The epidemiology of herpes zoster and potential cost-effectiveness of vaccination 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.

Health technology
A mass adult vaccination programme against varicella zoster virus (VZV) was examined. Either a live-attenuated or inactivated VZV vaccine (Oka strain) was used. VZV was associated with two distinct diseases, varicella (chickenpox) and herpes zoster (shingles).

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-utility analysis; cost-effectiveness analysis.

Study population
The study referred to the general population of individuals aged 45 years or older.

Setting
The setting was the community. The economic study was conducted in England and Wales.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1975 and 1999. The specific dates during which the resource use data were collected were not reported. The price year was 1998.

Source of effectiveness data
The effectiveness evidence was derived from completed studies and authors' assumptions.

Modelling
A decision analysis model was used to estimate the costs and benefits of the strategies of vaccination and no vaccination. The model did not consider the potential protective effect of vaccination in preventing varicella, because very few elderly adults (the target age group) are susceptible to VZV and zoster cases contribute very little to the overall transmission of varicella.

Outcomes assessed in the review
The outcomes estimated from the published studies were:

the population of England and Wales,
the mortality rate,
the mean annual incidence of a first episode of zoster,
the mean number of zoster episodes,
the mean number of consultations with a general practitioner (GP) per episode,
hospitalisations per episode,
the mean length of stay,
the percentage of post-herpetic neuralgia (PHN) per episode of zoster,
the case fatality ratio,
the percentages of zoster cases and PHN cases that experienced pain,
the proportions of severe pain cases and mild pain cases;
the mean lengths of a zoster episode and a PHN episode,
the utility weight with severe pain and with mild pain.

**Study designs and other criteria for inclusion in the review**
A systematic review of the literature was not performed. The primary studies used data from, for example, a hospital episodes statistics database, the Royal College of general practitioners weekly return service, and official estimates for mortality rates.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The effectiveness data came from approximately 16 primary studies.

**Methods of combining primary studies**
Estimates were derived from the literature using narrative methods.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The population of England and Wales that was older than 45 years of age was 20,390,000.

The mortality rate per 1,000 person-years was 26.3.

The mean annual incidence of first episode of zoster per 10,000 person-years was 79.2.

The mean number of zoster episodes was 1.45.

The mean number of GP consultations per episode was 1.45.

The proportion of hospitalisations per episode was 2.1%.

The mean length of stay was 15.9 days.

The PHN per episode zoster was 19.3%.

The case fatality ratio per 100,000 episodes was 0.24.

The percentage of zoster cases that experienced pain was 82% (range: 55 - 100).

The percentage of PHN cases that experienced pain was 100%.

The proportion of pain cases that was severe was 22.7% (range: 0 - 100).

The proportion of pain cases that was mild was 77.3% (range: 0 - 100).

The mean length of zoster episode was 2.0 weeks.

The mean length of a PHN episode was 1.40 years (range: 0.93 - 2.14).

The utility weight was 47% with severe pain and 73% with mild pain.

**Methods used to derive estimates of effectiveness**

The authors made some assumptions that were used to derive some effectiveness estimates.

**Estimates of effectiveness and key assumptions**

It was assumed that:

all VZV cases would result in contact with the health service;

the hospitalisation rates and length of stay in Wales were similar to those observed in England;

those who were effectively immunised by vaccination would gain complete protection against zoster;

there were no adverse events associated with vaccination that required health care usage;

the initial vaccine efficacy was 70%;

vaccine coverage was 60%;

vaccine protection ranged between 2.5 years and lifetime.

**Measure of benefits used in the economic analysis**

The main summary benefit measure used in the economic analysis was the quality-adjusted life-year (QALY). Life-
years gained without any adjustment for quality of life issues were also reported. The utility weights came from a study that used standard gamble techniques in a sample of 114 individuals aged 65 to 70 years (see Other Publications of Related Interest). The future benefits were discounted at an annual rate of 3%.

**Direct costs**
A 3% discount rate was applied because the long-term costs were evaluated. The unit costs were not reported separately from the quantities of resources used, except for the vaccine units. The health services included in the economic evaluation were inpatient day, GP consultation (including treatment), hospital case and PHN episode. The cost/resource boundary adopted in the study was that of the health care provider. The costs of GP consultation and inpatient stay were estimated from official sources. A fixed extra cost was added to the hospitalisation cost to cover treatment and infection control measures. The lifetime treatment costs were derived from a published study (see Other Publications of Related Interest). The authors made an assumption about the cost of the vaccine. Resource use was mainly derived from authors’ assumptions and published data. The price year was 1998. All of the costs estimated from earlier years were inflated using the hospital and community health service pay and prices index.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not included in the economic evaluation.

**Currency**
UK pounds sterling (£). The exchange rate between and US dollars ($) was 1 £ = $1.5.

**Sensitivity analysis**
One-way sensitivity analyses were conducted to test the robustness of the estimated cost per QALYs. The parameters varied were:

- the percentage of zoster cases that experience pain,
- the proportion of pain that was severe,
- the mean length of a PHN episode,
- the mean cost per GP consultation,
- the mean treatment cost per PHN episode,
- the cost per vaccine course,
- the discount rate for costs and benefits, and
- the assumption that the vaccine was 0% effective against GP consultation, or was 100% effective against PHN.

The values used were derived from the literature. The combined scenarios of low or high vaccine efficacy and duration of protection (2.5 years, 10 years, or life-long) were also considered.

**Estimated benefits used in the economic analysis**
In adults aged over 65 years in England and Wales, there were over 14,000 QALYs lost due to the pain caused by zoster and PHN (worst case 48,209, best case 10,986).
Cost results
The estimated annual costs to the health service providers in England and Wales due to zoster and PHN were over 47.6 million (worst case 73.8 million, best case 33.5 million).

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and QALYs of the vaccination programme relative to no vaccination.

The analysis revealed that a number of potential programmes were cost-saving. For example, the vaccination of 65-year-olds with a life-long efficacy of 70% would be cost-saving at a cost per course of lower than 30. Under the base-case assumption, the cost per QALY was 11,109 with life-long vaccine, 22,845 with 10 years of protection, and 65,961 with 2.5 years of protection and low vaccine efficacy. The corresponding figures with high vaccine efficacy were 27,255 (life-long), 8,684 (10 years) and 3,560 (2.5 years).

Several programmes may not be cost-saving but are still cost-effective, with a cost per QALY below the threshold of 10,000. However, when life-years were used as the summary benefit measure, most of the programmes were not cost-effective. Vaccination was cost-effective especially among the very elderly.

The sensitivity analysis showed that the longer the period of protection, the more cost-effective the vaccination option became. The estimated cost per QALY was particularly sensitive to the cost of the vaccine and to the parameters related to morbidity due to PHN.

Authors’ conclusions
From the perspective of the health care provider in England and Wales, vaccination of the elderly against varicella zoster virus (VZV) represented a cost-effective approach under several scenarios and assumptions.

CRD COMMENTARY - Selection of comparators
The rationale for the comparator was clear. No vaccination was selected because it represented the standard practice in the study setting. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were mainly derived from published studies and authors' assumptions. Both sources of data were quite mixed up in the paper. It appears that the authors made some assumptions that were supported by the literature, but it was unclear how such data were extracted from the published studies. A systematic review of the literature was not undertaken and data coming from the primary studies (whose designs were not reported) were combined using narrative methods. It was not stated whether the primary studies were comparable in terms of the patients and interventions studied. Finally, the validity of such studies was not mentioned. In terms of the assumptions made, the authors did not investigate their potential variability in the sensitivity analysis, which focused mainly on the epidemiological data found in the literature. These issues tend to cast some doubt on the internal validity of the effectiveness estimates used in the decision analysis.

Validity of estimate of measure of benefit
QALYs were used as the summary benefit measure in the economic analysis. This appears to have been appropriate, as QALYs capture all mortality and morbidity aspects of the interventions from the perspective of the patients. Patient-based utility values were, indeed, used and these came from a published study that used the standard gamble method. Few details of the decision model used in the economic analysis were reported, and the model was not depicted graphically in the paper. The use of QALYs enhances the comparability of the benefits of the present study with those obtained with other interventions implemented in the health care system.
Validity of estimate of costs
The perspective adopted in the study was stated. It appears that all the relevant categories of costs have been included in the economic evaluation. The indirect costs were not considered. The authors stated that their exclusion would have negligible impact, as productivity losses were minimal due to the advanced age of the patients involved in the study. The unit costs were analysed separately from the quantities of resources used, but only for a few items. The price year was reported, thus simplifying reflation exercises in other settings. Although the costs were treated deterministically in the base-case, several changes were investigated in the sensitivity analysis. The discount rate was also varied. Resource use was mainly estimated from the authors' assumptions. The sources of the cost data were reported.

Other issues
The authors did not compare their findings with those from other studies. They stated that their study represented the first analysis of the potential cost-effectiveness of vaccination against herpes zoster and PHN in England and Wales. The issue of the generalisability was not explicitly addressed. However, the authors stated that, since the UK had low treatment costs, the vaccination programme may be even more attractive in contexts with similar epidemiological patterns. Several sensitivity analyses were conducted, thus enhancing the external validity of the analysis.

Implications of the study
The study results suggested that a vaccination programme against VZV represents a safe and efficient strategy to improve the quality of life of elderly individuals in industrialised countries, such as England and Wales.

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Other publications of related interest


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