A serosurvey evaluation of the school-based measles 'catch-up' immunisation campaign in Victorian school-aged children

Michaela A. Riddell

Victorian Infectious Diseases Reference Laboratory and Department of Paediatrics, University of Melbourne, Victoria

Jennie A. Leydon, Antony Ugoni and Heath A. Kelly

Victorian Infectious Diseases Reference Laboratory

Abstract

Objective: To determine the proportion of Victorian primary school students protected against measles infection one year after the completion of the measles 'catch-up' immunisation campaign of 1998 and to compare this with the proportion of year 9 and 10 (aged 14-16 years) students.

Design & setting: Three-stage random cluster survey in Victorian primary and secondary schools.

Main outcome measures: Proportion of primary and year 9 and 10 secondary school students protected against measles infection one year after the completion of the mass 'catch-up' immunisation campaign. Secondary outcomes: the proportion of both primary and year 9 and 10 secondary school students protected against both mumps and rubella.

Results: Of 1,037 Victorian primary and 2,357 years 9 and 10 secondary school students invited to participate in this study, 403 (39%) and 752 (32%) respectively provided a blood specimen for serological testing for antibodies against measles, mumps and rubella. 94.8% (95% confidence interval, 91.5, 96.9) of primary school and 93.1% (90.9, 94.8) of year 9 and 10 students were protected against measles infection.

Conclusion: One year after the completion of the school-based measles 'catch-up' immunisation campaign the level of protection in Victorian primary school aged students is sufficient to prevent the continuing circulation of measles virus within this age group. The proportion of year 9 and 10 secondary school students protected against measles is also probably sufficient to prevent continuing circulation of wild type virus in Victoria, even though this age group was not specifically targeted by the 'catch-up' campaign.

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In 1968 the live attenuated measles vaccine was licensed in Australia. However, the vaccine was not included in the national immunisation schedule for infants until 1975.[1,2] The introduction of this vaccine, and subsequent revisions to the immunisation schedule, reduced the circulation of wild type virus and correspondingly reduced the incidence of measles-related illness.[3] However, inadequate vaccine uptake allowed measles transmission to continue throughout Australia.[4]

In 1988, the first national measles campaign was conducted. Vaccine coverage, however, failed to achieve sufficient protection against measles infection in the community and in 1993/94 a number of Australian States faced major measles epidemics, resulting in two reported deaths.[5-8] In 1998 the Commonwealth Department of Health and Family Services implemented the Measles Control Campaign (MCC). The cornerstone of the MCC was a school-based national 'catch-up' vaccination program of all primary school aged students with the measles, mumps and rubella (MMR) vaccine.

Victoria had the highest participation rate in the school-based campaign, with more than 84% of all eligible children vaccinated at school. Immunisation providers, other than the school campaign, accounted for a further 3% of vaccinations recorded for Victorian children.[9]

We aimed to determine the proportion of primary school students who were protected against measles infection one year after the completion of the campaign. We compared this with the proportion of year 9 and 10 secondary school students (aged 14-16 years) protected against measles, as these students were not specifically targeted by the vaccination campaign. As a secondary outcome we assessed the susceptibility in both groups to mumps and rubella virus infection.

Methods

Ethics approval for the study was obtained from the Department of Human Services (Victoria) Ethics Committee. Before recruitment of schools commenced, permission to contact school principals directly was sought from the Department of Education (School Community Support Branch), the Catholic Education Office and the Association of Independent Schools Victoria.

Study design and sample

We used a three-stage cluster sample[10] and based our sample size estimates on an expected 95% of primary school students and 85% of secondary school aged students being protected from measles infection.[11] We estimated that 264 primary and 707 year 9 and 10 students were needed to provide a sample of blood for the measurement of

Correspondence to:
M. Riddell, Epidemiology Division, Victorian Infectious Diseases Reference Laboratory, Locked Bag 815, Carlton South 3053. Fax: (03) 9342 2665; e-mail: michaela.riddell@mh.org.au

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measles-specific immunoglobulin class G (IgG). This calculation incorporated a design effect of 1.3 to allow for cluster sampling,[10] based on similarly designed surveys of immunisation coverage[12,13] to obtain a confidence interval (CI) around our estimates of the proportion of children protected from measles infection of ±3%.

Victorian Local Government Areas (LGAs) were used as the primary sampling unit for analysis since the 'catch-up' campaign in Victorian schools utilised existing immunisation services provided by LGAs. For the first stage, 22 of 78 LGAs were selected, with probability of selection proportional to the size of the primary school population in the LGA.

The second stage required a complete list of all schools, both primary and secondary, from all selected LGAs and subsequent selection of one primary and one secondary school (with probability of selection proportional to size of the whole school population). However, if an insufficient number of children agreed to participate in one school, the next randomly selected school in the same LGA was invited to participate, in addition to the first school.

A third sampling stage was required for the primary school sample since the level of immunisation coverage during the school-based 'catch-up' campaign increased with age (Virginia Kaltzis, Department Human Services, Victoria, personal communication). To ensure equal representation of the seven primary year levels throughout the 22 LGAs, each year level was randomly assigned to three LGAs. In some schools composite grades and, in one case, a small school population made it difficult to recruit from only one grade level. From each LGA, a minimum of 12 primary and 33 year 9 and 10 students were required to provide a blood specimen.

Recruitment

Schools were invited to participate by mail and by follow-up telephone call. Visits were made to schools that agreed to participate. Information seminars were given to the year 9 and 10 students and were offered to the parents of primary school students. Individual information packs containing a detailed information sheet for the parents, a consent form and a short questionnaire were given to each student. Information packs and questionnaires were available in English, Italian, Greek and Vietnamese. The questionnaire collected information on age, sex, language spoken at home, country of birth of student and parents, disease and vaccination history. Vaccination details were considered to be valid if a complete date (dd/mm/yy) was recorded and invalid if a history of vaccination was given without a date or the date was incomplete.

Specimen collection and testing

An experienced paediatric phlebotomist collected up to 10 mL of blood from each consenting student 30-45 minutes after treatment of the venepuncture site with anaesthetic cream (Amethocaine gel 4% 'Angel' Royal Children's Hospital Pharmacy, Melbourne, Australia). Specimens collected at the school were transported to the laboratory and stored at 4ºC within 48 hours.

Serum was tested for measles specific IgG at VIDRL using an Enzygnost anti-measles-virus/IgG enzyme immunoassay (Dade Behring, Marburg, Germany) in accordance with the manufacturer's instructions. Mumps-specific IgG was determined using the Enzygnost anti-parotitis-virus IgG immunoassay (Dade Behring, Marburg, Germany) in accordance with the manufacturer's instructions. Rubella-specific IgG was determined using the Beckman Access immunoassay system (Beckman Instruments, Chaska, MN, USA). For all three test antigens, initially equivocal specimens were retested. Students were considered protected from measles if their measles IgG was reported as positive. Students with an equivocal measles result were considered susceptible to modified measles. Protection from mumps was based on either a positive or equivocal test result as recommended by the manufacturer and antibody titres were not calculated. Students were considered protected from rubella virus infection if the rubella-specific IgG concentration, calculated from the standard curve of the internal standard of the assay, was determined to be >15 IU/mL.[14] Results were reported back to the parents or guardian(s) of students who provided a specimen with a recommendation for further vaccination if appropriate.

Data analysis

Data were analysed using the survey commands (svymean, svytab) of Stata 6.0 with LGA as the primary sampling unit.[15] This analysis allows adjustment of the standard errors based on the sampling strategy and the confidence intervals reflect the effects of clustering in the study population.

Results

Participation rates

Forty-seven primary and 40 secondary schools were approached to successfully recruit 25 (53%) primary and 25 (62.5%) secondary schools. Univariate analysis revealed no significant association of region (metro/non metro) or school governing body (government/non-government religious/non-government other independent) with school participation.

Participating primary schools reported 82.8% of their students vaccinated at school with MMR during the 'catch-up' campaign, which was not significantly different from the reported rate for Victoria (83.4%).[9] However, primary schools who refused to participate reported significantly lower MMR vaccination rates at school during the 'catch-up' campaign relative to participating schools (78.8%, Fisher's exact $p<0.001$).

Student response rates for the study are detailed in Table 1. Students were encouraged to return the questionnaire even if they did not wish to provide a blood specimen. For analysis of measles, mumps and rubella antibodies, 379 students aged 6-12 years (subsequently referred to as 'primary') and 739 students aged 14-16 years (subsequently referred to as 'secondary') provided a blood specimen. A further 90 primary and 161 secondary students returned the questionnaire but did not provide a blood specimen. Excluded from the analysis were 23 students aged five who provided a specimen but were not eligible for immunisation at school during the 1998 'catch-up' campaign and a further 14 students aged 13, 17, 18 and 19 who provided specimens.

Table 1: Student participant response rates.

	Number students invited	Number questionnaires returned (% invited)	Number who provided blood specimen (% quest. returned)
5-13 year olds	1,037	502 (48%)	403 (80.3%)
13-19 year olds	2,357	913 (39%)	752 (82.4%)

Primary school students who returned the questionnaire but did not provide a specimen were not significantly different from those students who provided a specimen with respect to school region, school governing body, age, vaccination history, language spoken at home and country of birth. The age and sex distribution of primary students who completed the questionnaire and gave a specimen was not significantly different from those primary students who completed the questionnaire but did not give a specimen. This was not true for female secondary school students, however, due to a much higher proportion of 14, compared to 15 and 16-year-old girls who returned the questionnaire and provided a sample for testing (p=0.008, data not shown). There was no significant difference in the proportion of students who provided a specimen, compared with those who completed the questionnaire but did not provide a specimen, based on their reported vaccination status or history of illness from measles, mumps or rubella.

Vaccination providers

Of 297 primary students (63% of sample) who nominated the provider of their second MMR, 205 (69%) reported vaccination at school during the 1998 school campaign, 35 (11.8%) reported vaccination at local council immunisation services and 49 (16.5%) reported vaccination at their GP or hospital clinic. Eight students reported vaccination in 'other school' campaigns. Fewer than 5% of secondary students reported vaccination in 1998 or 1999, while 63% reported vaccination with MMR in school vaccination programs prior to 1997.

Prevalence of antibodies to measles, mumps and rubella

The empirical design effect for this study with respect to seroprevalence of measles IgG antibodies in primary school students was 1.24.[10]

Figure 1 shows the immunoassay result for measles IgG by year of age with 95% CI for the positive test results. There was no statistically significant difference in the proportion of students positive for measles IgG for each year of age. When considering protection against clinical measles infection by age, the point estimates indicated more than 92% of students at each age, except nine-year-olds, were protected. However, since the sample number for each age group is small, the 95% CI are wide. There were no statistically significant differences in the geometric mean titre (mIU/mL) by age despite the majority of secondary students receiving a second dose of MMR more than two years prior to the serosurvey (data not shown).

Table 2 shows the proportion of students protected against measles, mumps and rubella and the difference in the proportions for each infection by sex and school level (primary vs. secondary). While it appears that higher proportions of females were protected against measles, mumps and rubella, these differences were not statistically significant. Higher proportions of primary school students were protected against measles, mumps and rubella than were secondary school students, but this difference was only statistically significant when considering the proportion of students protected against mumps infection. There was no statistically significant difference in the proportion of students protected against measles, mumps or rubella when considering region (metro/non-metro) and school governing body. Nor was there any significant difference in the proportion of students protected against measles or rubella, who were born overseas, compared

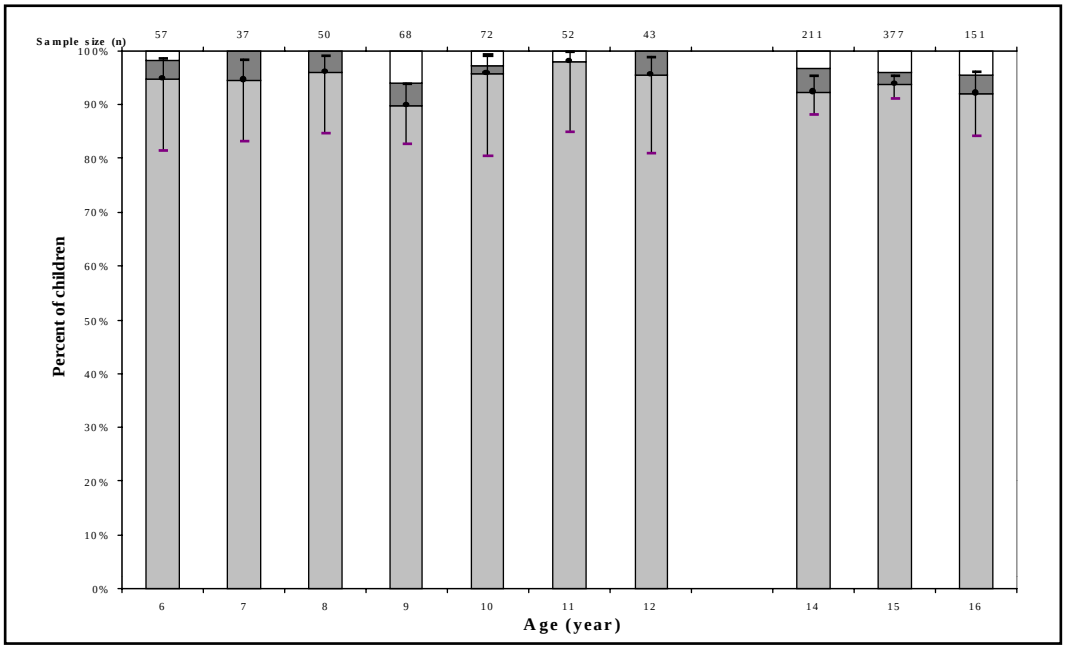

Figure 1: Measles IgG immunoassay result (95% CI for positive result) in Victorian school students, by age.

Table 2: Proportion of students protected against measles, mumps and rubella and difference in proportions by sex and school level.

		n	Measles % (95% CI)	Mumps % (95% CI)	Rubella % (95% CI)
Primary (6-12yo)	Male	189	94.2 (89.3–96.9)	89.9 (84.2–93.8)	97.9 (94.6–99.2)
	Female	190	95.3 (91.3–97.5)	94.2 (90.5–96.5)	99.5 (96.5–99.9)
	All	379	94.7 (91.3–96.8)	92.1 (88.9–94.4)	98.7 (96.5–99.5)
Difference in proportion	Female vs. Male		1.1% (-3.3–5.5)	4.3% (-0.9–9.5)	1.6% (-0.2–3.4)
Secondary (14-16yo)	Male	330	92.7 (89.2–95.2)	84.2 (79.7–87.9)	97.6 (95.3–98.8)
	Female	409	93.2 (90.7–95.0)	88.5 (85.0–91.3)	99.0 (97.6–99.6)
	All	739	93.0 (90.8–94.7)	86.6 (83.6–89.1)	98.4 (97.2–99.0)
Difference in proportion	Female vs. Male		0.4% (-3.0–3.8)	4.3% (-0.6–9.2)	1.4% (-0.7–3.5)
Difference in proportion	Primary vs. Secondary		1.8% (-1.3–4.8)	5.5% (1.8–9.2)	0.3% (-1.2–1.8)

with Australian-born students. However, the proportions of overseas-born primary (79.2%) and secondary (75.7%) school-aged students protected against mumps were significantly less than the proportions of Australian-born students (92.9% primary p=0.0005, 87.7% secondary p=0.003).

Reported immunisation and presence of antibodies

Table 3 shows the proportion of students protected against measles, mumps and rubella according to self-report of a second dose of MMR. The proportion of students protected against measles was not significantly different, whether the parental report of immunisation was valid (full date provided), invalid (incomplete or no date) or no/unsure. When assessing mumps protection, a validated report of MMR was significantly more likely to indicate protection. When considering rubella protection, parental report of uncertain or no vaccination was significantly more likely to indicate susceptibility, but there was no significant difference in the proportion of students protected against rubella when comparing students with a valid or invalid report of vaccination.

Discussion

Seroprevalence

We report here the seroprevalence of measles antibodies from a three-stage randomised cluster survey of Victorian primary and secondary school students collected one year after the completion of the 1998 school-based measles 'catch-up' vaccination campaign.

The level of immunity required in a community to prevent transmission of measles virus is thought to be between 92-95%.[16] A Victorian study conducted in 1994 found approximately 84% of year 2 (7-8 year olds) and 86% of year 7 (12-13 year olds) students were protected against measles.[11] These data suggested that prior to the 'catch-up' campaign measles immunisation coverage of Victorian school students might have been insufficient to prevent circulation of wild-type measles virus. However, our point estimate of 94.7% students protected indicates an adequate level of immunity has been achieved among primary school students following the immunisation program.

The National Centre for Immunisation Research and Surveillance (NCIRS) has evaluated population immunity in Australia using residual sera collected from diagnostic laboratories nationwide before and after the immunisation campaign.[9] The NCIRS estimated that 94.4% (95% CI, 90.9-96.8) of 267 Victorian primary school children were protected from measles infection (unpublished data, NCIRS), consistent with our results of 94.7% (91.3-96.8) of 379 students, despite the different sampling frames of the two studies. We found that 93.0% (95% CI, 90.8-94.7) of 739 secondary school students were protected against measles infection. This is again consistent with the

Table 3: Proportion of Victorian primary and secondary school students protected against measles, mumps and rubella according to reported vaccination with second dose of MMR.

Report of immunisation with second dose MMR	Number of students reporting immunisation with second dose MMR (n)	Number (%) students protected		
		Measles n (%)	Mumps n (%)	Rubella n (%)
Yes (valid date)[a]	436	411 (94.3%)	405 (92.9%)	435 (99.8%)
Yes (invalid date)[b]	346	325 (93.9%)	299 (86.4%)	342 (98.8%)
No/Unsure	230	213 (92.6%)	200 (87.0%)	220 (95.7%)
p-value[c]		0.62	0.02	0.0003

Notes:
(a) Day/month/year provided.
(b) Date incomplete or no date provided.
(c) Comparison of all three report categories.

results from the national evaluation where 91.7% (95% CI, 84.9-96.2) of 109 Victorian students of the same age as those in our study were found to be protected from measles infection (unpublished data, NCIRS).

Participation bias

The design employed in this study is subject to participation bias. In our sample we believe this bias has occurred at two stages. First, there is bias at the school level with respect to vaccination rates at school during the 'catch-up' campaign. Schools that did not participate in this study were less likely to appreciate the social value and benefits of a study such as ours.[17] This attitude may have extended to participation in the 'catch-up' campaign, explaining the lower proportion of children vaccinated at school during the 'catch-up' campaign in non-participating schools.

Second, there is evidence to suggest that our sample may be more likely to contain students who received an MMR vaccine. Over 28% of the primary school students who nominated a vaccination provider indicated they had been vaccinated outside the school-based campaign, a much higher proportion than the 3% vaccinated by other providers, reported for the whole of Victoria, during the campaign.[9] Our overall response rate indicates that less than 50% of the school population approached was represented in this sample. It would appear that this sample contains a high proportion of children of motivated parents who obtained vaccinations outside the school-based campaign and who thus may have been more likely to be protected against measles.

Despite this acknowledged bias, our estimate of the proportions of both primary and secondary school students protected against measles infection is not significantly different from the estimates for Victorian students obtained from the national evaluation.

Validity of parental report of immunisation

Another interesting finding in our study is that, at high levels of community-wide protection and vaccination coverage, as would occur following a successful mass immunisation campaign, the validation of parental report of immunisation records may not be necessary. This is in contrast to the current practice of only accepting validated parental records as evidence of immunisation.[18] For measles and rubella, even those participants who said they were not vaccinated or unsure of vaccination status were estimated to be sufficiently immune to prevent circulation of wild-type virus. For mumps, however, this was not the case.

Our results confirm that, one year after the measles 'catch-up' immunisation campaign, the Victorian primary school-aged community is protected from measles infection. The same is true of protection against rubella infection, although protection against mumps infection is less certain.

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