Respiratory syncytial virus vaccination

I. Introduction

Respiratory syncytial virus (RSV) is the main cause of acute lower respiratory infections in infants and young children [22], with almost all children having been infected by two years of age [10, 25] and an estimated 0.5–2% of infants requiring hospitalisation due to infection [18]. One recent study estimated in that in 2005, 33.8 million new episodes of RSV occurred worldwide in children younger than five years of age [22]. Symptoms of RSV range from those of a cold, more severe afflictions such as bronchiolitis and pneumonia [10]. While mortality due to RSV infection in developed countries is low, occurring in less than 0.1% of cases [32], little data is published about RSV morbidity and mortality in developing countries [34]. However, estimates of the hospitalisation costs are substantial [14, 30, 36], making RSV a significant economic and health care system burden.

Newborn infants are typically protected from RSV infection by maternal antibodies until about six weeks of age [8], and the highest number of observed RSV cases occur in children aged six weeks to six months [5, 27]. Immunity to RSV following an infection is short-lasting and reinfection in childhood is common [19]. Few studies have been undertaken to investigate transmission of RSV among adults, but it is thought that infection can occur throughout life [6, 15] and that in older children and adults, RSV manifests as a mild cold [10, 16]. RSV has been identified as a cause of mortality in the elderly with documented outbreaks in aged care settings [13, 31]; one such study found that up to 18% of pneumonia hospitalisation in adults aged above 65 years may be due to RSV infection [12].

In temperate climates RSV epidemics exhibit distinct and consistent seasonal patterns. Most RSV infections occur during the cooler winter months, whether wet or dry [34], and outbreaks typically last between two and five months [11, 23]. In a number of temperate regions a biennial pattern for RSV cases has been identified; see, for example, [4, 20, 28]. In tropical climates RSV is detected throughout the year with less pronounced seasonal peaks, and the onset of RSV is typically associated with the wet season [26, 34].

Immunoprophylaxis with the monoclonal antibody Palivizumab, while not preventing the onset of infection, has proven effective in reducing the severity of RSV-related symptoms [29]. However, prophylaxis is expensive and generally only administered to high-risk children, with recommendations varying across jurisdictions. There is currently no licensed vaccine to prevent RSV infection, despite about 50 years of vaccine research. Recent research has focused on the developed of live attenuated vaccines; several such vaccines are being evaluated in clinical trials, with other vaccines in preclinical development [9, 14]. With the possibility of a RSV vaccine becoming available, mathematical models can be powerful tools for planning vaccination roll-out strategies.

Several ordinary differential equation Susceptible-Exposed-Infectious-Recovered (SEIR) type mathematical models for RSV transmission have been published to date, such as those presented in [3, 7, 17, 21, 24, 33, 35] with a sine or cosine forcing term to account for seasonal variation in transmission. Weber *et al.* [33] present a SEIRS model which incorporates a gradual reduction in susceptibility to reinfection and maternally derived immunity, and fit the model to several data sets. Leecaster *et al.* [17] present a SEIDR model with both child and adult classes for the S, E and I compartments, and where the D class represents children in which infection was detected. The model is fit to seven years of data from Salt Lake City, USA.

Moore *et al*. [21] present an age-structured SEIRS model for children under two years of age and the remaining population. The model is fit to data from Perth, Western Australia. Capistran *et al*. [7] outline a SIRS model with seasonal forcing and propose a method to estimate the model parameters, demonstrated by fitting models to data from The Gambia and Finland. Paynter *et al*. [24] investigate the ecological drivers of RSV seasonality in the Philippines, where the model includes a second partially susceptible class, and second classes for latent and infectious individuals with a subsequent RSV infection. This work also applies a square wave transmission term that accounts decreased transmissability over the summer holidays, as well as a seasonally driven birth rate.

White *et al*. [35] describe nested differential equation models for RSV transmission and fit these to RSV case data for eight different regions. In the work of Arenas *et al*. [3], randomness is introduced into the differential equation model and the model fit to RSV hospitalisation data for Valencia, Spain.

Few papers have so far explored vaccination strategies for RSV. A newborn vaccination strategy is outlined in [1] for the Spanish region of Valencia, in order to estimate the cost-effectiveness of potential RSV vaccination strategies. The modelling approach removes a fraction of susceptible newborns into a vaccinated class, where they remained until they reached the next age group, at which point they move to the second susceptible class. This strategy assumes booster doses of the vaccine in the first year of life, such that the immunisation period would be at least equal to the immunity of those who have recovered from RSV infection. In subsequent work, an RSV vaccine cost analysis is conducted based on a stochastic network model, with children vaccinated at two months, four months and one year of age [2].

Details of what we plan to do...

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