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Tēnā koe s 9(2)(a)

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) to the Ministry of Health (the Ministry) on 30 May 2022. You requested:

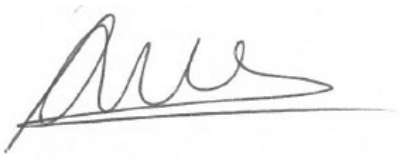
> *"Can I have a copy of the following report please?*
> *Roberts MG. 2004. A Mathematical Model for Measles Vaccination: Internal report to the Ministry of Health, New Zealand."*

Please find this report attached. This has been released to you with some information withheld under section 9(2)(a) of the Act to protect the privacy of natural persons. I have considered the countervailing public interest in release in making this decision and consider that it does not outweigh the need to withhold at this time.

I trust this information fulfils your request. Under section 28(3) of the Act, you have the right to ask the Ombudsman to review any decisions made under this request. The Ombudsman may be contacted by email at: info@ombudsman.parliament.nz or by calling 0800 802 602.

Please note that this response, with your personal details removed, may be published on the Ministry website at: www.health.govt.nz/about-ministry/information-releases/responses-official-information-act-requests.

Nāku noa, nā



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A mathematical model for measles vaccination *

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Abstract

A previously-published model of the dynamics of measles infections in New Zealand is used to evaluate the present vaccination strategy of MMR1 at 15 months and MMR2 before 5 years. The results show that achieving coverage of 90% or better at both vaccination opportunities is necessary if future epidemics of measles are to be prevented.

*Report prepared for *The Ministry of Health, Wellington.*

1 Introduction

The original mathematical model for the dynamics of measles in New Zealand was prepared in 1996 (Tobias & Roberts 1998). It successfully predicted the 1997 epidemic, which was curtailed by a mass vaccination campaign (Mansoor et al 1998; Roberts & Tobias 2000). A subsequent extension of this work in 1998 showed that the then current schedule of MMR1 at 15 months and MMR2 at 11 years was insufficient to prevent further epidemics. The schedule was changed in 2000 with MMR2 now being administered before 5 years (Anon. 2002a).

A variety of similar models for measles vaccination strategies have been developed by other authors for various regions (Agur et al 1993; Babad et al 1995; Edmunds et al 2000; Gay et al 1998; Wallinga et al 2001). These have invariably been based on sets of nonlinear differential equations, and the conclusions reached have been similar. The differences in the models have been in the details of the representation of the infectious period, and in the ways in which the age and contact structures of the population have been specified. As the time-course of a measles epidemic is short compared to that of demographic changes, details of the epidemic process are not relevant when examining population level changes over many years. In fact, it has been shown (Diekmann & Heesterbeek 2000) that the number infected in an epidemic depends only on the basic reproduction number (see below), and the numbers that are initially susceptible in each sub-population. It is therefore important to have a realistic representation of the population contact structure. The Royal Society (UK) report on the 2001 epidemic of Foot and Mouth Disease advocated that contact structures for infectious diseases should be described before epidemics occur, so that models may be speedily prepared. The report presented the

New Zealand measles model as an example of the successful use of modelling in epidemiology (Anon. 2002b).

The quantity that determines whether an epidemic will occur is the basic reproduction number of the infection, R_0. This is defined as the expected number of secondary infections that would arise from a single primary infection introduced into a fully susceptible population (Anderson & May 1991; Diekmann & Heesterbeek 2000). Clearly if $R_0 > 1$ an epidemic will occur following an introduction of infection. The best estimate we had for measles in New Zealand was $R_0 = 12.8$, the change in the birth rate (56780 p.a. in 2004, www.stats.govt.nz) could have reduced this slightly to $R_0 = 12.5$ (see results section). Recall that R_0 is calculated in the absence of control measures. We are interested in two related quantities:

- The basic reproduction number of the infection under vaccination, R_v, is the expected number of secondary infections that would arise from a single primary infection introduced into a vaccinated population at equilibrium. This is a robust indicator of the performance of a vaccination schedule. If $R_v < 1$ epidemics are prevented.
- The case reproduction number of the infection at time t, R_t, is the expected number of secondary infections that arise from a single infection at a particular time. This depends on the number in the population who are susceptible, either through prior infection or vaccination.

The dynamics of the process may be summarised as follows. Assume that the population has $R_t < 1$ for measles. As the number of susceptibles in the population increases, through children that miss their scheduled immunisations, then R_t increases. An epidemic occurs when R_t has increased above one. During the epidemic the number of susceptibles and hence R_t decreases.

In order to assess the efficacy of the vaccination campaign in the absence of precise information on levels of vaccination coverage, we assumed a range of plausible coverages at MMR1 and MMR2 and determined the corresponding value of R_v for each. For selected combinations we also numerically solved the model over a period of 150 years, not as a prediction of what will happen over that time period but in order to determine what the expected frequency of epidemics would be if this level of vaccination were to be in maintained. In all cases, if $R_v < 1$ epidemics are prevented.

2 Method

For this exercise we modelled the New Zealand population in the same way as in Roberts & Tobias (2000). We approximated the population structure by assuming that the birth rate was constant, and that deaths before the age of 25 could be neglected. Hence the four age groups active in the epidemic have constant size. The age groups were taken as 6 - 15 months, 15 months - 5 years, 5 years - 11 years and 11 years - 25 years. Hence MMR1 is applied as children pass from the first to the second group, and MMR2 from the second to the third. The same contact matrix was used as in Roberts & Tobias (2000). For a range of vaccination coverages for MMR1 and MMR2 (see Table 1) the basic reproduction number of the infection under vaccination, R_v, was calculated. In addition, for each combination of coverages the differential equation model was solved numerically until the epidemics settled into a regular pattern, and the inter-epidemic period was determined.

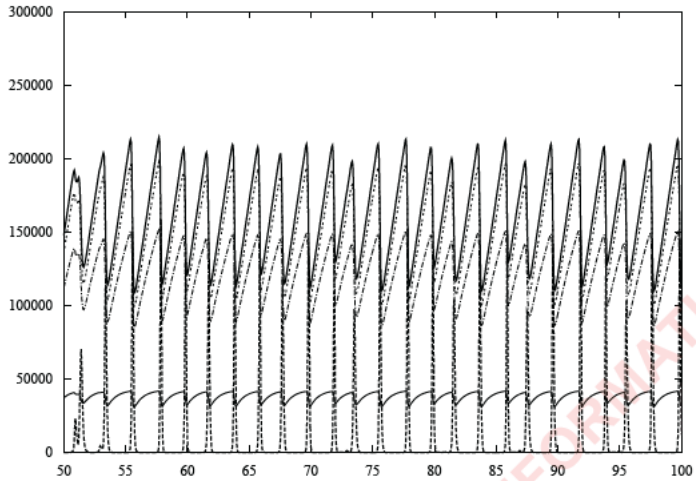
3 Results

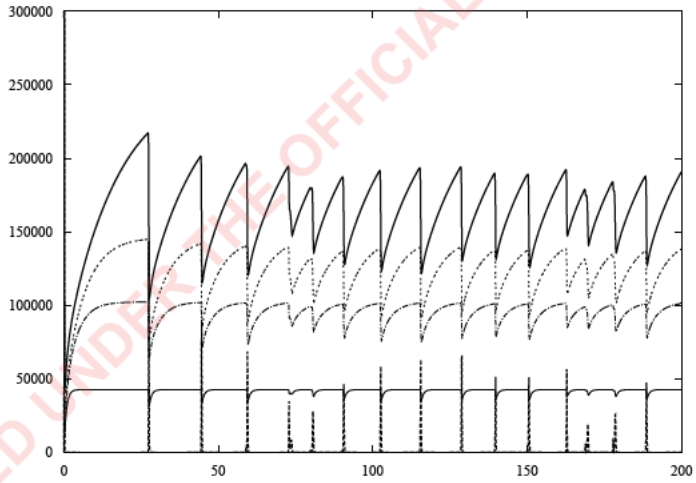
Calculated values of R_v for the various coverage levels of MMR1 and MMR2 that were considered are presented in Table 1.

	MMR1 coverage			
MMR2 coverage	80%	85%	90%	95%
60%	1.72^{2}	1.45^{5}	1.18^{7}	0.92
70%	1.43^{3}	1.21^{6}	0.99	0.77
80%	1.14^{4}	0.97	0.79	0.62
85%	1.00^{8}	0.85	0.70	0.55
90%	0.87	0.74	0.61	0.48
95%	0.75	0.64	0.53	0.42

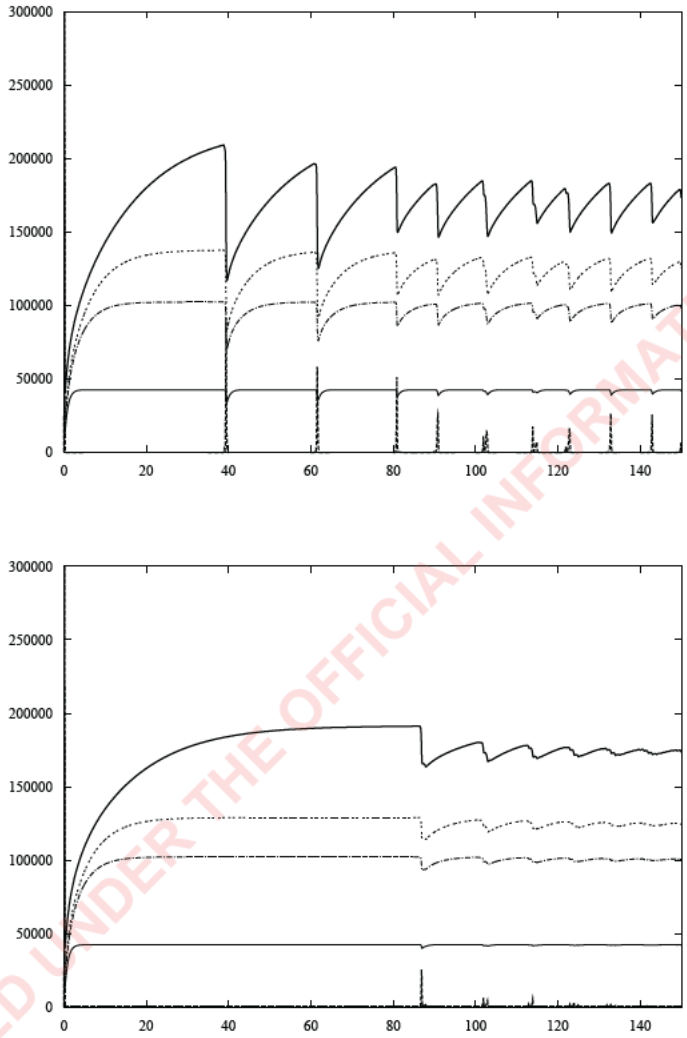
Table 1: The basic reproduction number of the infection under vaccination, R_v, for various coverage levels of MMR1 and MMR2. Superscripts refer to the figure number where numerical solutions are presented. If $R_v < 1$ then epidemics will not occur.

When no vaccination is applied, the system settles down to an epidemic every two years. This corresponds to an estimated $R_0 = 12.5$, similar to that which was observed in New Zealand in the 1960s (see Fig.1). The minimum level of vaccination investigated (MMR1 = 80%, MMR2 = 60%) resulted in $R_v = 1.72$ and a pattern of epidemics settling down to one every 12 years (see Fig.2). The other combinations of MMR1 and MMR2 coverage levels that resulted in $R_v > 1$ all resulted in epidemics recurring at intervals of between 10 and 20 years (Figs. 3-7). All other combinations of MMR1 and MMR2 resulted in $R_v \leq 1$ and the system settling down to a steady uninfected state with no epidemics, see Table 1 and Fig.8 for an example.

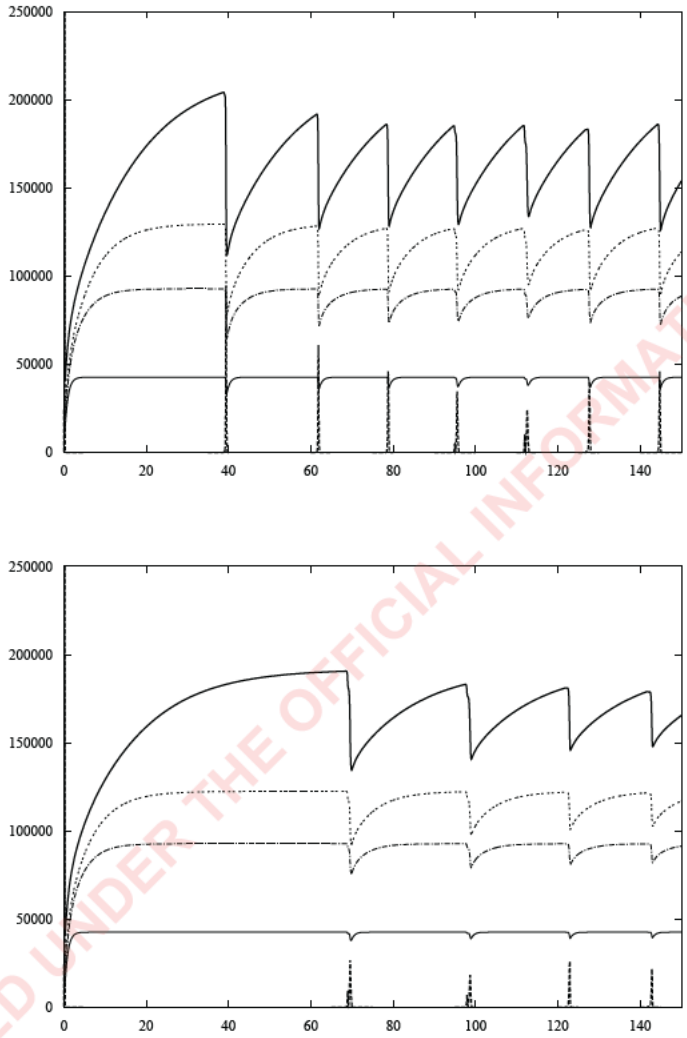




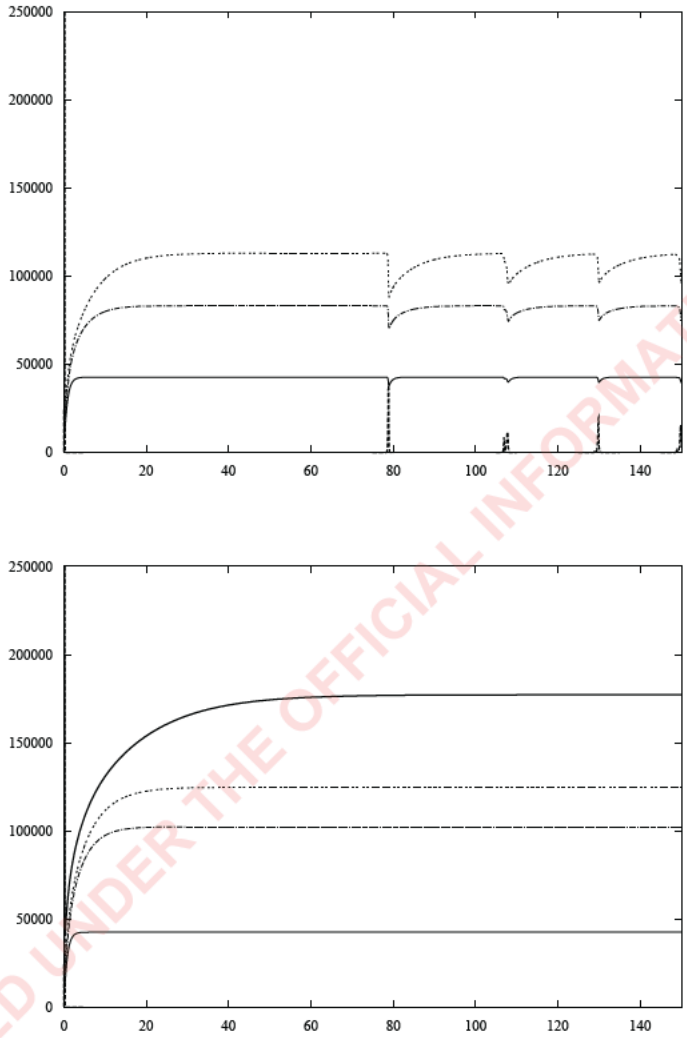
Figures 1 & 2. The epidemic pattern with no vaccination (top) and with MMR1 = 80%, MMR2 = 60% (bottom). The continuous curves show the cumulative numbers of susceptibles in the population in the age groups 6 months-15 months, 15 months - 5 years, 5 years - 11 years and 11 years -25 years, as determined by the model. The spikes show the numbers infectious during epidemics ($\times 10$).



Figures 3 & 4. The epidemic pattern with with MMR1 = 80%, MMR2 = 70% (top) and with MMR1 = 80%, MMR2 = 80% (bottom). The continuous curves show the cumulative numbers of susceptibles in the population in the age groups 6 months-15 months, 15 months - 5 years, 5 years - 11 years and 11 years -25 years, as determined by the model. The spikes show the numbers infectious during epidemics ($\times 10$).



Figures 5 & 6. The epidemic pattern with MMR1 = 85%, MMR2 = 60% (top) and with MMR1 = 85%, MMR2 = 70% (bottom). The continuous curves show the cumulative numbers of susceptibles in the population in the age groups 6 months-15 months, 15 months - 5 years, 5 years - 11 years and 11 years -25 years, as determined by the model. The spikes show the numbers infectious during epidemics ($\times 10$).



Figures 7 & 8. The epidemic pattern with MMR1 = 90%, MMR2 = 60% (top) and with MMR1 = 80%, MMR2 = 85% (bottom). The continuous curves show the cumulative numbers of susceptibles in the population in the age groups 6 months-15 months, 15 months - 5 years, 5 years - 11 years and 11 years -25 years, as determined by the model. The spikes show the numbers infectious during epidemics ($\times 10$).

4 Discussion

The model developed by Roberts & Tobias (2000) supported the change in the immunisation schedule that took effect in January 2001, at which time MMR2 was changed from delivery at 11 years to delivery before the age of five. These results were in line with those obtained by other authors, for example: Babad et al (1995) advocated a two-dose schedule for England and Wales, with the second vaccination given at age four; and Gay et al (1998) recommended a second vaccination at either 18 months or five years, to complement the first vaccination at 12 months in Canada. In addition, Agur et al (1993) found that vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals would prevent epidemics in Israel. These authors all agree that two vaccinations at no less than five years apart are necessary to prevent measles epidemics.

A different approach was taken by Wallinga et al (2001). These authors took existing policies in eight European countries and estimated the coverage rates required to reduce R_v below one. They found that results depended on the age at delivery, but no strategy succeeded if coverage rates were below approximately 87%. Our results presented in Table 1 are similar where coverage is assumed to be the same at MMR1 and MMR2. The results also show the absolute necessity of maintaining high coverage rates in order to prevent future epidemics. It is difficult to estimate the proportion of the school-age population that have been effectively immunised, but this is continuously being diluted by children who are not immunised. Wallinga et al (2000) noted that in Italy only MMR1 was offered at 18 months with no second vaccination opportunity, and that under most plausible assumptions for contact rates even 100% coverage would be insufficient to prevent epidemics.

Our final conclusion must depend on how much faith is placed in the model. The results are consistent with those of other authors, and from Table 1 it could be deduced that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics. However, a study by Glass et al (2004) in the Netherlands showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection. Our results indicate that overall targets or 90% or more will need to be achieved to prevent future epidemics in New Zealand.

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Appendix

The next generation matrix was calculated in a slightly different way to that in Roberts & Tobias (2000). In the absence of demographic influences the matrix is defined by

$$K_{i,j} = \frac{\beta C_{i,j} S_i}{\mu_j + \gamma}$$

where S_i is the steady state number susceptible in age group i. Correcting the next generation matrix for demographic influences yields

$$\tilde{K}_{i,j} = K_{i,j} + \frac{p_j \mu_j}{\mu_j + \gamma} K_{i,j+1}$$

for $j = 1, 2, 3$ and $\tilde{K}_{i,4} = K_{i,4}$. In the absence of vaccination the $p_j = 1$. In the presence of vaccination p_1 and p_2 are calculated from the MMR1 and MMR2 coverages and the vaccine efficacies (as percentages):

$$p_1 = 1 - \frac{\mathrm{EFF1}}{100}\frac{\mathrm{MMR1}}{100} \qquad p_2 = 1 - \frac{\mathrm{EFF2}}{100}\frac{\mathrm{MMR2}}{100}$$

All othe symbols are as in Roberts & Tobias (2000). The change made a small difference to the values of R_0 and R_v returned, but this was less than the round-off error in Table 1 and hence did not affect the results.