Cost effectiveness of pertussis vaccination in adults
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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 study examined two strategies for pertussis vaccination in adults. These were one-time adult vaccination at age 20 to 64 years, and adult vaccination with decennial boosters. One-time adult vaccination was included in the combined tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine programme. A third strategy, no adult pertussis vaccination, was also considered as a comparator, as it represented current practice.

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 166 million adults in the USA aged 20 to 64 years (i.e. all the US adult population up to 64 years).

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

Dates to which data relate
The clinical data were derived from studies published between 1965 and 2005. No dates for resource use were explicitly reported. The costs came from sources published between 2001 and 2006. The price year was 2005.

Source of effectiveness data
The clinical and epidemiological data used in the decision model were:
- disease incidence in adults and infants,
- ranges of severity of illness in adults with pertussis (mild cough, moderate cough, severe cough and pneumonia),
- vaccine efficacy and side effects (from year 1 to year 15 after vaccination), and
- coverage rates.

Modelling
An existing Markov model was modified to calculate the health benefits, risks, costs and cost-effectiveness of alternative vaccination strategies for healthy adults over an analytic horizon of a lifetime. Model pathways and probability of events were reported. A simplified version of the decision tree was presented in an appendix. A second
decision tree for infant disease, which was used in the sensitivity analysis, was constructed.

Sources searched to identify primary studies
The clinical data were derived from multiple sources, including the Massachusetts Department of Public Health. The authors also made some assumptions about uncertain model inputs. Expert opinion was used to determine vaccine-mediated immunity. No information on the other sources of data was provided.

Methods used to judge relevance and validity, and for extracting data
It was unclear whether a review of the literature was undertaken to identify the primary studies. Much of the data appears to have been obtained from US sources. No information on the methods used to pool the data was provided.

Measure of benefits used in the economic analysis
The summary benefit measures used were the pertussis cases prevented and quality-adjusted life-years (QALYs). Both measures were estimated using a modelling approach. The utility weights used to derive QALYs were estimated using data obtained from the only published study on preferences in adults with pertussis illness, where the time trade-off approach was used. The benefits were discounted at an annual rate of 3%.

Direct costs
The analysis of the direct costs covered medical costs and non-medical costs. Medical costs included laboratory tests, ambulatory visits, hospitalisation, use of chest radiography, antibiotics, and vaccine acquisition and administration. Non-medical costs included transportation, childcare and over-the-counter medications. The unit costs were not presented separately from the quantities of resources used. The costs were derived from published studies and official sources. The sources of resource use were not explicitly stated, but some quantities of resources used might have been derived from the same sources as those used to derive the costs. Overall, there was little information on the sources of the economic data. Discounting was relevant, as long-term costs were evaluated, and an annual rate of 3% was applied. The costs were updated to 2005 values using the gross domestic product deflator.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
Productivity costs (time missed from work) were included in the analysis, which was appropriate given the societal perspective adopted. However, no information on these costs was provided. The price year is assumed to have been 2005, as in the analysis of the direct costs.

Currency
US dollars ($).

Sensitivity analysis
An extensive univariate sensitivity analysis was carried out to assess the robustness of the model results to variations in model inputs such as impact of severity of disease, vaccine cost, vaccine efficacy, frequency of vaccine adverse events, time horizon and discount rate. Alternative values might have been derived from the literature, although it was not explicitly stated. An alternative scenario also considered the potential impact of herd immunity.

Estimated benefits used in the economic analysis
Only discounted benefits are presented in this abstract. The results were reported for different rates of incidence (from
10 to 500 cases per 100,000. The former figure (10 per 100,000) reflected national incidence rates from passive surveillance.

At an incidence rate of 10 per 100,000 there would be 763,000 cases of pertussis, of which 70,000 would be prevented with one-time adult vaccination and 239,000 would be prevented with decennial adult vaccination. The two programmes would generate a loss of 600 and 1,700 QALYs, respectively, since vaccine adverse events outweighed the benefits of disease prevention.

At an incidence rate of 350 per 100,000 there would be 26,097,000 cases of pertussis, of which 2,394,000 would be prevented with one-time adult vaccination and 4,987,000 would be prevented with decennial adult vaccination. The two programmes would save 83,200 and 180,200 QALYs, respectively.

At an incidence rate of 500 per 100,000 there would be 36,913,000 cases of pertussis, of which 3,385,000 would be prevented with one-time adult vaccination and 7,039,000 would be prevented with decennial adult vaccination. The two programmes would save 111,200 and 240,500 QALYs, respectively.

**Cost results**

At an incidence rate of 10 per 100,000, the cost of pertussis cases would be $301 million. The net cost (vaccination costs minus reduced medical and non-medical costs) would be $2,003 million with one-time vaccination and $4,535 million with decennial vaccination.

At an incidence rate of 350 per 100,000, the cost of pertussis cases would be $7,933 million. The net cost would be $674 million with one-time vaccination and $1,652 million with decennial vaccination.

At an incidence rate of 500 per 100,000, the cost of pertussis cases would be $9,415 million. The net cost would be $418 million with one-time vaccination and $1,104 million with decennial vaccination.

**Synthesis of costs and benefits**

Incremental cost-effectiveness ratios and cost-utility ratios were calculated in order to combine each vaccination programme with the strategy of no vaccination.

In terms of the cost-effectiveness ratios, the incremental cost per discounted pertussis case prevented with one-time adult vaccination ranged from $29,000 at an incidence of 10 cases per 100,000 to $120 at an incidence of 500 cases per 100,000 ($280 at an incidence of 350 per 100,000). The corresponding figures for the decennial adult vaccination programmes were $31,000 and $160 ($330).

In terms of the cost-utility ratios, both vaccination strategies were dominated by no vaccination at an incidence rate of 10 cases per 100,000. The incremental cost per discounted pertussis case prevented with one-time adult vaccination was $8,000 at an incidence of 350 cases per 100,000 and $4,000 at an incidence of 500 cases per 100,000. The incremental cost per discounted pertussis case prevented with decennial adult vaccination was $9,000 at an incidence of 350 cases per 100,000 and $5,000 at an incidence of 500 cases per 100,000.

In general, the analysis showed that, at an incidence rate lower than 120 per 100,000, the incremental cost per QALY of vaccination strategies was higher than a standard threshold of $50,000.

The results of the sensitivity analysis showed that the most influential model inputs were vaccine cost and vaccine efficacy. For example, a higher incremental vaccine cost of $35, a lower vaccine efficacy of 50%, or a shorter duration of pertussis illness shifted the curve upwards, so that a cost-effectiveness ratio threshold of $50,000 was exceeded unless the incidence rates were greater than 175 per 100,000. Changes in other model inputs did not alter the conclusions of the base-case analysis.

The alternative scenario indicated that, as the degree of herd immunity increased, the cost per QALY of the vaccination strategies decreased. In particular, herd immunity had a greater impact on cost-effectiveness when disease incidence was low, meaning that a certain threshold of cases prevented is needed for the intervention to appear cost-effective.
Authors’ conclusions
A programme of routine vaccination of adults aged 20 to 64 years with combined tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) was cost-effective if pertussis incidence in this age group was greater than 120 cases per 100,000.

CRD COMMENTARY - Selection of comparators
The choice of the comparators was appropriate since both the existing pattern of care and two feasible vaccination strategies were considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data were derived from published studies and authors’ opinions. However, no systematic search for data was reported and the method used to identify the primary studies was not described. Information on the primary studies was limited and the methods of evidence synthesis were not reported, thus it was not possible to assess the validity of the clinical estimates.

Validity of estimate of measure of benefit
Both a disease-specific measure (cases prevented) and a more generalisable measure (QALYs) were used in the analysis. They are both valid and commonly used outcomes of vaccination programmes. Discounting was performed in accordance with US guidelines, and the impact of changing the discount rate was investigated. The authors justified the source of the utility weights (only one published study) and the time trade-off approach taken would appear appropriate.

Validity of estimate of costs
The choice of the societal perspective was appropriate since all the relevant categories of costs were included. Limited information on the sources used to derive the unit costs and resource use was provided. The cost categories were reported but there was no detailed breakdown of the cost items. The costs were not treated stochastically but changes in some key cost items were considered in the sensitivity analysis. The price year was reported, thus simplifying reflation exercises in other time periods.

Other issues
The authors reported the results of other economic evaluations and provided reasons for the differences in their findings (mainly differences in incidence rates). The issue of the generalisability of the study results to other settings was not explicitly addressed, but alternative cost estimates for vaccination strategies were considered in the sensitivity analysis. The study involved adults aged 20 to 64 years and this was reflected in the authors’ conclusions.

Implications of the study
The study results appear to support the implementation of a routine Tdap vaccine programme, although the incidence of pertussis determined the cost-effectiveness of the programme.

Source of funding
Supported by the Agency for Healthcare Research and Quality, US Department of Health and Human Services, and the National Immunization Program and Centers for Disease Control and Prevention.

Bibliographic details
PubMedID
17296470

DOI
10.1016/j.amepre.2006.10.016

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Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Bordetella pertussis /immunology; Cost-Benefit Analysis; Female; Humans; Incidence; Male; Markov Chains; Middle Aged; Pertussis Vaccine /economics; Preventive Medicine /economics; United States; Whooping Cough /economics /microbiology /prevention & control

AccessionNumber
22007000528

Date bibliographic record published
31/07/2007

Date abstract record published
31/07/2007