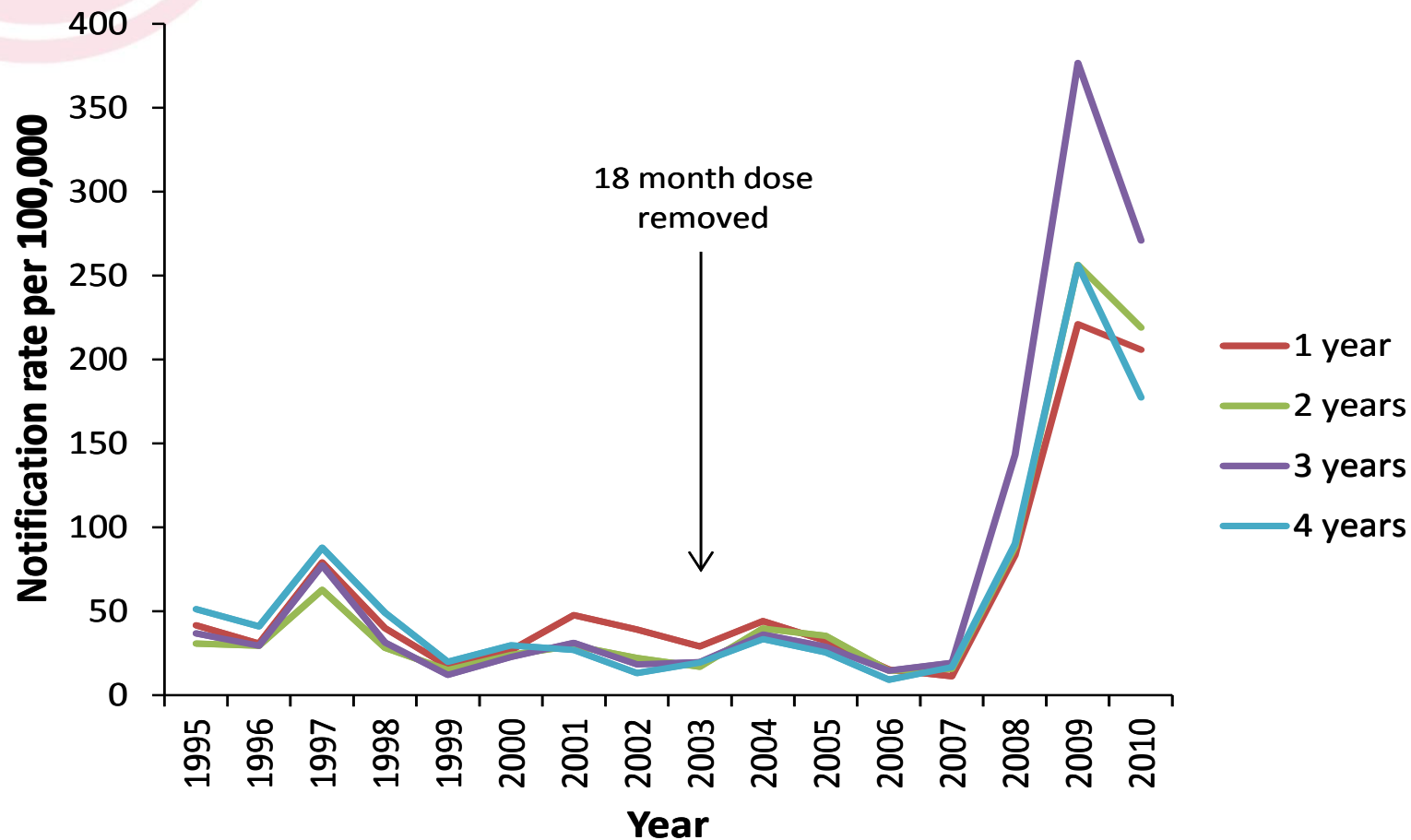


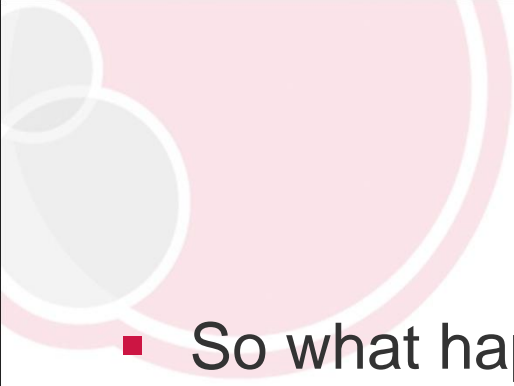
# **Pertussis vaccine effectiveness in Australia**

**Dr Helen Quinn and Prof. Peter McIntyre**

# Background

Pertussis notification rates in 1-4 year olds, 1995-2010



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- So what happened?
    - 18 month dose removal, something else
  
  - Seeking an answer
    - descriptive analysis
    - VE using screening method
    - VE by a case control study

# Descriptive cohort analysis

Age group	Rate* before dose removal†	Rate* after dose removal‡	IRR (95% CI)	Fold change in IRR
→ 6–17 months	56	77	1.4 (1.2–1.5)	1.0
→ 2 years#	22	78	3.5 (2.9–4.1)	2.5
→ 3 years#	23	107	4.8 (4.0–5.7)	3.4 ←
4 years	19	73	4.0 (3.3–4.8)	2.9
5 years	22	61	2.8 (2.3–3.3)	2.0

\* Notification rate per 100,000

† Period before 18-month dose removal: 1 January 2001 – 31 August 2003

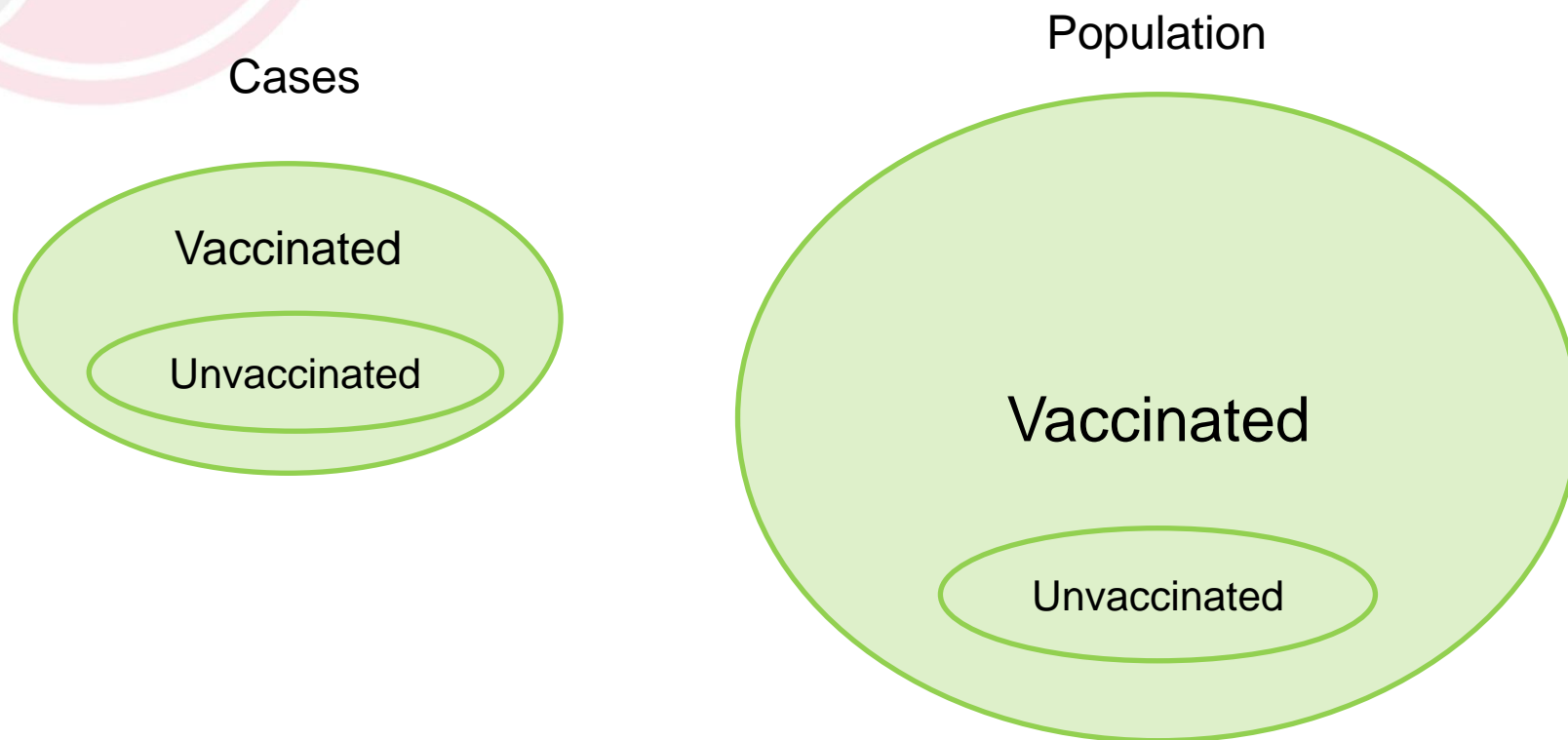
‡ Period after 18-month dose removal: 1 January 2004 – 31 December 2009

IRR comparing the notification rates before and after dose removal, for each age group

|| Compared to 6–17-month olds as the reference group with this IRR set to 1.0

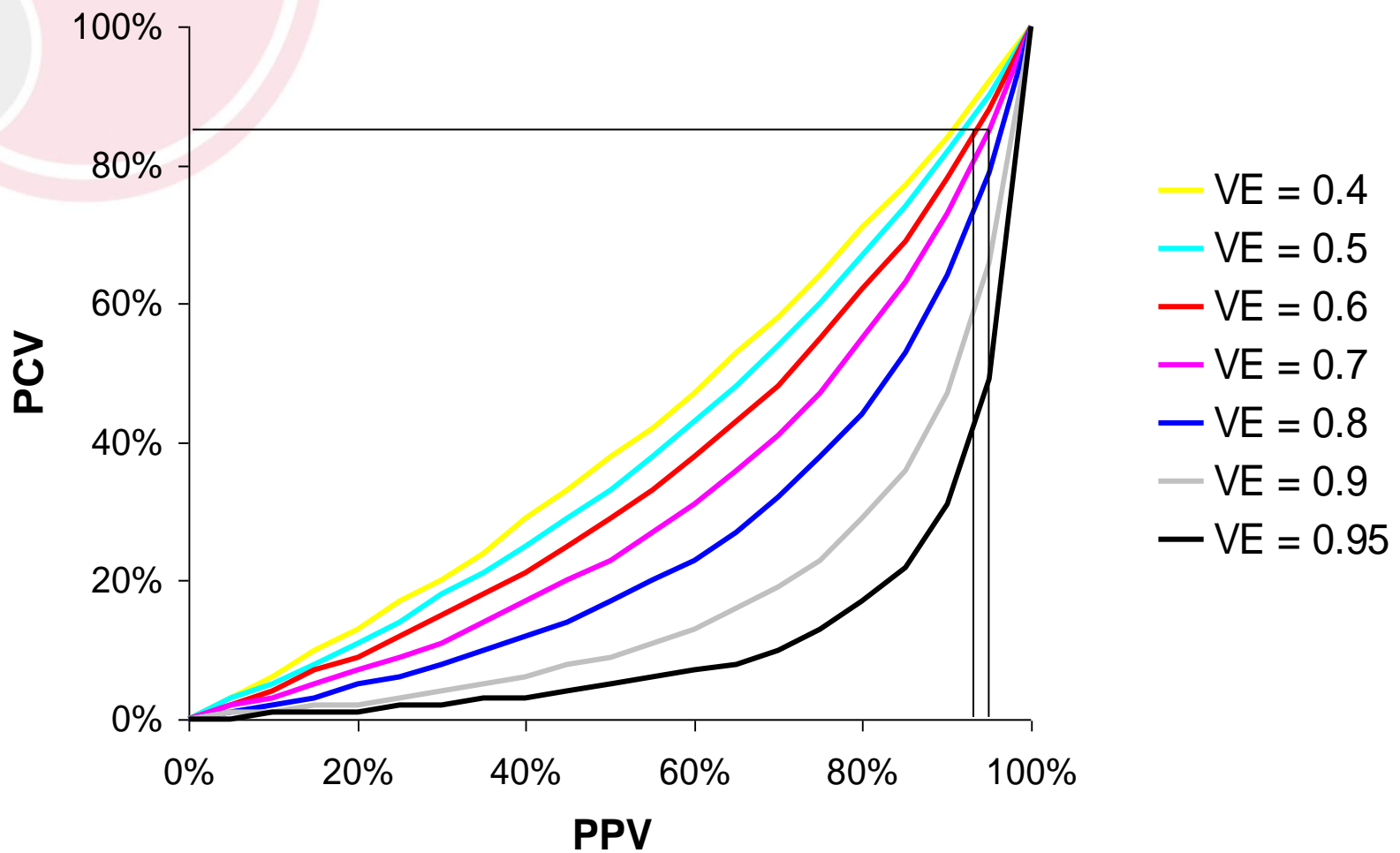
# For the period after dose removal, 3% of 2 year olds and 19% of 3 year olds were eligible for an 18 month dose

# VE using the screening method

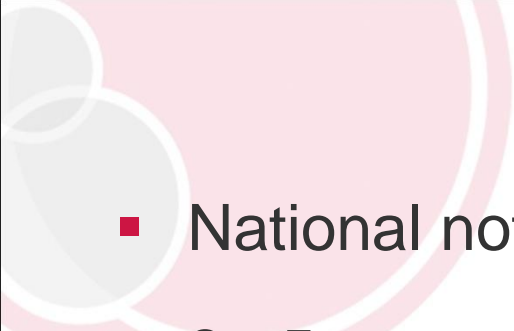


■  $(\text{---}) (\text{---})$

PCV = Proportion of cases vaccinated  
PPV = Proportion of population vaccinated



Source: Orenstein et al. Bull World Health Organ 1985; 63:1055-1068.

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- National notification data Jan 2001 - Dec 2009
  - 2 - 5 year olds
  - Limited to fully vaccinated field (not doses), excluded partially vaccinated
  - Eligibility for 18 month dose based on DOB (<1 Mar 2002)
  - Population vaccine coverage at 2 years from Australian Childhood Immunisation Register (ACIR)

# Vaccine effectiveness, by age

18 month booster	Age (years)	VE (95% CI)#
Yes	2	88 (81.6–92.1)
	3	89 (85.0–92.1)
	4	87 (82.0–91.2)
	5	90 (85.4–92.4)
No	2	78 (73.0–81.6)
	3	72 (66.4–76.7) ←
	4	86 (82.9–88.2)
	5	87 (84.0–89.6)

# Vaccine effectiveness, by age, during the 2001 and 2009 epidemics

Year	Age (years)	VE (95% CI)#
2001	2	89 (75.4–95.4)
	3	93 (85.9–96.1)
	4	73 (11.4–91.9)
	5	89 (77.0–94.3)
2009	2	75 (67.2–80.5)
	3	62 (50.6–70.3) ←
	4	81 (75.4–84.9)
	5	80 (72.6–85.2)

# Vaccine effectiveness, by vaccine type received

Primary series vaccine	Booster vaccine	VE (95% CI)#
DTPw	DTPw/DTPa*	91 (85.3–94.1)
DTPa	DTPa	87 (83.8–89.6)
DTPa	—	82 (79.7–83.3)

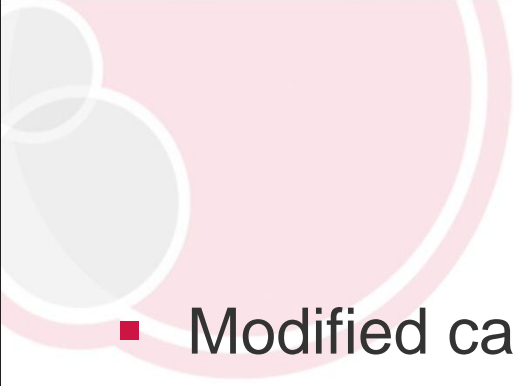
\* 12% had DTPw for their booster

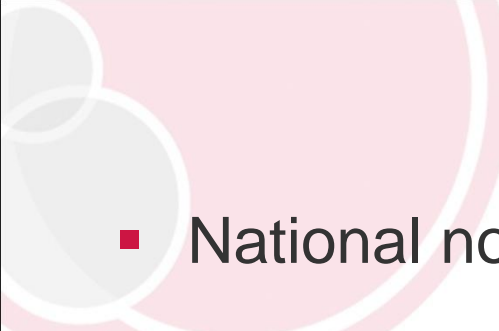
# VE using the case control method

- $$\left\{ \begin{array}{l} (—) \\ ( ) \end{array} \right\}$$

- Relative risk is approximated by the odds ratio in case control studies
- Conditional logistic regression models

ARV = Attack rate in vaccinated cases  
ARU = Attack rate in unvaccinated cases

- 
- Modified case control study
    - controls from ACIR
    - NCIRS de-identified line listing of enrolled children
    - **DOB**, sex, **state/territory**, postcode, **vaccine doses**, **vaccine dates**
    - No linkage to disease data
      - potential limitation?

- 
- National notification data Jan 2005 - Dec 2009\*
  - 2 month - 3 year olds
  - Dose based analysis
  - Hospitalised and non-hospitalised
  - Controls
    - matched by jurisdiction and +/- 1 day from DOB
    - ratio 1:4
    - only doses prior to case onset considered valid

\* ACT not included. WA cases with onset January 2006 - December 2009, TAS cases with onset January 2007 - December 2009.

# Vaccine effectiveness in infants, aged 2-11 months

Age (months)	Doses*	Not hospitalised VE (95% CI)#	Hospitalised VE (95% CI)#
2–5	1	48 (24.1–64.5)	56 (42.7–66.2)
	2	61 (37.2–76.1)	87 (79.1–92.0)
6–11	3	64 (47.0–76.1)	82 (66.0–90.3)

\* Children who received 0 doses were used as the referent in the regression analysis

# CI denotes confidence interval

# Vaccine effectiveness in children, aged 1-3 years

Age (years)	Doses*	Not hospitalised VE (95% CI)#	Hospitalised VE (95% CI) #
1	3	76 (66.7–82.0)	84 (65.8–92.9)
2	3	70 (59.5–77.7)	—†
3	3	59 (46.1–68.9)	—†
2–3	3	64 (56.5–70.9)	49 (-16.7–77.5)

\* Children who received 0 doses were used as the referent in the regression analysis

# CI denoted confidence interval

† Small case numbers

# Discussion

- All 3 methods provided consistent results
- VE in the expected range within 2 years of birth
  - similar to trial based data<sup>1,2</sup>
- Evidence of decreased VE estimates in children from 2 years of age, consistent with waning immunity

1. Zhang L, et al. Cochrane Database of Systematic Reviews 2010.

2. Jefferson T, et al. Vaccine 2003;21:2003-14.

- Other observational studies

- 7 published<sup>1-7</sup>

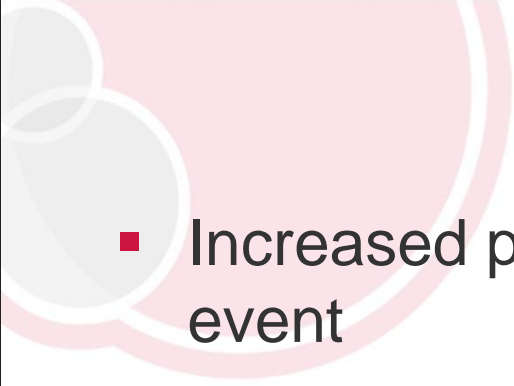
5 used screening method

Only 2 showed specific ages and vaccine type

Study	Vaccine type	Age	VE	Doses
1	DTPw (Australia)	2-4 years	85%	3 or 4
2	DTPw (UK)	3 years	86-93%	3
4	DTPw (Canada)	1-3 years	52% 81%	3 4

1. Torvaldsen S, et al. European J Epidem 2003;18:69-69.  
 2. Ramsay MEB, et al. Epidemiol Infect 1993;111:41-48.  
 3. Guris D, et al. J Inf Diseases 1997;176:456-63.  
 4. De Serres G, et al. Vaccine 2001;19:3004-8.

5. Rendi-Wagner P, et al. Vaccine 2006;24:5960-65.  
 6. Bisgard KM, et al. Pediatrics 2005;116:e285-e294.  
 7. Juretzko P, et al. CID 2002;35:162-167.

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- Increased pertussis in young children – a multifactorial event
    - lack of booster dose
      - lower VE estimates, waning immunity
    - acellular vaccines
      - lower VE than some whole cell pertussis vaccine
    - epidemic
      - ? increased identification of mild cases

# Where to from here?

*“there is a case for recommending a booster during the second year of life unless the epidemiology in a country provides compelling evidence that a booster is not needed until preschool”*

WHO Strategic Advisory Group of Experts on Immunization – Pertussis, 2010



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