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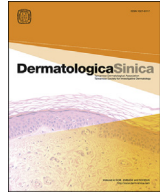
ORIGINAL ARTICLE

Cost-effectiveness analysis of herpes zoster vaccine in adults above 50 in Singapore

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ABSTRACT

Background/Objectives: Incidence of herpes zoster (HZ) increases with age. The vaccine to prevent HZ is available for those who are 50 and older. This study aims to investigate the cost-effectiveness of HZ vaccine on population older than 50 years old from a societal perspective in Singapore.
Methods: The established decision analytic (Markov) model was utilized to simulate the results of vaccination for adults who were older than 50 years of age, compared to those without vaccination. The total number of HZ cases, postherpetic neuralgia (PHN) cases, total direct cost of treatment and indirect cost due to productivity loss were estimated based on the characteristics of population, and treatment costs were collected from a local institute in Singapore. The public health consensus for the ICER benchmark in Singapore was S$65,000.
Results: One million individuals were simulated in this health economics analysis. Vaccination would reduce 48% of HZ cases and 33% of PHN cases over their life time. When a vaccination strategy for adults who are 50 years old and older was compared to a strategy with no vaccination, incremental cost-effectiveness ratio (ICER) was S$49,023 per quality adjusted life years (QALY) gained from the societal perspective.
Conclusion: The herpes zoster vaccination is likely to be cost-effective in societal perspective for adult over 50 years of age in Singapore.

Introduction

Aging is a worldwide concern and is no exception in Singapore. In 2004, about 35% of Singapore residents were above the age of 50, yet this cohort is expected to become 46% of total residents in 2014. Aging causes the immune system to weaken, which leads to increased risk of chronic and infectious diseases, including herpes zoster. Herpes zoster (HZ), also known as shingles or simply "zoster", is the reactivation of varicella zoster virus (VZV), which produces varicella. After treating varicella, the virus remains latent in sensory ganglia. In some individuals, latent VZV reactivates and replicates, perhaps as a consequence of waning cellular immunity, resulting in HZ.[1−8] HZ is characterized by a unilateral, vesicular cutaneous eruption with a dermatomal distribution that generally corresponds to the area of skin innervated by a single spinal or cranial sensory ganglion.[1−3]

The most significant clinical manifestations of HZ are acute neuritis and, postherpetic neuralgia (PHN),[9−11] which frequently results in disordered sleep, chronic fatigue, anxiety, and severe depression. Recent data indicated that the zoster associated pain may persist for months or even years after the rash has healed,[9−13] diminishing the patient's quality of life (QoL)[14−18] and functional capacity to a degree comparable to that in diseases such as congestive heart failure, myocardial infarction, diabetes mellitus type 2, and major depression.[3]

Early initiation of treatment with an antiviral agent (acyclovir, famciclovir, or valacyclovir) has been shown to reduce the severity of acute HZ, as defined by the time to HZ rash healing and the

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duration of HZ-associated pain. However, antiviral therapy has not consistently shown benefits in the treatment of PHN; data suggest that antiviral therapy has limited impact on the incidence of PHN, although it may shorten the duration of PHN pain.[8–11,19–31] It is then difficult to adequately treat HZ and PHN with antiviral and other medications. A recent Cochrane review showed that treatment with oral acyclovir does not have a significant impact on the incidence of PHN.[32] The authors highlighted the need for additional trials assessing the severity of pain and the patient QoL. Similarly, another meta-analysis showed that oral corticosteroids given acutely during HZ infection are ineffective in preventing PHN.[33] Prevention and treatment for HZ and PHN present a significant unmet medical need. A live, attenuated virus vaccine, was approved and indicated to prevent the herpes zoster for individuals on 50 years.[34,35]

Kawai et al. (2014)[36] summarized 15 studies analyzing the cost-effectiveness of herpes zoster vaccine, yet all of them were conducted in North America and European countries. Results from most of these studies showed that the herpes zoster vaccine is likely to be cost-effective in those countries. However, the cost-effectiveness of herpes zoster vaccine has not been evaluated in Asian countries, which shows a gap of epidemiological evidence of herpes zoster. This study aims to evaluate the cost-effectiveness of herpes zoster vaccine in Singapore setting.

Methods

The population and vaccination strategy

The herpes zoster vaccine investigated was approved to be used for immunocompetent adults 50 years old and above. The vaccine strategy was for all eligible adults, compared to the status with no herpes zoster vaccine. Prior to the cost-effectiveness study, the burden of illness study of herpes zoster was conducted at Singapore local institutes for herpes zoster patients who were over 50 years old when they visited the institutes for symptoms. Results of the burden of illness study were adopted as local inputs of the cost-effectiveness study.

Model settings and inputs

Population, clinical inputs and mortality
The pre-established decision analytic model was utilized for this analysis.[37] The structure of the model was depicted as Fig. 1. By applying the age-specific incidence rate of herpes zoster and the time-since-vaccination-specific efficacy of vaccine, the model estimated the total number of herpes zoster-related events for the two different vaccine strategies. Also, the direct cost incurred due to the herpes zoster, its complication, and vaccine-related outcomes were calculated based on Singapore data. All the costs were

discounted at a 3% annual discount rate. Beyond the direct payments from patients and the government, the indirect cost, which happened due to the loss of productivity, was also included in societal perspective. The population characteristics and clinical inputs adopted into the model were described in Table 1.

Also, as the figure showed, the model considered the mortality of zoster-free population and zoster-related mortality. Age-specific all-cause mortality rates were quoted from Department of Statistics, Singapore.[38] The probability of zoster-related mortality was adopted from the United States (U.S.) Center for Disease Control and Prevention's (CDC) mortality data since it's not identified in Singapore.[41]

Adjustment of quality of life, and healthcare resource utilization cost
The discomfort due to herpes zoster and its complications would discount the quality of life of patients. The quality of life of herpes zoster patients was adjusted based on the findings from existing literature (Table 2). Starting from the age-specific HZ incidence rates, the model simulated the number of HZ incidences of the cohort in one million seniors over 50 years old. Similar approached was adopted for PHN as well. The amount of quality adjust life years (QALY) loss caused by HZ and PHN were calculated by multiplying the number of HZ and PHN cases by the age-specific QALY loss per case (Table 2) for vaccinated and non-vaccinated seniors, respectively. The total QALY loss was driven by summing the values cross different age (in year) and causation of QALY loss (HZ and PHN). Beyond the impact of quality of life, the cost of herpes zoster vaccine, treatment of herpes zoster and its complication, and the indirect cost due to productivity loss were also adopted into the model. Inputs were summarized in Table 2 below.

Sensitivity analysis

To test the robustness of the results, we examined the scale of variation in results of fluctuating model parameter estimates such as economic costs and the incidence of adverse-events by 20% in both directions as the one-way sensitivity analysis. Also, the vaccine efficacy and durability analyzed in the model were tested by sensitivity analysis. Table 3 summarized the values of vaccine efficacy used in the analysis.

Results

In this study, we compared a vaccination strategy for adults who are 50 years old and older to a strategy with no vaccination. The model simulated the clinical and economic results for scenarios without and with HZ vaccination. For a hypothesized cohort with one million senior (≥50 years of age) people, if there is no HZ vaccination, the number of HZ and PHN will be 350,670 and 45,440, respectively. Total cost including productivity loss would be SGD
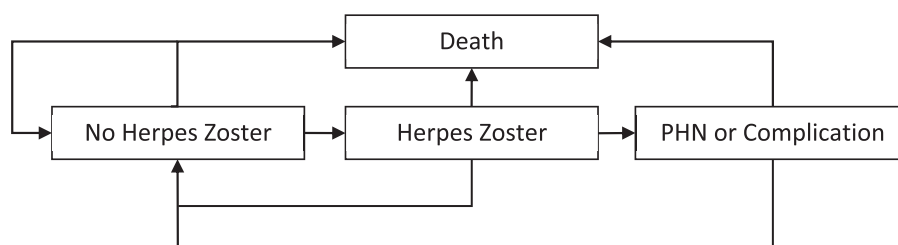
There are 4 mutual exclusive states of the disease progression of herpes zoster. The arrows represent the flow of patients between states.

Fig. 1 Herpes zoster cost-effectiveness model structure.