Pertussis modelling

Contributions of natural, vaccine immunity to epidemiology

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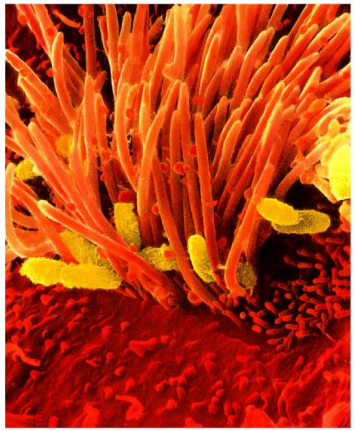
Pertussis: biology, epidemiology and prevention
Les Pensieres, Fondation Merieux Conference Centre, 11-13 November 2015

Overview

- Pertussis resurgence – Australia as a case study
- Modelling Australian pertussis trends
- Understanding the past, predicting the future
- Conclusions, context and next steps

Pertussis resurgence - background



- Resurgence of pertussis (whooping cough) observed recently in a number of developed countries
- Initial uncertainty re: ascertainment bias
- Associated infant deaths in US, UK indicate true increase

- How might vaccination have contributed to risi disease?
  - Waning immunity, loss of boosting
  - Lower effectiveness of new vaccines
  - Changes in bacterial population

Reported NNDSS pertussis cases: 1922-2013*

*2013 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service

Australia as a case study – in context

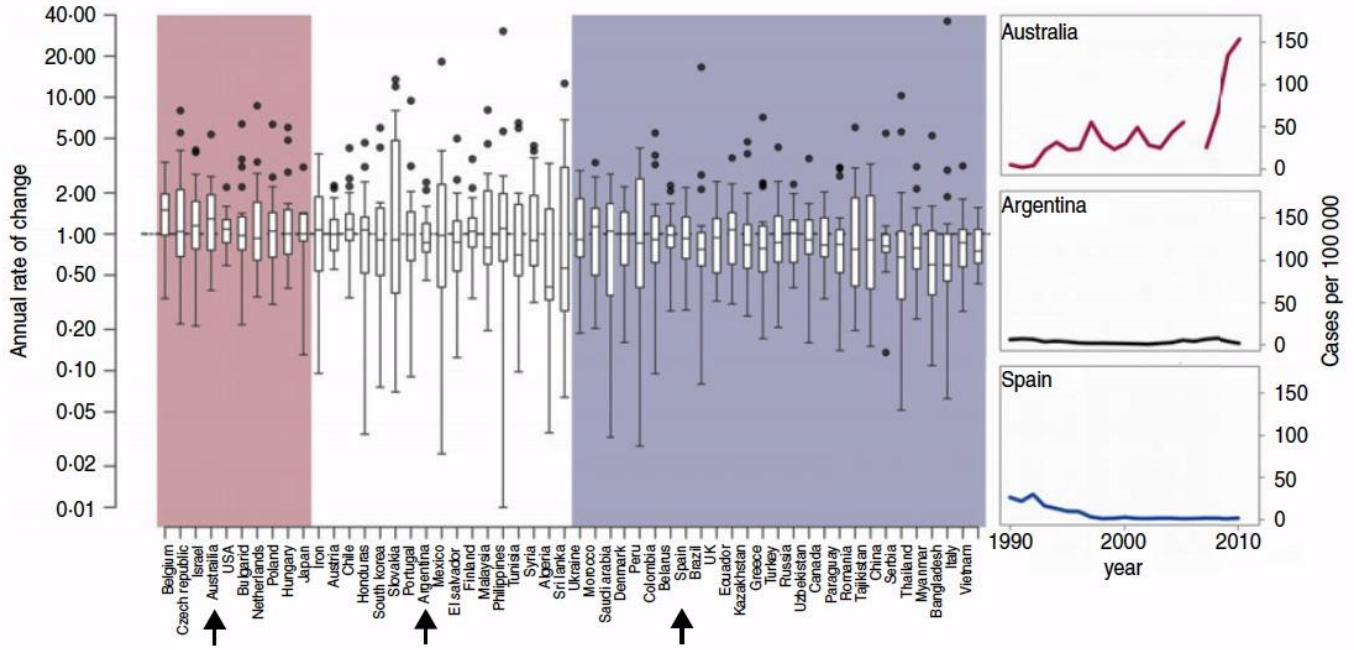
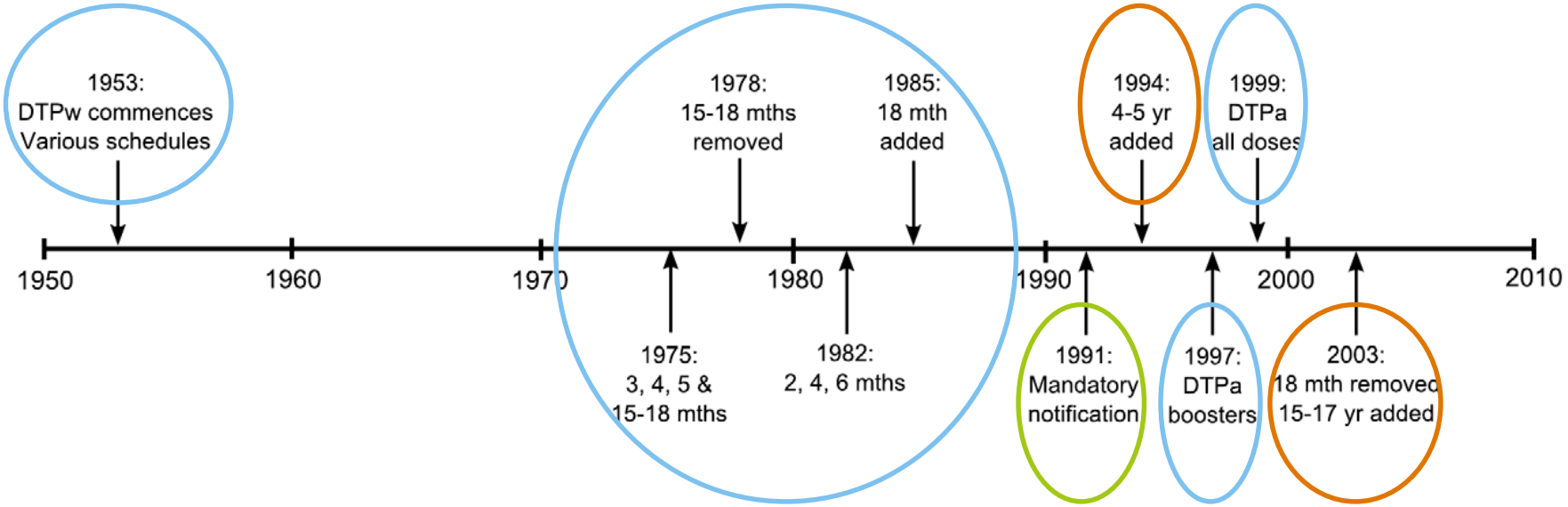


Fig. 1 [*colour online*]. Boxplot of annual rates of change of pertussis incidence between 1990 and 2010 for countries that met our inclusion criteria: mean DTP3 vaccine uptake of >80% between 1990 and 2010; populations of >5 million individuals; and >80% complete case count records for this time period. The pink area indicates countries with significantly positive trends in incidence based on Kendall's tau rank correlation ($P<0{\cdot}05$), white indicates countries for which trends were not significant, and blue indicates countries with significantly decreasing trends. Note that rates of change are plotted on a log scale. Representative time-series of countries with increasing (Australia), stationary (Argentina), and decreasing (Spain) trends are shown on the right.

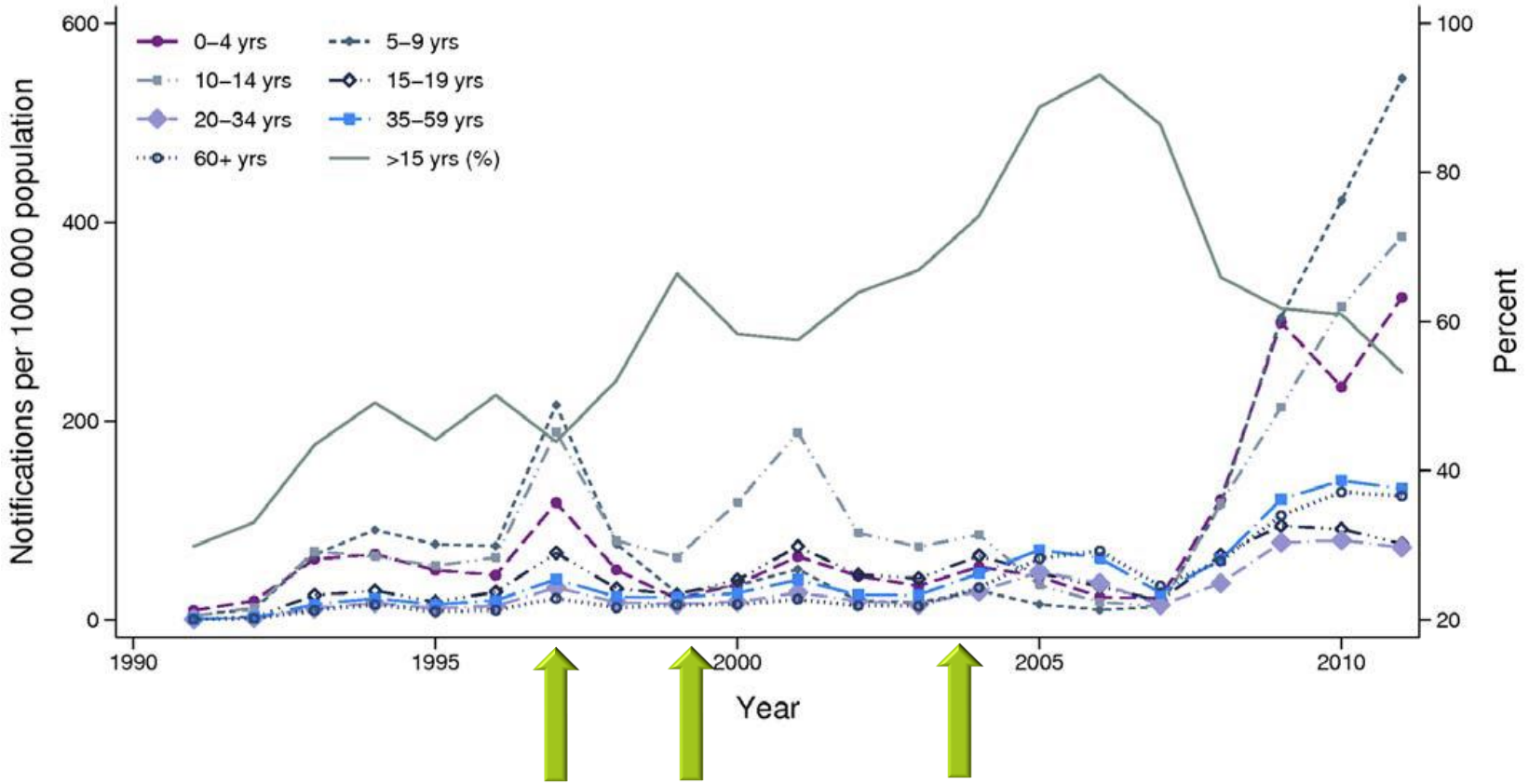
Jackson & Rohani, Epidemiol Infect 2014

Use of pertussis vaccines in Australia



Campbell et al PLoS ONE 2012

Pertussis resurgence in Australia



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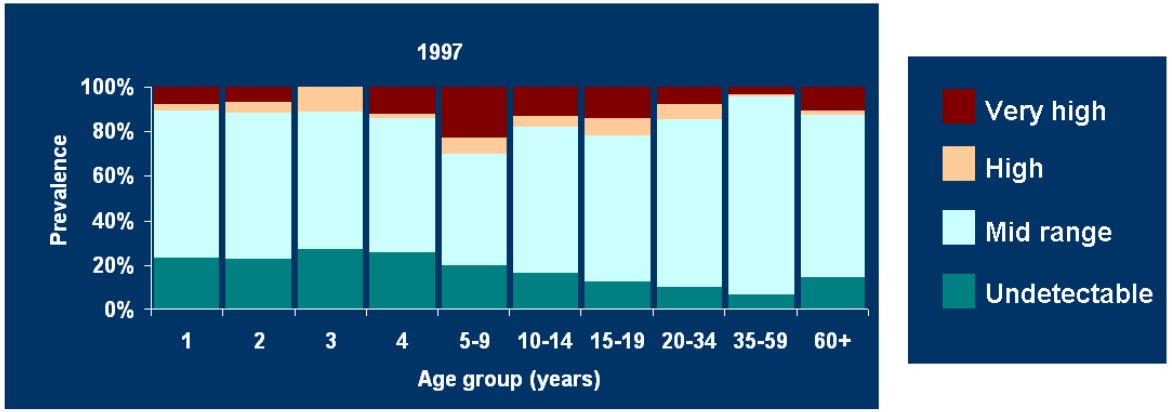
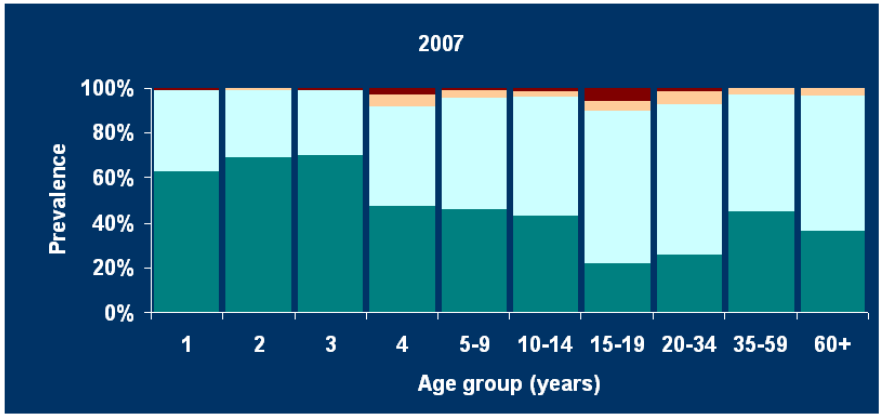
Australian pertussis seroepidemiology

Collected during and shortly after epidemic



Collected in trough before large epidemic



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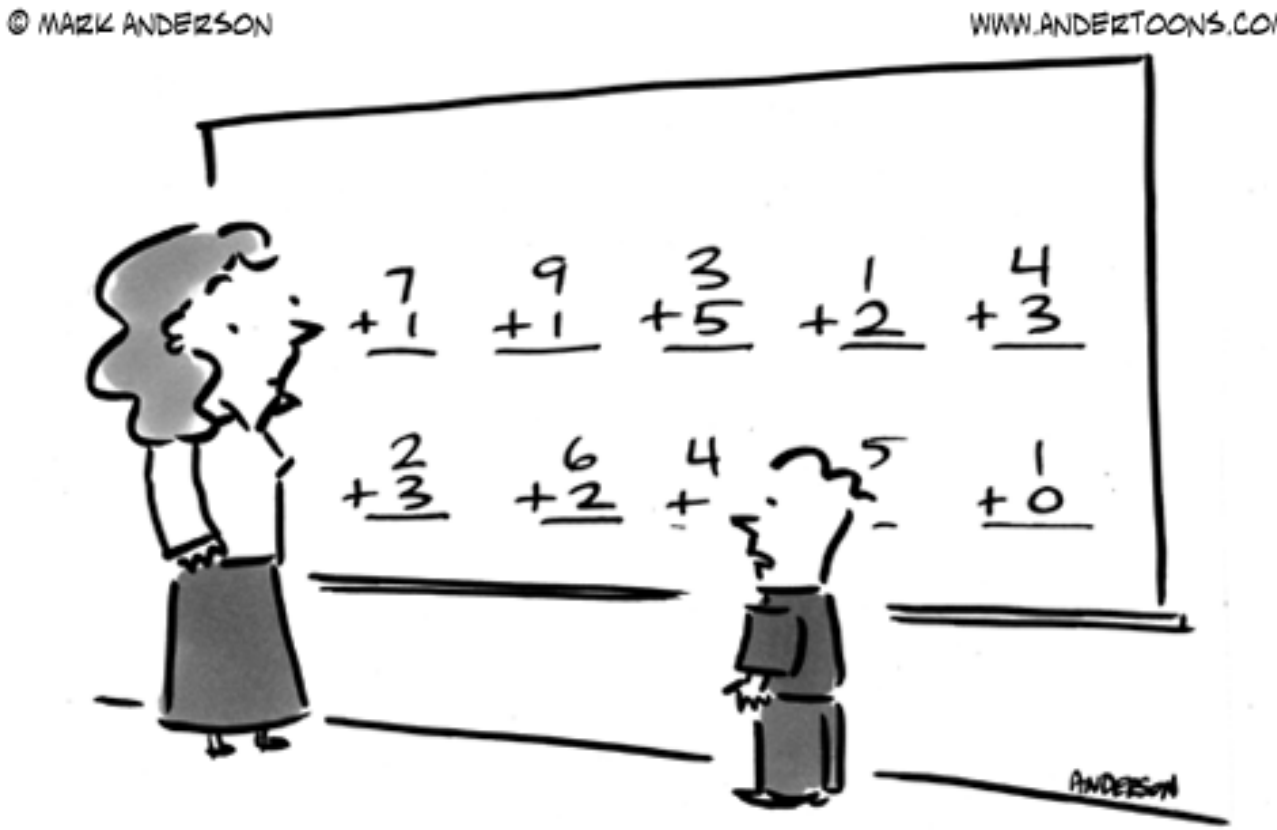
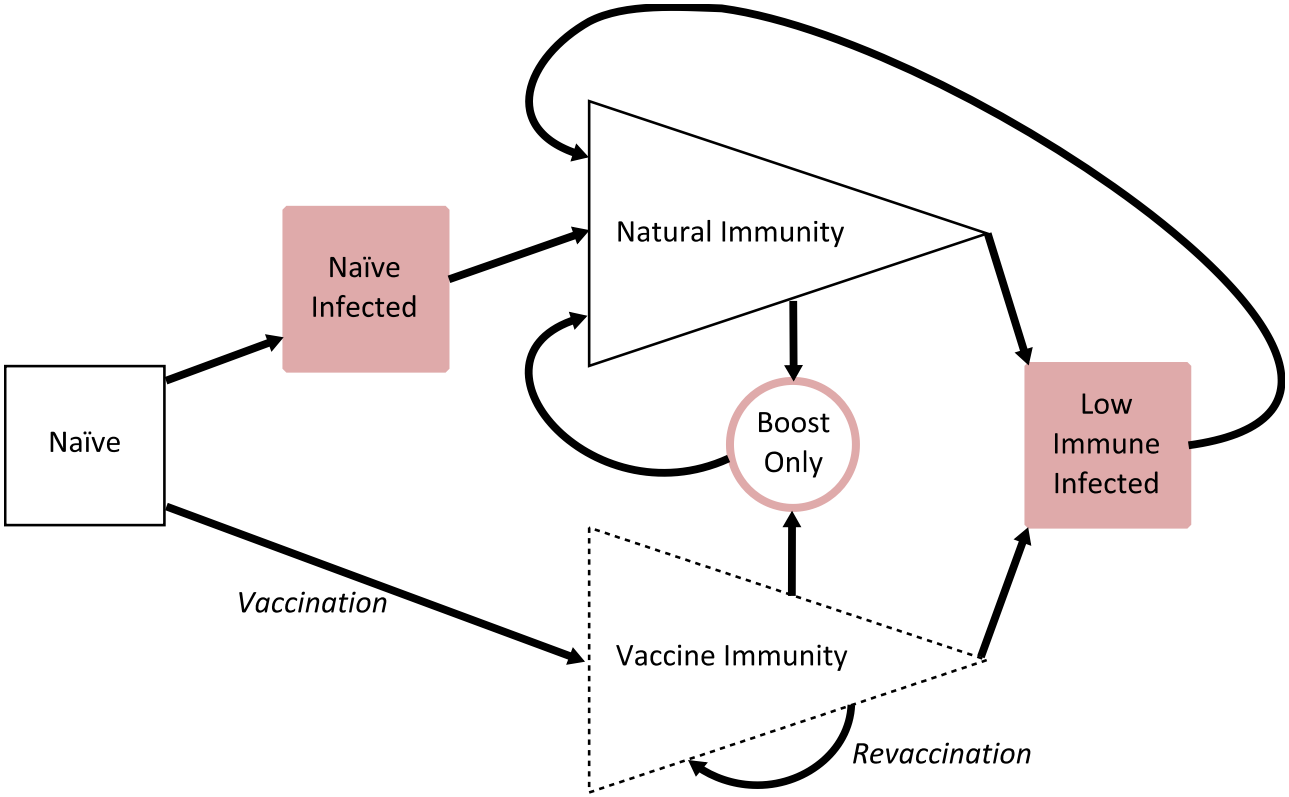
Modelling Australian pertussis trends



"All I'm saying is we plug these into Excel, let it do its thing, and then we can all play until lunch!"

Vaccine/natural immunity interaction



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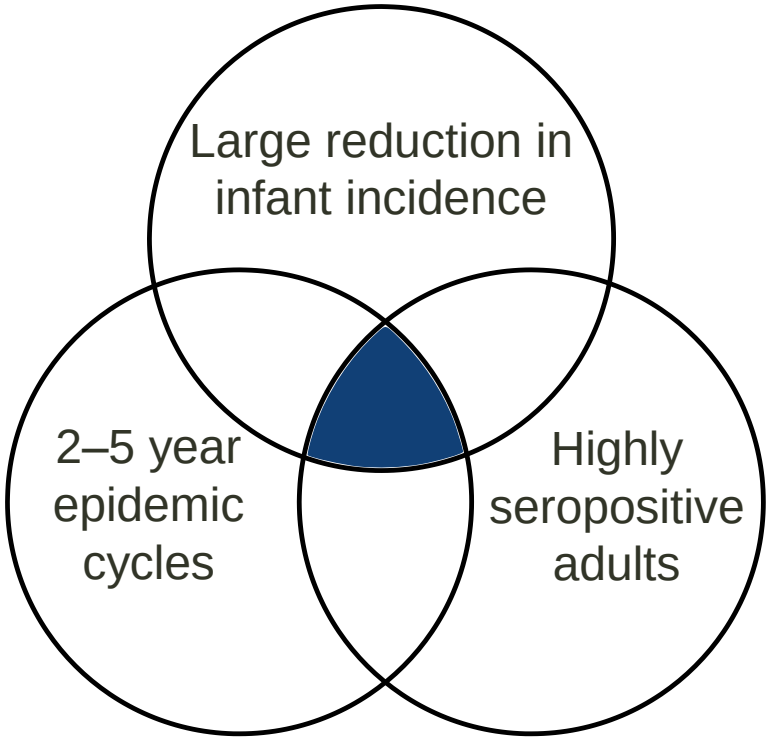
Pertussis model attributes

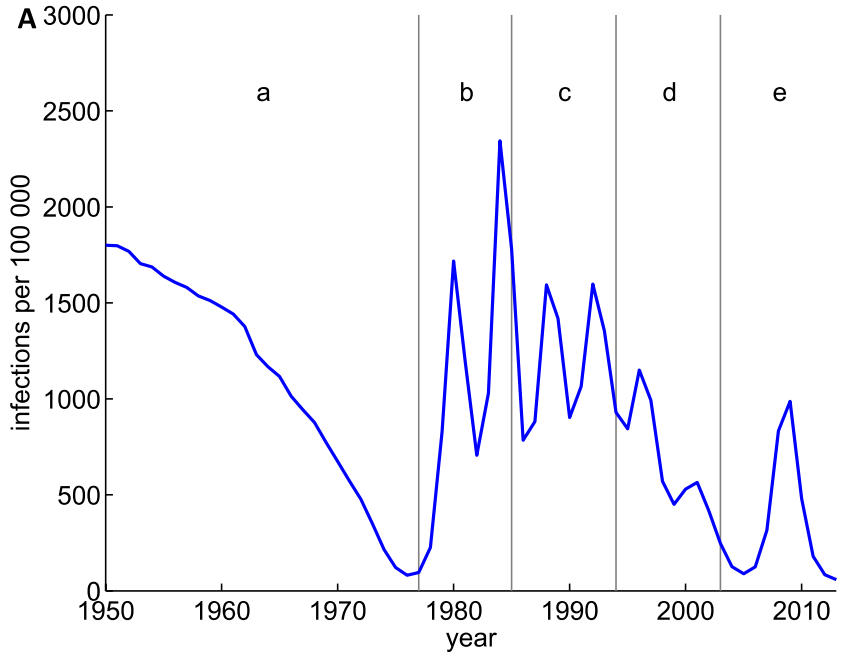
- Compartmental - susceptible, infected, recovered
- Age-structured – relates to disease risk, vaccine timing
- Dynamic – prevalence drives incidence in susceptibles
- Model of *infection,* as opposed to symptoms or disease
- Model states are associated with pertussis AB levels: used as a marker of infection, vaccination

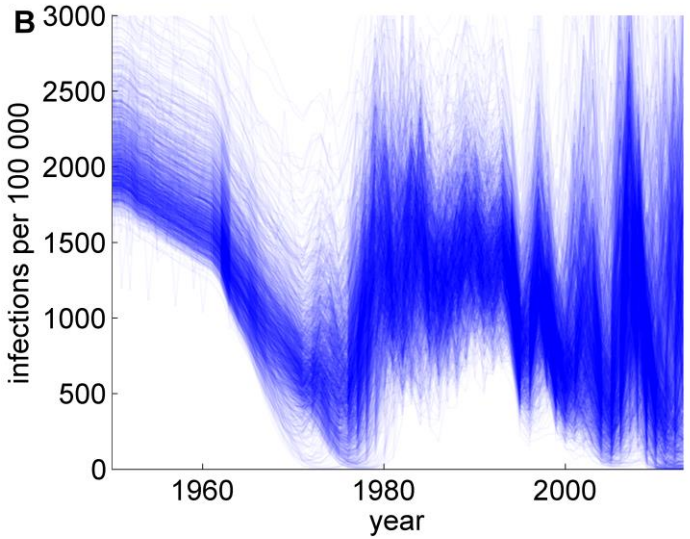
Model simulation and selection

- Model parameters varied simultaneously
  - Plausible parameter distributions based on local data, literature review
  - 200,000 parameter combinations tested
  - Qualitative match to 3 criteria *and* large epidemic post removing toddler dose



Selected simulations (n=2,321)





**Naïve and low immune infections*

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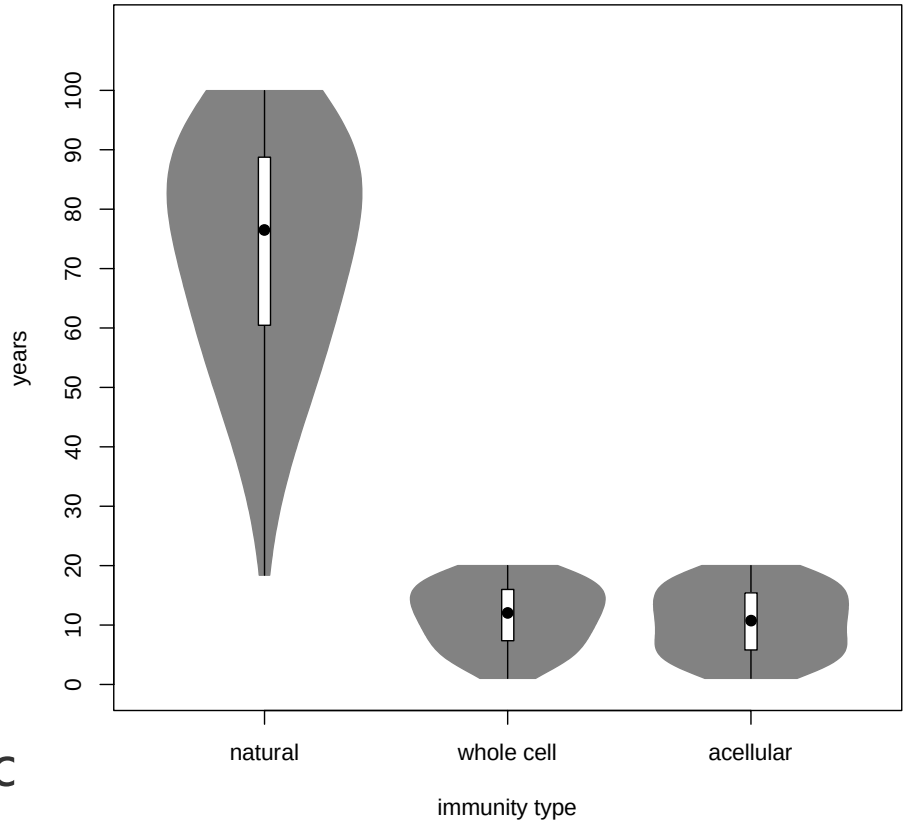
Understanding the past

- Natural immunity duration is far longer than either vaccine
- Coverage fluctuations open up opportunity for outbreaks
- Cycles of immunity and waning post outbreak have implications decades later
- Schedule change has opened up susceptible 'pockets' to fuel the most recent epidemic



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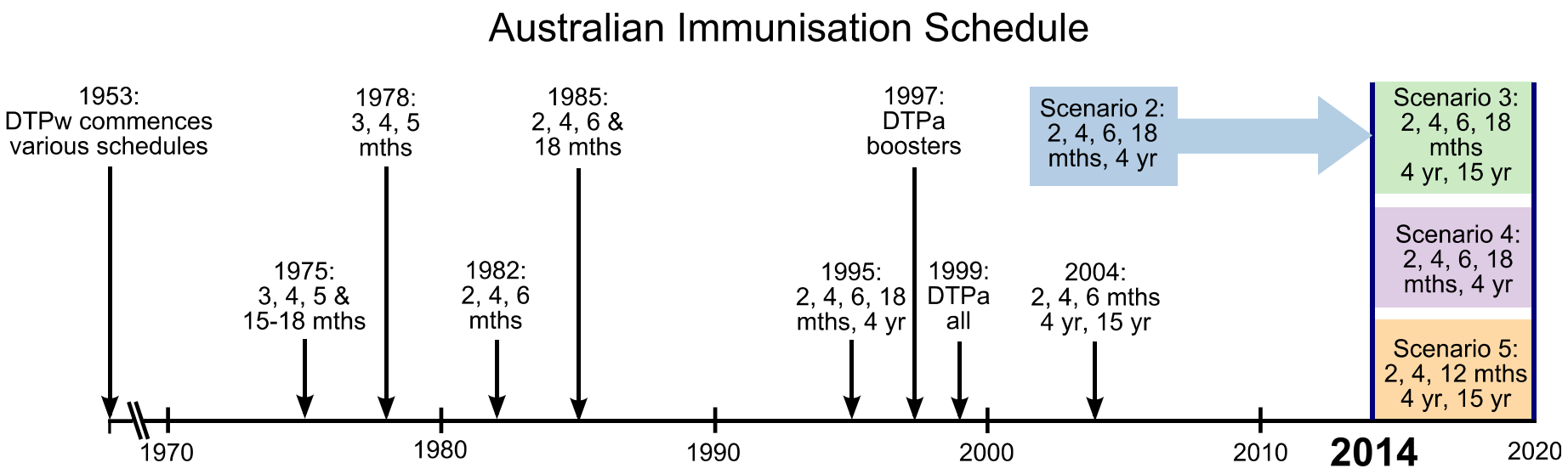
Looking backwards and forwards



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Impact of schedule changes

	median incidence difference per year per 100,000 (99% CI)			
	Historical 2003-2013	Future 2014-2020		
age	With 18mth dose/ Without 15yr dose	Addition of 18mth dose	Replacement of 15yr dose with 18mth dose	Delay third dose to 12mth
< 8 wks	62 (28, 86)	-253 (-278, -223)	145 (115, 164)	-6 (-8, -5)
8 wks to < 1yr	9 (5,13)	-37 (-43, -33)	17 (14, 20)	30 (26, 35)
18mth to <4yr	-282 (-313, -247)	-337 (-366, -311)	-276 (-303, -247)	-15 (-17, -13)
15yr to <30yr	98 (91, 103)	-21 (-23, -19)	160 (154, 168)	-0.7 (-0.7, -0.6)

**Best strategy: 43% reduction toddlers, 8% reduction infants*

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Conclusions

- Multiple factors have contributed to pertussis resurgence in Australia and elsewhere
- Ongoing transmission of pertussis seems inevitable
- A six-dose vaccine schedule (reintroducing the toddler booster) is expected to have some impact on transmission, and hence disease
- Additional mitigation strategies are needed to protect infants at highest risk of severe outcomes

Context and next steps

- Other groups have used models to consider the drivers of pertussis resurgence in their own context
  - Yoon Choi, Public Health England, UK
  - Manoj Gambhir, Centers for Disease Control, US
- WHO-supported model comparison exercise underway to assess model applicability to other data and settings
- Development of models of maternal immunisation approaches in household structured populations

Acknowledgements

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UNSW

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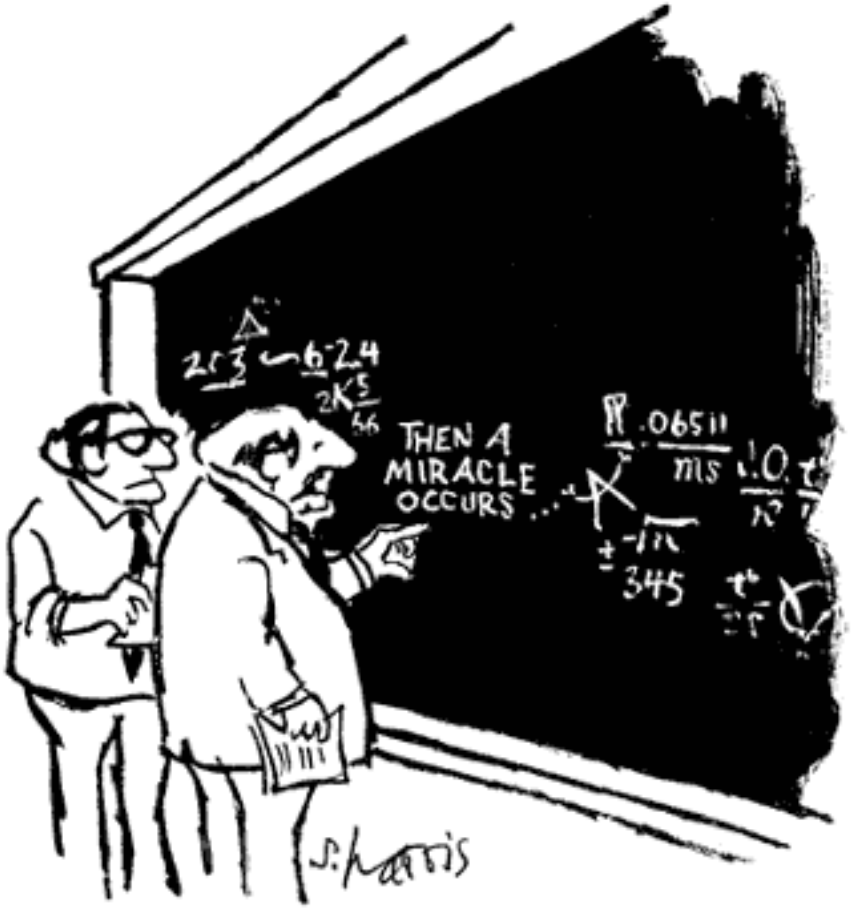

"I think you should be more explicit here in step two."

Thank you!

Any questions?