Estimating the cost-effectiveness of vaccination against herpes zoster in England and Wales
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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 evaluated the cost-effectiveness of routine vaccination, with herpes zoster vaccine, of the elderly (over 60 years) in England and Wales. The authors concluded that vaccination of the elderly against herpes zoster was likely to be cost-effective, especially at 70 years of age. The methodology seems to have been appropriate and was well reported. The conclusions reached by the authors appear to be valid and fairly robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to evaluate the effectiveness and cost-effectiveness of routine vaccination with a herpes zoster (HZ) vaccine, for the elderly (over 60 years) in England and Wales.

Interventions
Zostavax (Merck & Co. in the USA, Sanofi Pasteur MSD in Europe), which consists of a live attenuated (OKA strain) varicella zoster virus, was compared with the current policy of no mass vaccination. Although a one dose schedule was used for the baseline scenario, a two dose schedule was also evaluated.

Location/setting
England and Wales/primary care.

Methods
Analytical approach:
A Markov cohort model with a lifetime horizon was programmed in Excel. The authors stated that a health care provider perspective was taken.

Effectiveness data:
The evidence came from a selection of seemingly known, recent, relevant studies. The authors used their judgement to select the most appropriate estimates from the evidence found in the literature. The main efficacy parameters were the proportion of vaccinees who responded (vaccine take) and the decline in vaccine efficacy with time (vaccine wane). These were considered to be positively correlated and were estimated by fitting a model to the large-scale randomised clinical trial data. Other efficacy parameters included the age-specific incidence rates, mortality (all-cause and HZ specific), pain score, and rate of ophthalmic zoster.

Monetary benefit and utility valuations:
The vaccine efficacy in terms of the severity and duration of pain, as well as of acute HZ and post herpetic neuralgia, was extrapolated and combined with quality of life (QoL) weights to obtain quality-adjusted life-year (QALY) losses. QoL estimates were derived from studies which evaluated the European QoL (EQ-5D) scores associated with mild, moderate and severe pain. The methodological details were clearly described in several Appendices.

Measure of benefit:
QALYs gained were the primary outcome and future benefits were discounted at 3.5% per annum.

Cost data:
The cost categories were general practitioner visits due to HZ or post herpetic neuralgia, hospitalisation costs by age,
vaccine cost per dose, and administration. Nationally representative sources or registries were used to obtain the estimates. Future costs were discounted at 3.5% per annum. All costs were presented in 2006 UK pounds sterling (£), with appropriate adjustments for previous year costs.

Analysis of uncertainty:
Several sensitivity analyses were undertaken. Probabilistic sensitivity analyses and cost-effectiveness acceptability curves were simulated for each age group, on the assumption that the parameters were independent, except for the vaccine efficacy parameters, which were tested in 15 combinations of take and wane. The parameter distributions were adequately described. Univariate sensitivity analysis was performed, varying individual parameters across a range, or 95% confidence interval, of their distribution. Several scenarios were tested: the inclusion of QoL detriments over time; exclusion of specific HZ mortality; taking into account the future increase in life expectancy; the assumption that vaccine only protected against developing cases and did not reduce the severity of HZ, nor the likelihood of developing post-herpetic neuralgia if HZ occurred; an additional efficacy against post-herpetic neuralgia after adjustment for possible “excess” cases in the placebo group; the inclusion of the costs of infection control measures; calculation of hospitalisation rates using admissions which reported HZ in any of the first three diagnostic fields; and accounting for the short term injection site reactions.

Results
In the 65-year-old cohort, discounted QALYs lost over their lifetime were 6,206 with no vaccine compared with 5,106 in the vaccine group. The overall discounted costs were £7,603,000 in the no vaccine group compared with £30,044,500 in the vaccine group. This translated to a cost per QALY gained with vaccination (incremental cost-effectiveness ratio, ICER) of £20,412 and a cost per case prevented of £2,004.

At a maximum willingness-to-pay for a QALY gained of £30,000, the probability that vaccination at 65 years would be cost-effective was 87%, whereas vaccination at 70 years had a 98% chance of being cost-effective. This was based on the assumption that the vaccine provided additional protection against post-herpetic neuralgia, if this assumption did not hold then there was an 80% chance of vaccine for 70-year-olds being cost-effective.

The sensitivity analysis showed that the ICER was most sensitive to vaccine cost and efficacy parameters, as well as the estimated incidence of zoster and parameters that described the QALYs lost from HZ. It was also sensitive to the age at vaccination. Booster doses were less cost-effective than the first dose.

Authors' conclusions
The authors concluded that vaccination of the elderly against herpes zoster was likely to be cost-effective, specially at 70 years of age. If introduced, good quality surveillance data should be collected to evaluate the duration of protection. They stated that the introduction of the vaccine, would result in a significant increase in the overall proportion of the health budget spent on herpes zoster. In addition they suggested that due to their interaction, combined varicella and zoster vaccination programmes should be evaluated using a comprehensive cost-effectiveness model.

CRD commentary
Interventions:
The authors clearly reported the interventions and their details, which appeared to be relevant for the England and Wales setting.

Effectiveness/benefits:
Although no systematic review was described, the efficacy data appear to have been based on the main randomised clinical trial of the vaccine. Whist we can surmise that all of the main trials were identified and included, it is not explicit. A more systematic approach to reviewing the evidence would have ensured that the best available evidence was identified and made this fact transparent to the reader. The authors clearly explained and described how they extrapolated the trial results and combined them with QoL weights to derive the QALY losses. They also outlined details of other alternative approaches which were tested. The parameters were subjected to extensive sensitivity analysis to help characterise and outline the impact of any uncertainty.

Costs:
The authors included all the relevant costs for the reported perspective. They also stated that the exclusion of productivity costs would not have a major impact because this age group was mainly retired. The unit costs of care, treatment parameters and their sources were clearly presented. Further, the price year and method of inflation for costs from previous years was given. Overall, the costing was reporting clearly and in detail.

Analysis and results:
The study was based on a thorough analysis which, with the aid of some detailed appendices, was reported in a clear and comprehensive fashion. The authors undertook extensive analysis of the uncertainty and fully presented the main findings of this alongside the baseline results. The structure and details of the model, such as health states, cycle length, etc. were not presented. Overall, the level of reporting was good and enabled the logic and concept of the analysis to be followed.

Concluding remarks:
The methodology seems to have been appropriate and was clearly and transparently reported. The conclusions reached by the authors appear to be valid and fairly robust.

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