

# Use of linked data for estimation of the effectiveness of vaccination programs in Queensland

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# Vaccine effectiveness studies involving data linkage

- Rotavirus vaccine effectiveness
- Varicella vaccine effectiveness
- Pertussis vaccine effectiveness
- Hepatitis B assessment of post-exposure prophylaxis for infants born to hep B +ve mothers

# Calculation of vaccine effectiveness

- Screening method
  - compares vaccine coverage in cases (PCV) and population (PPV)
  - PPV obtained from Australian Childhood Immunisation Register
  - partially vaccinated children excluded from cases and population
  - possible in QLD (and NT) because both jurisdictions have local immunisation registers

$$VE = \left( 1 - \left( \frac{PCV}{(1-PCV)} \times \frac{(1-PPV)}{PPV} \right) \right) \times 100$$

# Rotaviruses (RV)

- most common cause of severe childhood gastroenteritis worldwide
- approximately 450,000 deaths in children <5 years of age
- publicly funded RV vaccination introduced in mid-2007

# RV study: aims

- Assess changes in RV epidemiology since commencement of the publicly funded vaccination program using routinely collected health data
- Calculate vaccine effectiveness (VE) of (i) pentavalent RV vaccine in QLD, and (ii) monovalent RV vaccine in NT, in preventing RV notifications, RV and non-RV gastroenteritis hospitalisations and gastroenteritis ED presentations

# RV study: methods (QLD)

## Data linkage by the Health Statistics Unit:

- Notifiable conditions system (NOCS)
- QLD hospital admitted patient data collection (QHAPDC)
- Emergency department information system (EDIS)
- Auslab (from Pathology QLD)
- Vaccination information and vaccination administration system (VIVAS)

# RV study data linkage (QLD)

QHAPDC



EDIS

# RV study data linkage (QLD)

NOCS



VIVAS

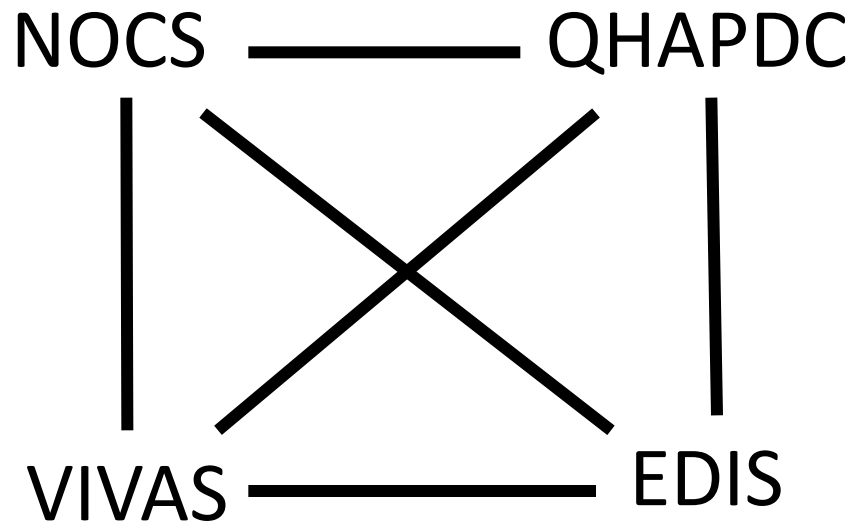
QHAPDC



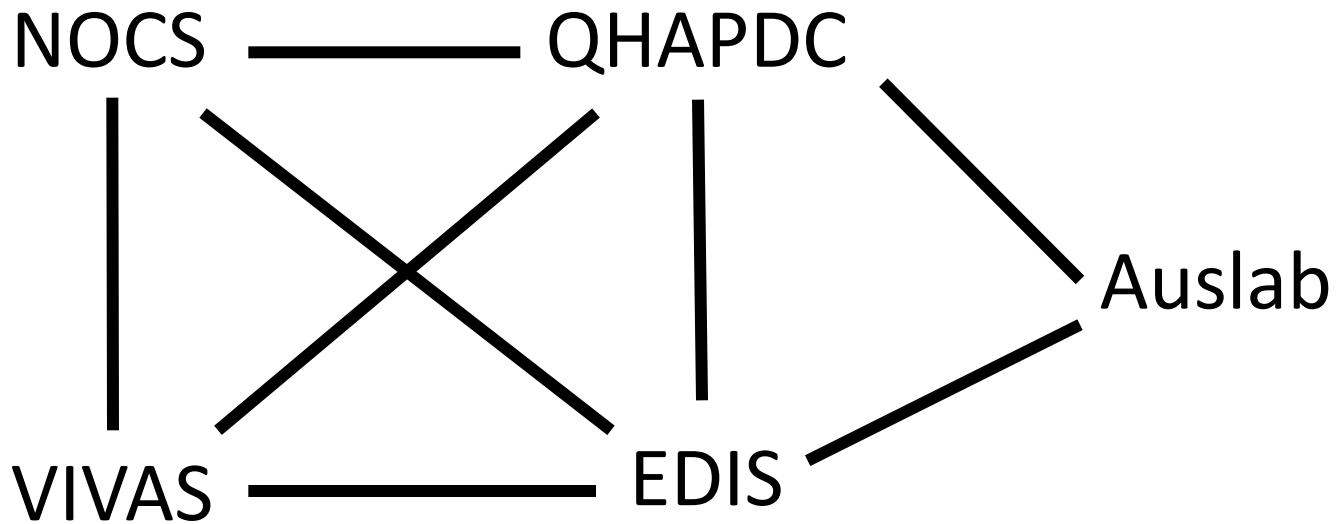
EDIS



# RV study data linkage (QLD)



# RV study data linkage (QLD)



## RV study: expected outcomes (QLD)

- RV VE estimates for prevention of notification, ED presentation and hospitalisation for RV and non-RV acute gastroenteritis in children under 5 years between 2009 and 2011, among Indigenous and non-Indigenous children

# RV vaccination and febrile seizures

- RV-related illnesses are associated with both febrile and afebrile seizures
- recent retrospective cohort study of US children found a protective association between full RV vaccination and childhood seizures resulting in emergency department (ED) presentation or hospital admission in the year following vaccination [1]
- Using our linked dataset containing febrile, but not afebrile, seizure outcome data, we sought evidence of a similar effect in QLD children

[1] Payne et al 2014

# RV vaccination and febrile seizures: results

Birth cohort	Age range	Vaccinated cases	Total cases	PPV (%)	VE [%] (95% CI)
<b>Any ED presentations for febrile seizures</b>					
May 2007–April 2008; May 2008–April 2009; May 2009–April 2010	8m–2y7m	1301	1530	87.7-90.9	35.8 (26.0 – 44.2)
May 2007–April 2008; May 2008–April 2009	1yr8m–3y7m	454	544	86.7-90.3	34.7 (18.1 – 48.0)
May 2007–April 2008	2y8m–4y7m	92	137	85.8	66.2 (51.6 – 76.4)
<b>Any hospital admissions for febrile seizures</b>					
May 2007–April 2008; May 2008–April 2009; May 2009–April 2010	8m–2y7m	389	460	87.7-90.9	38.0 (20.1 – 51.9)
May 2007–April 2008; May 2008–April 2009	1y8m–3y7m	110	142	86.7-90.3	56.4 (35.3 – 70.7)
May 2007–April 2008	2y8m–4y7m	23	33	85.8	62.0 (19.2 – 82.1)

# RV vaccination and febrile seizures: conclusions

- Our results support the recent US finding
- Reduction in seizures from RV vaccination may result in substantial benefits to children, their parents and the health system more broadly

# RV vaccination and febrile seizures

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Brief Report

## Febrile Seizures in the Era of Rotavirus Vaccine

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A protective association between rotavirus vaccination and childhood seizures in the year after vaccination was recently reported from the United States. In the state of Queensland, Australia, the authors found that rotavirus vaccine was 35.8% and 38.0% effective at preventing emergency department presentation and subsequent hospitalization, respectively, for febrile seizures among children up to two years following vaccination.

**Key words.** rotavirus vaccine; febrile seizures.

# Background – chicken-pox and varicella vaccine

- Caused by varicella-zoster virus (VZV)
- Primary infection – chicken-pox, VZV establishes latency in dorsal root ganglia and can reactivate manifesting as herpes zoster
- Usually mild disease occurring in childhood, causing complications in 1% (pneumonia, 2<sup>nd</sup> bacterial skin infections, acute cerebellar ataxia, encephalitis)
- More severe in adults and immunocompromised
- Publicly funded varicella vaccine (VV) introduced as an 18-month dose in November 2005
- VV replaced by MMRV at 12-months of age in July 2013
- No assessment of effectiveness of single dose VV in Australia

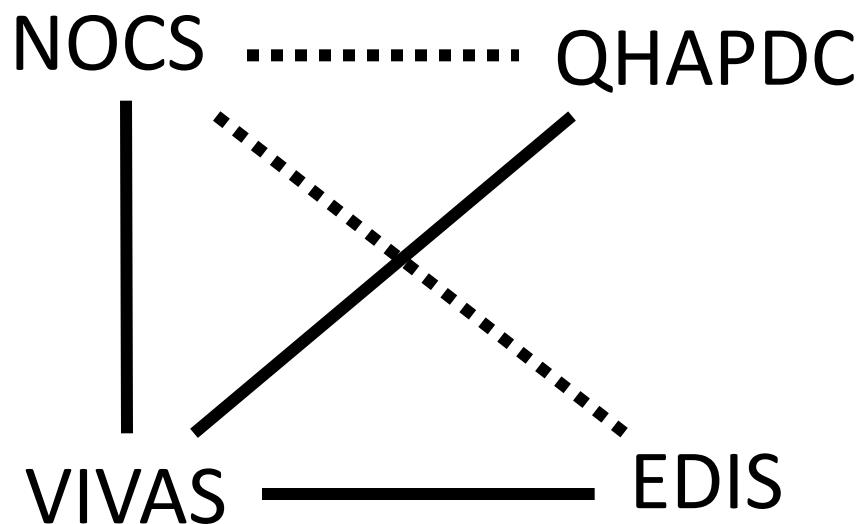


# Varicella VE study

## Aim

- Assess the impact and effectiveness of a single dose of varicella vaccine (VV or MMRV) in Queensland

# Varicella study data linkage



## Linked datasets:

1. "NOCS-VIVAS"
2. "QHAPDC-VIVAS"
3. "EDIS-VIVAS"

# Expected outcomes and benefits of varicella research

- novel results on persisting VE for single dose of vaccine in Australia from a population based study
- evidence base for decision making about the publicly funded varicella vaccination program, including:
  - providing evidence on which to compare the change in schedule to MMRV vaccine given at 12 months of age, and
  - inclusion of a 2nd dose of varicella vaccine into the National Immunisation Program
- by supporting an evidence based vaccination program, contribute to high uptake of effective vaccines, and reduction in varicella morbidity

# Pertussis (whooping cough) studies: aims

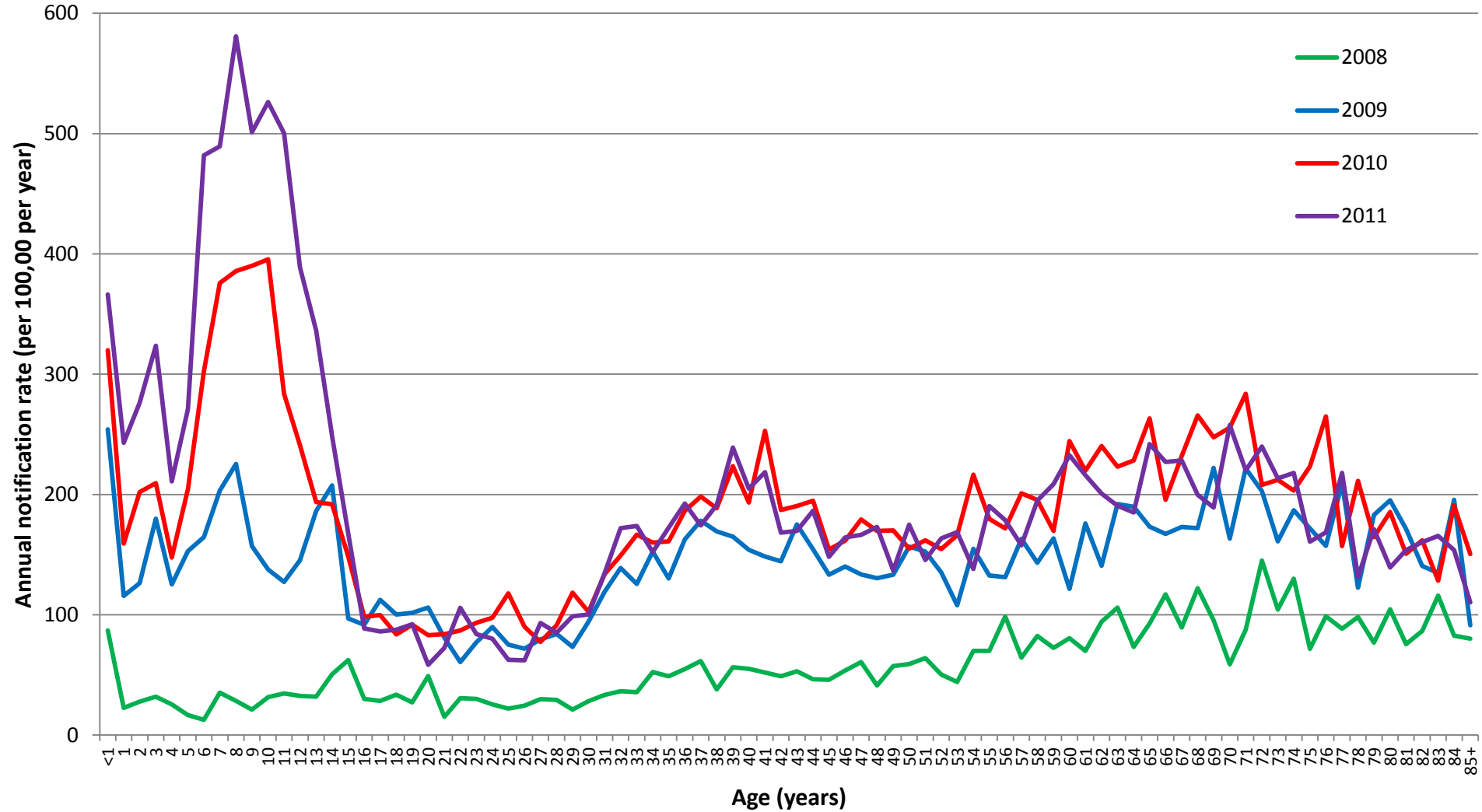
## Study 1:

- Compare the effectiveness of whole-cell pertussis versus acellular pertussis vaccine

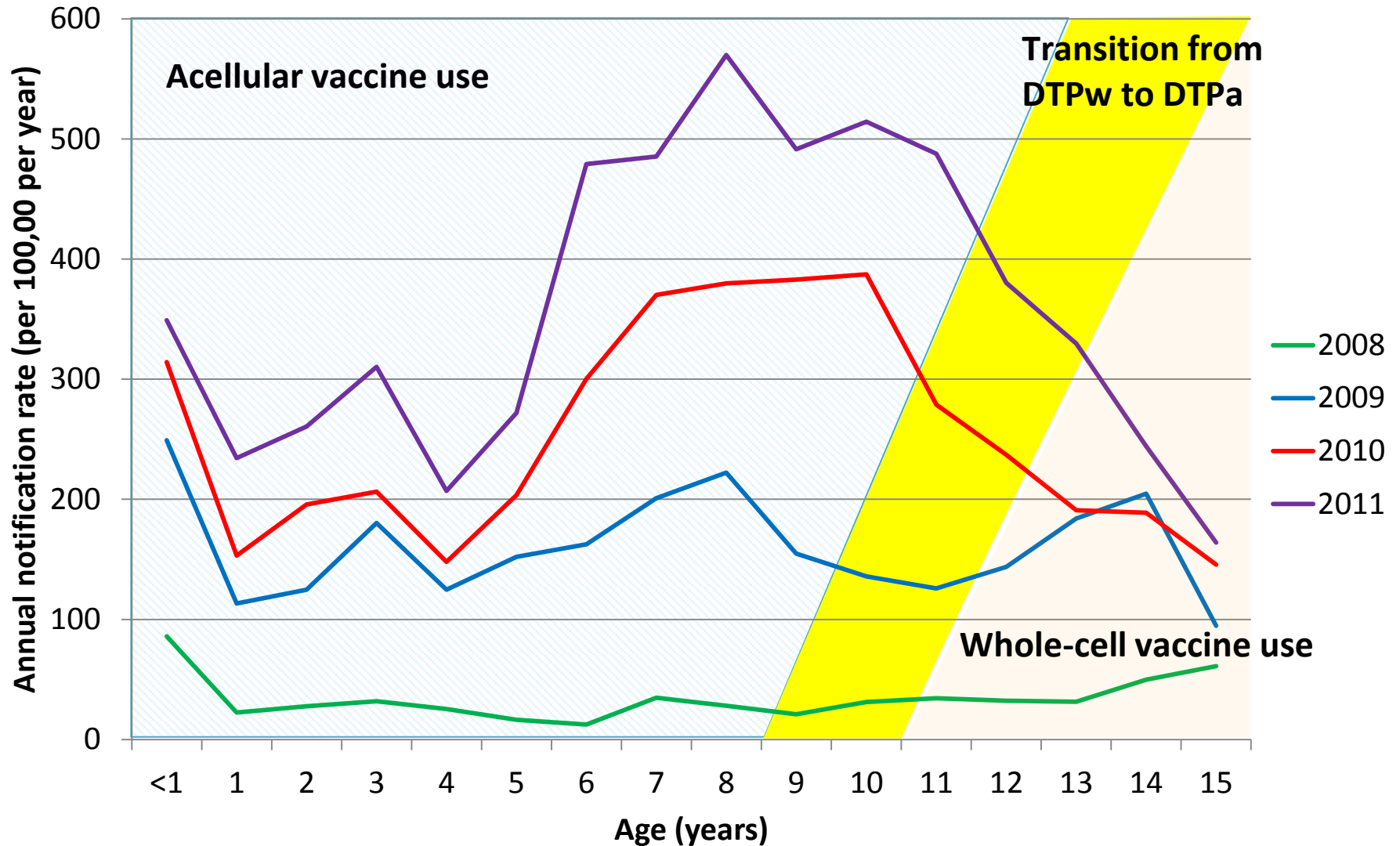
## Study 2:

- Assess the absolute effectiveness of acellular pertussis vaccine

# Age-specific pertussis notification rates, QLD, 2008-2011



# Age-specific pertussis notification rates, QLD, 2008-2011



# Pertussis study 1: methods

- Linked pertussis notification (NOCS) and vaccination records (VIVAS)
- Inclusion criteria:
  - born in 1998
  - $\geq 3$  doses of pertussis-containing vaccine  $< 1$  year of age
  - QLD vaccine service provider

# Pertussis study 1: methods

Children analysed by number and order of DTPw doses <1 year, during 2009-2011

- 3+ DTPw only
- 3+ DTPa only
- mixed-course 3+ doses DTPw/DTPa
  - 1 dose DTPw in 3+ dose course
    - DTPw as 1<sup>st</sup> dose
    - DTPa as 1<sup>st</sup> dose
  - 2+ doses of DTPw in 3+ dose course
    - DTPw as 1<sup>st</sup> dose
    - DTPa as 1<sup>st</sup> dose



# Pertussis study 1: results

- Denominator:
  - 40,694 (69.9%) of 58,233 children born in 1998 with a VIVAS record included in analysis
- Cases:
  - 242 individuals notified as pertussis cases 2009-2011
  - 2 cases had second notifications - excluded

# Counts, annual incidence-rates/ratios for pertussis notifications in 2009-2011 for children born in 1998

Primary-course	Notifications (count)	Average annual incidence-rate <sup>a</sup>	Incidence-rate ratio (95% CI)
<b>Pure course</b>			
DTPa primary-course (n=9,827)	110	373.1	3.29 (2.44, 4.46)
DTPw primary-course (n=22,956)	78	113.3	reference
<b>Mixed course</b>			
1 <sup>st</sup> dose DTPa (n=978)	12	409.0	3.61 (1.79, 6.67)
1 <sup>st</sup> dose DTPw (n=6,933)	42	201.9	1.78 (1.20, 2.63)
<b><i>Mixed course by number of DTPw</i></b>			
<b><i>1 dose of DTPw only</i></b>			
1 <sup>st</sup> dose DTPa (n=549)	6	364.3	3.22 (1.15, 7.32)
1 <sup>st</sup> dose DTPw (n=2,501)	20	266.6	2.35 (1.36, 3.89)
<b><i>2+ doses of DTPw</i></b>			
1 <sup>st</sup> dose DTPa (n=429) <sup>b</sup>	6	466.2	4.12 (1.47, 9.37)
1 <sup>st</sup> dose DTPw (n=4,432) <sup>c</sup>	22	165.5	1.46 (0.87, 2.37)

<sup>a</sup> Rate per 100,000 per year

<sup>b</sup> Only 2 children had 3 doses of DTWP ≤12 months of age

<sup>c</sup> Only 40 children had 3 doses of DTWP ≤12 months of age

# Conclusions and possible explanations

- Infant priming with DTPw associated with lower risk of pertussis than priming with DTPa only, more than a decade following primary vaccination
- Most important factor may be the first vaccine received - recent evidence from Oregon, USA, concurs with our findings
- Different immune responses from acellular and whole-cell priming
- Linked epitope suppression
  - initial exposure “locks in” the immune response to certain epitopes,
  - inhibits response to other linked epitopes on subsequent exposure<sup>1</sup>

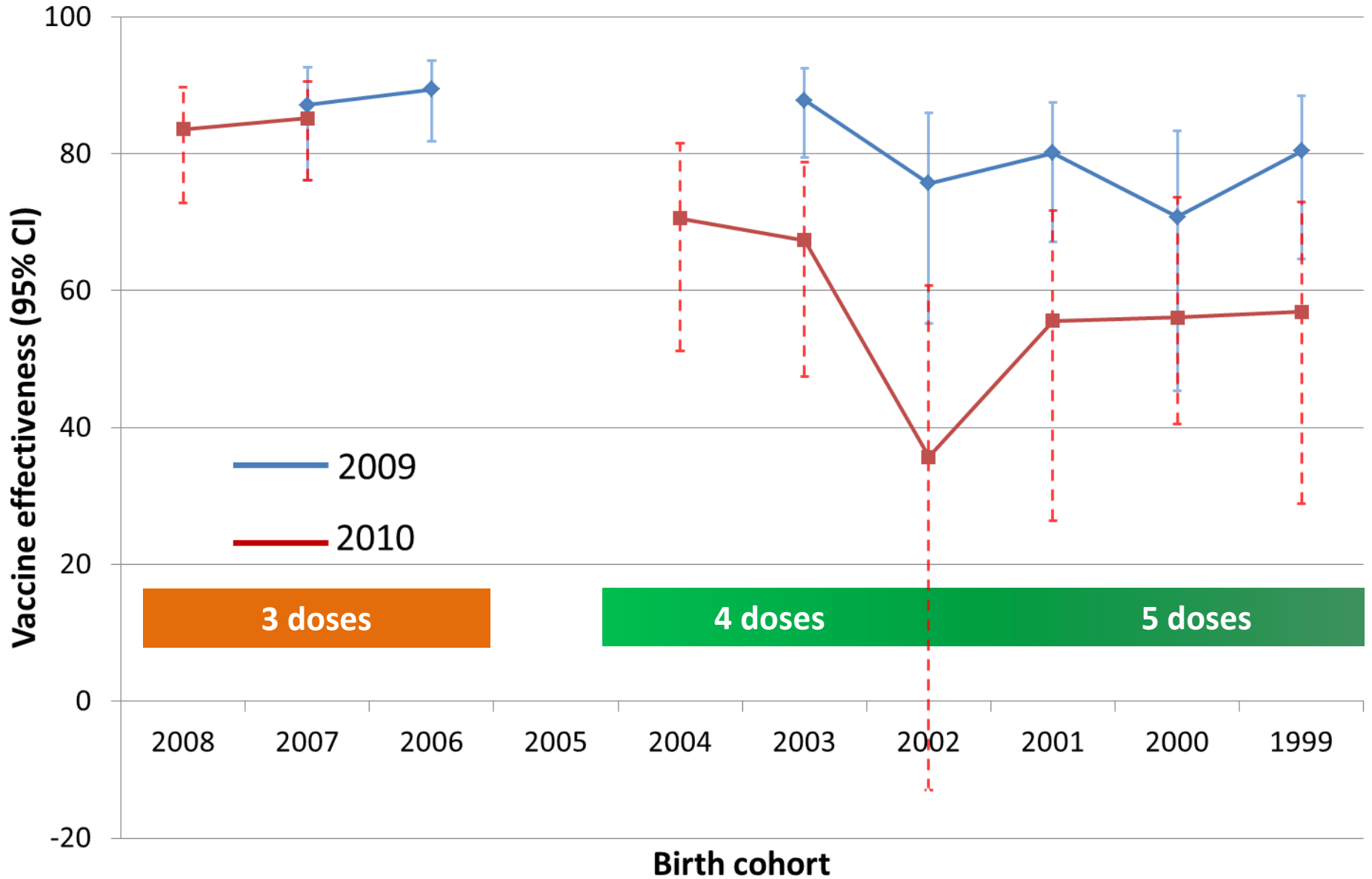
1. Cherry JD et al. Antibody response patterns to *Bordetella pertussis* antigens in vaccinated (primed) and unvaccinated (unprimed) young children with pertussis. Clin Vaccine Immunol. 2010;17(5):741-747.

## Pertussis study 2: methods

- Linked pertussis notification (NOCS) and vaccination records (VIVAS)
- Screening method:

$$VE = \left( 1 - \left( \frac{PCV}{(1-PCV)} \times \frac{(1-PPV)}{PPV} \right) \right) \times 100$$

# Pertussis VE against notification, 2009 and 2010, QLD



# Discussion and conclusions

- Although less protective than whole-cell vaccine, acellular vaccine provided very good protection for young children against notification in 2009/2010
- Overall, enduring high - moderate level of protection in older children against notification in 2009/2010
- Why lower VE estimates in 2010?
  - PCR detection of milder illness against which vaccine is less effective?
  - True decrease in effectiveness?

# Outcomes and benefits of pertussis research

- Improved understanding of current pertussis epidemiology and vaccine effectiveness both nationally and internationally
- Results shared in peer reviewed literature

# Hepatitis B study: aims

- Describe the epidemiology of hepatitis B infection and hepatitis B vaccination coverage in Queensland
- Assess hepatitis B neonatal post-exposure prophylaxis/prevention program:
  - completeness in delivering hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine birth dose to infants born to hep B +ve mothers
  - completeness of the infant hep B vaccination course among children born to B +ve mothers
  - number of children receiving serological testing through Pathology Queensland, of children born to hep B +ve mothers, by vaccination status
  - incidence of hep B infection among children born to hep B +ve mothers and fathers, by receipt of HBIG and/or vaccine,
  - incidence of vaccine failures, program failures or missed opportunities

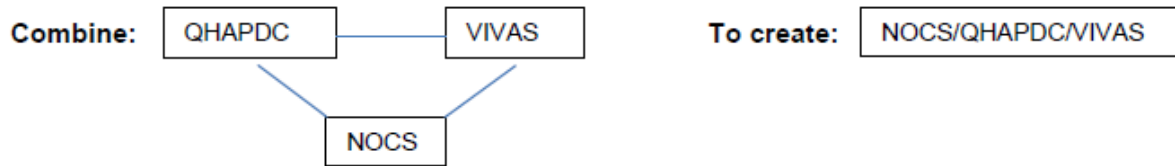


# Hep B study: methods

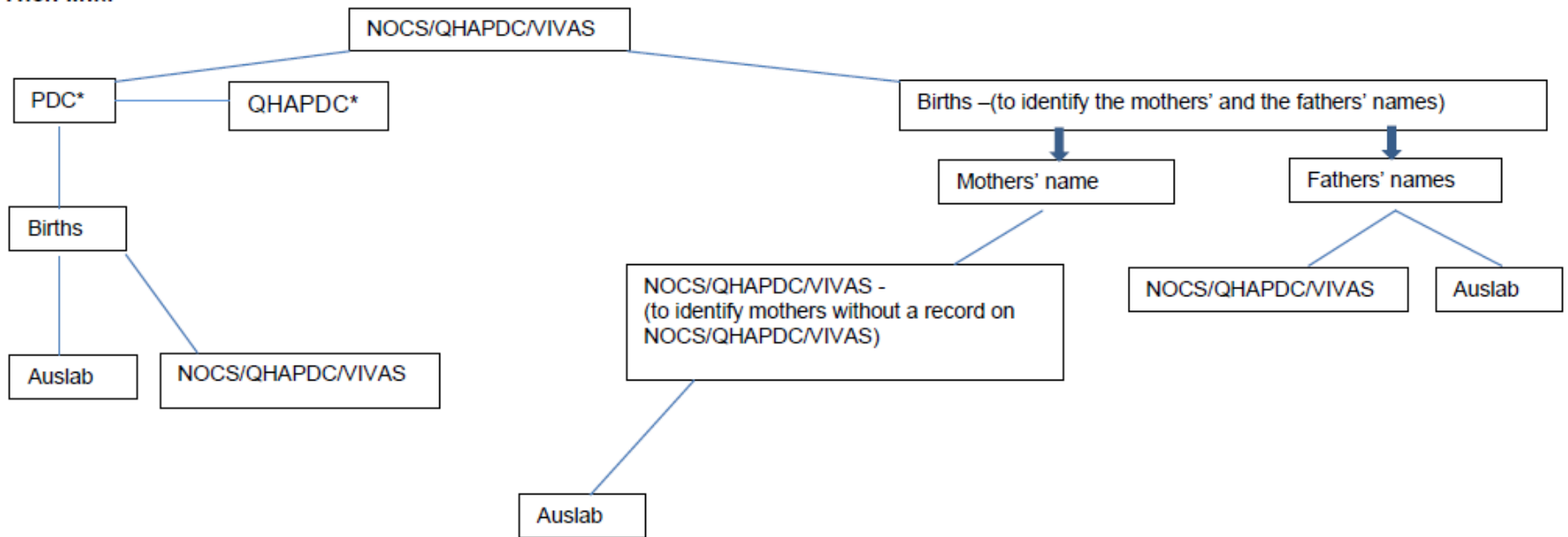
## Data linkage by the Health Statistics Unit:

- NOCS
- VIVAS
- QHAPDC
- Auslab
- Perinatal data collection (PDC)
- Births, deaths and marriages (BDM)

# Requested data linkage



**Then link:**



\* PDC with unnamed data (prior to 1 July 2007 for public, from 1 July 2007 for private) to be linked to QHAPDC to obtain mother's name & address

# Expected benefits from data linked vaccine research

- Efficient use of routinely collected data to answer public health questions and evaluate large, expensive publicly funded vaccination programs
- Studies are providing previously unavailable results on vaccine effectiveness in Australia (sometimes internationally relevant) and contribute to vaccine program evaluation
- Provide evidence base to inform decision making related to vaccine programs and support improvements in vaccination programs for public health benefit

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