Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Cost-effectiveness of varicella vaccine against herpes zoster and post-herpetic neuralgia for elderly in Japan

Shu-ling Hoshi *, Masahide Kondo, Ichiro Okubo

Department of Health Care Policy and Health Economics, Faculty of Medicine, University of Tsukuba, 1-1-1, Tennoudai, Tsukuba, Ibaraki 3058577, Japan

ARTICLE INFO

Article history:
Received 12 October 2016
Received in revised form 18 April 2017
Accepted 19 April 2017
Available online xxxx

Keywords:
Cost-effectiveness
Economic evaluation
Herpes zoster
Varicella vaccine
Vaccination
Quality-adjusted life year

ABSTRACT

Background: The extended use of varicella vaccine in adults aged 50 and older against herpes zoster (HZ) was recently approved in Japan, which has raised the need to evaluate its value for money.
Methods: We conducted a cost-effectiveness analysis with Markov modelling to evaluate the efficiency of varicella vaccine immunisation programme for the elderly in Japan. Four strategies with different ages to receive a shot of vaccine were set, namely: (1) 65–84, (2) 70–84, (3) 75–84 and (4) 80–84 years old (y.o.). Incremental cost-effectiveness ratios (ICERs) compared with no programme from societal perspective were calculated. The health statuses following the target cohort are as follows: without any HZ-related disease, acute HZ followed by recovery, post-herpetic neuralgia (PHN) followed by recovery, post HZ/PHN, and general death. The transition probabilities, utility weights to estimate quality-adjusted life year (QALY) and disease treatment costs were either calculated or cited from literature. Costs of per course of vaccination were assumed at ¥10,000 (US$91). The model with one-year cycle runs until the surviving individual reached 100 y.o.
Results: ICERs ranged from ¥2,812,000/US$25,680 to ¥3,644,000/US$33,279 per QALY gained, with 65–84 y.o. strategy having the lowest ICER and 80–84 y.o. strategy the highest. None of the alternatives was strongly dominated by the other, while 80–84 y.o. and 70–84 y.o. strategy were extendedly dominated by 65–84 y.o. strategy. Probabilistic sensitivity analyses showed that the probabilities that ICER is under ¥5,000,000/US$45,662 per QALY gained was at 100% for 65–84 y.o., 70–84 y.o., 75–84 y.o. strategy, respectively, and at 98.4% for 80–84 y.o. strategy.
Conclusion: We found that vaccinating individuals aged 65–84, 70–84, 75–84, and 80–84 with varicella vaccine to prevent HZ-associated disease in Japan can be cost-effective from societal perspective, with 65–84 y.o. strategy as the optimal alternative. Results are supported by one-way sensitivity analyses and probabilistic sensitivity analyses.

1. Introduction

Herpes zoster (HZ) results from reactivation of the varicella-zoster virus (VZV) in sensory ganglia after a long latency period following primary infection from varicella [1,2]. Epidemiological data of reports from high-income settings noted that age-adjusted HZ incidence in the total population ranging from 3.4 to 5.0 per 1000 person-years, while for those aged over 65 are from 8.0 to 11.0 per 1000 person-years [3]. The most common serious complication of HZ is post-herpetic neuralgia (PHN), i.e., persistent pain beyond the acute phase of vesicular rash [3]. Antiviral therapy can shorten the length and severity of acute HZ, but therapy must be started as soon as the rash appears [3]. In Japan, there are two large-scale epidemiological studies, which reported age-specific HZ incidence rates, namely: Miyazaki study and Shozu Herpes Zoster (SHEZ) study [4,5]. The former reported an HZ incidence rate of 7.48 per 1000 person-year for adult aged 50 and over, while the latter at 5.3–8.2. Although healthcare in Japan is easily accessible, percentage of HZ patients visiting within the ideal period for antiviral chemotherapy, day 0–2, is still low at 37% [6].

A single dose, high-potency, live-attenuated Oka VZV vaccine against HZ (Zostavax®) has been licensed for use among immunocompetent adults ≥50 years old [3], and has been used in over 60 countries for individuals ≥50 years old. The vaccine is formulated with a minimal potency of 194,000 plaque-forming units (PFU) and administered as a single 0.65 ml subcutaneous injection [7]. Cost-effectiveness studies from high-income countries found HZ vaccination to be less than US$50,000 per quality-adjusted life year (QALY) in 12 out of 15 studies, when the vaccine is given to those

* Corresponding author.
E-mail address: hoshi@hcs.tsukuba.ac.jp (S.-l. Hoshi).

http://dx.doi.org/10.1016/j.vaccine.2017.04.046
0264-410X/

60–79 years old, and in 5 out of 5 studies when given to ≥65 years old [8].

Zostavax® is not available in Japan, while a Japan-approved Oka varicella vaccine with similar annual mean titer at 42,000–67,000 PFU per dose exists [9] (Table S1). In March 2016, the Ministry of Health, Labour and Welfare (MHLW) approved the extended use of varicella vaccine in adults aged 50 and older against HZ. On June 22, 2016, the Health Science Council in charge of Immunisation and Vaccine added varicella vaccine against HZ as one of the topics for discussion in one of their recent conferences [10], which has raised the need to evaluate its value for money. This study aimed to appraise the value for money of giving varicella vaccine to the Japanese elderly, likewise, also explored the appropriate age for vaccine uptake due to varying incidence of HZ, PHN, and vaccine efficacy.

2. Method

We conducted a cost-effectiveness analysis with Markov modelling to evaluate the efficiency of varicella vaccine immunisation programmes among Japanese elderly from a societal perspective. Incremental cost-effectiveness ratios (ICERs) were calculated to determine resource use efficiency. The software used in this study is TreeAgePro 2016 [11].

In defining immunisation programmes and constructing the model, we conducted a literature survey to find out the best available evidence (Table S2).

2.1. Programme and model

The target population of the immunisation programmes to be evaluated were those aged 65–84 in 2016 [12]. We set four different strategies with different ages to receive a vaccine shot, namely: (1) 65–84 years old (y.o.), (2) 70–84 y.o., (3) 75–84 y.o., and (4) 80–84 y.o. We set the upper age at 84 and the lower age at 65 due to the uncertainty of long-term vaccine efficacy of patients under 65 as well as beyond 85 years old. Since the coverage rate of seasonal influenza vaccine in 2014 was 50.6% [13], we expect that varicella vaccine coverage for HZ among elderly to be lower, hence, we assumed the vaccine uptake rates to be at 40% for all four strategies.

A static Markov model of courses followed by the cohort under consideration was constructed based on epidemiological data, vaccine effectiveness and models from previous studies [14–34]. Five mutually-exclusive health states were modelled: health (without any HZ-related diseases), acute HZ followed by recovery, PHN followed by recovery, post HZ/PHN, and general death (Fig. 1). Our model did not include VZV-related complications (ophthalmic, neurological, or ocular) due to insufficient data in Japan. A Markov cycle for each stage was set at one year, the model continued until the surviving individual/s reached 100 y.o. Adverse effects associated with vaccination were not considered in our model based on systematic reviews [35]. Death directly from HZ/PHN was omitted because the occurrence is rare in Japan.

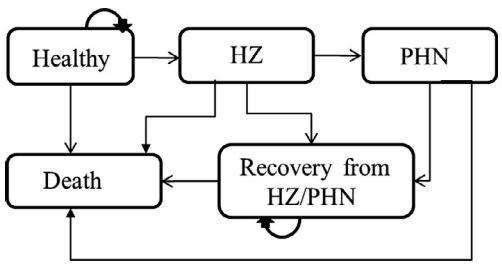

Fig. 1. Markov model.

2.2. Outcomes estimation

Outcomes in terms of QALY were estimated by assigning transition probabilities and utility weights from literature with incidence rates taken from the relevant Japanese studies; Miyazaki study and SHEZ [4,5]. Miyazaki study, a retrospective study conducted from 1997 to 2006 in Miyazaki Prefecture, reported the HZ incidence at 6.36, 8.08, 7.8, and 6.39 per 1000 person-year for persons aged 60–69, 70–79, 80–89, and 90 and over, respectively. While, SHEZ, a prospective cohort study, which recruited participants aged ≥50 from 19,058 residents between 12, 2008 and 11, 2009, reported higher HZ incidence than Miyazaki study, at 6.5 11.3, 10.8 per 1000 persons for men, 12.4, 14.1 13.6 per 1000 persons for women. In our model, HZ incidence was conservatively adopted from Miyazaki study, while proportion of PHN cases among HZ cases, namely 19.4%, 12.5%, 34.8% for men and 10.8%, 24.7%, 32.0% for women for person age 60–69, 70–79 and ≥80, respectively, were from SHEZ, because data related to PHN is not available in the Miyazaki study. Rates of general death are from vital statistics [36].

2.3. Vaccine effectiveness

The approval of extended use of varicella vaccine in adults ≥50 years old against HZ in Japan was through an application based on public knowledge. This type of application is submitted on the pretense that overseas usage of drug and medical literature published both in Japan and other countries are sufficient to prove that the drug's safety and efficiency is public knowledge within the medical and pharmacological community, and does not require additional clinical studies be conducted, either in whole or in part. Therefore, we used the vaccine effectiveness (VE) of varicella vaccine in reducing HP/PHN incidence rates from overseas' studies on Zostavax®.

Even though the Shingles Prevention Study, Short-Term Persistence Sub-study and Long-Term Persistence Sub-study (LTPS), have continuously reported VE by year after vaccination [37–39], these studies were not able to demonstrate how VE changed with chronological age (age at start of each year since vaccination) and duration after vaccination. We believe that the duration of protection and chronological age are important factors in evaluating HZ vaccination strategy cost-effectiveness, hence, we adopted the VE of model 3 from Li et al.'s study [40]. We further conservatively assumed that the vaccine will decrease HZ incidence and PHN proportion per HZ case, with no direct effects on PHN decrease. Age-specific VE data are shown in Table 1 and Fig. S1.

2.4. Utility weights

Since no study has reported the utility weights or health-related quality-of-life of HZ/PHN in Japan, we estimated these data based on two studies. Drolet et al. reported mean ED-5D score of HZ in different follow-up points after onset of rash as: 0.52 (0 day), 0.68 (30 days ~ 180 days) for patients 61–70 years old; 0.63 (0 days), 0.61 (30 days), 0.63 (90 days), 0.65 (180 days) for patients over 70 years old [41]. They also reported that "the score remained stable after 90 days (with a change of 0.2 points observed per week)". We therefore estimated the utility weights at 0.73 for 210 days and at 0.81 for 270 days and after. These figures were then weighted by the proportion of local patients with pain by month reported by Imafuku et al., which were 73.3%, 12.4%, 5.1%, 2.5%, 1.3%, 0.9% for month 0 to month 6, respectively [42]. These calculations were used to estimate average HZ QALY at 0.9548 for individuals age 60–69 and 0.9544 for those ≥70 years old, while, PHN utility weights, 0.79 (60–69 years old) and 0.76 (≥70 years old), were the averages of month 0 to month 12.

Please cite this article in press as: Hoshi S-I et al. Cost-effectiveness of varicella vaccine against herpes zoster and post-herpetic neuralgia for elderly in Japan. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.04.046