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Cost-effectiveness of an influenza vaccination program offering intramuscular and intradermal vaccines versus intramuscular vaccine alone for elderly

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ABSTRACT

Background: Intradermal (ID) injection is an alternative route for influenza vaccine administration in elderly with potential improvement of vaccine coverage. This study aimed to investigate the cost-effectiveness of an influenza vaccination program offering ID vaccine to elderly who had declined intramuscular (IM) vaccine from the perspective of Hong Kong public healthcare provider.
Methods: A decision analytic model was used to simulate outcomes of two programs: IM vaccine alone (IM program), and IM or ID vaccine (IM/ID program) in a hypothetic cohort of elderly aged 65 years. Outcome measures included influenza-related direct medical cost, infection rate, mortality rate, quality-adjusted life years (QALYs) loss, and incremental cost per QALY saved (ICER). Model inputs were derived from literature. Sensitivity analyses evaluated the impact of uncertainty of model variables.
Results: In base-case analysis, the IM/ID program was more costly (USD52.82 versus USD47.59 per individual to whom vaccine was offered) with lower influenza infection rate (8.71% versus 9.65%), mortality rate (0.021% versus 0.024%) and QALYs loss (0.00336 versus 0.00372) than the IM program. ICER of IM/ID program was USD14,528 per QALY saved. One-way sensitivity analysis found ICER of IM/ID program to exceed willingness-to-pay threshold (USD39,933) when probability of influenza infection in unvaccinated elderly decreased from 10.6% to 5.4%. In 10,000 Monte Carlo simulations of elderly populations of Hong Kong, the IM/ID program was the preferred option in 94.7% of time.
Conclusions: An influenza vaccination program offering ID vaccine to elderly who had declined IM vaccine appears to be a highly cost-effective option.

1. Introduction

Every year the public healthcare provider of Hong Kong is burdened by the surge of cases with influenza-like illness during peak influenza season, and public hospitals are crowded by severe influenza admissions [1]. It was estimated that nearly 1000 excess deaths were associated with influenza annually in Hong Kong and 95% of the excess deaths occurred in elderly [2].

Vaccination is a cost-effective method to avert influenza cases and corresponding losses in direct medical cost, productivity as well as quality-adjusted life-years (QALYs) [3]. Seasonal influenza vaccination for elderly (aged 65 years or above) in Hong Kong is subsided by the government and promoted by wide-scale communication activities, yet the vaccination coverage rate of elderly in Hong Kong was only 39.1% [4], indicating that most of elderly remain unprotected from influenza.

Intramuscular (IM) injection has been the conventional delivery route of influenza vaccine for elderly and needle anxiety is a limiting factor [5] for vaccine compliance. Intradermal (ID) injection is recently available as an alternative route of administration for influenza vaccine. Hollow microneedle delivery system for ID influenza vaccine consists of a finer and smaller-gauged microneedle of 1.5 mm long and 30 gauge needle, compared to the 25–37.5 mm and 22–25 gauge needle for IM injection. ID influenza vaccine targeted at the epidermal Langerhans cells stimulates a greater immune response in the recipients than intramuscular injection, and therefore achieves a dose sparing effect [6]. The use of microneedle delivery system for vaccination has potential advantages in improving vaccine coverage rate for elderly [7]. Quantification of the economic and clinical impact of ID influenza vaccine in elderly population would assist formulation of public health policy on seasonal influenza vaccination program. This study aimed to investigate the cost-effectiveness of an influenza

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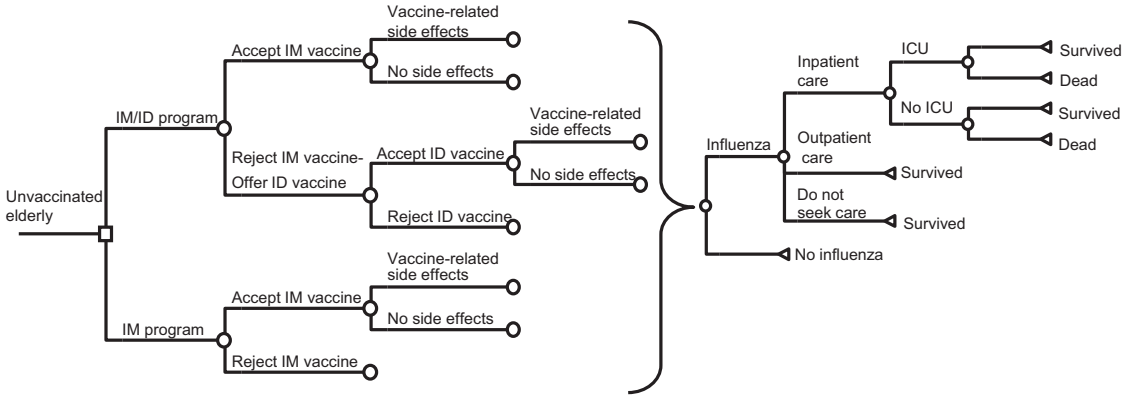

Fig. 1. Simplified decision-analytic model.

vaccination program offering both IM and ID delivery systems versus a program with IM injection alone for elderly from the perspective of public healthcare provider in Hong Kong.

2. Methods

2.1. Model design

In Hong Kong, the Elderly Vaccination Subsidy Scheme (EVSS) provided by the government covers all elders for seasonal influenza vaccination [8]. Our prior decision-analytic model on influenza [9] was adapted and modified to simulate the outcomes of two influenza vaccination programs: (1) IM injection alone (IM program) and (2) IM or ID injection (IM/ID program) for prevention of seasonal influenza over one-year time horizon in a hypothetic cohort of elderly aged 65 years (Fig. 1). Elderly with contraindications to influenza vaccine, including past medical history of severe allergic reaction toward any components of the vaccines, were excluded in the present model. Direct medical cost, infection rate, mortality rate and QALY loss due to influenza were simulated for each study arm.

In both vaccination programs, individuals could accept or decline the offered vaccine formulation. The IM/ID program would first offer IM influenza vaccine. Those who rejected the IM formulation would be further offered ID influenza vaccine, and they might or might not accept ID vaccine. In the IM program, only the IM formulation of influenza vaccine would be offered. For those individuals who were vaccinated, typical side effects such as injection site reaction, headache and myalgia might occur. All individuals (vaccinated or not) in the model might be infected by influenza. The patients infected with influenza might seek medical care, receiving outpatient care only or be admitted for inpatient care. All patients who were hospitalized might survive or die, with or without being admitted to the intensive care unit (ICU).

2.2. Clinical inputs

The model parameters were listed in Table 1. A literature search on MEDLINE over the period of 2000–2016 was performed using the keywords “influenza infection”, “intradermal vaccine”, “vaccine effectiveness”, “influenza mortality” and “utility score”. The selection criteria of clinical studies of influenza infection were: (1) reports were written in English; (2) etiology of respiratory illnesses was identified, and (3) mortality rate and/or ICU admission rate were reported. Relative treatment effect (such as vaccine efficacy) and side effect are considered to have high transferability even if derived from clinical trials conducted in a population different from the local population [10]. Baseline risk and healthcare resources utilization are considered to have low transferability, and published data from Hong Kong (if available) were preferred. All articles retrieved by this process were screened for relevance to our model. A manuscript was included if it had data pertaining to the model inputs. For variable that was reported in multiple studies, the weighted average was used to estimate the base-case value. The high and low values of the variable reported in literature were tested in sensitivity analysis.

The IM vaccine coverage rate in elderly (39.1%) was reported by a survey on over 3000 individuals of different age groups in Hong Kong [4]. The ID vaccine coverage rate (63.3%) among those who were not vaccinated by IM vaccine (but in whom vaccination was recommended based on the age of 65 years and above) was estimated from findings of a survey on over 1200 individuals in Europe [7]. The occurrence rate of side effects with parenteral influenza vaccine (inactivated form of virus) were estimated from systematic review of clinical studies on outcomes of influenza vaccination in elderly [11,12]. A meta-analysis reported no significant differences in the occurrence of systemic reactions with ID and IM influenza vaccines and the reported relative risk (1.00; 95% CI = 0.67–1.51) [13] was adopted in the present model. The influenza infection attack rate in unvaccinated elderly (10.6%; range 2.0–17.5%) was estimated from findings of an age-specific epidemiology study on seroprevalance rates in Hong Kong [14]. The influenza infection rate of vaccinated elderly was calculated by the following formula: Infection rate of unvaccinated person $\times$ (1 – vaccine effectiveness).

The seroprotection rate induced by the ID vaccine was reported to be comparable to IM vaccine [13], and similar effectiveness was assumed for both ID and IM vaccines. The 2014–2015 seasonal influenza vaccine effectiveness for older adults (23%) was used as base-case model input, ranging from the lowest and highest vaccine effectiveness for elderly reported in 2010–2015 (22–43%) [15–19]. The case-hospitalization ratio (4.21%), probabilities of seeking outpatient care in non-high-risk elderly (62%) and high-risk elderly (82%), and proportion of high-risk individuals (51.2%) in elderly were retrieved from outcome analyses and epidemiology studies [20,21]. The ICU admission rate [22–24] and mortality rate in hospitalized elderly patients aged 65 years or older were retrieved from outcome analyses of severe influenza infection in Hong Kong [25,26]. The risk of mortality in older patients (aged 85 years or above) was included to estimate the outcomes in elderly of advanced age [27].

2.3. Utility inputs

The QALYs lost by each vaccinated or infected individual were calculated using the utility loss (utility $\text{score}_{\text{elderly}}$ – utility $\text{score}_{\text{event}}$), and the duration of time-spent in each of following

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