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MODELLING THE EFFECT OF VACCINATION ON THE MENINGOCOCCAL B EPIDEMIC IN NEW ZEALAND

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Abstract

A nation-wide vaccination campaign began in New Zealand in 2004 with the aim of stopping the epidemic of meningococcal B disease. Approximately 80% of those under 20 years of age when the campaign was launched were vaccinated with three doses of a tailor-made vaccine. We propose a framework for a mathematical model based on the susceptible–carrier–infectious–removed (SCIR) structure. We show how the model could be used to calculate the predicted yearly incidence of infection in the absence of vaccination, and compare this to the effect that vaccination had on the course of the epidemic. Our model shows that vaccination led to a considerable decrease in the incidence of infection compared to what would have been seen otherwise. We then use our model to explore the potential effect of alternative vaccination schemes, and show that the one that was implemented was the best of all the possibilities we consider.

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1. Introduction

Infection with meningococci can cause a variety of diseases, but the most common are meningitis (the swelling of the membranes and fluid that cover the brain and spinal cord) and/or septicaemia (blood poisoning) [13]. Meningococcal disease is caused by a bacterium, *Neisseria meningitidis*, which colonizes the upper respiratory tract. The infection is transmitted by either aerosolized droplets of respiratory secretions, or by contact with these secretions (for example, sharing a glass or kissing [3, 13]). Once the bacteria have been acquired, they bond to the cells at the back of the throat and nasal passage. The bacteria can then manoeuvre their way into the bloodstream where they may invade and multiply in the cerebrospinal fluid. The colonization of the nasopharynx can continue for months, causing a persistent source of infection

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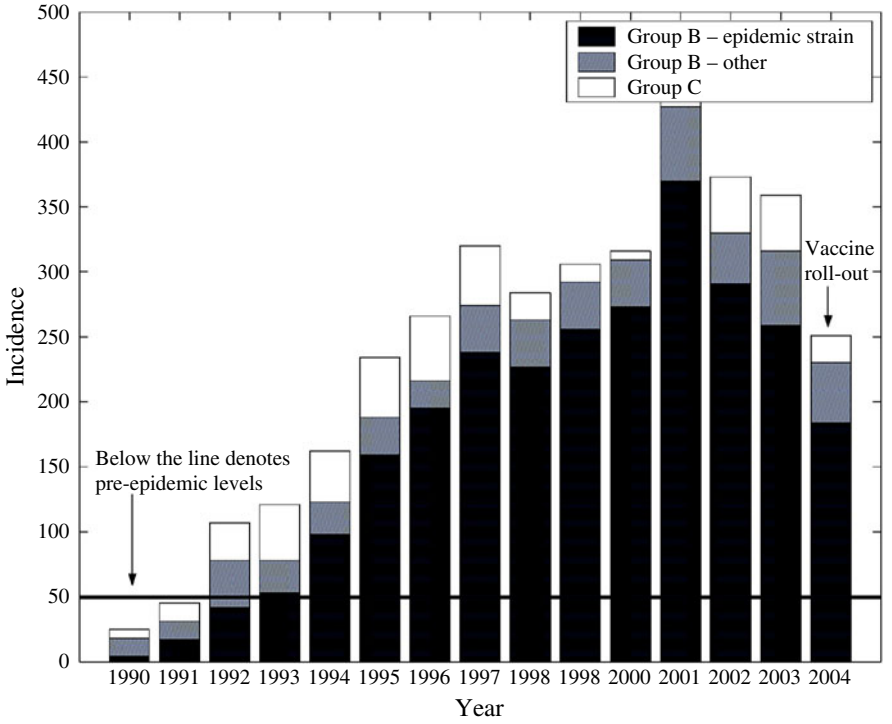

FIGURE 1. The recorded number of meningococcal cases of infection (data sourced from CBG Health Research Limited [5]). The group B epidemic strain was responsible for the majority of meningococcal disease cases.

to others. In most people, antibodies kill the bacteria before they can cause the disease [19]. However, it is possible to carry the meningococci and be infectious while not showing any symptoms of infection. Infection with the invasive form of meningococcal disease leads to a quick onset of symptoms including headache, nausea and vomiting, with approximately two thirds of cases presenting a rash. Acute infection can lead to death within 24 hours.

There are numerous serogroups of the bacterium, with serogroup B being the causative strain (defined as B4:P1.7b,4 subtype) of the New Zealand epidemic: this was a novel strain of the disease and a tailor-made vaccine was required. New Zealand's epidemic of meningococcal B disease began in mid-1991, and in 2004 an immunization programme was introduced in the hope of ending the epidemic. The annual number of cases of meningococcal disease in New Zealand can be seen in Figure 1, noting that the epidemic strain is responsible for the majority of these cases. Approximately 80% of cases of meningococcal disease occur in people aged 0–19 years, and within this age group the majority are seen in under-five-year-olds [14].

There are a number of mathematical models of meningococcal disease, with many of them investigating the bacterial level of the infection process and a smaller portion modelling the spread and control of the infection. To date, we are unaware of any published mathematical modelling papers looking specifically at the New Zealand meningitis epidemic, as the majority of published models take their data from epidemics and vaccination campaigns in Europe and the United States. We present a framework for a mathematical model, incorporating the known infection mechanism and process, and apply this framework to the New Zealand epidemic data. We then illustrate how our framework could be utilized to investigate the potential outcomes of alternative vaccination strategies.

1.1. Infection dynamics The carriage state of the infection, where a person is infected and infectious but shows no signs of the illness, makes meningococcal disease hard to monitor in the population, and yet these people play a large part in the spread of infection. Thus we have included an explicit carrier state in our model as well as an invasively infected state.

Tuckewell et al. [23] did not include a carriage state in their model, but assumed that the infection was at steady state with carriers and noncarriers in equilibrium. Ancel et al. [1] did not explicitly include a carrying population, but they had two strains of infection: one more likely to cause the invasive form of the infection and one likely to stay benign. Trotter et al. [21] only considered the population to be in two states: those carrying the infection and those not. However, these authors were mainly concerned with the sensitivity of techniques used to identify whether the infection is present in carriers and the infection and recovery rates, rather than with the actual spread of the infection in the population.

As a large number of cases are seen in the under-20-year-old age bracket, sectioning the population into age classes would be beneficial when creating a model, as has been shown in a number of papers [6, 9, 12, 20, 21, 23]. Tuckwell et al. [23] state that the most effective vaccination campaign over a 10-year period is to immunize all of the population aged between 2 and 20 years. Trotter et al. [20, 22] showed that the most effective campaign targeted teenagers, thus maximizing herd immunity and reducing the prevalence of carriage to an extent that it took years to recover.

Stollenwerk and co-workers have published a number of papers on the modelling of invasive meningococcal disease [9, 16–18]. They implemented an $SIRYX$ model, in which the I class are those infected with a benign strain of meningococcal (note that this is different than the I used in the model presented here, where I are those invasively infected with the disease: Stollenwerk's I is analogous to the C in the present model), the Y class are those infected with a mutant strain of the infection that can cause acute infection, and class X are the severely affected hosts. Those in the acutely infected class cannot infect others, but can return to the susceptible class. Carriers, I class, can develop the mutant strain of infection and become Y class, but the chance of this is extremely small. From the I and Y classes, individuals become removed, but the removed class then feeds back into the susceptible class. There was no age structure

in the models, which were implemented stochastically using a Markov process. A constant population size was imposed, with 25% of the population being in the benign carriage class, I, at any time. The average duration of both carriage and immunity was 10 months. By letting there be seasonal changes in transmission, the model produced seasonal changes in carriage rates which led to variations in the incidence of disease. Yet the seasonality in transmission did not yield any variation in the yearly incidence rate unless both the benign and the mutant strain were present. It is this diversity in the strains that the authors concluded are crucial for epidemics of meningococcal disease to occur.

Trotter and co-workers published a number of papers on modelling meningococcal disease in England and Wales, and looked at the impact of the vaccine against the epidemic strain [20–22]. They split the population into nine compartments and 75 one-year age cohorts, and let the prevalence of carriage be dependent on age with low prevalence in young children, peaking in teenagers, and implemented their model using differential equations. They did not explicitly model the invasive meningococcal disease, but calculated the incidence based on carriers. They assumed that co-infection with more than one strain is not possible, and that the duration of carriage is only 3 months (this is decreased to better fit the model to the known data). Their model produced a good fit to the England and Wales epidemic data, with an estimated basic reproduction number of 1.36. They concluded that the most effective use of vaccination is to target teenagers to generate herd immunity in the population [22].

A difference equation model with discrete time and monthly age groups for the effects of vaccination on a nonspecific disease was presented by Tuckwell et al. [23] and then applied to meningococcal disease. The population was compartmentalized according to their immune status, and immunity followed from nonfatal infection or from successful vaccination. Carriers of the infection were not specifically included in the model, carriers and noncarriers were assumed to be in equilibrium, and the per capita rates of fatal and nonfatal cases were fixed, which implies that these rates are small relative to the overall birth and death rates, so the carriage rates do not change significantly. This lack of change in carriage rates has been noted in most of the models, with the assumption that a certain percentage of the population is always in a carrier state. The authors modelled various vaccination schedules using parameter estimates from an epidemic of meningococcal C disease in France. The best vaccination schedule, in regard to the number of deaths and cases of infection avoided, was to vaccinate the entire population—which would be impossible—but it was shown that comparable results were achieved by vaccinating everyone in the population between 2 and 20 years of age. However, the scheme in which only one-year-olds are vaccinated also performed as well in terms of cases avoided, but not deaths avoided per dose of vaccine.

Ancel Meyers et al. [2] and Coen et al. [6] both modelled two strains of infection. Ancel Meyers et al. [2] used two different strains of meningococcal: a fast phase shifting strain that causes the invasive diseases and a wild strain that does not cause invasive infection but where the host becomes a carrier (thus able to infect others),

where phase shifting is the mutational mechanism causing the bacterial genes to switch on and off to evade the immune defences of the host. They presented two models, one where the population is split into two groups with respect to the strains, and another where secondary infection is allowed with a different strain. This study was mostly concerned with within-host infection dynamics, and the necessity of the two strains to cause an epidemic (limiting the model to one strain did not cause epidemics in the population), and did not compare results to data. Coen et al. [6] investigated meningococcal disease and carriage, as well as carriage of *N. lactamica*, which is an organism related to *N. meningitidis*. They presented three models for the incidence of carriage and disease, and used an estimated duration of carriage of 13.3 months, based on data from Belgian school children. The model that best fitted their data was one where acquisition of meningococcal carriage was inhibited by carriage of *N. lactamica* and carriage rates depended on age, with infants having the greatest pre-carriage rates of illness.

An age structured partial differential equation model was presented by Martcheva et al. [12], assuming an age distributed rate of carriage, which peaks at 45% in teenagers and young adults. There was no immunity in the model (apart from at birth), either from infection or from carriage, and no mortality rate due to infection. The authors investigated the stability of the disease-free state, the existence and stability of the endemic equilibrium, and the persistence of the disease, comparing these to known data.

All of the studies mentioned here are based on epidemic data from outside New Zealand, not the B strain of the disease. To create a model specifically for New Zealand, we utilize some of the ideas and assumptions made in other papers, then include the vaccination campaign that was initiated and the long time span of the epidemic.

2. Model framework

2.1. Nonstructured population Initially, we consider the population as a whole and compartmentalize in the following way: susceptible to infection, S; acutely infected and infectious, I; carrier (infectious but asymptomatic), C; and recovered, R. To be infected, a susceptible needs to have contact with either a carrier or an acutely infected person, with force of infection λ. Once infected, that person may either become a carrier (proportion p) or acutely infected (proportion $1 - p$). If they become a carrier, there is a small probability that they will develop acute infection (rate σ); otherwise they will eventually move to the recovered compartment (rate γ_1). An acutely infected person may only recover and move to the recovered compartment (rate γ_2): we do not specifically include death due to infection. After some time in the recovered compartment, people move back to the susceptible compartment (rate γ_3).

Although we are unaware of any cases of multiple infections with meningococcal B, the possibility of being a carrier multiple times has been used in other literature [4, 21, 24]. Noninfection related deaths are included in each compartment, and

Table 1. Parameter values used for the nonstructured population model.

Parameter	Description/movement	Value
$B(t)$	Live birth numbers	http://www.stats.govt.nz
p	$S \to C$	0.999
σ	$C \to I$	10^{-5} year^{-1}
μ	Death rate	$1/70$ year^{-1}
γ_1	$C \to R$	1.3 year^{-1}
γ_2	$I \to R$	10 year^{-1}
γ_3	$R \to S$	0.09 year^{-1}
α	Infectiousness of carriers relative to invasively infected	0.8 year^{-1}
β	Transmission coefficient	2.39 year^{-1}

all births, $B(t)$, are into the susceptible compartment with the yearly birth numbers taken from Statistics New Zealand (see http://www.stats.govt.nz). This framework is depicted in Figure 2 and in the following equations:

$$\frac{dS}{dt} = B(t) - (\lambda + \mu)S + \gamma_3 R, \tag{2.1}$$

$$\frac{dC}{dt} = p\lambda S - (\sigma + \gamma_1 + \mu)C, \tag{2.2}$$

$$\frac{dI}{dt} = (1-p)\lambda S + \sigma C - (\gamma_2 + \mu)I, \tag{2.3}$$

$$\frac{dR}{dt} = \gamma_1 C + \gamma_2 I - (\gamma_3 + \mu)R, \tag{2.4}$$

with

$$\lambda = \frac{\beta}{N}(I + \alpha C). \tag{2.5}$$

We calculate the basic reproduction number by finding the largest eigenvalue of the next generation matrix, K [7]. The first column of K represents the expected number of carriers (first row) and acutely infected (second row) individuals produced by one carrier, and the second column represents the expected number of carriers (first row) and acutely infected individuals (second row) produced from one acutely infected person:

$$K = \begin{pmatrix} \dfrac{\beta p}{\sigma + \gamma_1 + \mu}\left(\alpha + \dfrac{\sigma}{\gamma_2 + \mu}\right) & \dfrac{\beta p}{\gamma_2 + \mu} \\ \dfrac{1}{\sigma + \gamma_1 + \mu}\left(\sigma + \alpha\beta(1-p) + \dfrac{\sigma\beta(1-p)}{\gamma_2 + \mu}\right) & \dfrac{\beta(1-p)}{\gamma_2 + \mu} \end{pmatrix}.$$

Calculating the largest eigenvalue of K using the parameters given in Table 1, we have $R_0 = 1.45$. To compare the results of the model with known data, we calculate

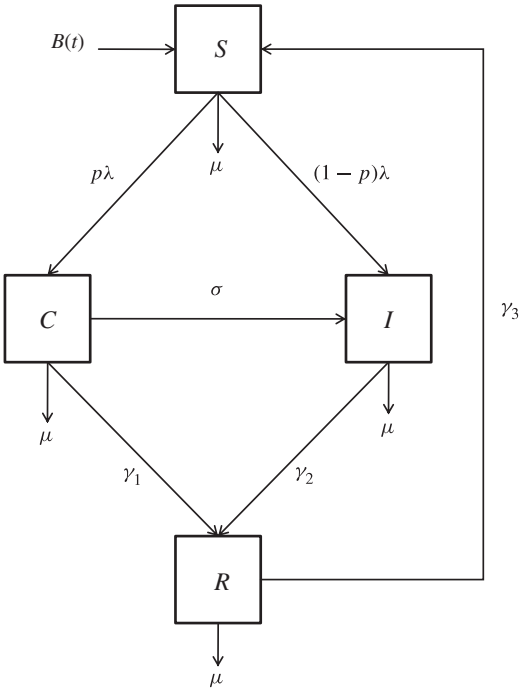

FIGURE 2. Flow diagram for the progression of individuals through the infection process. After being infected, a person can either become a carrier, C, or acutely infected, I. A small proportion of carriers will become acutely infected, but most will become temporarily immune, R. From being acutely infected, people also become temporarily immune. There is a natural mortality rate from each infection stage and births are into the susceptible class only. After immunity wanes, people go back to being fully susceptible to infection.

the yearly incidence of infection, i, by solving equations (2.1)–(2.5) numerically and setting

$$i = (1 - p)\lambda S + \sigma C.$$

The results are shown in Figure 3 (parameter values given in Table 1 with justification discussed in Section 4). We also include vaccination in the model, by reducing the number of people in the susceptible class and increasing the recovered class by the same number (we assumed that 30% of the total population were under 20 years old and thus eligible for vaccination). The vaccination campaign in New Zealand ran from 2004 to 2006, with approximately 80% of under those under 20 years old (when the vaccination campaign began) receiving three doses, after which the vaccine had an estimated 69% effectiveness (see the New Zealand Ministry of Health website: http://www.health.govt.nz) [10].

2.2. Structured population We extend our model by splitting the population into eight age classes. This is to allow for differences, according to age, in the probabilities of developing carriage or acute infection, and also to make our

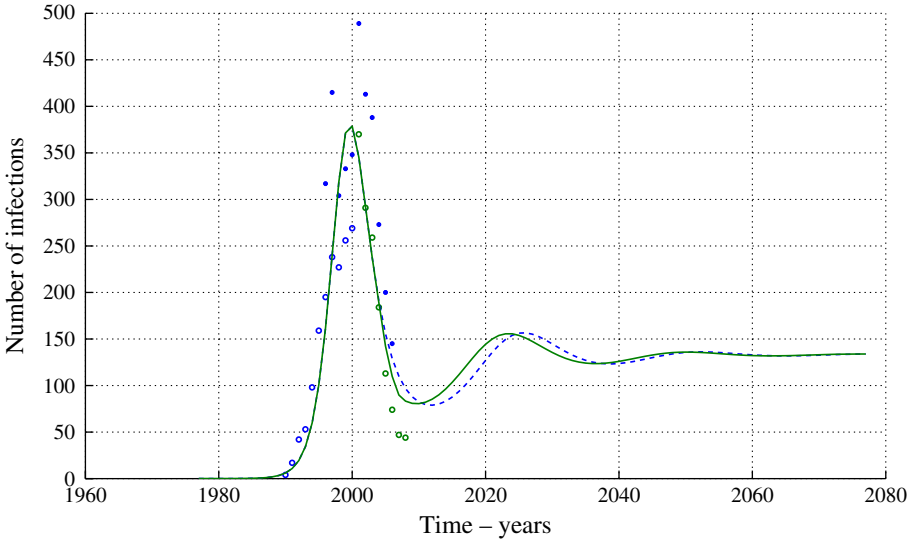

FIGURE 3. The yearly incidence of infection. The solid line is the result from our model with the population as a whole and no vaccination included, the dashed line is when vaccination is included, the circles are the recorded incidence of the epidemic strain of meningococcal disease, and the filled dots are the recorded incidence of all strains of meningococcal disease. Parameter values are listed in Table 1.

results more comparable with the recorded incidence of infection data. We use the framework outlined previously, but now allow movement from each compartment to the corresponding compartment in the next age class (for example, from carrier age class 2 to carrier age class 3). We also include a seasonal forcing term, as the incidence of infection is notably higher in the winter/spring months [8]. The effects of vaccination are included by reducing the number of susceptibles that move into the next age class and letting there be a proportion of susceptibles that move to the recovered compartment of the next age class. The equations are listed in the appendix and detailed parameter values are given in the first author's PhD thesis [11, p. 147].

We use banded mixing rates and different weighting for inter-age class contacts for adults and children. Banded mixing takes into account that those in similar age ranges are more likely to mix with each other. This produces a diagonally structured matrix, with the highest mixing rates on the diagonal, decreasing outwards. The highest activity levels are for age classes 2–6 (1–19 years old), as they are most likely to take part in activities that would lead to the spread of the infection, for example, children putting objects in their mouths at pre-school or teenagers sharing drink bottles. The parameter values were chosen based on activity levels previously used for the New Zealand epidemics of measles [15].

Solving this system numerically and calculating the yearly incidence of infection (see the previous section), we compare our model results to the data as shown in Figure 4. To calculate the basic reproduction number for this model, we construct

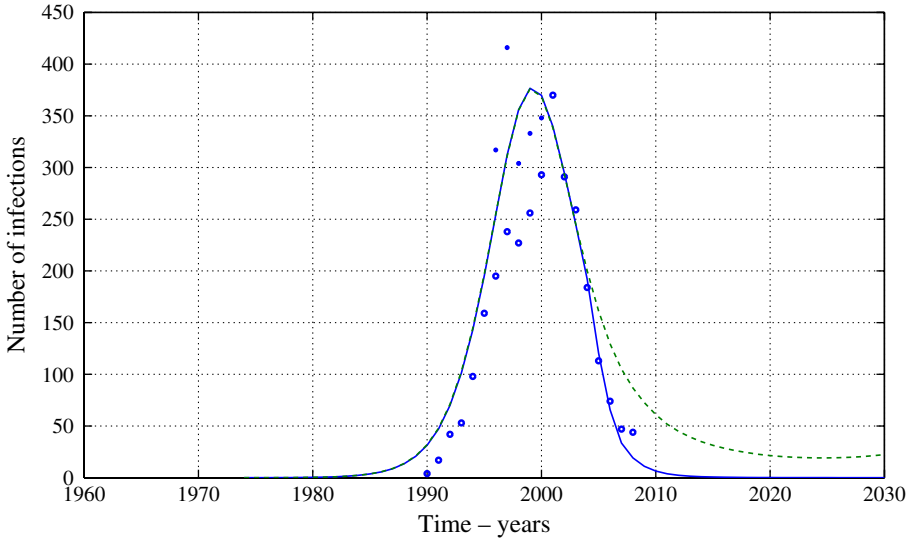

FIGURE 4. The yearly incidence of infection. The solid line is the predicted total incidence from our eight age class model when vaccination is not included, the dashed line is when vaccination is included, and the circles are the recorded incidence of infection.

the next generation matrix in a similar manner to that for the nonstructured population model, obtaining $R_0 = 1.26$.

3. Different vaccination schemes

Using the age structured population model, we now explore the effects that other possible vaccination schemes could have had on the epidemic. We consider 13 different schemes, all implemented over the same two-year period, using the coverage rates and effectiveness for the vaccination programme that was implemented; these schemes are summarized in Table 2.

To compare the different schemes, we look at the lowest incidence of infection after the vaccination campaign (after 2006), and then at the highest incidence of infection for the next peak in the epidemic and when both of these occur (results shown in Table 2). The vaccination schemes where only one age group is vaccinated (V_0, V_1, V_5, V_9 and V_{12}) do not have as great an effect as the ones where multiple age groups are vaccinated, yet they still bring the incidence of infection between epidemics significantly lower than would occur with no vaccination. Vaccinating the first three age groups, that is vaccinating at 6 weeks, 1 year and 5 years old, has the largest effect on the incidence of infection, as shown by vaccination schemes $V_{0,1,5}$, $V_{0,1,5,9}$, $V_{1,5,9}$ and $V_{0,5,9}$. Our last vaccination scheme (vaccinating everyone but the 19-year-olds) produces similar results to the campaign that was implemented, with the lowest number of cases after vaccination reaching 3 (compared to 2 with the current scheme), and the next epidemic peak occurring in 2043 with 356 cases (compared to a peak in

TABLE 2. The vaccination schemes and the results of these schemes used to explore the effect of vaccination on the incidence of infection and time until the next epidemic, implemented using the same two-year period for vaccination and vaccine effectiveness as in our previous model. Annual incidence numbers have been rounded up to the nearest integer.

Scheme symbol	Conditions: vaccination given at ages indicated	Lowest annual incidence after 2006 vaccination and year	Next peak incidence and year
NV	No vaccination	43, 2015	219, 2034
CV	All under 20 years (implemented scheme)	3, 2018	361, 2043
V_0	Birth (6 weeks old)	23, 2016	287, 2036
V_1	1 year	20, 2017	269, 2037
V_5	5 years	23, 2015	260, 2035
V_9	9 years	28, 2016	247, 2035
V_{12}	12 years	31, 2016	241, 2035
$V_{0,1}$	Birth and at 1 year	13, 2017	293, 2038
$V_{1,5}$	1 and 5 years	11, 2017	301, 2039
$V_{5,9}$	5 and 9 years	15, 2016	286, 2037
$V_{9,12}$	9 and 12 years	21, 2016	266, 2036
$V_{0,1,5}$	Birth, 1 and 5 years	7, 2018	326, 2040
$V_{0,1,5,9}$	Birth, 1, 5 and 9 years	4, 2018	346, 2042
$V_{1,5,9}$	1, 5 and 9 years	7, 2018	326, 2040
$V_{0,1,5,9,12}$	Birth, 1, 5, 9 and 12 years	3, 2018	356, 2043

the same year of 360 cases). The scheme where only those under 12 years old are vaccinated ($V_{0,1,5,9}$) also produces fairly low numbers, with the incidence dropping to 4 cases in 2018 then peaking again in 2042 with 346 cases. The vaccination schemes that only cover two age classes ($V_{0,1}$, $V_{1,5}$, $V_{5,9}$ and $V_{9,12}$) do not have as great an impact on the incidence as the schemes that cover more than two groups; however, with the two age group schemes the most improvement is seen from vaccination at 1 year and 5 years old. We have applied rounding to all the peak yearly incidence figures stated: these values resulted from a continuous state model which produced noninteger figures for what is in essence a discrete-state process.

None of the vaccination schemes prevent a future epidemic, but they all alter the severity and timing of it. With the current vaccination scheme, our model predicts a future epidemic peaking in 2043 with 361 cases (compared to a peak in 2034 with 220 cases with no vaccination). The peak number of cases for a future epidemic increases as the number of cases after vaccination decreases. The vaccination scheme $V_{0,1,5,9,12}$ gave us a low of 3 cases in 2018 and a peak of 356 cases in 2043, which is comparable to the current scheme. This proposed scheme may probably have been recommended, as it does not require the vaccination of teenagers. The scheme that was implemented included vaccinating teenagers who may have already left school, therefore making a significant coverage harder to gain.

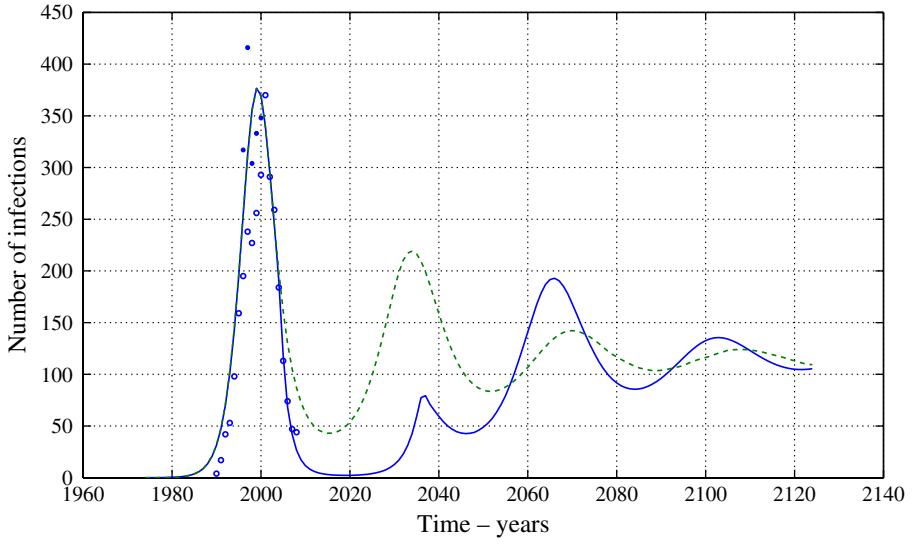

FIGURE 5. The solid line shows the model results for the eight age class meningococcal model with the vaccination included in 2004–2006 and then again in 2035–2037 at the same coverage rates and effectiveness. The dashed line shows the incidence of infection if there were no vaccination.

As future epidemics are not eliminated by a two-year vaccination campaign, vaccination is likely to be repeated. As launching a nation-wide vaccination campaign is expensive and difficult, it would only be done when deemed necessary. The current vaccine had to be designed specifically for the New Zealand epidemic strain, which is what caused the delay in implementing the vaccination campaign, but it is now ready for future epidemics. The New Zealand Ministry of Health [8] deems an epidemic of meningococcal disease to be more than 50 cases of infection per year. If we wait for there to be 50 cases of infection (year 2035) before implementing a similar vaccination scheme (using the coverage levels and effectiveness from the previous section), we obtain the results shown in Figure 5. With a two-year vaccination campaign, the immediate epidemic is avoided, but the incidence rate drops below 50 per year until 2051, when the same vaccination scheme could be implemented to avoid the epidemic. A longer-running vaccination scheme may be beneficial in the future to stop the rapid appearance of another epidemic peak. For all scenarios there will be future epidemics, yet these can be combated by vaccination.

4. Discussion

The results from the nonstructured population model follow the general trend of the epidemic data, slightly overestimating the number of cases near the epidemic peak in 2001 and after 2005 (Figure 3). By structuring the population into age classes and allowing for differences according to age in the probabilities of developing carriage and acute infection, our model shows a closer approximation to the recorded incidence

of infection for 2005–2007 (Figure 4). Other models were constructed without the possibility of reinfection (results not shown here), resulting in the incidence of infection steadily increasing to an endemic steady state. When the possibility of reinfection is included, only then do we obtain the peaked epidemic curve that relates to the known incidence data, which leads us to the conclusion that being infected multiple times plays a crucial role in the spread of the infection. A refinement to this model would be to allow carriage to occur multiple times (with a period of immunity between infections), whereas those who have suffered acute infection would remain immune for life.

We have shown that the epidemic of meningococcal disease was already declining when the nation-wide vaccination campaign was launched. However, the introduction of the vaccine reduced the incidence of infection to a predicted low of three cases per year, compared to 43 per year with no vaccination. With such low numbers of infection, it would be possible for there to be stochastic fade-out of the infection, meaning that small epidemics could occur as the infection gradually phases out of the population. However, this fade-out may be due to the decline of the invasively infected hosts while the number of carriers within the population continues to increase (results not shown here; see the first author's PhD thesis [11]). As the carriers act as a reservoir for infection, it is this population who will most likely be responsible for causing future epidemics. The model also predicts future epidemics, yet these can be brought under control by another two-year vaccination campaign similar to the one that has already been implemented.

The duration of carriage we used for the age structured model is relatively short compared to the 9–10 months estimated for American and European populations, and the lower 4.1 months for Nigeria [4]. Our average duration of carriage is just over 5 months, which is slightly longer than the average 2 months found by Trotter et al. [22] when modelling the impact of the serogroup C vaccination campaign in England and Wales. We assumed that vaccination gives complete protection against infection and carriage, whereas Trotter et al. allowed a small possibility that there could be carriage or infection after vaccination. Both models assumed that the vaccination gave waning protection; in our model this was for the time that would be spent in the recovered class (between 1 and 24 years, depending on age) and in the model of Trotter et al. protection lasted for an average of 15 months. The similarities in parameter estimates and results in our model and that of Trotter et al. [22] are surprising, as they are two very differently structured models in terms of compartmentalizing the state of an individual in relation to the disease. The United Kingdom routinely vaccinates infants against meningococcal C, and launched a nation-wide vaccination campaign in 1999 to vaccinate those under 25 who had not been vaccinated, in the hope of ending the epidemic. Both models predict that there will be future epidemics of meningococcal disease if another vaccination campaign is not initiated.

The estimated basic reproduction number of 1.26 is low compared to some other diseases. As it is so low, we would expect that a vaccination campaign would be an ideal way to combat an epidemic. Even with the effective reproduction number

being decreased below one through the effects of vaccination, the infection will not be totally eliminated from the population, seeding future epidemics. As we have seen with the nation-wide vaccination campaign that ended in 2006, the incidence of infection decreased and this campaign could be implemented in the future to avoid another epidemic.

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Appendix A. Equations for the model with population structure

For the structured population model, we have a system of 32 equations. For the first age group,

$$\begin{aligned}
\frac{dS_1}{dt} &= (1 - P_0(t))B(t) - (\lambda_1 + \mu_1)S_1 + \gamma_3 R_1,\\
\frac{dC_1}{dt} &= p_1\lambda_1 S_1 - (\sigma_1 + \gamma_1 + \mu_1)C_1,\\
\frac{dI_1}{dt} &= (1 - p_1)\lambda_1 S_1 + \sigma_1 C_1 - (\gamma_2 + \mu_1)I_1,\\
\frac{dR_1}{dt} &= BP_0(t)\gamma_1 C_1 + \gamma_2 I_1 - (\gamma_3 + \mu_1)R_1,
\end{aligned}$$

and for age groups $j = 2, \ldots, 8$,

$$\begin{aligned}
\frac{dS_j}{dt} &= \mu_{j-i}S_{j-i}(1 - P_{j-i}(t)) - (\lambda_j + \mu_j)S_j + \gamma_{3j}R_j,\\
\frac{dC_j}{dt} &= \mu_{j-i}C_{j-i} + p_j\lambda_j S_j - (\sigma_j + \gamma_{3j-2} + \mu_j)C_j,\\
\frac{dI_j}{dt} &= \mu_{j-i}I_{j-i} + (1 - p_j)\lambda_j S_j + \sigma_j C_j - (\gamma_{3j-1} + \mu_j)I_j,\\
\frac{dR_j}{dt} &= \mu_{j-i}(R_{j-i} + S_{j-i}P_{j-i}(t)) + \gamma_{3j-2}C_j + \gamma_{3j-1}I_j - (\gamma_{3j} + \mu_j)R_j.
\end{aligned}$$

Here

$$\lambda_n = \omega(t)\frac{\beta}{N}\sum_{k=1}^{8} m_{nk}(I_k + \alpha C_k),$$

$$\omega(t) = \begin{cases} (1+\delta)/(2\delta(\tau_2 - \tau_1) + 1 - \delta) & \text{if } \tau_1 < \tau < \tau_2 \\ (1-\delta)/(2\delta(\tau_2 - \tau_1) + 1 - \delta) & \text{otherwise,} \end{cases}$$

where $n = 1, \ldots, 8$, τ is the decimal part of t, τ_1 is set to be 1 July (0.5) and τ_2 is 1 September (0.67). Hence there is lower transmission in the summer months than in the winter months. The mean value of ω is one, and for our numerical solutions we have used $\delta = 0.4$. This is the same seasonal forcing as used for modelling measles in New Zealand [15].

The contact/mixing matrix for the structured population model, $M = (M_{ij})$, is constructed to take into account the different activity levels of each age class and inter-age class contacts:

$$M_{ij} = \begin{cases} a_i & \text{if } i = j \\ \epsilon_2 \sqrt{a_i a_j} & \text{if } (i, j) \in \{(7, 6), (7, 8), (8, 6), (8, 7)\} \\ \sqrt{\epsilon_1 \epsilon_2} \sqrt{a_i a_j} & \text{if } \{i \geq 7, j \leq 5\} \text{ or } \{i \leq 6, j \geq 7\} \text{ or } \{j = 6, i = 2, \ldots, 5\} \\ \epsilon_1 \sqrt{a_i a_j} & \text{otherwise.} \end{cases}$$

The mixing parameters used are: $a_1 = 1$, $a_2 = 5$, $a_3 = 6$, $a_4 = 6$, $a_5 = 5$, $a_6 = 4$, $a_7 = 2$, $a_8 = 1$, $\epsilon_1 = 0.7$ and $\epsilon_2 = 0.5$.

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