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The cost-effectiveness of trivalent and quadrivalent influenza vaccination in communities in South Africa, Vietnam and Australia

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ABSTRACT

Background: To inform national healthcare authorities whether quadrivalent influenza vaccines (QIVs) provide better value for money than trivalent influenza vaccines (TIVs), we assessed the cost-effectiveness of TIV and QIV in low-and-middle income communities based in South Africa and Vietnam and contrasted these findings with those from a high-income community in Australia.
Methods: Individual based dynamic simulation models were interfaced with a health economic analysis model to estimate the cost-effectiveness of vaccinating 15% of the population with QIV or TIV in each community over the period 2003–2013. Vaccination was prioritized for HIV-infected individuals, before elderly aged 65+ years and young children. Country or region-specific data on influenza-strain circulation, clinical outcomes and costs were obtained from published sources. The societal perspective was used and outcomes were expressed in International$ (I$) per quality-adjusted life-year (QALY) gained.
Results: When compared with TIV, we found that QIV would provide a greater reduction in influenza-related morbidity in communities in South Africa and Vietnam as compared with Australia. The incremental cost-effectiveness ratio of QIV versus TIV was estimated at I$4183/QALY in South Africa, I $1505/QALY in Vietnam and I$80,966/QALY in Australia.
Conclusions: The cost-effectiveness of QIV varied between communities due to differences in influenza epidemiology, comorbidities, and unit costs. Whether TIV or QIV is the most cost-effective alternative heavily depends on influenza B burden among subpopulations targeted for vaccination in addition to country-specific willingness-to-pay thresholds and budgetary impact.

1. Introduction

Seasonal influenza has been estimated to cause between 3 and 5 million cases of severe illness and 250,000–500,000 deaths globally each year [1]. The elderly, very young children and people with specific health conditions are at highest risk of developing serious complications [2]. In addition, influenza imposes a significant economic burden involving health care costs and productivity losses. In low- and middle-income countries (LMICs), costs due to seasonal influenza may have a considerable economic impact, estimated at 2–6% of gross domestic product (GDP) per capita,

Abbreviations: GDP, gross domestic product; ICER, incremental cost-effectiveness ratio; HIV, human immunodeficiency virus; IBS, individual based simulation; I$, international $; LMICs, low- and-middle income countries; NMB, net monetary benefit; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; QIV, quadrivalent influenza vaccine; SAR, symptomatic attack rate; TIV, trivalent influenza vaccine; WHO, world health organization; WTP, willingness-to-pay.

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compared to only 0.04–0.13% of GDP per capita in high income countries [3].

Annual vaccination is currently the most effective way of preventing influenza disease [1]. The commonly used trivalent influenza vaccines (TIVs) contain strains of two influenza A sub-types (H1N1 and H3N2) and one influenza B lineage (either Victoria or Yamagata), based on recommendations from the World Health Organization (WHO). Over the last decade, vaccine protection was regarded as sub-optimal in some years due to mismatches with the dominant circulating B lineage, or due to co-circulation of both B lineages in the same season [4]. In a response to this, quadrivalent influenza vaccines (QIVs) have been developed containing both B lineages (Victoria and Yamagata).

Previous cost-effectiveness analyses on influenza vaccination have had a focus on high-income countries with few economic studies of influenza vaccination in LMICs [3,5–7]. For instance, in a recent paper QIV was found to be cost-effective in the United States [8]. Some LMICs are now considering whether seasonal influenza vaccination should be introduced in their vaccination programs and whether this should involve TIVs or QIVs. Significantly, cost-effectiveness outcomes are not directly transferrable between countries, due to differences in circulating strains, demographics, climate, co-morbidities, health care infrastructure and budgets. For example, a study in South Africa, a country with considerable human immunodeficiency virus (HIV) prevalence, estimated that the incidence of influenza-associated severe lower respiratory tract infections was 4–8 times higher in HIV-infected individuals as compared with HIV-uninfected individuals [9].

In this study we analyzed the cost-effectiveness of influenza vaccination with TIV and QIV in three communities: Agincourt, a low-income rural community in South Africa; Thai Nguyen, a middle-income urban community in Vietnam; and Albany, a high-income urban/rural community in Australia. For this purpose, individual based simulation (IBS) models for each of the three communities were developed and interfaced with a health economic analysis model, capturing the specific demographics and health profiles of each community. As circulation of the different influenza B lineages and corresponding TIV vaccine matches are hard to predict, we studied the impact of TIV and QIV using retrospective data, over the period 2003–2013 (11 seasons).

2. Methods

2.1. Model overview

An overview of the analytic methodology used in this study is shown in Fig. 1; parenthesized numbers below refer to numbered items in the figure. Population and geographic data was used to build models for communities in South Africa, Vietnam and Australia (1). For each country, influenza strain circulation data was used to calibrate strain-specific influenza transmission parameters for the years 2003–2013 (2). For each of these combinations of communities and study years (39 in total), 3 different vaccination strategies were created: no vaccination, vaccination with TIV (using the actual influenza B strain present in the vaccine used in that country in that year), and vaccination with QIV (using both influenza B lineages) (3). For each combination of community, year and vaccination strategy (in total 117 scenarios) established individual based influenza spread simulation models (4) were used to assess the incidence of symptomatic influenza, stratified by age and HIV status (5). Influenza spread simulations also generated counts of work-days lost due to influenza (6).

These outputs, along with community, age, and HIV status-specific risk parameters (7) served as input to a health outcomes model (8), which generated numbers of clinical visits, hospitalizations and deaths due to influenza (9). Using cost and quality of life parameters (10), an economic analysis process (11) subsequently took the health outcomes counts, work-days lost and generated total costs and quality-adjusted life year (QALY) losses for each scenario. The differences between corresponding no-vaccination and vaccination scenarios served to calculate incremental cost-effectiveness ratios (ICERs) for the TIV and QIV vaccination strategies. Sensitivity analyses were performed to assess the robustness of results due to uncertainty in health outcome parameters, cost parameters and the stochastic nature of influenza spread.

2.2. Individual based simulation models

2.2.1. Community models

The main characteristics of each community are shown in Table 1. Agincourt represents a low-income rural area in northern South Africa, with HIV prevalence at ~16% in the adult population and a relatively low life-expectancy. The lower-middle income community of Thai Nguyen is located in north Vietnam near Hanoi and represents an urban setting and a relatively low HIV prevalence in adults (2.3%). Albany reflects a combined urban and rural community in Western Australia, representative of high-income countries with high life-expectancy and low HIV prevalence (0.2%). Current seasonal influenza vaccination coverage is moderate in Albany (20%), negligible in Agincourt (<2%) and absent in Thai Nguyen.

Each model was constructed using community-specific census and health data, and represents a community of individuals, each labelled with age (in bands 0–5, 6–12, 13–17, 18–24, 25–44, 45–64, 65+ years) and HIV status (see supplementary methods Table S1 for more details). Census and local government data was used to assign each individual to a number of contact groups (i.e. groups which the individual meets daily, including households, school classes, or groups of work colleagues). The size and overlapping memberships of contact groups is a key determinant of influenza spread, and these groups were constructed taking into account community-specific details including employment rate, workplace size, school attendance, number and size of schools, and household sizes. The IBS community models of Agincourt and Albany have been described in more detail previously [10,11]. The community model of Thai Nguyen in Vietnam was developed using the same methodology as the other models and is described in detail in the supplementary material.

2.2.2. Influenza transmission

As the simulation software runs, individuals come into daily contact with other individuals in their contact groups, where influenza transmission from infectious to susceptible individuals may occur: a stochastic choice determines if transmission fails, or results in symptomatic or asymptomatic infection. The model is able to capture the infection history of each individual regarding infection status, i.e. susceptible, infected, infectious or immune (due to infection or vaccination). Separate infectivity status was recorded of each of the four seasonal influenza strains A(H3N2), A(H1N1), B Yamagata, and B Victoria. The output of the IBS-model consisted of the number of symptomatic influenza cases and number of work days lost. A work-day lost was deemed to have occurred when an individual who would have otherwise attended a workplace withdrew to their household, either due to influenza infection themselves, or because one or more children in the household was ill with influenza. Main input parameters of the IBS-model are listed in the supplementary methods Table S2. The annual attack rate of influenza infection in each unvaccinated community was set at 21% and annual symptomatic attack rate (SAR) at 5% [12,13]. However, as the SAR of 5% has been determined in a setting where seasonal influenza vaccination