Economic evaluation of MF59 adjuvanted vaccine against influenza in the high-risk elderly population in France

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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
The study examined the MF59 adjuvanted vaccine, an adjuvanted trivalent influenza vaccine prepared from influenza virus Type A and B strains combined with an oil-in-water emulsion adjuvant.

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of high-risk elderly, defined as those over the age of 65 years and suffering from heart or lung disease.

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

Dates to which data relate
The effectiveness and resource use data were mainly derived from studies published between 1994 and 2002. The price year was unclear.

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

Modelling
A cohort model was used to assess the costs and consequences of adjuvanted vaccine against influenza in comparison with standard non-adjuvanted vaccination in the high-risk elderly. The model considered the attack rate in the relevant population, and subsequent cases, general practitioner (GP) visits, hospital admissions and deaths. Adverse events were not considered. The time horizon of the analysis was one year.

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

the size of the high-risk elderly population,
vaccination coverage,

excess primary care visits,

the antibiotic prescribing rate,

excess hospitalisations due to influenza,

excess mortality rate due to influenza, and

vaccine efficacy, calculated using a specific relationship between immunogenicity and efficacy.

**Study designs and other criteria for inclusion in the review**

It was unclear whether the primary studies were identified selectively, or by means of a systematic review of the literature. Data were estimated from multiple sources, including national statistics and published and unpublished studies.

**Sources searched to identify primary studies**

Not reported.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

Not reported.

**Number of primary studies included**

Five primary studies appear to have been the main sources of the clinical data.

**Methods of combining primary studies**

The primary studies were not combined because each study provided a single estimate.

**Investigation of differences between primary studies**

Not reported.

**Results of the review**

The size of the high-risk elderly population was 1,000,000.

Vaccination coverage was 61%.

The level of excess primary care visits was 31%.

The antibiotic prescribing rate was 59%.

Among the excess hospitalisations due to influenza, 2.3% were for influenza and pneumonia and 8.1% were for other respiratory conditions.

The excess mortality rate due to influenza was 2.3%.
The effectiveness of vaccination in the high-risk elderly was:

63.9% with standard vaccination and 73.5% with adjuvanted vaccination (case reduction 26.6%) for A/H3N2 strain;

63.1% with standard vaccination and 66.9% with adjuvanted vaccination (case reduction 10.4%) for A/H1N1 strain; and

56.5% with standard vaccination and 66.8% with adjuvanted vaccination (case reduction 23.8%) for B strain.

**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**
The attack rate was assumed to be 5%.

It was assumed that a reduction in cases led to only half as great a reduction in downstream consequences (health care resources, utilisation and costs, and mortality), thus a transfer rate of 50% was assumed.

It was assumed that mortality resulted in a mean of 7 years of life lost.

**Measure of benefits used in the economic analysis**
The summary benefit measures that were combined with the costs were the deaths averted and life-years gained. The number of influenza cases avoided was also reported. The life-years gained were discounted.

**Direct costs**
The analysis of the costs was carried out from the perspective of the health care system. The cost categories included were vaccine, vaccine administration, primary care consultations, antibiotic prescriptions, and hospitalisations. The unit costs were presented separately from the quantities of resources used for most items. Resource use was estimated from published data. The costs came from a study published in 1999 and from French hospital statistics. The cost of adjuvanted vaccination was based on data coming from countries where the new vaccine had already been licensed. Discounting was not relevant, as the time horizon of the model was one year, and was not performed. The price year was not reported.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
Euros (EUR).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to assess the robustness of cost-effectiveness ratios to variations in some uncertain assumptions made in the model. Specifically, the attack rate, discount rate for benefits, life expectancy, and transfer rate. Wide variations in these data were tested. The best- and worst-case scenarios were also identified.
Estimated benefits used in the economic analysis
The expected number of influenza cases avoided with adjuvanted vaccine against influenza in comparison with standard non-adjuvanted vaccination in the high-risk elderly was 3,813 for A/H3N2 strain, 1,477 for A/H1N1 strain, and 3,397 for B strain.

The incremental deaths avoided were 48 for A/H3N2 strain, 19 for A/H1N1 strain, and 43 for B strain.

The incremental life-years gained were 337 for A/H3N2 strain, 130 for A/H1N1 strain, and 300 for B strain.

Cost results
The incremental costs with adjuvanted vaccine against influenza in comparison with standard non-adjuvanted vaccination in the high-risk elderly were EUR 899,481 for A/H3N2 strain, EUR 1,621,074 for A/H1N1 strain, and EUR 1,027,863 for B strain.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated to combine the costs with each of the two benefit measures used in the analysis.

The incremental cost per death averted with adjuvanted vaccine against influenza in comparison with standard non-adjuvanted vaccination in the high-risk elderly was EUR 18,701 for A/H3N2 strain, EUR 87,040 for A/H1N1 strain, and EUR 23,985 for B strain.

The incremental cost per life-year gained with adjuvanted vaccine against influenza in comparison with standard non-adjuvanted vaccination in the high-risk elderly was EUR 3,759 for A/H3N2 strain, EUR 17,496 for A/H1N1 strain, and EUR 4,821 for B strain.

The sensitivity analysis showed that higher attack rates were associated with lower cost-effectiveness ratios. In particular, when the attack rate approached 10% (the rate observed in practice), adjuvant vaccination was dominant because it was more effective and less expensive than standard vaccination.

Changes in life expectancy and discount rate showed that the cost per life-year gained ranged from EUR 3,426 to EUR 26,383. The choice of the discount rate had a minor impact on the results of the model.

Changes in the transfer rate suggested that, even when the transfer rate fell as low as 30%, adjuvanted vaccination was cost-effective.

Overall, the best case for adjuvanted vaccination was high attack rate, no discounting, and a proportionate change in effects. The worst case was the opposite, namely low attack rate, high discounting, and small changes in knock-on effects.

Authors' conclusions
Adjuvanted vaccination against influenza in the high-risk elderly was cost-effective in comparison with standard vaccination, regardless of the circulating influenza strain.

CRD COMMENTARY - Selection of comparators
The authors provided justified their choice of the comparator (standard non-adjuvanted vaccination). The 'do-nothing' option was not considered as a comparator since the new vaccine was compared with the available existing therapeutic strategy, which was standard non-adjuvanted vaccination. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were mainly derived from published studies. However, a systematic review of the literature was presumably not performed to identify the primary estimates. There was no information on the design and characteristics of the primary studies, which limits the possibility of assessing the validity of the primary data. The methods used to extract and combine the primary estimates were not described, and the issue of heterogeneity across the primary studies was not addressed. The robustness of the clinical estimates was investigated in sensitivity analyses, especially for those estimates that were based on opinions rather than on published sources.

**Validity of estimate of measure of benefit**

Two benefit measures were used in the analysis. Specifically, life-years gained, which are comparable with the benefits of other health care interventions, and deaths avoided, which can also be generalised to other diseases. Both measures were appropriate for assessing the impact of the vaccination strategies on patient health. Discounting was applied to future life-years gained, as recommended in French guidelines for economic evaluations. The impact of changes in the discount rate was tested in the sensitivity analysis. The authors did not assess the impact of the intervention on quality of life, owing to the lack of robust evidence on this aspect of health.

**Validity of estimate of costs**

The perspective of the study was clearly reported and only direct medical costs were considered in the analysis. The source of the data was reported for all items. A breakdown of the costs was provided and most unit costs were presented. Utilisation rates were also provided. This enhances the possibility of replicating the analysis in other settings. No statistical analyses of the costs were carried out. These costs were specific to the French setting and the impact of alternative estimates was not investigated. The price year was not reported, which will make reflation exercises in other time periods difficult.

**Other issues**

The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. Some data used in the analysis were specific to the study setting. However, the sensitivity analysis, in part, addressed this issue by considering different attack rates and alternative estimates of life expectancy. The authors pointed out that the analysis was based on conservative assumptions and the impact of key data was tested in the sensitivity analysis, which represents a further strength of the analysis. It was also noted that the analysis used data related to all elderly patients, thus higher event rates would have been achieved if data referring to high-risk elderly patients had been used. The study referred to the high-risk elderly, but the authors stated that some of their conclusions may also be valid for the general population of elderly people.

**Implications of the study**

The study results support the use of adjuvanted vaccination against influenza in high-risk elderly people.

**Source of funding**

Funded by Chiron Vaccines.

**Bibliographic details**


**Other publications of related interest**


Indexing Status
Subject indexing assigned by CRD

MeSH
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