VALUE IN HEALTH ▮ (2016) ▮▮▮–▮▮▮

Available online at www.sciencedirect.com

ScienceDirect

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

Cost-Effectiveness of Quadrivalent versus Trivalent Influenza Vaccine in the United States

Pieter T. de Boer, MSc[1,], Pascal Crépey, PhD[2,3], Richard J. Pitman, PhD[4], Bérengère Macabeo, PharmD[5], Ayman Chit, PhD[6,7], Maarten J. Postma, PhD[1,8,9]*

[1]*Unit of PharmacoTherapy, -Epidemiology & -Economics (PTE2), Department of Pharmacy, University of Groningen, Groningen, The Netherlands;* [2]*EHESP Rennes, Sorbonne Paris-Cité, Paris, France;* [3]*Aix-Marseille Univ, UMR EPV 190, Marseille, France;* [4]*ICON Health Economics, Oxford, UK;* [5]*Sanofi Pasteur, Lyon, France;* [6]*Sanofi Pasteur, Swiftwater, PA, USA;* [7]*Lesli Dan Faculty of Pharmacy, Toronto, Ontario, Canada;* [8]*Institute of Science in Healthy Aging & healthcaRE (SHARE), University Medical Center Groningen (UMCG), Groningen, The Netherlands;* [9]*Department of Epidemiology, University Medical Center Groningen (UMCG), University of Groningen, Groningen, The Netherlands*

ABSTRACT

Background: Designed to overcome influenza B mismatch, new quadrivalent influenza vaccines (QIVs) contain one additional B strain compared with trivalent influenza vaccines (TIVs). **Objective:** To examine the expected public health impact, budget impact, and incremental cost-effectiveness of QIV versus TIV in the United States. **Methods:** A dynamic transmission model was used to predict the annual incidence of influenza over the 20-year-period of 2014 to 2034 under either a TIV program or a QIV program. A decision tree model was interfaced with the transmission model to estimate the public health impact and the cost-effectiveness of replacing TIV with QIV from a societal perspective. Our models were informed by published data from the United States on influenza complication probabilities and relevant costs. The incremental vaccine price of QIV as compared with that of TIV was set at US $5.40 per dose. **Results:** Over the next 20 years, replacing TIV with QIV may reduce the number of influenza B cases by 27.2% (16.0 million cases), resulting in the prevention of 137,600 hospitalizations and 16,100 deaths and a gain of 212,000 quality-adjusted life-years (QALYs). The net societal budget impact would be US $5.8 billion and the incremental cost-effectiveness ratio US $27,411/QALY gained. In the probabilistic sensitivity analysis, 100% and 96.5% of the simulations fell below US $100,000/QALY and US $50,000/QALY, respectively. **Conclusions:** Introducing QIV into the US immunization program may prevent a substantial number of hospitalizations and deaths. QIV is also expected to be a cost-effective alternative option to TIV.

Keywords: cost-effectiveness, influenza, quadrivalent influenza vaccine, vaccination.

Key Points

What is already known about the topic?
Recently approved quadrivalent influenza vaccines (QIVs) contain one extra B lineage as compared with trivalent influenza vaccines (TIVs). Therefore, QIVs offer improved protection during seasons with cocirculation of both type-B lineages or when TIV is mismatched against the sole circulating influenza B strain. A number of static models have predicted that shifting from TIV to QIV is a potential cost-effective intervention in the United States.

What does the article add to existing knowledge?
We use a dynamic model to study the cost-effectiveness of switching from TIV to QIV in the United States. Static models do not incorporate disease transmission dynamics, whereas dynamic models do (herd effects). Ignoring disease transmission can be a significant source of bias in infectious disease modeling studies. Moreover, some previous cost-effectiveness studies ignored cross-protection of TIV against the mismatched influenza B lineage.

What insights does the article provide for informing health care–related decision making?
Shifting from TIV to QIV is expected to reduce the number of influenza B cases by 27.2% over the next 20 years. Using the societal perspective, the incremental cost-effectiveness ratio was estimated at US $27,411 per quality-adjusted life-year gained. The probabilistic sensitivity analysis showed that the results are robust. This article illustrates that, using a dynamic model, cost-effectiveness is estimated to be below a potential willingness-to-pay threshold of US $50,000/quality-adjusted life-year gained.

Introduction

Seasonal influenza is a viral infectious disease caused by influenza type-A (H1N1 and H3N2) viruses or influenza type-B viruses

Source of financial support: This study was funded by Sanofi Pasteur.

* *Address correspondence to* Pieter T. de Boer, Department of Pharmacy, University of Groningen, Groningen 9713AV, The Netherlands. E-mail: p.t.de.boer@rug.nl.

1098-3015$36.00 – see front matter http://dx.doi.org/10.1016/j.jval.2016.05.012

(Yamagata and Victoria). Surveillance data show that B strains represent on average 24% of viral isolates in the United States and from the 2001-2002 season to the present, both B lineages have cocirculated each season at varying levels and with no regularity [1]. In the United States, the average annual public health burden of seasonal influenza (types A and B) is estimated at 24,000 deaths and 95,000 hospital admissions; however, in severe seasons, this can increase to 49,000 and 270,000, respectively [2,3]. Also, the economic burden of influenza is significant. Annual influenza-related medical costs in the United States have been estimated at US $10 billion and productivity costs at US $16 billion [4]. Seasonal vaccination against influenza is regarded as the most effective strategy to prevent influenza disease [5]. Traditional influenza vaccines are trivalent, containing strains of two influenza A subtypes (one of each H1N1 and H3N2) and one strain of an influenza B lineage (Victoria or Yamagata), according to recommendations of the World Health Organization. However, over the decade 2001 through 2012, mismatches between the circulating B lineage and the B strain of the vaccine occurred in 5 of the 10 seasons in the United States because of the cocirculation of both influenza B lineages [1]. Two recent meta-analysis have demonstrated that TIV offers suboptimal protection when there is a mismatch between circulating influenza B and B vaccine strains (B-lineage vaccine efficacy is 71%–77% when TIV influenza B is lineage matched and 46%–49% when mismatched) [6,7].

To address the problem of influenza B matching, quadrivalent influenza vaccines (QIVs) were developed and licensed in the US market in 2012 [8]. In addition to strains of the two influenza A subtypes, QIVs contain strains from both type-B lineages (Victoria and Yamagata). The US Centers for Disease Control and Prevention (CDC) estimated that QIV might have prevented on average 340,000 influenza cases, 2,700 hospitalizations, and 170 deaths within the seasons 2001-2002 to 2008-2009 [9]. Moreover, two economic evaluations demonstrated that the cost-effectiveness of shifting from TIV to QIV was favorable [10–12].

However, published economic evaluations of QIV versus TIV in the United States so far are based on static models. The static approach assumes a constant risk of infection and does not incorporate the indirect protection that the successfully immunized proportion of the population provides to those individuals who are still susceptible, by reducing the risk of transmission (herd effects). Dynamic models simulate disease transmission by taking into account contact patterns between humans and the risk of transmission per contact, which allows the model to account for herd effects [13]. Because influenza vaccination impacts disease transmission, the dynamic approach can be regarded as the more appropriate approach to quantify the epidemiological and economic impact of replacing TIV by QIV [14]. The aim of this study was to assess the cost-effectiveness of QIV versus TIV for seasonal vaccination in the United States on the basis of a dynamic modeling approach.

Methods

Overview

The cost-effectiveness model uses an age-structured dynamic transmission model to estimate the impact of QIV over TIV in terms of clinical outcomes, costs, and health effects. Clinical outcomes included outpatient visits, hospitalizations, and deaths. Costs were assessed from the third-party payer's (TPP's) perspective, considering reimbursed direct medical costs only, as well as from the societal perspective, which also accounts for out-of-pocket-paid over-the-counter medication and indirect costs due to productivity losses. Final outcomes of the study were incremental costs per quality-adjusted life-year (QALY) gained and incremental costs per life-year (LY) gained.

Model Design

The dynamic transmission model developed by Crepey et al. [15] was used to estimate age-stratified numbers of symptomatic influenza B cases under the QIV and TIV strategies. The model is a variation on the compartmental SEIR model, where individuals can be susceptible to infection (S), exposed but not infectious (E), infectious (I), or recovered (R) from an infection and therefore immune for a certain time period. A vaccination compartment was added to account for individuals effectively protected from infection by vaccination. The model accounted for cross-protection, that is, the protection that vaccination against or natural infection by a B lineage offers against the opposite B lineage. A more detailed description of the dynamic model and main input parameters can be found in Supplemental document A and Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.05.012.

For the economic model, we used an age-structured decision tree model (Fig. 1), developed in Excel 2010 and linked to the dynamic model described above. The output of the dynamic model, age-stratified symptomatic influenza cases, served as input to the economic model. First, the age groups of the dynamic model were recategorized in the economic model to align with available data on economic parameters (0–23 months, 2 years, 3–4 years, 5–11 years, 12–17 years, 18–49 years, 50–64 years, 65+ years), using age-distribution data of the US population [16]. Next,

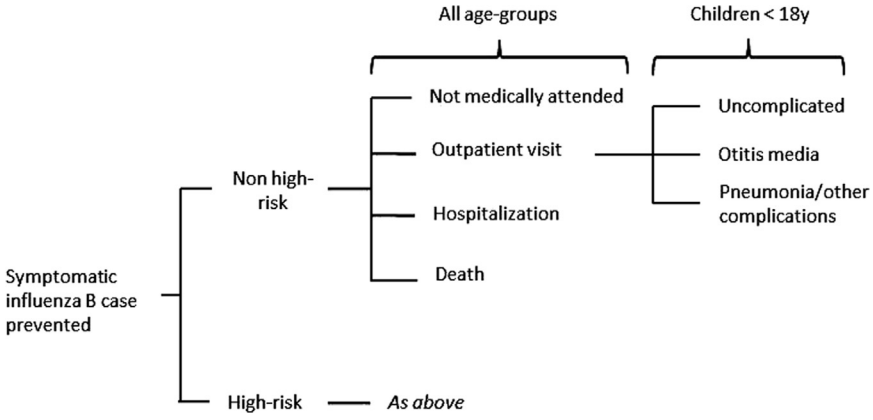

Fig. 1 – Flow diagram of the economic decision tree model.