Modelling Measles

Predicting and Preventing Measles Epidemics in New Zealand: Application of a mathematical model
Preface

In 1996 the Ministry of Health, with assistance from AgResearch, developed a mathematical model of measles dynamics in New Zealand. The model successfully predicted an epidemic in 1997 and was instrumental in the decision to carry out an intensive MMR (measles-mumps-rubella) immunisation campaign in that year. While the epidemic began some months earlier than anticipated in 1997, it was nevertheless brought rapidly under control, and its impact on the population was much reduced.

In order to prevent the occurrence of further measles epidemics in New Zealand, an extended version of the measles model has since been developed and applied to the critical question of the optimal timing of MMR immunisation.

This document brings together the results of both applications of the measles model. While most interest resides in the use of the model to assist decision making with regard to immunisation policy, both reports are included for ease of reference. The success of the model in predicting the 1997 measles epidemic provides support for its use in immunisation policy formulation.

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Acknowledgements

Part A was prepared in April 1998 by Martin Tobias (Ministry of Health) and Mick Roberts (AgResearch), with assistance from Osman Mansoor (Ministry of Health).

Part B is a second edition, prepared in February 1998, of a report presented to the Ministry of Health in January 1997 and includes minor revisions. Both editions were written by Martin Tobias (Ministry of Health) and Mick Roberts (AgResearch).
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Part A: Optimal Timing of MMR Immunisation

Introduction

Measles immunisation was introduced in New Zealand in 1969, but coverage was inadequate to alter the pattern of two- to three-yearly epidemics until 1980 (Ministry of Health 1996). In 1978, a five-year measles epidemic elimination programme was instituted. The coverage achieved by that programme is not known, yet coverage increased sufficiently to defer the next epidemics to 1985 and then 1991. In November 1990, the measles vaccine was replaced by the measles-mumps-rubella vaccine (MMR). A second dose of MMR, scheduled at age 11 years, was not added until 1992, in response to the 1991 measles epidemic (Dow and Mansoor 1996).

In the 1990s, coverage has been only a little above 80 percent for the first scheduled dose (Stehr-Green et al 1992; McNicholas and Baker 1995). Coverage for the second dose is likely to be about the same, although there are no national data on this episode. The 1997 measles epidemic confirmed mathematical modelling which showed that current levels of coverage will result in further large-scale measles epidemics about every six years, despite the addition of the second dose (Tobias et al 1997).

To help guide a decision about the optimal timing of the MMR doses, the mathematical model developed earlier has been used.

Method

The dynamics of measles were modelled under varying immunisation strategies in a population with the size and age structure of New Zealand’s, using a deterministic multi compartment (susceptible-infected-recovered (SIR)) model. The model had the same structure as that used in 1996 to predict the next measles epidemic (Roberts and Tobias 1997, revised version included as Part B of this report), but with a greater number of age classes to facilitate investigation of different immunisation schedules. Full details of the mathematics of the model are given under Model Structure.

Immunisation parameters

Schedules

The Ministry sought advice from its Infectious Diseases Advisory Committee (IDAC). IDAC consists of experts from outside the Ministry, and provides technical advice to the Ministry on infectious disease issues. IDAC confirmed the following four possible schedules as representing the range of realistic options:

<table>
<thead>
<tr>
<th>Schedule label</th>
<th>MMR1</th>
<th>MMR2</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>12 months</td>
<td>15 months</td>
<td>Earliest possible time for both doses</td>
</tr>
<tr>
<td>Preschool</td>
<td>15 months</td>
<td>3 years</td>
<td>MMR2 at or around entry to child care</td>
</tr>
</tbody>
</table>
### Catch-up opportunities

As well as the scheduled events, entry to an early childhood centre (modelled at three years of age) and to school (at five years of age) provide ‘catch-up’ opportunities. For the preschool schedule, only catch-up at the age of five years applies, as there is a scheduled immunisation event at three years of age.

### Immunisation coverage

For the first scheduled immunisation event (‘MMR1’), four coverage rates were modelled:

<table>
<thead>
<tr>
<th>MMR1 Coverage Label</th>
<th>Rate (%)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>80%</td>
<td>Low</td>
</tr>
<tr>
<td>Intermediate</td>
<td>85%</td>
<td>The current rate</td>
</tr>
<tr>
<td>High</td>
<td>90%</td>
<td>Realistically achievable</td>
</tr>
<tr>
<td>Target</td>
<td>95%</td>
<td>Challenging</td>
</tr>
</tbody>
</table>

For the second scheduled immunisation event (‘MMR2’), coverage was assumed to be dependent on behaviour at MMR1:

<table>
<thead>
<tr>
<th>Category</th>
<th>Coverage at MMR2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children immunised at MMR1</td>
<td>90</td>
</tr>
<tr>
<td>Children not immunised at MMR1</td>
<td>Variable, depending on schedule (see below)</td>
</tr>
</tbody>
</table>

For those children not immunised at MMR1, coverage at MMR2 was assumed to increase with time elapsed from the MMR1 episode until school entry, when it was assumed to stabilise at 70 percent (reflecting the fact that this represents a ‘hard to reach’ group of children, even when ‘captive’ at school):

<table>
<thead>
<tr>
<th>MMR2 coverage for children not immunised at MMR1</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant schedule</td>
<td>5</td>
</tr>
<tr>
<td>Preschool schedule</td>
<td>50</td>
</tr>
<tr>
<td>School schedule</td>
<td>70</td>
</tr>
<tr>
<td>Current schedule</td>
<td>70</td>
</tr>
</tbody>
</table>

Coverage at catch-up opportunities was assumed to vary from 0 to 50 percent, with the exception of the preschool schedule. As there is only one catch-up opportunity for the preschool schedule, 75 percent catch-up at five years of age was allowed for this schedule only.
Catch-up was considered to apply equally to children who had missed one or both scheduled immunisations, depending on the schedule concerned.

### Vaccine failure

Vaccine efficacy involves both the proportion of children who fail to respond to an immunisation (primary vaccine failure) and the proportion who respond initially but subsequently lose protective immunity (secondary vaccine failure).

#### Primary vaccine failure

The literature on the short-term efficacy of MMR vaccines is conflicting. Variables such as vaccine formulation, cold chain integrity, and injection technique can influence response. Initially a primary vaccine failure rate of 10 percent was modelled (12 percent for the infant immunisation schedule to allow for interference from residual maternal antibody at age 12 months), as had been used in the earlier measles model (Roberts and Tobias 1997). Subsequently a number of selected scenarios were simulated with a primary vaccine failure rate of only 5 percent, although this may be unrealistically high (protection does not necessarily correspond to seroconversion).

The question has often been raised as to whether children who fail to respond to their first immunisation are more likely to fail again when re-immunised. Although there is little evidence to support this theory, for these children primary vaccine failure rates of both 10 percent and 20 percent were modelled.

#### Secondary vaccine failure

A meta-analysis of published data found no evidence for secondary vaccine failure, with vaccine given after the age of 12 months using US-manufactured vaccines, and estimated the 95 percent confidence intervals for secondary failure at between 0 and 0.15 percent per annum (Anders et al 1996). Accordingly, two secondary vaccine failure rates were modelled: 0 percent and 0.5 percent per year post immunisation, to bracket the possible range.

### Simulation

For each schedule (infant, preschool, school, and current) and MMR1 coverage rate (low, intermediate, high, and target), the model was run for six scenarios based on catch-up and vaccine performance (giving a total of 96 scenarios):

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Catch-up rate at three years of age</th>
<th>Catch-up rate at five years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%, 50%</td>
<td>Not applicable</td>
<td>0%, 50%</td>
</tr>
<tr>
<td>Preschool</td>
<td>0%, 50%</td>
<td>0%, 75%</td>
</tr>
<tr>
<td>School</td>
<td>0%, 50%</td>
<td>0%, 50%</td>
</tr>
<tr>
<td>Current</td>
<td>0%, 50%</td>
<td>0%, 50%</td>
</tr>
</tbody>
</table>

For each schedule and coverage rate, the model was run for six scenarios based on catch-up and vaccine performance (giving a total of 96 scenarios):

<table>
<thead>
<tr>
<th>Scenario number (symbol)</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>No catch-up, low failure</td>
</tr>
<tr>
<td>NF</td>
<td>No catch-up, high failure</td>
</tr>
<tr>
<td>Schedule</td>
<td>Description</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>C3</td>
<td>50 percent catch-up at three years of age, low failure</td>
</tr>
<tr>
<td>C3F</td>
<td>50 percent catch-up at three years of age, high failure</td>
</tr>
<tr>
<td>C5</td>
<td>* 50 percent catch-up at five years of age, low failure</td>
</tr>
<tr>
<td>C5F</td>
<td>* 50 percent catch-up at five years of age, high failure</td>
</tr>
</tbody>
</table>

* For the preschool schedule catch up of 75 percent.

‘Low failure’ means 10 percent primary vaccine failure rate and no secondary vaccine failures. ‘High failure’ means 20 percent primary vaccine failure for children who failed to respond to their first dose (10 percent otherwise), and a secondary vaccine failure rate of 0.5 percent per year post immunisation.

Simulations were carried out over a 20-year modelling period (i.e., from 1998 to 2018), with a step length of one week. All calculations were performed using Mathcad 7 Professional (MathSoft 1997).

### Output

#### Reproduction ratio with immunisation (R<sub>v</sub>)

The basic reproduction ratio (R<sub>0</sub>) of an infectious disease is defined as the average number of secondary cases generated by a primary case in a fully susceptible population (Anderson and May 1991). R<sub>0</sub> for measles in New Zealand is estimated by the model to be 12.8. Given this R<sub>0</sub> and seasonal variability in transmission, the model predicts epidemics every two years in New Zealand (in the absence of immunisation).

R<sub>v</sub> is similarly defined as the average number of secondary cases generated by a primary case in a population rendered incompletely susceptible as a result of immunisation. If R<sub>v</sub> < 1, disease elimination occurs. In practice, a safety margin is needed because of seasonal variation in transmissibility and heterogeneities in the population (for example, the geographic clustering of ‘pockets’ of susceptibles). This means that R<sub>v</sub> needs to be well below 1, probably 0.8 or less before elimination becomes realistic.

#### Inter-epidemic period (IEP)

The complete model, run over 20 years, was plotted for selected strategies, to display visually the timing and scale of predicted epidemics. A mathematical relationship exists between R<sub>v</sub> and the IEP, and visual representation of future epidemics adds no new information. Nevertheless, it was considered helpful to display the model output in this graphical form as well. However, the results should not be interpreted literally. For example, the prediction that a particular immunisation strategy will yield an IEP of 16 years is not equivalent to a prediction that an epidemic will occur in exactly 16 years’ time. In fact, depending on the success internationally in preventing measles epidemics, such a long IEP may, in reality, be equivalent to disease elimination.

### Results

#### R<sub>v</sub>

The model output is summarised in terms of R<sub>v</sub> for different schedules, coverages, and scenarios, in Tables 1-6 (and shown graphically in Figures 1-6).
### Table 1. $R_v$ values, scenario N

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Schedule</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>2.6</td>
<td>2</td>
<td>1.5</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>1.5</td>
<td>1.2</td>
<td>0.9</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>School</td>
<td>1.4</td>
<td>1.2</td>
<td>0.9</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2.6</td>
<td>2.2</td>
<td>1.7</td>
<td>1.3</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. $R_v$ values, scenario NF

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Schedule</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>2.9</td>
<td>2.3</td>
<td>1.7</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>1.6</td>
<td>1.3</td>
<td>1</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>School</td>
<td>1.5</td>
<td>1.3</td>
<td>1</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2.6</td>
<td>2.2</td>
<td>1.8</td>
<td>1.4</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. $R_v$ values, scenario C3

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Schedule</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>2.2</td>
<td>1.8</td>
<td>1.3</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>School</td>
<td>1</td>
<td>0.9</td>
<td>0.7</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>1.8</td>
<td>1.6</td>
<td>1.4</td>
<td>1.1</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4. $R_v$ values, scenario C3F

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Schedule</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>2.5</td>
<td>2</td>
<td>1.6</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>School</td>
<td>1.1</td>
<td>1</td>
<td>0.8</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>1.9</td>
<td>1.6</td>
<td>1.4</td>
<td>1.2</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5. $R_v$ values, scenario C5

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Schedule</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>School</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6. $R_v$ values, scenario C5F

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Infant</th>
<th>Preschool</th>
<th>School</th>
<th>Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>2.5</td>
<td>1.4</td>
<td>1.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2</td>
<td>1.2</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>High</td>
<td>1.6</td>
<td>0.9</td>
<td>0.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Target</td>
<td>1</td>
<td>0.7</td>
<td>0.7</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Figure 1. Scenario N

Figure 2. Scenario NF
Figure 3. Scenario C3

Figure 4. Scenario C3F

Figure 5. Scenario C5
The key points to emerge from examination of these tables and charts include:

**Schedule and coverage variables**

At low coverage, no schedule will lead to measles elimination. At intermediate coverage, only the school schedule yields an $R_v$ below 1.0, and then without an adequate safety margin (and only if catch-up is high and vaccine failure low).

At high coverage, both the school and preschool schedules are capable of measles elimination ($R_v$ of 0.8 or below). At this coverage, the school schedule slightly outperforms the preschool schedule, whereas the opposite is the case at target coverage. Essentially, these schedules are equivalent.

Target MMR1 coverage (95 percent) is not required for measles elimination, provided the timing of the second dose is modified (to either school or preschool entry). Yet if the current schedule is continued, measles will not be eliminated at any (realistic) level of coverage, catch-up and vaccine failure.

**Catch-up and failure variables**

Unless coverage at scheduled opportunities is at target level, a catch-up programme is also required for measles elimination. For example, with the school schedule and high (90 percent) coverage, $R_v$ is 0.7 with preschool catch-up but 0.9 without it.

On the other hand, given high coverage at both scheduled and catch-up ages, vaccine failure is of little consequence.

**Inter-epidemic period**

Simulations of selected immunisation strategies over the next 20 years are shown in Figures 7–11.
Figure 7. ‘No immunisation’ situation

Figure 7 shows the ‘no immunisation’ situation (R_V = R_0 = 12.8). Epidemics occur every two years. The number of susceptibles in the population builds up to a threshold of 184,000, at which point an epidemic is triggered. The epidemic stops when the number of susceptibles has been reduced to approximately 100,000.
Figure 8. ‘Current’ situation

Figure 8 shows the model conditions approximating the current situation. This yields an $R_v$ of 2.0 and displays an inter-epidemic period of approximately six to seven years, with epidemics averaging about 60,000-80,000 cases.
Figure 9. ‘Best results with current schedule’ situation

Figure 9 shows the best results that could be achieved with the current immunisation schedule, ie, assuming 95 percent coverage, high catch-up, and low vaccine failure rates. Under these assumptions, the model predicts an $R_v$ of 1.1, and an epidemic occurs after 16 years.

In reality this should be interpreted to mean that epidemics might never occur, depending on the success of other countries in controlling measles. However, it also implies that sufficient susceptibles would (re)accumulate in the population to create the potential for epidemics to occur (albeit no more frequently than 15- or 16-yearly) until global eradication of the virus was achieved.
Figure 10. ‘Best possible results’ situation

Figure 10 shows the best result obtainable from any strategy-scenario combination: with 95 percent coverage at 15 months, 50 percent coverage at three years, 75 percent catch up at five years, and low vaccine failure rates, $R_v = 0.58$. The figure shows that the susceptible population slowly increases, then begins to decrease again close to 20 years out from the present without ever reaching the critical size necessary for an epidemic to occur. The simulations for other strategies yielding $R_v < 1$ (and especially $< 0.8$) show a similar pattern.
Finally, selected strategies were rerun, with the primary vaccine failure rate reduced to 5 percent. This made little difference to the respective $R_v$ values, and the graphical representations of IEPs were not observably different. For example, the current situation yields an $R_v = 2.04$ at ‘usual’ failure rates, which reduces to 2.01 if vaccine efficacy is assumed to be 95 percent. The simulation (Figure 11) should be compared with Figure 8; little difference is discernible in the timing or size of the predicted epidemics.

**Conclusions**

- If nothing is done, the next measles epidemic will occur in 2003 or 2004 and involve approximately 60,000-80,000 cases.

- As long as the current MMR schedule (15 months and 11 years) remains in force, measles epidemics will continue to occur.

- Bringing forward the second dose of vaccine (MMR2) to three years of age or six years of age (approximately) is necessary to prevent the further occurrence of measles epidemics in New Zealand.
• A change in the immunisation schedule alone will probably be insufficient by itself to eliminate measles from New Zealand. Coverage at 15 months of age needs to increase to 90 percent (or more), and effective opportunities for catch up immunisation are also required, to be certain of success.

• The timing of the second dose is not critical from an epidemiological perspective, provided this dose is administered between the ages of approximately three and approximately six years. Immunisation at or around school entry may offer logistic advantages.

Discussion

There is only limited evidence on the impact of different strategies for controlling measles. The consensus is that the most important factor is high coverage with one dose. The second dose counters vaccine failure (increasing vaccine efficacy) and failure to vaccinate (increasing coverage). The model shows that of these two effects, it is the latter (increasing coverage) that is more important until coverage with the first dose exceeds 95 percent. Similar results have been found by others (Williams et al 1995).

Until recently, the World Health Organization (WHO) has not actively promoted two-dose schedules, as it has considered achieving high coverage with one dose to be the priority (Rosenthal and Clements 1993). The WHO is now promoting delivery of the second dose through mass campaigns as a means of reaching children who would not normally access primary health care services. The effectiveness of this approach has been demonstrated in the Americas (Quadros et al 1996). The other approach with demonstrated effectiveness is high coverage with two scheduled doses, which led to the elimination of indigenous measles in Finland (Peltola et al 1994, 1997).

In Finland, MMR has been scheduled at 14-18 months of age and again at six years of age (prior to school entry) since 1982. The vaccine used in Finland has been MMR II (MSD) vaccine, the same vaccine now used in New Zealand. The coverage achieved in Finland exceeds 95 percent for both doses.

By contrast, in 1982 Sweden introduced a two-dose MMR schedule at 18 months of age and 12 years of age. Initial experience showed declining incidence of measles from 1982 to 1986, with achievement of over 90 percent coverage for both doses (Bottiger et al 1987). More recent experience has not been fully reported, although a 1994 paper describing serological response reports continuing success with the Swedish schedule (Christenson and Bottiger 1994). The WHO database shows a declining number of cases in Sweden from 1986 to 1996, although no data were reported for 1994 and 1995. Since 1995 coverage in Sweden at 12 years of age has been 99 percent for one dose and 90 percent for two doses (personal communication, JM Olive, WHO).

The very high coverage, relative homogeneity of the population, and low population density may be factors contributing to the success of measles control in Sweden despite an apparently suboptimal schedule.

Mathematical modelling in France has replicated the findings of this New Zealand study, and has led to the recommendation that MMR2 be brought forward to the time of school entry (or earlier) to enable elimination of measles (personal communication, Daniel Levy-Bruhl, INSERM, 1998).

A serological study of Canadian children supports delivery of the second dose before school entry (Ratnam et al 1996). Some areas in Canada are giving the second dose at 18 months of age while others are delivering it around school entry (Ratnam et al 1997).

The United Kingdom and United States schedule MMR2 at school entry. The Australians are currently considering a change in the timing from the current 10–16 years (Forrest et al 1988).

The 1997 measles epidemic in New Zealand, modelling results presented in this report, limited serological data, and international practice, all support bringing forward the timing of MMR2.
The only evidence against such a change appears to be the success of Sweden in eliminating measles with a similar schedule to that currently used in New Zealand. However, this assumes firstly that Sweden will not in fact experience another measles epidemic over the next decade, and secondly that New Zealand is capable of achieving and sustaining MMR immunisation coverage rates of similar magnitude to those achieved in Sweden.

In deciding whether to bring the second dose of MMR forward, the impact of such a change in the childhood immunisation schedule on diseases other than measles must also be considered. There are also logistic aspects to consider. The results of epidemiological modelling, reported herein, represent only one input into the decision-making process. Finally, it must be emphasised that unless coverage increases, no schedule will prevent further measles epidemics.

Model Structure

A model population with a structure similar to that of New Zealand’s was constructed as follows. The annual birth rate was assumed constant at $B = 57,435$ births per year$^{-1}$. For each age class (see Table 7) the class size was fixed at class width $x B$, and the transition rate to the next class at (class width)$^{-1}$. For example, Class 5 covers three years of age to six years of age, $N_5 = 172,305$ and $m_5 = 1/3$. Hence, model class sizes remain constant and deaths are neglected up to the age of 25.

The disease transmission model was constructed in a manner compatible with Roberts and Tobias (1997). In the previous report, four age classes were used corresponding to the present classes 1–2, 3–5, 6–7 and 8 respectively, with activity levels $a_1$ to $a_4$, and inter-level activity reduced by a factor $\varepsilon$.

We therefore use the contact rate matrix $C$ equal to:

\[
\begin{pmatrix}
  a_1 & a_1 & \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_1 a_4} \\
  a_1 & a_1 & \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_1 a_4} \\
  \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & a_2 & a_2 & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} \\
  \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & a_2 & a_2 & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} \\
  \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & a_2 & a_2 & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} \\
  \varepsilon \sqrt{a_1 a_2} & \varepsilon \sqrt{a_1 a_2} & a_2 & a_2 & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} \\
  \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} & a_3 & a_3 \\
  \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_1 a_3} & \varepsilon \sqrt{a_2 a_3} & \varepsilon \sqrt{a_2 a_3} & a_3 & a_3 \\
  \varepsilon \sqrt{a_1 a_4} & \varepsilon \sqrt{a_1 a_4} & \varepsilon \sqrt{a_2 a_4} & \varepsilon \sqrt{a_2 a_4} & \varepsilon \sqrt{a_3 a_4} & a_4
\end{pmatrix}
\]
to represent within and between class contacts for the model with eight age classes.

The model equations for the susceptible ($S_i$) and infectious ($I_i$) populations are:

$$\frac{dS_i}{dt} = \mu_0 N_0 - \left( \mu_1 + \omega(t) \beta \sum_{j=1}^{8} C_{ij} I_j \right) S_i$$

$$\frac{dI_i}{dt} = \omega(t) \beta S_i \sum_{j=1}^{8} C_{ij} I_j - (\mu_1 + \gamma) I_i$$

and for $i = 2 \ldots 8$:

$$\frac{dS_i}{dt} = \nu_{i-1} S_{i-1} - \left( \mu_i + \omega(t) \beta \sum_{j=1}^{8} C_{ij} I_j \right) S_i$$

$$\frac{dI_i}{dt} = \mu_{i-1} I_{i-1} + \omega(t) \beta S_i \sum_{j=1}^{8} C_{ij} I_j - (\mu_i + \gamma) I_i$$

The effect of vaccination is to reduce the incoming transition rate to class $i + 1$ from $\mu_i$ to $\nu_i$. The seasonality function was defined by:

$$\omega(t) = \begin{cases} 
1.0895 & \text{for } 0.1615 < \text{dec}(t) < 0.9151 \\
0.7263 & \text{otherwise} 
\end{cases}$$

where $\text{dec}(t)$ is the decimal part of time $t$ (years). Next generation matrices were calculated with $\omega(t) = 1$.

The matrix $M_0$ is equal to:

$$M_0 = \begin{pmatrix}
\frac{\beta C_{11} N_1}{\mu_1 + \gamma} & \frac{\beta C_{12} N_1}{\mu_2 + \gamma} & \frac{\beta C_{13} N_1}{\mu_3 + \gamma} & \ldots & \frac{\beta C_{18} N_1}{\mu_8 + \gamma} \\
\frac{\beta C_{21} N_2}{\mu_1 + \gamma} & \frac{\beta C_{22} N_2}{\mu_2 + \gamma} & \frac{\beta C_{23} N_2}{\mu_3 + \gamma} & \ldots & \frac{\beta C_{28} N_2}{\mu_8 + \gamma} \\
\frac{\beta C_{31} N_3}{\mu_1 + \gamma} & \frac{\beta C_{32} N_3 + \mu_2}{\mu_2 + \gamma} & \frac{\beta C_{33} N_3}{\mu_3 + \gamma} & \ldots & \frac{\beta C_{38} N_3}{\mu_8 + \gamma} \\
\mu_2 + \gamma & \mu_2 + \gamma & \mu_2 + \gamma & \ldots & \mu_2 + \gamma \\
\ldots & \ldots & \ldots & \ldots & \ldots \\
\frac{\beta C_{81} N_8}{\mu_1 + \gamma} & \frac{\beta C_{82} N_8 + \mu_2}{\mu_2 + \gamma} & \frac{\beta C_{83} N_8}{\mu_3 + \gamma} & \ldots & \frac{\beta C_{88} N_8}{\mu_8 + \gamma} \\
\frac{\beta C_{89} N_8}{\mu_9 + \gamma} & \frac{\beta C_{810} N_8}{\mu_9 + \gamma} & \frac{\beta C_{811} N_8}{\mu_9 + \gamma} & \ldots & \frac{\beta C_{818} N_8}{\mu_8 + \gamma} \\
\frac{\beta C_{819} N_8}{\mu_9 + \gamma} & \frac{\beta C_{820} N_8}{\mu_9 + \gamma} & \frac{\beta C_{821} N_8}{\mu_9 + \gamma} & \ldots & \frac{\beta C_{88} N_8}{\mu_8 + \gamma} \\
\mu_9 + \gamma & \mu_9 + \gamma & \mu_9 + \gamma & \ldots & \mu_9 + \gamma \\
\ldots & \ldots & \ldots & \ldots & \ldots
\end{pmatrix}$$

and $M_v$ is equal to the same matrix, but with $N_i$ replaced with $S_i^*$, the steady state value of $S_i(t)$. The Basic Reproduction Ratio $R_0 = \rho(M_0)$, and the Basic Reproduction Ratio under vaccination $R_v = \rho(M_v)$, where $\rho$ signifies spectral radius of a matrix. Parameter values are given in Table 8.
Table 8. Parameter values used in the model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a_1$</td>
<td>activity level</td>
<td>1</td>
</tr>
<tr>
<td>$a_2$</td>
<td>activity level</td>
<td>2</td>
</tr>
<tr>
<td>$a_3$</td>
<td>activity level</td>
<td>6</td>
</tr>
<tr>
<td>$a_4$</td>
<td>activity level</td>
<td>3</td>
</tr>
<tr>
<td>$\varepsilon$</td>
<td>factor reducing inter-class activity</td>
<td>0.4</td>
</tr>
<tr>
<td>$\beta$</td>
<td>disease transmission coefficient</td>
<td>$2.005 \times 10^{-4}$ year$^{-1}$</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>$1/(\text{mean time infectious})$</td>
<td>52 year$^{-1}$</td>
</tr>
</tbody>
</table>

With these parameter values we obtain $R_0 = 12.8$, which is consistent with the results in Roberts and Tobias (1997).
Part B: A Model of Measles Dynamics in New Zealand*

Summary

An SIR model has been used to explore the dynamics of measles in New Zealand. The model predicts that the current vaccination programme has increased the inter-epidemic period from two to six years, which is consistent with observations. The model also demonstrates that the vaccination programme has changed the age structure of the susceptible population and hence the threshold at which an epidemic is triggered, with children under five years now playing a smaller part in epidemics, and those over 16 years having an increasing role. The predicted timing and sizes of measles epidemics are very sensitive to assumed values of the basic reproduction ratio, $R_0$, and the assumed mixing pattern between age classes.

Introduction

Until the introduction of the measles vaccination in 1970 there was an epidemic of measles in New Zealand every two years. The effect of the vaccination programme has been to lengthen the inter-epidemic period, and the last epidemic occurred in 1991 (Cullen and Walker 1996). In this paper we use a deterministic SIR model with four age classes (see Anderson and May 1991; Agur et al 1993; Grenfell and Bolker 1994) to investigate the dynamics of measles in New Zealand, predict the timing of the next epidemic and explore the changes in the age-distribution of measles cases since the initiation of the vaccination programme.

Method

Demographics

The population was divided into six age classes, numbered 0–5, as shown in Table 9. The boundaries of the age classes were chosen using the assumption that those aged less than six months or more than 25 years take no part in the epidemic, and because vaccination is scheduled to occur at 1.25 years of age, five years of age and 11 years of age.

Table 9. Age classes used in the model

| Class 0: | 0–0.5 years |
| Class 1: | 0.5–1.25 years |
| Class 2: | 1.25–5 years |
| Class 3: | 5–11 years |
| Class 4: | 11–25 years |

In order to construct a model population that approximates that of New Zealand, it was assumed that the annual number of births ($B$) is constant, and that the death rate in age classes 0–4 (all ages less than 25 years) is so small that it can be neglected. Hence the number in age class $i$ for $i = 0 \ldots 4$, is $N_i = Bw_i$ where $w_i$ is the class width (0.5, 0.75, 3.75, 6 or 14 years respectively). The transition rates between age classes were then calculated as the reciprocals of the class widths, $\mu_i = 1/w_i$. For example, the transition rate from class 0 to class 1 is $\mu_0 = 1/w_0 = 2$ years$^{-1}$. This procedure ensures that the class sizes $N_i$ remain constant. All assumed parameters are listed in Table 10, and all derived parameters in Table 11.

The SIR model

Age classes 1–4 were subdivided into $S$, susceptibles, $I$, infectives and $R$, immune. As the numbers in each class are constant, it was not necessary to model the immune classes explicitly. The equations for age class 1 are:

$$\frac{dS_1}{dt} = \mu_0 N_0 - \left( \mu_1 + \omega(t)\beta \sum_{j=1}^{4} c_{1j} I_j \right) S_1$$

$$\frac{dI_1}{dt} = \omega(t)\beta S_1 \sum_{j=1}^{4} c_{1j} I_j - (\mu_1 + \gamma) I_1$$

Children enter from class 0 as susceptibles at rate $\mu_0$, and leave by moving to class 2 at rate $\mu_1$. Susceptibles may also become infected, by contact with an infective individual, after which they become immune (enter the $R$ class) at rate $\gamma$.

The equations for age classes 2–4 are similar. We have:

$$\frac{dS_i}{dt} = (1 - P_{i-1}(t)) \mu_{i-1} S_{i-1} - \left( \mu_i + \omega(t)\beta \sum_{j=1}^{4} c_{ij} I_j \right) S_i$$

$$\frac{dI_i}{dt} = \mu_{i-1} I_{i-1} + \omega(t)\beta S_i \sum_{j=1}^{4} c_{ij} I_j - (\mu_i + \gamma) I_i$$

for $i = 2, 3, 4$. Vaccination may occur at ages 1.25 years, five years or 11 years, the proportion of the population that is protected being $P_1$, $P_2$, or $P_3$ respectively.

The infection process

Consider first the situation with a single age class. If the number of contacts that an individual makes with another per unit time is $C$, then the number of contacts with an infectious individual is $CI$. If the number of new infectives formed per infectious contact is $\bar{\beta}$, then the rate at which susceptibles become infected (force of infection) is $\bar{\beta}CI$. With four age classes, the force of infection in class $i$ is:

$$\lambda_i(t) = \omega(t)\beta \sum_{j=1}^{4} c_{ij} I_j$$

$$= \omega(t)\beta (c_{i1} I_1 + c_{i2} I_2 + c_{i3} I_3 + c_{i4} I_4)$$

It is convenient to estimate contact rates relative to those in one selected class, for example age-class 1. The parameter $\bar{\beta}$ then has dimension year$^{-1}$. 

---

Modelling Measles 19
We therefore need to estimate the relative contact rates ($c_{ij}$), the seasonality function ($\Omega(t)$) and the transmission rate ($\tilde{B}$).

**Relative contact rates**

Suppose that an individual in age class $i$ has an activity level measured by $a_i$. Under the proportionate mixing assumption, the number of contacts per unit time between individuals in age class $i$ and individuals in age class $j$ is proportional to $\sqrt{a_i a_j}$, and under the preferred mixing assumption this is true for within-class contacts, but between-class contacts are assumed to be zero. We have combined the two assumptions, by choosing a parameter $\varepsilon < 1$ to weight between-class contacts (see Hethcote 1995). We estimated relative contact rates by setting $a_1 = 1$, estimating the other within-class activity rates $a_2, a_3, a_4$ relative to $a_1$, and constructing the matrix:

$$
\begin{pmatrix}
c_{11} & c_{12} & c_{13} & c_{14} \\
c_{21} & c_{22} & c_{23} & c_{24} \\
c_{31} & c_{32} & c_{33} & c_{34} \\
c_{41} & c_{42} & c_{43} & c_{44}
\end{pmatrix} = 
\begin{pmatrix}
1 & \varepsilon\sqrt{a_2} & \varepsilon\sqrt{a_3} & \varepsilon\sqrt{a_4} \\
\varepsilon\sqrt{a_2} & a_2 & \varepsilon\sqrt{a_2a_3} & \varepsilon\sqrt{a_2a_4} \\
\varepsilon\sqrt{a_3} & \varepsilon\sqrt{a_2a_3} & a_3 & \varepsilon\sqrt{a_3a_4} \\
\varepsilon\sqrt{a_4} & \varepsilon\sqrt{a_2a_4} & \varepsilon\sqrt{a_3a_4} & a_4
\end{pmatrix}
$$

This plays a similar role to the familiar WAIFW matrix (Anderson and May 1991; Keeling and Grenfell 1997).

**The seasonality function**

A function $\Omega(t)$ was used to simulate the variation in disease transmission with the season of the year. Two forms were used: a sine wave:

$$\omega(t) = 1 + \delta \cos ((2t + 1)\pi)$$

and a step function:

$$\omega(t) = \begin{cases} 
\kappa (1 + \delta) & \text{for } \tau_1 < \tau < \tau_2 \\
\kappa (1 - \delta) & \text{for } \text{otherwise}
\end{cases}$$

where $\tau$ is the decimal part of $t$ and $\kappa = 1/(2\delta(\tau_2 - \tau_1) + 1 - \delta)$. Hence transmission is at its lowest at the beginning and end of the year ($\Omega(0) = 1 - \delta$ for the sine wave, $\Omega(0) = \kappa(1 - \delta)$ for the step function) and its highest in the middle of the year ($\Omega(0.5) = 1 + \delta$ or $\kappa(1 + \delta)$ respectively). The mean value of $\Omega$ is 1, and $\delta < 1$. Grenfell and Bolker (1994) modelled measles transmission using a sine wave and $\delta = 0.362$. For the step function model we used $\tau_1 = 0.1615$ and $\tau_2 = 0.9151$, corresponding to high transmission between 28 February and 1 December, and lower transmission throughout the summer.

**The transmission rate**

The basic reproduction ratio ($R_0$) is defined as the average number of secondary cases that would be caused by a typical primary case over its entire infectious period, in a completely susceptible population. According to McLean (1994) $R_0 = 18$ for measles in Africa; Rhodes and Anderson (1996) chose $R_0 = 11$ for their model of measles in the Faroe Islands; and most authors quote $R_0$ in the range of 12-18 (see Anderson and May 1991; Grenfell and Bolker 1994). We set $R_0$ to a range of values for the model without seasonality ($\delta = 0$) and hence fixed the value of $\tilde{B}$. This was done by noting that $R_0$ is equal to the spectral
radius of the next-generation matrix (Diekmann et al 1990). This is the matrix \(M_0\) of secondary cases in the next generation due to primary cases in this generation.

\[
M_0 = \begin{pmatrix}
\frac{\beta_{c_1}N_1}{\mu_1+\gamma} & \frac{\beta_{c_2}N_1}{\mu_1+\gamma} & \frac{\beta_{c_3}N_1}{\mu_1+\gamma} & \frac{\beta_{c_4}N_1}{\mu_1+\gamma} \\
\frac{\mu_2+\gamma}{\beta_{c_1}N_1} & \frac{\mu_2+\gamma}{\beta_{c_2}N_1} & \frac{\mu_2+\gamma}{\beta_{c_3}N_1} & \frac{\mu_2+\gamma}{\beta_{c_4}N_1} \\
\frac{\mu_4+\gamma}{\beta_{c_1}N_1} & \frac{\mu_4+\gamma}{\beta_{c_2}N_1} & \frac{\mu_4+\gamma}{\beta_{c_3}N_1} & \frac{\mu_4+\gamma}{\beta_{c_4}N_1} \\
\mu_4+\gamma & \mu_4+\gamma & \mu_4+\gamma & \mu_4+\gamma
\end{pmatrix}
\]

**Vaccination**

Vaccination rates were based on the proportion of children vaccinated at each of the three ages, and the vaccine efficacy. For example, if a proportion \(q\) of the population are vaccinated, and the vaccine efficacy is 90 percent, then the proportion protected is \(p = 0.9q\). When there is no disease and \(p_1, p_2, p_3\) are constant, the numbers that are susceptible in each age class are:

\[
\begin{align*}
S_1^* &= \frac{\mu_0N_0}{\mu_1} \\
S_2^* &= \frac{(1-p_1)\mu_1S_1^*}{\mu_2} \\
S_3^* &= \frac{(1-p_2)\mu_2S_2^*}{\mu_3} \\
S_4^* &= \frac{(1-p_3)\mu_3S_3^*}{\mu_4}
\end{align*}
\]

The basic reproduction ratio under vaccination is then \(R_v\), which is equal to the spectral radius of:

\[
M_v = \begin{pmatrix}
\frac{\beta_{c_1}S_1^*}{\mu_1+\gamma} & \frac{\beta_{c_2}S_1^*}{\mu_1+\gamma} & \frac{\beta_{c_3}S_1^*}{\mu_1+\gamma} & \frac{\beta_{c_4}S_1^*}{\mu_1+\gamma} \\
\frac{\mu_2+\gamma}{\beta_{c_1}S_1^*} & \frac{\mu_2+\gamma}{\beta_{c_2}S_1^*} & \frac{\mu_2+\gamma}{\beta_{c_3}S_1^*} & \frac{\mu_2+\gamma}{\beta_{c_4}S_1^*} \\
\frac{\mu_4+\gamma}{\beta_{c_1}S_1^*} & \frac{\mu_4+\gamma}{\beta_{c_2}S_1^*} & \frac{\mu_4+\gamma}{\beta_{c_3}S_1^*} & \frac{\mu_4+\gamma}{\beta_{c_4}S_1^*} \\
\mu_4+\gamma & \mu_4+\gamma & \mu_4+\gamma & \mu_4+\gamma
\end{pmatrix}
\]

**The Jacobian matrices**

These represent the linearisation of the model equations about the steady state (again with \(\delta = 0\)). In general the Jacobian matrices are 8 x 8, but when \(I_i = 0\) for \(i = 1, 4\) the eigenvalues of the Jacobian are \(-\mu_i\), for \(i = 1 \ldots, 4\), and the eigenvalues of:

\[
J_0 = \begin{pmatrix}
\beta_{c_1}N_1 - \mu_1 - \gamma & \beta_{c_2}N_1 - \mu_2 - \gamma & \beta_{c_3}N_1 - \mu_3 - \gamma & \beta_{c_4}N_1 - \mu_4 - \gamma \\
\beta_{c_2}N_2 + \mu_1 & \beta_{c_3}N_2 + \mu_2 & \beta_{c_4}N_2 + \mu_3 & \beta_{c_4}N_3 + \mu_4 \\
\beta_{c_3}N_3 + \mu_2 & \beta_{c_4}N_3 + \mu_3 & \beta_{c_4}N_4 + \mu_4 & \beta_{c_4}N_4 + \mu_4 \\
\beta_{c_4}N_4 + \mu_3 & \beta_{c_4}N_4 + \mu_4 & \beta_{c_4}N_4 + \mu_4 & \beta_{c_4}N_4 + \mu_4 \\
\end{pmatrix}
\]

The Jacobian matrix with vaccination, \(J_v\), is the same but with \(N_i\) replaced with \(S_i^*\) wherever it occurs. The eigenvalues of matrices \(J_0\) and \(J_v\) were calculated as checks on the expected system behaviour; if all eigenvalues of \(J_0\) have negative real parts then \(R_0 < 1\), but if one or more eigenvalue has a positive real part then \(R_0 > 1\).

**Parameter values assumed**

The parameter values assumed for the model are shown in Table 10 below.
Table 10. The parameter values assumed for the model

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
<th>Value</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B$</td>
<td>Nett birth rate</td>
<td>57,435 people/year$^{-1}$</td>
<td>NZYB</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Transition rate, infective to immune</td>
<td>52 year$^{-1}$</td>
<td>GB</td>
</tr>
<tr>
<td>$a_1$</td>
<td>Activity level in age class 1</td>
<td>1</td>
<td>MoH</td>
</tr>
<tr>
<td>$a_2$</td>
<td>Activity level in age class 2</td>
<td>3</td>
<td>MoH</td>
</tr>
<tr>
<td>$a_3$</td>
<td>Activity level in age class 3</td>
<td>6</td>
<td>MoH</td>
</tr>
<tr>
<td>$a_4$</td>
<td>Activity level in age class 4</td>
<td>3</td>
<td>MoH</td>
</tr>
<tr>
<td>$q_1$</td>
<td>Proportion vaccinated at 1.25 years</td>
<td>0.84</td>
<td>MoH*</td>
</tr>
<tr>
<td>$q_2$</td>
<td>Proportion vaccinated at 5 years</td>
<td>0.1</td>
<td>MoH*</td>
</tr>
<tr>
<td>$q_3$</td>
<td>Proportion vaccinated at 11 years for first time</td>
<td>0.7</td>
<td>MoH*</td>
</tr>
<tr>
<td>$q_4$</td>
<td>Proportion vaccinated at 11 years for second time</td>
<td>0.9</td>
<td>MoH*</td>
</tr>
<tr>
<td></td>
<td>Efficacy of first vaccination</td>
<td>90%</td>
<td>MoH</td>
</tr>
<tr>
<td></td>
<td>Efficacy of second vaccination</td>
<td>99%</td>
<td>MoH</td>
</tr>
</tbody>
</table>

Sources are NZYB: Statistics NZ (1996), GB: Grenfell and Bolker (1994), and MoH: Ministry of Health (unpublished data). Proportions vaccinated (MoH*) as given in the table are for the current control programme.

Numerical solution

The model was solved numerically using the Rkadapt function of Mathcad Plus 6.0 (MathSoft Inc., 1995). The time period for solution was 1962 < $t$ < 2000, where $t=1962$ implies 1 January 1962, and the number of time steps was set at 1983 (equivalent to a step size of one week). Initially the equations were solved with no vaccination ($P_1(t) = P_2(t) = P_3(t) = 0$) to establish a ‘no-control’ pattern of epidemics. This was used to specify starting values (at 1962) for state variables that gave the correct pre-control epidemic timing, ie, epidemics in 1963, 1965, 1967 and 1969. The equations were then solved using historical vaccination values; since 1970, between 30 percent and 84 percent of children were vaccinated at the age of 1.25 years:

$$Q_1(t) = \begin{cases} 
0.30 & \text{if } 1970 \leq t < 1974 \\
0.50 & \text{if } 1974 \leq t < 1978 \\
0.70 & \text{if } 1978 \leq t < 1979 \\
0.77 & \text{if } 1979 \leq t < 1980 \\
0.82 & \text{if } 1980 \leq t < 1993 \\
0.84 & \text{if } 1993 \leq t \\
0.00 & \text{otherwise} 
\end{cases}$$
and between 10 percent and 40 percent of previously unvaccinated children were vaccinated at five years of age:

\[ Q_2(t) = \begin{cases} 
0.20 (1 - Q_1(t)) & \text{if } 1970 \leq t < 1978 \\
0.30 (1 - Q_1(t)) & \text{if } 1978 \leq t < 1980 \\
0.40 (1 - Q_1(t)) & \text{if } 1980 \leq t < 1987 \\
0.10 \left(1 + \frac{3}{4}(1991 - t)\right) (1 - Q_1(t)) & \text{if } 1987 \leq t < 1991 \\
0.10 (1 - Q_1(t)) & \text{if } 1991 \leq t \\
0.00 & \text{otherwise.}
\end{cases} \]

Since 1992, 70 percent of previously unvaccinated children were vaccinated at 11 years of age:

\[ Q_3(t) = \begin{cases} 
0.70 (1 - Q_1(t) - Q_2(t)) & \text{if } 1992 \leq t \\
0.00 & \text{otherwise}
\end{cases} \]

and 90 percent of previously vaccinated children were given a second vaccination:

\[ Q_4(t) = \begin{cases} 
0.90 (Q_1(t) + Q_3(t)) & \text{if } 1992 \leq t \\
0.00 & \text{otherwise}
\end{cases} \]

The effective vaccination proportions are therefore:

\[
\begin{align*}
P_1(t) &= 0.9Q_1(t) \\
P_2(t) &= 0.9Q_2(t) \\
P_3(t) &= 0.9Q_3(t) + 0.099Q_4(t)
\end{align*}
\]

The final multiplier is 0.099 because \( Q_4 \) are vaccinated for the second time. The vaccine is 90 percent effective first time, 99 percent effective second time, but only 10 percent of those previously vaccinated remain susceptible hence, 9.9 percent are transferred from the susceptible to immune \((R)\) class.

The process was repeated using different values of \( \varepsilon, \delta, \) and \( R_0 \) until combinations were found that gave an output that mirrored historical epidemic data. The solution was then continued until the year 2000.

## Results

### Parameters and other quantities derived

Parameters fixed as a consequence of those that were assumed are shown in Table 11 below.

### Table 11. Parameter values derived from the model

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N_1 )</td>
<td>Number in age class 1</td>
<td>4.308 x 10^7 people</td>
</tr>
<tr>
<td>( N_2 )</td>
<td>Number in age class 2</td>
<td>2.154 x 10^7 people</td>
</tr>
<tr>
<td>( N_3 )</td>
<td>Number in age class 3</td>
<td>3.446 x 10^7 people</td>
</tr>
<tr>
<td>( N_4 )</td>
<td>Number in age class 4</td>
<td>8.041 x 10^7 people</td>
</tr>
</tbody>
</table>
The parameter values that produced a reasonable agreement between the occurrence of epidemics and the observed historical pattern were $e = 0.4$ and $\tilde{\beta} = 2.002 \times 10^{-7}$, leading to $R_0 = 12.8$ and $R_v = 2.85$ with current vaccination procedures. A step function with $d = 0.2$ was used to model variations in transmission due to seasonal effects. The corresponding spectral radii of the Jacobian matrices $J_0$ and $J_v$ were 615 and 96.3 respectively.

**Numerical results**

Table 12 shows the epidemics predicted to occur in the years 1962 to 2000, compared with the actual epidemics that occurred prior to 1996.

**Table 12. Observed and predicted epidemic years**

|----------|------|------|------|------|------|------|------|------|------|------|

The results from the simulations for $S$, the total number of susceptibles in age classes 1–4, and $I$, the total number of infectives in age classes 1–4, are shown in Figure 12, and Figure 13 shows the age class distribution over time for the susceptible population. In addition, the cumulative numbers of susceptibles in each age class immediately prior to the 1969, 1991 and 1997 epidemics are shown in Table 13, and the drop in numbers of susceptibles during these epidemics is shown in Table 14.
**Figure 12.** Predicted numbers of susceptibles and infectives, all ages combined

Predicted numbers of susceptibles and infectives in the combination of age classes 1–4, giving the age range 0.5 years to 25 years, for the years 1962 to 2000. The upper trace shows the numbers of susceptibles (thousands) and the lower trace the numbers of infectives (hundreds). On the time scale 62 equals 1 January 1962.

**Figure 13.** Predicted numbers of susceptibles and infectives by age class

Predicted numbers of susceptibles (hundreds of thousands) in age classes 1–4 for the years 1962 to 2000. The traces are (reading from bottom to top) $S_1$, $S_2$, $S_1 + S_2$, $S_1 + S_2 + S_3$, $S_1 + S_2 + S_3 + S_4$. Hence the gaps between the traces represent $S_1$, $S_2$, $S_3$ and $S_4$ respectively. The age classes are 1:0.5-1.25 years, 2:1.25-5 years, 3:5-11 years, 4:11-25 years, hence the uppermost trace is identical to that in Figure 12. On the time scale 62 equals 1 January 1962.
Table 13. Predicted cumulative numbers (thousands) of susceptibles at different ages immediately prior to the 1969, 1991 and 1997 epidemics.

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt; 0.5 years</th>
<th>0.5-1.25 years</th>
<th>&lt; 5 years</th>
<th>1.25-5 years</th>
<th>&lt; 11 years</th>
<th>5-11 years</th>
<th>&lt; 25 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1969</td>
<td>28.7</td>
<td>69.8</td>
<td>163.1</td>
<td>121.2</td>
<td>198.5</td>
<td>199.3</td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>28.7</td>
<td>71.4</td>
<td>168.0</td>
<td>129.6</td>
<td>206.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>28.7</td>
<td>71.9</td>
<td>163.7</td>
<td>118.6</td>
<td>199.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 14. Predicted drop in numbers (thousands) of susceptibles at different ages during the 1969, 1991 and 1997 epidemics.

<table>
<thead>
<tr>
<th>Year</th>
<th>0.5-1.25 years</th>
<th>1.25-5 years</th>
<th>5-11 years</th>
<th>11-25 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1969</td>
<td>10.8</td>
<td>55.4</td>
<td>29.3</td>
<td>5.1</td>
</tr>
<tr>
<td>1991</td>
<td>9.0</td>
<td>21.5</td>
<td>29.6</td>
<td>15.3</td>
</tr>
<tr>
<td>1997</td>
<td>9.1</td>
<td>19.4</td>
<td>27.7</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Discussion

We have used a model to explore the dynamics of measles in New Zealand, and the consequences of the current vaccination policy. In constructing the model we have assumed an unchanging population size and structure, with a constant birth rate and no deaths prior to the age of 25 years. The derived sizes of age classes 1–4 (Table 11) differ from the current sizes of those classes (43,058, 220,417, 332,020, 757,140, Tobias, personal communication) by no more than 6.2 percent. Similarly the maximum death rate for these classes is $8.8 \times 10^{-5}$ year$^{-1}$ (class 4, New Zealand Official Yearbook (Statistics NZ 1996)), which is negligible compared to the transition rate from that class ($\mu_4$, see Table 11). The results presented in this paper should therefore be viewed as predictions for a hypothetical population with these characteristics, with the suggestion that the model population is sufficiently near to the New Zealand population, with its changing birth rate and age structure, for the results to be similar to those observed.

In the model we have used highly simplified mechanisms for disease transmission. It was assumed that each age class mixed homogeneously within itself, with a lesser degree of contact between age classes. The classes were chosen for convenience, the boundaries between them being the ages at which vaccination may occur. The step function with $\delta = 0.2$ was used to introduce seasonality to the model, purely on the basis that it gave the best fit to the observed pattern. Similarly values of $R_0$ and $\epsilon$ were selected on the basis of the best historical fit to data. Initial conditions at 1962 were obtained by solving the model with no vaccination over a 70-year period so that a regular pattern of biannual epidemics developed. The precise epidemic timing was found to be sensitive to the initial conditions, as well as to the values of $R_0$ and $\epsilon$ chosen. Hence it is the overall pattern of epidemics, and not the precise year in which they occurred, that is important when considering the results.

Although the qualitative nature of the predictions remains unchanged for small variations in the parameter values, the precise timing of epidemics is sensitive to changes in $R_0$, $\epsilon$, and $\delta$. In addition, we used a step function to model the effect of seasonality with transmission rather than a sine wave (see ‘The Infection Process’), which is consistent with changes in transmission rates being due to closer contact during the school year, rather than being dependent on weather. Recently Keeling and Grenfell (1997) have shown that a measles model is less prone to fade out in the inter-epidemic period if the time in the infectious period is normally rather than exponentially distributed, and Ferguson et al (1996) obtained a similar result by assuming a finer age structure (more classes). These are refinements that could be applied to our model in the future.
The results presented in Figure 12 clearly show that an epidemic is ‘triggered’ when the number of susceptibles has built up to critical level. This number (approximately 200,000) is consistent with critical community sizes found by other authors. During the epidemic the size of the susceptible pool drops rapidly, matched by a sharp peak in the number of infectives. The results show an initial inter-epidemic period of two years, lengthening to six or more years following the introduction of vaccination (see also Table 12). The model fails to predict the 1977 epidemic, consequently shows the 1980 epidemic a year early, and then predicts the next epidemic late in 1991, spilling over into 1992 (as occurred). It predicts that the next epidemic will occur in 1997.

The apparent change in the critical number of susceptibles required to trigger an epidemic, and in the epidemic size following vaccination, is due to changes in the age structure of the susceptible population caused by the control programme. The age structure of the susceptible population is shown in Figure 2, and the peak numbers of susceptibles prior to the 1969 and 1997 epidemics are shown in Table 13. It can be seen that the 1969 epidemic occurred mainly in the under-11 age classes, whereas for the 1997 epidemic the 11-25 year age class plays a more significant role. As vaccination at 11 years was introduced in 1992, it is those now over 16 years of age (not shown separately) that will now make the most significant contribution to the epidemic.

Finally, the results presented in Table 14 confirm the changing age structure of epidemics. The drop in the number of susceptibles during an epidemic is approximately equal to the number of measles cases, and the table clearly shows a change towards the older age classes between the last epidemic to occur prior to vaccination (1969) and the last recorded epidemic (1991).

**Conclusions**

Our SIR model for the dynamics of measles in New Zealand predicts that an epidemic would occur every two years in the absence of control measures, and that the current vaccination programme has increased the inter-epidemic period to six years. This is consistent with observations.

The model demonstrates that an epidemic occurs when the number of susceptibles in the population reaches a threshold. However, the vaccination programme has changed the age structure of the susceptible population and hence the threshold at which an epidemic is triggered.

The model demonstrates that prior to the control programme, measles epidemics occurred primarily in the 1.25–11-year age classes, but under the vaccination programme older children and young people play a more important role in epidemics.

The predicted timing and sizes of measles epidemics are very sensitive to assumed values of the basic reproduction ratio, $R_0$, and the assumed mixing pattern between age classes. The most likely scenario is a current inter-epidemic period of six years, indicating that the next epidemic would occur in 1997 if the current pattern of intervention continued. However, the estimate represents only the mean of a stochastic process with a large variance, and a later occurrence of the next epidemic would still be consistent with the results.

The model could be used to explore the effects of different intervention options designed to prevent future measles epidemics, for example changing the timing of measles vaccinations from 11 years to five years, or a pulse immunisation programme to reduce the size of the pool of susceptible children and/or adolescents.
References


