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Estimating the clinical impact of introducing paediatric influenza vaccination in England and Wales☆

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ABSTRACT

Influenza causes a significant burden of disease each year in England and Wales, with the young and the elderly suffering the greatest burden. Children are recognised as playing an important role in the dissemination of the influenza virus. This study examines the population impact of implementing a programme of paediatric vaccination.

A dynamic transmission model was used to simulate the impact of vaccination programmes with varying levels of coverage across pre-school and school age children. These analyses suggest that vaccinating as few as 50% of 2–18 year olds could result in a substantial reduction in the annual incidence of influenza related morbidity and mortality across the population. Herd immunity may extend this protection to the young and the elderly. It is assumed that such programmes would be implemented in concert with the current strategy of vaccinating the elderly and younger at risk groups with an inactivated vaccine.

In England and Wales, paediatric vaccination of two to eighteen year olds reduced the estimated number of general practice consultations, hospitalisations and deaths arising from influenza A and B infections by up to 95%. This translates into an annual average reduction of approximately 52,000, 1500 and 1200 events, respectively.

A policy of paediatric vaccination could significantly reduce the clinical burden of influenza in England and Wales, in all age groups, with the added value of herd immunity helping to protect the young and the elderly who are at highest risk of complications.

1. Introduction

Influenza is a highly infectious disease affecting 5–15% of the overall population worldwide [1] every year, predominantly in the autumn and winter season in temperate regions. Incidence rates are highest in children, especially in congregate settings with rates of up to 50% in children attending day care centres [2]. The burden of influenza in children is substantial, with frequent primary care (general practice) consultations in children under the age of 2 years [3] and in school age children [3,4], as well as a high hospitalisation rate in young children [3,5–7]. As children are thought to be the principal transmitters of influenza in the community [2,8,9], adequate childhood vaccination may efficiently disrupt the transmission and spread of influenza in the population, leading to the indirect protection (herd immunity) of close household contacts and of the wider community, including vulnerable risk groups with chronic underlying medical conditions and the frail elderly.

Individuals at risk of influenza related complications include those with chronic respiratory, heart, liver or kidney disease, and the immunosuppressed, as well as all individuals over the age of 64 years [10].

Although at risk individuals are currently targeted for seasonal vaccination in England and Wales and a number of other European countries, vaccination rates in most countries are suboptimal although coverage of the elderly is often better than that of clinical risk groups [11,12]. A recent survey has shown that vaccination rates in the elderly differ considerably across Europe [12], being highest in the UK (70.2%) and lowest in Eastern European countries such as Poland (13.9%). Furthermore, evidence is accumulating that vaccination of the elderly with an inactivated vaccine offers only partial protection. Reported estimates of vaccine effectiveness vary widely in the elderly, ranging from 20% to over 50% [13,14].

Vaccination rates in individuals with a chronic medical condition considered at a high risk of developing complications due to influenza are also low, ranging from 56% in the UK to 11% in Poland.

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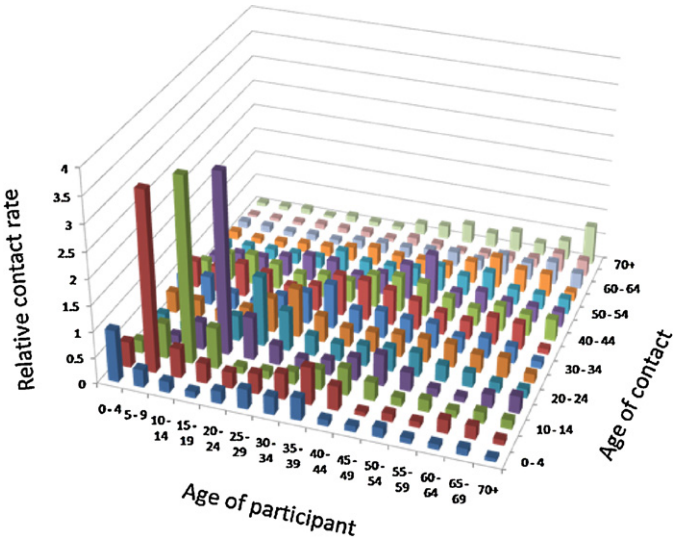

Fig. 1. Who Acquires Infection From Whom (WAIFW) matrix for Great Britain, as derived by the POLYMOD study [16] for both physical and non-physical contacts.

Vaccination rates have increased marginally over the last few years. Non-vaccinated individuals constitute a hard to reach group. In those EU member states where vaccination rates are low due to the absence of funding, childhood vaccination may be an attractive option. Provided adequate coverage is achieved, not only will children be protected but herd immunity could offer protection to at risk groups across the age ranges.

2. Aims and objectives

The aim of this paper is to estimate the potential clinical impact of paediatric influenza vaccination in England and Wales. Specific objectives were to develop a demographic model of England and Wales, to capture the population structure over time, and to create a dynamic transmission model simulating the transmission of influenza and the current influenza vaccination policy. A set of risk functions were developed to translate the incidence of infection into clinical outcomes. The resulting model was used to estimate the impact of vaccinating pre-school and school aged children with a live attenuated influenza vaccine. Clinical impact was quantified as the mean annual number of averted influenza infections and the related general practice consultations, hospitalisations and deaths, over a 15-year time horizon.

3. Methods

3.1. Demographics and age dependent mixing

The model adopts a realistic age structure (RAS), starting with population data for England and Wales in 1980, provided by the Office for National Statistics (ONS). These data are single year of age stratified population numbers [15]. Individuals within the model are aged on a monthly basis. Mortality from causes other than influenza starts from age 65 and thereafter is assumed to be a constant risk, corresponding to a mean life expectancy of 25 years for individuals aged 65 (Table 1).

Individuals in different age groups mix with one another as defined in a UK specific age stratified contact matrix developed by the POLYMOD study [16]. Such matrices are usually referred to as 'Who Acquires Infection from Whom' (WAIFW) contact matrices (Fig. 1) and provide a relative measure of the frequency of contact between individuals of different or similar ages.

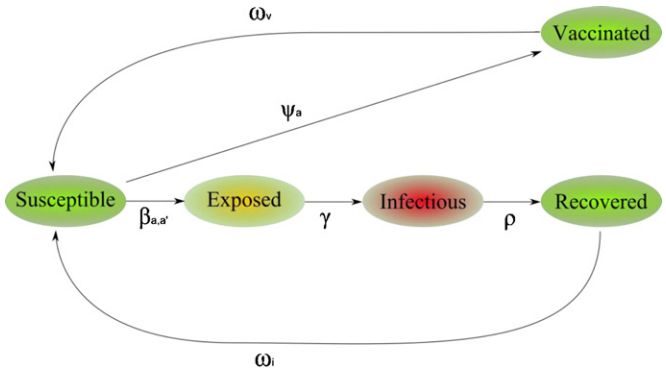

Fig. 2. The structure of the age stratified influenza SEIRS model. These compartments represent the infection status of the population and do not relate to clinical presentation. Infected individuals may or may not be symptomatic. ψ_a is the age dependent rate of vaccination. See Table 1 for a list of the remaining parameters.

3.2. Dynamic transmission model

An influenza transmission model was developed, building on an approach set out previously [17]. For the purposes of this model, influenza is assumed to occur as two sub-types of influenza A (e.g. H1N1 and H3N2) and as influenza B. All subtypes are assumed to be immunologically distinct and to occur every two years, with the A subtypes alternating to give an annual peak in incidence between week 40 and week 20 of the following year.

The dynamic transmission model subdivides the population into 5 subgroups, the Susceptible, Exposed, Infectious, Recovered and Vaccinated populations (Fig. 2). This stratification is based on the influenza virus infection status of members of the population and not on clinical presentation. A set of linked differential equations (see Appendix A) describes the flow of individuals between these subgroups and the system is solved numerically using a fourth order Runge–Kutta method with adaptive step control [18].

Exposed (latently infected) individuals are assumed to be infected for an average of 2 days before becoming infectious [19]. They remain infectious on average for a further 2 days [19], during which time the intensity and duration of viral shedding is assumed to be uniform across the age bands.

Once an individual has recovered from infection, they are assumed to be immune to reinfection with the same subtype. This immunity wanes over time as a result of the combined effects of a gradual decline in immunological memory and antigenic drift on the part of the virus. The resulting duration of protection was assumed to last for 6 and 12 years for influenza A and influenza B, respectively [17].

3.3. The basic reproductive rate

The basic reproductive rate (R_0) is defined as the number of secondary infections arising from one primary infection in a totally susceptible population [20,21]. Using data from past pandemics, R_0 for influenza has been estimated to range from 1.6 to 3.9 [22,23]. A value for the transmission coefficient was chosen, corresponding to a conservative R_0 of 1.8, calculated using the dominant eigenvalue of the next generation matrix [24,25].

3.4. Seasonality

The incidence of influenza follows a marked seasonal pattern. Peak incidence was assumed to occur on December 22 and to reach a minimum on June 23. The magnitude of the basic reproduction number at the peak of influenza incidence compared to baseline was set to 1.43 [17].