Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

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

Cost-effectiveness and public health impact of alternative influenza vaccination strategies in high-risk adults

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ARTICLE INFO

Article history:
Received 14 March 2017
Received in revised form 19 July 2017
Accepted 21 July 2017
Available online xxxx

Keywords:
High dose influenza vaccine
Cost-effectiveness analysis
Influenza vaccination policy

ABSTRACT

Purpose: High-dose trivalent inactivated influenza vaccine (HD-IIV3) or recombinant trivalent influenza vaccine (RIV) may increase influenza vaccine effectiveness (VE) in adults with conditions that place them at high risk for influenza complications. This analysis models the public health impact and cost-effectiveness (CE) of these vaccines for 50–64 year-olds.

Methods: Markov model CE analysis compared 5 strategies in 50–64 year-olds: no vaccination; only standard-dose IIV3 offered (SD-IIV3 only), only quadrivalent influenza vaccine offered (SD-IIV4 only); high-risk patients receiving HD-IIV3, others receiving SD-IIV3 (HD-IIV3 & SD-IIV3); and high-risk patients receiving HD-IIV3, others receiving SD-IIV4 (HD-IIV3 & SD-IIV4). In a secondary analysis, RIV replaced HD-IIV3. Parameters were obtained from U.S. databases, the medical literature and extrapolations from VE estimates. Effectiveness was measured as 3%/year discounted quality adjusted life year (QALY) losses avoided.

Results: The least expensive strategy was SD-IIV3 only, with total costs of $99.84/person. The SD-IIV4 only strategy cost an additional $0.91/person, or $37,700/QALY gained. The HD-IIV3 & SD-IIV4 strategy cost $1.06 more than SD-IIV4 only, or $71,500/QALY gained. No vaccination and HD-IIV3 & SD-IIV3 strategies were dominated. Results were sensitive to influenza incidence, vaccine cost, standard-dose VE in the entire population and high-dose VE in high-risk patients. The CE of RIV for high-risk patients was dependent on as yet unknown parameter values.

Conclusions: Based on available data, using high-dose influenza vaccine or RIV in middle-aged, high-risk patients may be an economically favorable vaccination strategy with public health benefits. Clinical trials of these vaccines in this population may be warranted.

1. Introduction

High-risk conditions, such as chronic cardiac or pulmonary disease that increase the risk of influenza complications, are major factors determining morbidity and mortality due to influenza A [1,2]. Influenza vaccine policy seeks to prevent the substantial morbidity [3] and mortality [4] associated with influenza among high-risk persons through the use of the most effective vaccines. Thus, high-dose inactivated influenza vaccine is currently recommended for individuals over age 65 years because of their age-specific reduction in immunological response and the increasing prevalence of chronic conditions in this age group. High-dose influenza vaccine has been shown to elicit higher immunological response [5] and improve protection against influenza [6], compared with the standard-dose influenza vaccine.

Due to the aging of the baby boomer generation, the US population includes an increasing proportion of middle-aged adults with chronic conditions that place them at high risk for influenza

Abbreviations: SD-IIV3, standard-dose trivalent inactivated influenza vaccine; HD-IIV3, high-dose trivalent inactivated influenza vaccine; RIV, recombinant trivalent influenza vaccine; IDA, Influenza Decision Analysis; SD-IIV4, standard-dose quadrivalent influenza vaccine; QALY, Quality-adjusted life year.

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http://dx.doi.org/10.1016/j.vaccine.2017.07.069
0264-410X/

complications. The growth of this high-risk population suggests a need to consider vaccine options that could better prevent influenza. Currently, the standard-dose inactivated influenza vaccine (SD-IIV) is recommended for all adults 50–64 years of age, whether they are high risk or not, but the vaccine's effectiveness in recent years has been modest [7]. Similar to older adults, there is some evidence suggesting that 50–64-year-old adults with conditions that increase influenza risk may produce suboptimal responses to standard-dose influenza vaccine and that these high risk individuals may benefit from high-dose vaccine [8].

Two influenza vaccine options offer the potential to better protect high-risk, middle-aged adults: (1) high-dose trivalent inactivated influenza vaccine (HD-IIV3); and (2) recombinant trivalent influenza vaccine (RIV). However, studies examining their effectiveness in this age group have not been completed. Cost-effectiveness analyses offer a relatively inexpensive and responsive method of evaluating new vaccination strategies. For example, a cost-effectiveness analysis has demonstrated that high-dose trivalent influenza vaccine is economically reasonable for use in individuals ≥65 years of age, given its increased effectiveness [9].

An evaluation of the cost-effectiveness of HD-IIV3 and RIV in high-risk middle-aged adults is warranted to help guide influenza vaccine policy. This study uses a Markov decision analysis to examine several strategies that include HD-IIV3 or RIV for vaccinating high-risk, 50–64-year-old adults to determine their cost-effectiveness and the public health impact that may be realized through their use.

2. Methods

2.1. Population and model dynamics

The decision analytic Markov model used in this analysis extended the Influenza Decision Analysis (IDA) model, which was developed to evaluate alternative influenza vaccination strategies in the U.S. population, to a high-risk, 50–64-year-old U.S. population [9]. The dynamics of the decision tree, including detailed descriptions of cost and benefit valuations and model assumptions, have been previously reported [9]. The enhanced model used in the present analysis retains the same event logic, where the probabilities of vaccination, illness, complications, treatment, recovery, and death are computed for a hypothetical cohort of individuals for each of 10 monthly cycles corresponding with a single influenza season.

In the Markov state transition model, five strategies for 50–64 year-olds were compared: no vaccination, only standard-dose trivalent influenza vaccine offered (SD-IIV3 only), only standard-dose quadrivalent influenza vaccine offered (SD-IIV4 only), high-risk patients receiving HD-IIV3 and non-high-risk individuals receiving SD-IIV3 (HD-IIV3 & SD-IIV3), and high-risk patients receiving HD-IIV3 and non-high-risk individuals receiving SD-IIV4 (HD-IIV3 & SD-IIV4). The analysis took a societal perspective, following the recently updated recommendations of the Panel on Cost-Effectiveness in Health and Medicine [10].

The present model differs from the original IDA model [9] in the population age cohort and the vaccination strategies recommended for high-risk and non-high-risk 50–64-year-old patients. The model was supplemented with logic to allow the comparison of strategies with unknown vaccine effectiveness, as the comparator strategies are either too new to have generated reliable population data or have not been routinely used in the high-risk, middle-aged population. The potential cost-effectiveness of RIV was modeled in a secondary analysis in which RIV was substituted for HD-IIV3 in the HD-IIV3 & SD-IIV3 and the HD-IIV3 & SD-IIV4 strategies. This analysis was conducted as a hypothesis-generating exercise to explore scenarios where inclusion of RIV might alter the favored vaccination strategy.

2.2. Measures

Parameters used in the model are shown in Table 1. Whenever possible, costs, utilities, and probabilities were selected from the most current and robust data sources, as noted. Though several values of vaccine efficacy required new estimations based on analogous data in related populations, previously developed peer-reviewed estimates were selected when available.

A systematic review and *meta*-analysis of all published reports provided a pooled value for SD-IIV3 vaccine effectiveness of 59% in the adult non-elderly population [11]. This was used as the base case vaccine efficacy for the subset of non-high-risk adults 50–64 years old. The efficacy of SD-IIV3 was reduced by 10% for high-risk patients per recent findings among working-age adults [8]. Reliable estimates of the effectiveness of HD-IIV3 in high-risk adults <65 years old were not available. Therefore, HD-IIV3 effectiveness among high-risk 50–64 year olds was calculated as an increase in relative effectiveness over SD-IIV3. The magnitude of this difference was assumed to be similar to the observed difference (0.242) reported in randomized trial data in the ≥65-year-old population [6]. The relative difference in effectiveness of SD-IIV4 versus SD-IIV3 was calculated by applying the protection offered by SD-IIV3 against influenza A strains to the average likelihood of infection from the influenza B lineage not included in the vaccine from 1999–2000 through 2013–14 [12]. Because VE against influenza B has recently been greater than that of influenza A, this assumption could bias against IIV4. Additionally, no cross-protection against influenza B is assumed to be offered in IIV3 variants. This assumption may bias against IIV3 variants. Similarly, RIV effectiveness was calculated as a relative effectiveness increase over SD-IIV3 from a randomized trial of adults aged 50 years or more [13], converting that study's relative effectiveness compared to SD-IIV4 (=0.31) to relative effectiveness vs. SD-IIV3, using the average likelihood of influenza B due to the non-vaccine lineage (as above), to facilitate comparisons between HD-IIV3 and RIV.

Adverse event risk was assumed to be the same among all vaccine types [6]. Quality-adjusted life years (QALYs) lost due to influenza-related causes were used to quantify strategy effectiveness and were discounted at 3% per year. All costs, except for RIV which was not available in 2014, were adjusted to 2014 levels based on the U.S. Consumer Price Index [14]. Expected event frequencies for hospitalization and death due to influenza in the modeled cohort were calculated using the base case parameters of the model (Table 1) multiplied by the U.S. Census estimated 2014 50–64-year-old population.

2.3. Sensitivity analysis

One-way and multi-way sensitivity analyses were conducted to test the stability of model results under varying parameter values as shown in Table 1. One-way comparisons demonstrate the effect of individual parameters; multi-way analyses plot model results when selected parameters are varied simultaneously across their plausible ranges.

3. Results

In the primary analysis comparing alternative influenza vaccination strategies in middle-aged, high-risk adults, no vaccination and the HD-IIV3 & SD-IIV3 strategy were more costly and less effective than other strategies and thus were dominated (Table 2). SD-IIV3 only was the least expensive strategy, with total influenza

Please cite this article in press as: Raviotta JM et al. Cost-effectiveness and public health impact of alternative influenza vaccination strategies in high-risk adults. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.07.069