Economic analysis of influenza vaccination and antiviral treatment for healthy working 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
Several strategies for influenza vaccination and antiviral treatment were examined. These were:

- no vaccination and no intervention (base-case);
- no vaccination and treatment with zanamivir;
- no vaccination and treatment with rimantadine;
- no vaccination and treatment with oseltamivir;
- vaccination and no intervention;
- vaccination and treatment with zanamivir;
- vaccination and treatment with rimantadine; and
- vaccination and treatment with oseltamivir.

Type of intervention
Primary prevention.

Economic study type
Cost-benefit analysis.

Study population
The study population comprised healthy adults aged 18 to 50 years without any significant co-morbid conditions.

Setting
The setting was the community. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness evidence came from studies published between 1978 and 2001. The dates relating to resource use were not reported. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies and authors' assumptions.
Modelling
A decision tree was constructed to model all the costs and benefits of alternative strategies for the vaccination and treatment of healthy working adults. The time horizon of the model was a complete influenza season. A simple structure of the tree was reported in the paper.

Outcomes assessed in the review
The outcomes assessed from the literature were:

- the probability of influenza illness;
- vaccine efficacy;
- the probabilities of side effects of the central nervous system from using rimantadine, gastrointestinal (GI) side effects from using rimantadine, and GI side effects from using oseltamivir;
- the prevalence of influenza B virus;
- the probabilities of using antibiotic therapy for influenza infection and using antibiotic and antiviral therapy for influenza infection;
- work time lost for one episode of influenza without treatment;
- work time gained from using zanamivir or oseltamivir;
- the duration of symptoms; and
- the duration of symptom relief from the use of rimantadine, zanamivir or oseltamivir.

The prevalence of influenza B virus was not based on published studies, but on the average yearly rate in the UK for the last 10 years.

Study designs and other criteria for inclusion in the review
A formal review of the literature was not undertaken. The design of the primary studies was reported for only some studies, such as clinical trials and meta-analyses.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
The model inputs were obtained from 17 primary studies.

Methods of combining primary studies
Not stated.
Investigation of differences between primary studies
Not stated.

Results of the review
The probability of influenza illness was 15% (range: 1 - 35), while vaccine efficacy was 68% (range: 50 - 86).

The probability values were 2% (range: 0 - 5) for side effects of the central nervous system from using rimantadine, 1% (range: 0 - 5) for GI side effects from using rimantadine, and 9% (range: 5 - 15) for GI side effects from using oseltamivir.

The prevalence of influenza B virus was 16% (range: 1 - 86).

The probability values were 17% (range: 0 - 40) for using antibiotics for influenza infection and 11% (range: 0 - 40) for using antibiotic and antiviral therapy for influenza infection.

The work time lost for one episode of influenza without treatment was 2.8 days (range: 0.5 - 7).

The work time gained from the use of zanamivir or oseltamivir was 0.5 days (range: 0.1 - 1).

The duration of symptoms was 5 days (range: 3 - 7).

The duration of symptom relief was 1.27 days (range: 0.77 - 1.77) from the use of rimantadine, and 1 day (range: 0.6 - 1.3) from the use of zanamivir or oseltamivir.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
It was assumed that vaccination or antiviral therapy would not affect mortality or provide any long-term health benefits. The work time gained from the use of rimantadine was assumed to have been 0.5 days (range: 0.1 - 1). In general, the assumptions made were conservative.

Measure of benefits used in the economic analysis
The summary benefit measure used was the benefit of vaccination. This was defined as the economic value of symptom relief and avoided side effects. It was assessed using the willingness-to-pay for a day of symptom relief and for avoided drug side effects. The conjoint analysis approach was used in a group of 210 patients seeking primary care at a family practice clinic in North Carolina.

Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe. The unit costs were reported separately from the quantities of resources. The costs of antiviral treatments were reported for completed courses. The health services included in the economic evaluation were vaccine, time lost for vaccination, physician visit, rimantadine therapy, zanamivir therapy, oseltamivir therapy, and one course of antibiotics. It was assumed that any benefits of vaccination would not save costs from physician visits. The cost/resource boundary of the study was that of the health service payer for the direct costs. The costs were estimated using data coming from manufacturers, prior studies, and payer databases (i.e. Current Procedural Terminology). The resource use data were derived from assumptions and standard sources (i.e. 5-day course of antiviral therapies). The price year was 2001.

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

**Indirect Costs**
The indirect costs were considered since a societal perspective was applied. Daily wages were estimated from the Bureau of Labor Statistics. The days of work time lost were estimated from the literature. The daily wage was reported separately from the number of days of work lost. No discounting was applied. The price year was 2001.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted on all inputs to address the issue of variability in the data. The ranges used were derived from the literature for most items, and were plausible ranges for the remaining items. A probabilistic sensitivity analysis was also conducted by varying all parameters simultaneously for 1,000 iterations. The parameters were entered as triangular distributions, but other probability distributions (normal and uniform) were considered. Threshold sensitivity analyses were also used for key inputs.

**Estimated benefits used in the economic analysis**
The conjoint analysis revealed that the patient's willingness-to-pay was $15.49 for a day of relief from influenza, $61.79 for a day of relief from nausea, and $56.39 for a day of relief from dizziness. The estimated total benefits for each strategy were not reported.

**Cost results**
The estimated costs for each strategy were not reported. Only the unit costs for vaccination, antiviral therapies and physician visits were presented.

**Synthesis of costs and benefits**
The net benefit (benefits of vaccination minus the costs of vaccination and treatment) was calculated to combine the costs and benefits of the strategies under examination.

The net benefit compared with the base-case strategy (no vaccination and no treatment) was:

- $30.97 with vaccination and treatment with rimantadine;
- $30.13 with vaccination and treatment with zanamivir;
- $29.50 with vaccination and no intervention;
- $29.39 with vaccination and treatment with oseltamivir;
- $4.61 with no vaccination and treatment with rimantadine;
- $1.97 with no vaccination and treatment with zanamivir; and
- -$0.032 with no vaccination and treatment with oseltamivir.

The sensitivity analysis showed that the model inputs with the greatest impact on the estimated net benefit were the prevalence of influenza and the number of workdays affected by influenza-related illness. Specifically, if the influenza prevalence was lower than 6.3%, then non-vaccination would be more cost-beneficial than vaccination. Similarly, if less than 0.98 workdays were lost because of influenza infection, then non-vaccination would be more cost-beneficial.
However, both values were quite far from the baseline assumptions. Variations in other inputs did not change the results of the base-case analysis.

The probabilistic sensitivity analysis showed that strategies including vaccination were favoured over non-vaccination in 95% of iterations. Vaccination plus antiviral therapy was the optimal strategy in 79% of iterations.

In terms of antiviral therapies, vaccination with rimantadine was the preferred strategy in 35% of iterations, followed by vaccination plus zanamivir with 31% of iterations. Non-vaccination and no-antiviral therapy were never the preferred strategy.

Authors’ conclusions
All of the vaccination strategies had a higher net benefit than strategies without vaccination. Among antiviral strategies, rimantadine and zanamivir were the most cost-beneficial options.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear since the authors covered all possible strategies for the management of influenza. The choice of the antiviral treatments reflected the drugs usually prescribed for influenza infection. Amantadine was also available for influenza treatment, but it was not considered as a possible treatment option because it was less efficacious than rimantadine and had more side effects. The strategy of no vaccination and no treatment was appropriately selected to reflect standard care. You should decide whether this is relevant to your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness aimed to identify the relevant model inputs, which were derived from published studies. A formal review of the literature was not undertaken and there was limited information on the design of the primary studies. Therefore, it was difficult to assess the validity of the primary estimates. However, some of the studies were clinical trials and meta-analyses, which increased the robustness of the estimates used in the model. The methods used to extract and combine the primary estimates were not reported. Some assumptions were also made. Uncertainty surrounding all model inputs was investigated in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was estimated using the willingness-to-pay approach, which was consistent with the cost-benefit design. The method used to elicit monetary preferences was reported.

Validity of estimate of costs
The analysis of costs was appropriately carried out from a societal perspective. As such, it appears that all the relevant categories of costs have been included in the analysis. The unit costs, source of the data, quantities of resources used and price year were reported, which facilitate replication of the results and reflation exercises in other settings. The costs were treated deterministically in the base-case, but extensive probabilistic sensitivity analyses were conducted to investigate the robustness of the estimated costs. However, the results of the cost analysis were not reported.

Other issues
The authors compared their findings with those from two published trials. They found the results were consistent with one study but disagreed with the results of the other. However, the authors justified the reasons for the differences in the conclusions of the analysis. The issue of the generalisability of the study results to other settings was not addressed, but extensive sensitivity analyses were conducted. These enhanced the external validity of the analysis. The authors noted some limitations of their study. First, the limited literature available on the efficacy of antiviral therapies. Second, the impact of factors, such as income, on willingness-to-pay estimates. Third, the lack of consideration of specific issues, such as post-exposure prophylaxis with antivirals. A further point was the fact that no distinction was made
between real influenza and influenza-like illness.

**Implications of the study**
The authors suggested that head-to-head trials of the strategies under evaluation in the current study should be conducted to identify, appropriately, the optimal treatment for the management of influenza in healthy working adults.

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**Other publications of related interest**


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