Potential cost-effectiveness of adjuvanted herpes zoster subunit vaccine for older adults in Hong Kong

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ARTICLE INFO

ABSTRACT

Background: Adjuvanted herpes zoster (HZ) subunit vaccine is recommended for adults aged ≥50 years. This study aimed to investigate cost-effectiveness of HZ subunit vaccine for older adults at different age in Hong Kong.
Methods: A life-long Markov model was designed to simulate outcomes of four alternatives: Vaccination at model entry (age 50 years); deferring vaccination to 60 years; deferring vaccination to 70 years; and no vaccination. Outcome measures included direct cost, indirect cost, HZ and post-herpetic neuralgia incidences, quality-adjusted life years (QALYs) loss, and incremental cost per QALY saved (ICER). Model clinical inputs were derived from literature. HZ treatment costs were collected from a cohort of HZ patients (n = 218). One-way and probabilistic sensitivity analyses were performed.
Results: In base-case analysis, vaccination at 50 years showed highest QALYs saved and increment cost (0.00258; USD166), followed by deferring to 60 years (0.00215 QALYs saved; USD102) and deferring to 70 years (0.00134 QALYs; USD62) when comparing to no vaccination. ICERs of vaccination arms versus no vaccine (46,267–64,341 USD/QALY) were between 1–3 × gross domestic product (GPD) per capita in Hong Kong (USD43,530–USD130,590). One-way sensitivity analyses found vaccine cost to be the common and most influential parameter for ICER of each vaccination strategy to become <1 × GDP per capita. In probabilistic sensitivity analysis, vaccination at 50 years, deferring to 60 years and 70 years were accepted as cost-effective in 90% of time at willingness-to-pay (WTP) of 78,400 USD/QALY, 57,680 USD/QALY and 53,760 USD/QALY, respectively.
Conclusions: Cost-effectiveness of each strategy is highly subject to the vaccine cost and WTP threshold per QALY saved.

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1. Introduction

Varicella zoster virus causes herpes zoster (HZ) upon reactivation in patients who were previously infected in earlier stage of life. HZ manifestations include severe pain, followed by vesicles along the dermatome(s). Truck, head and neck are most commonly affected, while ophthalmic complications are also common. Post-herpetic neuralgia (PHN), referring to the pain that persisted beyond the acute phase of HZ, also frequently occurs. Epidemiologic findings suggested that one-third of Chinese population developed HZ within their lifetime and the incidence increased with age from 5.18 cases per 1000 people at 40–50 years old to

11.77 cases per 1000 in those above 70 years old. Hospitalizations and medical cost per HZ patient also increased with age [1]. Population census ranked Hong Kong to be one of the cities with longest life-expectancy. The life expectancies at birth for men and women were 81 years and 87 years, respectively, and 54% of seven millions were females and the ≥50 years age groups accounted for 40% of the entire population in 2016 [2]. With increasing size of aging population, it is anticipated that the HZ prevalence will increase over time in Hong Kong.

A live-attenuated vaccine against HZ was first available in 2006 for adults aged 60 years and older, was later approved by Food and Drug Administration (FDA) in 2011 for adults aged 50 years and older. The live-attenuated vaccine reduced HZ cases by 51% and PHN cases by 67% for adults aged 60 years or older [3]. Further age-stratified clinical findings showed that the vaccine efficacy

against HZ in elderly aged 70 years (38%) or older was significantly lower than the efficacy (70%) in the 50–59 years age group [3,4].

Adjuvanted HZ subunit vaccine was recently approved in 2017 by the FDA for adults aged 50 years. Clinical trials data found the overall vaccine efficacy against the HZ incidence for adults aged 50 years and older to be 97% [5]. The efficacy for age groups 50–59, 60–69, 70–79 and ≥80 years were above 90% [5,6]. The Advisory Committee on Immunization Practices (ACIP) recommended it for healthy adults aged 50 years and older and for adults who had previously vaccinated with the live-attenuated HZ vaccine [7].

With aging population and prolonging life expectancy, the adult population at risk for HZ is high in Hong Kong. Universal varicella vaccination was implemented in children vaccination program subsidized by the Hong Kong government in 2014 and possibly reduced the exogenous boosting effect used to be available from those shedding zoster virus in the community. The adult vaccination program subsidized by government currently does not include zoster vaccine. To assist the decision-making process of public healthcare providers and the government on the implementation of HZ subunit vaccine in Hong Kong vaccination program, this study therefore aimed to investigate the cost-effectiveness of HZ subunit vaccine for older adults at different age from the perspective of Hong Kong society.

2. Methods

2.1. Model design

A Markov model was designed to simulate the potential life-long economic and clinical outcomes of zoster vaccination in a hypothetical cohort of immunocompetent older adults and have with no contraindications for HZ subunit vaccine. The age of hypothetical cohort was 50 years old at the entry of model. Four vaccination strategies were examined: (1) Vaccination at entry of model (vaccination at age 50 years), (2) no vaccination for next 10 years and vaccinated at age 60 years (defer vaccination to age 60 years),

(3) no vaccination for next 20 years and vaccinated at age 70 years (defer vaccination to age 70 years), and (4) no vaccination.

Markov modeling is a form of decision analysis in which hypothetical subjects proceed through health states over time based on probability inputs of the model (Fig. 1). Subjects of all study arms entered the model at the age of 50 years old at the Markov health state "well" and transit to other health states (including well, HZ, PHN, resolved HZ and death) in the next cycle. The time horizon of Markov model was 50 years with monthly cycle. Primary outcomes measures of the model included direct medical costs, indirect costs, incidence of HZ and PHN and HZ-related quality-adjusted life-years (QALYs) loss.

In the three vaccination arms, a person might develop adverse events after receiving vaccination and require medical attention. All subjects in the present model, vaccinated or not, might survive or die from all causes in each cycle. Those subjects who survive might experience HZ and receive treatment in outpatient or inpatient setting. Those who were admitted for inpatient treatment might develop complications (such as nervous system infection, ophthalmicus, Ramsay Hunt Syndrome, secondary skin and soft tissue infection (SSTI), disseminated HZ), and might die or survive. Zoster patients who survived might develop PHN, and the duration of PHN varied by age and gender of patients.

2.2. Clinical inputs

The model clinical parameters were listed in Table 1. Literature search on MEDLINE over the period 2000-present was performed using keywords "herpes zoster", "post-herpetic neuralgia", "neurologic complications", "meningitis", "ophthalmic complications", "herpes zoster vaccination", "adjuvanted herpes zoster subunit vaccine", "vaccine coverage", "vaccine safety", "outpatient care", "hospitalization", and "mortality". The selection criteria of clinical trials are: (1) reports in English; (2) patients aged 18 years or above; and (3) the incidence of events were reported. A manuscript was included if it had data relevant to the model inputs. Case
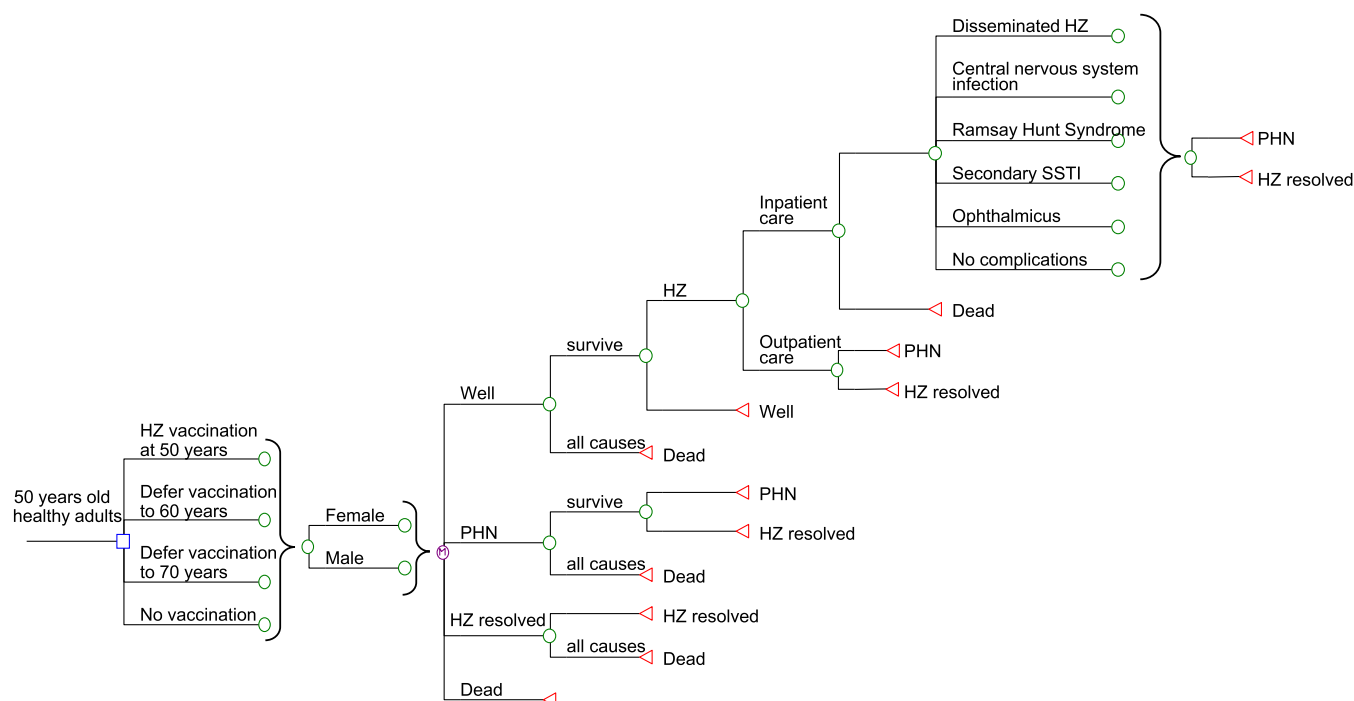

Fig. 1. Simplified Markov model.