Comparison of Potential Vaccine Strategies to Decrease Infant Pertussis

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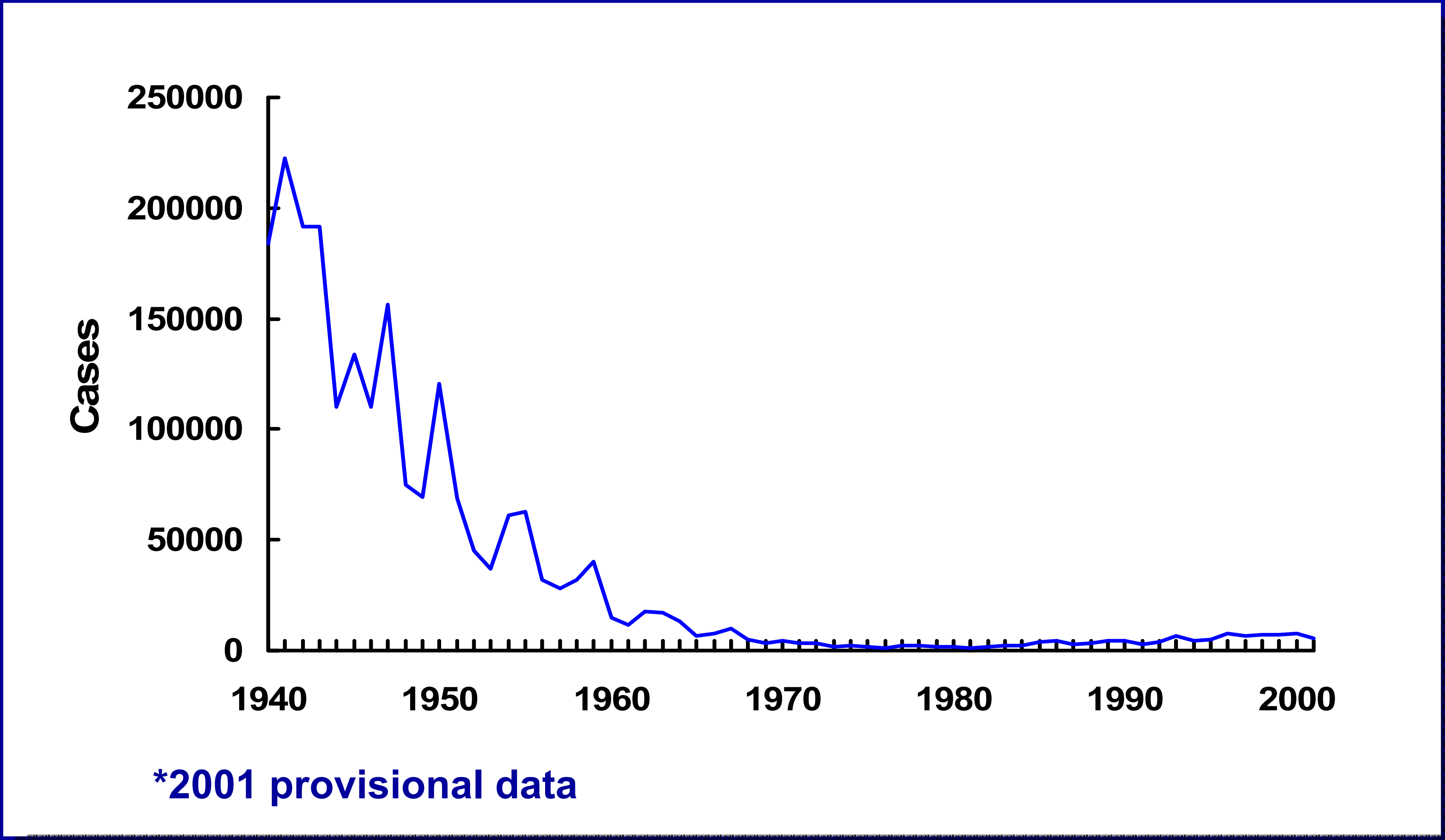
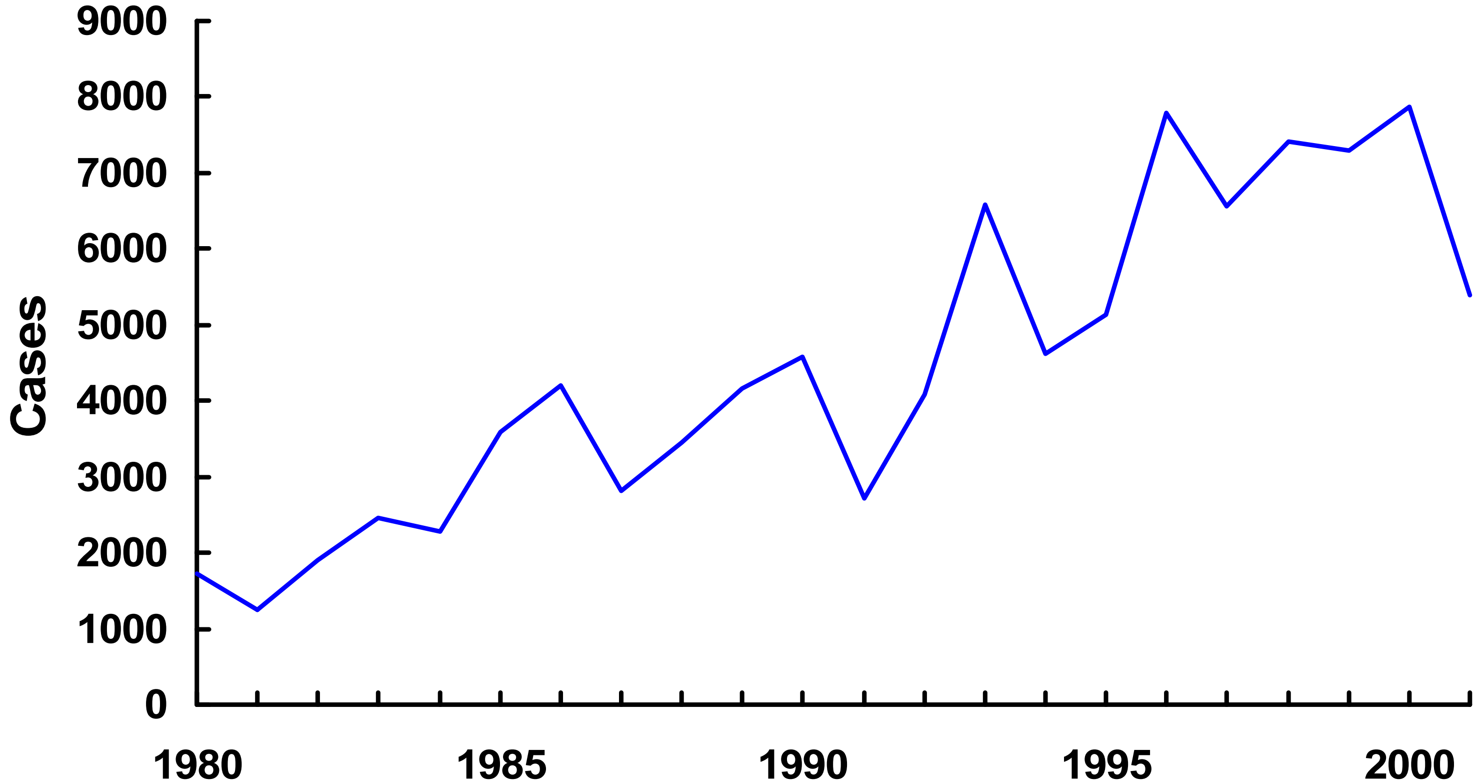
Pertussis – United States, 1940-2001*



CDC. *MMWR*. 2002;51(4):73-76.

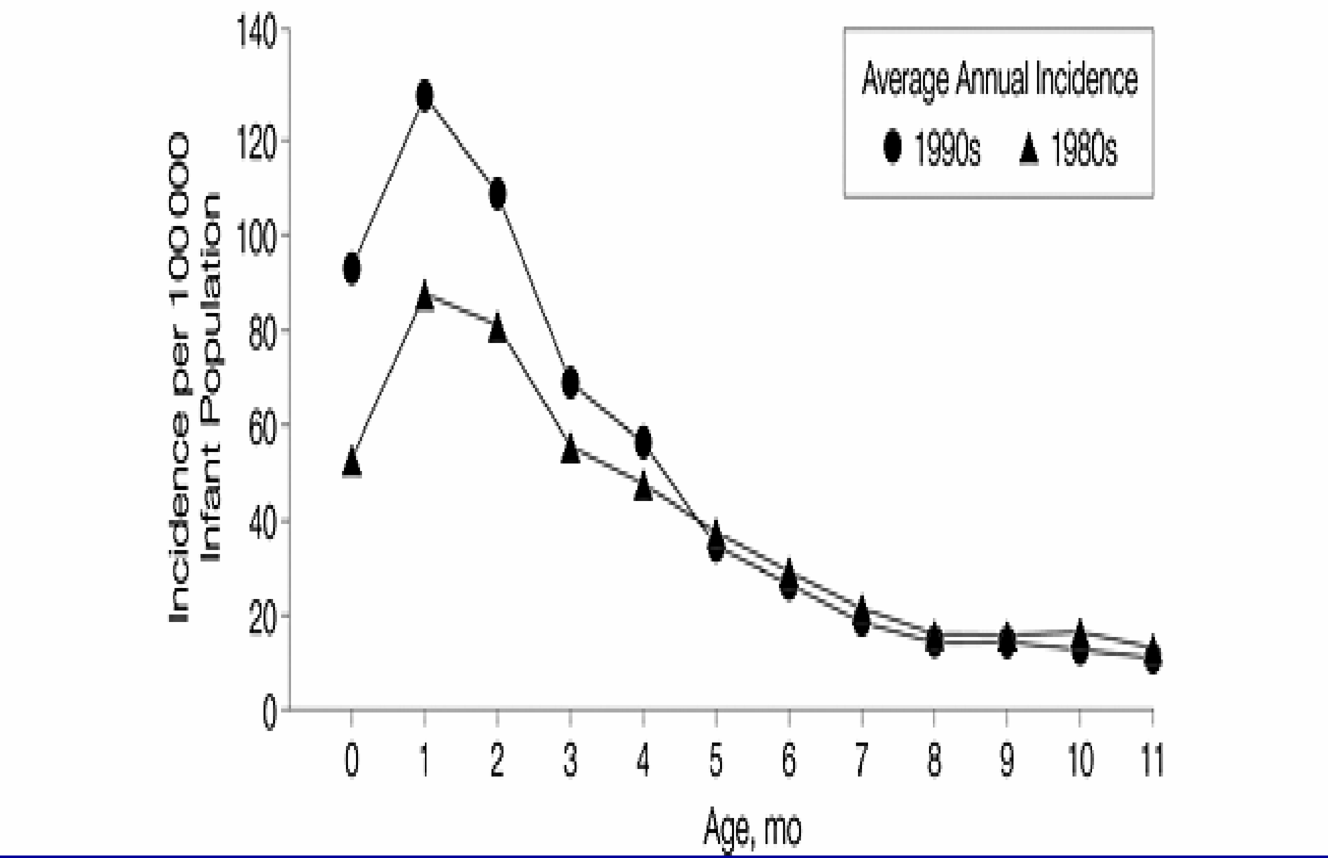
Pertussis – United States, 1980-2001*



***2001 provisional data**

CDC. *MMWR*. 2002;51(4):73-76.

Pertussis Trends
0-11 months of age



Tanaka M JAMA. 2003 Dec 10;290(22):2968-75.

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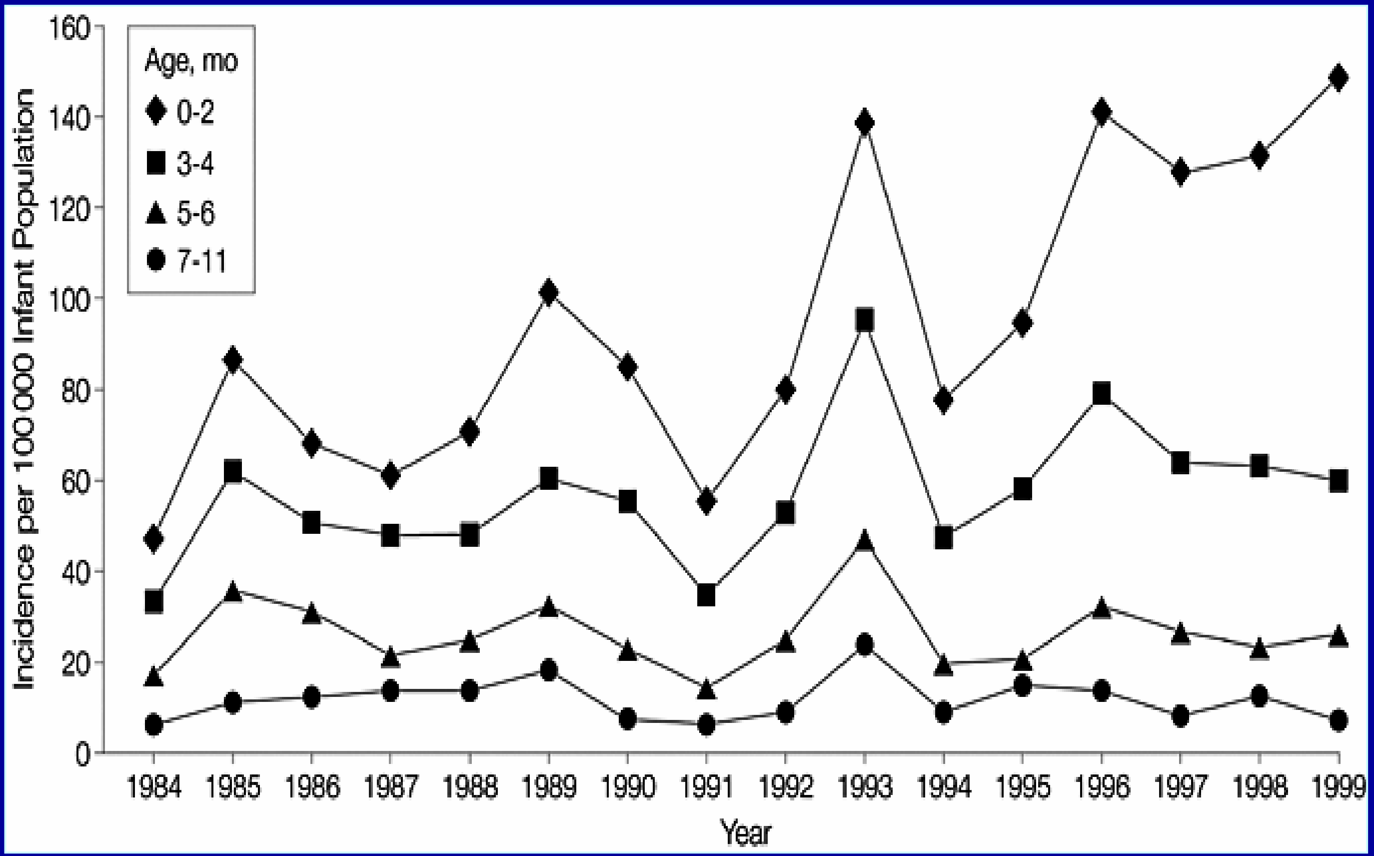

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Pertussis Related Deaths
1997-2000

Age	No. Cases	Deaths
< 6 mo	7203	56
6-11 mo	1073	1
1-4 yr	3137	1
5-9 yr	2756	2
10-19 yr	8273	0
≥ 20 yr	5745	2

MMWR; 2002:51;74-76

Epidemiologic Features of Children Hospitalized with in Canada

- 1082 cases requiring hospitalization
- 92% cases in children < I year of age; 79% in children < 6 months of age
- Mean age at hospitalization 12.4 weeks
- Ten deaths reported: 6 < 1 mo of age
- Source of infection known 40% of cases; sibling (53%), parent (20%), relative (12%), neighbor (8%), day care contact (3%)
- Most children too young to be fully vaccinated

Halperin et al. Clin Infect Dis 1999; 28: 1238-43

Potential Options to Reduce Neonatal Disease

- Maternal Immunization
- Universal Adolescent and Adult Immunization
- Infant Immunization
- Parental Immunization

Maternal Immunization

Natural History of Pertussis Antibody and Effect on Vaccine Response

- Sera were available from three distinct groups
  - Group 1: 34 paired maternal and cord sera
  - Group 2: 50 prevaccination sera from infants given either whole cell or acellular pertussis
  - Group 3: 17 unimmunized infants followed with sequential sera to assess antibody decline (1973)
- Antibodies to PT and FHA were measured by standardized ELISA methods (LLD= 2 EU)

Van Savage J, Decker MD, Edwards KM, Sell SH, Karzon DT.
J. Infect. Dis. 161:487, 1990

Maternal Transfer of Pertussis Antibody: Group 1

Antigen (ELISA) GMT (95% CI)	Maternal Sera	Cord Sera
PT	5 (2-13)	14 (6-32)
FHA	41 (26-66)	27 (15-49)
Aggln	34 (23-50)	35 (24-51)

Antibody Titers in Groups 2 and 3

Group	2	3	3	3	3
Mean Age (d)	61	55	93	125	148
PT	3 (2-4)	4 (2-8)	2 (1-4)	1 (1-1.4)	1 (1-1)
FHA	11 (1-17)	8 (3-21)	5 (2-13)	5 (2-12)	2 (1-5)

Antibody Decline in Unimmunized Infants

Antibody	Half-Life of Antibody
PT	36.3 days
FHA	40.3 days
Agglutinins	55.0 days

Geometric Mean Concentrations of IgG (95% CI): Pertussis Antigens

Antigen	Maternal Delivery	Cord	Infant (2 months)
PT	2.4 (1.9-3.1)	4.1 (3-5.5)	1.4 (1.2-1.7)
FHA	6.9 (5-9.5)	12.3 (8.8-17.3)	3.0 (2.3-3.8)
FIM	13.0 (9.2-18.5)	20.4 (14-29.6)	5.8 (4.5-7.4)

Healy, Munoz, Rench, Halasa, Edwards, Baker. JID in press

Universal Adolescent and Adult Immunization

Simulations of Pertussis Epidemiology in US: First Model

- Infectious period of 21 days, vaccine efficacy of 0.9 when routine vaccination at 2, 4, 6 months with boosters at 15-18 mos and 4-6 years, and 90% vaccine coverage
- Initial model used 384 nonlinear differential equations, 12 epidemiologic groups and 32 age groups
- Assumed adult immunization raises immunity slightly

Hethcote. An age-structured model for pertussis transmission. Math. Biosci. 1997;145:89

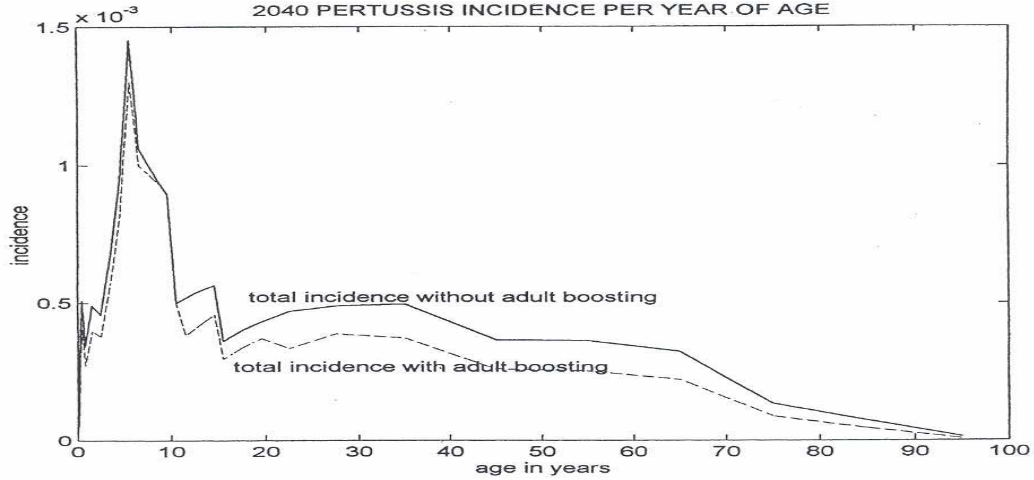

Fig. 6. Total pertussis incidence per year of age for various years using the first simulation model.

Simulations of Pertussis Epidemiology in US: Second Model

- Uses same epidemiologic data, forces of infection, vaccine schedule, and vaccination coverage
- Assumes that booster vaccination raises level of immunity to highest level

Hethcote. Simulations of pertussis epidemiology in the United States: effect of adult booster vaccination. Math. Biosci. 1999; 158: 47.

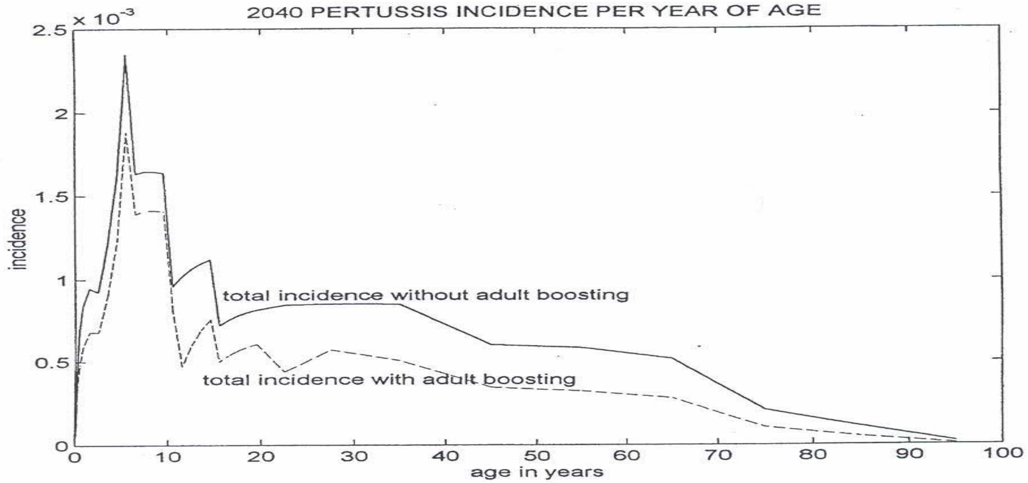

Fig. 10. Total pertussis incidence per year of age for various years using the second simulation model.

Effects of Adding Adult Booster

- In 1st model booster vaccinations for **ALL** adolescents and adults every 10 years leads to 9% reduction in both typical and atypical cases in children < 10 years and 26% reduction in those > 10 years
- In 2nd model booster vaccinations for **ALL** adolescents and adults every 10 years leads to 20% reduction in both typical and atypical cases in children < 10 years and 42% reduction in those > 10 years

Hethcote. Simulations of pertussis epidemiology in the United States: effect of adult booster vaccination. Math. Biosci. 1999; 158: 47.

Practical Implications of Adult Booster Doses

- If only 60% of adults get vaccine (as predicted), then the 1st model would reduce typical cases in children < 10 years by 2% and atypical cases overall by 12%
- With 60% vaccination of adults, the 2nd model reduces typical cases in children < 10 years by 17% and atypical cases by overall 22%

Hethcote. Simulations of pertussis epidemiology in the United States: effect of adult booster vaccination. Math. Biosci. 1999; 158: 47.

Summary of Adult Vaccination

- If the goal of adult boosting is to reduce the number or severity of atypical pertussis cases in adults, then these simulations suggest that adult boosting is effective.
- If the goal of adult boosting is to reduce pertussis incidence in infants and children, then the simulations warn that adult boosting will be relatively unsuccessful

Hethcote. Simulations of pertussis epidemiology in the United States: effect of adult booster vaccination. Math. Biosci. 1999; 158: 47.

Infant Immunization at Birth, at One Month of Age, or Parental Immunization

Pertussis Vaccination Strategies For Neonates; An Exploratory Cost-effectiveness Analysis

PA Scuffham and PB McIntyre

Vaccine In Press

Primary Aims of Study

- To compare the potential costs and health consequences of parental vaccination, a birth vaccination strategy, and a one month vaccination strategy with the practice of beginning vaccine at 2 months
- Secondary aim to identify areas of uncertainty to guide further studies

Methods

- Markov model used so differential timing of events can be modeled
- Cost of pertussis to Australian health system chosen as perspective and model populated using Australian data on incidence and cases
- Limited baseline analysis to notified cases only, including cases admitted to the hospital and deaths

Assumptions for Cost Analysis

- Hospitalization and death from pertussis in highly immunized populations occurs before first vaccination at 2 months of age
- Disability adjusted life years (DALYs) were used as the primary outcome
- Cost to public health system chosen with Monte Carlo simulations used

Three Alternative Strategies

- Parental vaccination at birth
  - Assumes 50% of infants infected by parents
  - Parents vaccinated at time of infant’s birth
- Infant vaccinated at birth
- Infant vaccinated at one month of age
  - Assumed vaccination at birth or one month was 67% as effective as vaccination at 2 mos

Primary Outcome Measures

- Disability-adjusted life years (DALY) was used as the primary outcome
- DALY is an index that combines morbidity and mortality according to weights for each state multiplied by time in that state
- DALY weights for global burden of disease
- DALY weight of one used for mortality multiplied by life expectancy for an infant

Costs of Strategies

Vaccine Strategy	Cost A$	DALYs (SD)	Cost per DALY averted A$
No change	$101.50	0.000243 (0.000203)	
Birth dose	$134.71	0.000133 (0.000122)	$330175
One month	$144.74	0.000184 (0.000164)	$735994
Parental	$174.88	0.000150 (0.000141)	$787504

Summary of Results

- Vaccination at birth was estimated to cost an additional A$33.21 per infant and to reduce cases, deaths, and DALYS by 45%
- Vaccination at 1 month cost an additional A$43.24 per infant and to reduce cases, deaths, and DALYS by 25%
- Parental vaccination at birth cost an additional A$73.38 and reduced cases, deaths, and DALYS by 38%

Additional Concerns

- Rates of hospitalization and death and efficacy of early vaccination have large effects on results
- Parental vaccination at birth was most cost-effective if protection persists for later children
- Policy implications are that all three strategies exceed the Australian guideline of cost effectiveness acceptability of $100,000 per life year gained

Conclusions about Vaccination Strategies for Infant Pertussis

- Infant pertussis cases are increasing
- Maternal immunization should be studied
- Universal adolescent / adult immunization will not eliminate neonatal disease
- Infant immunization programs will have greater impact than parental immunization programs and should be further evaluated