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Viral Vaccine-Preventable Diseases

- what happens between the laboratory and the Sunday Telegraph?

Peter McIntyre

Background

- Viral vaccines on the NIP
- Laboratory tests
- The notification “chain”
- Other data sources

Case studies

- A newly vaccine-preventable disease
  - Varicella
- Elimination - what does it mean?
  - Measles
- A re-emerging VPD
  - Mumps

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Viral Vaccines on the National Program

NIP **then..... early 1990s**

Birth	
2m	Diphtheria, Tetanus, Pertussis, Polio
4m	Diphtheria, Tetanus, Pertussis, Polio
6m	Diphtheria, Tetanus, Pertussis, Polio
12m	Measles, Mumps, Rubella
18m	
4y	
10-19y	Diphtheria, Tetanus
19-26y	
≥65y	

NIP **... now**

Birth	Hepatitis B
2m	Diphtheria, Tetanus, Pertussis, Polio, Hib, Hep B, Pneumo, Rota
4m	Diphtheria, Tetanus, Pertussis, Polio, Hib, Hep B, Pneumo, Rota
6m	Diphtheria, Tetanus, Pertussis, Polio, Hib, Hep B, Pneumo,(Rota)
12m	Measles, Mumps, Rubella, Hib, Men C, (Hep B)
18m	Varicella, Hepatitis A#, Pneumo#
4y	Diphtheria, Tetanus, Pertussis, Polio, Measles, Mumps, Rubella
10-19y	Diphtheria, Tetanus, Pertussis, Varicella (negs), Hep B, Meningococcus C, HPV, Influenz
19-26y	HPV
15-49	Influenza#, Pneumo#
≥65y	Influenza, Pneumo

 # Indigenous or high risk only, ages may vary

Long-standing “traditional” vaccines

- Polio
- Measles
- Mumps
- Rubella
- Hepatitis B

Disease	Vaccine type	Laboratory tests	Notifiable ?
Polio	Inactivated (2005)	Culture/PCR	Yes
Measles	Live attenuated	Serology PCR	Yes
Mumps	Live attenuated	Serology PCR	Yes
Rubella	Live attenuated	Serology PCR	Yes
Hepatitis B	Subcomponent	Serology	Yes

More recent viral vaccines and/or variable notification/lab status

- HPV (2007)
- Rotavirus (2007)
- Varicella (2005)
- Influenza (1999 - elderly)
- Hepatitis A (2007 - Indigenous children, some jurisdictions only)

Disease	Vaccine type	Laboratory tests	Notifiable
HPV	VLPs	Serology Cytology PCR	No
Rotavirus	Live attenuated	ELISA - stool PCR	Some states
Varicella	Live attenuated	Serology PCR	Some states
Influenza	Inactivated	Serology Culture PCR	Yes
Hepatitis A	Inactivated	Serology	Yes

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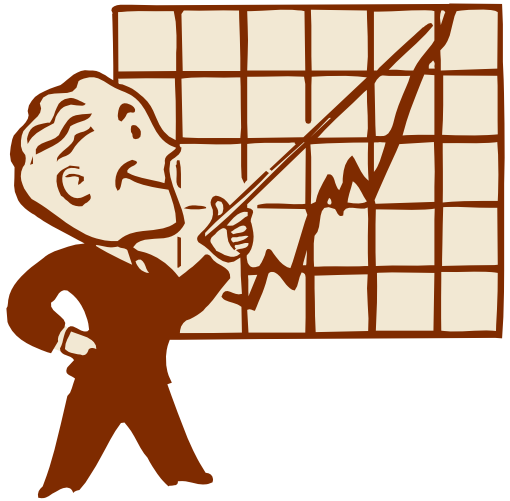
Surveillance of VPDs - some general principles

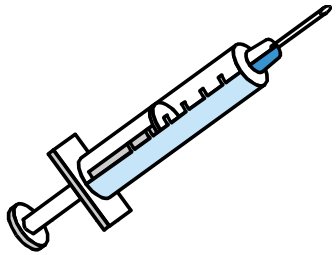
Definition of surveillance

- Information for public health action
  - systematic collection, analysis and interpretation
  - dissemination/feedback to those who need to know
  - use for disease prevention and control



VPD related surveillance

- Immunisation coverage
- Vaccine effectiveness
- Vaccine adverse events
- Epidemiology of the disease
  - indirect
    - serological surveys
  - direct
    - numbers (notified cases, laboratory reports, GP visits)
    - morbidity (absenteeism, GP visits, hospitalisations)
    - mortality (deaths)



Evolving surveillance needs

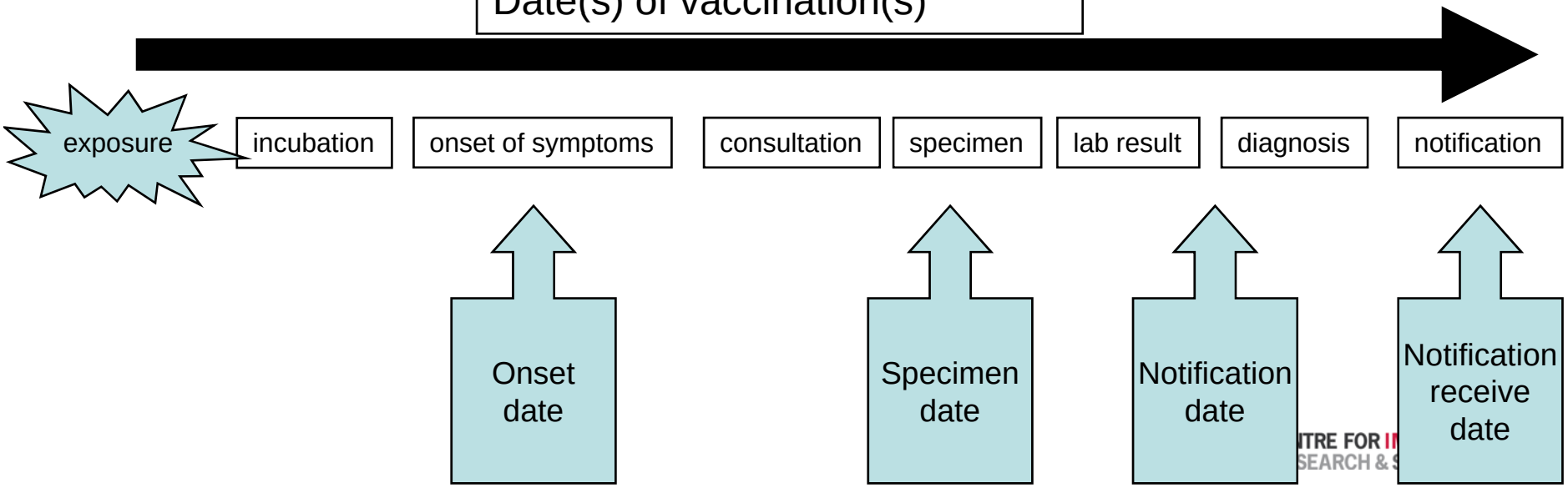
- Surveillance objectives & needs change over time
- More detailed information is required as
  - immunisation programs mature
  - disease incidence declines
- Surveillance tailored to the phase of disease control

Phases of a vaccination program

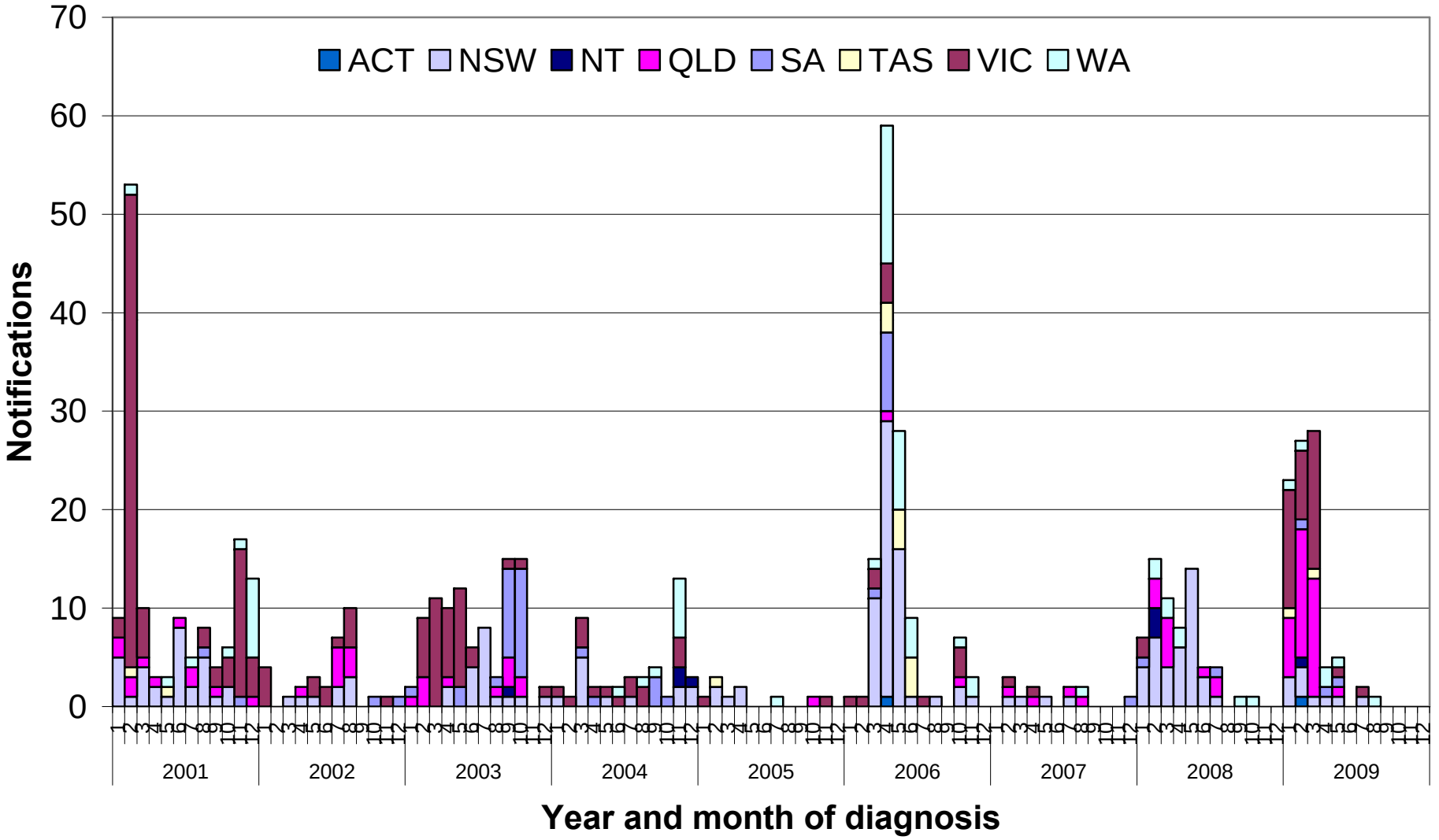
- **Pre-vaccination** phase
  - measure disease burden and identify at risk groups
- **Post program implementation** phase
  - measure impact of program
  - immunisation coverage and adverse event monitoring
- Established programs **moving towards elimination**
  - enhanced surveillance of each suspect case
  - rapidly detect and fully investigate all outbreaks

Detecting events in persons, place and time

Age
Sex
Indigenous status
Residential postcode
Confirmation status
Outbreak link
Organism details, genotype
Place of acquisition
Vaccination status
Vaccine type
Date(s) of vaccination(s)



Measles notifications and outbreaks



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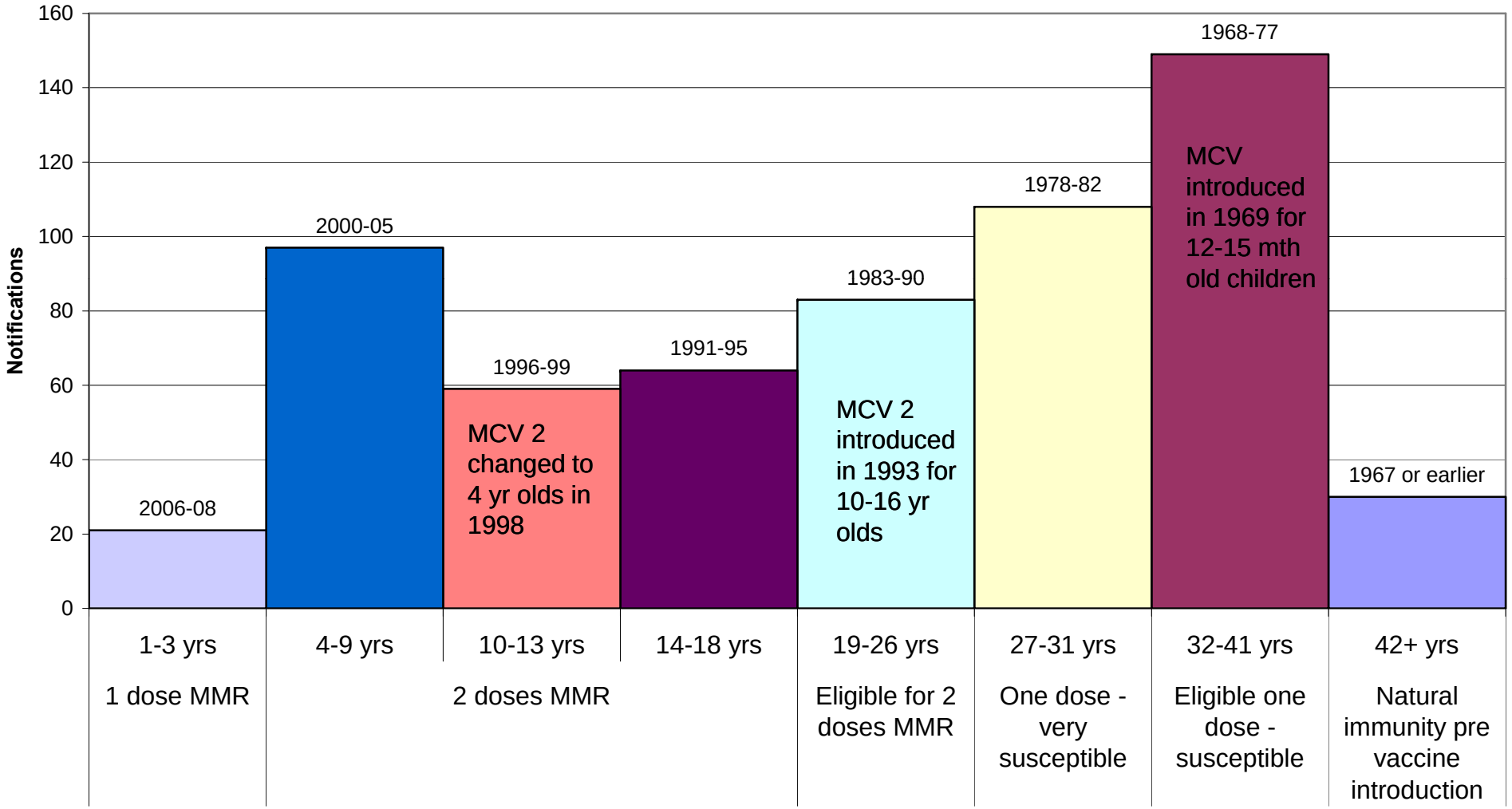
Source: NNDSS, 15 September 2009

Measles notifications, 2001-2009 by year of birth and MCV eligibility



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Source: NNDSS, 15 September 2009

Australia - measles elimination ?

Elimination of endemic measles transmission in Australia

Anita E Heywood,[a] Heather F Gidding,[b] Michaela A Riddell,[c] Peter B McIntyre,[a] C Raina MacIntyre[a] & Heath A Kelly[c]

Abstract Elimination of endemic measles transmission is the culmination of a range of control measures at a national level. Current documentation of elimination proposed by WHO's regional offices requires achieving specific targets for surveillance process indicators. We demonstrate how Australia, although not meeting these specific targets, has satisfied multiple criteria that justify the formal declaration of measles elimination. Our review shows that few countries previously declaring measles elimination have satisfied the current WHO surveillance targets. We argue that the requirements for recognition of measles elimination should not restrict countries to a particular type of surveillance system or surveillance criteria.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se halla una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة

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Measles notifications and vaccine coverage

Fig. 1. **Measles notification rates per million population, Australia, 1991–2007**[24]

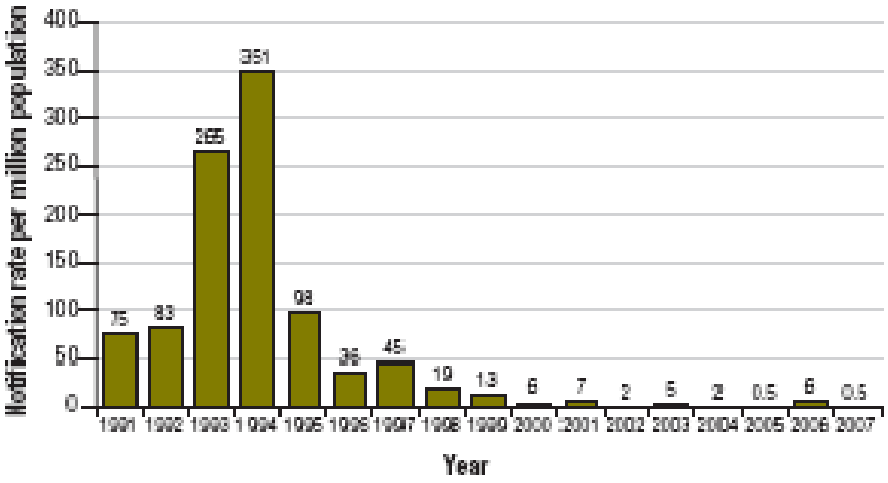
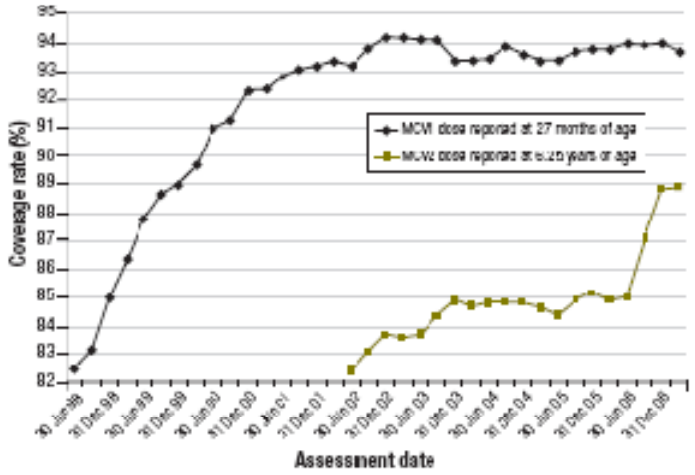


Fig 2 **Coverage rates of the first and second doses of measles-containing vaccine in Australia by assessment date as reported on the Australian Childhood Immunisation Register**[a]



MCV, measles containing vaccine.

[a] Assessment date: MCV1 is scheduled at 12 months of age and assessed at 27 months of age; MCV2 is scheduled at 4 years of age and assessed at 6.25 years of age to allow for delayed notification.

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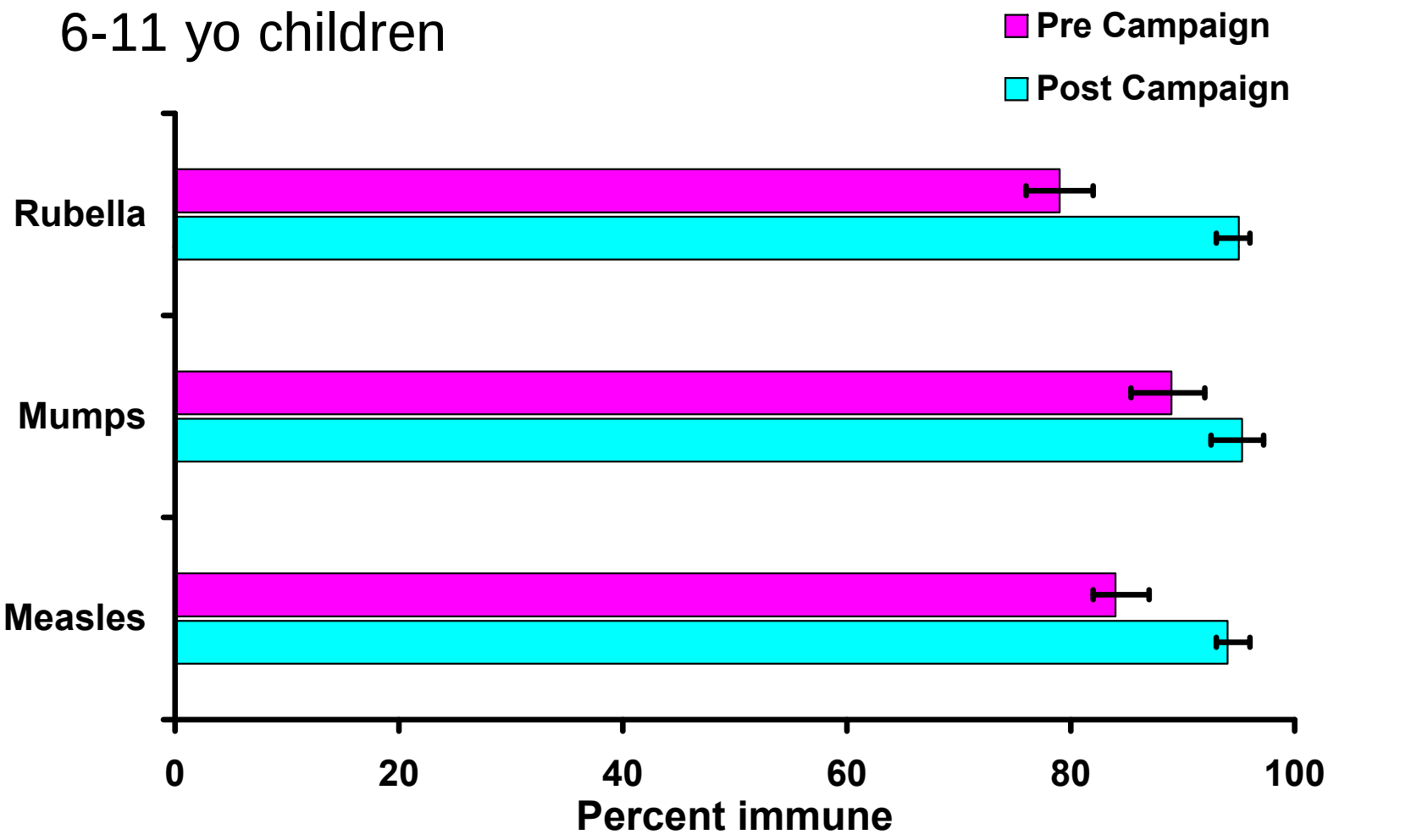
1998 Measles Campaign - serosurveillance



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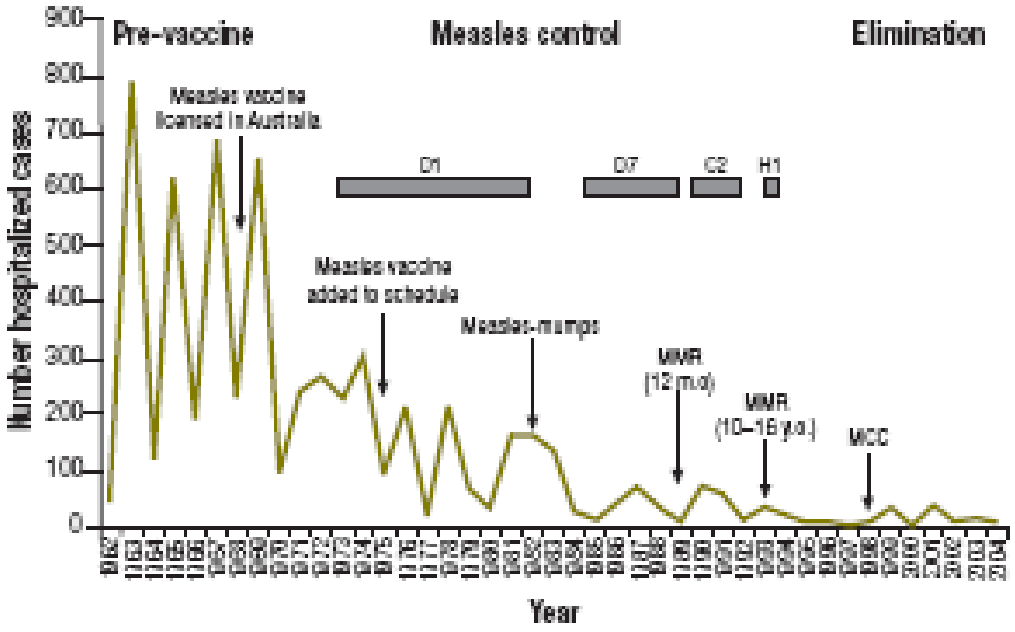
Documenting elimination of indigenous measles transmission in Australia - genotype patterns

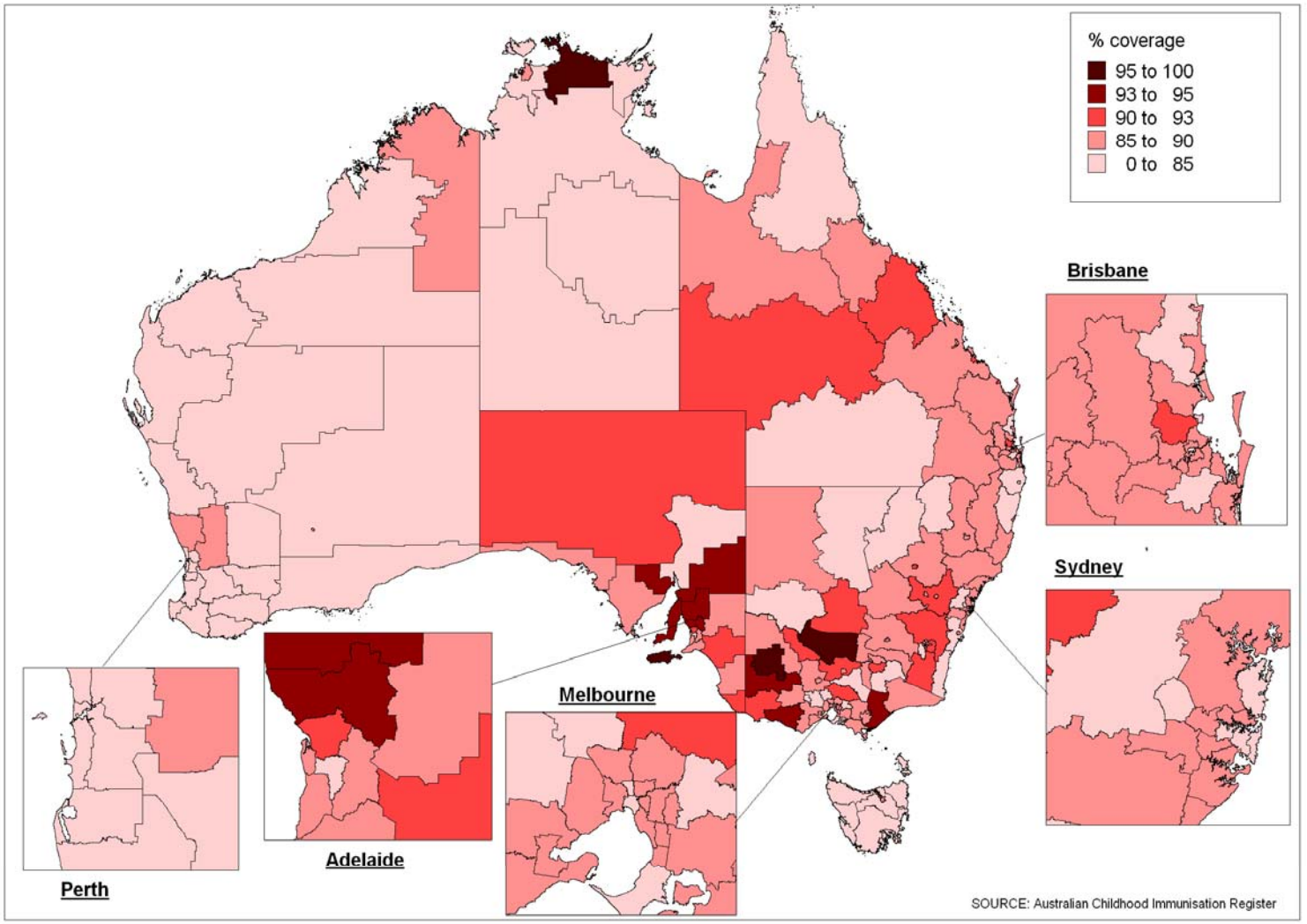
Fig. 3. Measles-associated hospitalizations and measles virus genotypes isolated in Victoria (1962–2004) during WHO-defined measles elimination phases[20,18,41,a]



MCC, measles control campaign; MMR, measles–mumps–rubella vaccine; m.o., months' old; y.o., years' old.

[a] Arrows reflect changes to measles immunization policy. Boxes show genotypes detected retrospectively (pre–1999) from measles virus isolates and clinical samples during the measles control phase. Measles virus isolates prospectively (1999–2004) detected during the elimination phase represent genotypes associated with imported cases or vaccine-related illness (not shown in figure). Prospectively isolated genotypes (number of isolates) include A (4 isolates detected), D3 (1), D4 (2), D5 (4), D7 (1), D8 (4), D9 (2), G2 (2), G3 (2), H1 (2) and H2 (1).

Vaccination coverage for 2 doses of rotavirus vaccine by 12 months of age, post-rota cohort, Australia



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Varicella in Australia – a “mild” disease?

Disease

- **~7 deaths/yr (most adults)**
- **~ 1500 hospitalisations (most children)**
- **> 200,000 cases**
  - **School/child care costs**
  - **Non-immune adults**

Varicella vaccine

- Live attenuated (oka strain)
- Varivax and Varilix
- From 12 months of age
- 1 dose < age 14 yrs
- 2 doses ≥ age 14 yrs
- side effects low
- protection >90% for severe disease

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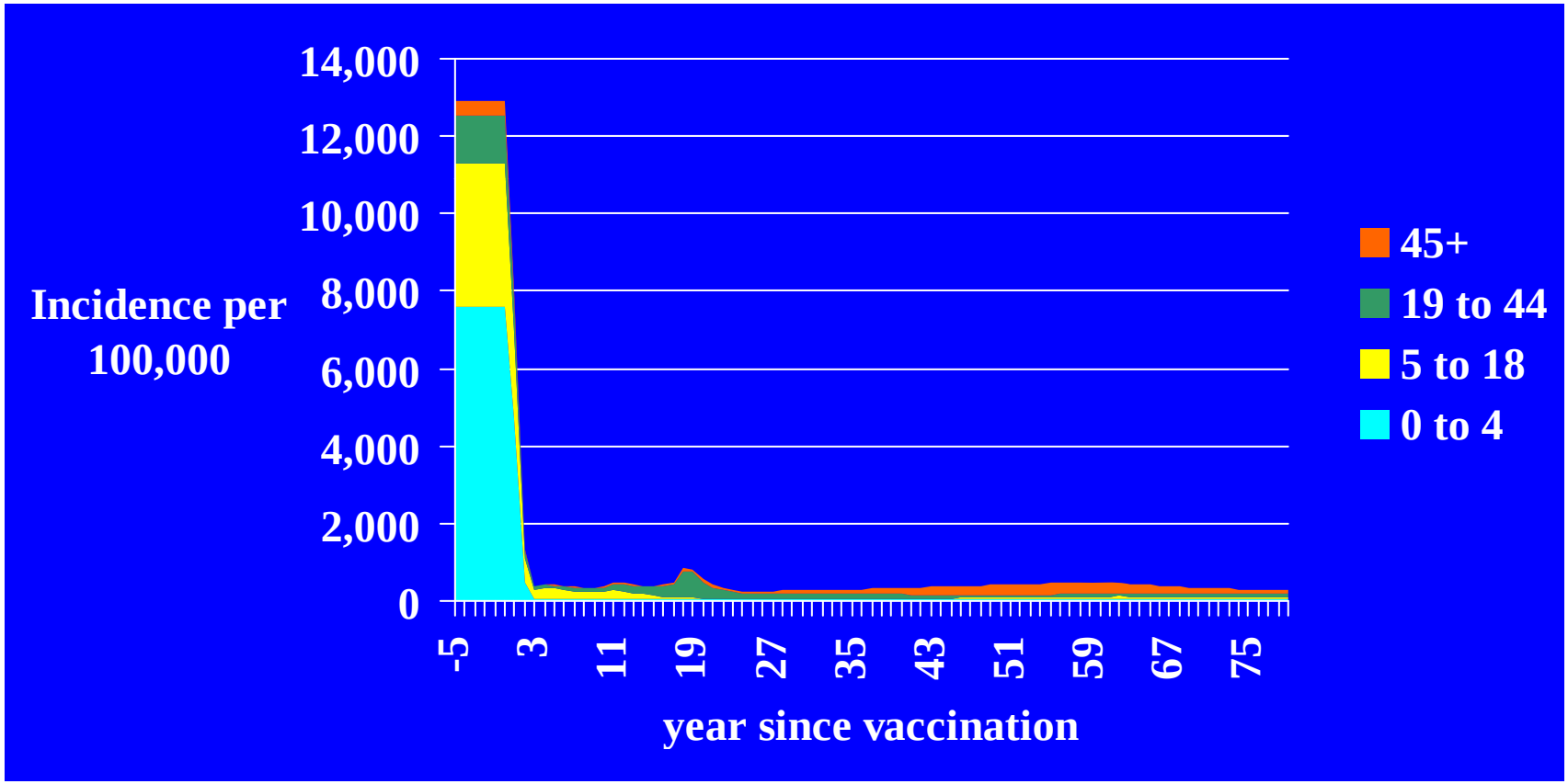
Vaccine coverage and varicella

Estimated age-specific varicella incidence over time following 100% coverage



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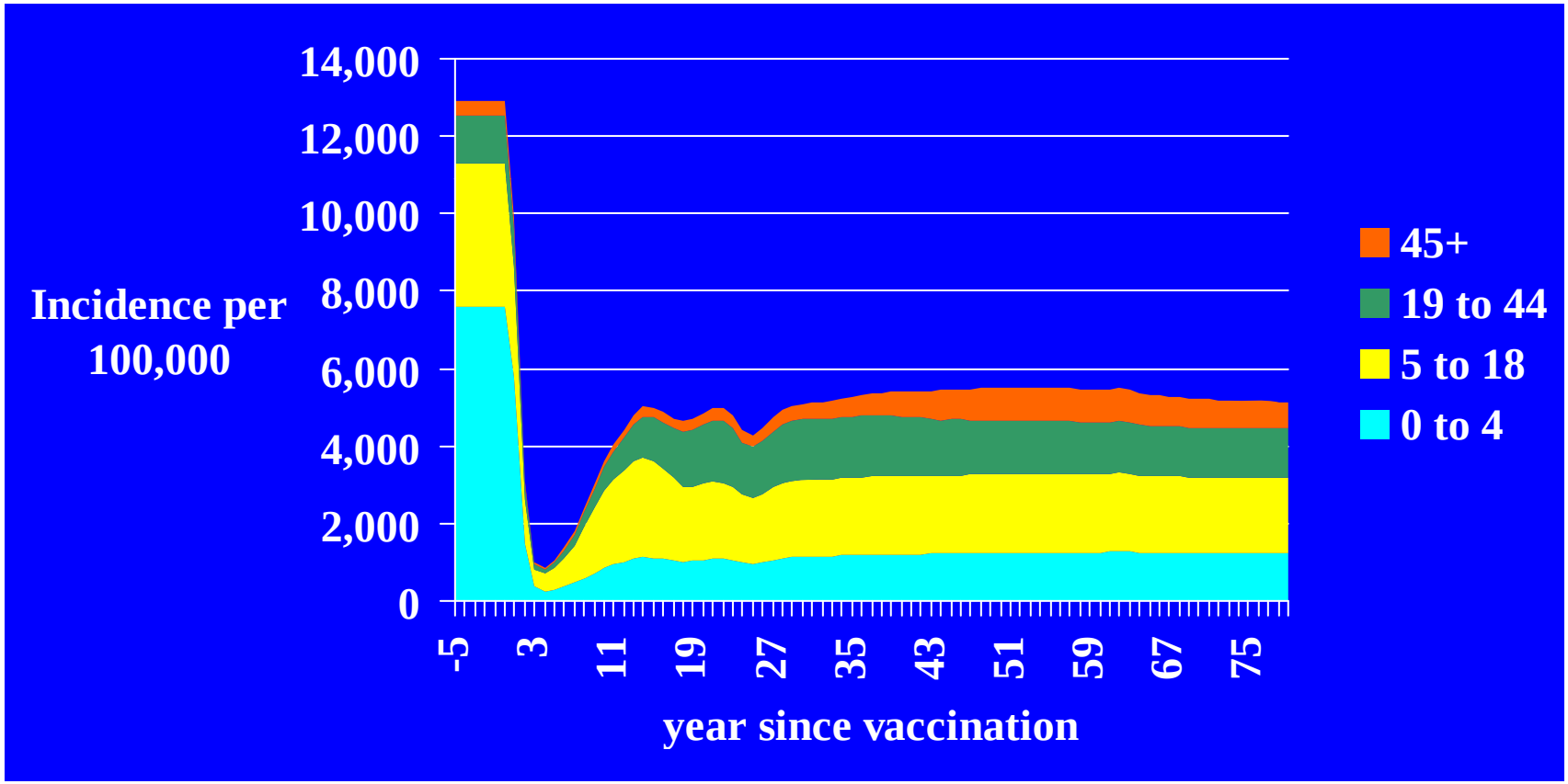
Estimated age-specific varicella incidence following 60% coverage



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Varicella vaccine program

- Varicella vaccine @ 18 months +
  - Schedule point available
- Vaccine licensed from 12 mo
- Trade-off between cases before 18 m and schedule
  - ~25% hospitalisations < 2yrs
  - ~20% of hosps <2yrs occur 12-18 months
- Vaccine @ 10-13 years for those without a history (no blood tests)
- Promote vaccination for persons >15y without a history, especially planning pregnancy (blood test required)

Varicella

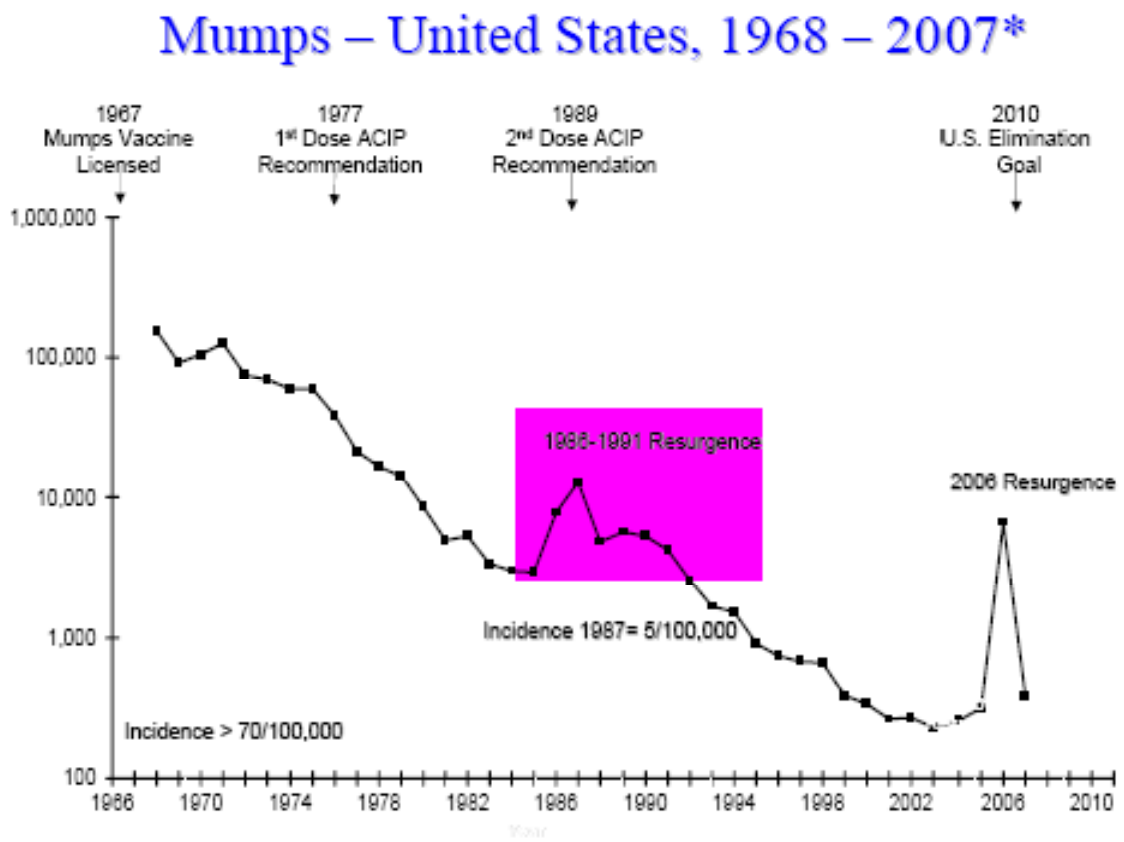
Breakthrough varicella

Challenges in varicella surveillance and monitoring

- Lots of cases
- Most do not present to GP, few lab tests
- Those that are lab tested probably atypical
- Only SA had varicella notifiable pre vaccine program
- Vaccine available in private market pre program

- **Conclusion** - monitor hospitalisations
- Early data show decrease in hospitalisations in targeted age group + older and younger children

Mumps in US - courtesy Jane Seward



National Notifiable Disease Surveillance System, *provisional data through Dec 31, 2007

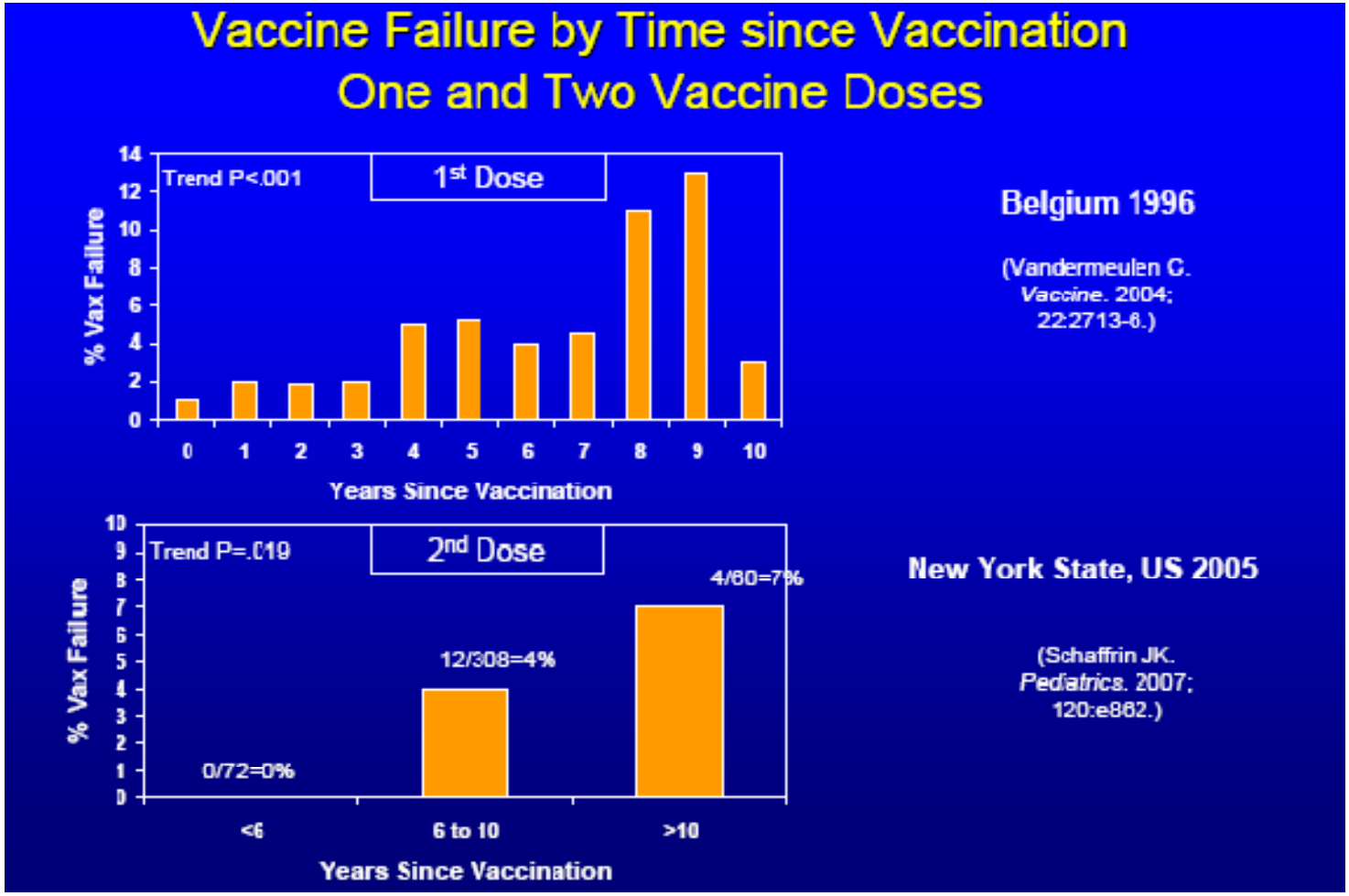
Mumps - other countries

Lessons Learned
National Mumps Outbreaks

- National incidence rates as indication of vaccine protection in populations
  - Pre-vaccine > 80/100,000*
  - UK outbreak 2005 ~100/100,000
  - US resurgence 1987 5/100,000
  - Canada outbreak 2007 4/100,000
  - US resurgence 2006 2/100,000

* likely ~ 500-1,500/100,000

Mumps - two dose failures



Lessons for Australia

- Most of our mumps resurgent cases are in young adults who have had one or no doses
- We need to maximise two dose coverage first
- Challenges ahead with diagnosing two dose vaccine failures
  - Serology and PCR not useful
  - Back to the “old days” of relying on clinical diagnosis + link to another clinical case

Summary and conclusions

- Laboratory contribution vital but some VPDs have no tests (eg HPV) and others interpretation a problem
- Need to consider in the context of the vaccine program maturity and coverage
- There is always another challenge around the corner - eg mumps

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