Pertussis in adolescents and adults: should we vaccinate

Lee G M, LeBaron C, Murphy T V, Lett S, Schauer S, Lieu T A

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The health technology under evaluation was a national pertussis vaccination programme for adolescents and adults. Six strategies were examined:

- no vaccination;
- 1-time adolescent vaccination;
- 1-time adult vaccination;
- adult vaccination with boosters;
- adolescent and adult vaccination with boosters; and
- postpartum vaccination.

Strategy 1, no vaccination, was used as the main comparator.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The hypothetical population of the study was a US cohort of 4 million 11-year-old adolescents over their lifetimes.

Setting
The setting was the community. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence and resource use data were derived from a review of the literature dated from 1965 to 2004, recent vaccine clinical trial data, and unpublished data provided by the Centers for Disease Control and Prevention and the Massachusetts Department of Public Health. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a review of the literature, recent vaccine clinical trial data, and unpublished data provided by the Centers for Disease Control and Prevention and the Massachusetts Department of Public Health. Where estimates were unavailable or uncertain despite these sources, the authors relied on a pertussis expert panel.
convened in November 2002 in Atlanta, Georgia.

Modelling
A Markov model was constructed to calculate the health benefits, risks, costs and cost-effectiveness of six vaccination strategies for healthy adolescents and/or adults. The analytical horizon was lifetime.

Outcomes assessed in the review
The outcomes assessed in the review included disease probabilities, vaccine probabilities, waning immunity and infant transmission.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
MEDLINE was searched from 1965 to 2004 for articles in the English language. Recent vaccine clinical trial data and unpublished clinical trials were obtained from the Centers for Disease Control and Prevention and the Massachusetts Department of Public Health.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Approximately 32 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The annual incidence of pertussis was 155 cases per 100,000 adolescents, 11 cases per 100,000 adults and 58.5 cases per 100,000 infants. Severe cough occurred among 58% of adolescents with pertussis and 67% of adults with pertussis. Pneumonia occurred among 1% of adolescents with pertussis and 3% of adults with pertussis.

The vaccine efficacy was 87%. The vaccine delivery rates for the adolescents and/or adult strategy were 76% among teenagers, 36% among those in their twenties, 34% among those in their thirties, 29% among those in their forties, 21% among those in their fifties, 14% among those in their sixties and 5% among those in their seventies. The vaccine delivery rate for the postpartum vaccination strategy was 66%.

The immunity was assumed to wane each year for 15 years, after which the individual was considered non immune.
The baseline model assumed that universal adolescent or adult vaccination would have no impact on infant disease. In an alternative analysis, the potential to reduce infant transmission for each strategy was varied, assuming the vaccine delivery rates used in the baseline analysis.

**Methods used to derive estimates of effectiveness**

Experts’ opinion was relied on where estimates were unavailable or uncertain. A modified Delphi process was used to obtain the estimates.

**Estimates of effectiveness and key assumptions**

Different assumptions about reduced infant transmission were used in an alternative analysis to address the potential impact of herd immunity. Each vaccination strategy was estimated to reduce infant disease as follows:

- no vaccination, 0%;
- 1-time adolescent vaccination, 17%;
- 1-time adult vaccination, 10%;
- adult vaccination with 10-year boosters, 17%; and
- adolescent and adult vaccination with 10-year boosters, 35%.

For the postpartum vaccination strategy, infant disease was estimated to be reduced by 40% in both baseline and alternative analyses, on the basis of 66% vaccine delivery and 87% vaccine efficacy and the assumption that caregivers were responsible for 70% of infant disease.

**Measure of benefits used in the economic analysis**

The measures of benefit were the pertussis cases prevented and the quality-adjusted life-years (QALYs). Preferences for study-specific health states were obtained from adults and parents of adolescents with confirmed pertussis disease in a separate study (Lee et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic detail). The time trade-off method was used to measure preference for health states.

**Direct costs**

The direct costs were disease costs and vaccine costs. The former (disease costs) included medical costs for cough and pneumonia for adolescents and adults, medical cost for respiratory disease, respiratory disease with hospitalisation, neurologic disease and death for infants. The latter (vaccine costs) included vaccine price, cost of vaccine administration, cost of vaccine visit, cost of local reaction, cost of systemic reaction and cost of anaphylaxis. The disease costs for adolescents and adults were based on a published study (Lee et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic detail). The medical costs for infants were estimated from health service utilisation data from the Massachusetts enhanced pertussis surveillance system multiplied by the unit cost per service, and from sources such as the Medicare fee schedule and the American Academy of Paediatrics fee schedule. The estimations of vaccine price and quantities were assumptions. The costs were adjusted for inflation to 2004 US dollars. Future costs were discounted at an annual rate of 3%, which was relevant as the time horizon was lifetime.

**Statistical analysis of costs**

No statistical analysis of the costs was reported.

**Indirect Costs**

The indirect costs included non-medical costs attributable to pertussis. The non-medical costs for adolescents and adults were based on a published study (Lee et al. 2004). The non-medical costs for infants were estimated to include the time
costs of work missed for one adult while the child received medical care (2 hours per office visit and 8 hours per day for hospitalisations). The median wage rate for female workers aged 25 to 35 years was used to calculate the time costs related to infant disease. The costs were adjusted for inflation to 2004 US dollars.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to evaluate the different assumptions about reduced infant transmission and other baseline assumptions. Two-way sensitivity analyses of significant parameters identified in the one-way analyses were also examined.

Estimated benefits used in the economic analysis
The health outcomes were modelled over the lifetime of a hypothetical cohort of 4 million adolescents. Approximately 85,000 cases would occur if no vaccination programme were implemented. Compared with no vaccination:

30,760 cases of pertussis would be prevented by the 1-time adolescent vaccination strategy,
1,180 by the 1-time adult vaccination strategy,
4,320 by the adult vaccination with boosters strategy,
34,980 by the adolescent and adult vaccination with boosters strategy, and
6,180 by the postpartum vaccination strategy.

Compared with no vaccination, 1,613 QALYs would be saved by 1-time adolescent vaccination, 1,600 by adolescent and adult vaccination with boosters, and 203 by postpartum vaccination. The 1-time adult vaccination and adult vaccination with boosters strategies resulted in 4 and 10 QALYs less, respectively, compared with no vaccination.

Compared with no vaccination:
1-time adolescent vaccination would potentially cause 60,800 local adverse events and 30,400 systemic adverse events;
1-time adult vaccination would potentially cause 28,700 local adverse events and 14,300 systemic adverse events;
adult vaccination with boosters would potentially cause 107,800 local adverse events and 53,900 systemic adverse events;
adolescent and adult vaccination with boosters would potentially cause 168,600 local adverse events and 84,300 systemic adverse events; and
postpartum vaccination would potentially cause 57,000 local adverse events and 28,500 systemic adverse events.

Cost results
With no vaccination programme, the overall costs for the cohort were $23.7 million from the health care payer perspective and $37.6 million from the societal perspectives. The adolescent and adult vaccination with boosters strategy had the highest total costs at $101.1 million (health care payer perspective) and $109.3 million (societal perspective), whereas the 1-time adolescent vaccination strategy cost $61.5 million (health care payer) and $70.6 million (societal).

Compared with no vaccination, the net costs for the cohort from the health care payer perspective were:
$37.8 million with 1-time adolescent vaccination,
$15.8 million with 1-time adult vaccination,
$39.5 million with adult vaccination with boosters,
$77.4 million with adolescent and adult vaccination with boosters, and
$54.2 million with postpartum vaccination.

Compared with no vaccination, the net costs for the cohort from the societal perspective were:

$33.0 million with 1-time adolescent vaccination,
$15.5 million with 1-time adult vaccination,
$38.6 million with adult vaccination with boosters,
$71.7 million with adolescent and adult vaccination with boosters, and
$52.7 million with postpartum vaccination.

**Synthesis of costs and benefits**
The estimated benefits and costs were combined by calculating the cost per case prevented and cost per QALY saved.

Compared with no vaccination, the 1-time adolescent vaccination strategy cost $1,200 per case prevented (health care payer perspective) and $1,100 per case prevented (societal perspective). The adolescent and adult vaccination with boosters strategy cost $9,400 per case prevented (health care payer) and $9,200 per case prevented (societal), compared with the next-best strategy of 1-time adolescent vaccination. All other strategies were dominated (i.e. they were more costly and less effective than alternative strategies).

When the incremental cost per QALY saved was examined, the baseline analysis demonstrated cost-effectiveness ratios of $23,000 per QALY saved (health care payer perspective) and $20,000 per QALY saved (societal perspective) for the 1-time adolescent vaccination strategy compared with no vaccination. All other strategies were dominated.

In sensitivity analyses, when the probability and cost estimates in the model were varied over plausible ranges, 1-time adolescent vaccination usually remained the most effective and cost-effective strategy, with a criterion of less than $50,000 per QALY saved. The adolescent and adult vaccination with boosters strategy became potentially cost-effective from the societal perspective only if two conditions were met simultaneously. More specifically, if the disease incidence for adolescent and adults was at least 6 times higher than the base-case assumptions and the cost of vaccination was less than $10. Adult vaccination strategies were more costly and less effective than adolescent vaccination strategies. The results were sensitive to assumptions about disease incidence, vaccine efficacy, frequency of vaccine adverse events, and vaccine costs.

**Authors' conclusions**
Routine pertussis vaccination of adolescents resulted in net health benefits and may be relatively cost-effective.

**CRD COMMENTARY - Selection of comparators**
No vaccination strategy, which appears to have represented current practice in the authors' setting, was reported to be the comparator. You should decide if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors relied on published and unpublished data, as well as a pertussis expert panel. It was not reported that a systematic review of the literature had been undertaken, and full details of the review were not reported. Since the authors chose the analytical horizon of a lifetime and incorporated waning immunity in their study, the long-term benefits of the vaccine could be assessed. The authors acknowledged that they might have underestimated the true impact of the vaccine in the population level given the uncertainty in the disease incidence rate.

**Validity of estimate of measure of benefit**
The authors used QALYs as the measure of benefits. These were derived from a published paper through modelling. This measure of benefit enables comparisons to be made across different health technologies. The methods used to derive the utility weights were reported. Sensitivity analyses around QALYs were conducted, and the method used to select the ranges was reported.

**Validity of estimate of costs**
The authors reported that the costs were estimated from both health care payer and societal perspectives. Therefore, both the direct and indirect costs were included. The resource use quantities and prices were taken from different sources, and sensitivity analyses of the quantities were conducted.

**Other issues**
The authors made some comparisons of their findings with those from other studies. However, the issue of generalisability to other settings was not explicitly addressed. The authors did not present their results selectively. The authors pointed out several limitations to their study. First, the limited information about how frequently pertussis is transmitted from one age group to another and how effective adolescent or adult vaccination would be in interrupting transmission to infants. Second, the uncertainty in terms of the duration of vaccine- and disease-mediated immunity, particularly because there is limited experience with currently available adolescent or adult boosters on the market.

**Implications of the study**
The authors stated that their findings underscore the need for additional research and surveillance efforts to assess accurately the true burden of pertussis in the population. Additional information about disease incidence, vaccine efficacy and vaccine adverse events would contribute to policy decision about vaccine use.

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**Other publications of related interest**

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