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Targeted vaccination in healthy school children – Can primary school vaccination alone control influenza?

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ABSTRACT

Background: The UK commenced an extension to the seasonal influenza vaccination policy in autumn 2014 that will eventually see all healthy children between the ages of 2–16 years offered annual influenza vaccination. Models suggest that the new policy will be both highly effective at reducing the burden of influenza as well as cost-effective. We explore whether targeting vaccination at either primary or secondary schools would be more effective and/or cost-effective than the current strategy.

Methods: An age-structured deterministic transmission dynamic SEIR-type mathematical model was used to simulate a national influenza outbreak in England. Costs including GP consultations, hospitalisations due to influenza and vaccinations were compared to potential gains in quality-adjusted life years achieved through vaccinating healthy children. Costs and benefits of the new JCVI vaccination policy were estimated over a single season, and compared to the hypothesised new policies of targeted and heterogeneous vaccination.

Findings and conclusion: All potential vaccination policies were highly cost-effective. Influenza transmission can be eliminated for a particular season by vaccinating both primary and secondary school children, but not by vaccinating only one group. The most cost-effective policy overall is heterogeneous vaccination coverage with 48% uptake in primary schools and 34% in secondary schools. The Joint Committee on Vaccination and Immunisation can consider a modification to their policy of offering seasonal influenza vaccinations to all healthy children of ages 2–16 years.

1. Introduction

Seasonal influenza can cause a significant health burden in the United Kingdom. It is estimated that approximately 10% of all respiratory admissions and deaths can be attributed to influenza. The highest admission rates for both influenza A and B strains are in children under five years of age and the highest influenza-attributed deaths rates occur in the group of elderly patients with co-morbidities [1].

The UK has had a long-standing influenza vaccination programme. Originally available to those in at-risk groups including those with underlying health conditions such as chronic heart disease, the programme was extended in 1998 to include people aged 75 years and over. Two years later it was extended again to include people aged 65 years and over. Pregnant women were included in 2010. Any proposed alterations to a national vaccination programme should be accompanied by a cost-effectiveness analysis using quality-adjusted life years (QALYs) as the measured benefit, according to guidelines written by both The National Institute for Health and Clinical Excellence (NICE) and the JCVI [2,3]. A cost-effective vaccination policy would have a cost per QALY ratio less than £20,000 per QALY, from the perspective of the healthcare provider [2]. In 2013 Baguelin et al. reported that it would be cost-effective to offer vaccination to children in addition to the other groups currently offered the vaccine [4].

Subsequently, the Joint Committee on Vaccination and Immunisation (JCVI) in 2012 recommended extending the influenza vaccination programme to all children between the ages of 2–16 years [5]. This extension would see a live-attenuated influenza vaccination (LAIV) offered to children each year with the majority of vaccines administered in school settings, and would become the largest vaccination programme in the UK measured in terms of number of doses administered. The LAIV is more effective than inactivated vaccines in children and adolescents and may also offer protection against drifted strains of influenza [6,7].

Children and adolescents attending schools play a large role in the spread of influenza in the community [8–10]. Transmission within schools is maintained because of the high number of close

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Table 1
Total population of England, clinically at-risk population and the number of seasonal influenza vaccinations administered to those clinically at-risk before new JCVI vaccination policy is implemented.

Age group	Total population [30]	At-risk population [21]	Vaccinated (baseline) [31]
0–3 years	2,680,335	138,573	71,504
4–10	4,221,738	218,264	112,624
11–16	3,771,682	194,996	100,618
17–64	33,703,747	1,742,484	899,122
65+	8,729,667	8,729,667	6,459,954

contacts between school children [11], as well as less acquired immunity in children [12] and a longer period of virus-shedding once infected [13,14]. Vaccinating children has the potential to reduce influenza episodes both in the vaccinated individuals, but also in individuals of all age groups who were not vaccinated, or who did not successfully seroconvert following vaccination. Several countries now offer annual influenza vaccination to healthy children as it has been repeatedly shown to be a cost-effective extension of existing national influenza vaccination programmes [15,16].

A pilot of the extended vaccination policy was implemented for the 2013–14 influenza season. Seven geographically discrete areas of England were chosen to offer vaccination against seasonal influenza (A/California/7/2009 (H1N1)pdm09-like strain, A/Victoria/361/2011 (H3N2)-like strain and B/Massachusetts/2/2012-like strain) to primary school age children between September 2013 and January 2014. Six of the seven geographical areas used a school-based vaccination programme for which the overall average coverage level was 56.27% (91,782/163,115) [17]. In addition, children aged 2–3 years were offered vaccination via primary care, with the intention to extend this to school-age children throughout England.

Previous modelling analyses demonstrating the cost-effectiveness of vaccinating healthy children have consistently assumed that children in both primary schools (aged 4–11 years) and secondary schools (11–16 years) would be simultaneously vaccinated [18,19]. For infectious diseases such as seasonal influenza, which has a low potential for transmission, it is possible to vaccinate a proportion of a population to eliminate the potential for sustained transmission (the threshold for "herd immunity" [20]). This threshold could be achieved with a successful vaccination policy implemented in only one of the two school groups. This study aims to establish whether a programme of targeted vaccination in either primary or secondary schools would be more cost-effective than a programme stretching across both school groups, and whether it will be able to eliminate influenza transmission for that season. Given that a range of coverage levels we also investigate how high coverage needs to be in order to maximise cost-effectiveness. For comparability, we have used epidemiological and economic parameters from previous influenza vaccination analyses to inform national immunisation [4,21], but adopted a simpler model to highlight key results related to optimally targeting age groups for paediatric vaccination.

2. Methods

This study uses a discrete time age-structured deterministic model with SEIR structure written in R version 3.0.2 using the tcltk2, mc2d, mgcv, MASS and lattice packages [22–27] to estimate the burden of disease. The model has age-structured compartments representing individuals susceptible to influenza infection (S), latently infected (E), infectious (I) and recovered (R). The model is linked to a decision tree model also written in R to determine the cost-effectiveness of each proposed vaccination policy in comparison to the old UK policy.

The SEIR framework has been modified to include classes of those vaccinated (V) as well as individuals assumed to have immunity from influenza due to exposure in previous seasons and therefore have associated antibodies in their immune systems (A). An individual in the model who has recovered from infection is assumed to have immunity from influenza for the remainder of the simulation (i.e. one influenza season). Persons successfully immunised also acquire immunity for the duration of the simulation but a fraction of those vaccinated were non-responders and remain susceptible [28]. All vaccination is assumed to take place at random within the targeted age groups before the annual influenza season commences when the first infection occurs.

Contact rates between age groups in the population can be critical for determining model outcomes [29]. In our model the population of England is divided into 5 age groups (0–3, 4–10, 11–16, 17–64 and 65+ years old) using 2011 mid-year estimates [30] (Table 1). Individuals have close contacts with others in the model according to the POLYMOD survey of contact frequency in Europe [11]. The mathematical model was informed with the age-dependent mixing patterns measured from the Great Britain arm of this eight-country survey in the form of a matrix of close contacts, $\beta_{i,j}$.

A significant proportion of influenza infections are subclinical. The definition of clinical influenza is fever with one other influenza-related symptom [32]. Clinical influenza incidence was estimated as a proportion of total infections generated by the model, derived from a review of volunteer challenge studies that found that 35% of individuals with influenza had fever, thereby providing an estimate of clinical influenza cases from suspected influenza infections [33].

2.1. Model calibration

The model was calibrated by fitting the incidence of clinical influenza to final size data of the 2006–07 influenza season in England to ensure our model produced results comparable to the model of Baguelin et al. used to inform England's original decision to vaccinate children [18]. Parameters for the proportion of each age group with prior immunity to influenza were estimated using Latin Hypercube sampling and binomial maximum likelihood estimation (Table 2). We drew 25,000 Latin Hypercube samples from uniform distributions over [0,1] for each of these parameters, and then selected those which minimised the binomial log-likelihood using the observed final size and the simulated final size for each age group (see Appendix for further details about the model and its calibration).

2.2. Modelling vaccination

We assumed that vaccination administered using LAIV requires one dose per individual. The baseline for all modelling scenarios was a continuation of the influenza vaccination policy in the UK prior to the introduction of paediatric vaccination (i.e. at-risk groups and adults over 65 years only). The outputs from this