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Cost-utility of quadrivalent versus trivalent influenza vaccine in Brazil – comparison of outcomes from different static model types

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ABSTRACT

Background: Influenza burden in Brazil is considerable with 4.2–6.4 million cases in 2008 and influenza-like-illness responsible for 16.9% of hospitalizations. Cost-effectiveness of influenza vaccination may be assessed by different types of models, with limitations due to data availability, assumptions, and modelling approach.

Objective: To understand the impact of model complexity, the cost-utility of quadrivalent versus trivalent influenza vaccines (QIV versus TIV) in Brazil was estimated using three distinct models: a 1-year decision tree population model with three age groups (FLOU); a more detailed 1-year population model with five age groups (FLORA); and a more complex lifetime multi-cohort Markov model with nine age groups (FLORENCE).

Methods: Analysis 1 (impact of model structure) compared each model using the same data inputs (i.e., best available data for FLOU). Analysis 2 (impact of increasing granularity) compared each model populated with the best available data for that model.

Results: Using the best data for each model, the discounted cost-utility ratio of QIV versus TIV was R$20,428 with FLOU, R$22,768 with FLORA (versus R$20,428 in Analysis 1), and, R$19,257 with FLORENCE (versus R$22,490 in Analysis 1) using a lifetime horizon. Conceptual differences between FLORA and FLORENCE meant the same assumption regarding increased all-cause mortality in at-risk individuals had an opposite effect on the incremental cost-effectiveness ratio (ICER) in Analysis 2 versus 1, and a proportionally higher number of vaccinated elderly in FLORENCE reduced the ICER in Analysis 2.

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Discussion

FLOU provided adequate cost-effectiveness estimates with data in broad age groups. FLORA increased insights (e.g., in healthy versus at-risk, paediatric, respiratory/non-respiratory complications). FLORENCE provided greater insights and precision (e.g., in elderly, costs and complications, lifetime cost-effectiveness).

Conclusion: All three models predicted a cost per QALY gained for QIV versus TIV in the range of R$19,257 (FLORENCE) to R$22,768 (FLORA) with the best available data in Brazil.

Background (Appendix A)

The annual number of confirmed influenza cases in Brazil was estimated to be between 4.2 and 6.4 million cases in 2008.[1] While data were limited due to likely underreporting, the influenza surveillance system reported that influenza-like illness was responsible for 4.4–16.9% of hospital consultations between 2000 and 2008.[2] Data on mortality were reported for influenza and pneumonia combined, and were highest among the youngest and eldest age groups in most Latin American countries. The highest proportion of deaths in children under five years in the region were reported for Ecuador (14.4% in 2003) and Brazil (13.5% in 2004).[1] The vaccination target group in Brazil has become progressively broader since 1999, and now includes people over 60 years old, children aged six months to four years, and a range of vulnerable people.[2]

By investing in disease prevention, influenza vaccination programs can increase the health of the entire population. Policy-makers need to choose which age- and risk-groups to vaccinate in order to achieve the best health outcomes. Investment costs need to be weighed up against the current health burden, expected health gains, and cost savings, to evaluate whether vaccination programs offer value for money compared to existing disease management options. Epidemiologic and economic models, combining current knowledge of the disease burden, transmission and impact on healthcare resources are frequently used to predict the health and economic consequences of vaccination. A range of model types are available with many different data requirements; more detailed approaches typically require more data, which can often be unavailable leading to increased use of assumptions, and ultimately reducing validity of a more complex approach.

Regarding the cost-effectiveness of influenza vaccination, a range of model types have been used, but with caveats relating to limitations in the modelling approach, lack of input data, and use of assumptions. Health policy guidelines recommend annual influenza vaccination in *consecutive* seasons, yet many influenza models consider cost-effectiveness in *one* year and apply a lifetime horizon to assess quality-adjusted life-years (QALYs) lost due to premature mortality.[3–5] These 1-year models may artificially oversimplify lifetime effects by assuming all influenza mortality occurs at one average age within an age group, and those who survive influenza would live their remaining life expectancy at a constant baseline utility. The population of these 1-year models is often broadly subdivided (e.g. children, adults, and elderly), however, there is considerable heterogeneity within those broad age bands, especially among the elderly (e.g., due to natural mortality, baseline utility and costs). Multi-cohort models in which cohorts enter the model at many different ages and are followed over a lifetime of consecutive influenza seasons, provide a more direct approach to influenza management than 1-year models, consider heterogeneity in the population, and allow for an appropriate attribution of QALYs over time.[6] However, detailed age-specific data may prove difficult to find.

This paper aims to understand the impact model complexity has on predicting results, and the pros and cons of different approaches. In order to do so, the impact of introducing influenza vaccination in Brazil was estimated using three distinct models, from a 1-year decision tree population model (FLOU) to a more complex life-time multi-cohort Markov model (FLORENCE), and with a moderately complex 1-year population model (FLORA). Thus FLOU, FLORA, and FLORENCE, each used increasing data and modelling complexity, were compared in terms of predicting outcomes with increasing precision. The models compared cases, costs and health outcomes of the following influenza vaccination strategies in Brazil: no vaccination, trivalent influenza vaccination (TIV), and quadrivalent influenza vaccination (QIV).

Methods

Model descriptions

FLOU (i.e. inFLuenza cOst-Utility) model

The FLOU model is a decision tree population model dividing the population into three age groups (paediatric, adult, and elderly; <18, 18–64, and ≥65 years, respectively), each subdivided into two risk groups (healthy and at-risk). The model uses a 1-year time horizon, while attributing lifetime QALY losses to premature deaths. Influenza cases could lead to general practitioner (GP) visits, hospitalization, and death following hospitalization or no hospitalization.

A distinction was made between healthy and at-risk populations for vaccination coverage and the probability of GP visits and hospitalization. The model calculated vaccination costs (vaccine price and administration), GP visit and hospitalization costs as well as baseline utilities, QALY loss due to influenza, hospitalizations, and mortality for each strategy.