

An earlier 2nd dose of MMR? Insights from modelling...

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Abstract

The Measles Control Campaign and subsequent high rates of infant measles-mumps-rubella (MMR) vaccination have led to the elimination of endemic measles transmission in Australia. Currently, the second dose of MMR vaccine is scheduled at 4 years of age. The likely availability of a combined MMR-Varicella (VZ) vaccine, as well as disease control objectives for measles, make it timely to look at moving the age of the 2nd dose of MMR down. This study looked at the effect of lowering the 2nd dose of MMR to 18 months of age on population immunity as measured by the value of the reproduction number in Australia. We found that such a shift would provide better population immunity until 2026, even if two-dose coverage falls from its current 85% to 76%.

We also considered the impact that waning immunity might have on elimination for both the current schedule and the proposed change, and find that for low rates of waning, the change of schedule would be beneficial provided two-dose coverage remains at 2006 (85%) levels. For high rates of waning, both schedules would fail to maintain elimination past 2011.

Methods

The reproduction number R is estimated on the basis of three sources of data (see Figure 1 for importance of R in elimination). The matrix used is shown in Equation 1.

•UK/Canada estimates of measles transmission between different age groups.

•Australian Childhood Immunisation Register (ACIR) data for measles coverage. For base case assumptions of MMR2 coverage when given at 18 months, we used DTPa coverage figures for the period when the 4th dose was given at 18 months (88% by 2 years, 91% by 4 years).

•Data from the 2002 measles serosurvey conducted by NCIRS and CIDM public health.

We assumed that the schedule change occurred at the beginning of 2007.

Waning of immunity is assumed to apply only to individuals born later than 1995 and to begin only once children reach 6 years of age.

$$(R_{0ij}) = \begin{pmatrix} 0.96 & 0.43 & 0.43 & 0.43 & 0.43 \\ 0.48 & 4.99 & 1.80 & 0.48 & 0.48 \\ 0.48 & 1.80 & 7.48 & 0.48 & 0.48 \\ 0.48 & 0.48 & 0.48 & 8.73 & 0.48 \\ 5.23 & 5.23 & 5.23 & 5.23 & 5.23 \end{pmatrix}$$

Equation 1: Next generation matrix

Introduction

Elimination of endemic measles transmission has occurred in Australia¹, largely due to the Measles Control Campaign (MCC) in 1998 and subsequent high rates of infant measles-mumps-rubella (MMR) vaccination. Projections based on simple mathematical models of measles transmission indicate that elimination status will be maintained until at least 2012 if coverage with MMR vaccine remains at present levels².

While this is encouraging, there is still potential for improving the timeliness of measles vaccination in Australia. Currently, the second dose of MMR vaccine is scheduled at 4 years of age, following a first dose at 12 months. This study considered what effect lowering the age of the 2nd dose of MMR (MMR2) to 18 months would have on population immunity and the elimination status of Australia in the near future. The recent introduction of varicella (VZ) vaccine at 18 months of age in the Australian schedule may facilitate such a change, either through separate delivery of MMR2 and VZ or the combined Measles Mumps Rubella Varicella (MMRVZ) vaccine.

In addition to examining sensitivity to vaccine coverage, we allowed for waning of vaccine-induced immunity³ and examined how this affected elimination status, and immunity amongst the population never exposed to wild-type virus.

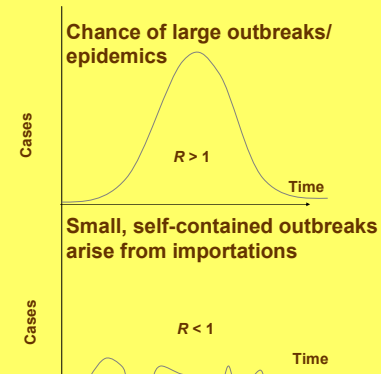


Figure 1: Qualitative behaviour due to R

Results

Our model suggested that a switch to a second dose at 18 months would enhance immunity in the 0-4 age-group: we find that the proportion susceptible in the 0-4 age-group falls from 26% to 21%, primarily because of better coverage in 2-4 year age band. The effect on immunity in younger cohorts is presented in Figure 2.

Figure 3 graphs R over time, and shows that R would be lower until 2021 with a change of schedule. This result was sustained even if MMR2 coverage fell to below current levels amongst school age children. However, the overall difference is small, and both schedules would maintain elimination in the absence of waning of immunity after two doses of MMR vaccine.

However, both the existing and the proposed schedules were highly sensitive to waning of vaccine derived immunity. Figure 4 shows the effect of assuming that 5% of individuals lose their protection every 10 years. Our model suggested that both schedules would cross $R=1$ in 2013.

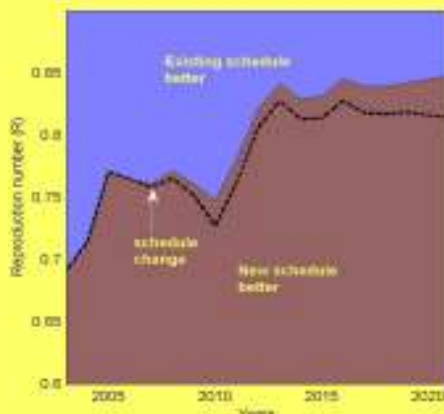


Figure 2: Predicted value of R for MMR2 at 18 months (dashed) as compared to existing schedule.

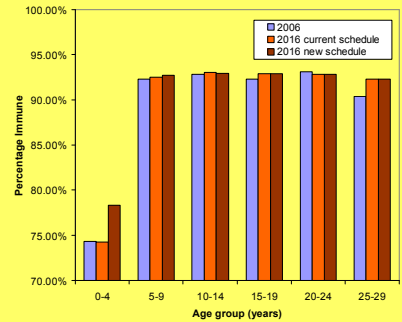


Figure 3: Comparison of projected immunity by cohort due to 18 month MMR2 in 2016 with current schedule in 2006 and 2016

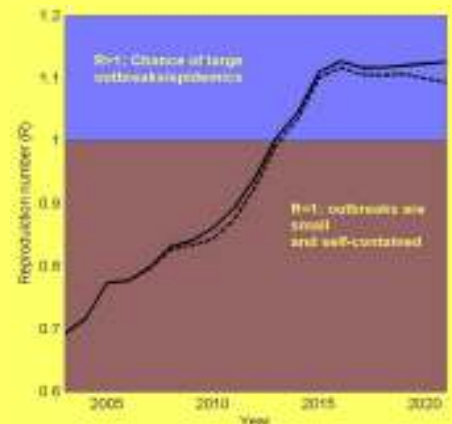


Figure 4: Effect of waning rate of 0.5% per year on R for existing (solid) and new (dashed) schedule

Discussion

Our base-case analysis suggested that lowering the age of MMR2 to 18 months would provide greater protection for children under 4 years of age, and increase population immunity to measles as a whole. While infants under one year of age would not receive a direct boost to immunity from the schedule change, they are likely to benefit indirectly from herd immunity given the projected rises in immunity in the 2-6 year age-range. This may be an important cohort to target, given increased utilisation of child-care, which may result in increased opportunities for infectious contacts with young infants.

The effects of a change in schedule on overall immunity and elimination status are predicted to be minor, with only a very small reduction in the value of R for Australia as a result of a schedule change. This change was relatively insensitive to reductions in 2-dose coverage, but highly sensitive to waning of immunity after 2-doses of MMR vaccine as shown in Figure 4.

If vaccine induced immunity does not wane, and coverage remains at 2006 levels, either schedule will maintain elimination status for measles in Australia until at least 2021. However, our analysis concludes that a change in schedule would increase levels of immunity in young children. The sensitivity of elimination status to waning of immunity suggests that this issue receive further attention via longitudinal studies.

References

- 1 Heywood A et al. (in preparation).
- 2 Gidding HF et al., accepted by Vaccine (Jan 07)
- 3 Kremer et al., Vaccine 2006; 24: 2594-2601.

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NCIRS- National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases