Economic evaluation of influenza pandemic mitigation strategies in the United States using a stochastic microsimulation transmission model

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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.

CRD summary
This study investigated the cost-effectiveness of 16 strategies to reduce the impact of an influenza pandemic. The authors concluded that the strategies of pre-pandemic vaccination and targeted antiviral prophylaxis (using oseltamivir) were effective and cost-saving compared with no intervention. The addition of school closures further reduced the attack rates, morbidity, and deaths and was cost-effective from a societal perspective. The methods were transparent and generally supported the authors’ conclusions, which were based on the available evidence.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to evaluate the costs and health effects of strategies to reduce an influenza pandemic in the community. The population was considered by contact groups (households, child-care centres, larger neighbourhoods, and work groups) and by age group (zero to four, five to 18, 19 to 64, and 65 years or older). Younger adults were further grouped into those at high or low risk, according to underlying chronic conditions.

Interventions
There were 16 single or combination strategies that were compared with no intervention. The strategies included vaccinating 70% of the population, preventive treatment with antivirals (oseltamivir) after exposure, school closures for 26 weeks, and case treatment only. Some of these strategies were also combined and assessed with different target groups for the antiviral prevention, with different stockpiles of antivirals for the population (full, 25% or 50%), or both.

Location/setting
USA/primary care.

Methods
Analytical approach:
A discrete-time stochastic simulation model was used to synthesise the published data from scientific literature and other sources. The model simulated the spread of disease among interacting individuals. The time horizon was six months (one pandemic wave) and the authors stated that their study was carried out from a societal perspective.

Effectiveness data:
The clinical data for the effectiveness of oseltamivir, the low-efficacy vaccine, and influenza-induced bronchitis, pneumonia, otitis media, and deaths, were from a selection of studies published between 1999 and 2007, as well as authors’ assumptions and unpublished data. Other clinical outcomes included influenza hospitalisations, transmission parameters, and quality of life improvements. Transmission parameters were from other published models. To determine the average number of secondary infections, produced by a typical infected person, in a fully susceptible population, 100 simulations were performed for each intervention and the results were averaged.

Monetary benefit and utility valuations:
The utility weights for influenza were from those reported in a clinical trial (Turner, et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details), while those for otitis media were from other published information. The weights for bronchitis were assumed to be the same as those for influenza.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and they were discounted at 3% per annum.

Cost data:
The direct medical costs were included for the treatment of influenza (separately for children and adults), physician visits, hospitalisations, antibiotics and over-the-counter medicines, vaccine drug and delivery, travel and time to obtain antiviral medications, and work lost due to school closures. The unit costs were based on US fees and price schedules, diagnosis-related groups, bulk prices to the government for oseltamivir drug and delivery, average wages for work losses, and expert opinion for health resource use. All costs were reported in US dollars ($) and the cost of oseltamivir was converted from Euros (EUR) to dollars using the Interbank rate on 5th July 2006.

Analysis of uncertainty:
Uncertainty was measured in one-way sensitivity analyses on the key model parameters (viral reproducibility, mortality, school closure costs, and probability of a pandemic), except the oseltamivir effectiveness estimates. The results of these analyses were presented in the main text and a supplement.

Results
The base-case results, for all 16 strategies and no intervention, were ranked by their QALYs. Thirteen of the strategies were dominated as they were more costly and less effective than another strategy. The three remaining non-dominated strategies were antiviral prophylaxis for household contacts and 60% of work or school contacts (full prophylaxis), full prophylaxis and school closure, and vaccination and school closure. These were considered in an incremental analysis.

For every 1,000 individuals, the total costs were $0.12 million for full prophylaxis, $2.73 million for full prophylaxis and school closure, and $2.73 million for vaccination and school closure. The total QALYs were 21,352 for full prophylaxis, 21,403 for full prophylaxis and school closure, and 21,403 for vaccination and school closure. Using full prophylaxis as the comparator, the incremental cost per QALY ratios were $48,472 for full prophylaxis and school closure, and $48,638 for vaccination and school closure.

The one-way sensitivity analyses showed that the ranking of the incremental cost-utility ratios was stable to variations in: the basic reproductive number (viral reproducibility) between 1.5 and 2.6; resource use for influenza treatment; and assumptions on mortality and school closure productivity losses.

Authors’ conclusions
The authors concluded that pre-pandemic vaccination and full targeted antiviral prophylaxis, using oseltamivir, were effective in mitigating influenza and were predicted to be cost-saving compared with no intervention. The addition of school closures increased the health benefits and was considered to be cost-effective from a societal perspective.

CRD commentary
Interventions:
The authors’ provided clear descriptions of the 16 strategies for pandemic influenza management.

Effectiveness/benefits:
The clinical effectiveness parameters were from relevant published research, which included a detailed systematic review (Turner, et al. 2003). The data sources were clearly reported, along with all of the assumptions made. The methods used to measure the utilities were not stated, but were referenced (Turner, et al. 2003) and this reference should be consulted to assess the quality of these data. Some supplementary material was provided.

Costs:
A societal perspective was taken and the relevant direct medical resources and productivity losses, during influenza illness and school closures were included, but the time taken to receive the vaccine was not included. The resources involved in a mass media campaign and dissemination of the vaccine were also not considered and might have had a significant impact on the conclusions. It was unclear whether the resource use associated with complications from antivirals and vaccines was included.
Analysis and results:
The authors acknowledged a number of limitations to their study and these included uncertainties about disease factors, such as infectivity, the antigenic nature of the virus, the feasibility of the timely availability of a pandemic vaccine, production capacity, and shelf life. Considerable variations in the parameters were investigated in the sensitivity analyses and did not change the key findings. These results were reported in appendices. The micro-simulation model took into account population heterogeneity (age, risk profile, and contact groups) and different treatment costs or resources for different age groups.

Concluding remarks:
Despite some limitations in the published evidence for the clinical estimates and viral disease characteristics, the methods were appropriate, transparent, and comprehensive. The conclusions reached by the authors appear to reflect the analysis time horizon of a single pandemic wave.

Funding
Supported by the National Institute of General Medical Sciences, and consultancy fees were received from F. Hoffmann-La Roche, Ltd, Basel, Switzerland (manufacturers of oseltamivir).

Bibliographic details

PubMedID
18671770

DOI
10.1111/j.1524-4733.2008.00437.x

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Antiviral Agents /economics /therapeutic use; Computer Simulation; Cost Savings; Cost-Benefit Analysis; Disease Outbreaks /economics /prevention & control; Humans; Influenza, Human /economics /epidemiology /prevention & control; Models, Biological; Models, Economic; Public Health /economics /methods; Quality of Life; Quality-Adjusted Life Years; Stochastic Processes; United States /epidemiology

AccessionNumber
22009100868

Date bibliographic record published
07/04/2009

Date abstract record published
22/09/2010