Pertussis immunization of adolescents in the United States: an economic evaluation
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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 authors assessed pertussis immunisation given in a combined pertussis-diphtheria-tetanus vaccine as an additional adolescent acellular booster dose. The comparator was the existing vaccination strategy of no booster vaccination during adolescence.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study hypothetical population comprised four cohorts of individuals. Specifically, infants (0 - 1 year old), children (1 - 10 years old), adolescents (11 - 18 years old) and adults (older than 18 years). The vaccination cohort was the adolescents, while the other cohorts allowed an analysis of herd effects.

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

Dates to which data relate
Epidemiological evidence and effectiveness evidence seem to have related to studies and reports published between 1992 and 2004. Resource use was modelled and informed by authors and expert assumptions. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies, supplemented by estimates provided by members of the Global Pertussis Initiative (GPI) (an expert forum of 37 members) and authors’ assumptions.

Modelling
The authors created an epidemiological model to assess the clinical and economic benefits associated with the technology of interest. Input data were informed by published literature, which was supplemented by expert opinion. Members of the GPI received a suggested value for parameters based on the literature and they were asked whether they agreed with the range. If they disagreed, they were asked for an alternative parameter estimate. Cohorts were modelled for each year of age over their lifetime (maximum 105 years).

The model assumed that infection in other age groups and in unvaccinated adolescents will be decreased because of reduced transmission of the disease resulting from the herd immunity effect of adding an adolescent booster vaccine.
The duration of herd immunity was assumed to be consistent with the protection conferred upon vaccinees.

**Outcomes assessed in the review**
The report was not completely clear as to which outcomes came from which published source. The majority of the epidemiological data seem to have come from the review of the literature, while the majority of the effectiveness data seem to have come from either published studies supplemented by GPI estimates or from GPI estimates alone. Outcomes from the review included case fatality for each age group, hospitalisations per case for each age group, encephalitis rate for each age group, and long-term disability per encephalitis case. The review was not reported to be systematic, and it seems to have selected those studies that provided data relevant to the epidemiological model.

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

**Sources searched to identify primary studies**
Not reported.

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

**Methods used to judge relevance and validity, and for extracting data**
The authors did not state any methods to judge the relevance and validity of the data.

**Number of primary studies included**
Fourteen primary studies seem to have been included in the review.

**Methods of combining primary studies**
In some cases parameter estimates from differing studies were presented to the GPI, who were then asked whether they agreed with the values.

**Investigation of differences between primary studies**
The authors discussed some differences between the results from primary studies, but did not thoroughly investigate such differences.

**Results of the review**
The percentage of case fatalities was 0.69% for infants, 0.05% for children, 0.00% for adolescents, and 0.03% for adults.

The percentage of hospitalisations per case was 58.5% for infants, 7.0% for children, 2.1% for adolescents, and 3.5% for adults.

The encephalitis rate was 0.19% for infants and 0.05% for children, adolescents and adults.

Long-term disability per encephalitis case was 33%.

**Methods used to derive estimates of effectiveness**
The authors used the opinions of the GPI to supplement their review.

**Estimates of effectiveness and key assumptions**

The vaccine wastage rate was 10%.

The adverse event (leading to a medical visit) rate was 2%.

The coverage rate was 80%.

The initial vaccine efficacy was 85%.

The duration of vaccine efficacy was 10 years.

The proportion of breakthrough cases was 45%.

The number of unreported cases per reported case was 7.6.

The percentage of unreported cases (mild) was 68%.

The reduced severity of mild cases was 45%.

The incidence per 100,000 person-years was less than 0.2 to 57.

The reduction in non-target cases (herd immunity) was 20%.

The duration of herd immunity was 10 years.

The distribution of herd immunity was 20% in infants, 30% in children, and 25% in adolescents and adults.

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

The authors estimated the number of pertussis cases, the number of individuals suffering permanent sequelae, the number of pertussis-related deaths, and the number of life-years gained. These outcomes were estimated through the model. The health benefits were discounted at an annual rate of 3%.

**Direct costs**

The costing analysis was conducted from the perspectives of the health care payer (direct costs only) and society. The direct costs included estimates of the acellular vaccine, physician visits, emergency room visits, hospitalisations, long-term disability, antibiotics and other drugs, diagnostic tests and prophylactic measures. The costs of wastage and the treatment of adverse reactions were also included. Where inputs had to be estimated from charges, a cost-to-charge ratio was applied. Data were sourced from published studies and databases in the authors’ setting.

The price year was 2002, and where prices did not relate directly to this year they were reflated using the Medical Care Inflation Index of the US Consumer Price Index. The costs were discounted at a rate of 3% per year after the first year, which was appropriate for the very long-time horizon adopted. The costs were adjusted to reflect national values using ratios based on geographic variations, derived using published data.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The authors estimated the lost time from paid work activities that could be due to the illness itself or from caring for...
someone with pertussis, or the lack of employability resulting from pertussis. Relevant data were sourced from published studies. These estimates were appropriate for the societal perspective adopted as they estimated the broader economic costs of pertussis. Discounting and reflation was the same as for the direct costs.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were carried out to explore the impact of uncertainty in parameter estimates on the outcomes of interest. These analyses particularly encompassed herd immunity efficacy and the waning of immunity over time.

Estimated benefits used in the economic analysis
The number of cases of pertussis was reduced by 68,408 under a base-case of 20% herd immunity, 20,696 with 5% herd immunity, and 116,120 with 35% herd immunity.

The number of deaths was reduced by 41 with 20% herd immunity, 11 with 5% herd immunity, and 72 with 35% herd immunity.

The number of life-years gained was 3,053 with 20% herd immunity, 779 with 5% herd immunity, and 5,327 with 35% herd immunity.

The number of cases of long-term disability was reduced by 7 with 20% herd immunity, 2 with 5% herd immunity, and 12 with 35% herd immunity.

Cost results
The total cost of immunising 80% of the target adolescent cohort was $74,063,016.

The total discounted direct medical savings resulting from immunisation were $48,544,246 with 20% herd immunity, $13,248,431 with 5% herd immunity, and $83,840,061 with 35% herd immunity.

The total discounted indirect savings resulting from immunisation were $18,273,612 with 20% herd immunity, $5,367,603 with 5% herd immunity, and $31,179,620 with 35% herd immunity.

The net social cost was $7,245,159 with 20% herd immunity, $55,446,983 with 5% herd immunity, and -$40,956,665 (saving) with 35% herd immunity.

The net direct cost was $25,518,770 with 20% herd immunity, $60,814,585 with 5% herd immunity, and -$9,777,045 (saving) with 35% herd immunity.

Synthesis of costs and benefits
With 35% herd immunity, immunisation offered greater benefits and reduced cost for all estimates of cost-effectiveness; it was a dominant strategy.

The direct cost per case avoided was $408 with 20% herd immunity and $3,178 with 5% herd immunity.

The direct cost per life-year gained was $22,023 with 20% herd immunity and $205,191 with 5% herd immunity.

The societal cost per case avoided was $115 with 20% herd immunity and $2,898 with 5% herd immunity.

The societal cost per life-year gained was $6,253 with 20% herd immunity and $187,081 with 5% herd immunity.
The authors reported that a strategy of immunising adolescents became cost-neutral from the health care provider perspective if herd immunity was slightly more than 30%. The cost per life-year gained remained below $50,000 if herd immunity was at least 12%. The results were sensitivity to the duration of the effectiveness of immunisation.

Authors' conclusions
"Adding an adolescent pertussis booster dose to the current infant and toddler immunization schedules in the United States would be cost-effective, given reasonable estimates of herd immunity, and applying the assumption that just under 12% of all pertussis cases are reported."

CRD COMMENTARY - Selection of comparators
The authors compared vaccination booster versus no vaccination booster for adolescents. The comparator of no vaccination represented current practice in the authors' setting, and may represent current practice in other settings.

Validity of estimate of measure of effectiveness
A systematic review of the literature was not undertaken. Instead, the authors seem to have selected those accounts that provided data relevant to their model. They highlighted a severe lack of evidence in this field, which made it difficult to estimate inputs with certainty. As a systematic review was not undertaken, few details on the search strategy and how data were elicited were given. However, the authors did give a detailed account of how GPI members were asked to assess and amend data found from published sources. Uncertainty around the outcome parameters was investigated in the sensitivity analyses. In their suggestions for further work, the authors called for further studies to be carried out to increase the evidence available in this field.

Validity of estimate of measure of benefit
The authors used the number of pertussis cases, the number of individuals suffering permanent sequelae, the number of pertussis-related deaths, and the number of life-years gained from vaccination as their summary measures of health benefit. These measures represent natural outcomes from vaccination and enable comparisons with similar vaccination evaluations.

Validity of estimate of costs
The authors estimated the costs from the perspectives of the health care payer and society, and included all cost categories appropriate to these two perspectives. In particular, an estimate of economic productivity lost, not just due to the initial illness but also for caring for sufferers and due to long-term disabilities, was made. The total costs were sensitive to several parameters, particularly the herd effects of immunisation. Thus, changes in the base-case did have an impact on the results and conclusions drawn. The authors carried out sensitivity analyses to explore these impacts. A breakdown of the costs into cost per case for differing age ranges was presented, which helps the reader to gain an understanding of the influence of age on the total costs. However, further breakdowns indicating the importance of hospitilisation versus medication and emergency room visits versus physician visits would have improved the reader's understanding of the key cost-drivers. The price year was reported, which will aid reflation exercises in other settings. Discounting was conducted and was appropriate given the long time horizon.

Other issues
The authors described and discussed results of similar studies in this field. One of these studies did not include a herd impact and the authors offered this as a possible explanation for differences in the results. The authors improved the generalisability of the study by adjusting unit costs to reflect national values. The results do not appear to have been presented selectively and the conclusions drawn were an accurate representation of the results presented. The main limitation of the study, as the authors acknowledged, was the lack of existing evidence for input into the model. The authors carried out a range of sensitivity analyses to explore the impact of this uncertainty and inform the agenda for future work.
Implications of the study
The authors did not make any recommendations for policy but the preference for the introduction of the booster vaccination was clear. Further work to improve the general body of evidence in this area was suggested.

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None stated.

Bibliographic details

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Other publications of related interest


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MeSH
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