Cost-benefit analysis of universal varicella vaccination in the U.S. taking into account the closely related herpes-zoster epidemiology

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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 health intervention examined in the study was universal varicella vaccination.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a cohort of individuals eligible for varicella vaccination.

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

Dates to which data relate
The clinical data came from studies published between 1965 and 2003. The costs and resource use data were derived from studies published in 1994 and 2001. The price year was unclear.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and author's assumptions.

Modelling
An analytic model was used to assess the clinical and economic impact of universal varicella vaccination in comparison with no vaccination. In particular, the model investigated the impact of universal varicella vaccination solely on the population as it existed in 2000 and as it progressively aged over the next 50 years. Whether or not the birth cohort was vaccinated influenced the age-specific HZ incidence rates that were applied to the population. Thus, the population when modelled without the effects of universal varicella vaccination would have the same initial set of (pre-licensure) age-specific incidence rates applied. The number of HZ cases gradually decreased in both models (with and without the effects of universal vaccination) as the initial population gradually aged and experienced mortality.

Outcomes assessed in the review
The outcomes estimated from the literature were the HZ incidence rates and mortality rates of the US population.
Study designs and other criteria for inclusion in the review
It appears that the primary studies have been identified selectively and not from a review of the literature. The mortality rates came from US Census data.

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
The clinical data were derived from four primary sources.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
An estimated 842,000 HZ cases among a US population of 275 million in 2000 was estimated (incidence rate of 306 per 100,000 person-years among individuals of all ages).

Seven recurrent cases occurred among 639 incident HZ cases among individuals of all ages during a 2-year (2000-2001) study.

HZ recurrence was an estimated 2,188 per 100,000 person-years (95% confidence interval, CI: 880 - 4,507), based on the average at-risk person-time of 320 person-years.

Another study reported 1,490 cases per 100,000 person-years (95% CI: 643 - 2,935).

Based on the data from these two studies, a rate of HZ recurrence of 2,000 per 100,000 person-years was used in the model.

Thus, the effective increase in the HZ incidence rate was 11 per 100,000 person-years or from 550 to 561 per 100,000 person-years.

All-age mortality rates were not reported.

Methods used to derive estimates of effectiveness
The author made some simplifying assumptions that were used in the model.

Estimates of effectiveness and key assumptions
It was assumed that 100% of the birth cohort was vaccinated each year. It was also assumed that vaccinees were protected 100% against breakthrough varicella disease, and that the recurrence of HZ was negligible or sub-clinical during their lifetime.

**Measure of benefits used in the economic analysis**
The main model output was the estimated number of HZ cases. However, it was not used as a summary benefit measure. In effect, a cost-consequences analysis was carried out.

**Direct costs**
The perspective adopted in the study was unclear. However, only the direct medical costs (i.e. hospitalisations, physician consultations and treatments) were considered. Vaccine costs and administration costs were not included. Aggregated costs were presented, thus the unit costs were not presented separately from the quantities of resources used. Medical cost-savings due to varicella vaccination were estimated from a published study. Similarly, another study (performed in the UK) provided the medical costs associated with HZ cases. The role and use of discounting was unclear. The price year was not reported.

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

**Indirect Costs**
The indirect costs were not considered in the analysis.

**Currency**
US dollars ($). Costs that were derived from UK sources using pounds sterling (£) were converted into dollars. The conversion rate was 1 = $1.50.

**Sensitivity analysis**
The author stated that a sensitivity analysis was performed to assess the variability in HZ cases. However, no information on this sensitivity analysis was provided.

**Estimated benefits used in the economic analysis**
With no intervention such as "booster" vaccinations among adults, an additional 14.6 million cases of HZ occurred over 50 years with universal varicella vaccination.

HZ cases reached a peak approximately 15 years following licensure, at a rate that was 70% higher than those occurring in the pre-licensure era.

Approximately 13% (36 million out of 275 million) and 18.5% (51 million out of 275 million) of the population alive in 2000 would have had onset of HZ during their lifetime without and with universal varicella vaccination, respectively. This represents a 42% increase in the number of HZ cases in the post-licensure period relative to the pre-licensure era.

The sensitivity analysis showed that the number of HZ cases varied depending on whether the predominant means of boosting is asymptomatic endogenous reactivation or periodic exogenous re-exposure.

**Cost results**
The extra cases of HZ would lead to a total cost of $4.1 billion (range: 2.7 - 6.1) or a mean cost of $280 per case. This would lead to approximately $80 million extra medical costs per year.
The model projected a net deficit (loss) in annual medical costs incurred during the first 30 years, with a break-even point at approximately 50 years. This was followed by a continuing rise in medical savings, which would eventually approach $460 million annually due to a reduction in cases of both varicella ($80 million) and HZ ($380 million) as vaccinated individuals continue to enter the older adult cohorts.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was performed.

Authors’ conclusions
The recently reported increase in herpes zoster (HZ) cases might have the effect of counterbalancing the medical cost-effectiveness of universal varicella vaccination, as other studies have shown. It was also stressed that the assumptions inherent to the current model were more realistic than previous models that neglected the influence of varicella on the closely related HZ epidemiology.

CRD COMMENTARY - Selection of comparators
The selection of the comparator (i.e. no vaccination) was appropriate. It might have reflected the standard care in the author's context. However, you should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a synthesis of published studies. However, few details of the design and characteristics of the primary studies were reported. Thus, it was difficult to assess the validity of the primary studies. Some assumptions were also made to derive model inputs that were not available from the literature. The issue of uncertainty was not extensively addressed in the sensitivity analysis, and only one clinical parameter was varied.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective of the study was not explicitly stated. Only the direct medical costs were included in the analysis. Since the costs were estimated from published studies, no details of the approach used to estimate the costs were reported. Thus it was difficult to assess the data. The medical costs associated with HZ were taken from a UK study and just converted to US dollars, which seems an inappropriate technique. However, the author stated that this could have underestimated the costs of HZ, given that US costs are usually higher than UK costs. The unit costs, quantities of resources used, price year and use of discounting were not reported, thus limiting the possibility of replicating the study in other settings. The author stated that the net cost deficit was likely to have been underestimated since the costs related to varicella vaccination were not considered.

Other issues
The author reported the results of other studies that evaluated the clinical impact of varicella vaccination. However, no explicit comparisons were made. The issue of the generalisability of the study results to other settings was not addressed and a very limited sensitivity analysis was performed. Thus, the external validity of the study was low.

Implications of the study
The study results suggested that universal varicella vaccination might increase the burden of HZ disease. The author stated that as future HZ incidence data become available, cost-effectiveness analyses could be carried out to refine current estimates.
Source of funding
None stated.

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Other publications of related interest


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