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Introducing vaccination against serogroup B meningococcal disease: An economic and mathematical modelling study of potential impact

Hannah Christensen[a,*], Matthew Hickman[a], W. John Edmunds[b], Caroline L. Trotter[a,1]

[a] School of Social and Community Medicine, University of Bristol, Bristol, UK
[b] London School of Hygiene and Tropical Medicine, London, UK

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ABSTRACT

Background: Meningococcal disease remains an important cause of morbidity and mortality worldwide. The first broadly effective vaccine against group B disease (which causes considerable meningococcal disease in Europe, the Americas and Australasia) was licensed in the EU in January 2013; our objective was to estimate the potential impact of introducing such a vaccine in England.
Methods: We developed two models to estimate the impact of introducing a new 'MenB' vaccine. The cohort model assumes the vaccine protects against disease only; the transmission dynamic model also allows the vaccine to protect against carriage (accounting for herd effects). We used these, and economic models, to estimate the case reduction and cost-effectiveness of a number of different vaccine strategies.
Results: We estimate 27% of meningococcal disease cases could be prevented over the lifetime of an English birth cohort by vaccinating infants at 2,3,4 and 12 months of age with a vaccine that prevents disease only; this strategy could be cost-effective at £9 per vaccine dose. Substantial reductions in disease (71%) can be produced after 10 years by routinely vaccinating infants in combination with a large-scale catch-up campaign, using a vaccine which protects against carriage as well as disease; this could be cost-effective at £17 per vaccine dose.
Conclusions: New 'MenB' vaccines could substantially reduce disease in England and be cost-effective if competitively priced, particularly if the vaccines can prevent carriage as well as disease. These results are relevant to other countries, with a similar epidemiology to England, considering the introduction of a new 'MenB' vaccine.

1. Introduction

Meningococcal disease is a leading infectious cause of death in young children in the UK [1] and remains an important cause of morbidity and mortality worldwide, despite improvements in critical care and the availability of vaccines against some capsular groups. Globally five capsular groups cause most disease (A, B, C, W, Y though X is increasing) and B and C are dominant outside Africa and Asia [2]. The key to reducing incidence is prevention through vaccination, because early signs of the disease can be non-distinct, the infection can progress rapidly, and can be fatal in 5–10% of cases even if treatment is initiated early [3].

Effective vaccines are available against capsular groups A, C, W and Y. The meningococcal serogroup C conjugate (MCC) vaccine was first introduced in the UK in 1999 [4] and subsequently by several other European countries, Australia and Canada [2]. MCC vaccination achieved high uptake rates, and has led to a considerable reduction in group C disease [5] due both to high vaccine effectiveness and protection against carriage, interrupting transmission and generating herd immunity [6]. Until recently there was no broadly effective vaccine against capsular group B (MenB) the most common cause of meningococcal disease in the UK and Europe [7] (MenB disease accounted for 89% of cases in England and Wales in 2009/10 [8]). Progress towards a MenB vaccine has been hindered because the serogroup B capsule shares homologous structures with human neural tissue, resulting in the polysaccharide being poorly immunogenic in people and concerns about a MenB capsular-based vaccine inducing auto-immunity [9]. New vaccines with the capacity to protect against MenB, based on protein antigens, are in advanced stages of development [10,11] and one, Bexsero, was granted an EU license in January 2013. Policy

Abbreviations: MCC, meningococcal serogroup C conjugate; MenB, capsular group B meningococci; QALYs, quality adjusted life years.

* Corresponding author at: School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, UK.
Tel.: +44 0117 92 87260.
E-mail addresses: hannah.christensen@bristol.ac.uk (H. Christensen), matthew.hickman@bristol.ac.uk (M. Hickman), John.Edmunds@lshtm.ac.uk (W.J. Edmunds), caroline.trotter@bristol.ac.uk, clt56@cam.ac.uk (C.L. Trotter).
[1] Present address: Department of Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge, CB3 0ES, UK.

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makers are now faced with decisions about if, and how, to introduce the vaccine.

To help inform policy decisions we developed mathematical and economic models to predict the potential impact of introducing a new vaccine in England, with the capacity to protect against MenB disease (henceforth referred to as a 'MenB' vaccine).

2. Methods

2.1. Model structures

It is unknown whether the new meningococcal vaccines will reduce carriage. Consequently, we developed two models (using Berkley Madonna software [12]) to assess the potential impact of these vaccines: a cohort model that assumes the vaccine prevents disease only, and a transmission dynamic model that also allows the vaccine to prevent carriage [13,14].

2.1.1. Details common to both models

The model populations are stratified into 100 single year of age classes. Incidence rates include all capsular groups of meningococcal disease because the new vaccines are not group specific. Following disease, individuals may survive with or without sequelae, or die. Survivors with sequelae are assumed to have a reduced quality of life and fatal cases lose the average life expectancy for the age at which they die. Individuals may die due to causes other than meningococcal disease; published mortality rates were adjusted to remove deaths due to meningococcal disease as these are explicitly modelled. Vaccinated individuals have a reduced risk of disease. Immunity from vaccination wanes over time, and individuals then have the same risks of infection as unvaccinated individuals. For each vaccination scenario the model results were compared to the situation without vaccination. Models were run for 100 years (time horizon) to capture the full benefits of vaccination and effects of invasive disease over the lifetimes of individuals.

2.1.2. Cohort model specific details

The cohort model was constructed using a Markov model, with monthly time steps. Individuals are born into a susceptible non-vaccinated state (Fig. 1). Meningococcal disease cases arise by multiplying the age-specific probability of disease (in a given interval) by the population. We assumed individuals only have disease once and are removed from the susceptible pool (instances of repeat invasive disease are rare and are associated with individuals with immune deficiencies and anatomical defects [15]). Years of life are weighted by the age-specific quality of life. The cohort sizes were based upon population figures for 2008.

2.1.3. Transmission dynamic model specific details

Individuals can have multiple episodes of asymptomatic carriage of meningococci in their lifetimes [16,17], therefore we used a Susceptible-Infected-Susceptible (SIS) model, with a daily time step, to represent the transmission dynamics of carriage in the population (Fig. 1). Individuals are born susceptible. They may then become carriers of a meningococcal strain (vaccine preventable or non-vaccine preventable), from which they recover and return to the susceptible state. We did not consider co-infection in the model because current evidence suggest carriage of multiple meningococcal strains is rare [18,19]. Cases of invasive disease are not explicitly included, but are generated from the number of new carriers arising over time (see Supplementary Material) using an age-specific case: carrier ratio. This ratio captures changes in disease risk given carriage acquisition across ages, which could be due to a number of factors including maturation of the immune system, physical changes in the pharynx, exposure to other pathogens and immunity following meningococcal carriage. Vaccinated individuals with vaccine induced immunity can have a reduced risk of becoming a carrier in addition to a reduced risk of disease.

2.2. Model parameters

Data sources used to estimate the parameters in the models, are summarised below and in Table 1 with further details provided in the Supplementary Material.

We used carriage prevalence estimates from a recent systematic review [20], with contact patterns estimated using a simple preferential mixing structure and recently published survey data on self-reported contacts [21]. Disease incidence naturally fluctuates over time; incidence peaked in the late 1990s and has declined since then. We therefore based disease incidence and case fatality upon hospital admissions from 2004/05–2005/06 to represent current low incidence. Data from 1997/98–2005/06 (adjusting for the decline in incidence due to MCC), which includes peak incidence years, were used to generate a 'higher' incidence comparator. We assumed all meningococcal disease cases were hospitalised and estimated those requiring augmented care from hospital admissions (1998/99–2005/06). We included published costs for time in hospital including augmented care [22], and all survivors of disease were assumed to have a hearing test and a follow-up review in line with recent NICE guidelines [23]. The proportion of survivors with minor and major sequelae following disease was estimated from a recent systematic review of sequelae following bacterial meningitis [24]. Those with sequelae were assumed to have a reduced quality of life (0.2 utility reduction [25–27]) compared to susceptible individuals, and survivors of disease without sequelae [28]. Long term costs of supporting those with mild and severe sequelae were estimated at £500 and £10,000 per year per individual respectively. For public health management we included costs of chemoprophylaxis (rifampicin for 3 adults and 2 children [29]) and staff time associated with contact tracing. Costs of outbreak control were not included.

Several vaccination strategies were considered (Table 2). Vaccination uptake for routine vaccination was assumed to equate to MCC in infants, and for catch-up cohorts, match the MCC catch-up programme [30]. Vaccine administration costs [31–34] were included separately from the cost of the vaccine itself, and were greater if given outside of current schedules. The full characteristics of the new meningococcal protein vaccines are not yet known; assumptions regarding vaccine effectiveness and duration of protection were based on data from trials, other meningococcal vaccines, such as the MCC or Outer Membrane Vesicle vaccines, and expert opinion. Data from trials of Bexsero have indicated, however, that the vaccine is immunogenic in infants [35], and adolescents [36], that responses are evident after two doses of the vaccine in infancy [37] and that it is possible to boost an individual's response [35]. Early genotypic estimates of strain coverage suggested 100% strain coverage was possible [38] however recent phenotypic approaches suggest strain coverage in England may be 73% (95% CI 57–87%), though these results are based on a method which may underestimate coverage [39]. In the base case model the vaccine was assumed to protect against all meningococcal strains. We included costs, but not quality of life losses, for adverse vaccine events. We assumed the vaccine cost £40 per vaccine dose in the base case, but varied this widely in the sensitivity analysis.

2.3. Scenario and sensitivity analysis

The cohort model was probabilistic, with distributions around the parameters reflecting uncertainty (Table 1). Where probabilistic analysis was not possible or appropriate (e.g. vaccine price will be fixed, but at a level currently unknown) we ran scenario analyses. Cost-effectiveness ratios from probabilistic results were calculated

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