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Review

Cost-effectiveness of vaccination against herpes zoster and postherpetic neuralgia: a critical review

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ABSTRACT

Objective: The objective of this study was to systematically review cost-effectiveness studies of vaccination against herpes zoster (HZ) and postherpetic neuralgia (PHN).
Methods: We searched MEDLINE and EMBASE databases for eligible studies published prior to November 2013. We extracted information regarding model structure, model input parameters, and study results. We compared the results across studies by projecting the health and economic impacts of vaccinating one million adults over their lifetimes.
Results: We identified 15 cost-effectiveness studies performed in North America and Europe. Results ranged from approximately US$10,000 to more than US$100,000 per quality-adjusted life years (QALY) gained. Most studies in Europe concluded that zoster vaccination is likely to be cost-effective. Differences in results among studies are largely due to differing assumptions regarding duration of vaccine protection and a loss in quality of life associated with HZ and to a larger extent, PHN. Moreover, vaccine efficacy against PHN, age at vaccination, and vaccine cost strongly influenced the results in sensitivity analyses.
Conclusion: Most studies included in this review shows that vaccination against HZ is likely to be cost-effective. Future research addressing key model parameters and cost-effectiveness studies in other parts of the world are needed.

1. Introduction

Herpes zoster (HZ) or shingles is caused by reactivation of latent varicella-zoster virus (VZV) and is typically characterized by painful, blistering rashes [1]. The lifetime risk of HZ is approximately 30%, with risk increasing sharply after 50 years of age [2–4]. Pain from HZ can substantially reduce patient quality of life and impair physical, functional, psychological, and social aspects of well-being [5]. The most common complication is postherpetic neuralgia (PHN), a devastating pain that can persist for months or even years [6]. Older patients have a greater risk of developing PHN [3,7].

ZOSTAVAX® is a live-attenuated VZV vaccine that has been demonstrated to significantly reduce the incidence of HZ by 51% and the incidence of PHN by 67% in a double-blind, placebo-control trial in adults 60 years of age or older ("The Shingles Prevention Study", SPS) [8]. The trial also demonstrated that the vaccine reduced the burden of illness due to HZ by 61%, defined using a composite measure of incidence, severity, and duration of pain. The Short Term Persistence Substudy (STPS) evaluated a subset of SPS population during the study period of 4 to 7 years after vaccination and demonstrated sustained vaccine efficacy (VE) [9]. Moreover, vaccine protection may persist for at least 7 to 10 years as observed in the Long Term Persistence Substudy (LTPS) [10]. In another trial ("Zoster Efficacy and Safety Trial" or ZEST), zoster vaccination has been shown to reduce the incidence of HZ by 70% in adults 50 to 59 years of age [11]. ZOSTAVAX® has been approved for use in adults 50 years of age and older in North America, Europe, and elsewhere.

Health economic evaluation of vaccination is one of the important components for evidence-based decision-making on adopting new vaccines. A number of cost-effectiveness studies of vaccination against HZ and PHN have been conducted but the results are divergent. The objective of this study was to systematically review cost-effectiveness studies, critically assess key model parameters that lead to diverging results, and discuss areas of future research.

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2. Methods

2.1. Study selection

We searched MEDLINE and EMBASE databases for eligible studies. For EMBASE, we used the following combinations of keywords: ('zoster' or 'shingles' or 'herpes zoster') and ('cost effectiveness' or 'cost' or 'economic') and ('vaccine' or 'vaccination'). For MEDLINE, we used MeSH/Text terms using the same combinations. We searched the literature up to November 2013. We also searched the references cited by the retrieved papers for additional references. We included published studies examining cost-effectiveness analyses of HZ vaccination. We excluded studies described in conference abstracts. In order to focus our review on HZ vaccination, we excluded a study that examined the combined impacts of varicella and zoster vaccination.

2.2. Data extraction

We extracted information regarding study characteristics (authors, published year, journal, country, and funding sources), model structure (model design, perspective, time horizon, and discount rate), model parameters (epidemiologic and economic parameters, health utilities, and vaccine characteristics including vaccine efficacy, duration of protection, and cost of vaccination), and results (number of prevented cases of HZ and PHN, gains in quality-adjusted life years [QALYs], incremental cost-effectiveness ratio [ICER], threshold used for cost-effectiveness, and sensitivity analysis).

2.3. Quality assessment

In order to assess the quality of each study, we used the recently developed Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [12]. The CHEERS checklist recommends 24 items for optimal reporting of health economic evaluations.

2.4. Synthesis of results

All studies examined the health and economic impacts of vaccinating adults over their lifetimes using cohort models. However, because assumptions about vaccine coverage and target populations for vaccination differed between countries, each study presented results assuming different sample sizes for the vaccinated cohort. We extrapolated the results assuming the same numbers of vaccinated adults (i.e., one million adults) to allow comparability between studies. Costs were converted into US dollars using exchange rates at the time of each study and then inflated into 2012 US dollars using the country-specific Consumer Price Index [13]. For each study, we projected the number of avoided cases of HZ and PHN, and gains in QALYs when vaccinating 1 million adults. ICER was computed comparing vaccination strategy to no vaccination strategy.

3. Results

The literature search yielded 745 citations, of which 726 were excluded after the title or abstract was examined. We excluded 4 articles because they were either reviews [14], or were examining the combined impacts of varicella and zoster vaccinations [15,16], or as they were conference abstracts [17]. We identified 15 studies examining the cost-effectiveness of HZ vaccination [18–32].

3.1. Quality assessment

We utilized the CHEERS checklist to assess quality of studies included in this review. Overall, all studies were of good quality and explicitly stated the study objective, target population, setting, study perspective, comparators, time horizon, discount rate, choice of health outcomes, and analytical methods. All studies reported study parameters in detail, incremental costs and outcome, limitations, funding source, and potential conflict of interests.

Several limitations in prior studies are worth noting. In some studies, it was unclear which data sources were chosen for parameter estimates in base case analysis when multiple sources were available. We also found that studies made various assumptions regarding VE over time. As long-term clinical data are not available, assumptions regarding duration of vaccine protection varied across studies in the base case analysis. Quality and methods for characterizing uncertainty in sensitivity analysis differed across studies. For many studies, the ranges selected to explore uncertainty of parameters in sensitivity analysis were unclear. While all studies conducted one-way sensitivity analyses, multivariate probabilistic sensitivity analysis was conducted in only 7 studies (Hornberger et al., 2006, Pellissier et al., 2007, Brisson et al., 2008, Najafzadeh et al., 2009, van Hoek et al., 2009, Bresse et al., 2013, and Ultsch et al., 2013) [18,20–22,24,31,32].

3.2. Model structure and study design

All analyses were performed in North America and Europe (Table 1). Of the 15 studies, 9 studies used Markov-cohort models [18,19,24–26,28,30–32], whereas others used decision analytic cohort models [20,21,23,29], static cohort models [27], or discrete-event-simulation models [22]. Furthermore, several studies incorporated model structures that divided health states of HZ and PHN based on the severity of pain [22,25,26,30,31]. Eight studies used the model structure of vaccinating a cohort across age groups (e.g., $\geq$ 60 years) [18–20,22,25,26,30,31], whereas seven studies used the model structure of vaccinating among a specific age group (e.g., 60 years) [21,23,24,27–29,32]. All studies used a lifetime time horizon.

Six studies performed cost-effectiveness analyses from the payer perspective [21–24,27,31], three from the societal perspective [18,19,28], and six from both the payer and societal perspectives [20,25,26,29,30,32].

3.3. Epidemiological parameter

Most studies used country-specific data for incidence rates of HZ in the general population (Table 1). However, two studies used the HZ incidence data from the SPS trial. Assumptions regarding rates of PHN varied across studies. Only three studies incorporated ophthalmic complications in their study [19,20,24].

3.4. Health utilities

All studies used the QALY as a measure of health outcome (Table 1). The estimates of average QALY lost due to HZ and PHN varied widely among studies. A large proportion of QALY loss among elderly populations was due to PHN. Most studies categorized severity of pain into four levels (severe, moderate, mild, and no pain) and calculated QALY loss in each pain state. A model developed by van Hoek et al., 2009 allows severity and duration of pain to increase with age and fitting a model on data from nine prospective cohort studies [24]. Most studies used QALY weights from studies by Coplan et al., Oster et al., or SPS data [20,33,34]. However, van Hoek et al. utilized a more comprehensive approach and used the data on QALY loss for HZ from the data on severity and duration