Predicting the next measles epidemic

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Key points

- A measles epidemic in 1997 was interrupted by a mass vaccination
- Estimates are available of both the number of cases and the number of effective vaccinations
- These data suggest that measles may be eliminated from New Zealand if current vaccination levels are maintained
- The mathematical model used in this study produces results in good agreement with the Ministry of Health's model

ABSTRACT

New Zealand experienced a measles epidemic in 1997 that was interrupted by a mass immunisation campaign. Recent mathematical modelling by the Ministry of Health has suggested that changes to the immunisation schedule are necessary if elimination of this parasite is to occur.

In this paper a different S-I-R model is used to consider various possible impacts of the 1997 epidemic and mass immunisation campaign on the period between epidemics, and on the prospect of eliminating measles from New Zealand.

Good agreement with the ministry's model is obtained for those cases where the 1997 mass immunisation campaign is not predicted to result in the elimination of measles before the next epidemic. However, measles may be eliminated in the next few years without the occurrence of a further epidemic if current vaccination levels are maintained.

This conclusion is sensitive to the value of key estimated parameters – the number of children immunised as part of the mass immunisation campaign in 1997, and the number of cases of measles that occurred in the interrupted 1997 epidemic.

INTRODUCTION

New Zealand experienced a measles epidemic in 1997 that was interrupted by a mass vaccination campaign. Recently there have been calls to eliminate measles from New Zealand1 and it seems likely that New Zealand will move the second dose of MMR from age 11 to somewhere around school entry at age five.2 A recent mathematical modelling exercise3 predicted that such a change would facilitate achievement of this goal.

Accurate predictions of the timing of the next measles epidemic, if New Zealand persists with its current immunisation strategy of two doses of MMR at ages 15 months and 11 years, provide a time-frame within which the new policy needs to be implemented.

The Ministry of Health's modelling3 predicts the next measles epidemic will occur in 2003 or 2004 if the measles vaccination schedule is not changed and if coverage is not improved. This implicitly assumes the number of susceptibles who were moved to the recovered (immune) class in 1997, as the result of either natural infection or immunisation, was equal to the number who would have been moved had the epidemic not been modified by the mass vaccination programme.

The object of this paper is to explore the sensitivity of the predicted six to seven year inter-epidemic period to different possible values of "the number of susceptibles who were movedssssss to the recovered class in 1997". We are interested in the question, what would the prediction be if more, or fewer, susceptible individuals had been infected in the epidemic or reached by the immunisation campaign? The available data provide only indirect estimates of both these variables. The actual number of cases, or of susceptible children immunised, may be quite different to that estimated. How would this affect the prediction?

There is consensus among mathematicians and epidemiologists that the inter-epidemic period represents the time it takes for the number of susceptibles in a host population to restock from the post-epidemic trough to a pre-epidemic peak. Earlier work by Tobias and Mansoor4 has suggested that some 60,000 susceptibles are infected in a New Zealand measles epidemic. The inter-epidemic period then is the time it takes to introduce 60,000 susceptibles into the host population. Introduction occurs by births, minus immigration, successful vaccination and secondary vaccine failure.

One intuition is that, if an uninterrupted 1997 epidemic would have infected 60,000 susceptibles and if the number actually moved into the recovered class in 1997 was only 30,000 (perhaps because only 5000 were infected and a further 25,000 were effectively vaccinated), then only 30,000 susceptibles need to be added to the host population before a further measles epidemic will occur. A rough guess would be that if this were the case the next measles epidemic would occur in 2000 or 2001, as immediately prior to 1997 epidemics had occurred at six-year intervals.

This paper generates tables in which various possibilities for the number of susceptibles actually moved into the recovered class in 1997 are matched to predicted inter-epidemic periods.

METHODS

The difference equation model used in this paper has previously been described.5,6 It provides good estimates of the inter-epidemic periods in New Zealand from 1948-1997. 6,7 For this paper we have used an approximation to the model that is based on the principle of mass action.8 This approximation has the desirable effect that, when the number of infectives is plotted against the number of susceptibles, closed orbits are produced.

Such a closed orbit (see Figure 1) corresponds to an epidemic cycle. There is a long period during which disease incidence is low, and a considerably shorter period of greatly increased incidence corresponding to an epidemic, before the period of low incidence is re-entered.

The figures do not provide any information about how long the process spends in each part of the orbit.

Figure 1 represents an idealised New Zealand. The number of births per year in this system is 54,000. All hosts live to age 65 and then die. Some 75 per cent of newborns are effectively vaccinated against measles, which has a basic reproductive rate of 16. In this system the inter-epidemic period is 6.54 years. The key thing to notice about Figure 1 is that the system returns to its starting point and retraces the same path after each epidemic.

A mass vaccination campaign will interrupt the epidemic cycle and break the closed orbit. The number of susceptibles is reduced by an amount equal to the number of effective vaccinations of susceptibles. The number of infectives (unchanged) and the reduced number of susceptibles provide the starting point for a new orbit. The period of this new orbit is calculated by observing how long it takes the system to traverse it. Elimination of the virus corresponds to the number of infectives falling below "one".

The new orbit depends on how many susceptibles are vaccinated and when in the epidemic cycle this takes place. We have considered two interruption points in the epidemic cycle corresponding to 5000 or 30,000 cases of natural infection in 1997 and various possible numbers of sus-ceptibles effectively vaccinated in 1997.

RESULTS

Tables 1 and 2 predict the inter-epidemic period of measles in New Zealand given that either 5000 or 30,000 cases of natural infection occurred in 1997 and for various numbers of susceptibles effectively vaccinated in the mass campaign.

If the 1997 epidemic was severely interrupted by the mass vaccination campaign so only 5000 rather than the expected 60,000 cases occurred, then the next measles epidemic would not be expected before 2002.

If the 1997 epidemic was interrupted by the mass vaccination campaign to the extent that only half the cases that would otherwise have occurred did so, the next measles epidemic would not be expected before 2003.

Importantly, measles may be eliminated as the result of the 1997 mass vaccination campaign if enough susceptibles were effectively vaccinated by that campaign.

This elimination would not be observed immediately. Rather, the incidence of measles would decrease from 1997 (with unmodelled seasonal variation) until, within a few years, the predicted number of cases would fall below one for a sustained period.

If there were only 5000 cases in the interrupted 1997 epidemic and if the mass vaccination campaign effectively vaccinated 70,000 or more susceptibles then elimination is predicted by this modelling exercise. If there were 30,000 cases and 50,000 or more successful vaccinations then elimination is also predicted.

Figure 2 demonstrates the move from the orbit of Figure 1 to a new orbit, as the result of a mass vaccination programme of short duration. In this figure, the shift (represented by the dashed straight line) is produced by vaccinating 70,000 children after 5000 cases of measles have occurred.

Although it is not obvious from the figure, there are never fewer than 10 infectives on the original orbit. On the new, wider orbit (represented by the continuation of the dashed line) there is a prolonged period when the number of infectives is predicted to be less than one. This can be seen more clearly in Figure 3 (where a log scale has been used for the number of infectives) and corresponds to elimination of measles in New Zealand.

A key point is that the model predicts elimination well before it occurs. If one point on a closed orbit is known, all the future ones can be calculated.

DISCUSSION

The model used in this exercise is a simple difference equation one that partitions the human population into susceptible, infective, and recovered classes. It has produced predictions in close agreement with those of the Ministry of Health.[2] More than that, it has raised the possibility that the 1997 mass vaccination campaign has perturbed the host-parasite system to the extent that measles will be eliminated from New Zealand in the near future if current vaccine coverage is maintained.

However, to establish that possibility two data are required – the number of cases of measles which occurred in 1997 and the number of susceptibles effectively vaccinated in the 1997 mass campaign.

There were 2169 notified cases of measles in 1997.[9] If one believes that about half of all cases were reported then the predicted time until the next epidemic and the number of successful vaccinations to trigger elimination are as in Table 1.

There were 314 hospitalisations due to measles in 1997. As there were some 640 hospitalisations in the 1991 epidemic[4] and an estimated 60,000 cases[4] this suggests the 1997 epidemic, although interrupted, resulted in the infection of about 30,000 susceptibles. However, there was only one hospitalisation coded as measles encephalitis compared to 10 in 1991.[9]

Table 2 gives the predicted inter-epidemic period and the required number of successful vaccinations to trigger elimination for the case where the 1997 epidemic was about half the (estimated) size of the 1991 one.

The Ministry of Health's modelling [3,4] estimates there were about 135,000 susceptible children from six months to 12 years of age at the beginning of 1997. Jones et al[10] estimated that in Auckland 57 per cent of children aged six to11 months were vaccinated, as were 56 per cent of those aged six to 10 years.

If these figures are accurate and if the vaccination estimates apply both nationally and to children in the one to five year age group, then inspection of the tables reveals New Zealand can expect, or is very close to achieving, the elimination of measles in the next few years if current vaccination rates are maintained.

We may be, as represented by Figures 2 and 3, on an orbit where the number of infectives will drop below one for a sustained period of time.

This has implications for public health purchasing in New Zealand. Serological testing of all suspected cases of measles and ring vaccinating around cases is currently recommended and could be critical if elimination is to occur. An extended vaccination campaign in 2000 in poorly vaccinated subpopulations might eliminate the remaining reservoirs of infection.

In summary, this paper has extended the Ministry of Health's recent measles modelling exercises by considering different possible starting values for the next epidemic cycle. Our results are in good agreement with those of the ministry for cases where measles will not be eliminated before the next epidemic.

Available data from the 1997 epidemic and associated mass vaccination campaign suggest that, as a result of the 1997 mass immunisation campaign, measles might be eliminated from New Zealand within the next few years if current immunisation rates are maintained.

Mathematical modelling of measles epidemics in New Zealand can only provide tentative conclusions. This model does not incorporate seasonal effects, age-related differences in transmission or population heterogeneity and so may not predict events in a real New Zealand if such features are influential. The Ministry of Health's model is more complex, but it has been necessary to provide "best guess" values for most parameters. It may model a different reality than New Zealand if those estimates are wrong.

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