# Epidemiology of a Measles Epidemic in Vietnam 2008–2010

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***Background.*** Vietnam conducted a measles catch-up supplementary immunization activity (SIA) during 2002–2003 that targeted children 9 months–10 years of age, followed by subnational SIAs targeting persons up to 20 years of age during 2004 and 2007–2008. A measles epidemic began among young adults in October 2008 in the northern region, spread nationwide during early 2009, and continued during 2010.

***Methods.*** We reviewed national epidemiologic and laboratory surveillance data. Measles cases were defined and classified according to World Health Organization recommendations.

***Results.*** From October 2008 through January 2010, 7948 confirmed measles cases were reported from 60 of 63 provinces, an incidence of 93 cases per million population. Incidence was 328 cases per million population among children age 1–4 years, 318 cases per million population among infants, and 271 cases per million population among persons aged 20–24 years. Few cases were reported among persons 7–17 or >27 years of age. Median age of cases trended downward over time in all regions.

***Conclusions.*** The 2002–2003 measles SIA protected its targeted age group, but this epidemic was not prevented by follow-up subnational SIAs in selected provinces during 2007–2008. Transmission began among young adults and was sustained among children. The outcome of Vietnam's 2010 SIA targeting children only and change in routine schedule may influence elimination strategies for other countries.

## BACKGROUND

### Routine Immunization

Vietnam's estimated 2009 population of 85,790,000 persons resides in 63 provinces of 4 regions. Measles-containing vaccine (MCV) was introduced into the routine immunization schedule in 1982. National coverage increased during the 1980s, reaching 89% by 1989, and varied from 93% to 97% during 1993–2009 (Figure 1), excluding 2007, when reported first-dose MCV (MCV1) coverage was 83% because of a nationwide stock out. MCV1 is administered at 9 months of age; a second dose of MCV (MCV2) was introduced in 2006 for children entering primary school and is administered at 6–7 years of age.

### Supplementary Immunization Activities

Beginning in 1999, Vietnam began conducting a series of subnational supplementary immunization activities (SIAs) in selected provinces. A national SIA targeting children aged 9 months to 10 years was conducted in the North Region in 2002 and in the South, Central, and Highland Regions in 2003. Older age groups (12–15 and 12–18 years) were targeted in selected districts of 20 provinces during 2004. In 2007, measles SIAs again were conducted in 17 of 29 provinces in the North Region, targeting persons 6–20 years of age; 4 of these (Lao Cai, Lai Chau, Dien Bien, and Ha Giang) also targeted children aged 9 months–5 years (Figure 2). In 2008, SIAs targeting persons 7–20 years of age were conducted in all 4 provinces in the Highland Region and in part of 1 province (Quang Nam) in the Central Region. Reported

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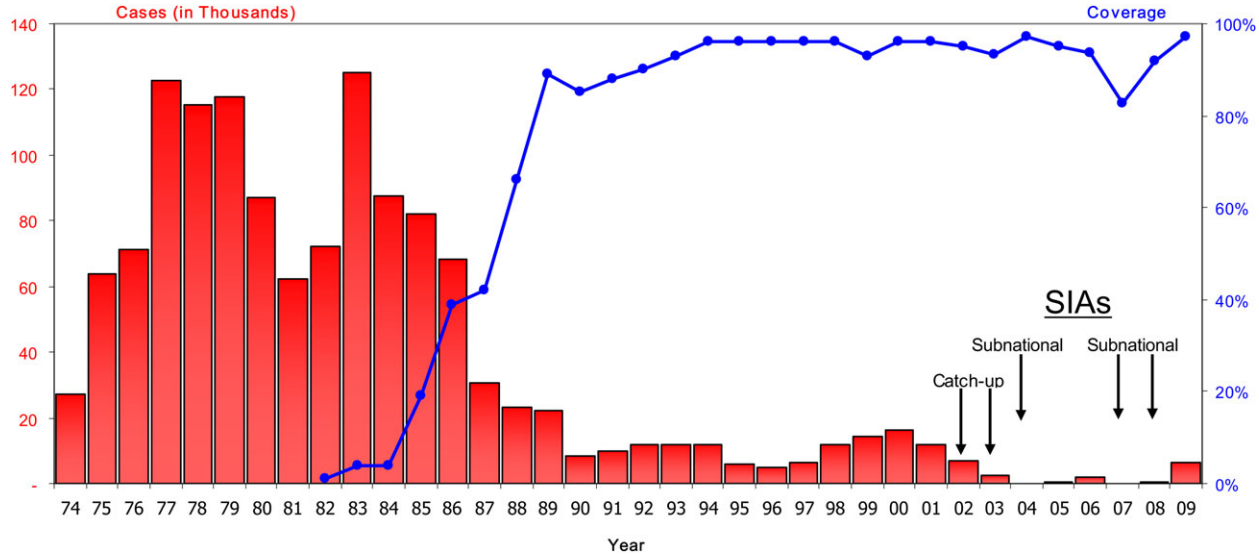


**Figure 1.** Reported measles cases and MCV1 coverage Vietnam, 1974–2009.

coverage in almost all provinces conducting SIAs since 2002 was ≥95%.

### Measles Incidence and Onset of the Epidemic

After the national SIA during 2002–2003, only 5 laboratory-confirmed measles cases were reported in 2004. Sporadic measles outbreaks were reported from 2004 through early 2008, often in the mountainous areas of the North Region; outbreak response immunization (ORI) appeared to contain the outbreaks.

In October 2008, outbreaks were reported from 3 provinces in the North Region, Vinh Phuc, Than Hoa, and Ha Noi. The Vinh Phuc outbreak involved 17 college students and was self-limited. The Thanh Hoa outbreak involved children <15 years of age and was halted in early December after ORI. Ha Noi's index case was a 19-year-old student from the Hanoi School of Public Health with rash onset on October 20. By the end of epidemiologic week 52, 84 cases had been confirmed from 13 of 14 districts in Ha Noi; 68 cases (81%) were 18–26 years of age. A total of 158 cases were reported from Vietnam during the last quarter of 2008. Measles transmission increased dramatically during early 2009 to involve ~8000 reported confirmed cases from 60 provinces as of January 2010. We describe the epidemiology of this epidemic.

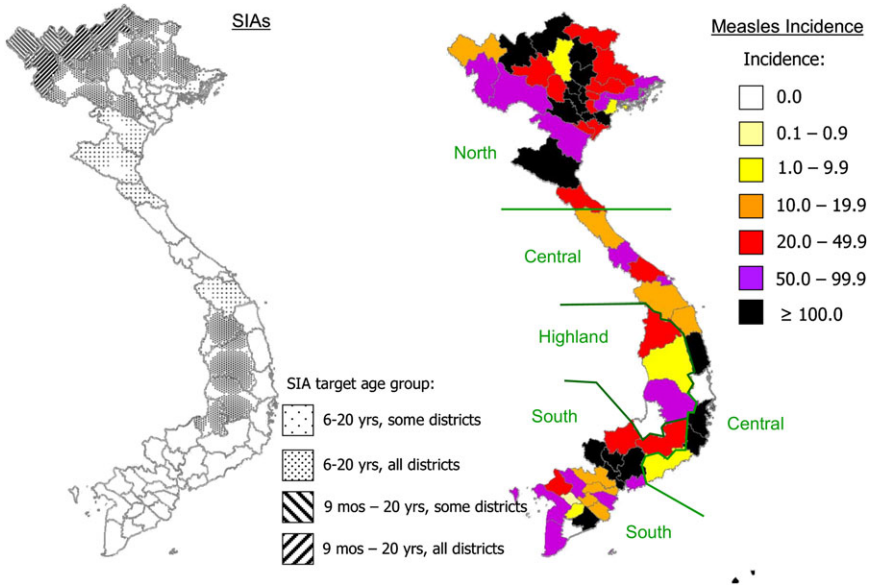


**Figure 2.** Subnational supplementary immunization activities (SIAs) conducted in 2007–08 and measles incidence during the epidemic period, by province, Vietnam.

## METHODS

### Case Definitions and Case Classification

A suspected case of measles was defined as a person of any age with fever, rash, and one of the following: cough, coryza, or conjunctivitis. Suspected cases were classified as either laboratory-confirmed, epidemiologically linked, clinically confirmed, or discarded, according to guidelines from the World Health Organization [1, 2].

### Data Sources

Two sources of surveillance data were used to identify and classify suspected measles cases: measles case investigation forms (CIFs) submitted to the National Institute of Hygiene and Epidemiology (NIHE) EPI Unit and monthly line listing forms submitted by the 4 regional measles laboratories. Because laboratory data submissions reported more IgM-positive cases than did CIFs submitted to the NIHE EPI Unit, we added epidemiologically linked and clinically confirmed cases from CIF submissions to the IgM-positive cases reported in laboratory reports to determine numbers of cases by time, place, and age. All IgM-positive cases included in the laboratory report forms were assumed to satisfy the clinical case definition of measles. Unless otherwise indicated, the term "measles cases" refers to cases confirmed by laboratory, epidemiologic linkage, and/or clinical criteria. Vaccination status was determined for lab-confirmed and epidemiologically linked cases only based on CIF submissions.

Population data by province and by age group for 2009 were obtained from the National Bureau of Statistics in Ha Noi and were based on the 2009 census. We assumed that the national percentage of population by age group, crude birth rates, and infant mortality rates were the same in every region.

### Analytic Methods

Data were analyzed using Stata software (StataCorp). For cases with unknown dates of rash onset, date of rash onset was approximated using the data from the rest of the measles cases on the median interval between date of rash onset and other subsequent dates, such as date of notification, date of investigation, date of specimen collection, and date of specimen receipt in the laboratory, in that order. The epidemic period was defined as October 2008 through January 2010.

Ninety-five percent confidence intervals (CIs) were determined for proportions, assuming a binomial distribution and for relative risks (RRs), using Taylor Series expansion [3]. Differences in proportions were considered to be statistically significant if their 95% CIs did not overlap. Yates' corrected $\chi^2$ test was used to assess statistical significance of differences of parametric data; the Kruskal-Wallis test was used for nonparametric significance testing. All $P$ values are 2-tailed.

## RESULTS

A total of 7948 confirmed measles cases were reported from October 2008 through January 2010 in 60 of 63 provinces of Vietnam, an incidence of 93 cases per 1 million population during the epidemic period. Among these, 5488 were laboratory confirmed, 2106 were confirmed by epidemiologic linkage, and 354 were clinically confirmed. Incidence during the epidemic period, by province, is given in Figure 2. Measles genotype H1 was detected from 6 cases in the North Region and 16 cases in the South Region.

### Temporal and Geographic Characteristics of the Epidemic

The epidemic dramatically increased in magnitude during the first quarter of 2009. (Figure 3) In the North Region, measles

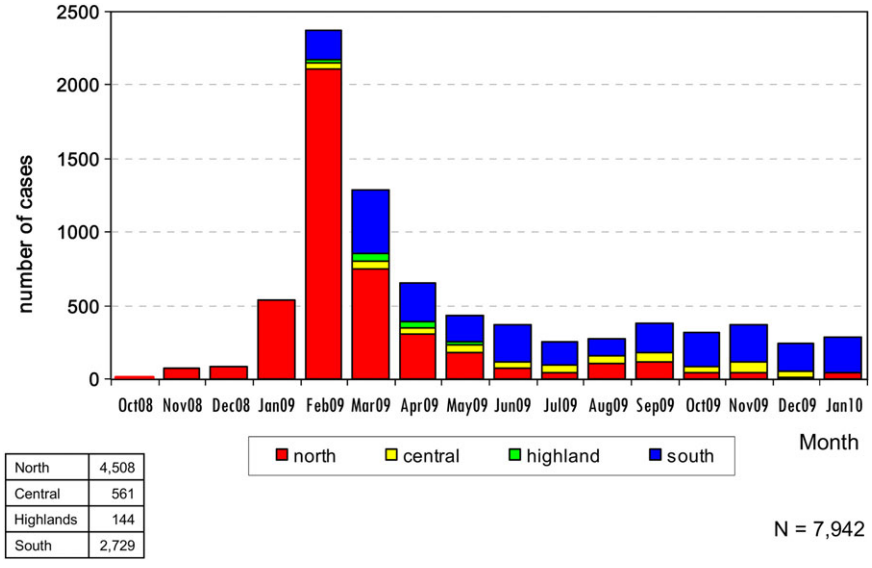


**Figure 3.** Measles, by month of rash onset and region Vietnam, October 2008–January 2010.

transmission peaked at 2108 cases in February and was followed by a progressive decrease to <100 cases per month from June onward. Transmission in the other 3 regions began at the end of January and early February 2009, peaked in March, and for the South and Central Regions, remained relatively stable thereafter at 100–250 and 40–80 cases per month, respectively, without any discernable trend. In the Highland Region, 3 cases were reported in January 2009, followed by 25–50 cases per month from February through May 2009 only.

The North Region was the most heavily affected by the epidemic, with 4508 (57%) confirmed cases (118 cases per million population). The South Region reported 2729 (34%) cases (84 cases per million population), followed by the Central Region with 561 (7%) cases (50 cases per million population) and the Highland Region with 144 (2%) cases (37 cases per million population). Localizing data were not available for 6 cases. Among the 2106 epidemiologically linked and 354 clinically confirmed cases, 2030 (96%) and 254 (72%), respectively, were from the North Region.

### Sociodemographic Characteristics of Measles Cases

***Age.*** Among 7512 cases for which data on age were available, the highest incidence was among persons aged 1–4 years (328 cases per million), followed by those aged <12 months (318 cases per million), 20–24 years (271 cases per million), 5–9 years (162 cases per million), 25–29 years (119 cases per million), and 15–19 years (105 cases per million). Persons aged 10–14 years and ≥30 years had relatively low measles incidence (41 and 9 cases per million, respectively).

Overall, 3953 (53%) of 7512 patients were ≥15 years of age. In contrast, during the years before the catch-up SIAs in the North (2002) and in the other 3 Regions (2003), 139 (5%) of 2643 measles cases were ≥15 years [4]. The percentage of infant cases occurring during 2008–2010 was similar to that during 2001–2002 (401 [5%] of 7512 vs 184 [7%] of 2643).

During the epidemic period, few cases were reported among persons aged 7–17 years or ≥27 years in any region, corresponding to the age groups targeted during the 2002–2003 SIAs and those born before the introduction of measles vaccine, respectively (Figure 4). However, in the North Region, 2100 (47%) of 4364 cases were 18–26 years of age, whereas in the South, Central, and Highland Regions, only 877 (28%) of 3126 cases were among this age group (RR, 1.72; 95% CI, 1.61–1.83). Conversely, in the North Region, only 1255 cases (29%) were <7 years of age, whereas in the South, Central, and Highland Regions, 1630 (52%) were in this age group (RR, .55; 95% CI, = 0.52–0.58). Differences in proportions of cases by age group and region were not substantially different when restricting analysis to laboratory-confirmed cases only. Among 388 confirmed cases <12 months of age, 228 (59%) were <9 months of age, representing a total of 3% of 7490 cases with age data.

Age distribution of measles cases varied over time and by region. (Figure 5) In the North, the median age of cases by month was 17–21 years from December 2008 through March 2009, decreased to 11–13 years during April–May, then decreased further to 1–7 years from June 2009 through January 2010. In the other 3 regions, the median age was 17–20 years during January and February 2010, then decreased to 5–8 years from March through November. The median age increased transiently to 18 years in December 2009 and 21 years in January 2010. The percentage of district index cases aged ≥15 years was 79% in the North Region, 71% in the Central Region, and 46%

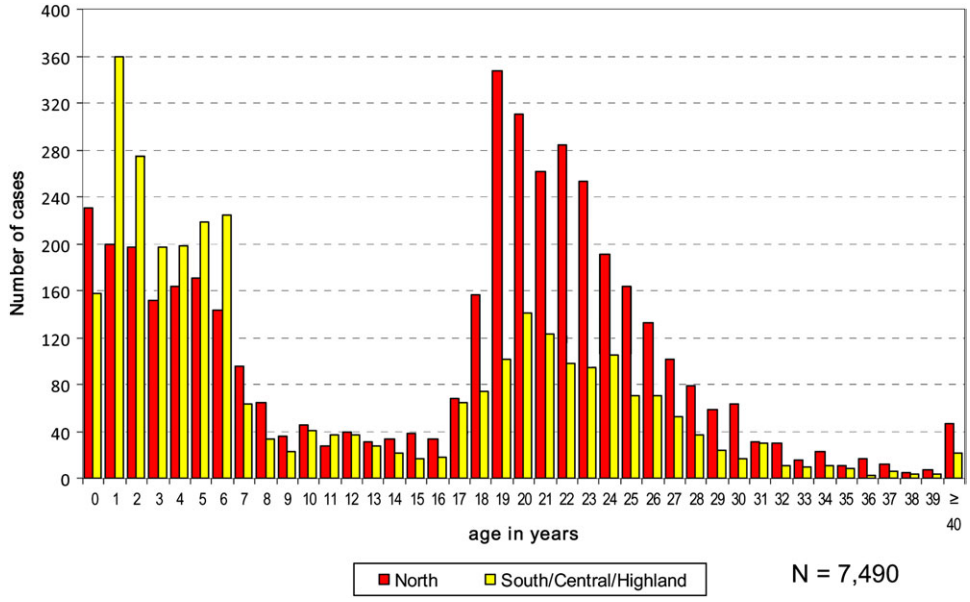


**Figure 4.** Measles cases by age and region, Vietnam, October 2008–January 2010.

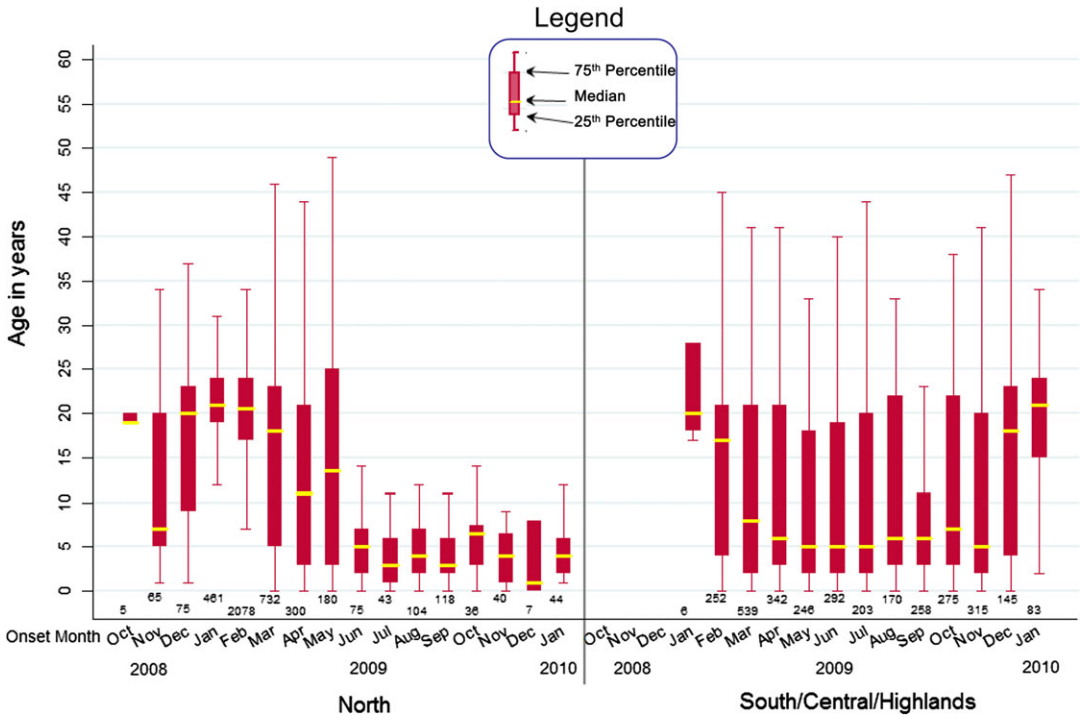


**Figure 5.** Age distribution of measles cases, by month and region, Vietnam, October 2008–January 2010.

in the South Region. Districts in the South Region were significantly more likely to report index cases <15 years of age than districts in the North Region (19 [57.6%] of 33 vs 36 [21.3%] of 169; RR, 2.70; 95% CI, 1.79–4.08).

***Sex.*** Among 7255 cases with data on sex, 3717 (51%) were male. Nationally, the number of male measles cases aged 1–4 years was significantly greater than females cases (926 [54.9%] of 1688; 95% CI, 52.5–57.3). Among the 4 regions, this difference was significant only in the South (423 [55.8%] of 758; 95% CI, 52.1–59.4). Also in the South, the number of male measles cases was significantly greater than female cases in the 5–9 year age group (233 [56.3%] of 414; 95% CI,51.3–61.1). In contrast, among young adults, the number of female cases was significantly greater than male cases in the South and Central Regions only. In the South Region, female cases accounted for 242 (58.3%; 95% CI, 53.4–63.1) of 415 and 111 (63.4%; 95% CI, 55.8–70.6) of 175 cases in the 20–24 and 25–29 year age groups, respectively. In the Central Region, 53 (63.1%; 95% CI, 51.9–73.4) of 84 and 30 (71.4%; 95% CI, 55.4–84.2) cases 20–24 and 25–29 years of age, respectively, were female.

***Vaccination Status.*** Data on vaccination status and age were available from 5254 laboratory and epidemiology linked confirmed cases. Overall, 1570 cases (30%) were vaccinated. Among 1011 cases aged 1–4 years, 480 (48%) were previously vaccinated, and 11 (2%) of these had received 2 doses of MCV. Among 704 cases aged 5–9 years, 376 (53%) were previously vaccinated, and 49 (13%) of these had received 2 MCV doses. Vaccine effectiveness among children receiving at least 1 measles vaccine dose was ~90% and ~86% among children aged 1–4 years and 5–9 years, respectively, assuming 90% of the population was vaccinated with MCV1 [5].

***Protection From Supplementary Immunization Activities During 2007–2008.*** Among the 22 provinces that conducted SIAs during 2007–2008, 5 that had targeted all districts in the province reported an unexpectedly high incidence of confirmed measles during the epidemic period, ranging from 63 to 549 cases per million population. Incidence ranged from 45 to 129 cases per million when restricting analysis to laboratory-confirmed cases only. Two of the 5 provinces had targeted persons 9 months to 20 years of age during the 2007 SIAs; in these provinces, 126 (54%) of 233 confirmed cases were aged 3–22 years who should have been protected; 57 (24%) were aged <3 years, and 50 (21%) were aged ≥23 years. The remaining 3 provinces targeted persons either 6 or 7 to 20 years of age during their SIAs in 2007 or 2008, respectively; in these provinces, 188 (34%) of 549 cases were 8–22 years of age and should have been protected; 199 (36%) were <8 years of age, and 162 (30%) were ≥23 years of age.

***Occupation.*** Occupational status data were reported for 579 (17%) of 3334 suspected cases reported from Ha Noi through 13 March 2009. Among cases in the 20–24 year age group, 151 (59%) of 257 suspected cases and 32 (74%) of 43 confirmed cases were in students from >50 colleges and universities.

## DISCUSSION

The epidemic's magnitude and geographic extent have been substantial, and the epidemiologic findings suggest both success and limitations of past elimination efforts. The rolling 2002–2003 catch-up SIA that targeted children aged 9 months to 10 years was successful in largely interrupting measles virus transmission and continued to protect persons who were 7–17 years of age during the 2009 epidemic. Incidence among children 5–9 and 10–14 years of age was very low, compared with other age groups and compared with reported measles cases before the 2002–2003 catch-up SIAs. However, the follow-up strategy of outbreak response immunization and subnational SIAs implemented during 2005–2008 and limited to provinces thought to be at risk for measles apparently left large numbers of susceptible children who acquired measles infection during this epidemic.

Young adults aged 18–27 years, many of whom were students, clearly played a large role in the initial spread of this epidemic. Persons in this age group likely remained susceptible to measles because most were born during the period of measles vaccine introduction into the routine immunization program and scaling up of coverage during 1983–1989; these young adults were less likely than older persons to have natural immunity because of decreasing risk of exposure to measles and also less likely than younger persons to have vaccine-induced immunity. The relatively high incidence among infants, particularly those $<$9 months of age, and the high attack rate among young adults suggest that many young mothers may never have been vaccinated or acquired natural immunity, leaving their newborn children at increased risk from birth because they lacked protective maternal antibody against measles. This risk should diminish over time as increasing numbers of women enter their child-bearing age years with vaccine-induced immunity.

Measles incidence was highest among young children who sustained the Vietnam measles epidemic beginning in the latter half of 2009 in the North and beginning in the second quarter in the South and Central Regions. A substantial number of children $<$7 years of age were susceptible to measles, because (1) 15% of those vaccinated at 9 months of age were unlikely to have seroconverted, (2) the MCV2 schedule did not target children until after entering primary school at 6 or 7 years of age, (3) low vaccination coverage in 2007 resulted from a measles vaccine stock out, and (4) follow-up SIAs in many provinces did not include children $<$7 years of age. Measles outbreaks are most likely to occur when the number of susceptible children reaches the size of one birth cohort [6].

The temporal evolution in age distribution from primarily adults to children and the large percentage of districts with adult index cases suggest that measles transmission began among susceptible adults and likely continued among them for several generations, particularly in the North Region. One reason for the earlier predominance of measles cases among children in the South, Central, and Highland Regions, compared with the North Region, may be related to the relatively higher proportion of female patients than male patients among those aged 20–24 and 25–29 years in the former. Children of infected mothers will inevitably be exposed to measles virus, whereas contact with young male adult family members, many of whom are away at school, may be less frequent. After measles virus began to spread rapidly, susceptible children became increasingly affected and involved in transmission.

Travel during the weeks before and after the Vietnamese New Year (Tet) holiday (26 January 2009) likely played an important role in the spread of measles virus in Vietnam, especially among young adults. The substantial decrease in median age and percentage of cases among young adults after several months of transmission suggest that, without involvement of children, transmission among young adults might have been self-limited. Recommended measles elimination strategies include wide age range catch-up SIAs that usually target children up to 14 years of age, and unless high routine MCV2 coverage exists, periodic follow-up SIAs to reduce the accumulation of susceptible children before reaching the size of a birth cohort [7]. If the 2002–2003 SIA had included persons aged up to 14 years instead of 10 years, persons up to $\geq$21 years of age would have been protected during 2008–2009, and the outbreaks among young adults from October through December in 2008 might not have occurred or ignited the larger nationwide epidemic. Had a nationwide follow-up SIA been conducted in 2007, targeting children born since the initial catch-up SIA, it is possible that measles virus transmission would have been self-limited after the initial spread among susceptible adults. Selective subnational SIAs were not effective in preventing this epidemic.

To eliminate measles by 2012, Vietnam is planning to conduct a nationwide SIA targeting children 1–5 years of age during the fourth quarter of 2010, followed by a change in the scheduled age of routine MCV2 administration from 6 years to 18 months of age beginning in 2011. In so doing, Vietnam will assure a high level of population immunity in all birth cohorts up to age 18 years as of 2010 and up to age 20 years as of 2012. Experience in the Americas suggests that ensuring immunity of persons up to 15 years of age can interrupt measles virus transmission in most circumstances, even when young adults comprise a large percentage of cases. Vaccinating children 6 months to 15 years was effective in rapidly terminating a 1993 outbreak in Peru although 44.0% of cases occurred in persons $>$15 years of age [7]. A similar phenomenon was seen during a 1997 measles outbreak in Sao Paulo, Brazil, in which adults aged 20–29 years accounted for more than half of all cases [8]. An SIA targeting children aged 6 months to 4 years of age appeared to have little impact on measles transmission; subsequent expansion of the target age to 14 years resulted in a substantial decrease in the weekly number of measles cases. However, Sao Paulo also immunized high-risk

adults such as students, migrant workers, military recruits, health care workers, and employees in the tourism industry, an approach being considered by Vietnam.

The number of birth cohorts requiring high levels of population immunity to eliminate endemic measles virus transmission is uncertain. Similar to Vietnam, many priority countries and areas of the Western Pacific Region introduced MCV into their national immunization programs during the 1980s and reached high levels of coverage by 1990 or later. Subsequent SIAs conducted in many of these countries to close immunity gaps will likely result in high levels of population immunity in successive birth cohorts up to 20–25 years of age in 2012, the target year for measles elimination. Large-scale immunization of persons beyond this age may not be necessary to eliminate measles in these countries, as measles virus transmission among persons born around the time of vaccine introduction may not be sustainable, and high levels of natural immunity are likely to exist among prevaccine introduction birth cohorts. The outcome of Vietnam's strategy and that of other Western Pacific Region countries and areas will help determine whether ensuring high population immunity among cohorts born around the time of measles vaccine introduction and scale-up is necessary to achieve measles elimination in other Regions.

## Funding

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