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Cost-effectiveness of vaccination against herpes zoster in adults aged over 60 years in Belgium

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ABSTRACT

Aim: To assess the cost-effectiveness of vaccinating all or subgroups of adults aged 60 to 85 years against herpes zoster.
Methods: A deterministic compartmental static model was developed (in freeware R), in which cohorts can acquire herpes zoster according to their age in years. Surveys and database analyses were conducted to obtain as much as possible Belgian age-specific estimates for input parameters. Direct costs and Quality-Adjusted Life-Year (QALY) losses were estimated as a function of standardised Severity Of Illness (SOI) scores (i.e. as a function of the duration and severity of herpes zoster disease).
Results: Uncertainty about the average SOI score for a person with herpes zoster, the duration of protection from the vaccine, and the population that can benefit from the vaccine, exerts a major impact on the results: under assumptions least in favour of vaccination, vaccination is not cost-effective (i.e. incremental cost per QALY gained >€48,000 for all ages considered) at the expected vaccine price of €90 per dose. At the same price, but under assumptions most in favour of vaccination, vaccination is found to be cost-effective (i.e. incremental cost per QALY gained <€5500 for all ages considered). Vaccination of age cohort 60 seems more cost-effective than vaccination of any older age cohort in Belgium.
Discussion: If the vaccine price per dose drops to €45, HZ vaccination of adults aged 60–64 years is likely to be cost-effective in Belgium, even under assumptions least in favour of vaccination. Unlike previous studies, our analysis acknowledged major methodological and model uncertainties simultaneously and presented outcomes for 26 different target ages at which vaccination can be considered (ages 60–85).

1. Introduction

Herpes zoster (HZ), also known as shingles or zona, is a viral disease characterized by a painful dermatomal skin rash. The lifetime probability of getting HZ has been estimated at approximately 30% [1], but the probability to get HZ increases with age, and is larger for immunocompromised persons [2]. Also the duration and severity of the pain increases with age [3,4]. Recently, a vaccine has been shown to be efficacious in preventing HZ for people aged 60 and older (Zostavax®) [5]. Several studies evaluated the cost-effectiveness of HZ vaccination programs [6–15], but their conclusions differed with respect to whether vaccination is likely to be cost-effective, and at which age vaccination is likely to be (most) cost-effective. Some of these differences are due to country-specific differences in HZ-related health care use and costs. Hence, it is crucial that for each country a separate cost-effectiveness analysis is performed, based on as much country-specific information as possible.

The only study that has assessed the cost-effectiveness of HZ vaccination in Belgium, derived almost all evidence on HZ burden from other countries [6]. In the meantime, data on the burden of HZ in Belgium have been extracted from representative Belgian databases and specific surveys have been conducted and analyzed [7], These newly obtained data provide the opportunity to conduct a more relevant analysis of the cost-effectiveness of HZ vaccination in Belgium.

Furthermore, previous studies have shown that the cost-effectiveness of HZ vaccination is sensitive to the age at which vaccination is administered [8–11,14,15]. Our study aims to improve on these studies by estimating a more precise age (in years) at which vaccination is most cost-effective. Unlike previous published analyses our study aims to account for major sources of methodological and model uncertainties simultaneously, including uncertainty about the subgroups which can benefit from the

Abbreviations: HZ, herpes zoster; QALY, Quality-Adjusted Life-Year; SOI, severity of illness.

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vaccine, uncertainty about the interpretation of efficacy outcomes from the pivotal trial and uncertainty about the choice of vaccine efficacy model, which expresses in our analysis the joint influence of age at vaccination and time since vaccination on the level and duration of vaccine efficacy.

2. Methods

2.1. Model and methodological choices

A static cohort model was developed (and implemented in R [16]) to obtain the age-specific annual number of herpes zoster episodes and deaths in Belgium with and without vaccination. Individuals belonging to a single age cohort are modelled to transition between 3 states (healthy; herpes zoster; and death) in yearly cycles, until everybody is absorbed in the 'death state'. The life table method is used to estimate state membership of the cohort model [17]. Twenty-six age cohorts (60 up to 85) are followed over time, so that the impact of vaccination at different ages can be investigated (e.g. only vaccinating at 60, only vaccinating at 61, vaccinating all people aged 60–65, and so on). The number of herpes zoster episodes with and without vaccination is compared based on the direct costs (health care payer perspective) and consequences (life-years lost and Quality-Adjusted Life-Years (QALYs) lost) related to the episodes. These costs and consequences are discounted at 3% and 1.5% respectively, according to Belgian guidelines [18].

2.2. Estimation of the values of the parameters within the model

Demography – Rather than using Belgian demographic data from a single or several years, a Gompertz curve is fitted on such data reflecting average Belgian demography (data from years 1990 to 2007 obtained from Statbel: http://statbel.fgov.be/nl/statistieken/cijfers/bevolking/structuur/leeftijdgeslacht/belgie/index.jsp, accessed 12/07/2011). Life expectancy is extracted from the same database, for the latest available year (2007).

HZ incidence and health care use – The age-specific number of HZ hospitalizations in Belgium is available for years 2000 up to 2007 from a national database; the number of visits for HZ to a sentinel system of general practitioners in Belgium is available for years 2006–2008 [7]. By fitting a generalized additive model [19] to these data, estimates are obtained for the average hospitalization rate for HZ and the average rate at which people consult a general practitioner at least once for HZ. A representative survey among HZ hospitalized patients in Belgium showed that 10.5% of these patients did not visit a general practitioner for HZ, but were either (i) admitted directly through the emergency department, (ii) referred to the hospital through a specialist doctor, or (iii) hospitalized for another reason and got HZ in the hospital [7]. Hence, we estimate the age-specific HZ incidence by adding 10.5% of the estimated average HZ hospitalization rate to the estimated average rate at which people consult a general practitioner at least once for HZ. The average age specific HZ mortality rate is based on Belgian death certificates. The opinion of five experts independently evaluating death certificates containing HZ as a possible cause of death differed substantially. Therefore the cost-utility will be assessed for a scenario least in favour of vaccination (i.e. assuming no deaths due to HZ), and a scenario most in favour of vaccination (i.e. assuming the number of HZ-related deaths equals all registered deaths with HZ as a possible cause, without the ones for which at least four experts agreed they were not due to HZ).

Vaccine coverage and costs – The marginal intervention costs consist of the purchasing costs as well as the marginal administration costs of the vaccine. The Centres for Disease Control and Prevention report a price per dose of Zostavax® of $105.9 (€85.5, 10-pack, 1 dose vial) and $116.7 (€94.2, 1-pack, single dose 0.65 mL vials); the private sector price per dose of Zostavax® is $153.9 (€124.3, 10-pack, 1 dose vial) and $161.5 (€130.4, 1-pack, single dose 0.65 mL vials) (http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm#adult, accessed 21/06/2010). A price per dose of €90 is used, as this is likely to reflect the price for bulk purchase by a publicly funded program. Because vaccines in this age group are delivered by general practitioners in Belgium, the administration costs were set to €21.53, based on the cost of one consultation. Based on the experience with influenza and pneumococcal vaccines for this target group, vaccine uptake (or coverage) is assumed to be 30%, and independent of age and gender. It is varied in scenario analyses between 10% and 70%.

Vaccine efficacy – A single trial (the Shingles Prevention Study) measured efficacy of the Zostavax® vaccine in preventing HZ [5]. However, three major sources of uncertainty remain regarding the protective efficacy of the vaccine:

1. The Shingles Prevention Study excluded immunocompromised persons and persons with other conditions (e.g. diabetes mellitus). Hence, vaccine efficacy in such persons is unclear, because it was not measured.
2. The Shingles Prevention Study measured efficacy of the Zostavax® vaccine against the burden of illness due to HZ (primary endpoint), against the number of HZ cases and against the number of post herpetic neuralgia cases [5]. A choice has to be made about which endpoint to use in a cost-effectiveness analysis.
3. Vaccine efficacy data from the Shingles Prevention Study for a follow-up period of 5 years are published [5] (and have been presented in a poster for a follow-up period of 7 years [20]). Also, vaccine efficacy data for an average follow-up period of 3 years are available separately for 5-year age groups (i.e. persons vaccinated at age 59–64, 65–69, and so on) [21]. Bilcke et al. [22] showed that a range of different models fit the data equally well, but result in very different estimates for vaccine efficacy against the number of HZ cases as a joint function of age at vaccination and time since vaccination. For instance, depending on the chosen vaccine efficacy model, vaccination is expected to protect persons against HZ for 7 years up to lifelong, and is expected to reduce HZ incidence in people vaccinated for instance at age 80 by between 35% and 41% for the first year after vaccination.

We account for these 3 major sources of uncertainty simultaneously by presenting results of the cost-effectiveness analysis for a scenario least and most in favour of vaccination.

The following assumptions are made on vaccine efficacy for the scenario least in favour of vaccination: We assume only people compliant with the Shingles Prevention Study (i.e. mainly immunocompetent persons) can benefit from vaccination, and we assume vaccination only decreases the number of HZ cases. Choosing the vaccine efficacy model which results in estimates least in favour of vaccination is less straightforward: for instance the vaccine efficacy model which predicts lowest efficacy for vaccination at age 60, is different to the vaccine efficacy model which predicts lowest efficacy for vaccination at age 70 (for details see ref. [22]). Hence, the following approach was used to determine the vaccine efficacy model and associated vaccine efficacy estimates which result in cost-effectiveness values least in favour of vaccination, for each age at vaccination separately:

- Step 1: Age-specific cost-effectiveness values are obtained using the vaccine efficacy estimates from one vaccine efficacy model as input, and assuming the choices least in favour of vaccination for the other uncertainties (listed in Table 1). This results in 26