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Saturday, June 10, 2017 (Room 7)

16:30 - 17:25 WS #164: Update on Public and Private Vaccination
17:35 - 18:30 WS #176: Update on Public and Private Vaccination (Repeated)

Update: Public and Private Vaccination

Nikki Turner
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The University of Auckland
June 2017

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Te Whare Wānanga o Tāmaki Makaurau

Index

- 2017 National Immunisation Schedule
  - HPV
  - Varicella
  - Other
  - High risk groups
- Private Market Vaccines
- Communication Issues

2017 schedule changes summary

Vaccine changes	Vaccine	Eligibility	Introduced
HPV	Gardasil 9® (HPV9)	For young men and young women: <15 years: two doses >15 - 26 years: three doses	1 January 2017
Varicella	Varilrix® (Varicella)	One dose 15 months Catch-up at 11 years*	1 July 2017
Rotavirus vaccine	Rotarix® (RV1)	First dose by 14 weeks Second by 24 weeks	1 July 2017

* For previously unvaccinated children with no history of chickenpox infection

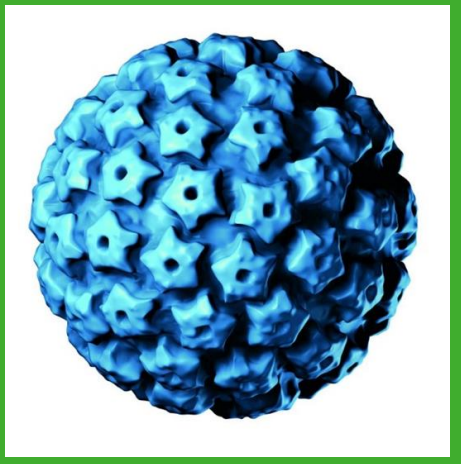
2017 further changes – brand only

Schedule changes	Vaccine	Eligibility	
Pneumococcal	Synflorix® PCV10	No change*	1 July 2017
MMR	Priorix® MMR	No change	1 July 2017
Hib	Hiberix® Hib	No change	1 July 2017

* Prevenar13 remains for high risk pneumococcal programme

HPV vaccination

For boys and girls



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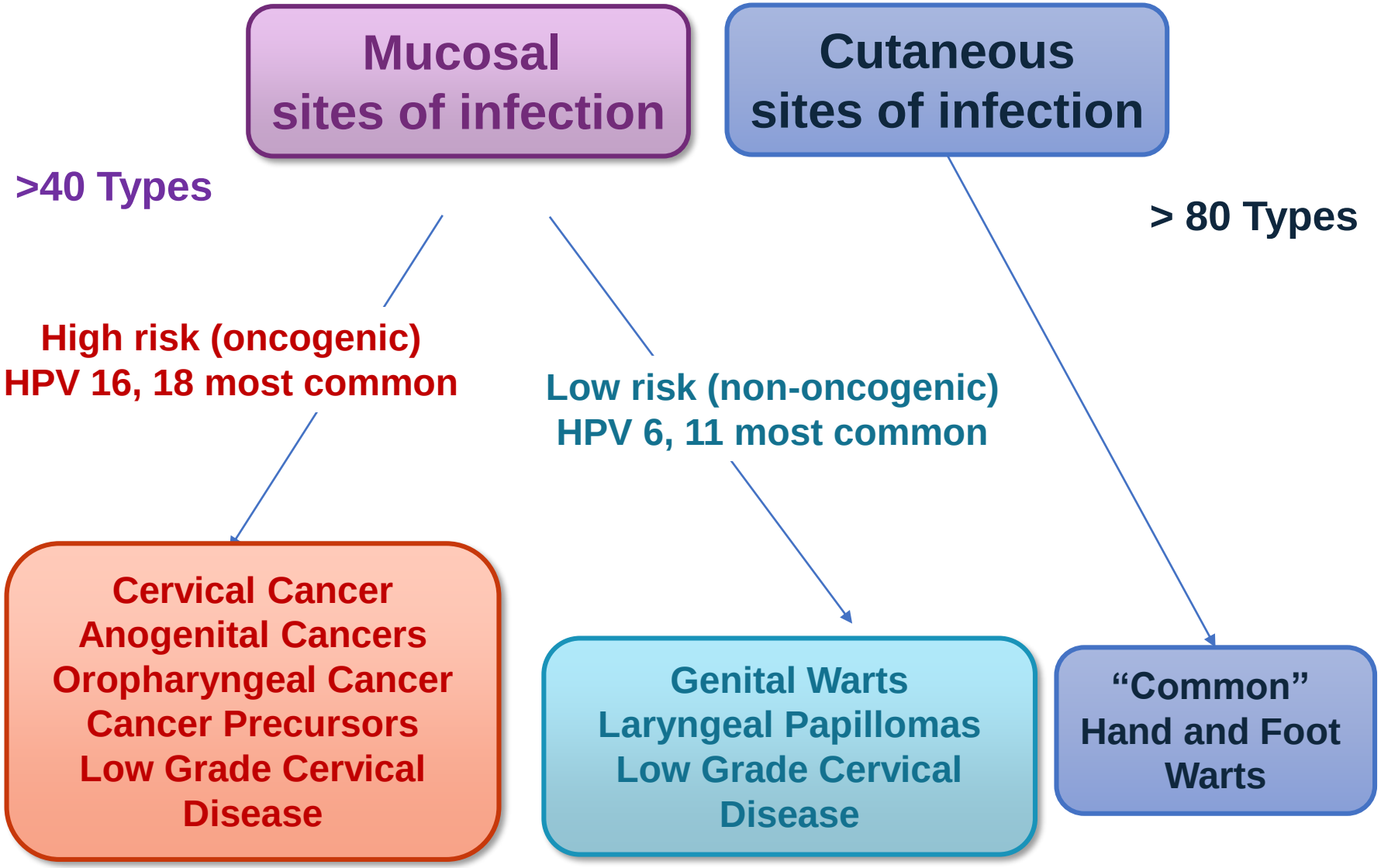
HPV Types Differ in Disease Association



Why go to 9 serotypes?

HPV9 vaccine and cervical cancer

HPV4 covers >70% of oncogenic types

HPV9 covers >87% of oncogenic serotypes

Richard Roden, Wu T (2006) How will HPV vaccines affect cervical cancer? Nature Reviews Cancer 6, 753-763 doi:10.1038/nrc1973

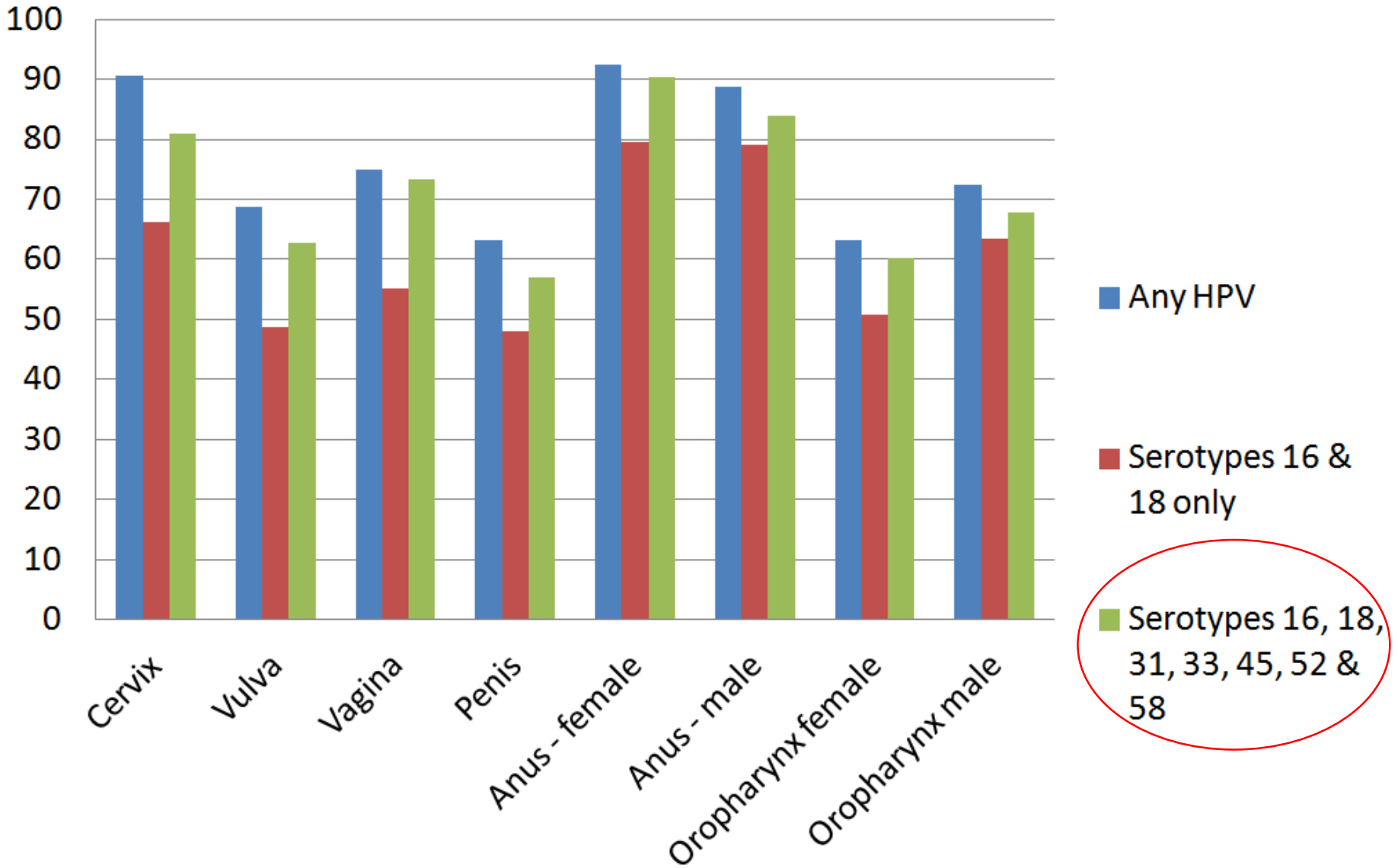
Why give it to both sexes?

Cancers caused by high-risk HPV types

Cervix	• >99%
Penis	• >60%
Vulva, Vagina	• >70%
Anus	• >90%
Oropharynx	• >70%

http://www.cdc.gov/hpv/parents/cancer.html

Average annual % of cancer cases attributable to HPV, by anatomic site and sex, United States 2008-2010



Adapted from: Saraiya M, Unger E, Thompson T, et al (2015) Assessment of HPV types in cancers: Implications for current and 9-valent HPV vaccines. *Journal of National Cancer Institute* 107 (6) Table 4

But is it safe?

Gee, J., Weinbaum, C., Sukumaran, L., & Markowitz, L. E. (2016). Quadrivalent HPV vaccine safety review and safety monitoring plans for nine-valent HPV vaccine in the United States. *Human vaccines & immunotherapeutics*, *12*(6), 1406-1417.

HPV vaccine

profile

- Extensive post-market surveillance HPV4
  – no safety signals raised
- Summary of post-market safety associations
  - Syncope (related to injection reaction)
  - Possible skin infections (probably injection site reactions misclassified)
  - Pregnancy (contraindicated but inadvertent admin)
    - No theoretical risk (not a live vaccine)
    - No differences in outcome pregnant/non pregnant

Haupt et al An overview of Quadrivalent HPV vaccine safety 2006 – 2015 PIDJ Sept 2015

HPV Vaccines safety

- Large number of investigations for specific outcomes
  - Case reports do not equal causality
  - No association with many conditions including:
    - Autoimmune disease (MS, connective tissue disease, GBS,type1 diabetes, thyroiditis, ITP
  - Extensive investigations for venous thromboembolism – do not support an association
  - No association with poor outcomes when accidentally given in pregnancy
  - MS – one study suggested an increased risk in 30 day period after vaccination, overall the data does not support this finding
  - POTS case reports. EMA review to date, no increase
  - Complex regional pain syndrome, fibromyalgia – not expected to be linked

EMA report
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Human_papillomavirus_vaccines/human_referral_prac_000053.jsp&mid=WC0b01ac05805c516f

Post licensure studies - most compare outcomes in vaccinated with unvaccinated

Table 1. Post-licensure published quadrivalent human papillomavirus vaccine (4vHPV) safety studies.

System or review (country)	Year of Publication	Number of doses evaluated		Description	Methods	Findings
VAERS (US)[a]	2009	N/A	600,000 doses	Summary of 12,424 VAERS reports following 4vHPV between 2006–2008	Spontaneous reporting; data mining for disproportional reporting	Disproportional reporting of syncope and VTE
Vaccine Safety Datalink (US)[b]	2011	600,558	General safety	Large database used for active surveillance and research; safety assessment of 9 pre-specified health outcomes among females vaccine recipients aged 9–26 years	Cohort design with weekly sequential analyses of electronic medical data	No statistically significant increase in risk for the outcomes monitored; non-significant elevated risk detected for VTE
Institute of Medicine review (US)[c]	2011	N/A	346,972 doses	Review of available 4vHPV safety data	Review of published studies, case reports, and surveillance systems	No evidence to support association among 12 outcomes; anaphylaxis causally associated with 4vHPV; syncope associated
Post-marketing commitment to FDA (US)[d]	2012	346,972	General safety, VTE, neurologic, death	General follo adm two orga		weeks ther
Post-marketing commitment to FDA (US)[e]	2012	346,972	Autoimmune	Assessm auto follo 4vH care		als for
VAERS (US)[f]	2013	N/A	696,420 doses	Review follo 200		ing cerns
Register-based cohort study (Denmark and Sweden)[g]	2013	696,420	Autoimmune, Neurologic, VTE	Assessm auto conc follo fem		ween
VAERS (US)[h]	2014	N/A	General safety	Review follo 2006–2014		ing cerns
Pharmacoepidemiologic General Research Extension (France)[i]	2014	N/A	500,345 doses	Assessment of 6 different autoimmune outcomes following 4vHPV among 211 cases and 875 controls aged 14–26 years	Case-control study with recruitment of cases and controls through registries	No increased risk for combined endpoint of six autoimmune disorders
Register-based cohort study (Denmark)[j]	2014	500,345	VTE	Assessment of VTE following 4vHPV among women aged 10–44 years	Self-controlled case series using national patient registers	No increased risk for VTE

Outcomes include autoimmune, neurological, blood clots, CNS, CRPS, other specified conditions....

1,924,581

1,426,399

1,240,000

System or review (country)	Year of Publication	Number of doses evaluated	addressed	Description	Methods	Findings
Register-based cohort stud (Denmark and Sweden)[f]		,581	Autoir	t of multiple sclerosis er demyelinating s of the central s system among aged 10–44 years	Cohort design using data linked to national registers	No association with the development of multiple sclerosis and other demyelinating diseases
Vaccine Safety Datalink (US)[l]	2015	1, 240, 000	VTE	Assessment of VTE among adolescents and young adults aged 9–26 years	Self-controlled case series; cases confirmed by medical record review	No increase risk for VTE
Sentinel System (US)[m]	2015	1,423,399	VTE	Assessment of VTE among females aged 9–26 years	Self-controlled risk interval design; cases confirmed by medical record review	No increased risk for VTE
VAERS (US)[n]	2015	N/A	Neurologic	Review of 21 CRPS-related VAERS reports following 4vHPV between 2006 and 2015	Spontaneous reporting; clinical review of CRPS cases	Lack of evidence to suggest an association; data suggest CRPS following HPV vaccine is rare
Post-marketing commitment to FDA (US)[o]	2015	N/A	Pregnancy	Review of 4,919 reports of pregnancy following 4vHPV between 2006–2012	Voluntary reporting to pregnancy registry	Data were reassuring with no elevated reporting of adverse pregnancy outcomes
VAERS (US)[p]	2015	N/A	Pregnancy	Review of 147 VAERS pregnancy reports following 4vHPV between 2006 and 2013	Spontaneous reporting; data mining for disproportional reporting	No unexpected patterns fetal adverse events after 4vHPV
Vaccine Safety Datalink (US)[q]	2016	1,355,535	Death	Evaluation of deaths among individuals aged 9–26 years	Case-centered method; medical record review	Rate of death was lower than the national expected rate of death in this population

Abbreviations

CRPS- Chronic Regional Pain Syndrome, FDA- Food and Drug Administration, HIV- Human immunodeficiency virus, 4vHPV- Quadrivalent Human Papillomavirus vaccine, VAERS- Vaccine Adverse Event Reporting System, VTE- Venous thromboembolism

Sources

[a]Slade, B.A., et al., Post-licensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. JAMA, 2009. 302(7): p. 750–757.
[b]Gee, J., et al., Monitoring the safety of quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink. Vaccine, 2011. 29(46): p. 8279–8284.
[c]Institute of Medicine. Adverse Effects of Vaccines: Evidence and Causality. 2011.
[d]Klein, N.P., et al., Safety of quadrivalent human papillomavirus vaccine administered routinely to females. Arch Pediatr Adolesc Med, 2012. 166(12): p. 1140–8.
[e]Chao, C., et al., Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. J Intern Med, 2012. 271(2): p. 193–203.
[f]Stokley S, et al., Human Papillomavirus Vaccination Coverage Among Adolescent Girls, 2007–2012, and Postlicensure Vaccine Safety Monitoring, 2006–2013 — United States. MMWR Recomm Rep, 2013. 62(29); p. 591–595
[g]Arnheim-Dahlstrom, L., et al., Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. BMJ, 2013. 347: p. f5906.
[h]Stokley S, et al., Human papillomavirus vaccination coverage among adolescent girls, 2007–2012, and post-licensure vaccine safety monitoring, 2006–2013 — United States. MMWR Recomm Rep. 2014. 63(29); p. 620–4.
[i]Grimaldi-Bensouda, L., et al., Autoimmune disorders and quadrivalent human papisslomavirus vaccination of young female subjects. J Intern Med, 2014. 275(4): p. 398–408.
[j]Scheller, N.M., et al., Quadrivalent human papillomavirus vaccine and the risk of venous thromboembolism. JAMA, 2014. 312(2): p. 187–8.
[k]Scheller, N.M., et al., Quadrivalent HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. JAMA, 2015. 313(1): p. 54–61.
[l]Naleway, A.L., et al., Absence of venous thromboembolism risk following quadrivalent human papillomavirus vaccination, Vaccine Safety Datalink, 2008–2011. Vaccine, 2016; 34(1): p. 167–71.
[m]Yih, W.K., et al., Evaluation of the risk of venous thromboembolism after quadrivalent human papillomavirus vaccination among US females. Vaccine, 2016; 34(1): p. 172–8.
[n]Weinbaum C, et al.. HPV Vaccination and Complex Regional Pain Syndrome: Lack of Evidence. EBioMed, 2015. 2(9): p. 1014–1015.
[o]Goss, M.A., et al., Final report on exposure during pregnancy from a pregnancy registry for quadrivalent human papillomavirus vaccine. Vaccine, 2015. 33(29): p. 3422–8.
[p]Moro, P.L., et al., Safety of quadrivalent human papillomavirus vaccine (Gardasil) in pregnancy: adverse events among non-manufacturer reports in the Vaccine Adverse Event Reporting System, 2006–2013. Vaccine, 2015. 33(4): p. 519–22.
[q]McCarthy, N.L., et al. Lack of association between vaccination and death in individuals 9–26 years of age. Pediatrics, 2016; 137(3): p. 1–8.

HPV9 vaccine

- 15,000 subjects in 31 countries
- HPV9 slightly more reactogenic than HPV4
  - injection site reactions: only significant difference was in injection site swelling
  - common systemic events all slightly higher e.g. headache 14.6% (13.7% with HPV4), pyrexia 5% (4.3% with HPV4)
- No serious adverse events
  - anaphylaxis is possible

Moreira E D, Block S L, Ferris D et al (2016) Safety profile of the 9-valent HPV vaccine: a combined analysis of 7 phase III clinical trials Pediatrics 2016;138 (2) e2015438

Does it work?

Effectiveness of HPV4 vaccine

- Over 130 published studies to June 2016
  - Maximal reduction of around 90% for HPV infection, genital warts and cervical abnormalities (57 studies)
- Profound reduction in genital warts (e.g. Australia and Denmark)
  - Mediocre coverage also leads to significant reductions
  - Elimination of genital warts may be possible

Garland SM, Kjaer SK, Muñoz N, et al. Impact and Effectiveness of the Quadrivalent Human Papillomavirus Vaccine: A Systematic Review of Ten Years of Real-World Experience. Clin Infect Dis 2016:ciw354.

I wish to wait till my child is older before giving HPV vaccine

Immunogenicity

The younger the better response

NB but likely to be reduced in immunocompromised hosts

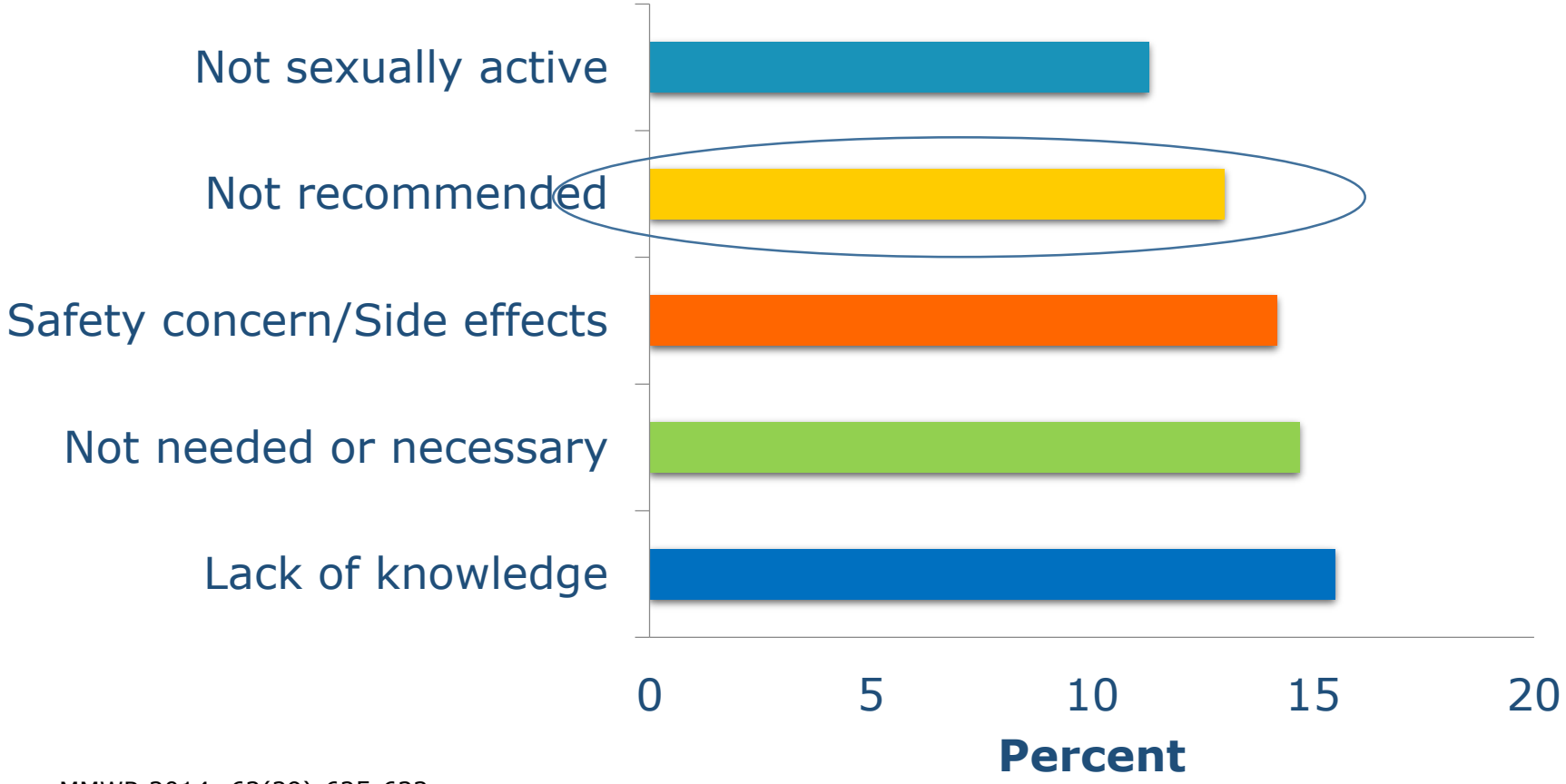
http://www.who.int/immunization/sage/meetings/2014/april/1_HPV_Evidence_based_recommendationsWHO_with_Appendices2_3.pdf

HPV delivery in primary care

- Two doses funded – **The standard schedule**
  - For to 11-14 year olds who decline in school based programme
- Three dose schedule **– catch-up if missed or high risk**
  - Aged 15-26 years old
  - Aged 9 – 26 with confirmed HIV, transplant patients
  - Immunocompromised (not funded under 15 yrs)
- Completion of the course is only funded if first dose was given before turning 27 years

- **Resource permitting (?!)** primary care can recall 14 – 26 year olds who have not completed a course of HPV vaccine
  - ?maybe start with a standard recall at 14 years for all unvaccinated

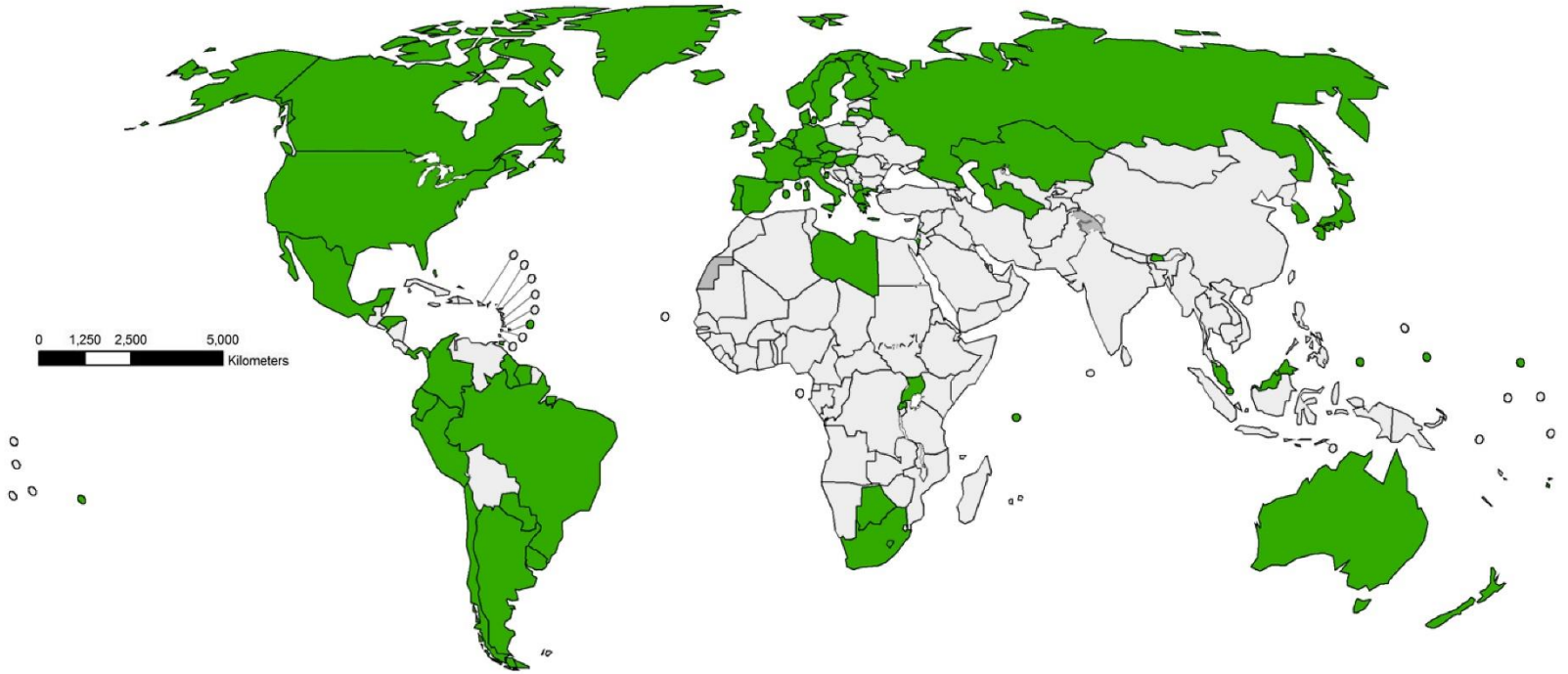
Reasons parents won't initiate HPV vaccination for children



MMWR 2014; 63(29);625-633;

- I am already sexually active, is there any benefit in the vaccination
- A 48 year old woman is requesting to be vaccinated
- 2 doses versus 3 doses
- Avoiding embedding myths
- How to recall/catch up in real GP land

Countries with HPV vaccine in the national immunization programme to date



* Includes partial introduction

Data source: WHO/IVB Database, as of 16 December 2016
Map production Immunization Vaccines and Biologicals (IVB),
World Health Organization

WHO

USEFUL SUMMARY REFERENCE

Human papillomavirus vaccines: WHO position paper, May 2017
Weekly epidemiological record (WER), World Health Organization

http://apps.who.int/iris/bitstream/10665/255353/1/WER9219.pdf?ua=1

Varicella Vaccines

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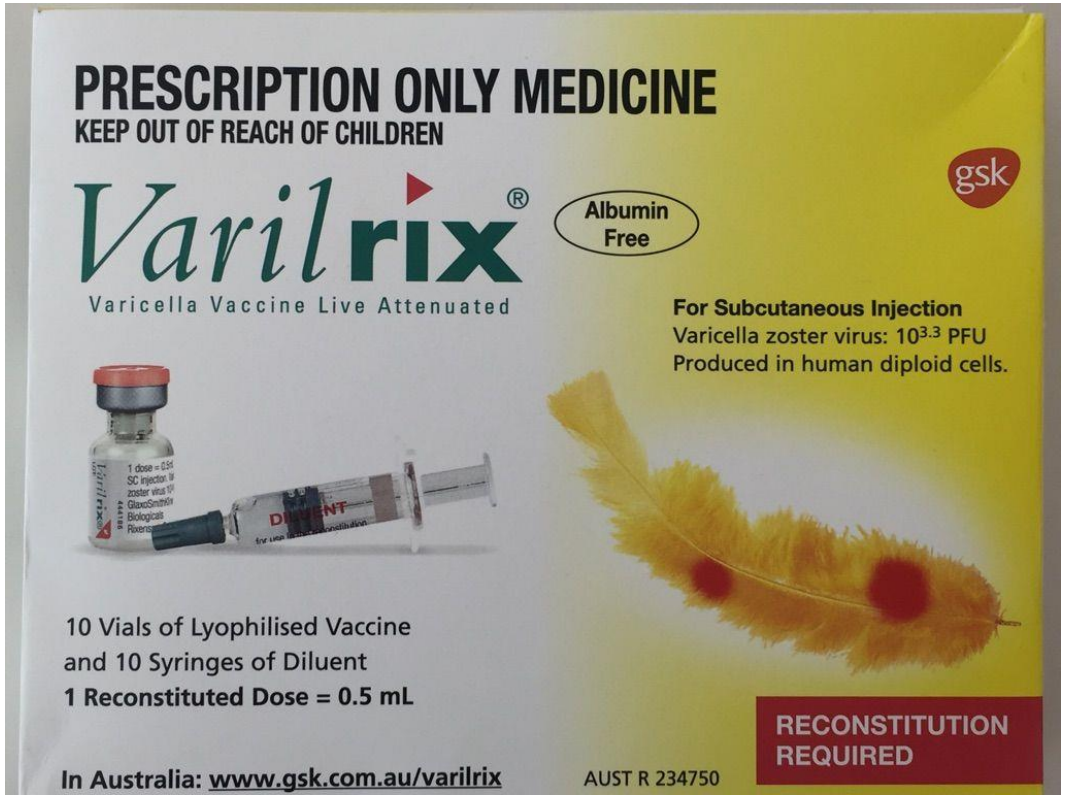
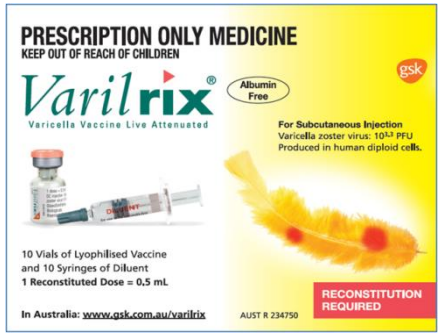


V

MMRV

(licensed but not currently available)

NEW schedule

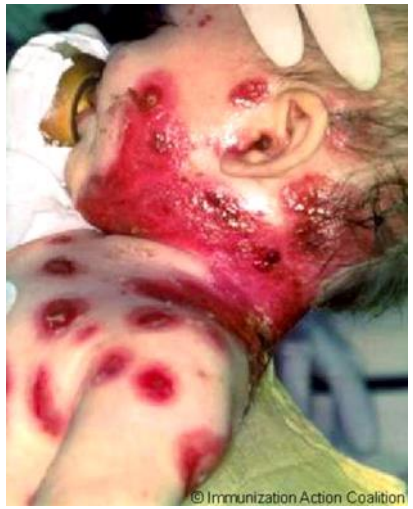


From 1st July 2017 on National Schedule

- Single dose at 15 months alongside Hib, PCV10 and MMR
- Four injections different sites

- Funded Catch-up dose for 11 year olds previously unvaccinated with no history of chickenpox infection
- Funding criteria for special groups remain the same

Why add a vaccine in for such a mild disease?



NZ epidemiology

- Ubiquitous in NZ childhood
- Hundreds hospitalized per year
  - One tenth of cases occur in immuno-suppressed children
- 1-2 per year long term disability or death
  - Most deaths in adults
- 0.5 case per year of severe congenital varicella

Ministry of Health (2016) Immunisation Handbook 2014 (2nd edition) URL: http://www.health.govt.nz/system/files/documents/publications/immunisation-handbook-2014-2nd-edn-apr16.pdf

Varicella complications

Majority of complications occur in otherwise healthy individuals

Skin/soft tissue bone joint infections	Central nervous system complications	Respiratory complications
• Secondary skin infections • Scarring • Septic arthritis • Osteoarthritis • Necrotizing fasciitis	• Acute cerebellar ataxia • Encephalitis • Meningitis • Central facial palsy • Reye's syndrome	• Pneumonia • Broncholitis

Ministry of Health (2016) Immunisation Handbook 2014 2nd Ed. Wellington: Ministry of Health.

Effectiveness

Single Dose

- Approx. 80% effective
- Against severe disease 95% plus
- Breakthrough cases less severe

Two dose

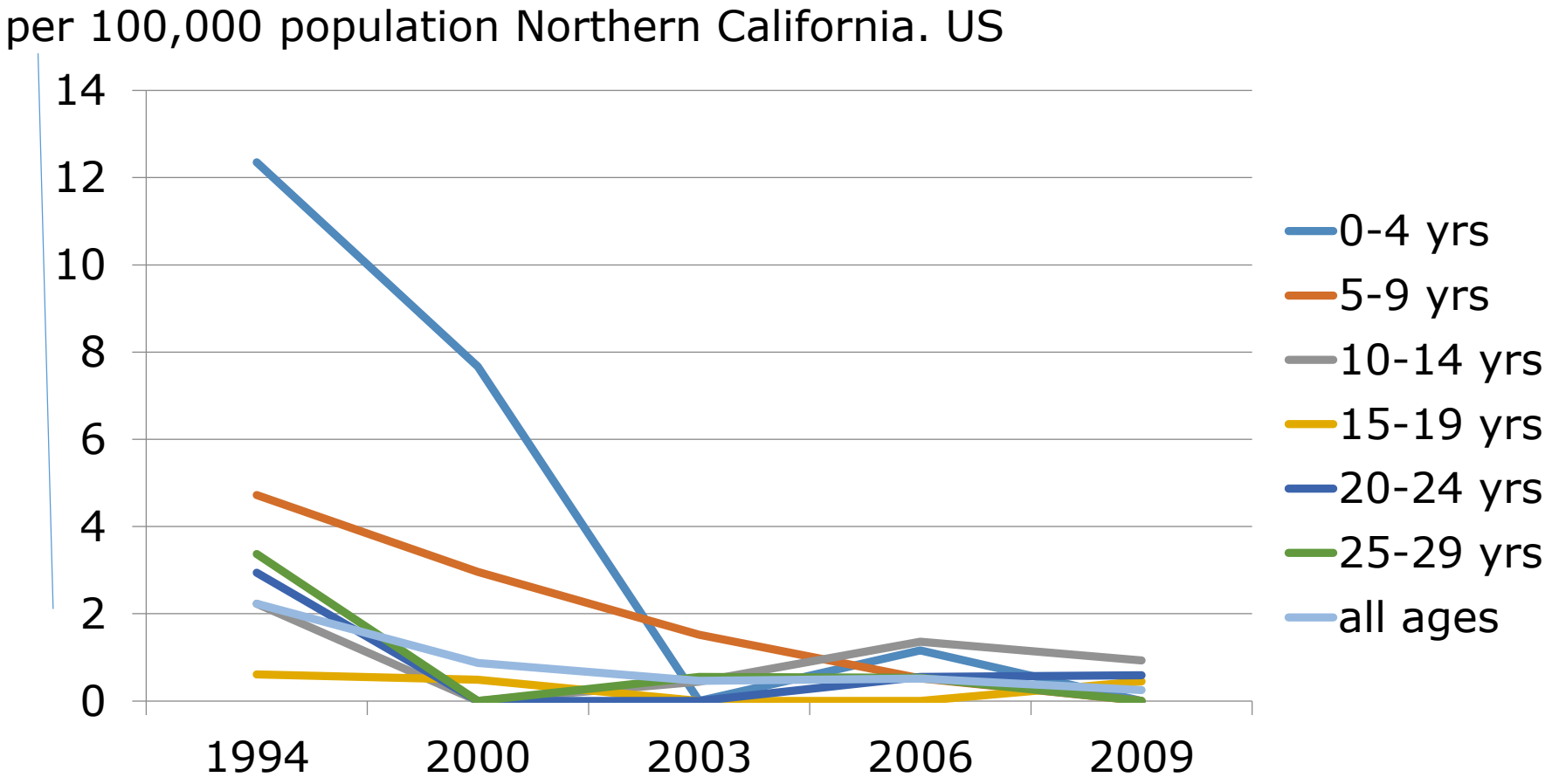
- 93% -100% against severe disease

- Breakthrough varicella in vaccinated people
  - Usually attenuated
  - Severity does not increase with time post vaccination

- Immunocompromised
  - Effectiveness unclear
  - Disease severity reduced
  - Mild immunosuppression still get seroconversion

SAGE. Systematic review of available evidence on effectiveness and duration of protection of varicella vaccines.: WHO; 2014
Available from: http://www.who.int/immunization/sage/meetings/2014/april/presentations_background_docs/en/

Impact of varicella vaccination program in United States



Baxter R, Tran T, Ray P, et al. (2014 Impact of vaccination on the epidemiology of varicella: 1995-2009 Pediatrics 134 (1) 24-30

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Duration of protection

- One dose
  - Not yet defined, but breakthrough disease does not become more severe with time
  - US study VE declined from 88.8% to 81.8% after >10 years
  - Some effect from circulating wild disease causing boosting
    - Therefore reductions in circulating disease may reduce duration of protection

- Two-dose probably long lasting
  - NB second dose also acts as a booster
    (unlike measles vaccination)
  - No breakthrough after 14 years post two doses
  - Many countries introduce a few years after starting one dose
  - Universal 2 dose in US since 2006

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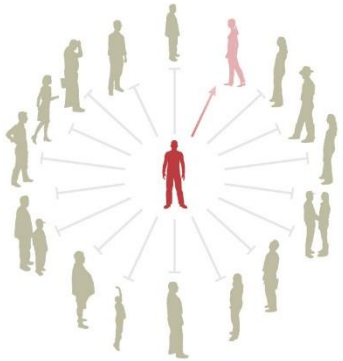
SAGE. Systematic review of available evidence on effectiveness and duration of protection of varicella vaccines.: WHO; 2014
Available from: http://www.who.int/immunization/sage/meetings/2014/april/presentations_background_docs/en/

Herd immunity

YES



http://graphics8.nytimes.com/newsgraphics/2015/02/02/measles-facts/01f7c7331715b51a58bc4380fd8031c56bcd27a1/herd-3-artboard-10.jpg

Where universal programmes have been implemented significant declines in cases and hospitalisations have been seen, including those not vaccinated – infants and immunocompromised

Waye A, Jacobs P, Tan B. The impact of the universal infant varicella immunization strategy on Canadian varicella-related hospitalization rates. Vaccine. 2013;31(42):4744-8.

Varilrix®

- **<u>Live</u>** attenuated Oka strain of varicella-zoster virus
- Each 0.5ml reconstituted contains
  - ≥ $10^{3.3}$ plague-forming units (PFU) attenuated varicella virus, human albumin, lactose, neomycin, polyalcohols
- From 9 months of age
  - 1 or 2 doses in children, 2 doses >12 years
- Minimal interval between doses: 4 weeks
- Can be given at the same time as other vaccines

  (DTaP-containing vaccines, hepatitis B, Hib, MMR, Hepatitis A, pneumococcal conjugate vaccines)

Contraindications

Immunocompromised

Includes:

- **Primary or acquired T-cell deficiency states**
- **High dose steroids for >2 weeks**
- **Active untreated Tb**

But limited capacity for virulence or replication:

- Mild immunocompromised benefits probably outweigh risks eg
  - HIV on treatment,
  - 2 years post bone marrow transplantation
  - 6 months post chemotherapy
  - HIV-positive with mild or mod immunosuppression

CAUTION, TAKE ADVICE

- Can treat with antivirals if breakthrough disease

Refer page 502 NZ Immunisation Handbook 2014

AEFIs

- Generally mild and self limiting
  - Fever: Possible 5-12 days post vaccination
  - 1-3% localized rash
  - 3-5% generalized varicella-like rash
    - 5-26 days post vaccination
    - Usually 2-5 lesions, can be maculopapular

- **? Transmission of vaccine virus to others:**
  - **Possible but extremely rare**
  - **Err on the side of caution**
    - **If there is a post-immunisation rash isolate from any immunosuppressed contacts, cover rash**

- Noted but not necessarily causally linked
  - Encephalitis, ataxia, thrombocytopenia, anaphylaxis <0.01%

Why not use MMR-V so requires less injections

N.B. MMR-V is not currently available in New Zealand

Giving MMR-V combined vaccine at 15 months is associated with a significant increased risk of febrile convulsions

- This does not occur when used as a second dose
- This also does not occur with separated MMR and varicella vaccines given at the same time

Therefore separated vaccines were chosen to reduce the risk of febrile convulsion

SAGE. Safety of varicella and MMRV vaccines: A systematic review 2014.
Hambidge SJ, Newcomer SR, Narwaney KJ, et al. Timely versus delayed early childhood vaccination and seizures. Pediatrics. 2014;133(6):e1492-9.

Multiple injections!!

Get all four at 15 months

Find out more at immune.org.nz

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Supported by an unrestricted grant from GSK.

Recommended not funded

All adolescents/adults with no previous history of varicella or vaccination

Particularly consider

- - born in tropical countries (lower childhood incidence)
- High risk environments eg
  - – us (healthcare workers)
    - early childcare,
    - Institutional care
    - Hostels,
    - Military
    - Correctional institutes

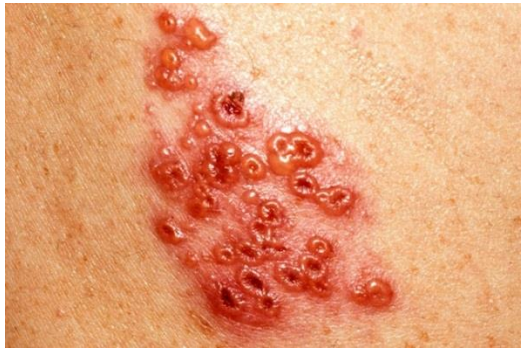
Post exposure prophylaxis

A single dose is highly effective when administered within 3-5 days of exposure (79 – 100%)

Break through cases tend to be more mild

World Health Organization. Varicella and herpes zoster vaccines: WHO position paper, June 2014. Wkly Epidemiol Rec. 2014;89(25):265-87.
Macartney K, Heywood A, McIntyre P. Vaccines for post-exposure prophylaxis against varicella (chickenpox) in children and adults. Cochrane Database Syst Rev. 2014;6:CD001833.
Marin M. Updated recommendations for use of VariZIG - United States, 2013. American Journal of Transplantation. 2013;13(10):2765-7.

But what about the effect on shingles



Herpes zoster

1. Zoster does occur post vaccination but lower rates

- 48/100 000 in vaccinated versus 230/10 000 in unvaccinated
- US study vaccinated children had 79% lower incidence of zoster

2. Could rates of zoster rise with a highly vaccinated population? - probably NO

If zoster is prevented by exogenous boosting (ie exposure to circulating varicella) then theoretically stopping varicella circulating could increase the incidence of zoster in older groups

- BUT - No definite increase has been demonstrated in countries that have introduced varicella vaccination. No definitive increase has been seen overall in the US or Australia
- Probably key role of endogenous boosting

Weinmann S, Chun C, Schmid DS, et al. Incidence and clinical characteristics of herpes zoster among children in the varicella vaccine era, 2005-2009. J Infect Dis. 2013;208(11):1859-68.
Hales CM, Harpaz R, Joesoef MR, et al. Examination of links between herpes zoster incidence and childhood varicella vaccination. Ann Intern Med. 2013;159(11):739-45.
Heywood AE, Wang H, Macartney KK, et al. Varicella and herpes zoster hospitalizations before and after implementation of one-dose varicella vaccination in Australia: an ecological study. Bull World Health Organ. 2014;92(8):593-604.

- I want to offer my child protection earlier that 15 months
- I don’t wish to give 4 injections at once
- Why doesn’t the national schedule offer a two dose regime
- I wish to use the MMRV, rather than separate injections
- How do I protect my immunosuppressed patient who has never had chicken pox
- How do I know if I need the vaccine , do I need a blood test?

Rotavirus Vaccine
Brand change

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Effectiveness against any rotavirus disease

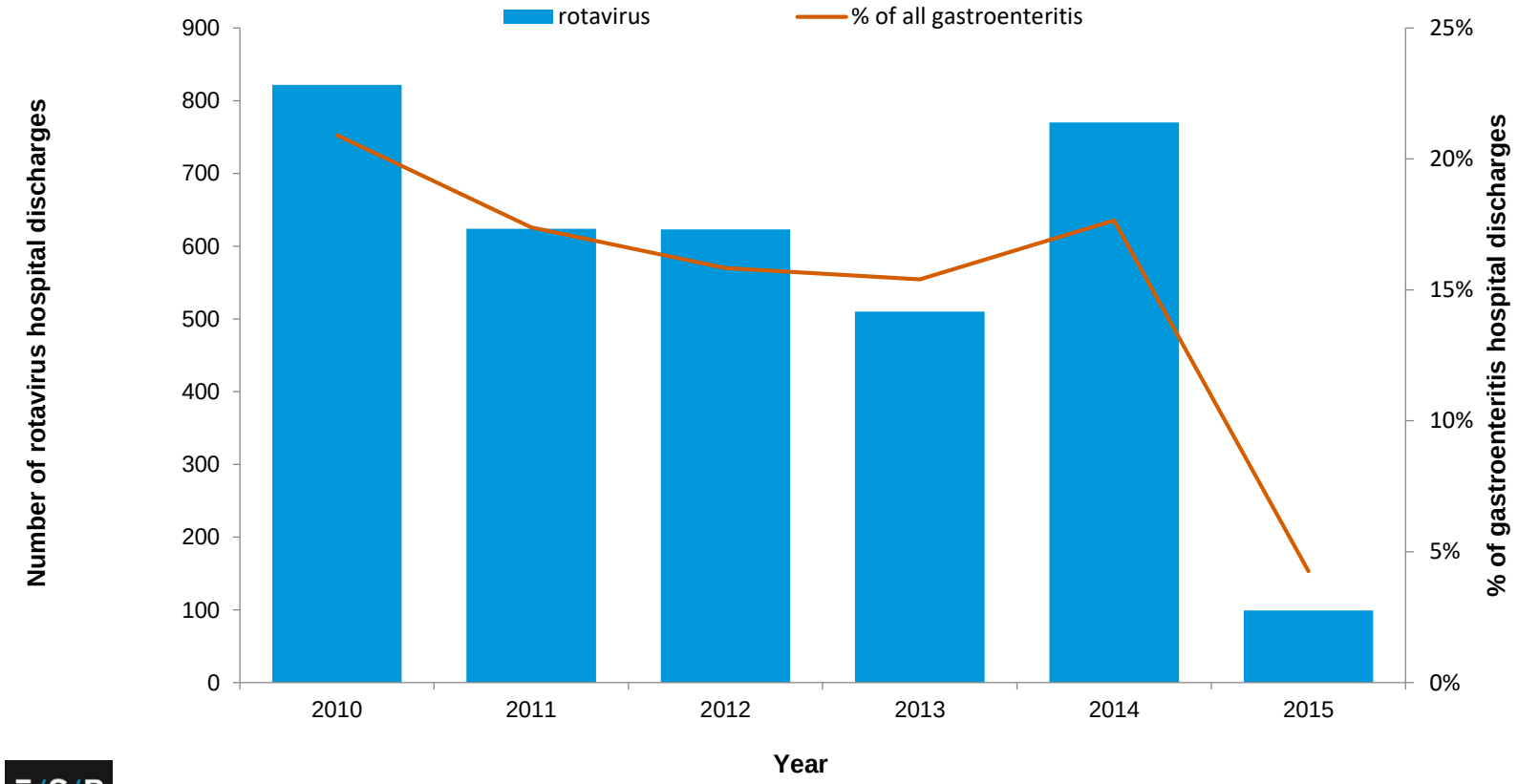
Similar for both vaccines

- 44-51% low income settings
- 76-86% middle income settings
- 80-85% higher income settings

- More effective against severe disease

- Some cross protection seen against other strains

Hospitalisation data children <5 years 2010-15



Institute of Environmental Science and Research Ltd – unpublished data

Delivery

- First dose 6 weeks, second dose 3 months
  - First dose MUST be complete by 15 weeks
  - Second dose MUST be complete by 25 weeks of age
- Administer first
  - Sucrose content reduces pain for injectable vaccines
- Handwashing
- Interchangeability
  - No data, but expected to be fine
  - If started with Rotateq®, can complete with Rotarix®
    - Must be within the 25 weeks

IMAC video resources

Four in a row – best practice for multiple vaccines

CHICKENPOX Disease and Vaccine

The Immunisation Advisory Centre

Pneumococcal conjugate Vaccine

Brand change

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Current Conjugate Pneumococcal Vaccines

PCV10 (Synflorix®)

- 1,4,5,6B,7F,9V,14,18C,19F, 23F
- Conjugate
  - Protein D from non-typeable H. influenza
  - Tetanus toxoid
  - Diphtheria toxoid (CRM_{197})
- Theoretical advantage in Protein D conjugate may offer better protection against OM
  - Not proven
- International evidence shows some cross-protection to 19A

PCV13 (Prevenar13®)

- Same 10 serotypes
- Also includes 2, 3, 19A
- Conjugate:
  - Diphtheria toxoid(CRM_{197})

Pneumococcal vaccine change

- PCV10 (Synflorix) is funded from 1st July 2017
- Overall the data shows that both PCV10 and PCV13 (Prevenar 13) vaccines act similarly in overall disease reduction
- PCV10 has demonstrated cross protection for serotypes not included
- PCV13 and 23PPV (Pneumovax 23) will continue to be funded for *high risk groups only*

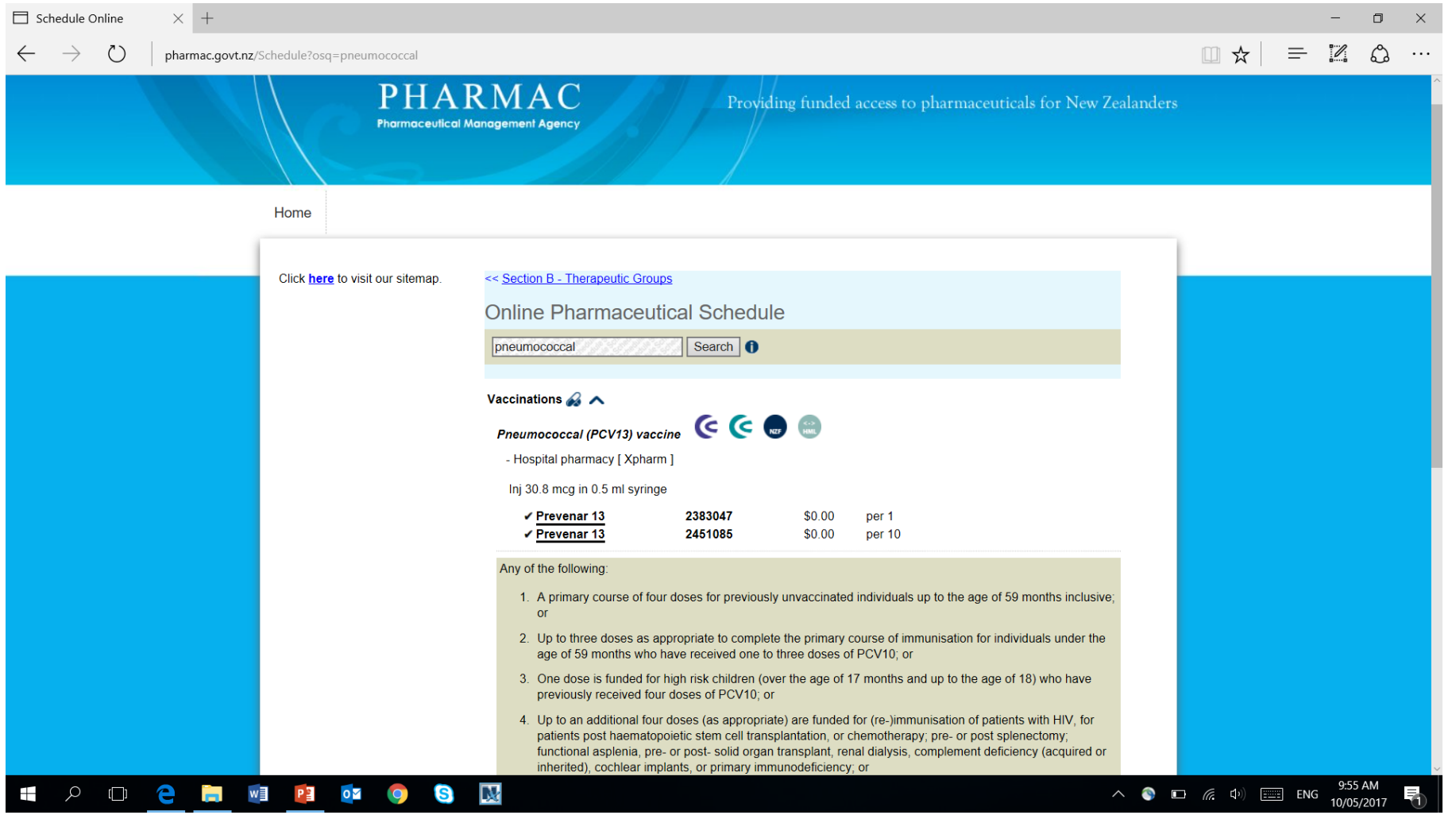
High risk groups for pneumococcal disease

Use PCV13 followed by PPV23

FUNDED

HIV, chemotherapy pre or post splenectomy, functional asplenia, pre or post transplant or haemopoietic stem cell transplant, renal dialysis, complement deficiency, cochlear implants, primary immundeficiency

Other groups being considered…..


Schedule Online
pharmac.govt.nz/Schedule?osq=pneumococcal
PHARMAC
Pharmaceutical Management Agency
Providing funded access to pharmaceuticals for New Zealanders
Home
Click here to visit our sitemap.
<< Section B - Therapeutic Groups
Online Pharmaceutical Schedule
pneumococcal
Search
Vaccinations
Pneumococcal (PCV13) vaccine
- Hospital pharmacy [Xpharm]
Inj 30.8 mcg in 0.5 ml syringe
✔ Prevenar 13 2383047 $0.00 per 1
✔ Prevenar 13 2451085 $0.00 per 10
Any of the following:
1. A primary course of four doses for previously unvaccinated individuals up to the age of 59 months inclusive; or
2. Up to three doses as appropriate to complete the primary course of immunisation for individuals under the age of 59 months who have received one to three doses of PCV10; or
3. One dose is funded for high risk children (over the age of 17 months and up to the age of 18) who have previously received four doses of PCV10; or
4. Up to an additional four doses (as appropriate) are funded for (re-)immunisation of patients with HIV, for patients post haematopoietic stem cell transplantation, or chemotherapy; pre- or post splenectomy; functional asplenia, pre- or post- solid organ transplant, renal dialysis, complement deficiency (acquired or inherited), cochlear implants, or primary immunodeficiency; or
ENG
9:55 AM
10/05/2017

Funded high risk programme – - try the IMAC website resource

http://www.immune.org.nz/sites/default/files/resources/ProgrammeScheduleChanges20170113V01Final_0.pdf

Funded vaccines for special groups from 1st January 2017

Please refer to individual vaccines for detailed eligibility criteria and to the electronic *Immunisation Handbook 2014 (3rd edition)* for vaccine administration schedules

Asplenia - Functional or Pre- or Post-Splenectomy Immunisation Programme
• Hib, influenza, meningococcal, pneumococcal, and Tdap vaccines

Chemotherapy - following
• Hib, HPV, influenza, pneumococcal, Tdap, and varicella vaccines
Also consider immunosuppression for longer than 28 days
• Hepatitis B and meningococcal vaccines

Cochlear implant
• Hib, influenza, and pneumococcal vaccines

Error of metabolism at risk of major metabolic decompensation
• Influenza and varicella vaccines

Haematopoietic stem cell transplantation (HSCT) - following
• Hib, HPV, influenza, meningococcal, pneumococcal, Tdap, and varicella vaccines
Also consider immunosuppression for longer than 28 days
• Hepatitis B vaccine

Hepatitis A case - contact with
• Hepatitis A vaccine

Hepatitis B case - contact with Infants born to mothers who are hepatitis B surface antigen (HBsAg) positive
• Hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) at birth
Household and sexual contacts of known acute hepatitis B cases or carriers
• Hepatitis B vaccine

Hepatitis C positive individual
• Hepatitis B vaccine

HIV positive individual
• Hepatitis B, HPV, influenza, meningococcal, pneumococcal, and varicella vaccines

Immune deficiency/immunosuppression
Individuals with an immune deficiency
• Influenza, meningococcal, and pneumococcal vaccines
Household contacts of children or adults who will be/are immunosuppressed
• Varicella vaccine
Prior to elective immunosuppression for longer than 28 days
• Varicella vaccine
Following immunosuppression for longer than 28 days
• Hepatitis B, Hib, influenza, meningococcal, and Tdap vaccines

Influenza Immunisation Programme
» Pregnancy,
» Children aged 6 months to under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness,
» Individuals aged 6 months to under 65 years with an eligible medical condition,
» Individuals aged 65 years or older.
• Influenza vaccine

Kidney disease
• Hepatitis B, Hib, influenza, pneumococcal, Tdap, and varicella vaccines

Liver disease
• Hepatitis A and varicella vaccines

Meningococcal disease case - contact with
• Meningococcal vaccine

Needle stick injury - following
• Hepatitis B vaccine

Non-consensual sexual intercourse - following
• Hepatitis B vaccine

Pneumococcal disease - increased risk
• Additional pneumococcal vaccine

Pregnancy
• Influenza and Tdap vaccines in every pregnancy

Rubella - women of childbearing age who are not immune to rubella
• MMR vaccine

Solid organ transplantation
Prior to solid organ transplantation
• Hib, meningococcal, pneumococcal, Tdap, and varicella vaccines
Following solid organ transplantation
• Hepatitis A, hepatitis B, Hib, HPV, influenza, meningococcal, pneumococcal, and Tdap vaccines

Tuberculosis - infants and children aged under 5 years at risk of tuberculosis (TB) exposure
• BCG vaccine

VACCINE KEY

BCG: tuberculosis
Hib: *Haemophilus influenzae* type b
HPV: human papillomavirus
MMR: measles, mumps, rubella
Tdap: tetanus, diphtheria, acellular pertussis
Varicella: chickenpox

The Immunisation Advisory Centre

For more details, visit **immune.org.nz**

Funded vaccines for special groups from 1st January 2017

The Immunisation Advisory Centre

Please refer to individual vaccines for detailed eligibility criteria and to the electronic *Immunisation Handbook 2014 (3rd edition)* for vaccine administration schedules

Asplenia — Functional or Pre- or Post-Splenectomy Immunisation Programme
- Hib, influenza, meningococcal, pneumococcal, and Tdap vaccines

Chemotherapy — following
- Hib, HPV, influenza, pneumococcal, Tdap, and varicella vaccines

Also consider immunosuppression for longer than 28 days
- Hepatitis B and meningococcal vaccines

Cochlear implant
- Hib, influenza, and pneumococcal vaccines

Error of metabolism at risk of major metabolic decompensation
- Influenza and varicella vaccines

Haematopoietic stem cell transplantation (HSCT) — following
- Hib, HPV, influenza, meningococcal, pneumococcal, Tdap, and varicella vaccines

Also consider immunosuppression for longer than 28 days
- Hepatitis B vaccine

Hepatitis A case — contact with
- Hepatitis A vaccine

Hepatitis B case — contact with

Infants born to mothers who are hepatitis B surface antigen (HBsAg) positive
- Hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) at birth

Household and sexual contacts of known acute hepatitis B cases or carriers
- Hepatitis B vaccine

Hepatitis C positive individual
- Hepatitis B vaccine

HIV positive individual
- Hepatitis B, HPV, influenza, meningococcal, pneumococcal, and varicella vaccines

Immune deficiency/immunosuppression

Individuals with an immune deficiency
- Influenza, meningococcal, and pneumococcal vaccines

Household contacts of children or adults who will be/are immunosuppressed
- Varicella vaccine

Influenza Immunisation Programme
- » Pregnancy,
- » Children aged 6 months to under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness,
- » Individuals aged 6 months to under 65 years with an eligible medical condition,
- » Individuals aged 65 years or older.
- Influenza vaccine

Kidney disease
- Hepatitis B, Hib, influenza, pneumococcal, Tdap, and varicella vaccines

Liver disease
- Hepatitis A and varicell…

Meningococcal disease ca…
- Meningococcal vaccine

Needle stick injury — foll…
- Hepatitis B vaccine

Non-consensual sexual in…
- Hepatitis B vaccine

Pneumococcal disease —
- Additional pneumococcal vaccines

Pregnancy
- Influenza and Tdap vaccines in every pregnancy

Rubella — women of childbearing age who are not immune to rubella
- MMR vaccine

Solid organ transplantation

Prior to solid organ transplantation
- Hib, meningococcal, pneumococcal, Tdap, and varicella vaccines

Following solid organ transplantation
- Hepatitis A, hepatitis B, Hib, HPV, influenza, meningococcal, pneumococcal, and Tdap vaccines

Influenza vaccine
- Pregnant women in every pregnancy during vaccination season
- Children aged 6 months to under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness
- Individuals aged 65 years and older
- Individuals aged 6 months to under 65 years with certain medical conditions, as per the Influenza Kit, including individuals pre- or post-splenectomy; or with Down syndrome, cochlear implant, error of metabolism at risk of major metabolic decompensation

Useful, evidence-based vaccines not currently on NZ schedule

Families and individuals wish to be offered

How do we systematically do this?

My suggested priority list :

Pneumococcal PCV13 + PPV 23: High risk

Varicella: Non immune adolescents/adults

Meningococcal: Infants/toddlers and young adults

Shingles: Older adults

Influenza: Family contacts of at risk

Pertussis: Occupational, Cocoon protection

More ways to help protect your family

PURCHASED VACCINES

The National Immunisation Schedule provides free immunisations against some diseases. There are other vaccines you can buy that are worth considering.

CHILDREN	PROTECTS AGAINST	VACCINE BRAND NAME
Babies from 6 weeks to one year	Meningococcal C meningitis	NeisVac-C®
Older babies, toddlers and children	Meningococcal C meningitis	NeisVac-C®
	Meningococcal A,C,Y and W135 meningitis	Menactra® or Nimenrix®
	Chickenpox (varicella)	Varilrix® or Varivax®
ADOLESCENTS		
Adolescents and young adults	Meningococcal C meningitis	NeisVac-C®
	Meningococcal A,C,Y and W135 meningitis	Menactra® or Nimenrix®
Non-immune adolescents	Chickenpox (varicella)	Varilrix® or Varivax®
ADULTS		
People aged 27 or older	Human papillomavirus (HPV) cervical and other cancers and genital warts	Gardasil®9
People aged 50 or older	Shingles (herpes zoster)	Zostavax®
People aged 65 or older	Pneumococcal pneumonia	Prevenar®13
		Pneumovax®23
Adults with chronic respiratory disease	Pneumococcal pneumonia	Prevenar®13
		Pneumovax®23
	Whooping cough (pertussis)	Boostrix®
Non-immune adults	Chickenpox (varicella)	Varilrix® or Varivax®
PEOPLE IN CLOSE CONTACT WITH NEWBORN BABIES		
Healthcare professionals and family members of infants	Whooping cough (pertussis)	Boostrix® or Adacel®
	Influenza	Influvac®, Vaxigrip®, Fluvax® or FluQuadri™
Non-immune close contacts	Chickenpox (varicella)	Varilrix® or Varivax®
ADULTS AT GREATER RISK OF SOME DISEASES		
Men who have sex with men	Human papillomavirus (HPV) cancers and genital warts	Gardasil®9
	Hepatitis A	Havrix® or Avaxim®
	Hepatitis B	Engerix-B®
	Hepatitis A + B	Twinrix®
Intravenous drug users	Hepatitis A	Havrix® or Avaxim®
	Hepatitis B	Engerix-B®
	Hepatitis A + B	Twinrix®
OCCUPATIONAL Healthcare, childcare, carers, sewerage, sex workers, laboratory staff		
At risk of exposure to faecal material	Hepatitis A	Havrix® or Avaxim®
At risk of exposure to blood or body fluids	Hepatitis B	Engerix®-B
Healthcare professionals	Influenza	Influvac®, Vaxigrip®, Fluvax® or FluQuadri™
Non-immune childcare professionals	Chickenpox (varicella)	Varilrix® or Varivax®

For more information:

0800 IMMUNE (0800 466 863) or visit immune.org.nz

The Immunisation Advisory Centre

?role of Pneumococcal vaccines in the elderly

The role of Pneumococcal vaccines in elderly is unclear
There is probably a role for HIGH RISK groups eg COPD
- **Personally I recommend PCV13 followed by PPV23**

PCV13 (conjugate)

- CAPITA study (Bronten et al March 25 2015 NEJM)

  In Dutch population

  - 75% (41 – 92) effective against vaccine-strain invasive IPD
  - 45% (14 – 63) effective against vaccine-strain types community-acquired pneumonia
  - Efficacy lasted up to 4 years

  - Adults >65yrs: 13% of all pneumonia was vaccine-strain
  - **No significant effect against all-cause pneumonia**

PPV23 (polysaccharide)

- Some effectiveness against IPD, not against pneumonia

Who could benefit from Pneumococcal vaccination ?

Weycker D et al, BMC Health Services Research (2016) 16: 182

Risk Group	RR (IPD and all cause pneumonia)
Healthy	0
Asplenia	19.0 (18.7 – 19.4)
Diseases of WBC	14.8 (14.6 -15.1)
Congenital immunodeficiency	12.9 (12.6 – 13.3)
Chronic renal failure	12.2 (12.0 – 12.3)
Chrnic lung disease	10.4 – 10.6
Chroniic liver disease	6.6 (6.4 – 6.7)
Immunological conditions/drugs	6.9 (6.8 – 6.9)

AND MORE : RR 2.5 - >6

Alcohol dependence; asthma; chronic oral steroid use; diabetes; Downs, neuromuscular/seizure disorders, RA/Crohns/Lupus, Smokers, cocclear implant;HIV

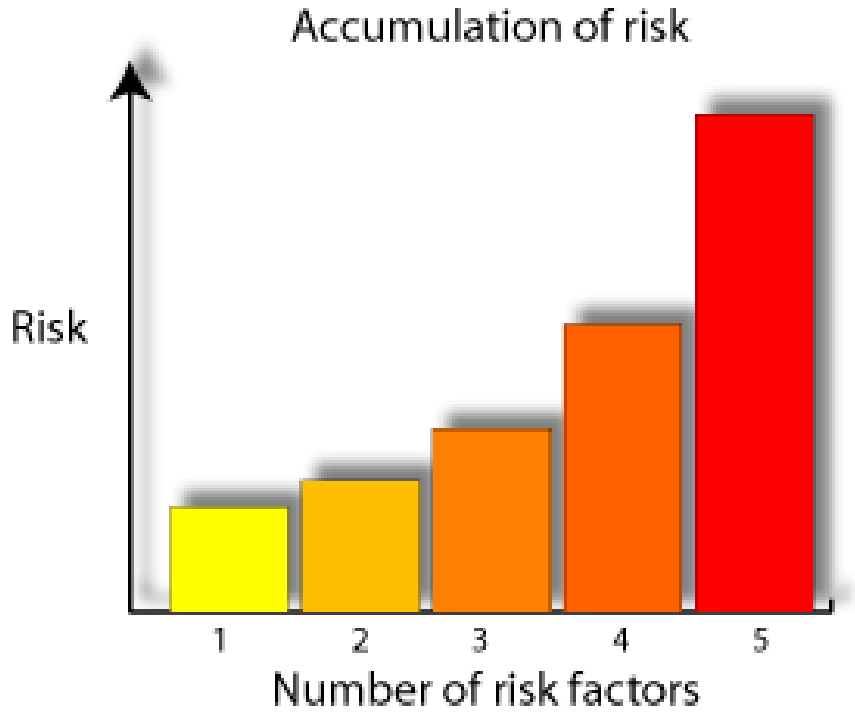
And the concept of stacking

More morbidities add more risk

E.g. COPD + alcohol disorder

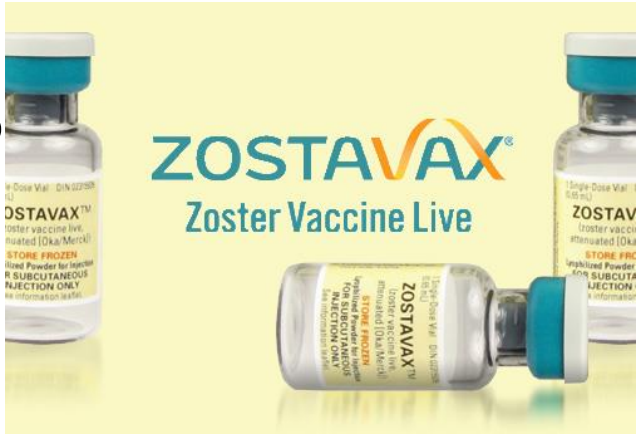
Diabetes + smoker

Asthma + Diseases of WBC ……+ smoker



Shingles - Zostavax

- VE
  - 60 yrs plus
    - Zoster reduction 51% NNT = 58
    - Post herpetic neuralgia reduction 67%
    - Longevity unclear, >5 yrs

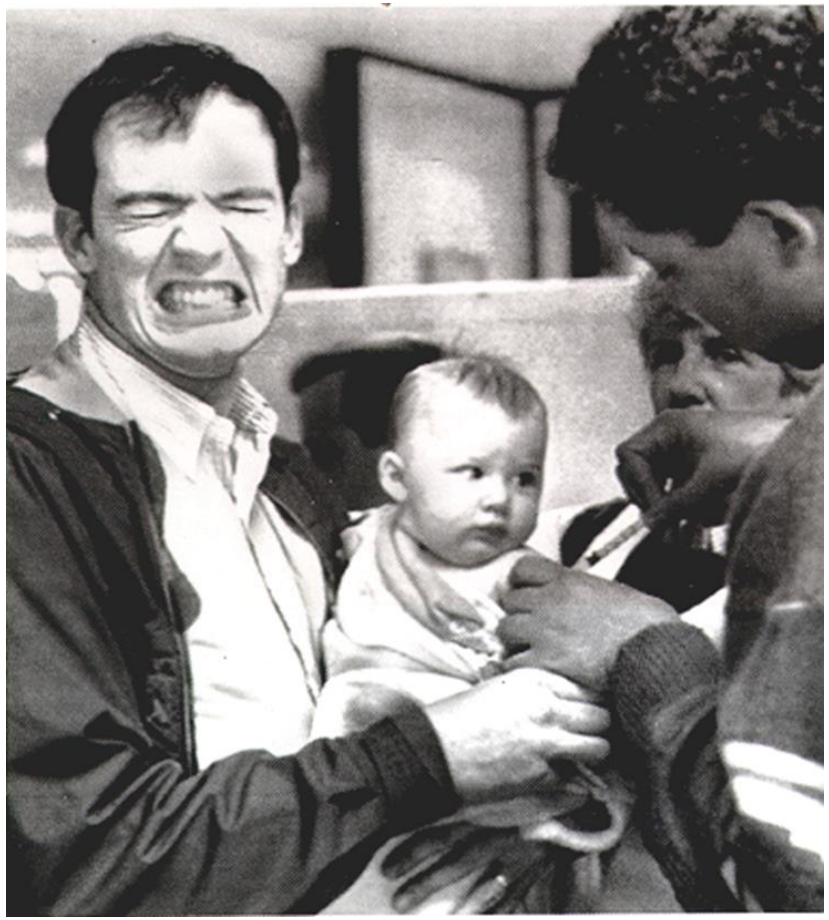


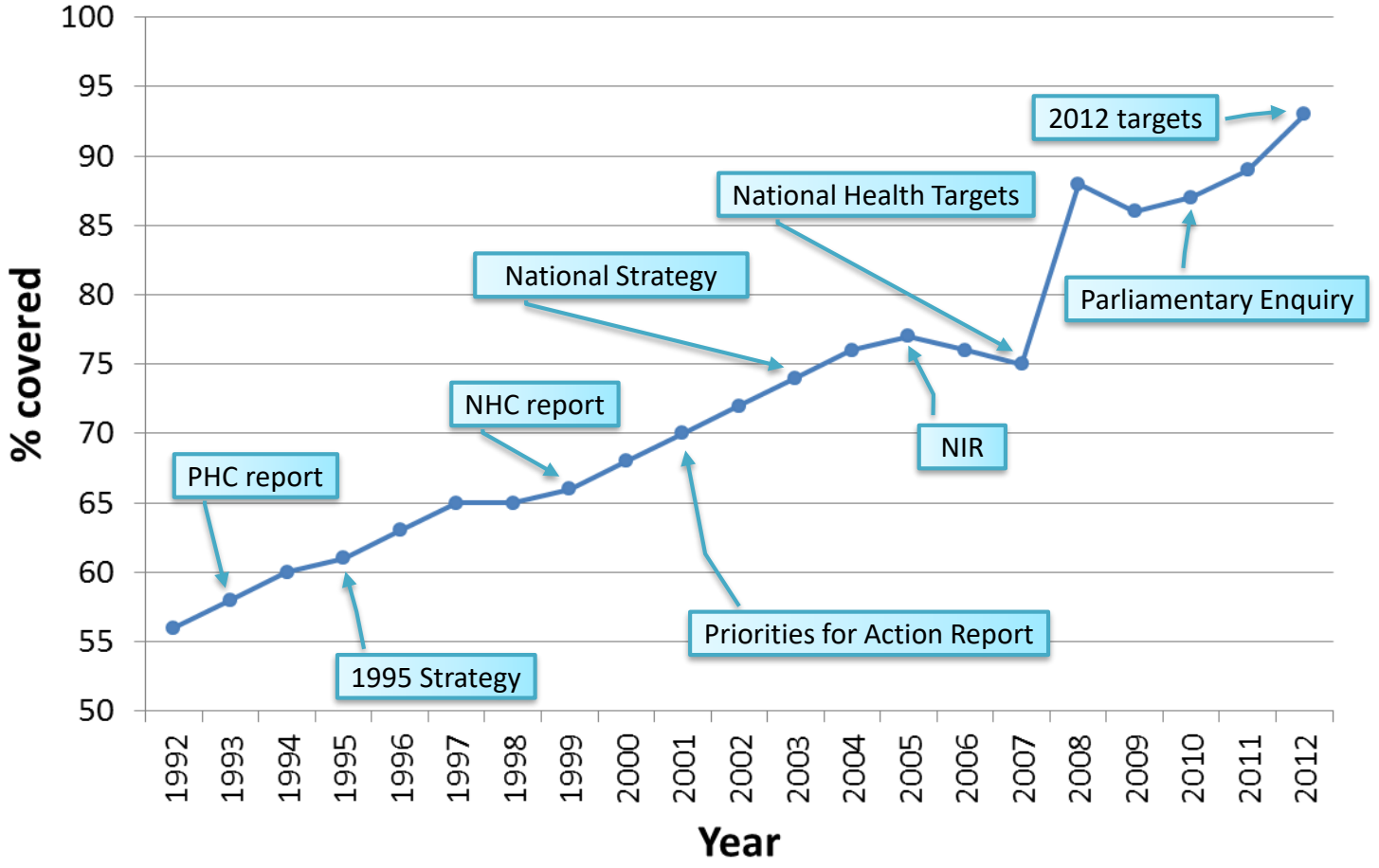
- Contraindications
  - Anaphylaxis to any components, neomycin
  - Immunodeficiency/ immunosuppressed
  - Pregnancy
  - Active untreated Tb

- Who to advise
  - Elderly …..
  - Higher risk
    - RA, IBD, COPD, Asthma, CKD, Depression, IDDM (BMJ 2014;348:g2911)

  Aims
  - Keep independent living
  - Reduce increased frailty with onset of zoster

Vaccine hesitancy
- conversations and confidence





Percentage fully immunised by two years of age

Turner N, unpublished; using combined data from national surveys and the NIR

Why are we improving

- Commitment at all levels – national target
- Feedback loops – DHBs and PHOs
- Provider engagement and confidence
  - More focus , higher priority
  - Less missed opportunities
- SYSTEMS
  - Early ENROLMENT - and follow up
  - Precalls/recalls/audits
  - PMS/NIR
  - Providers to OIS
- **Confident health sector spills over to confident public**
  - **Less anti-science in the media now**
  - **No overall increase in decline rates, pockets/local communities**

What is the question?

- My child is sick
- My child is not at high risk
- My child is too young
- Vaccines are unsafe
- I don’t trust the authorities

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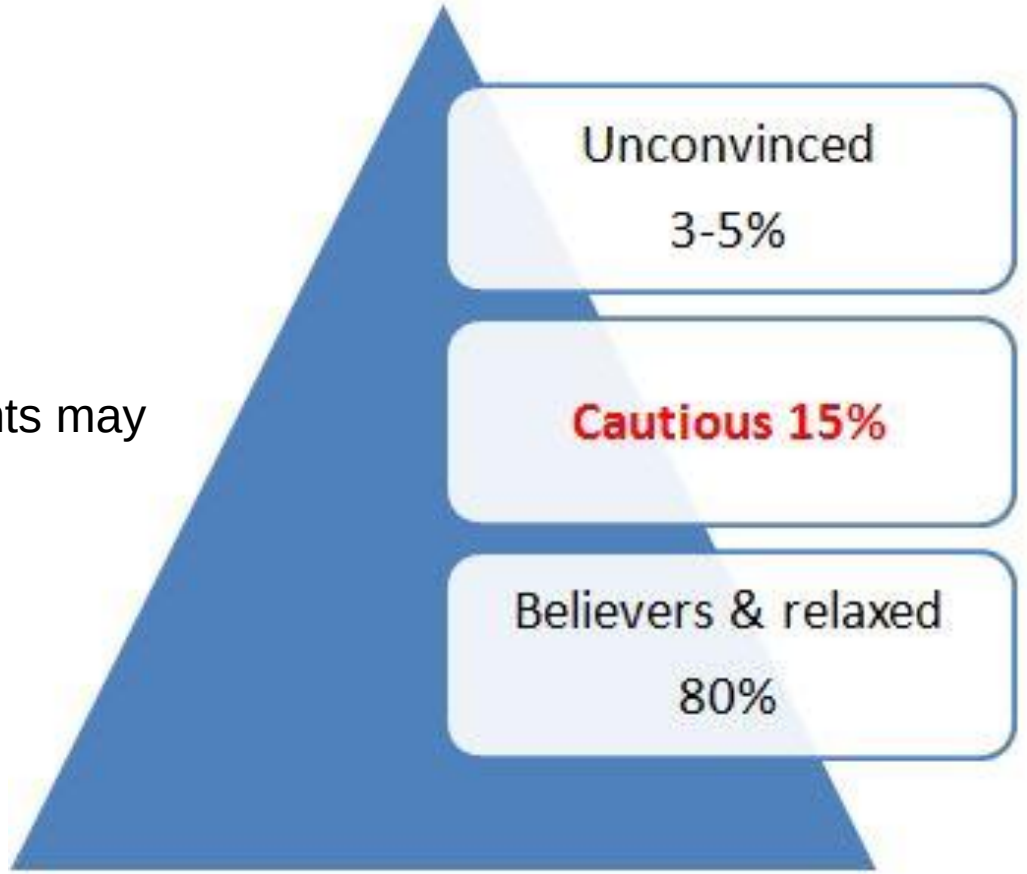
The vaccine acceptance spectrum

Vaccine hesitant parents may need more time

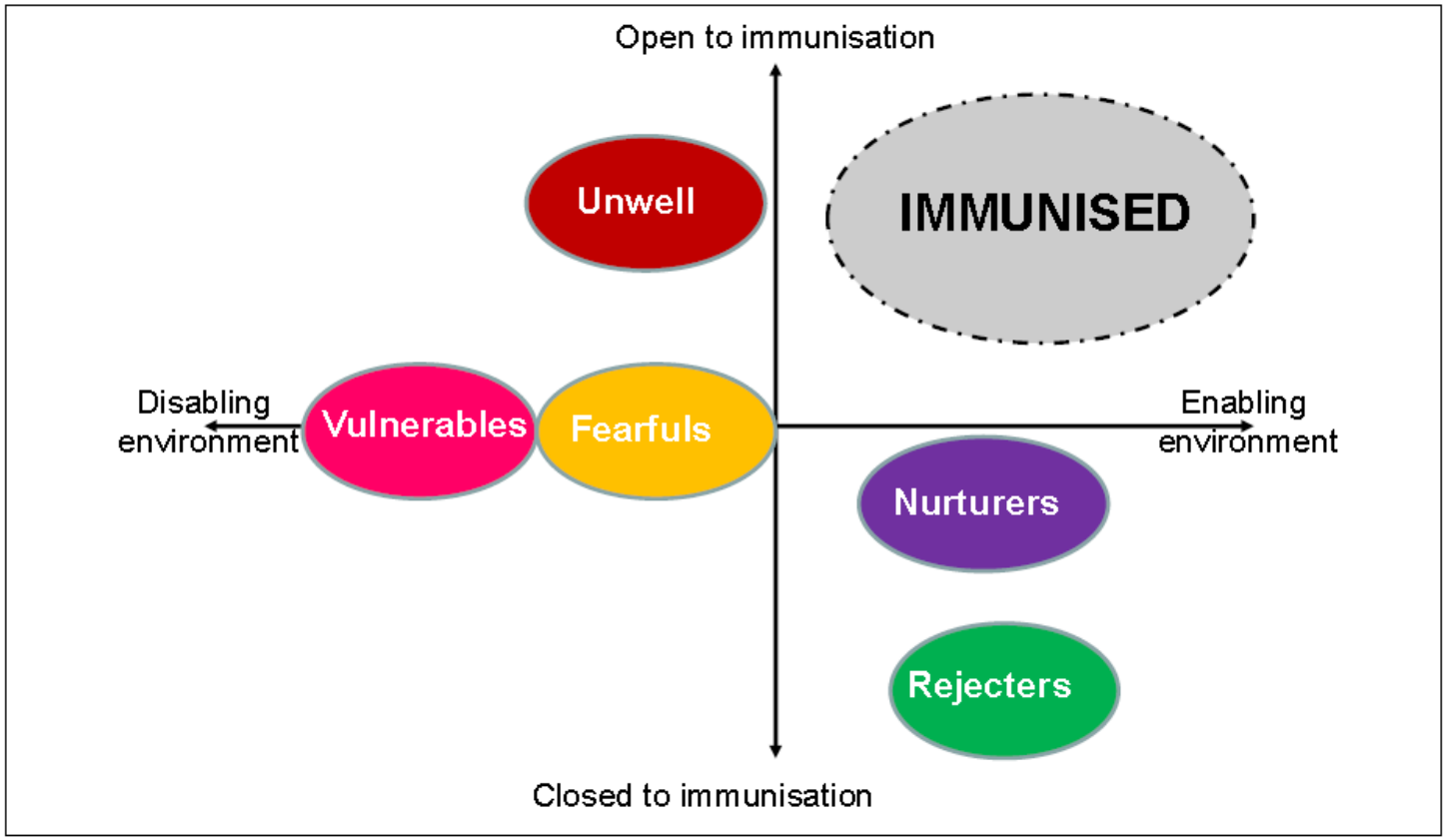


Source:
Leask et al 2012
Benin et al 2009

Tailor communications- no ‘one size fits all’

Vaccination decisions are complex

Figure 1: Typology matrix



Litmus Group (2013*) Immunisation Audience Research- Delayers of Infant Immunisation.* Ministry of Health, New Zealand

Recommend, recommend, & recommend

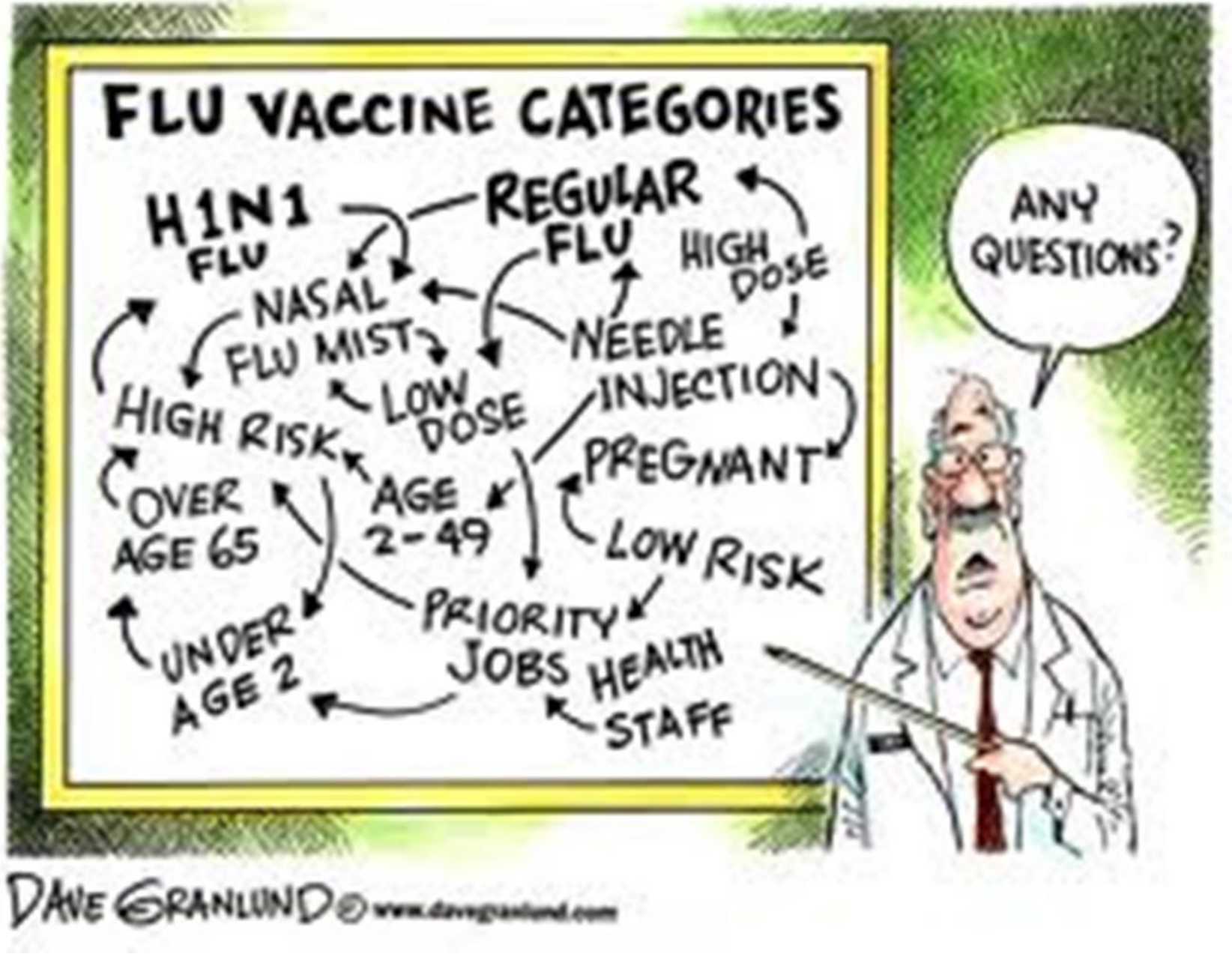
- **Assume parents** are ready to vaccinate
- Make **unequivocal** recommendations
- Do not sit on the fence

  “I recommend that you vaccinate your baby, child, preteen”

  “I do recommend this vaccine”

  “John is 12 years old so we will give him Boostrix and HPV vaccine today”

- HPV is a very safe vaccine


FLU VACCINE CATEGORIES
H1N1 FLU
REGULAR FLU
HIGH DOSE
NASAL FLU MIST
NEEDLE INJECTION
LOW DOSE
HIGH RISK
PREGNANT
OVER AGE 65
AGE 2-49
LOW RISK
PRIORITY JOBS
UNDER AGE 2
HEALTH STAFF
ANY QUESTIONS?
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(466863)

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Extra slides

HPV4 and HPV9: Very similar vaccines, - more aluminum adjuvant in HPV9

HPV4 vaccine (Gardasil®, Seqirus/MSD) contains:

- 40 µg of HPV16 L1 VLP, 20 µg of HPV18 L1 VLP, 20 µg of HPV6 L1 VLP and 40 µg of HPV11 L1 VLP
- 225 µg of aluminium hydroxyphosphate sulphate.

HPV9 vaccine (Gardasil9, Seqirus®/MSD) contains:

- 30 µg of HPV6 L1 VLP, 40 µg of HPV11,60 µg of HPV 16, 40 µg HPV18, 20 µg of HPV 31, 33, 45, 52 and 58
- 500 µg of aluminium hydroxyphosphate sulphate.

No preservatives or antibiotics

Also contain sodium chloride, L-histadine, polysorbate, sodium borate, traces of yeast protein, water for injection

HPV9

Pivotal study 14,215 women aged 16 – 26

- Double blind phase 2b-3 trial
- Three doses of HPV4 or HPV9 at 0,2, and 6 months

- Incidence rates of high-grade disease related to HPV 31,33,45,52 and 58 was 0.1 per 1000 person years in HPV9 and 1.6 per 100 person years in HPV4

- **HPV9 efficacy 96.7%** (80.9 – 99.8)

Joura EA, Giuliano AR, Iversen O-E, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. N Engl J Med 2015;372:711-23.

Impact of varicella vaccination programmes

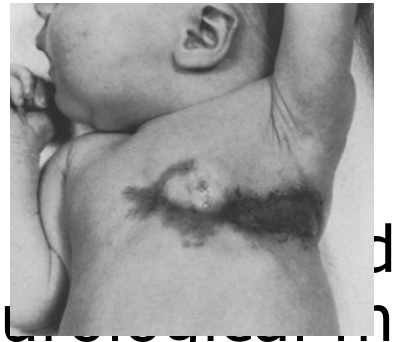
- Significant reductions in severity of disease, hospitalisations and circulation of varicella in all regions that have introduced varicella

  - US (one dose in 1995, two doses in 2007)
    - 90-95% reduction in varicella in 5-19 yr olds
    - No evidence of shift in burden to older age groups
    - 10 fold reduction in varicella hospitalisations
    - 99% decline in mortality fur <20yrs
    - Declines in all age groups, including infants too young to be vaccinated

  - Similar impacts in Germany (1 dose 2004, 2 dose 2007) ,Saudi Arabia (2 dose 1998) Canada (1 dose 2000-2007, six provinces dose 2), Italy and Spain region by region,
  - Australia: Single dose 2005, second dose as MMRV 2013

Baxter R, Tran TN, Ray P, et al. Impact of vaccination on the epidemiology of varicella: 1995-2009. Pediatrics. 2014;134(1):24-30.
Leung J, Bialek SR, Marin M. Trends in varicella mortality in the United States: Data from vital statistics and the national surveillance system. Human Vaccines and Immunotherapeutics. 2015;11(3):662-8.

Risk of congenital varicella syndrome (CRS)



- Varicella infection during pregnancy
- Risk greatest in first 20 weeks
- May result in skin scarring, limb defects, ocular anomalies and neurological malformations
- Disease in very late pregnancy (5 days before to 2 days after delivery) may result in severe neonatal varicella infection

Borzyskowski M, Harris R, and Jones R (1981) The Congenital Varicella Syndrome Eur J Paediatrics 137 (335-338

Safety profile
Varicella vaccine

Immunocompetent

- Most frequently reported reactions mild and primarily injection site reactions (systematic review SAGE)
  - Site pain, swelling, redness : 28%
- Local or generalized rash fairly frequent (up to 5%)
- ITP with adolescent vaccination, rare but possible – all mild and acute
- Anaphylaxis reported but very rare

No increase risk of cerebellar ataxia, encephalitis or ischaemic stroke

SAGE. Safety of varicella and MMRV vaccines: A systematic review 2014 Available from: http://www.who.int/immunization/sage/meetings/2014/april/presentations_background_docs/en/

Safety profile
Varicella vaccine (2)

Immunocompromised

- Higher risk in children with cell-mediated immunity deficiencies
- Can use cautiously in children closely monitored oncology situations, treatments regimes for juvenile arthritis
- Undiagnosed immunocompromised – rash, vaccine strain viral reactivation and subsequent infections dissemination, pneumonitis, meningitis, hepatitis, fatal outcomes

SAGE. Safety of varicella and MMRV vaccines: A systematic review 2014 Available from: http://www.who.int/immunization/sage/meetings/2014/april/presentations_background_docs/en/

Vaccines

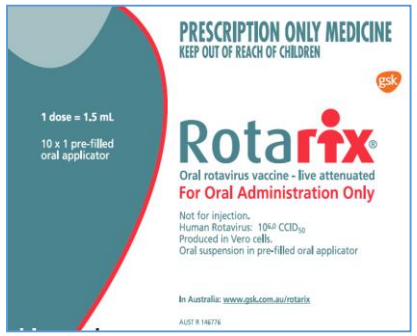
Rotarix® (RV1)

- Live attenuated
- Human rotavirus strain
- P1A[8]G1
- oral
- 2 dose
- Second dose no later than 25 weeks of age

Rotateq® (RV5)

- Live attenuated
- Pentavalent human-bovine assortment
- G types 1-4(VP7) and P[8] (VP4
- oral
- 3 dose
- 3rd dose no later than 8 months of age

RV1 presentation



- Each pack contains:
  - 10 vials of lyophilized vaccine and 10 oral applicators prefilled with diluent with 10 transfer adapters
- Composition
  - Live attenuated vaccine
  - Animal Vero cell line used for culture
  - High in sucrose – give before injections to mitigate injection pain/distress
- Storage
  - Store in packaging at 2-8°Celsius
  - Do not freeze
  - Discard if frozen
- Reconstitution
  - Store reconstituted vaccine in packaging at 2-8°Celsius
  - Administer within 24 hours of reconstitution
  - discard after 24 hours

Pneumococcal Vaccines in NZ

- Prevenar® and Pneumovax 23® introduced 2006 for high risk groups only
- Prevenar® on the national schedule 2008
- Replaced by Synflorix® (PCV10) July 2011
  - PCV13 and PPV23 remained for high risk children
- Replaced by Prevenar13® July 2014
- Return to Synflorix® July 2017

MMR vaccine (Priorix®) brand change

- Priorix® in packs of 10, will replace M-M-R l l vaccine brand from 1st July 2017 when stocks are used up
- Presented as a whitish to slightly pink pellet in a single dose glass vial for reconstitution with the diluent
- The sterile diluent is clear and colourless and presented in a pre-filled *single dose syringe*
- The reconstituted vaccine may vary in colour from clear peach to fuchsia pink due to slight variations in the pH
- Administer as the last injection in a set for mitigation of pain and distress

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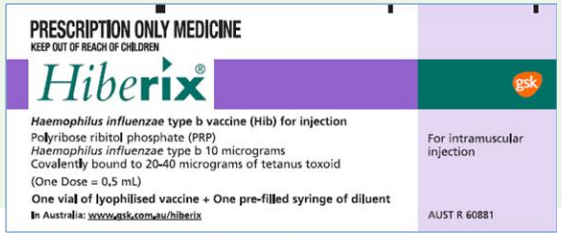
Haemophilis Influenzae type b **vaccine brand change**

- Hiberix® in single dose packs will replace ActHib® vaccine brand for the 15 month event from 1st July 2017 when stocks are used up
- Hiberix® is a lyophilised vaccine presented as a white powder in a glass vial for reconstitution with the diluent
- The sterile diluent is presented in a pre-filled syringe for reconstitution
- Hiberix® vaccine has been used on the New Zealand Immunisation schedule in the past
- Give first at the 15 month event



THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
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The Immunisation Advisory Centre