Effectiveness and cost-effectiveness of expanded antiviral prophylaxis and adjuvanted vaccination strategies for an influenza A (H5N1) pandemic
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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 three strategies for vaccinating against, and treating illness from, a pandemic of influenza H5N1. The authors concluded that an expanded vaccination strategy, with 40% population coverage, combined with the current US antiviral stockpiles, was most effective and was cost-effective. The methods were transparent and the findings were clearly reported. The authors’ conclusions appear to reflect the scope of the analysis.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to evaluate the cost-effectiveness of three vaccination and response strategies for an influenza A (H5N1) pandemic. The population was a hypothetical cohort of 8.3 million US metropolitan residents, representing the population of New York City. At the start of the pandemic, it was assumed that 1,000 people were infected.

Interventions
Three scenarios were compared with no intervention. The stockpiled strategy was vaccination and the administration of antiviral drugs, using the usual US supplies. The expanded antiviral strategy was the usual supply of vaccination, with the antiviral drugs extended to 40% of the population. The expanded vaccination strategy was the usual supply of antiviral drugs, with vaccination extended to 40% of the population. All strategies were in addition to non-pharmaceutical public health hygiene measures.

Location/setting
USA/primary care.

Methods
Analytical approach:
A compartmental epidemic model and a Markov model were used to synthesise the published data from studies and official sources. The analysis had a lifetime horizon and the authors stated that it was carried out from a societal perspective.

Effectiveness data:
The clinical data for the efficacy of the vaccine and antiviral drugs were from a selection of relevant published studies, government statistics, authors’ assumptions, and a meta-analysis of an extended duration of neuraminidase inhibitor prophylaxis against influenza (Khazeni, et al. 2009, see ‘Other Publications of Related Interest’ below for bibliographic details). The clinical outcomes included influenza transmission rate, clinical attack rate, case-fatality rate, deaths, deaths averted, and vaccine or antiviral adverse reactions.

Monetary benefit and utility valuations:
The influenza-related health state values were derived from published studies, using the European Quality of life (EQ-5D) questionnaire, and from authors’ assumptions.

Measure of benefit:
The measure of benefit used was the quality-adjusted life-year (QALY) and these were discounted at an annual rate of 3%.

Cost data:
The direct medical costs were included for vaccine antigen, adjuvant and administration, antiviral drugs, dispensing, rotation of stockpile, health care for adverse vaccine or antiviral treatment effects, general health care, and hospitalisations. The patient time taken in receiving the vaccine was also included and valued from US Bureau of Labor Statistics. The unit costs were based on wholesale prices and were from a selection of relevant published sources, government departments, and personal communications with experts. Future costs were discounted at 3% per annum and adjusted to 2009 US dollars ($) using the Gross Domestic Product deflator.

Analysis of uncertainty:
The uncertainty was measured in one-way sensitivity analyses on all the model parameters and a probabilistic sensitivity analysis, using Monte Carlo simulations. The results were presented graphically and in the main text and appendices. Cost-effectiveness acceptability curves were presented in the appendices.

Results
There were 67,822 deaths with no intervention. 38,061 with the stockpiled strategy, 35,077 with expanded antiviral treatment, and 21,882 with expanded vaccination. The discounted QALYs gained over no intervention were 404,030 with expanded vaccination, 282,329 with expanded antivirals, and 258,342 with the stockpiled strategy.

Over the cohort lifetime, the total discounted costs were $1,497,403 million with no intervention, $1,499,704 million with the stockpiled strategy, $1,500,339 million with expanded antivirals, and $1,501,284 million with expanded vaccination.

The incremental costs per QALY were $10,844 for expanded vaccination compared with the stockpiled strategy and $8,907 for the stockpiled strategy compared with no intervention. Expanded antiviral prophylaxis was dominated by extension, which means that its incremental cost per QALY was higher than another more effective intervention.

There was an 88% probability that the incremental cost per QALY for expanded vaccination would be less than $50,000 and only a 5% probability that another strategy would have higher QALYs and lower costs. The one-way sensitivity analyses found that the results were robust to changes in the assumptions and inputs, varying within ±$2,000 in most cases.

Authors' conclusions
The authors concluded that the expanded vaccination strategy was the most effective and cost-effective, based on the current knowledge of vaccine efficacy and influenza transmission rates. They suggested that further research should be conducted into the safety and efficacy of influenza H5N1 vaccines for children.

CRD commentary
Interventions:
Clear and comprehensive dosing and population coverage details were given for the three strategies of influenza H5N1 management. You should decide if these are feasible options in your own setting.

Effectiveness/benefits:
The clinical effectiveness data were derived from relevant published research, including systematic reviews. The sources were clearly reported as were all the assumptions and justifications for their use. The methods used to measure the utilities were briefly reported and the source studies should be consulted to assess the quality of these data.

Costs:
A societal perspective was taken and all the relevant medical resources appear to have been included. Patient time was estimated, but productivity lost due to influenza was not included and neither was a media campaign or other resources needed for mass vaccinations that were assumed to be completed over 10 days. Adverse events and resource use data were from expert opinion due to a lack of published data. Detailed information on the costing methods was available in
the appendices.

Analysis and results:
The authors reported a number of limitations to their study and these included a population model that assumed a homogeneous mix of individuals and disease transmission rates, an assumption of continued effectiveness of the vaccine without strain mutation, and a reliance on expert opinion. The details of the probabilistic sensitivity analysis methods, such as the parameter distributions and the number of simulations, and its results, including 95% confidence intervals, were provided in the appendices. Further discussion on the logistics of implementing the vaccination strategies on a large scale would have been useful.

Concluding remarks:
: There were some limitations, such as a lack of evidence to substantiate the estimates used, but the methods were appropriate, transparent, and comprehensive. The conclusions appear to reflect the scope of the analysis.

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