



Dr Pam Jackson

Paediatrics

Update on Paediatric Vaccinations - Concurrent Workshop Repeated

Friday, 16 August 2013

Start 4:30pm

Start 5:35pm

Duration: 55mins

Duration: 55mins

Kandinsky

Kandinsky



South GP CME 2013

General Practice Conference & Medical Exhibition

15-18 August | Edgar Centre | Dunedin

Pertussis and Varicella Update

August 2013
Dr Pam Jackson

Declaration of conflict of interest

- Sponsorship for this meeting GSK
- Some slides provided by GSK
- Sponsorship for respiratory meeting Boehringer
- Working on rotavirus vaccine with MCRI
- General Paediatrician

Whooping cough



Pertussis is epidemic

- 18 months
- Not seasonal
- Across ages
- Infants hospitalised



Pertussis in NZ

- From 1873 – 1944 – 3.9 yearly epidemics
- Introduced vaccine in 1945, (acellular 2000)
- From 1945 – 2004 – 3.5 yearly epidemics
- Implies no impact on pertussis outbreaks



**WAS THE WHOOPING COUGH
EPIDEMIC CAUSED BY**

UNVACCINATED KIDS?

HulkAndBudd.com

NZ hospital discharges

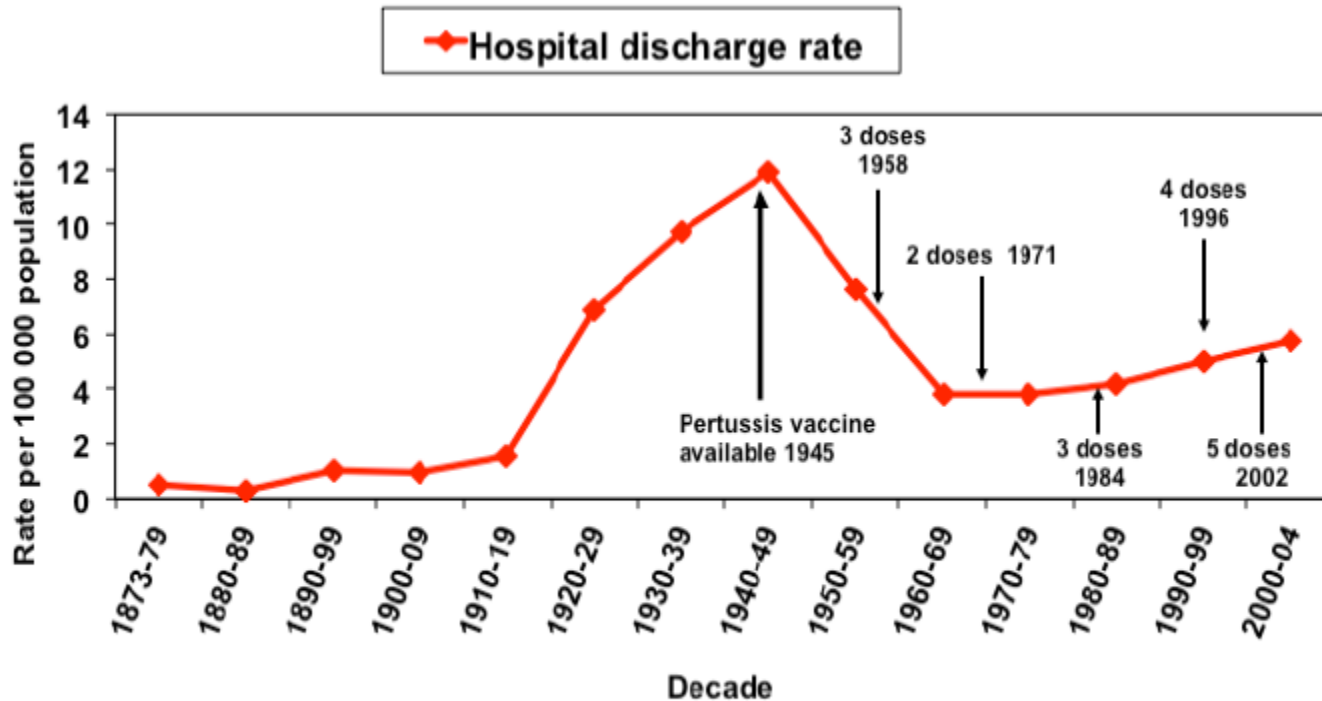


Figure 1: Annual pertussis hospital discharge rate per decade per 100,000 person years from 1873 to 2004.¹

But why continued high rates?

- NZ had rates 6x US, 4x Australia, 3x UK
- Poor immunisation coverage
- Poorer immunisation timeliness
- Tinkering with schedule

Vaccine coverage – 95%



Delay in vaccination

YOU'LL BE PLEASED TO KNOW WE'RE
FINALLY GETTING THE SWINE FLU VACCINE
YOU NEED IF YOU JUST WAIT PATIENTLY
FOR TWO OR FOUR
MORE WEEKS!



Any delay in vaccination → 5x ↑
risk of hospitalisation



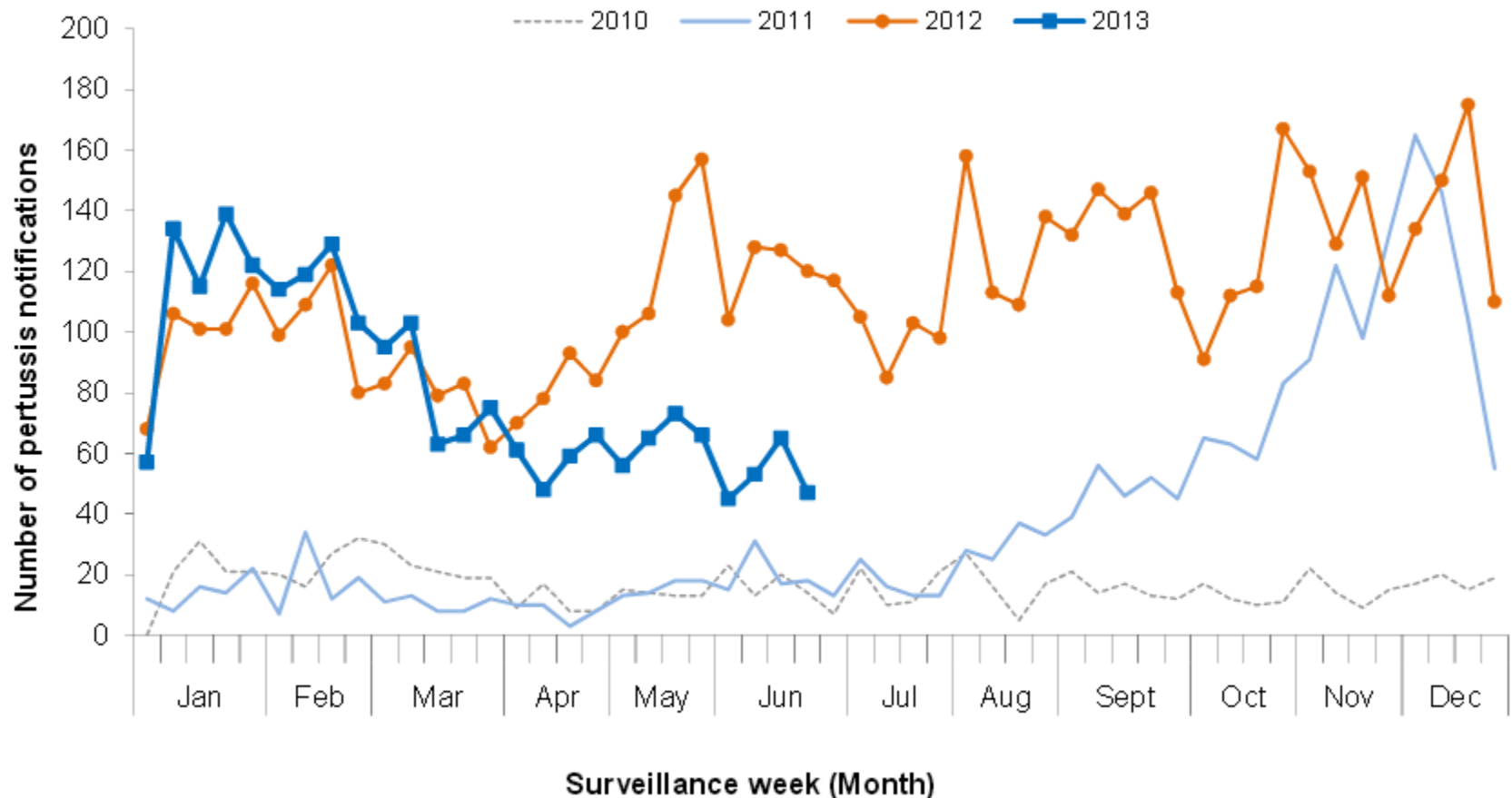
Epidemic in NZ began 2011

- 780 cases April – June 2013
- 303 confirmed, 364 probable
- 7.1% less than 1 year old
- 34 hospitalised, no deaths



Notifications 2010 - 2013

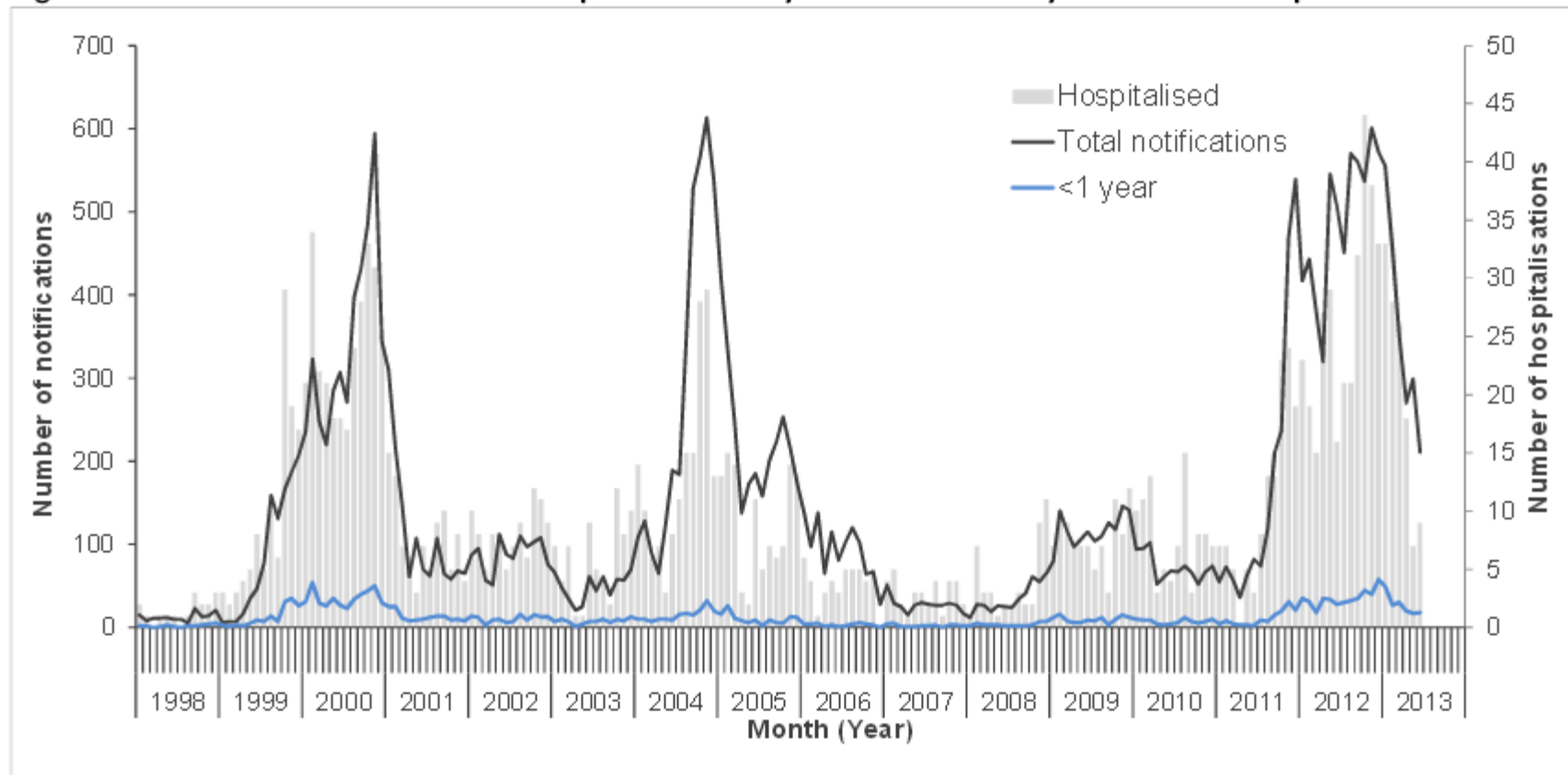
Figure 1: Number of pertussis notifications by week reported, 2010 - 2013



Notification and hospitalisation

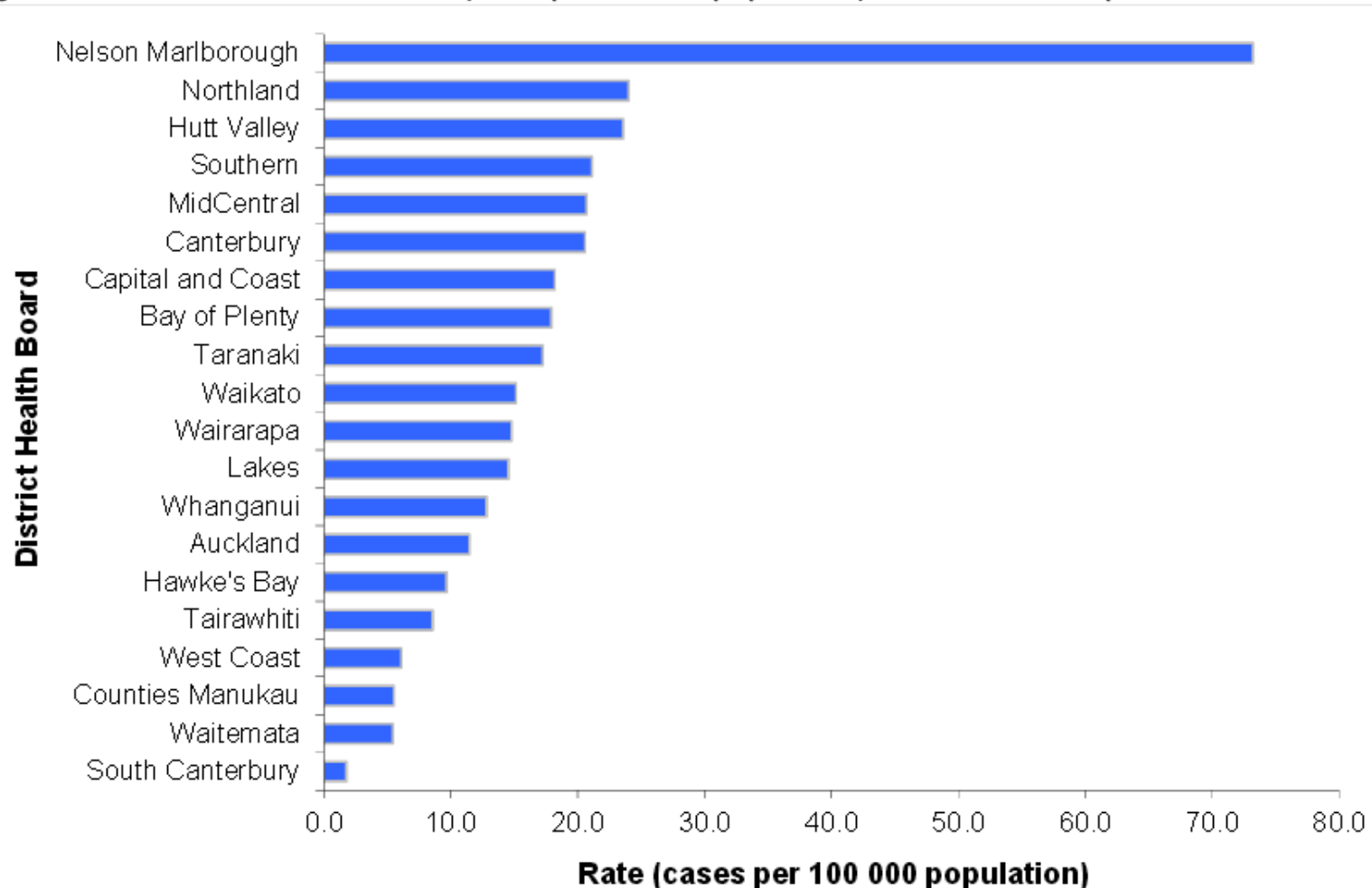
June 2013

Figure 2: Pertussis notifications and hospitalisations by calendar month-year since 1998 up to 30 June 2013



Notification by region

Figure 4: Pertussis notifications rates (cases per 100 000 population) in Quarter two: Apr-Jun 2013



Pertussis by age

Table 1: Pertussis cases and rates by age group in Quarter two: Apr-Jun and June 2013

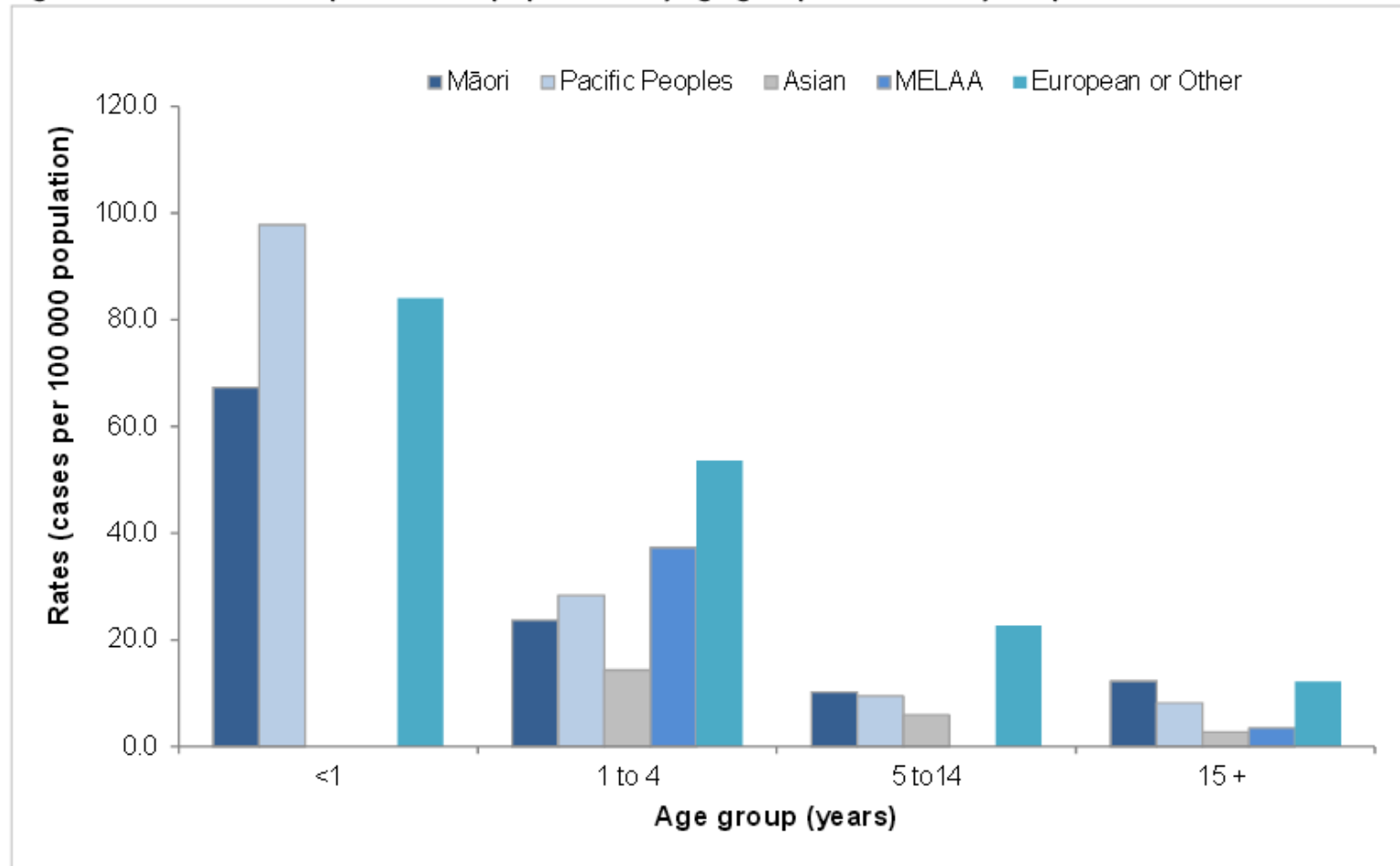
Age group (Years)	Quarter two: Apr-Jun 2013			June 2013	
	All cases	Rates ¹	Hosp	New Cases	Hosp
<1	47	77.6	22	13	5
1 to 4	110	43.8	0	27	0
5 to 9	77	26.4	2	15	1
10 to 14	33	11.4	0	9	0
15 to 19	28	9.0	2	6	1
20 to 29	80	12.7	1	17	1
30 to 39	88	15.8	0	21	0
40 to 49	106	16.9	5	27	1
50 to 59	61	10.7	0	10	0
60 to 69	47	11.0	1	14	0
70+	30	7.1	0	5	0
Unknown	0	-	0	0	0
Overall	707	16.0	33	164	9

¹Rate of pertussis cases per 100 000 population calculated using 2012 mid-year population estimates.

Hosp: hospitalisation counts

Pertussis and ethnicity

Figure 3: Pertussis rates per 100 000 population by age group and ethnicity in April to June 2013



Note: Denominator data used to determine rates are based on the proportion of people in each ethnic group from the estimated resident 2006 census population applied to the 2012 mid-year population estimates from Statistics New Zealand.

Immunisation status - 2013

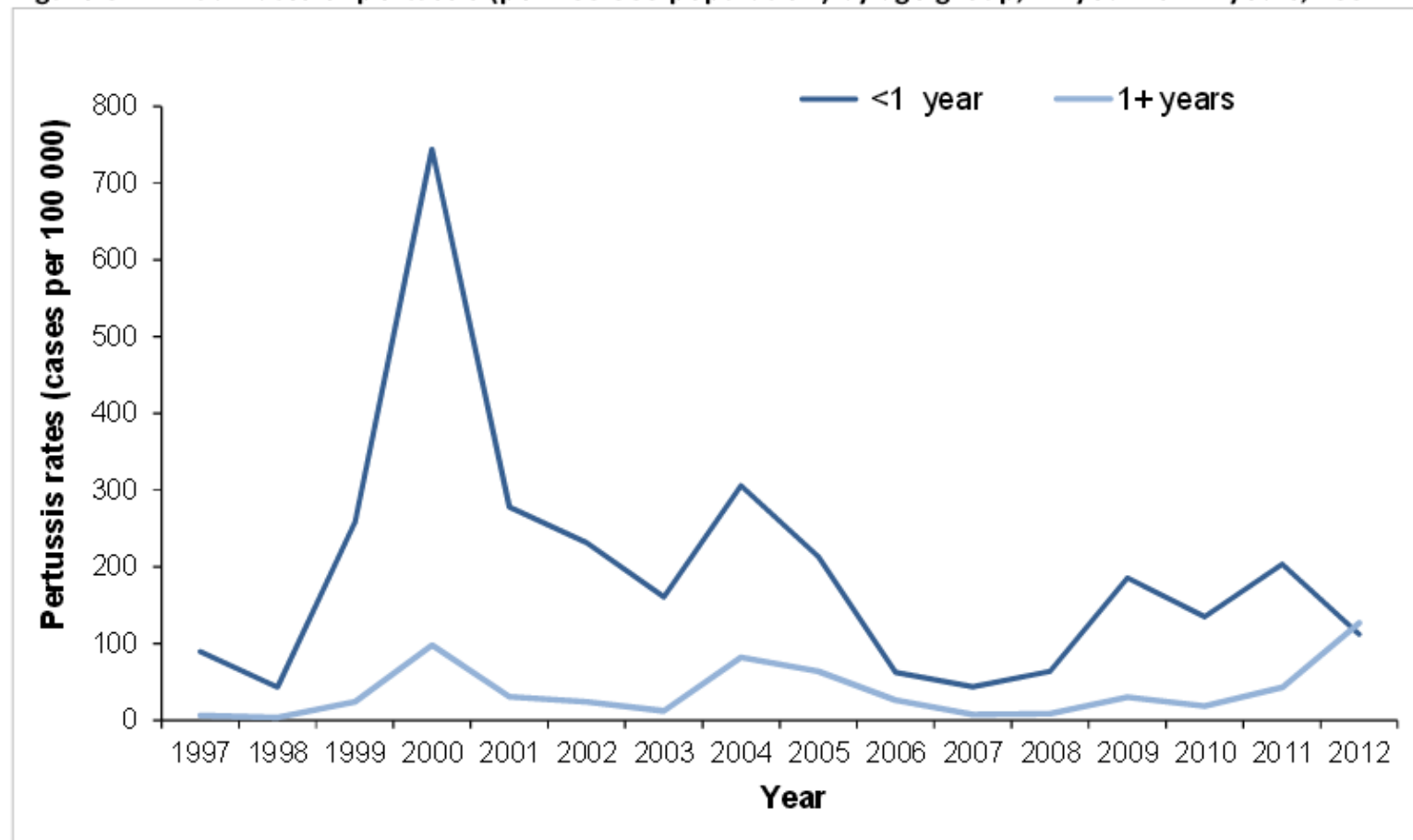
Table 4: Immunisation status of confirmed pertussis cases notified in April to June 2013

Age Group	Total cases	One dose	Two doses	Three doses	Four doses	Five doses	Vaccinated (no dose info)	Not vaccinated	Unknown
<6wks	7	0	0	0	0	0	0	7	0
6wks - 2mths	11	5	0	0	0	0	0	6	0
3-4 mths	3	2	1	0	0	0	0	0	0
5mths - 3yrs	50	1	1	25	2	1	4	14	2
4 - 10yrs	70	0	0	4	18	2	6	25	15
11+ yrs	162	5	1	2	4	3	20	29	98
Unknown	0	0	0	0	0	0	0	0	0
Total	303	13	3	31	24	6	30	81	115

Note: Immunisation status has been extracted from Episurv notifications. Health professionals use a range of sources to update immunisation status including the NIR, parental recall or Well Child book records.

Annual rates by age

Figure 6: Annual rates of pertussis (per 100 000 population) by age group, <1 year vs. 1+ years, 1997-2012



Note: Rate of pertussis notified cases per 100 000 population calculated using mid-year population estimates.

Infants are at the most risk!

Data from USA

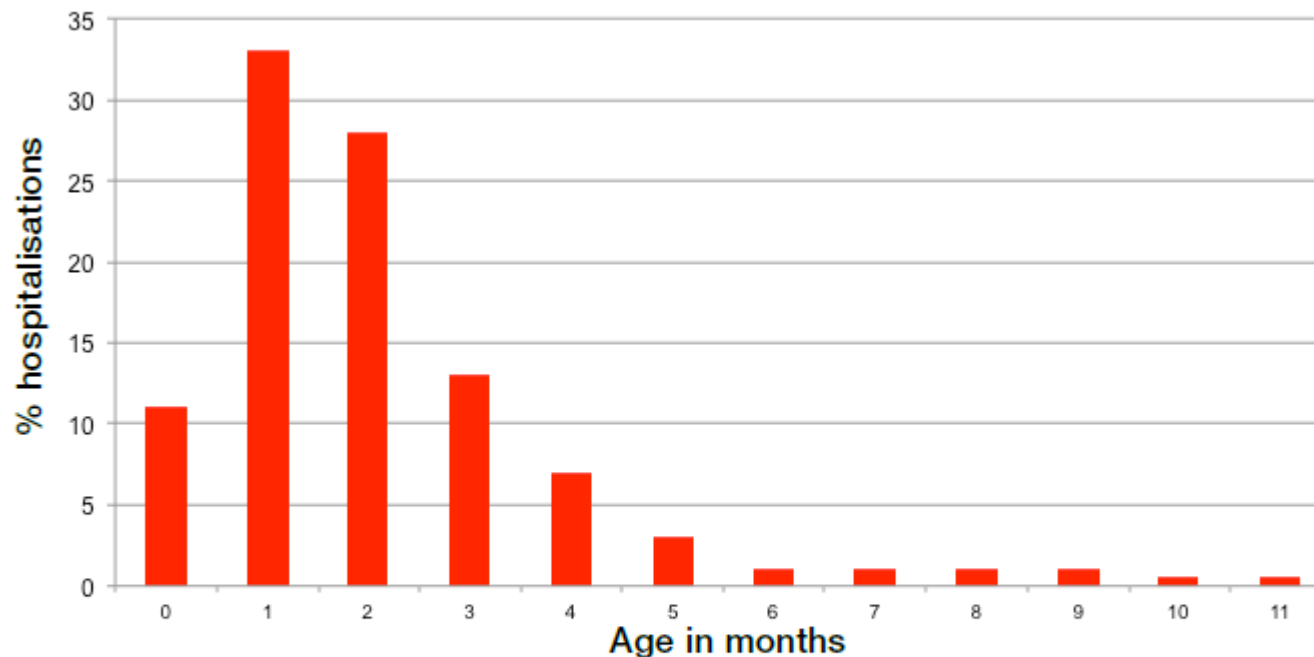
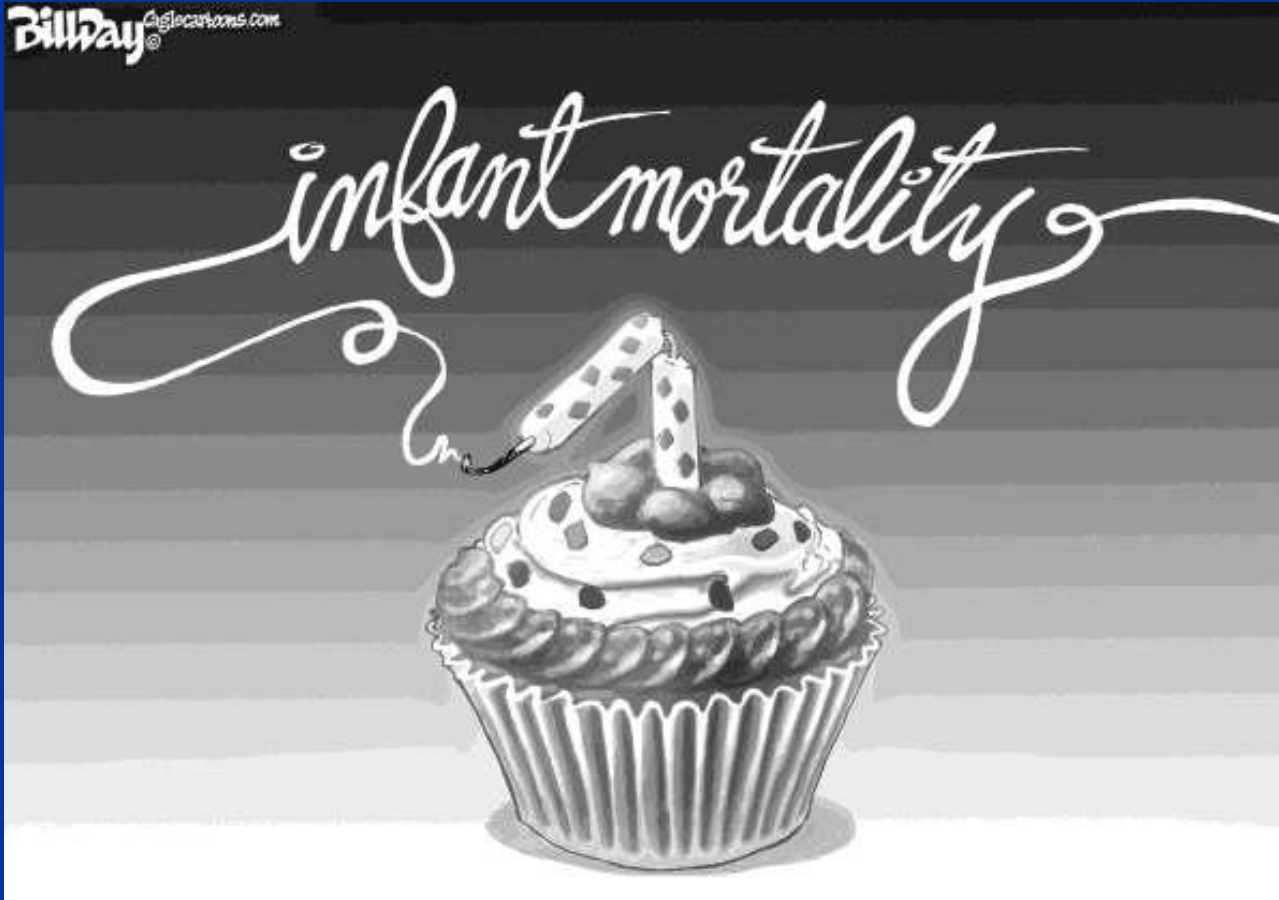


Figure 2. Average annual incidence of pertussis hospitalisations and number (percent) of hospitalisations according to age group in the US Kids' Inpatient Database (2000 and 2003).³



In 1940s more infant deaths were due to pertussis than measles, diphtheria, polio and scarlet fever combined.

NZ Schedule

New Zealand National Immunisation Schedule from 1 July 2011

Age	DTaP-IPV-HepB/Hib	PCV	Hib	MMR	DTaP-IPV	Tdap	HPV	Td	Influenza
6 weeks	Infanrix®-hexa	Synflorix®							
3 months	Infanrix®-hexa	Synflorix®							
5 months	Infanrix®-hexa	Synflorix®							
15 months		Synflorix®	Act-HIB™	M-M-R® II					
4 years				M-M-R® II	Infanrix®-IPV				
11 years (school year 7)						Boostrix®			
12 years (school year 8) Girls only							Gardasil®		
							Gardasil®		
							Gardasil®		
45 years								ADT™ Booster	
65 years								ADT™ Booster	Brand varies annually

In New Zealand 2005

- Immunisation coverage 80%
- Timeliness only 40%



Immunisation coverage

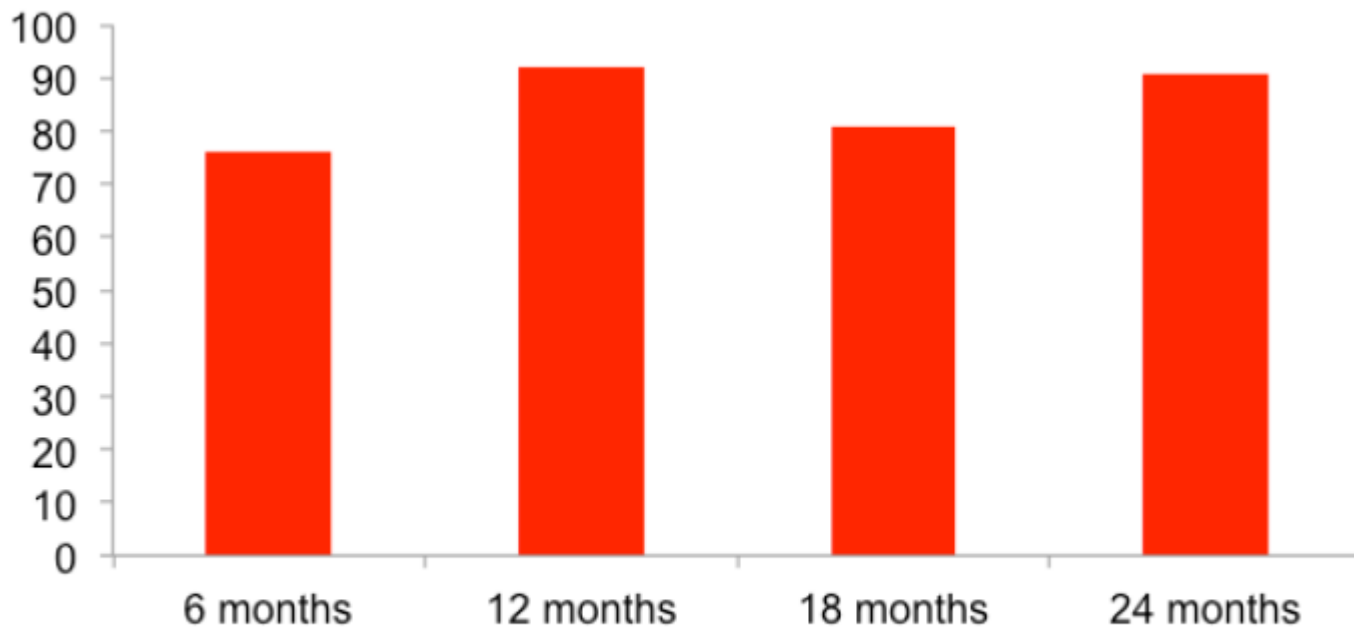


Figure 3: Delayed immunisation and risk of pertussis hospitalisation in infants.¹⁵

Pertussis threatens the very young

- No protection from maternal antibodies
- No protection from breastmilk
- Waning adult immunity



Immunisation target groups

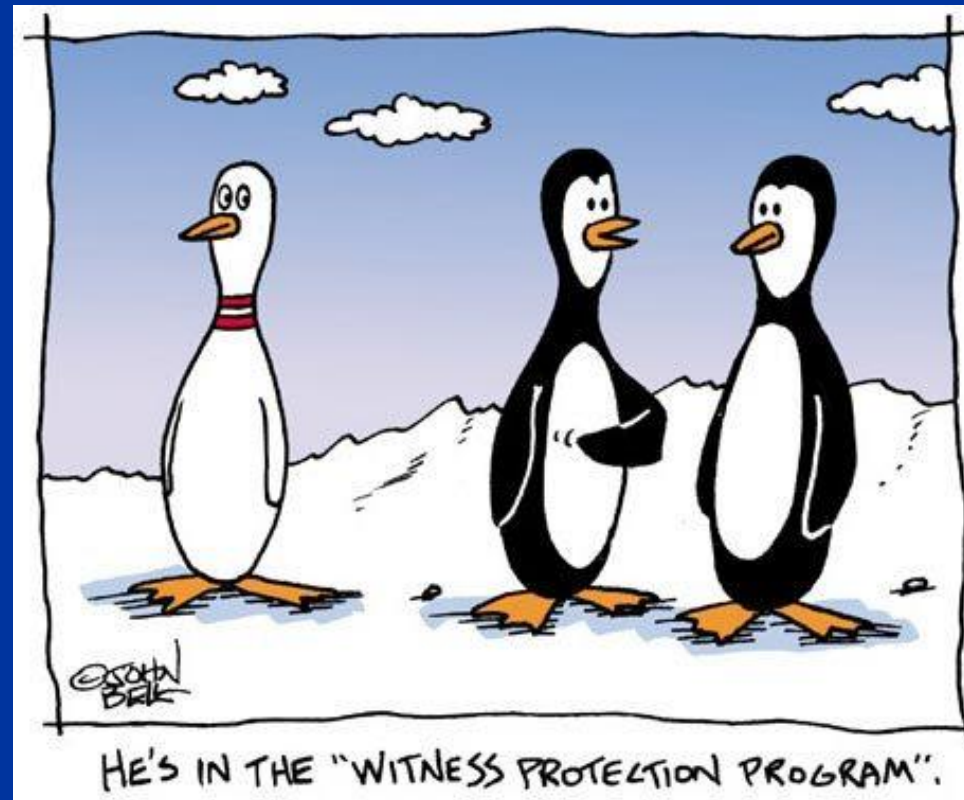
- Older siblings
- Women after childbirth
- Close contacts – cocooning
- Healthcare workers
- Childcare workers



Other preventions

- Treat to reduce spread
- Isolate from vulnerable
- Antibiotic prophylaxis

(Not infectious after 21 days of cough or 4-5 days of antibiotic)





Not Vaccinated? No Kisses!

Get the adult whooping cough vaccine.
www.VaccinateYourFamily.org

NZ recommendations

- Increase immunisation coverage
- Timeliness of immunisation
- Vaccinate pregnant women 28-38 weeks
- Vaccinate children aged 11 years
- Healthcare workers – DHB dependent

Medsafe data sheet

Use In Pregnancy (Category B₂)

- *Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. Therefore, Boostrix should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the foetus. When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria/tetanus vaccines. As with all inactivated vaccines, one does not expect harm to the foetus.*

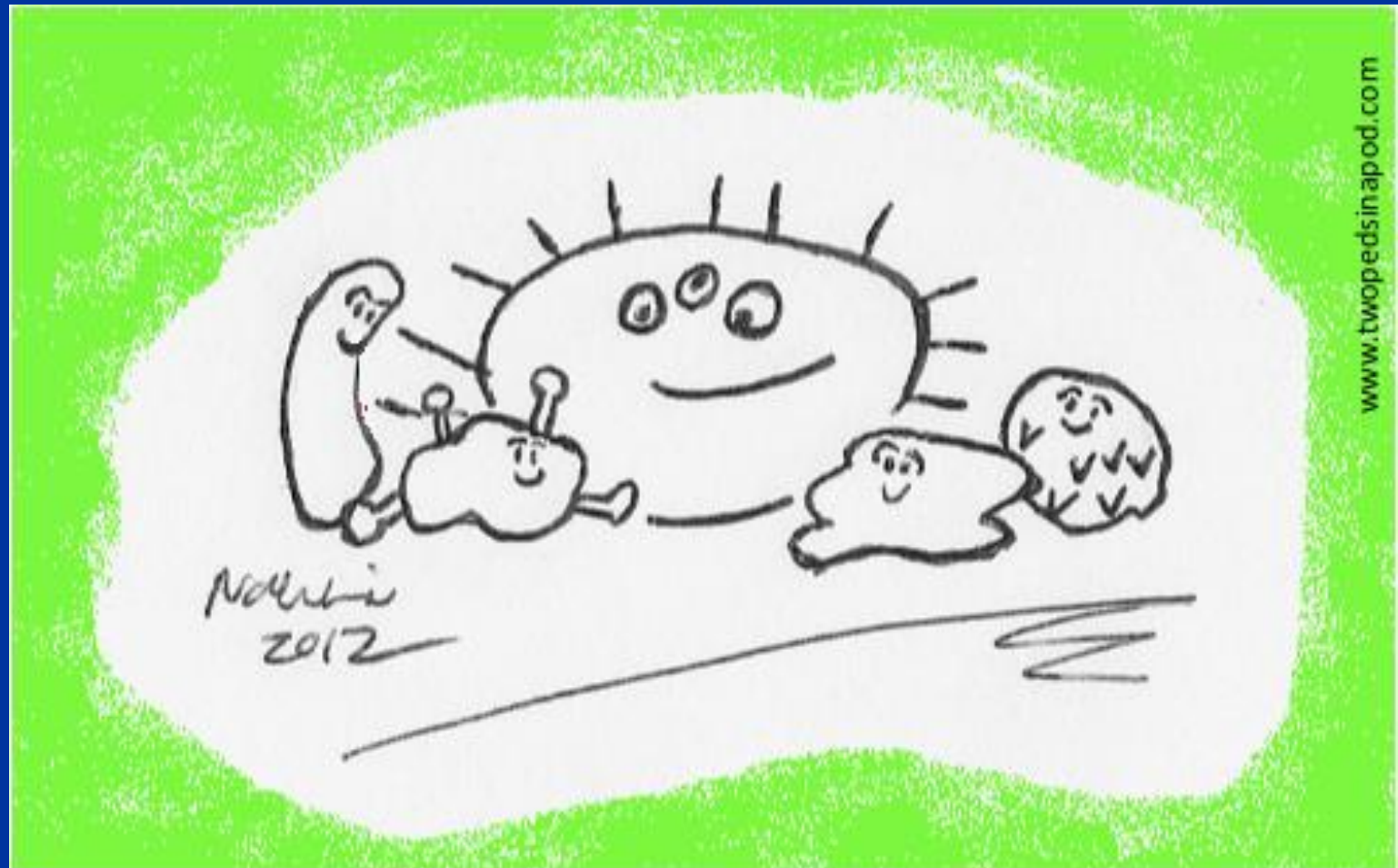
Pertussis summary

WE HAVE...

- A large pertussis epidemic
- Greater problem than other countries

WE NEED TO...

- Deliver complete and timely vaccine
- Deliver cocooning strategies



*Germ family reunion in the post-vaccine era:
"Grampa, tell us again how all you had to worry about
was bleach and hot water."*

Boostrix® (combined diphtheria-tetanus-acellular pertussis (dTpa or Tdap) vaccine) is available as an injection. A 0.5mL dose contains not less than 2.5LfU of diphtheria toxoid, not less than 5LfU of tetanus toxoid, and three purified *Bordetella pertussis* antigens (8mcg of pertussis toxoid, 8mcg of filamentous haemagglutinin, and 2.5mcg of 69kDa outer membrane protein). *Boostrix* is a private-purchase prescription medicine for booster vaccination against diphtheria, tetanus, and pertussis in individuals aged 10 years and older – a prescription charge will apply. Adequate data on use during pregnancy or breastfeeding are not available; therefore prescribing decisions should be based on the possible risks and benefits for each patient. **Contraindications:** known hypersensitivity to any component of the vaccine, encephalopathy after previous pertussis vaccination, or transient thrombocytopenia or neurological complications after previous vaccination against diphtheria and/or tetanus. **Precautions:** do not administer intravenously; ensure medical treatment is readily available in case of rare anaphylactic reaction following administration. **Common side effects** include fever, malaise, fatigue, headache, irritability, loss of appetite, vomiting, diarrhoea, and local reactions such as pain, redness, bruising, itching, or swelling at the injection site. Before prescribing *Boostrix*, please review the full Data Sheet at www.medsafe.govt.nz. *Boostrix* is a registered trade mark of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. **Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.** TAPS DA1313IG/AU13/BOO/0029/13

The preventable reality of varicella.

Dr Pam Jackson





© Original Artist
Reproduction rights obtainable from
www.CartoonStock.com



Search ID: cza0806

"NO, YOU MAY NOT CONNECT THE DOTS!"

Varicella zoster

- Neurotropic herpes virus
- Highly infectious – 90% secondary infections
- Transmitted person to person
 - Inhalation of aerosol
 - Vesicular fluid
 - Through conjunctivae
- Incubation period 7-21 days
- Infectious period 2 days pre-rash till crusted

Epidemiology of V-Z virus infection. Inf Dis Clin N Amer 1996; 10: 571-81



Chicken Pox

©RCH Clinical Practice Guidelines (www.rch.org.au/clinicalguide) / Kids Health Info



Chicken Pox

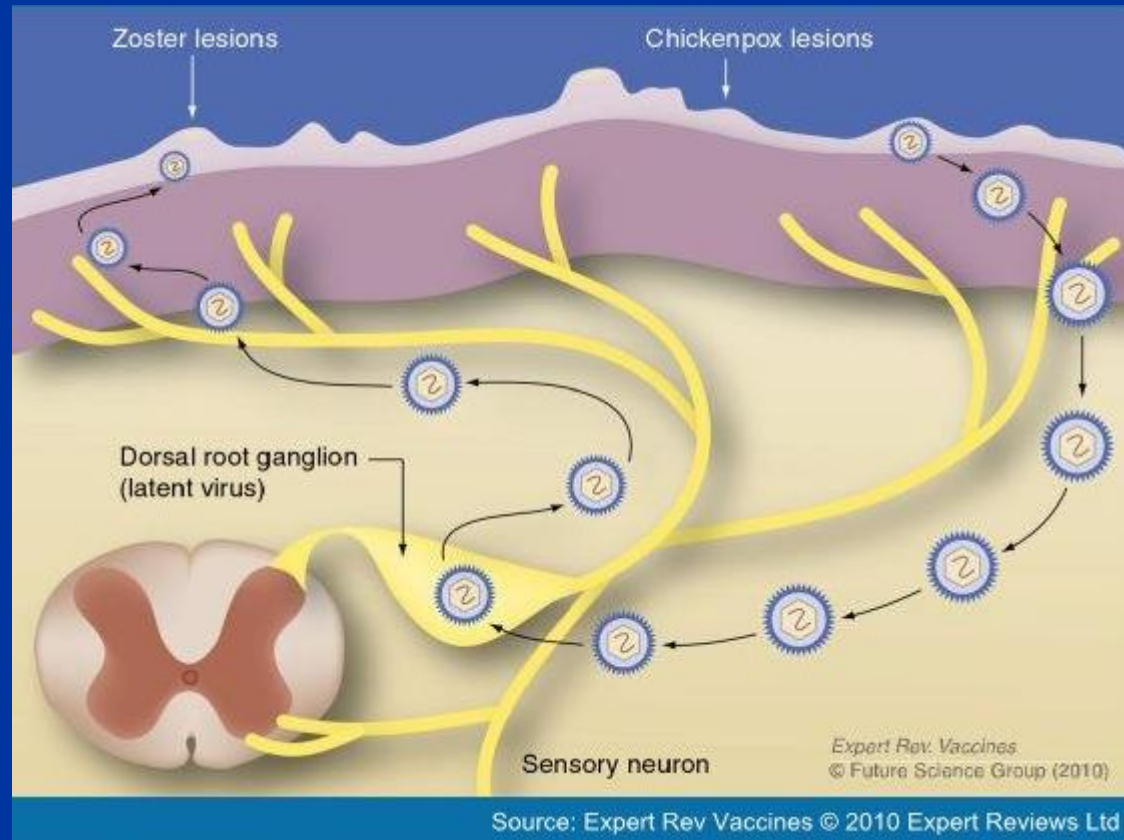
©RCH Clinical Practice Guidelines (www.rch.org.au/clinicalguide) / Kids Health Info



Dewdrop on a rose petal

What is peculiar to V-Z?

- Stays in the sensory nerve ganglia
- Can cause herpes zoster



© Original Artist
Reproduction rights obtainable from
www.CartoonStock.com



"YOU'VE GOT THE SHINGLES"

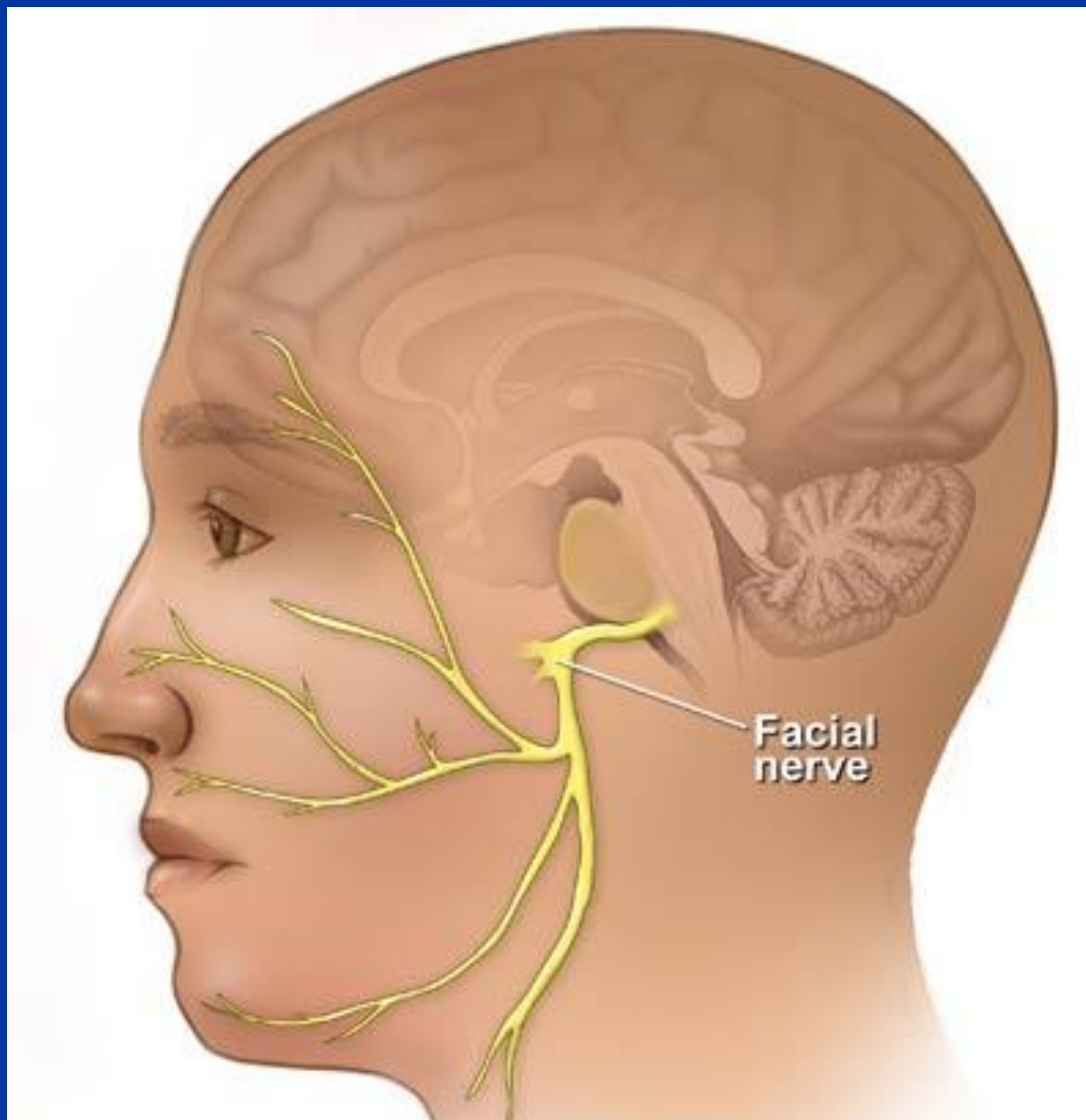
search ID: rjo1084







15



Chickenpox not so benign

Amanda Cameron

New Zealand is in the middle of a chickenpox outbreak and a disturbing number of parents are unaware how dangerous the disease can be, according to an expert in childhood infections.

Emma Best, paediatric in-

Key points

- Chickenpox puts 200 New Zealanders in hospital each year.
- Only about 8 per cent of one to two-year-olds are vaccinated against the disease.
- Chickenpox parties reflect misunderstanding about the disease's potential seriousness.

varicella zoster virus (VZV) and develop an immunity to it.

If asked whether chickenpox parties are a good idea, health professionals should tell parents the disease is potentially very serious in some children and a vaccine can provide immunity without making children sick, Dr Best says.

Speaking at a GSK-sponsored dinner in Auckland last month, she told the audience of about 40 GPs and practice nurses that there are two VZV vaccines available in New Zealand, though neither of them are funded.

Varilrix (GlaxoSmithKline) and Varivax (Merck Sharpe & Dohme) are both live attenuated vaccines with at least 95 per cent efficacy in inducing immu-

Varicella in NZ

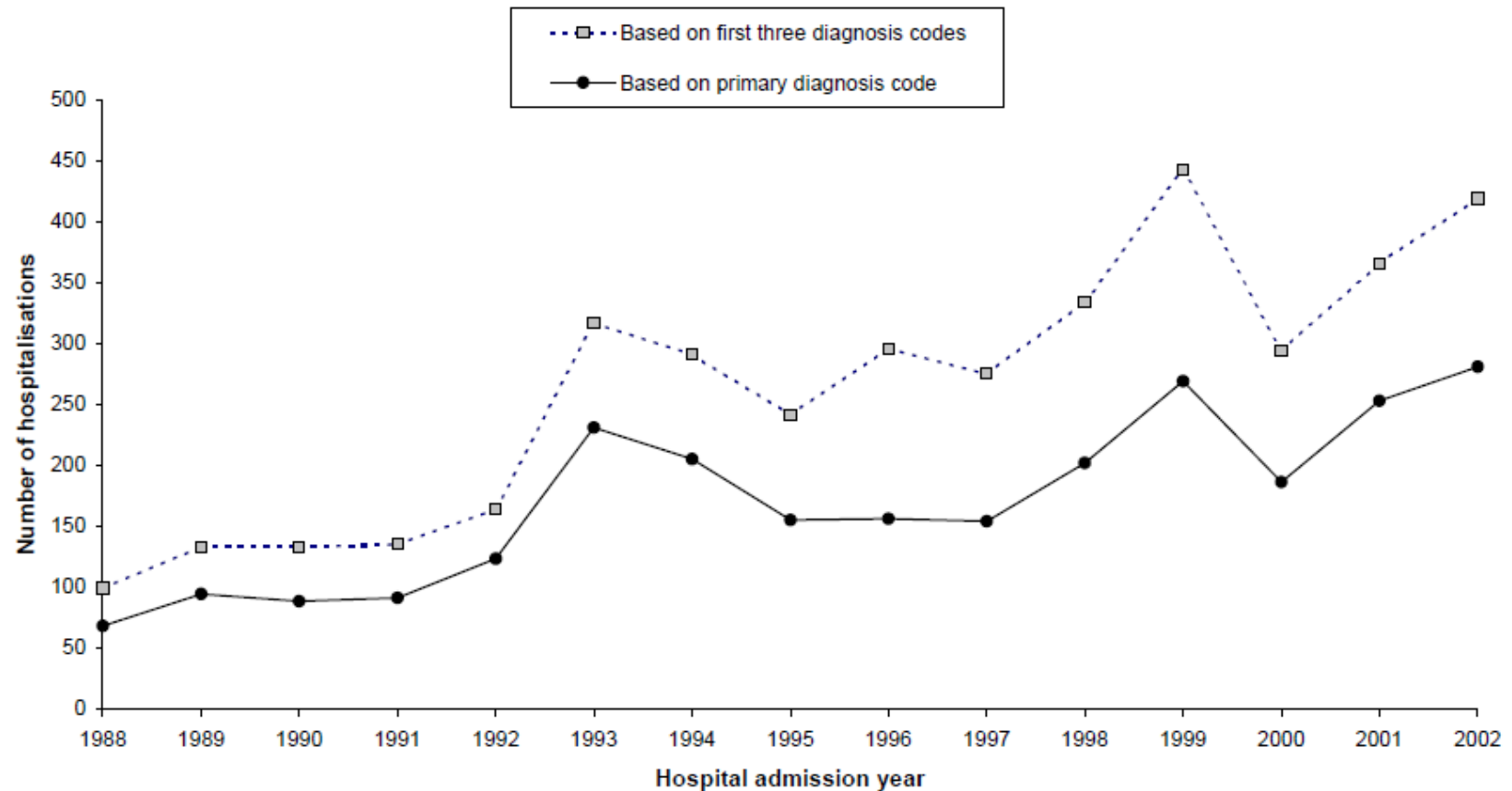
- Not notifiable
- Assume epidemiology of other temperate climates
- 3% of children infected as infants
- 10% of children infected each year
- At 14 years <10% susceptible
- At age 40 >97% exposed

NJMJ 1998 – Tobias et al

Varicella in NZ

- One death per year in NZ
- 5 children to ICU – 2010
- 50,000 get varicella
- 200 are hospitalised
- Meningoencephalitis 1-2 per 10,000
- Acute cerebellar ataxia 1 in 4,000

*Varicella hospitalisations by year,
1988 - 2002*



Definition of contact of varicella

- Household contact
- Playmate contact for more than one hour
- Mother of newborn develops infection one week before to one week after delivery
- Very expensive in isolation etc.....

HEY CHECK IT OUT!
I HAVE THE
CHICKEN POX!



Severity of varicella

- Most cases 2-400 lesions
- Severe cases >1,000 lesions
- Worse in adults – 13x more likely to be hospitalised
- Infants <1 year 6x more likely to be hospitalised
- More severe disease in immunocompromised
- 0.3-0.5 deaths per million estimated

YOU DON'T THINK IT'S
HUMAN POX, DO YOU DOCTOR?

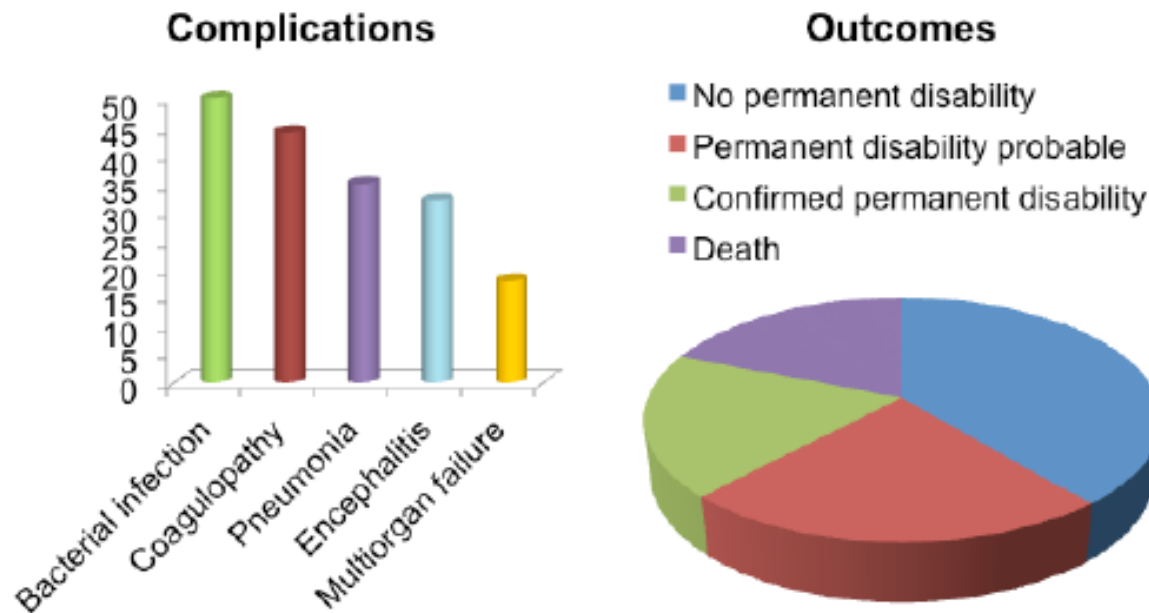
ARE YOU SCARED?!
...YOU BIG CHICKEN!



Complications of varicella

- Skin and soft tissue infections – grp A strep
 - Pneumonia
 - Dehydration
 - Encephalitis – including ataxia
-
- 1980 – association with Reyes syndrome
 - Congenital varicella 1.1% risk in 1st 20 weeks

Complications varicella



34 children, 79% Maori or Pacific

Figure 5: Varicella admissions to the Starship Paediatric Intensive Care Unit 2001-2011.²⁴

Secondary bacterial infection

- Skin and soft tissue infections
 - Necrotising fasciitis
 - Osteomyelitis
 - Other serious invasive infections
-
- NZ has a high rate soft tissue infections
 - 330/100,000 children
 - 700/100,000 infants







1



Other organs

- Liver disease

Haemorrhagic varicella



Congenital varicella

- First recognised 1947 *
- Many abnormalities
 - Low birth weight
 - Scarring
 - Limb hypoplasia
 - Microcephaly
 - Cortical atrophy
 - Chorioretinitis
 - Cataracts
- Incidence 0.6% 2-12 weeks gestation
- 1.4% 13-28 weeks gestation
- 0% after 28 weeks

Reprod Toxicol 2006; 21: e410-20

Congenital varicella

- Most risky at 13-23 weeks gestation
- Immunoglobulin may be helpful
- Immunisation of women best protection









Varicella active protection

- 2 preparations available in NZ – not funded
- 9 months to 13 years
- Susceptible contact of immunosuppressed
- To ring fence patient unable to vaccinate
- 3-5 days post exposure

- One dose under 14 – 2 if over 14 years

Indications for vaccination

- All children going to daycare
- Children with eczema or atopy
- Immunosuppressed *
- Children about to be immunosuppressed
 - Inflammatory bowel disease
 - Cancer or leukaemia
 - Rheumatological conditions etc
- Family of those immunosuppressed
- During an outbreak
- Susceptible women prior to pregnancy

*VARILRIX is contraindicated in subjects with a total lymphocyte count less than 1200 per mm³ or presenting other evidence of lack of cellular immune competence such as subjects with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infect

Contraindications to vaccination

- Anaphylaxis to previous, gelatin or neomycin
- Pregnancy
- Immunodeficiency
- High dose steroids 14 days or longer
- Another live vaccine within 4 weeks

Reactogenicity

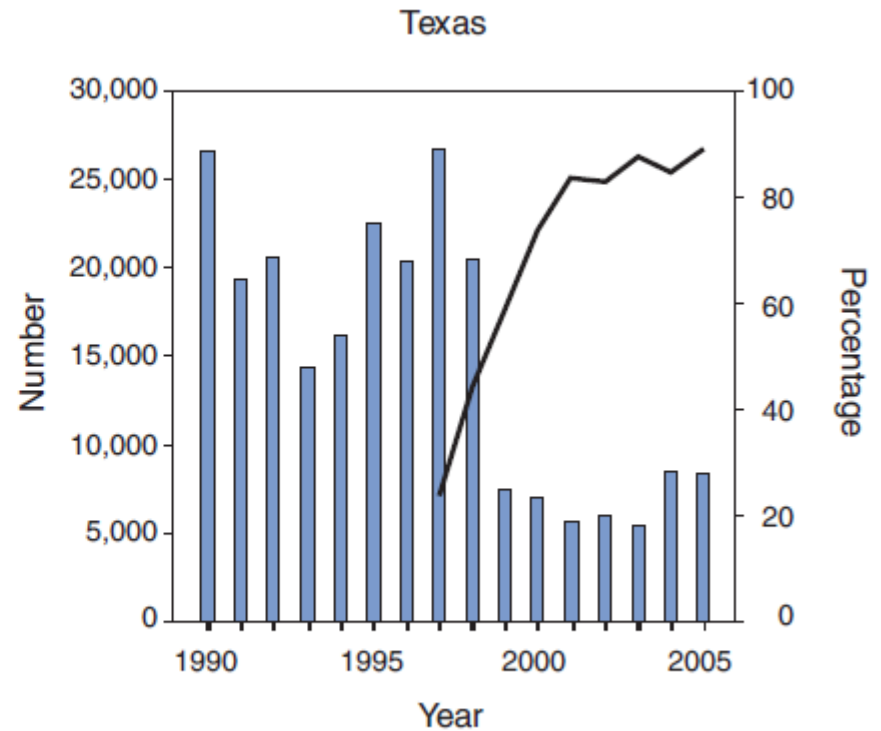
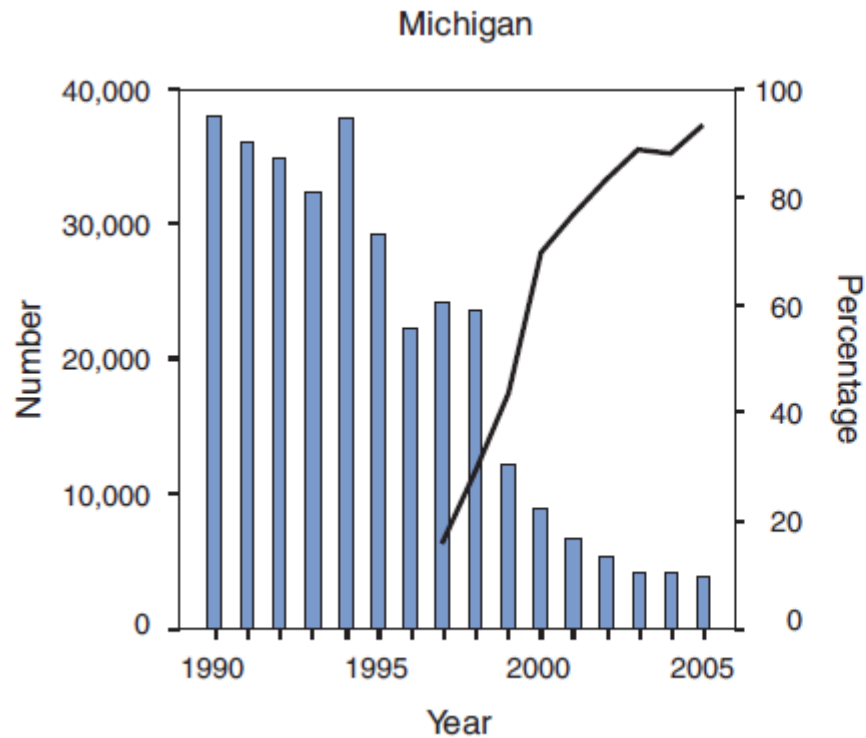
- Fever – 1:10 or less
- Mild rash – 1:20 or less
- Seizure due to fever – 1:1,000 or less
- Pain or swelling at site – 1:5
- No serious adverse events from pre-licensure trials
- Post licensure serious adverse events 2.9:100,000
 - Encephalitis, ataxia, erythema multiforme, pneumonia, thrombocytopenia, seizures, neuropathy, anaphylaxis and death

Causal link not established in all – plausible for thrombocytopenia, ataxia and encephalitis.

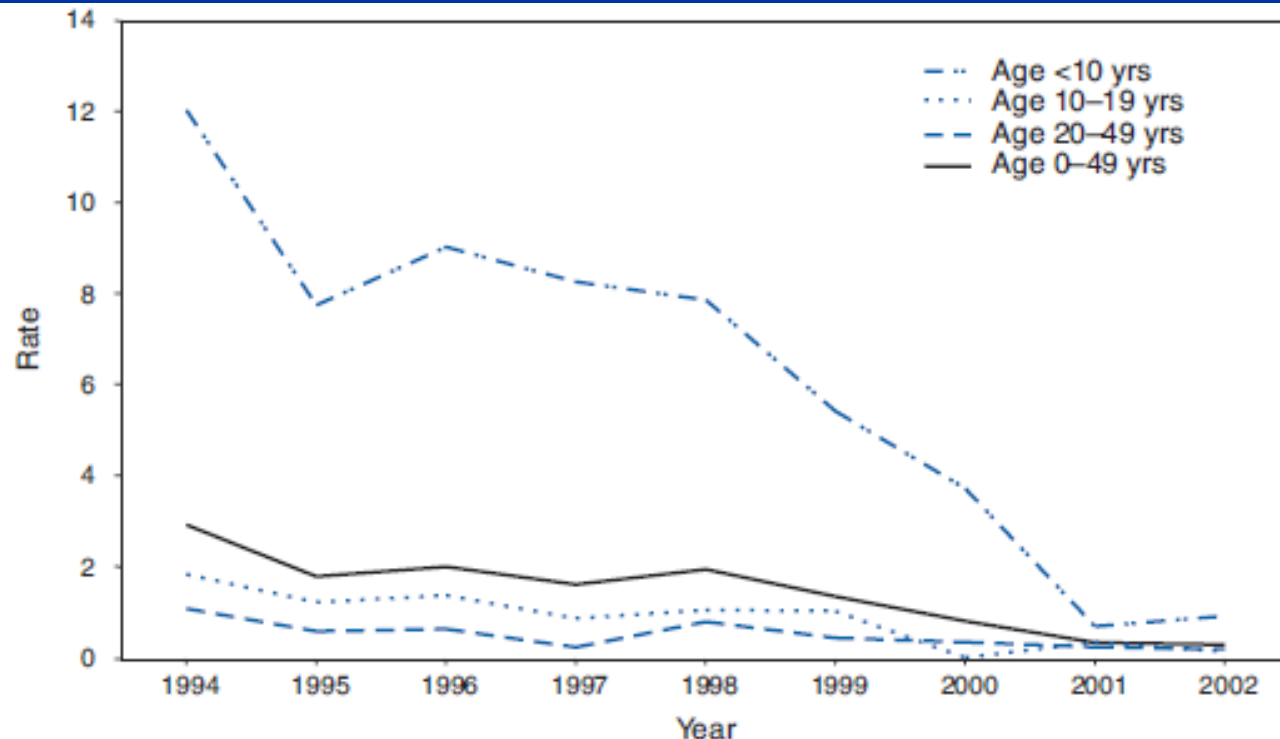
USA and varicella



USA introduced vaccination 1995



Varicella hospitalisation rates USA

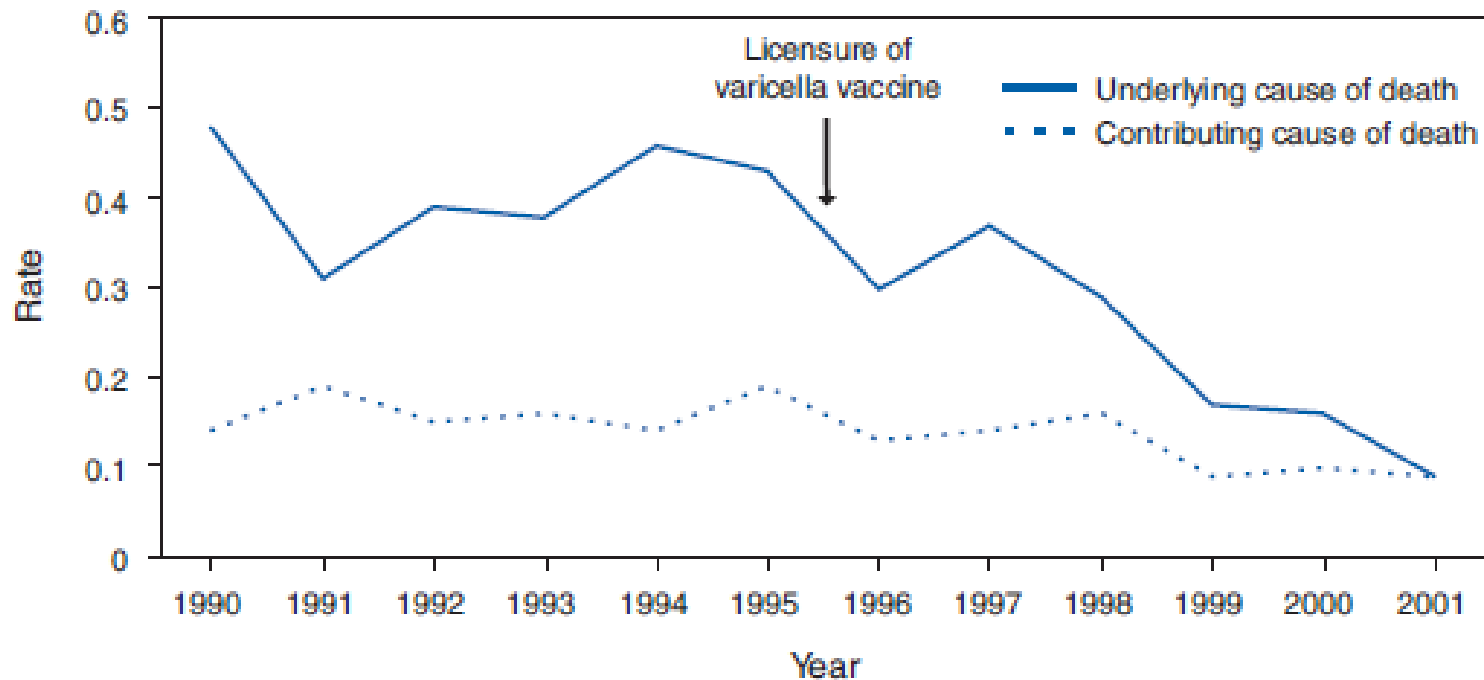


Source: Zhou F, Harpaz R, Jumaan AO, Winston CA, Shefer A. Impact of varicella vaccination on health care utilization. JAMA 2005;294: 797-802.

* Varicella was the primary diagnosis code.

† Per 100,000 population.

Varicella mortality USA



Source: Nguyen HQ, Jumaan AO, Seward JF. Decline in mortality due to varicella after implementation of varicella vaccination in the United States. *N Engl J Med* 2005;352:450–8.

* Per 1 million population.

USA 2001-5 varicella outbreaks

- Immunisation coverage 96-100%
- In elementary schools
- Vaccine efficacy similar 72-85%
- Highest attack in younger
- Outbreaks lasted 2 months
- Index case vaccinated (mild disease)



What about zoster after immunisation?

- Zoster more likely in aging
- Immunosuppression
- Those who have had early infection
- Overall rate of 15-30% zoster in population in their lifetime
- Major effect is post-herpetic neuralgia

Proc R Soc Med 1965; 58: 9-20

Epidemiol Inf 2001; 127: 305-14

Is there some data on zoster?

- Study of leukaemic children – 4.1 years follow up
- 2% rate herpes zoster in vaccine recipients
- 15% herpes zoster in controls
- Subset evaluation – HZ 3x lower in recipients of vaccine than in matched controls *
- Data for healthy children – studies suggest risk is lower

*NEJM 1991; 325: 1545-50

PIDJ 1999; 18: 1041-6

Clin Dis N Am 1996; 10: 595-608

J Inf Dis 2003; 188: 945-7

[Pediatr Infect Dis J.](#) 2009 Nov;28(11)

HSZ and varicella vaccination

- Zoster is not notifiable
- There is no baseline data to study
- There are many studies showing no consistent trends

J Gen Int Med 2005; 20: 748-53

Epidemiol Inf 2005; 133: 245-53

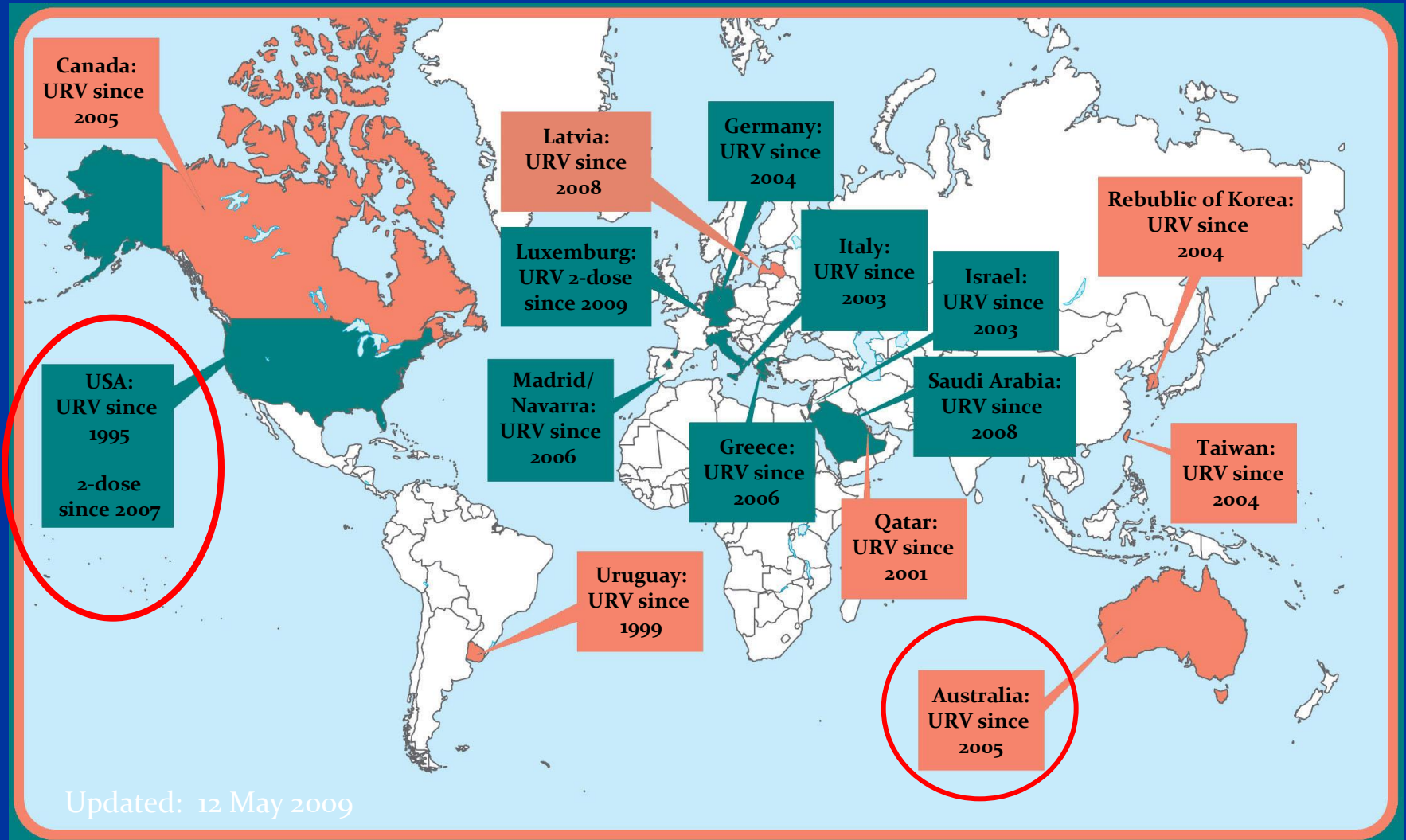
BMC Public Health 2005; 5: 68



Varicella vaccination

- Basic “Jenner” properties
- Live vaccine in low dose confers protection
- Prevents primary infection and disease
- Can induce herd immunity if coverage high enough
- So protection for vaccinated and unvaccinated

Map of countries using *Varilrix*® in universal routine vaccination (URV) programmes



Cost effectiveness of varicella vaccination in NZ

- Economic cost-benefit analysis done 1999 for NZ
- \$0.67 return for every \$1 spent direct costs
- \$2.79 benefit for every dollar spent on vaccination when indirect costs considered

Slide from Dr Emma Best Starship Infectious Diseases Paediatrician

Adverse events and safety

- Local soreness ~ 1: 5
 - Fever ~ 1: 20
 - Local rash ~ 1: 20
 - VZV infection (mild) ~ 1: 50
-
- 5% get mild rash 3 - 4 weeks after vaccination
 - Mean number of vesicles = 5

Serious adverse events

- 2.8 per 100,000 doses
- Anaphylaxis
- Thrombocytopenia
- Ataxia, encephalitis, stroke
- Pneumonia

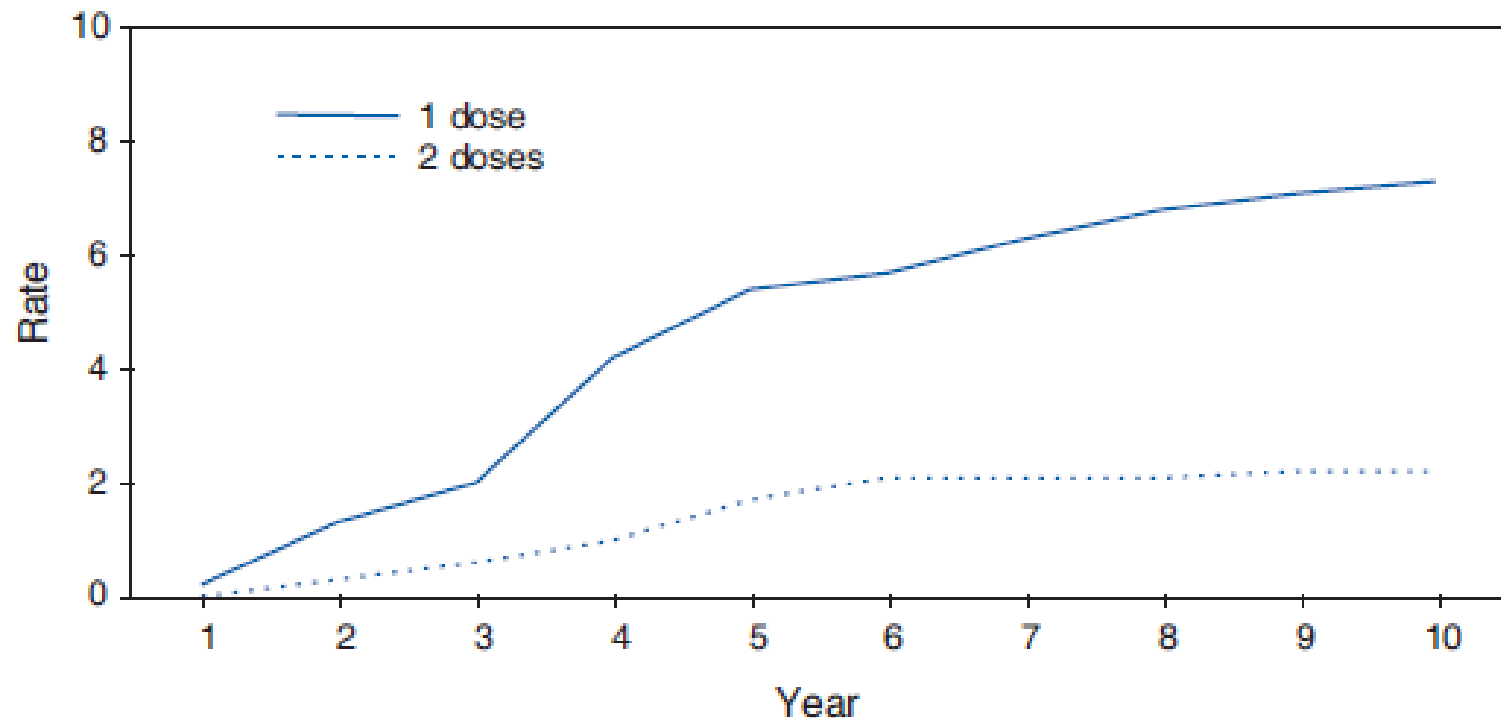
- Undiagnosed immune deficiencies – disseminated vaccine strain
- No deaths

Breakthrough varicella

- Could still be due to wild virus
- Greater than 42 days after vaccination
- Usually mild - <50 lesions
- Lasts 4-6 days
- Contagious
- Rash may be maculo-papular

Milder disease

Breakthrough



Source: Kuter B, Matthews H, Shinefield H, et al. Ten year follow-up of healthy children who received one or two injections of varicella vaccine. *Pediatr Infect Dis J* 2004;23:132–7.

* Per 100 person-years at risk.

After vaccination

- Still may get breakthrough infection
 - Milder
 - Still infectious
- May be more susceptible to wild type if immunosuppressed

© Original Artist

Reproduction rights obtainable from
www.CartoonStock.com



**WORSE CASE OF CHICKEN POX
I'VE EVER SEEN!**

Adverse events

- Need to know if wild type or vaccine type
- Pain and redness at the site
- >11,00 studied
- 4% rash – increased if 2 dose schedule
- Infectious if rash develops – up to 6 weeks
- Zoster can occur – much less common

Varicella in USA

- No shift in age of disease
- Fewer deaths under 50 years
- No change in deaths over 50 years
- No increased varicella or zoster in adults

JAMA 2002; 287: 606-11

Lancet Inf Dis 2002; 2: 454

Post exposure prophylaxis

- Administration of Varilrix[®]
- Within 48 hours of exposure prevented 87.5%
- After 72 hours did not prevent but attenuated

Arch Argent Pediatr 2002; 100: 25-30

Vaccine 2004; 23: 325-8

Future perspectives for NZ

- Immunisation schedule update in 2014
- Measles, mumps, rubella, varicella =MMR-V – Priorix-tetra[®]

Varilrix® Product Information

Varilrix is registered in New Zealand and not currently available on the NZ Immunisation Schedule

Varilrix® (live attenuated varicella vaccine) is available as an injection, 0.5mL per dose. **Varilrix is a private-purchase prescription medicine** for immunisation and prophylaxis against varicella (chickenpox) in adults and children older than 9 months. A prescription charge will apply. Children aged 13 years and older need two doses with an interval between doses of at least 6 weeks. Two doses at least 6 weeks apart are also recommended for children aged between 9 months and 12 years, to provide optimal immune responses against varicella virus.

Contraindications: acute severe febrile illness, lack of cellular immunity (e.g. leukaemia, lymphoma, HIV infection, or immunosuppressive therapy), known systemic hypersensitivity to neomycin, or pregnancy. Pregnancy should also be avoided for 3 months after vaccination. **Precautions:** do not administer intradermally or intravenously. Ensure medical treatment is readily available in case of fainting or rare anaphylactic reaction following administration. Use caution in patients with serious chronic diseases (such as chronic renal failure, autoimmune diseases, collagen diseases, or severe bronchial asthma). Avoid salicylates for 6 weeks after vaccination. Vaccination should be delayed for at least 3 months after a patient has received immunoglobulins or a blood transfusion. If a measles vaccine is not given at the same time as Varilrix, it should be delayed by at least 1 month. **Common side effects** include mild rash; pain, redness and swelling at the injection site; and small numbers of papulo-vesicular eruptions. Uncommon side effects include fever, headache, cough, vomiting, lymphadenopathy, and arthralgia. Before prescribing *Varilrix*, please review the full Data Sheet at www.medsafe.govt.nz. *Varilrix* is a registered trade mark of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. TAPS DA1313IG/13AU/BOO/0029/13.

Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.



Why wouldn't you protect me?