High Rate of Acellular Pertussis Vaccine Failure in Pre-Adolescents in a North American Outbreak

Maxwell A. Witt
Paul H. Katz, MD MPH
David J. Witt, MD

Background

- 2010 saw the largest epidemic of *B. pertussis* in California in more than 50 years
- Marin County was at the epicenter of the epidemic
- The impetus for this study was to identify the risks to unvaccinated children in a county with a high rate of Personal Belief Exemptions (PBE)
- The results addressed this target group but revealed significant limitations in durability of the current vaccine

Pertussis Vaccine, Background

- Acellular Pertussis Vaccine (aP) was introduced in 1991 and has been the sole available vaccine since 2002
- aP was licensed for adolescents and adults in 2005
- It has been suggested that the efficacy of aP may be less than whole cell pertussis vaccine (wP)
- The durability of aP has not been well-studied.

Zhang, L, et al, Acellular vaccines for preventing whooping cough in children, Cochrane Database of Systemic Reviews 2011, Issue 1

Methods

- KPMC, San Rafael is the sole source of care for 135,0000 persons and includes 40% of the Marin county, CA population
- Kaiser Permanente uses a fully electronic record which captures all visits, labs and hospitalizations

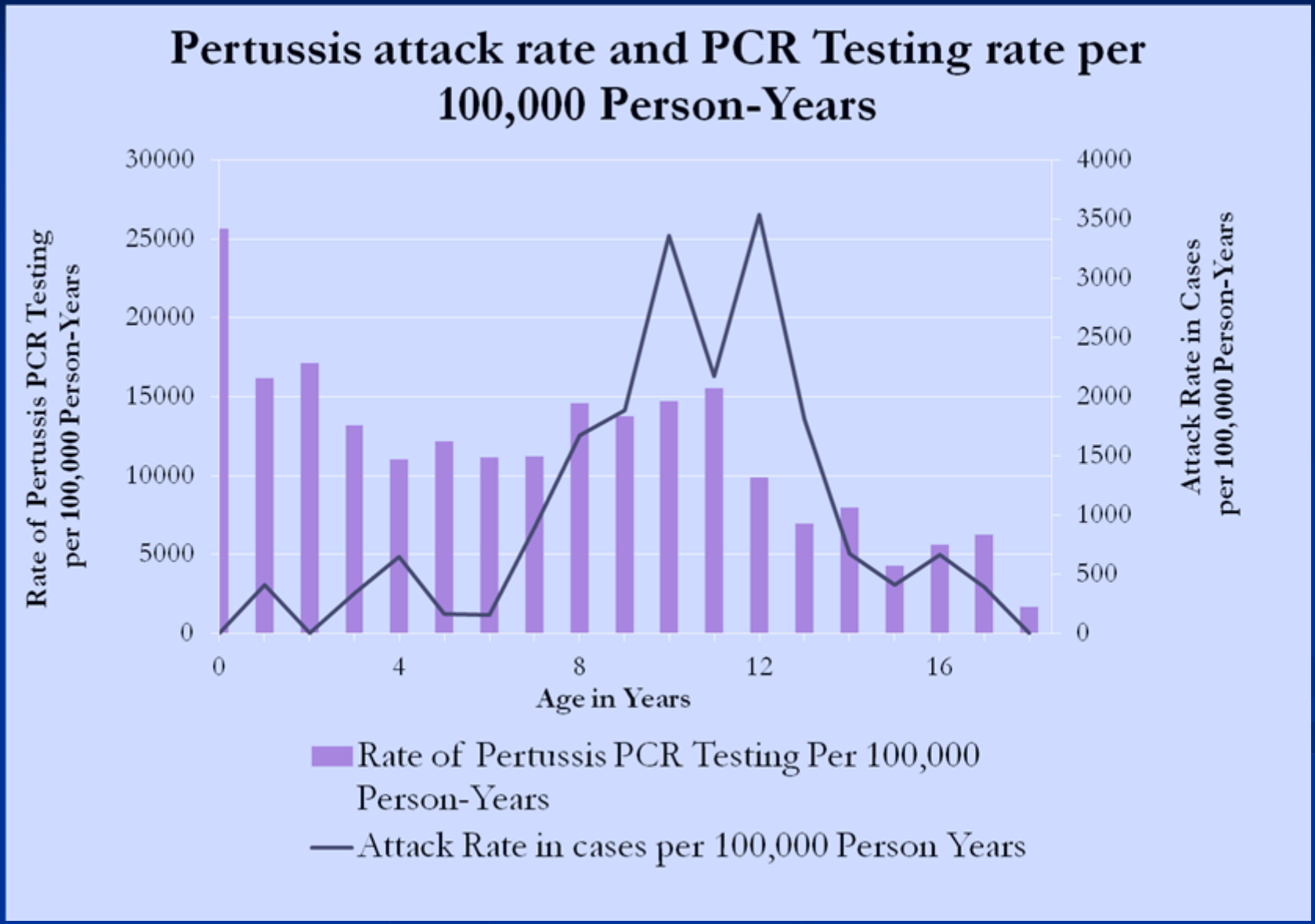
Methods

- At the beginning of the outbreak, an informal practice agreement was adopted, to test all patients who presented with prolonged cough for *B. pertussis*
- All patients with a positive PCR for *B. pertussis* or *B. parapertussis* at the medical center were identified from March 1-October 31, 2010
- Demographics and vaccine status were determined from medical records.

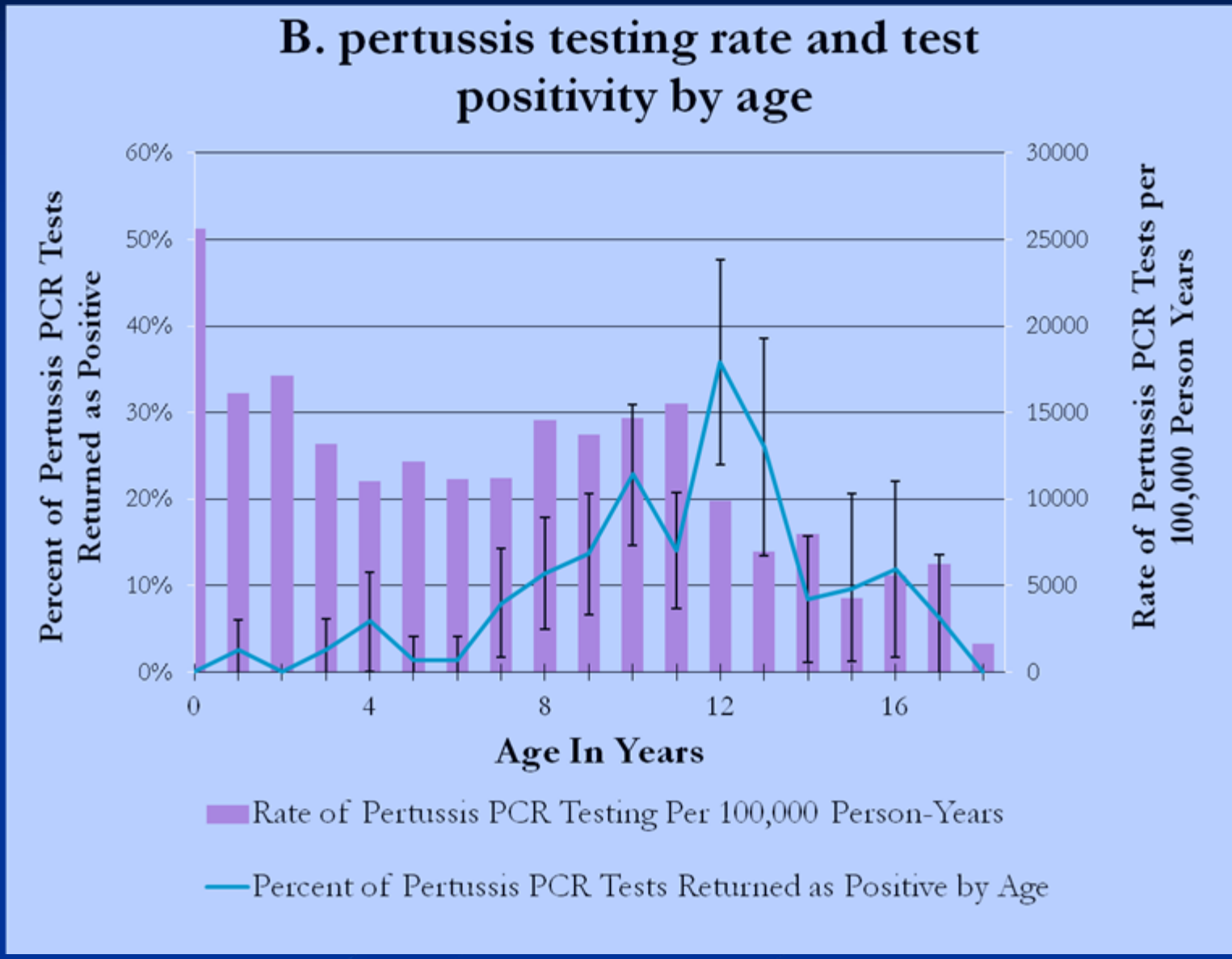
Results

- 171 patients with *B. Pertussis* were identified
  - 132 age <18, and 103 age <=12.
- Vaccination rates of patients in the <=12 age group:
  - 85% fully vaccinated
  - 7% under vaccinated
  - 8% never vaccinated.

Case and Testing Rates By Age



Pertussis PCR Tests Positive By Age (%)

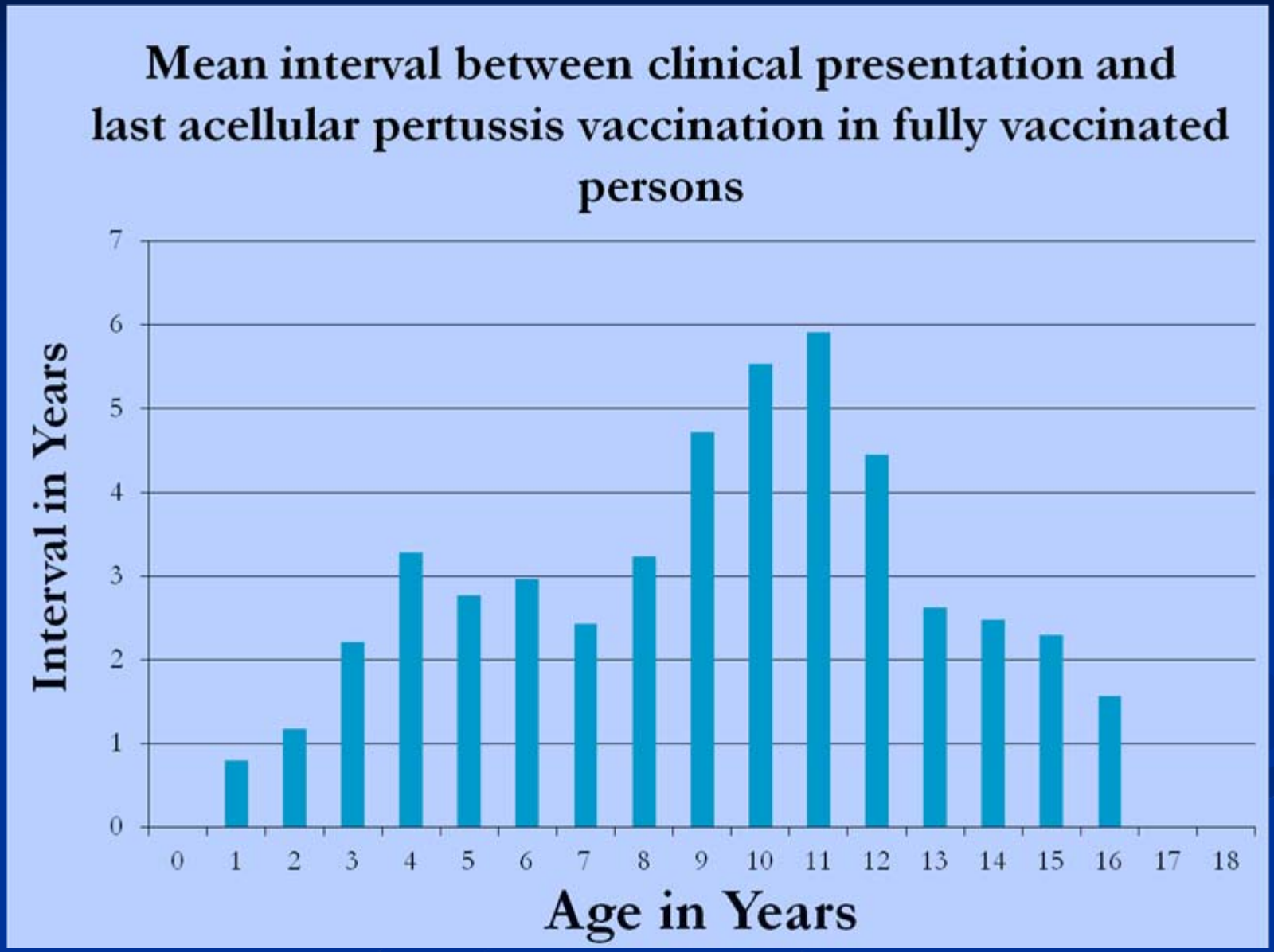


Results

Table 3. Attack Rate in Vaccinated and Under and Unvaccinated Patients			
Age Group	Attack Rate in Vaccinated Persons*	Attack Rate in Under and Unvaccinated Persons*	P-Value
2-7	359	606	0.57
8-12	2453	3211	0.43
13-18	452	2189	0.009
2-18	1011	2073	0.01

*Per 100,000 person-years

Results


Mean interval between clinical presentation and last acellular pertussis vaccination in fully vaccinated persons
Interval in Years
0
1
2
3
4
5
6
7
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Age in Years

Analysis

- PCR testing for both IS481 (*B. pertussis*) and IS1001 (*B. parapertussis*) allowed for exclusion of *B. holmesii*
  - A specimen positive for both sequences would suggest infection by *B. holmesii*
  - No such specimens were found
  - No isolates of either *B. holmesii* or *B. bronchiseptica* were identified among those submitted to the CDPH (Personal communication K. Harriman, CDPH)

Analysis

- There was no statistically significant difference in attack rates between un/undervaccinated children and fully vaccinated children in the 2-7 and 8-12 year age groups
- There was a significantly higher rate of disease in un/undervaccinated children in the 13-18 age group and when all age groups were examined in the aggregate ($p = 0.009$ and 0.01 respectively)

Analysis

- Testing rate was similar for all ages except infants and older teens, ruling out selection bias
- There was a sharp increase in attack rate from ages 8-14, peaking at age 12 ($p=0.002$, one sample t-test)
- Based on these attack rates, the Vaccine Effectiveness was demonstrated to be markedly reduced in the 8-12 year age group.

Analysis

Table 1. Vaccine Effectiveness by age.

Age Group (Years)	PPV	PCV	Effectiveness (%)	Effectiveness: 95% Confidence Intervals
2-7	91%	86%	41%	21-54%
8-12	89%	86%	24%	0-40%
13-18	89%	62%	79%	73-84%
2-18	90%	81%	51%	44-58%

* PPV= Proportion of the Population fully Vaccinated
PCV= Proportion of Cases fully Vaccinated

Conclusions

- There may be an increasingly susceptible population as the interval since last vaccination increases within this population.
- aP is highly effective in the first three years following vaccination
- An increase in disease appears to correspond to an interval of greater than three years from last vaccination.
  - Vaccine Effectiveness is markedly reduced after this time period among our population
  - This suggests that the vaccine may be not as durable as previously thought.

Conclusions

- The lower than expected durability, paired with the current vaccine schedule and imperfect vaccine coverage, appears to result in a reduced level of herd immunity in the 8-13 age group.
- If these findings are verified, strategies for control of pertussis might include:
  - Earlier and/or additional booster doses
  - Targeted vaccination programs to address insufficient immunity in outbreak situations