
Effects of adverse events on the projected population benefits and cost-effectiveness of using live attenuated influenza vaccine in children aged 6 months to 4 years

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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 assessed the cost-effectiveness of vaccination with live attenuated influenza vaccine or with inactivated influenza vaccine, for children younger than five years, considering the impact of adverse events. The authors concluded that the live attenuated vaccine was similar in cost-effectiveness to the inactivated vaccine, under a wide range of assumptions on the incidence of adverse events. The methods were valid and should ensure that the authors' conclusions are robust.

Type of economic evaluation

Cost-effectiveness analysis, cost-utility analysis

Study objective

This study assessed the cost-effectiveness of vaccination with live attenuated influenza vaccine or with inactivated influenza vaccine in children younger than five years, focusing on the impact of adverse events.

Interventions

The three options were no vaccination, inactivated influenza vaccine, and live attenuated influenza vaccine.

Location/setting

USA/primary care.

Methods

Analytical approach:

The analysis was based on a published decision-tree model that considered three cohorts of children aged: six to 23 months; two years (24 to 35 months); and three to four years. The outcome was influenza occurring within one year of vaccination, but a lifetime horizon was considered to capture the effects of long-term sequelae or death. The authors stated that a societal perspective was adopted.

Effectiveness data:

The clinical data were from a selection of relevant studies. A clinical trial provided some of the data for the live attenuated vaccine adverse events. Experts' opinions were used where there were no published studies and some assumptions were required. The vaccine efficacy in preventing influenza infection and the probability of medically attended vaccination-related adverse events were the key inputs for the analysis.

Monetary benefit and utility valuations:

The utility values were from published studies and studies carried out by the authors of this analysis.

Measure of benefit:

Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%. Other model outcomes, such as hospitalisations, deaths, and influenza episodes avoided, were reported.

Cost data:

The economic analysis included both the direct and indirect costs of vaccine acquisition and administration, physician visits for uncomplicated influenza, otitis media, or pneumonia, parents' time, hospitalisations due to vaccination-related

adverse events, wheezing episodes requiring physician or emergency department visits, prescription medications, and long-term sequelae (including lifetime care and special education). The quantities of resources were from published studies and experts' opinions. Most of the costs were based on Centers for Disease Control and Prevention (CDC) negotiated prices. They were in US dollars (\$) and a 3% annual discount rate was applied. The price year was 2006.

Analysis of uncertainty:

One-way sensitivity analyses were carried out on all the inputs to the model, using published or assumed ranges of values. A probabilistic sensitivity analysis was carried out, using a Monte Carlo simulation.

Results

In children aged six to 23 months, the expected costs, compared with no vaccination, were \$71,000 with live attenuated and \$63,000 with inactivated vaccine. The QALYs were 3.6 with live attenuated and 3.0 with inactivated vaccine. Including wheezing-related adverse events in the live attenuated vaccine arm, the incremental cost per QALY gained over no vaccination was \$20,000 with the live attenuated vaccine and \$21,000 with the inactivated vaccine.

In children aged two years, the expected costs were \$64,000 with live attenuated and \$59,000 with inactivated vaccine. The QALYs were 2.9 with live attenuated and 2.4 with inactivated vaccine. The incremental cost per QALY gained was \$23,000 with live attenuated vaccine and \$25,000 with inactivated vaccine, over no vaccination.

In children aged three to four years, the expected costs were \$67,000 with live attenuated and \$62,000 with inactivated vaccine. The QALYs were 2.0 with live attenuated and 1.7 with inactivated vaccine. The incremental cost per QALY gained was \$33,000 with live attenuated vaccine and \$37,000 with inactivated vaccine.

The exclusion of wheezing-related adverse events did not substantially alter the base-case findings. Wide confidence intervals around the mean outcomes were observed. The most influential inputs were the probability of influenza illness, the probability of influenza-related hospitalisation, and the total vaccination costs. No parameter variation, except for the influenza illness rate, led to an incremental cost per QALY for live attenuated vaccine of more than \$40,000.

Authors' conclusions

The authors concluded that the live attenuated vaccine had similar cost-effectiveness to the inactivated vaccine, considering a wide range of assumptions on the incidence of adverse events.

CRD commentary

Interventions:

The selection of the comparators was appropriate because the available vaccination strategies were considered. No vaccination was a relevant strategy. A direct comparison of the two immunisation strategies was not carried out.

Effectiveness/benefits:

The clinical data were selected without a review of the literature. Little information on the sources was provided and it is not possible to judge the quality of the clinical inputs. The authors did not state the method used to synthesise data from several sources. Experts' opinions were used for some items, where data were not readily available from the literature. Extensive sensitivity analysis was conducted on all the model parameters. QALYs were an appropriate benefit measure as the disease has a substantial impact on both survival and quality of life. The authors did not state the instrument used to elicit the preferences. Some utility weights were from adults and patients with other conditions, as there was a lack of estimates for children. The other outcome measures were specific to influenza.

Costs:

The cost categories were consistent with the economic viewpoint. Most of the unit costs were presented in an online appendix, but some costs were reported as category totals. The data sources were reported, but were not fully described for the resource use, some of which was based on authors' opinions. The price year and discounting were reported. The inclusion of the costs of vaccination-related adverse events was a key part of the analysis, but their exclusion did not substantially alter the base-case findings.

Analysis and results:

The incremental results were reported for each immunisation strategy, compared against no vaccination. The uncertainty was satisfactorily investigated. Conventional predefined probability distributions were assigned to the model inputs. The authors pointed out that the exclusion of herd immunity effects could limit their analysis. Several assumptions, especially for the utility values for hospitalisation, were based on expert opinion rather than published evidence, and might have introduced uncertainty into the analysis.

Concluding remarks:

The methods were valid and this should ensure that the authors' conclusions are robust.

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