Burden of paediatric respiratory syncytial virus disease and potential effect of different immunisation strategies: a modelling and cost-effectiveness analysis for England

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Summary

Background Vaccines and prophylactic antibodies against respiratory syncytial virus (RSV) are in development and likely to be available in the next 5–10 years. The most efficient way to use these products when they become available is an important consideration for public health decision makers.

Methods We performed a multivariate regression analysis to estimate the burden of RSV in children younger than 5 years in England (UK), a representative high-income temperate country, and used these results to assess the potential effect of different RSV immunisation strategies (targeting vaccination for infants, or pregnant women, or prophylactic antibodies for neonates). We did a cost-effectiveness analysis for these strategies, implemented either separately or concurrently, and assessed the effect of restricting vaccination to certain months of the year.

Findings We estimated that RSV is responsible for 12 primary care consultations (95% CI 11·9–12·1) and 0·9 admissions to hospital annually per 100 children younger than 5 years (95% CI 0·89–0·90), with the major burden occurring in infants younger than 6 months. The most cost-effective strategy was to selectively immunise all children born before the start of the RSV season (maximum price of £220 [95% uncertainty interval (UI) 208–232] per vaccine, for an incremental cost-effectiveness ratio of £20 000 per quality-adjusted life-year). The maximum price per fully protected person that should be paid for the infant, newborn, and maternal strategies without seasonal restrictions was £192 (95% UI 168–219), £81 (76–86), and £54 (51–57), respectively.

Interpretation Nearly double the number of primary care consultations, and nearly five times the number of admissions to hospital occurred with RSV compared with influenza. RSV vaccine and antibody strategies are likely to be cost-effective if they can be priced below around £200 per fully protected person. A seasonal vaccination strategy is likely to provide the most direct benefits. Herd effects might render a year-round infant vaccination strategy more appealing, although it is currently unclear whether such a programme would induce herd effects.

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Introduction

Respiratory syncytial virus (RSV) is a highly seasonal respiratory virus (the season runs from from late autumn to early spring).[1] Exposure to RSV does not lead to long-lasting protection and hence people can have many infections over their lifetime.[2] Infection mainly leads to mild disease, but in very young children (aged <6 months), elderly people, and immunocompromised patients it can result in serious disease or death.[3]

Currently, the only effective preventive strategy against RSV is passive immunisation with palivizumab, a humanised monoclonal RSV-specific antibody. Because of its high price, this antibody is only used in the highest-risk groups of individuals during the RSV season (November to February)—usually young children who are born prematurely and have other respiratory or cardiac conditions.[4,5] However, around 60 RSV vaccine and monoclonal antibody candidates are in development, 16 of which are in clinical trials,[6,7] although trial results in adults aged 60 years and older for the most advanced vaccine candidate (Resolve RSV-F vaccine) have not shown efficacy.[8] Besides older adults, other potential candidates are pregnant women (to protect newborn babies through passive immunity), newborn babies (through passive immunisation with antibodies), and infants. An RSV vaccine could possibly be licensed in the next 5–10 years.[9] Additionally, at least one extended, half-life monoclonal antibody designed to protect infants from birth, along with at least three maternal vaccines, are in clinical trials.[6]

Decision makers will need to understand the potential health and economic effects of the different vaccine and antibody options to select strategies that maximise the effect of health-care resources. Although the exact characteristics of future maternal or infant vaccines or prophylactic antibodies for newborn babies are unknown, understanding the burden of RSV disease and the drivers of vaccine effects and value can help to inform decisions about prioritisation of vaccination or antibody strategies, and protocols for clinical trials.[7] Such analyses can also

Research in context

Evidence before this study

Respiratory syncytial virus (RSV) disease is the primary contributor to childhood lower respiratory tract infections. More than 60 biological candidates for RSV prophylaxis (vaccines and prophylactic monoclonal and polyclonal antibodies) are undergoing development, of which more than 25% have progressed to human trials, and one or more is likely to be licenced in the next 5–10 years. The candidates target different patient populations, and the optimum prophylactic strategy is yet to be determined. We did a search of the scientific literature, based on expert opinions. Despite some previous studies separately assessing the incidence of RSV-attributable clinical disease, and the economic impact of vaccination, as yet there have been no studies that combine this information, and few published studies can be used by decision-making bodies to assess the cost-effectiveness of different RSV vaccination strategies.

Added value of this study

We used data from laboratory reports and on health-care attendances for acute respiratory illness to estimate disease burden and health-care costs associated with RSV in England (UK). The estimates agreed with those from previous studies, while providing greater insight into the timing of outbreaks and ages most affected. We present the first quantitative analysis to highlight how the month of birth affects RSV-attributable health-care outcomes in a temperate climate. We then assessed the effect and cost-effectiveness of various vaccine and antibody strategies in pregnant women and young children. We showed that children born immediately before the RSV season, which runs from late autumn to early spring, have a two-fold higher risk of primary-care attendance and a four-fold higher risk of being admitted to hospital than children born after the season.

Implications of all the available evidence

Given the difference in these risks between children born before and after RSV season, the most cost-effective strategies, and ones that have the potential to avert the most severe disease and deaths, are those that protect children born just before the RSV season, such as maternal vaccination or long-lasting prophylactic monoclonal antibodies.

identify and help to ensure that data are obtained in advance about the key drivers of cost-effectiveness.

So far, few studies are available to inform about the potential cost-effectiveness of different RSV vaccination strategies[10] and the need for further cost-effectiveness information has been identified as a priority by WHO's Strategic Advisory Group of Experts on Immunisation.[11] To help to address this need, we present a detailed analysis of the disease burden of RSV and the associated health-care costs in England (UK). We then used England as an example of a high-income country in the temperate zone that is considering RSV vaccination in the future. This allowed us to illustrate general principles and to explore the potential effect and cost-effectiveness of different vaccine and antibody strategies to protect young children in high income, temperate climates with a similar epidemiology to England.

See Online for appendix

Methods

Disease burden estimation

Most people who present to health-care services with respiratory symptoms are not routinely tested for RSV, so the incidence of primary care attendances and hospital admissions for RSV has to be inferred. We used a statistical regression model[12] to ecologically link clinical attendances for acute respiratory infection to organisms detected in routine clinical microbiological testing, based on temporal trends in both datasets, similar to our work estimating the burden of seasonal influenza.[12] Similar methods have been previously used to explore the burden of seasonal organisms, including RSV, influenza virus, and rotavirus.[13,14] We synthesised information from general practice attendances and hospital admissions for acute respiratory symptoms and positive laboratory reports for respiratory pathogens with data from the scientific literature[15] to explore the detailed age distribution of these clinical attendances in children younger than 5 years. Full details of our methods are in the appendix (p 1).

Economic model

We used a static cohort model (ie, a model that does not account for the indirect or herd effects of vaccination) to explore the potential direct effect of paediatric vaccination or long-lasting monoclonal antibody use on its recipient (appendix p 5). We used the results of the model to estimate the net cost and cost-effectiveness of the interventions. We estimated the maximum cost-effective price (MCEP) per fully protected individual that could be paid for both the purchase and the administration costs of a course of vaccines or prophylactic antibodies (including any required booster doses), so as not to exceed the threshold of £20 000 per quality-adjusted life-year (QALY) gained, which is commonly used as a measure of cost-effectiveness in England.[16] This value is close to the UK's gross domestic product per capita, which has been suggested[17] as a possible threshold to use for an intervention to be deemed very cost-effective. The maximum price payable for each fully vaccinated individual for a range of assumptions on vaccine efficacy is in the appendix (p 10). Further details including cost-related and health-related quality-of-life parameters are in table 1, and the appendix (p 9).