A cost-benefit analysis of testing for influenza A in high-risk 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
Two strategies for treating influenza in high-risk individuals were examined. One was empirical treatment with four alternative therapies (amantadine, rimadidine, zanamivir, or oseltamivir). The other was a rapid test and the treatment of test-positive patients.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-benefit analysis.

Study population
The study population comprised a hypothetical cohort of unvaccinated patients older than 65 years and those older than 50 years who had chronic obstructive pulmonary disease, asthma or other chronic respiratory tract conditions, pre-existing malignancy, diabetes, or cardiac diseases. Only influenza A strains were considered.

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

Dates to which data relate
The effectiveness data were derived from studies published between 1999 and 2002. The resource use and cost data came from studies published between 1996 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' assumptions.

Modelling
A decision tree model was constructed to examine the economic costs and benefits of the alternative strategies under evaluation. A simplified structure of the tree was provided. The three alternatives considered were test and treat (when test is positive), treat all patients, and no treatment. In the test-and-treat arm, given the sensitivity and specificity of the test, true negatives, true positives, false positives and false negatives were considered. In the case of a positive test (true or false), the use of antiviral drugs could lead to side effects, while in the case of a negative test (true or false), complications may arise. In the treat-all arm, the use of antiviral drugs may lead to side effects. Finally, in the no treatment arm, complications may occur in the case of flu. The time horizon of the model was one month.

Outcomes assessed in the review
The outcomes estimated from the literature were test sensitivity and specificity, the probability of drug side effects, and the probability of influenza complications.

**Study designs and other criteria for inclusion in the review**
It was not stated whether a systematic review of the literature was undertaken to identify relevant primary studies. No information on the design and characteristics of the primary studies was reported.

**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**
Eleven primary studies provided evidence.

**Methods of combining primary studies**
Average values were calculated when multiple sources were available.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The sensitivity of the test was 72.5% (range: 50 - 95) and the specificity was 90% (range: 80 - 100).

The probability of drug side effects was 3% (range: 0 - 6).

The probability of influenza complications was 0.5 (range: 0.3 - 5).

**Methods used to derive estimates of effectiveness**
A key assumption on the efficacy of anti-influenza treatment was made.

**Estimates of effectiveness and key assumptions**
It was assumed that patients receiving anti-influenza treatment would return to work one day earlier than patients receiving no treatment.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the increase in productivity. This was based on the patient being able to return to work earlier because of the beneficial effect of treatment (as estimated already). The unit cost of productivity gains was based on the hourly wage plus the benefits for a worker in the USA.
Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe (one month). Some unit costs were presented separately from the quantities of resources used. The economic evaluation considered diagnostic tests, medications, outpatient visits, the treatment of adverse events, and insurance co-payments for hospital or outpatient services. The cost of the initial visit to the clinician was not considered since all patients would have already incurred this expense. The cost/resource boundary of the health care system and the patient was adopted in the analysis of the direct costs. The cost of a visit for diagnostic codes for influenza was estimated by calculating the weighted average visit costs for respiratory tract infections. Other resource use data were derived from authors’ opinions and published evidence. The costs came from reimbursement rates, average wholesale prices, hospital sources and published data. Diagnostic tests costs were based on the average cost of five currently commercially available test kits. All of the costs were adjusted to 2002 values using the medical component of the Consumer Price Index.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs (i.e. productivity losses) were not considered on the cost side of the analysis.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out on all model inputs to examine the robustness of the base-case results to variations in base-case assumptions. Two-way sensitivity analyses were also performed on some key inputs. The results were presented as threshold analyses representing the point at which the economic value assigned to an earlier recovery altered the decision for the entire range of pre-test probabilities. The ranges of values used were mainly derived from the literature.

Estimated benefits used in the economic analysis
The estimated benefits were not reported.

Cost results
The estimated costs were not reported.

Synthesis of costs and benefits
A cost-benefit ratio was calculated to combine the economic costs and benefits of the alternative diagnostic and treatment strategies under examination. As already stated, the results were presented using a threshold analysis.

When using amantadine, the preferred strategy was no treatment with a probability of influenza less than 5% and empiric treatment with a probability of 5% or higher (test and treat was never cost-beneficial).

When using rimantadine, the preferred strategy was no treatment with a probability of influenza less than 11% and empiric treatment with a probability of 11% or higher (test and treat was never cost-beneficial).

When using zanamivir, the preferred strategy was no treatment with a probability of influenza less than 19%, test and treat with a probability of influenza between 19 and 28%, and empiric treatment with a probability greater than 28%.

When using oseltamivir, the preferred strategy was no treatment with a probability of influenza less than 22%, test and
treat with a probability of influenza between 22 and 36%, and empiric treatment with a probability greater than 36%.

The sensitivity analysis showed that whenever the probability of the patient having influenza was better than about 50%, empiric treatment remained preferable. For the non-neuraminidase inhibitors, even at these extreme values, empiric treatment always was less expensive than testing.

When drug side effects were set at 10% and the cost of side effects increased to $300 per episode, empiric treatment saved money compared with no treatment when the probability of disease was more than 50%.

When the benefits assigned to increased productivity were reduced (to account for the fact that some patients could not be of a working age), both amantadine and rimantadine were cost-beneficial in comparison with no treatment, providing that the probability of influenza was greater than 50%.

Authors' conclusions
The two most important factors to consider in the decision of whether to treat empirically or test a patient for influenza were the probability that the patient has influenza and the drug that will be used for treatment. In particular, the analysis showed that when influenza was probable (greater than 50% chance), then empiric treatment was the best strategy regardless of the drug used. However, when influenza was less likely (20 to 40% chance), testing was a cost-beneficial strategy only if a neuraminidase inhibitor (zanamivir or oseltamivir) was used. Only when it was fairly certain that the patient did not have influenza was no treatment the most cost-beneficial approach.

CRD COMMENTARY - Selection of comparators
The selection of the comparators appears to have been appropriate as the interventions examined in the study represented possible strategies for the treatment of patients with influenza symptoms. The drugs considered were commonly used therapies. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from published evidence. However, it was unclear whether a systematic review of the literature had been undertaken to identify relevant studies. In fact, the primary studies appear to have been identified selectively. The authors did not describe the design and characteristics of the primary sources. Thus, it was not possible to examine the validity of the studies used. A key assumption was also made. The issue of uncertainty was extensively addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was disease-specific and is only comparable with other interventions for the treatment of influenza. Therefore, it is not possible to compare the benefits assessed in the current study with those of other health care interventions.

Validity of estimate of costs
The economic analysis covered all possible categories of costs, although indirect costs were evaluated on the side of the benefits. Information on the unit costs and quantities of resources used was not provided separately for all items. The source of the data was reported for most categories of costs. Discounting was not relevant because only short-term costs were considered. The price year was reported, which will aid reflation exercises. The costs were treated deterministically, but the economic estimates were varied in the sensitivity analysis.

Other issues
The authors compared their findings with those from other studies and observed consistent results. The issue of the generalisability of the study results to other settings was implicitly addressed in the sensitivity analysis, the results of which were extensively reported. This enhances the external validity of the analysis. The authors noted some limitations...
of their study. First, the benefit measure was difficult to measure since most of the patients were old and not of a working age. However, the sensitivity analysis revealed that this did not represent a key model variable. Second, in a real-world setting, the patient population may be different from the patients considered in the current study. High-risk patients usually receive vaccination, while the study considered only unvaccinated individuals.

Implications of the study
The study results supported the use of empiric treatment for patients with symptoms of influenza under most circumstances considered in the decision model. The authors stated that the findings of their study may help guide testing or treatment decisions for high-risk patients.

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Other publications of related interest


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