm this estimate and establish the impact of the programme on the budget annually over the timeframe of interest, based on assumptions around increasing coverage and expected savings has not occurred. Likewise, both the ‘new technology’ scenario (eg, universal vaccination) needs to be modelled alongside the ‘baseline scenario’ (eg, status quo).

Is the universal public funding of varicella vaccination affordable and sustainable?

Vaccination policy is driven by several factors, including vaccine safety and efficacy, avertable disease burden, acceptability, and societal value (Kim 2011). One measure of value is an intervention's cost-effectiveness, defined as the additional cost required per additional unit of health benefit produced as compared with the next-most-effective alternative (as discussed in section 0). However, it is important to differentiate cost-effectiveness (value for money) from affordability (financial resources required); indeed, interventions with high value may not always be affordable (Kim 2011).

Evaluating single diseases or interventions in isolation is a restrictive approach to prioritising investment (Kim 2011). Individual vaccines may appear cost-effective compared with the status quo or a particular investment threshold, but the overall vaccination program may be unaffordable or provide less value than other bundled preventive health services targeting the same age group. This has been suggested in New Zealand by the Immunisation Awareness Society, with respect to funding for the pneumococcal vaccine, at the expense of other measures that might improve the health of this age group such as encouraging breastfeeding up to the age of two and ensuring that all children have a healthy and nutritious diet, free from high-sugar and high-fat junk and fast food (Immunisation Awareness Society 2012).

Kim (2011) also note that real-world obstacles should be integrated into analyses; for example, shortages in vaccine supply (as experienced with influenza vaccines and herpes zoster vaccines) can influence cost-effectiveness results. To make cost-effectiveness analysis a more practical tool, analysts should evaluate investments across multiple diseases and interventions and include the influences of nonmonetary constraints (Kim 2011).

Taking this on board, an investigation across other diseases suggests that there are a number of new vaccines on the horizon which might place pressure on the budget for vaccines in the future, such as a vaccines for rotavirus, cancer (including prostate cancer (Blue Cross Technology Evaluation Center 2010)), diabetes and Alzheimer’s (Poland et al 2002). In February 2011, researchers also successfully studied a universal flu vaccine, which might protect against all strains of influenza for ten years at a time (ImmuneForGood 2012).

Furthermore, there is an international trend in the expansion of existing recommendations for some vaccines currently listed on the New Zealand schedule. For example, while currently HPV is only on the New Zealand National Immunisation Schedule for girls aged 12 years, there is an indication overseas that this should be expanded to girls over 12 years (Marchetti and Morelli 2009). Similarly, while the pneumococcal conjugate vaccine is only listed on the schedule for children <15 months, the FDA approval of a conjugate pneumococcal vaccine for adults (PCV-13) in December 2011 (Fekete 2012) may also place pressure on future vaccine budgets. ACIP have not yet made a recommendation, but this is expected in 2012.
Likewise, suggestions have been made around the potential of extending the programme of school-based adolescent immunisations to include the provision of both additional primary immunisations as well as important booster doses of vaccines given earlier in childhood (Finn et al 2011). It has been argued that, such a programme, if well designed, would ensure that individual protection from vaccine preventable disease was maximised prior to school leaving and, of equal importance in some cases, that herd immunity was sustained more effectively in the population as a whole.

However, at this stage, the cost-effectiveness of universal vaccination for varicella is only directly comparable with universal vaccination for rotavirus due to the need for consistent methods. When compared with universal vaccination of infants against rotavirus, universal vaccination for varicella in children aged 15 months and 4 years, is more cost-effective; rotavirus vaccination would cost $62,000/QALY (Rosevear and Urlich 2012a), compared with the most expensive scenario for varicella vaccination, which is estimated to cost, at most (scenario 1), $16,000/QALY (Rosevear and Urlich 2012b).

Programme Budgeting & Marginal Analysis (PBMA): Is universal varicella vaccination a better option than any of the other initiatives in vaccines?

One of the best ways to determine the impact that funding a new vaccine will have on the budget, and how affordable and sustainable it is in the future, is to not just look at alternative vaccines and interventions on the horizon, but also to look at those interventions that are currently funded, but may be of less value than the new one under consideration. This process is called programme budgeting & marginal analysis, and normally starts by looking within specific programme budgets before looking across them.

Within the budget for vaccines, Cochrane reviews have identified two low value vaccine schedules (Cochrane Collaboration 2012). For example, they recommend that patients with chronic obstructive pulmonary disease (COPD) should not receive the influenza vaccine because the addition of intranasal live attenuated virus for influenza does not confer any added benefit (Cochrane Collaboration 2012) and that vaccines for preventing influenza in healthy adults should be discouraged (Cochrane Collaboration 2012).

While in New Zealand the universal vaccination of all adults for influenza is not publicly funded (targeted to those over 65 years and certain ‘at risk groups’), a substantial amount of money is spent annually on promoting the vaccine40, and the Immunisation Handbook 2011 does not list the vaccine as contraindicated for patients with COPD. With this considered, it may be worth examining the current immunisation schedule to see if money can be saved through better use of existing vaccines, and whether the funding of varicella vaccination through these savings is a better use of public money.

Similarly, it is possible that better gains may be made from increasing the coverage of existing vaccines on the schedule, to get them closer to the level that would achieve ‘herd immunity’, rather than investing in a new vaccine. To identify which vaccines this might apply to would require further investigation through mathematical modelling.

How difficult would it be to disinvest in this vaccination programme in the future?

Anecdotally, once a vaccine has been placed on the schedule, it is difficult to remove, and thus disinvestment is difficult. However, why this is, and whether the difficulty of disinvestment varies by vaccine is unclear and requires further investigation – possibly with clinical advisors, such as the Royal College of Pathologists Australasia (RACP) or the Royal New Zealand College of General Practitioners (RNZCGP).

40 Health Report number: 20111006
Funding

Varicella is usually a mild and transient disease treated in the community by children’s caregivers, resulting in only 0.5% of varicella cases being hospitalised, and about 1.2 deaths annually. Given that caregivers’ lost productivity is the most significant impact (as opposed to morbidity experience by the child), and that vaccination is only cost saving from a societal perspective, if the primary reason for vaccination was to reduce productivity loss from varicella, it will be important to confirm that such loss indeed occurs. Furthermore, given that savings are accrued to the wider society, whether that be employers or individuals (rather than the health sector), there is also a rationale for exploring whether Vote: Health is the appropriate funding source, or whether funding by individuals, employers or another government department, is more appropriate.

Should funding of the varicella vaccine come from Vote: Health or elsewhere?

While the Ministry of Health (Vote: Health) will bear the cost for the vaccination programme, it could be argued that the primary benefits of the programme (increased productivity) may be more closely aligned with the priorities of other government agencies (eg, Ministry of Economic Development and Ministry of Social Development) than those of the Ministry of Health. A similar argument could be made with respect to individuals funding vaccination themselves (to insure against loss of income) or employers (to insure against the lost productivity).

From a clinical standpoint, varicella is predominantly a relatively benign disease in children that is short-lived and results in few deaths or hospitalisations. From an economic standpoint, universal vaccination is cost-saving from a societal perspective because it reduces the time taken off work by caregivers to care for sick children. As the main drivers of the ‘cost’ of varicella are these productivity costs, rather than medical costs, a universal vaccination programme will increase the costs to Vote: Health, while the benefits (increased productivity), may be more closely aligned with a different Vote. If it is determined that the societal costs of varicella warrant intervention, then it is worth considering whether the costs of the vaccination programme should be funded by the budget anticipated to accrue the savings.

If varicella is a burden on society, and results in a significant loss of income for individuals or productivity losses for employers, prior to making any decision based on the anticipated ‘productivity savings’ from publicly funded vaccination, further investigation into the reasons why individuals or their employers are not currently funding vaccination should be undertaken.

Scuffham et al (1999) argues that the rationale for a fully-subsidized routine programme must rest upon observations regarding the extent to which the market, left to its own devices, fails to achieve socially optimal outcomes. With regards to the public funding of the varicella vaccine, this means that the cost, as oppose to awareness of the availability of a safe & effective vaccine, and perceptions of the seriousness of the disease, is the main reason uptake is low. Currently it is unclear whether caregivers associate their children getting varicella with a significant loss of income or whether employers believe the productivity of their business is significantly affected by caregivers taking sick days to care for children with varicella. Further work to establish caregiver’s preferences around varicella vaccination, and the cause of current ‘market failure’ in New Zealand is required.

It is also possible that the cause of market failure may vary by population group. For instance, while cost and information may be the primary determinants of uptake among Maori and individuals residing in the most deprived areas, information and changing perceptions may be the primary determinants of uptake among Europeans and those residing in the least deprived areas. If this is the case, and it is shown that cost is the primary barrier to particular groups not having the varicella vaccine, there may be a stronger case for targeting the public funding of varicella vaccination to individuals on low incomes,
and those susceptible to infection (see section 0) rather than universally funding vaccination for all. However, limiting the volumes of ‘publicly funded vaccine’ may reduce the bargaining strength of the government, making it less able to secure the vaccine at a good price, for both those for whom it is subsidised, and those able to privately pay

Conclusion

Overall, current evidence suggests that the single-antigen varicella vaccine is safe and effective for use in most children aged 15 months and 4 years, alongside existing immunisations on the schedule. However the quadrivalent MMRV vaccine is only recommended for use for the second dose at 4 years due to its links with febrile seizures in children of 15 months. While there is sufficient evidence to indicate the currently available single-antigen varicella and MMRV vaccines are safe & effective for most individuals that receive them, there is a suggestion that universal varicella vaccination may have an adverse impact on the unvaccinated population through increasing the risk of herpes zoster in unvaccinated adults. This potential outcome has implications for both the cost-effectiveness and ethics of a universal varicella vaccination programme.

Regardless of whether there is an increase in herpes zoster or not, a universal vaccination programme will still be cost-saving from a societal perspective, where the expected productivity gains will continue to outweigh any increased costs to the health sector. Conversely, an increase in herpes zoster is likely to substantially reduce the cost-effectiveness of vaccination for the health payer. Simulation models undertaken overseas suggest that the cost-effectiveness of universal vaccination from a health payer’s perspective could be improved through the addition of a herpes zoster vaccination programme for adults. However, these models still showed potentially negative benefits in the first 30-50 years, which were only partly mitigated through the introduction of a herpes zoster vaccine, and even after 100 years, vaccination was still not cost-saving to the health payer.

In the New Zealand model, decreasing the number of doses of the vaccine, from two to one, increased the cost-effectiveness of universal vaccination to both society and the health payer, but was still not cost-saving to the health payer. Universal vaccination only became cost-saving to the health payer when the price of the vaccine decreased by more than half (from $57 to $25) and this scenario did not factor in an increase in the incidence of herpes zoster which may occur.

An additional consideration is not just whether a universal varicella vaccination programme is cost-saving, but whether it represents the best use of public money when compared with other potential spending. While a two-dose varicella vaccination programme at 15 months and 4 years is more cost-effective when compared with vaccination against rotavirus, it remains uncertain whether money would better be spent on increasing coverage rates for existing vaccines on the schedule, or saved to fund other, potentially more beneficial vaccines on the horizon (ie, against cancer and Alzheimer’s).

Options

The decision to publicly fund the universal vaccination of children aged 15 months and 4 years is complex and hinges on a number of uncertainties, which may, depending on the level of risk decision-makers are comfortable with, require further research and analysis. The different options, their associated strengths and weakness, and the potential next steps required are summarised in Table 5. Which option that is chosen will depend on what decision-makers hope to achieve through publicly funding varicella vaccination. For instance, what is the main problem they are hoping to solve, or the main outcome they wish to obtain?

If the main priority is to reduce the morbidity associated with all cases of the disease (mild & severe), and to reduce the time taken off work by parents to care for sick children (ie, to
increase productivity gains) then option 1 may be best. If the main priority is to prevent most mild cases and all severe cases of the disease, and reduce the time taken off work by parents to care for sick children, then option 2 might be best. If the main priority is to reduce severe cases of the disease (but not the mild cases), in the most cost-effective way to the health payer, and manage uncertainty around potential increases in herpes zoster, then option 3 might be best. If the main priority is to produce cost savings for the health sector, then option 4 might be best.

**Table 5: Strengths and weakness of different options for publicly funding varicella vaccination in New Zealand**

<table>
<thead>
<tr>
<th>Option</th>
<th>Strengths</th>
<th>Weaknesses</th>
<th>Next Step</th>
</tr>
</thead>
</table>
| 1      | Public funding of two-dose vaccination for all children at 15 months and 4 years. | - reduces incidence of mild and severe varicella and associated hospitalisations  
- reduces incidence of herpes zoster in vaccinee  
- cost-saving to society  
- not cost-saving to health payer and potentially significant costs to health system due to increases herpes zoster in the short-term.  
- significant investment in surveillance required. | - investigate further likely cost of herpes zoster to health sector through another economic model which includes herpes zoster vaccine in 75+  
- further investigate likely costs of surveillance  
- further investigate likely savings and priority to society through focus groups  
- investigate other options for funding (ie, different Vote) |
| 2      | Public funding of single-dose vaccination for all children at 15 months. | - more cost-effective to society & health payer than option 1  
- reduces incidence of herpes zoster in vaccinee  
- prevents all severe cases of varicella and decreases hospitalisations  
- some mild cases of break through varicella  
- still not cost-saving to health payer and still uncertain impact on herpes zoster | - same as above |
| 3      | Targeted public funding of vaccination & private purchase for others (with or without subsidy for low income) | - prevents most severe cases of varicella  
- reduces incidence of herpes zoster in vaccinee  
- may be more ethical & equitable than option 4  
- wild-type virus still circulates so increase of herpes zoster due to lack of boosting unlikely  
- cost-effectiveness to society reduced (unlikely to still be cost-saving).  
- price of vaccine may increase due to small numbers  
- screening costs in cases of uncertain history  
- risk to immune compromised population higher than in options 1 & 2 | - determine number of people likely to be eligible for full subsidy.  
- investigate likely impact on vaccine price  
- investigate which form of targeting would be most cost-effective from both a societal and health payer’s perspective through more economic modelling  
- focus groups with public to determine willingness to pay to offset costs of time lost to work |
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>- If uptake is significant, same issues under options 1 &amp; 2 regarding herpes zoster will arise</td>
</tr>
</tbody>
</table>
| 4 | No public funding of varicella vaccination, only private purchase (ie, status quo) | - Cost-saving to the health payer  
- Wild-type virus still circulates so increases of herpes zoster due to lack of boosting unlikely |
|   |   | - Current incidence of varicella and herpes zoster and related hospitalisations likely to continue  
- Societal costs from lost productivity will continue  
- Private costs of vaccine remain high due to lack of bulk purchasing by government  
- Equity issues associated with ‘user pays’ – unequal impact on low income groups. |
|   |   | No further work required. |
Glossary of Terms

**Budget Impact Analysis (BIA)** or Financial analysis

A procedure for comparing only the financial costs and cost offsets of competing options, rather than comparing their clinical and economic costs and benefits (Ryan 2010).

**Cost-benefit analysis (CBA)**

An economic evaluation that compares the proposed technology with its main comparator(s) in which both costs and benefits are measured in monetary terms to compute a net monetary gain/loss or benefit gain/loss (Ryan 2010).

**Cost-effective (value for money)**

A proposed technology is considered cost-effective for a specified main indication if the incremental benefits of the proposed technology versus its main comparator(s) justify its incremental costs and harms (Ryan 2010).

**Cost-utility analysis (CUA)**

An economic evaluation that compares the proposed technology with its main comparator(s) in which costs are measured in monetary terms and outcomes are measured in terms of extension of life and the utility value of that extension, e.g. using quality-adjusted life years (QALYs) (Ryan 2010).

**Critical appraisal**

A strict process to assess the validity, results and relevance of evidence (Ryan 2010).

**Disability-adjusted life years (DALYs)**

A unit of healthcare status that adjusts age-specific life expectancy by the loss of health and years of life due to disability from disease or injury. DALYs are often used to measure the global burden of disease (Ryan 2010).

**Discount rate**

The interest rate used to discount or adjust future costs and benefits so as to arrive at their present values, e.g. 3.5%. This is also known as the opportunity cost of capital investment (Ryan 2010).

**Discounting**

The process used in economic analyses to convert future costs or benefits to present values using a discount rate. Discounting costs reflects societal preference for costs to be experienced in the future rather than the present. Discounting benefits reflects a preference for benefits to be realised in the present rather than at a later date (Ryan 2010).

**Economic evaluation**

Application of analytical methods to identify, measure, value, and compare costs and consequences of alternatives being considered; addresses issue of efficiency to aid decision making for resource allocation. It is an umbrella term covering CBA, CEA, CMA and CUA (Ryan 2010).

**Effectiveness**

The extent to which a technology produces an overall health benefit (taking into account adverse and beneficial effects) in routine clinical practice (contrast
with **Efficacy** *(Ryan 2010).*

**Efficacy**

the extent to which a technology produces an overall health benefit (taking into account adverse and beneficial effects) when studied under controlled research conditions (contrast with **Effectiveness**) *(Ryan 2010).*

**Epidemiology**

the study of the distribution and determinants of health-related conditions or events in defined populations *(Ryan 2010).*

**Generalizability**

the problem of whether one can apply or extrapolate results obtained in one setting or population to another. Term may also be referred to as ‘transferability’, ‘transportability’, ‘external validity’, ‘relevance’, or ‘applicability’ *(Ryan 2010).*

**Health outcome**

a change (or lack of change) in health status caused by a therapy or factor when compared with a previously documented health status using disease-specific measures, general quality of life measures or utility measures *(Ryan 2010).*

**Health payer’s perspective**

economic analysis is taken from the perspective of the funder, and excludes costs and savings to other (non-healthcare) government departments. This does not prevent these costs from being considered in a qualitative manner elsewhere in the report *(Grocott et al 2007).*

**Health technology assessment (HTA)**

this is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner. Its aim is to inform the formulation of safe, effective health policies that are patient focused and seek to achieve best value *(Ryan 2010).*

**Incidence**

the number of new cases of a disease or condition that develop within a specific timeframe in a defined population at risk. It is usually expressed as a ratio of the number of affected people to the total population *(Ryan 2010).*

**Incremental costs**

the absolute difference between the costs of alternative management strategies of the same medical condition, disease or disorder *(Ryan 2010).*

**Marginal benefit**

the additional benefit (e.g. in units of health outcome) produced by an additional resource use (e.g. another healthcare intervention) *(Ryan 2010).*

**Marginal cost**

the additional cost required to produce one additional unit of benefit (e.g. unit of health outcome) *(Ryan 2010).*

**Perspective**

this is the viewpoint from which an economic evaluation is conducted. Viewpoints that may be adopted include that of the patient, the public
Prevalence  
the number of people in a population with a specific disease or condition at a given time and is usually expressed as a ratio of the number of affected people to the total population (Ryan 2010).

Productivity costs  
the costs associated with lost or impaired ability to work because of morbidity or death (Ryan 2010).

Quality-adjusted life year (QALY)  
a unit of healthcare outcomes that adjusts gains (or losses) in years of life subsequent to a healthcare intervention by the quality of life during those years. QALYs can provide a common unit for comparing cost-utility across different technologies and health problems. Analogous units include Disability-Adjusted Life Years (DALYs) and Healthy-Years Equivalents (HYEs) (Ryan 2010).

Societal perspective  
economic evaluations taken from a ‘societal perspective’ include costs and consequences beyond those experienced by the health sector or potentially beyond the scope of the health sector’s control. These costs would include not only those to other government departments, but also productivity costs.
References


Harpaz R, Yawn BP. 2009. Trends in rates of herpes zoster-related hospitalizations: are they real, are they costly, and are they linked to varicella vaccination? Infection Control & Hospital Epidemiology 30:495-6; author reply 6-7.


Immunisation Advisory Centre. 2012. The Cost of Immunising in General Practice. The Cost of Immunising in General Practice.


Appendix 1: Immunisation Programme

The government subsidises a number of free immunisations through the National Immunisation Schedule, which is a mix of universal programmes (everyone of a particular age is eligible) and targeted programmes (only people with certain conditions are eligible). The largest component is the annual influenza immunisation programme targeted at adults over 65 and people with conditions that put them at risk from influenza. The most familiar component is the series of childhood immunisations to protect babies from infectious diseases like diphtheria, whooping cough, measles, and polio. There are also immunisations delivered in schools to Year 7 and 8 students. One of the six health targets is for 95% of 2-year olds to be fully immunised by July 2012.

Generally, the Ministry of Health purchases vaccines, while the District Health Boards (DHBs) are responsible for funding and planning how they get delivered to their communities. Most immunisations are given at general practices that are paid a fixed fee by DHBs for each immunisation visit. But immunisations are also given by special outreach services, public health units, in hospitals, and in some workplaces. Many immunisations are now recorded on the National Immunisation Register, which allows very accurate monitoring of immunisation coverage and also helps providers identify children and families who may have missed out.

The Immunisation Team oversees the whole immunisation system and specifically carries out these functions:

1. recommending to the government which vaccines should be free and for whom
2. purchasing and ordering vaccines worth around $50 million per year
3. communicating with providers and the public about immunisation programmes
4. servicing three advisory groups: the Immunisation Technical Forum, the Immunisation DHB Forum, and the Immunisation Coverage Forum
5. business owner of the National Immunisation Register
6. using data from the National Immunisation Register to identify the demographic, geographic, or programme factors that influence immunisation rates
7. project managing specific programmes like the annual influenza programme and the new human papillomavirus vaccine programme to prevent cervical cancer
8. publishing the Immunisation Handbook
9. managing contracts to deliver some national immunisation services
10. liaising with District Health Boards to share good practice and monitor progress towards the health target

Appendix 2: HTA repositories searched
Search terms: Varicella, Herpes Zoster, VZV Vaccination

Listed below are the various HTA agencies/repositories that were searched.

Agency for Healthcare Research and Quality

*No HTA found

Australia and New Zealand Horizon Scanning Network – Technologies Assessed

*No HTA found

MSAC

*No HTA found

CADTH

Varicella-Zoster Vaccine Implementation: Clinical Evidence and Guidelines
http://cadth.ca/media/pdf/K0270_Varicella_Zoster_Vaccine_final.pdf

VACCINE FOR HERPES ZOSTER
http://cadth.ca/media/pdf/412_No67_herpes_zoster_vaccine_edrug_e.pdf

Use of Varicella Vaccine in Healthy Populations
http://www.canadiantaskforce.ca/recommendations/2001_09_eng.html

Danish Centre for Evaluation and Health Technology Assessment

*No HTA found

Belgian Health Care Knowledge Centre

[Cost-utility of Vaccination against Chickenpox in Children and against Herpes Zoster in Elderly in Belgium]
Institute of Health Economics

Economics of Childhood Immunisations in Canada: Data Book (Varicella is a core component)

Ontario Health Technology Advisory Committee

*No HTA found

National Coordinating Centre for Health Technology Assessment

*No HTA found

Quality Improvement Scotland

*No HTA found

National Horizon Scanning Centre

*No HTA found

VA Technology Assessment

*No HTA found

California Health Technology Assessment

*No HTA found

Washington Health Technology Assessment

*No HTA found

Ludwig Boltzmann Institut für Health Technology Assessment
*NO HTA found

**Haute Authorité de Santé**

*No HTA found

**Norwegian Knowledge Centre for the Health Services**

*No HTA found

**Swedish Council on Technology Assessment in Health Care**

*No HTA found

**Catalan Agency for Health Technology Assessment and Research**

*No English HTA found

**Blue Cross Technology Evaluation Centre**

*No HTA found

**AETMIS**

*No HTA found

**McGill Technology Assessment Unit**

*No HTA found

**MONASH Center for Clinical Effectiveness**

*No HTA found

**Centre for Reviews and Dissemination**

Varicella-Zoster (not full text)

http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?AccessionNumber=32003000629
Appendix 3: Search strategies

Search strategy for EMBASE – English Only

Search Completed 16-November-2011
Database: Embase <1996 to 2011 Week 45>

Search Strategy:

--------------------------------------------------------------------------------
1  varicella.mp. (9482)  
2  chickenpox/ (5050)  
3  exp herpes zoster/ (8746)  
4  1 or 2 or 3 (16591)  
5  chickenpox vaccine/ (2785)  
6  varicella zoster vaccine/ (1144)  
7  exp vaccine/ (132353)  
8  vaccin*.mp. (186156)  
9  4 and (5 or 6 or 7 or 8) (4559)  
10 limit 9 to (meta analysis or "systematic review") (57)  
11 exp United States/ or exp Europe/ or exp Canada/ or exp Australia/ or exp New Zealand/ or New Zealand.cp. (1206025)  
12 9 and 11 (1134)  
13 10 or 12 (1181)  
14 limit 13 to (english language and yr="2009 -Current") (287)

*****************************************************************************

Search strategy for EMBASE – Non-English Only

Search Completed 16-November-2011
Database: Embase <1996 to 2011 Week 45>

Search Strategy:

--------------------------------------------------------------------------------
1  varicella.mp. (9482)  
2  chickenpox/ (5050)  
3  exp herpes zoster/ (8746)  
4  1 or 2 or 3 (16591)  
5  chickenpox vaccine/ (2785)  
6  varicella zoster vaccine/ (1144)  
7  exp vaccine/ (132353)  
8  vaccin*.mp. (186156)  
9  4 and (5 or 6 or 7 or 8) (4559)  
10 limit 9 to (meta analysis or "systematic review") (57)  
11 exp United States/ or exp Europe/ or exp Canada/ or exp Australia/ or exp New Zealand/ or New Zealand.cp. (1206025)
12 9 and 11 (1134)
13 10 or 12 (1181)
14 limit 13 to english language (984)
15 limit 13 to yr="2009 -Current" (340)
16 15 not 14 (53)

Search strategy for Ovid MEDLINE® - English Only
Search Run 2-November-2011
Database: Ovid MEDLINE(R) <1948 to October Week 3 2011>
Search Strategy:

1 varicella.mp. (9737)
2 Chickenpox/ (6165)
3 herpes zoster.mp. (10305)
4 1 or 2 or 3 (18834)
5 chickenpox vaccine/ or herpes zoster vaccine/ (1625)
6 vaccin*.mp. (228309)
7 exp vaccines/ (154421)
8 5 or 6 or 7 (232634)
9 4 and 8 (3122)
10 limit 9 to meta analysis (6)
11 9 and systematic review*.mp. (4)
12 exp United States/ or exp Europe/ or exp Canada/ or exp Australia/ or exp New Zealand/ or New Zealand.cp. (2187652)
13 9 and 12 (908)
14 10 or 11 or 13 (916)
15 limit 14 to (english language and yr="2009 -Current") (151)

Cochrane Library

#1 (varicella):ti,ab,kw 311
#2 MeSH descriptor Chickenpox explode all trees 125
#3 "herpes zoster":ti,ab,kw 637
#4 (#1 OR #2 OR #3) 860
#5 MeSH descriptor Chickenpox Vaccine explode all trees 133
#6 MeSH descriptor Herpes Zoster Vaccine explode all trees 22
#7 (vaccin*):ti,ab,kw 9563
#8 MeSH descriptor Vaccines explode all trees 6435
#9 (#5 OR #6 OR #7 OR #8) 9598
#10 (#4 AND #9) 184
#11 (#10), from 2009 to 2011 12

**Search strategy for Ovid MEDLINE® - Non-English Only**

Database: Ovid MEDLINE(R) <1948 to October Week 3 2011>

Search Strategy:

--------------------------------------------------------------------------------
1 varicella.mp. (9737)
2 Chickenpox/ (6165)
3 herpes zoster.mp. (10305)
4 1 or 2 or 3 (18834)
5 chickenpox vaccine/ or herpes zoster vaccine/ (1625)
6 vaccin*.mp. (228309)
7 exp vaccines/ (154421)
8 5 or 6 or 7 (232634)
9 4 and 8 (3122)
10 limit 9 to meta analysis (6)
11 9 and systematic review*.mp. (4)
12 exp United States/ or exp Europe/ or exp Canada/ or exp Australia/ or exp New Zealand/ or New Zealand.cp. (2187652)
13 9 and 12 (908)
14 10 or 11 or 13 (916)
15 limit 14 to yr="2009 -Current" (182)
16 limit 14 to english language (790)
17 15 not 16 (31)

*includes one non-English reference sourced from Cochrane Library full search
National Health Committee (NHC) and Executive

The National Health Committee (NHC) is an independent statutory body which provides advice to the New Zealand Minister of Health. It was reformed in 2011 to establish evaluation systems that would provide the New Zealand people and health sector with greater value for the money invested in health. The NHC Executive is the secretariat that supports the Committee. The NHC Executive's primary objective is to provide the Committee with sufficient information for them to make recommendations regarding prioritisation and reprioritisation of interventions. They do this through a range of evidence-based reports tailored to the nature of the decision required and time-frame within which decisions need to be made.


Published in December 2014 by the National Health Committee
PO Box 5013, Wellington, New Zealand
ISBN: 978-0-478-44472-8 (online)
HP 6105

This document is available on the National Health Committee’s website:
http://www.nhc.health.govt.nz/

Disclaimer

The information provided in this report is intended to provide general information to clinicians, health and disability service providers and the public, and is not intended to address specific circumstances of any particular individual or entity. All reasonable measures have been taken to ensure the quality and accuracy of the information provided.

If you find any information that you believe may be inaccurate, please email to NHC_Info@nhc.govt.nz.

The National Health Committee is an independent committee established by the Minister of Health. The information in this report is the work of the National Health Committee and does not necessarily represent the views of the Ministry of Health.

The National Health Committee makes no warranty, express or implied, nor assumes any legal liability or responsibility for the accuracy, correctness, completeness or use of any information provided. Nothing contained in this report shall be relied on as a promise or representation by the New Zealand government or the National Health Committee.

The contents of this report should not be construed as legal or professional advice and specific advice from qualified professional people should be sought before undertaking any action following information in this report.

Any reference to any specific commercial product, process, or service by trade name, trademark, manufacture, or otherwise does not constitute an endorsement or recommendation by the New Zealand government or the National Health Committee.