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Comparison of population-based measles-rubella immunoglobulin G antibody prevalence between 2014 and 2019 in Lao People's Democratic Republic: Impacts of the national immunization program

Shinsuke Miyano[1,#,*], Emilia Vynnycky[2,3,#], Chansay Pattamavone[4], Yasunori Ichimura[1], Yoshio Mori[5], Phonethipsavanh Nouanthong[6], Kongxay Phounphenghack[4], Chankham Tengbriacheu[4], Bouaphne Khamphaphongphane[7], Lauren Franzel[8], Tae Un Yang[8], Hendrikus Raaijimarkers[9], Kenichi Komada[1], Tomomi Ota[1], Masafumi Funato[1], Makoto Takeda[5], Masahiko Hachiya[1]

[1] *Bureau of International Health Cooperation and World Health Organization (WHO) Collaborating Center for Health Systems Development, National Center for Global Health and Medicine, Tokyo, Japan*
[2] *United Kingdom Health Security Agency, London, UK*
[3] *London School of Hygiene & Tropical Medicine, London, UK*
[4] *National Immunization Program, Mother and Child Health Center, Ministry of Health, Lao People's Democratic Republic (Lao PDR), Vientiane, Lao PDR*
[5] *Department of Virology III and WHO Global Specialized Laboratory for Measles and Rubella, National Institute of Infectious Diseases, Tokyo, Japan*
[6] *Institute Pasteur du Laos, National Immunization Technical Advisory Group, Ministry of Health, Lao PDR, Vientiane, Lao PDR*
[7] *National Center Laboratory and Epidemiology, Ministry of Health, Lao PDR, Vientiane, Lao PDR*
[8] *Vaccine-Preventable Diseases and Immunization Team, WHO Lao PDR, Vientiane, Lao PDR*
[9] *Health and Nutrition Section, UNICEF, Lao PDR, Vientiane, Lao PDR*

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ABSTRACT

Objectives: We evaluated the effectiveness of the Lao People's Democratic Republic's measles-rubella immunization program using the seroprevalence from two cross-sectional surveys.
Methods: The nationwide surveys occurred in 2014 and 2019 using a multistage cluster sampling, both requiring samples from 2184 individuals from 52 randomly selected villages. Immunoglobulin G titers, measured using enzyme-linked immunosorbent assay, were considered positive at ≥120 mIU/ml (measles) and ≥10 IU/ml (rubella). We calculated the vaccination-related reduction in the force of rubella infection and the number of congenital rubella syndrome cases averted in 2019.
Results: We collected 2135 (women: 55.2%, mean age: 23.2 years) and 2001 (52.7%, 23.1 years) samples in 2014 and 2019, respectively. During 2014-2019, immunoglobulin G prevalence increased from 83.9% (95% confidence interval [CI]: 83.8-84.0) to 98.3% (97.7-98.8) for measles and from 75.4% (75.3-75.5) to 87.8% (86.4-89.2) for rubella. The most plausible reduction in the average force of rubella infection was 100% (95% CI: 28-100) since vaccination started, averting 78 (95% CI: 42-128) congenital rubella syndrome cases in 2019.
Conclusion: This is the first population-based study for measles and rubella at two different time points in developing countries. Measles and rubella seroprevalence increased significantly during 2014-2019, greatly exceeding the immunity thresholds for their elimination.
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Introduction

In Lao People's Democratic Republic (PDR), the Expanded Program on Immunization was launched in 1979, establishing both a system of outreach and fixed-site immunization services, covering all villages nationwide by 1991. The Eighth National Health Sec-

* Corresponding author at: (S. Miyano); Tel: +81-(0)3-3202-7181 (ext. 5430); Fax: +81-(0)3-3205-7860
E-mail address: s-miyano@it.ncgm.go.jp (S. Miyano).
# These authors contributed equally.

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tor Development Plan 2016-2020 included a goal of 95% vaccination coverage for measles and rubella by 2020 [1]. The official routine immunization coverage has steadily improved during the last 5 years, reaching 89% for the measles and rubella-containing vaccine (MRCV) in 2019 [2].

In February 2014, the first nationwide seroprevalence survey was conducted to measure the antimeasles and antirubella immunoglobulin (Ig) G prevalence to estimate the population immunity, evaluate previous vaccination effectiveness, and the number of averted congenital rubella syndrome (CRS) cases [3,4]. The estimated IgG prevalence was 83.9% and 75.4% for measles and rubella, respectively. The IgG prevalence of measles was significantly lower in the target age groups (5-21 years) of the 2011 supplementary immunization activity (SIA), which used MRCV, than in young adults (22-39 years; 86.8% [95% confidence interval (CI): 84.5-91.8] vs 99.0% [95% CI: 98.3-99.8]), whereas the IgG prevalence of rubella was significantly higher (88.2% [95% CI: 84.5-91.8] vs 74.6% [95% CI: 70.7-78.5]). In the SIA target age groups, the prevalence of measles IgG increased with age. The number of CRS cases estimated to have been prevented in 2013 ranged from 16 to 92, depending on the assumed postvaccination reduction in the force of infection.

The survey findings led the national immunization program (NIP) to conduct two SIAs targeting those aged 9 months to 10 years in 2014 and 9 months to 5 years in 2017 (100% and 97% coverage, respectively). The incidence per 1 million dramatically decreased during 2014-2018 from 10.7 to 1.4 for measles and from 2.8 to 2.2 for rubella [5,6], making the NIP and relevant partners regard the direct measurement of herd immunity as a better approach to obtaining reliable data on the occurrence of these vaccine-preventable diseases [3,7–10] and to start to consider steps to eliminate measles in Lao PDR by 2022 [11].

Thus, we conducted the second nationwide seroprevalence survey in 2019 to assess the change in IgG prevalence for measles and rubella between 2014 and 2019 that could be caused by routine immunization and two SIAs in 2014 and 2017. Mathematical modeling was then used to assess the effectiveness of the immunization program over the last 5 years by estimating the reduction in the force of infection and the number of CRS averted in 2019 using data from both surveys [3,4].

Materials and methods

Study population and required sample size

Although this survey covered different people in different areas from those in 2014, both surveys used the same multistage random cluster sampling design [3], allowing the results to be compared between the surveys. In the 2014 survey, to evaluate the 2011 SIA, the population included both those who would have been covered (aged 5-21 years) and not covered (aged 1-2 and >21 years) by the SIA. To separate the two groups clearly for comparison of immunity level, those aged 3-4 years were excluded because some of them could be covered by the SIA and others could not because their date of birth is often ambiguous because calendar and traditional ages are often confused in rural villages [12,13]. The required sample size was calculated using the same method as in the previous survey, resulting in 2184 samples [3].

Sampling strategies

A three-stage random cluster sampling design was adapted using a sampling method recommended by the World Health Organization (WHO) [14,15]. For the first stage, 26 of 148 districts were randomly selected by applying probability proportionate-to-size sampling based on the latest population census of 2005 obtained from the Department of Statistics, Lao PDR. For the second stage, two villages per district were randomly selected using proportionate-to-size sampling (52 villages in total). For the third stage, 42 participants per village, including eight, six, six, 16, and six aged 1-2, 5-14, 15-21, 22-39, and ≥40 years, respectively, were randomly selected from a household list using a paper-based lottery, meeting the required sample size (2184 samples).

Sample collection and laboratory examination

Survey teams of two were organized in each selected district to conduct a brief face-to-face interview to obtain the demographic information and blood collection by finger prick [16] from the individuals sampled from two villages in the same district. A small amount of blood was put onto filter paper (Whatman 903®) using capillary tubes, dried well, and transported to the WHO Measles and Rubella Regional Reference Laboratory, as well as the Global Specialized Laboratory in the Department of Virology III, National Institute of Infectious Diseases (NIID), Tokyo, Japan, for the laboratory examinations. The antimeasles and antirubella IgG titers were measured using commercially available enzyme-linked immunosorbent assay kits (Enzygnost Anti-measles virus/IgG and Anti-rubella virus/IgG, Siemens Healthcare Diagnostics). The Optical Density (OD) values were converted to quantitative data, and we presented the results with cut-off points of 120 mIU/ml for antimeasles IgG that has been considered to be protective against symptomatic disease according to past studies [16–18] and 10 IU/ml for antirubella IgG that has been recommended by the latest WHO position paper [19] because several studies demonstrated that a secondary immune response was elicited by patients with antibody levels >10 IU/ml after a challenge with a live attenuated vaccine or reinfection [20–23].

Estimated number of averted CRS cases by mathematical modeling

We fitted the catalytic models to age-specific rubella seroprevalence data from both 2014 and 2019 simultaneously to estimate the prevaccination force of infection, the sensitivity of the antibody assay for both surveys, and the average reduction in the force of infection resulting from the introduction of vaccination. Eight catalytic models, denoted as AA, AB, BA, BB, CC, CD, DC, and DD (see Supplementary Table A.1 and A.2), were fitted to the data from both surveys by maximum likelihood. The best-fitting value for the prevaccination force of infection was then used to estimate the CRS incidence per 100,000 live births in 2019 among women in 5-year age groups between those aged 15 and 49 years and those aged 15-49 years and what it might have been if the rubella-containing vaccine had not been introduced. The methods are similar to those used previously [4]. For each model, we also computed the basic reproduction number (R_0) and the net reproduction number R_n for rubella by 2019 as a result of vaccination. Further details are in the Appendix.

The CIs on the prevaccination force of infection, its average reduction after vaccination was introduced, the sensitivity of the antibody assay, the CRS incidence for each catalytic model, and the number of CRS cases prevented by vaccination and the reproduction numbers were obtained by bootstrapping, using 1000 bootstrap datasets generated using the approach used by Shkedy *et al* [24]. In the sensitivity analyses, we repeated the analyses conducted previously [4] but just using data from the seroprevalence survey in 2019 to estimate the force of infection from before the introduction to vaccination using assumptions for the average reduction in the force of infection after vaccination was introduced of 0, 25%, 50%, 75%, and 100%. Further details are in the Appendix.

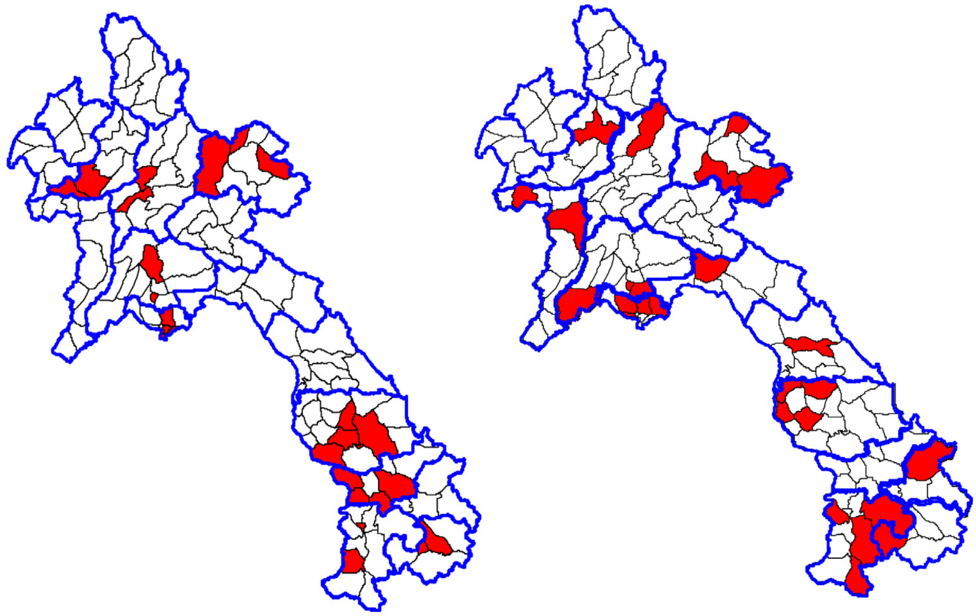

Figure 1. Selected 26 districts (52 villages) for the survey (left: 2014, right: 2019).

Statistical analysis

The statistical analysis was conducted using STATA version 14.0 (StataCorp., College Station, TX, USA). The calculations of the overall prevalence among the participants considered the sampling design and each individual's sampling weight. All estimates and standard errors were calculated by considering the multistage cluster sampling design and the weight of each sample. The Clopper-Pearson exact method was used to calculate the 95% CIs for the estimated prevalence in each group.

Ethical approval

Written informed consent was obtained from all selected participants. When the participants were aged <18 years, it was obtained from their parents or legal representatives. The participants' names were not recorded. The research proposal was approved by the Ministry of Health; Lao PDR (06/NECHR); National Center for Global Health and Medicine, Japan (NCGM; NCGM-3038); and National Institute of Infectious Diseases, Japan (NIID-1012).

Role of the funding source

This survey was supported by the NCGM Intramural Research Fund (grant numbers 25-8, 19A01 and 22A01) and the Grant for the NIP, Lao PDR (grant number FY2019). However, the funders had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

Participants' characteristics

The survey teams visited all 52 selected villages from the 26 districts between June 3 and 14, 2019, and completed blood sampling on 2043 people (93.5% of the required sample size; Figure 1). After 42 samples were excluded from the study due to improper blood sampling on the filter paper or missing demographic information, 2001 samples were included for the laboratory analysis of measles and rubella (91.6% of the required sample size). The mean age was 23.1 years (95% CI: 22.4-23.9), ranging from 1 to 89 years (Table 1). Men accounted for 47.3% of all the selected subjects. The places of residence were the north for 26.9%, the central region for 50.0%, and the south for 23.1%. Regarding the ethnic group, 59.7% were Lao Loum, and 40.3% were from other groups.

Table 1
Demographic characteristics of the survey participants (n = 2001).

Variable		n (%)
Age	Mean (range)	23.1 years (1-89)
Age group (years)	1-2	354 (17.7)
	5-14	311 (15.5)
	15-21	342 (17.1)
	22-39	607 (30.3)
	≥40	387 (19.4)
Sex	Male	946 (47.3)
Region	North	539 (26.9)
	Central	1000 (50.0)
	South	462 (23.1)
	Lao Loum	1195 (59.7)
Ethnicity	Khmu	293 (14.6)
	Hmong	323 (16.1)
	Others	188 (9.4)
	N/A	2 (0.1)

Measles

Of the 2001 samples, 1966 tested positive for antimeasles IgG. The estimated IgG prevalence was 97.5% (95% CI: 96.7-98.0) for measles after considering the sampling design and individual sampling weight. Figure 2 summarizes the results of the IgG antibodies against measles for each age group. When the results were compared among the age groups, seropositivity of IgG antibodies of >95.0% was detected in all age groups, except for those aged 1-2 years, who had the lowest seroprevalence of 90.6% (95% CI: 77.4-96.4). Compared with the results in the previous survey in 2014, the overall estimated prevalence was significantly higher in 2019 (97.5% [95% CI: 96.7-98.0] vs 83.9% [95% CI: 83.8-84.0]), and it was increased, especially in the groups aged ≤14 years.

Rubella

Of the 2001 samples, 1743 tested positive for antirubella IgG. The estimated IgG prevalence was 86.8% (95% CI: 85.2-88.2).

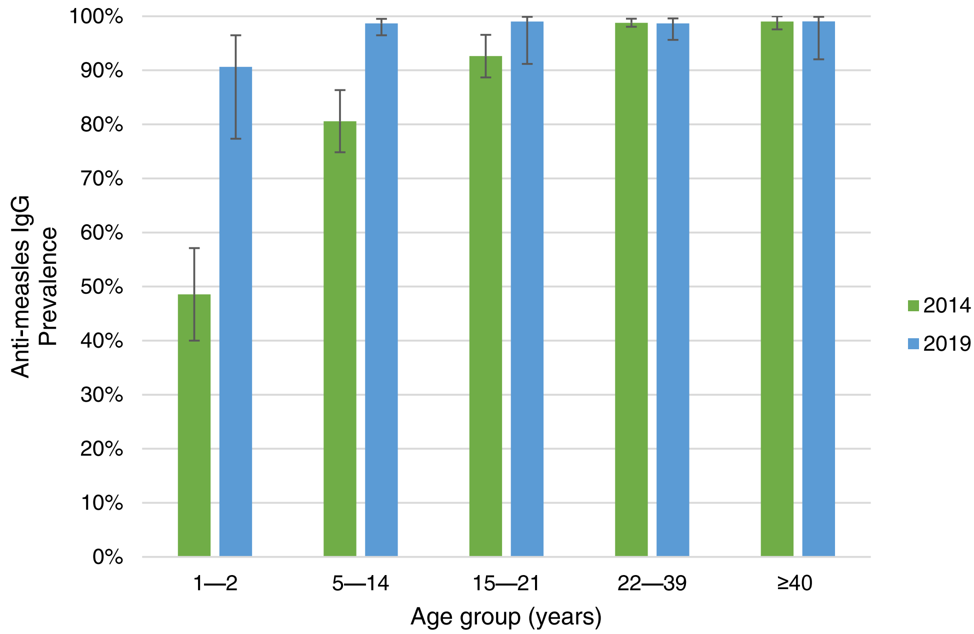

Figure 2. Estimated antimeasles IgG seroprevalence among different age groups in 2014 and 2019. Ig, immunoglobulin.

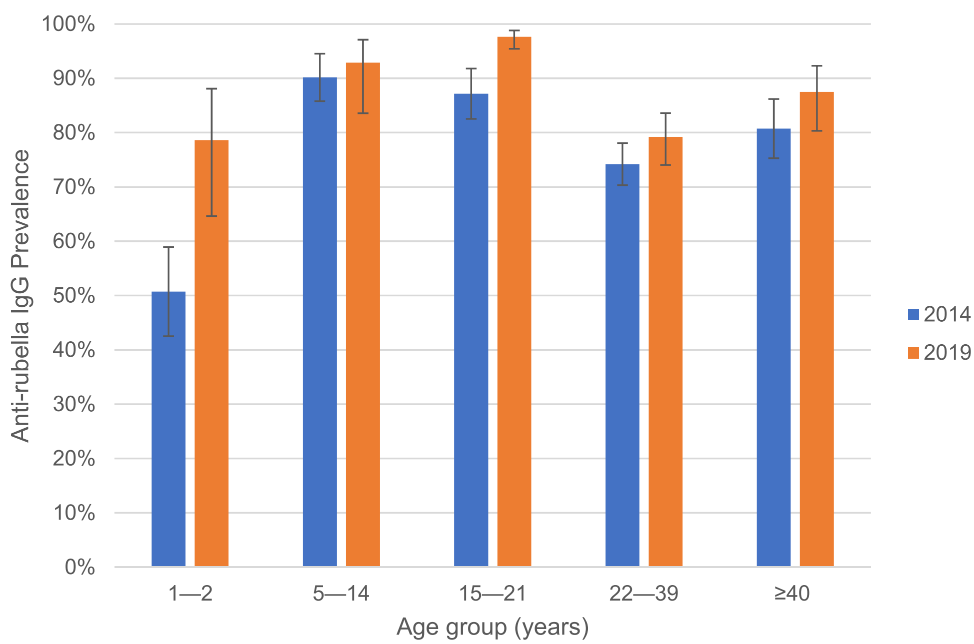

Figure 3. Estimated antirubella IgG seroprevalence among different age groups in 2014 and 2019. Ig, immunoglobulin.

Figure 3 summarizes the results of the IgG antibodies against rubella for the individual age groups. A seroprevalence of >80.0% was observed in most age groups covered by the past SIAs and routine immunization, except for the age groups of 1-2 and 22-39 years. Compared with the results in the previous survey in 2014, the overall estimated prevalence was significantly higher in 2019 (86.8% [95% CI: 85.2-88.2] vs 75.4% [95% CI: 75.3-75.5]). The seroprevalence increased in individuals aged 1-2 years (from 50.7% [95% CI: 42.5-58.9] in 2014 to 78.6% [95% CI: 64.6-88.1] in 2019) and 5-14 years (from 90.2% [95% CI: 85.8-94.5] in 2014 to 92.9% [95% CI: 83.6-97.1] in 2019), who had been covered in the recent SIAs in 2014 and 2017 and routine immunization services. However, those aged 22 years and older, including those aged 26 years and older who had not been covered by any vaccination programs of MRCV, had a lower seroprevalence than other age groups in both 2014 and 2019.

Estimated number of averted CRS cases

As presented in Appendix Table A.4 and Figure 4, the fit of the eight catalytic models fitted to the rubella seroprevalence data from both surveys simultaneously was generally similar. Three models (AA, AB, and CC) resulted in a plausible estimate for the reduction in the force of infection after the introduction of rubella vaccination, with the lower limit of the 95% CI being above zero (Appendix Table A.4). Of these three models, model AB was con-

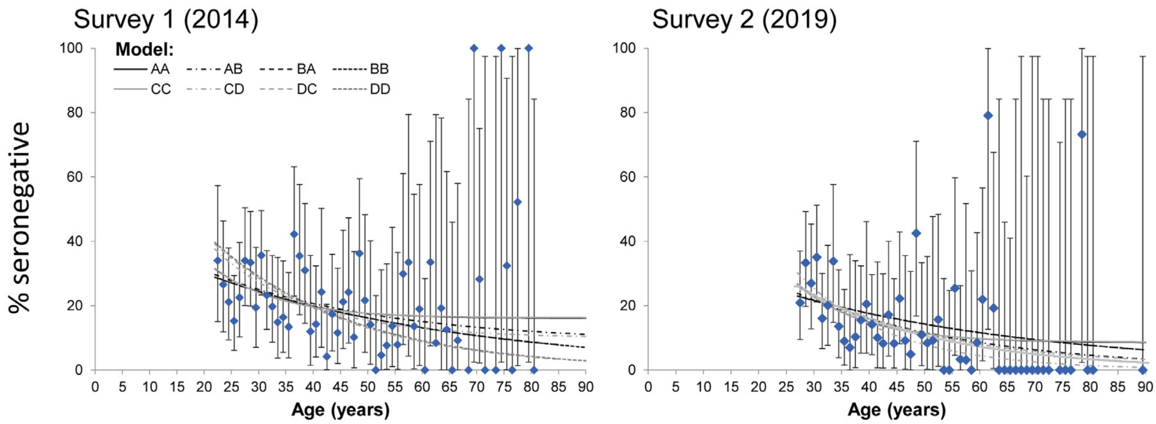

Figure 4. Comparison between the predictions of age-specific percentage seronegative obtained using the best-fitting catalytic model and the data used when fitting to both surveys simultaneously.
The bars reflect the 95% confidence intervals in the observed data.

Table 2
Best-fitting estimates of the prevaccination force of infection, estimated reduction in the force of infection after 2011, and CRS incidence and numbers of CRS cases prevented obtained for the most plausible model (AB) fitted to data from both surveys simultaneously (deviance = 136 on 105 degrees of freedom).

Outcome		Estimate (95% confidence interval)
Force of infection (per 1000 susceptible)	<15-year-olds	89 (72-105)
	≥15-year-olds	31 (17-48)
% reduction in the force of infection because of vaccination		100 (28-100)
CRS incidence per 100,000 live births in 2019	Without vaccination	122 (66-199)
	With vaccination	0 (0-70)
Estimated number of CRS cases in 2019	Without vaccination	78 (42-128)
	With vaccination	0 (0-45)
Number of CRS cases prevented in 2019		78 (33-126)

CRS, congenital rubella syndrome.

sidered the most plausible, with the highest estimates of the sensitivity of the antibody assay and different values for the force of infection for rubella for children and adults. For this model, the estimate for the reduction in the force of infection after the introduction of rubella vaccination was 100% (95% CI: 28-100). The estimates for the other models were considered implausible because the force of infection is estimated to have either increased since vaccination started or the lower 95% CI on the reduction in the force of infection was negative.

For the most plausible model, the CRS incidence per 100,000 live births was estimated to have decreased from 122 (95% CI: 66-199) if vaccination had not occurred to zero (95% CI: 0-70) with vaccination (Table 2). These incidence estimates correspond to 78 (95% CI: 42-128) CRS cases born in 2019 if vaccination had not occurred and zero (95% CI: 0-45) as a result of vaccination being introduced, resulting in 78 (95% CI: 33-126) cases prevented in 2019 due to vaccination. Due to the absence of data from surveillance on the numbers of CRS cases in Lao PDR, the extent to which these estimates under- or overestimate the true CRS incidence is unclear. For the most plausible model, the basic reproduction number for rubella was estimated to be 2.2 (95% CI: 2-2.7) and the estimated net reproduction number by 2019 was around 0.3 (95% CI: 0.3-0.4; Appendix Table A.4). When the catalytic models were fitted just to the data for 2019, making assumptions for the average reduction in the force of infection after the introduction of vaccination, the best-fitting values for the selected model (B) was similar to those estimated using the catalytic models to both datasets simultaneously (Table 3). The findings for the remaining models are in Appendix Table A.5. In addition, the estimated force of infection for children (83 per 1000, 95% CI: 63-102) was comparable to that estimated just using the data for 2014. For adults, however, the estimated prevaccination force of infection was almost two-fold higher than that estimated just using data from 2014 (19 per 1000, 95% CI: 9-127); although, the 95% CIs overlapped.

Discussion

The estimated antimeasles IgG prevalence has increased to a level that is much higher than that estimated in the survey 2014, especially in children and young adolescents aged 5-14 years. During the same period, the number of measles cases reported to the national surveillance decreased from 10.7-1.4 per 1 million population from 2014-2018 [5,6]. The estimated antirubella IgG prevalence has reached and exceeded the required threshold of 76-79% in all age groups that the WHO considered highly effective in the prevention of rubella and CRS in highly endemic countries [19]. Significant increases were observed among those aged 15-21 years between the surveys in 2014 and 2019. It could imply that both routine immunization and recent SIAs in 2014 and 2017 were effectively implemented to increase their immunity because those services covered those age groups. We estimated that 78 (95% CI: 33-126) CRS cases were prevented in 2019 through rubella-containing vaccination administered either routinely or SIAs. Unlike our previous estimates, which just used seroprevalence data from 2014 and made assumptions about the reduction in the post-vaccination force of infection, our current estimates were based on the data from 2014 and 2019. As such, we were also able to estimate the average reduction in the force of infection resulting from the introduction of rubella vaccination (100%, 95% CI: 28-100). Although the CIs on the reduction is wide, a reduction in the force of infection is likely to have occurred, given findings from studies considering the seroprevalence data collected before and after the mass campaigns [25].

Studies sometimes present the estimates of the reproduction number of an infection. In our analyses, we have presented the es-

Table 3
Summary of the best-fitting estimates of the prevaccination force of infection obtained from the selected models when fitted to the data from either 2014 or 2019 or both.

Assumed or estimated reduction in force of infection since 2011	Force of infection per 1000 (susceptible) before 2011, estimated using data from:					
	2014 only		2019 only		Both 2014 and 2019	
	<15-year-olds	≥15-year-olds	<15-year-olds	≥15-year-olds	<15-year-olds	≥15-year-olds
0%	79 (41-124)	18 (9-128)	63 (34-88)	36 (21-54)	-	-
25%	80 (45-126)	18 (9-128)	68 (42-92)	36 (21-54)	-	-
50%	82 (49-127)	19 (9-128)	73 (49-95)	36 (21-54)	-	-
75%	82 (52-129)	19 (9-127)	78 (56-98)	36 (21-54)	-	-
100%	83 (56-130)	19 (9-127)	83 (63-101)	36 (21-54)	-	-
100% (95% confidence interval: 28-100)					89 (72-105)	31 (17-48)

timates of the average force of infection for rubella. For rubella, the average force of infection for children and adults is helpful statistics because, using equations, such as those presented in these analyses, it is possible to estimate the burden of CRS and the number of CRS cases prevented, which is relevant for rubella. In contrast, although reproduction numbers are useful for indicating the trend in the incidence of an infection in the overall population, they do not provide insight in the CRS incidence, which depends on both levels of susceptibility in women of childbearing age and the force of infection that they experience. Reproduction numbers also rely on assumptions about the contact patterns between the different age groups, which are not always known in populations.

Our previous study conducted in 2014 found that the IgG prevalence against both measles and rubella was low compared with the reported SIA coverage, suggesting that vaccine management, especially vaccine temperature control, was not properly conducted [3]. Lao PDR and partners have made an effort to strengthen cold-chain management by replacing old refrigerators and freezers with the assistance of partners in the last 5 years, which could have improved the vaccine management, resulting in the improvement of IgG prevalence for both measles and rubella and averted CRSs. Although national immunization coverage has often been used as a performance indicator of immunization, and the coverage of MRCV was reported as 96%, 97%, 100%, and 97% in 2007, 2011, 2014, and 2017, respectively, in Lao PDR, the current study clearly demonstrated that the reported coverage was sometimes inconsistent with the actual level of population immunity. Blindly planning immunization implementation based solely on the reported coverage might fail to cover the populations with low antibody titers, creating a breeding ground for outbreaks. Based on the previous survey results, the NIP conducted two rounds of SIAs covering the age groups that the survey identified as having lower immunity than the required herd immunity.

However, the IgG prevalence against measles and rubella in the age group of 1-2 years is still in the lower range of the herd immunity threshold. Other seroprevalence studies conducted in several provinces in Lao PDR have also found a low prevalence of measles antibodies among infants and young age groups, given routine and SIA vaccination services [26–29]. This might indicate heterogeneity in the measles vaccination among provinces or between rural versus urban areas. The IgG prevalence against rubella of those aged 1-2 years and 22-39 years were still within the range of the herd immunity threshold; although, it was much lower than that of other age groups. On this basis, we recommend that the NIP further strengthens the routine immunization program for those aged 1-2 years and provide another immunization opportunity for those aged 22-39 years, especially women of childbearing age and those aged over 26 years who have not been vaccinated by any national immunization services. Because these adult populations make up the core of the labor force and have limited time to access health services due to their work [12,13], immunization services must be provided along with other services. Furthermore, recent estimates suggest that the COVID-19 pandemic has potentially disrupted immunization delivery services, with an estimated 7.9% reduction in the worldwide measles-containing vaccine first dose coverage in 2020 compared with that expected [30]. According to WHO, the reported worldwide measles cases increased by 79% in the first 2 months of 2022 compared with the same period of 2021 [31]. Because the rubella vaccination accompanies the measles vaccine, the prolonged disruption of both routine immunization services and SIAs could increase the burden of CRS by leading to increasing proportions of women of childbearing age who are still susceptible to infection. To control the COVID-19 pandemic and mitigate its negative impact on MRCV coverage, the COVID-19 vaccination program could be used as an opportunity to provide MRCV simultaneously, as soon as there has been a further study of the efficacy, safety, and adverse events after immunization when MRCV is co-administered with COVID-19 vaccines.

This is the first report describing the elevation of antimeasles and antirubella IgG prevalence obtained by comparing two nationally representative survey data from Lao PDR 5 years apart in 2014 and 2019. The current survey results quantitatively detected the change in IgG prevalence before and after the two rounds of SIAs, as well as residual antirubella immunity gaps among children aged 1-2 years and women of childbearing age. The evidence obtained from the surveys should help to optimize immunization strategies for eliminating measles and rubella. The response rates were high in both surveys, and the design effect of prevalence was calculated to be 0.87 and 0.96, which was acceptable because we set it at 1.6 before the survey. We also used the same type of filter paper for the sample collection in both surveys and examined the samples using the same enzyme-linked immunosorbent assay kits in the same WHO Global Specialized Laboratory. These enabled us to assess the change in herd immunity between 2014 and 2019 and evaluate the effectiveness of the SIAs in 2014 and 2017 and the routine immunization program conducted after the survey in 2014. Because the surveys produced national representative data, the results enabled the country to request the National Verification Committee and Regional Verification Commission for measles and rubella elimination to examine whether the country is in a state of measles and rubella elimination.

We note that our estimates are subject to some limitations. The people surveyed in 2019 were different from those surveyed in 2014. However, the regions and study population were selected in both surveys to ensure a nationally representative population. Furthermore, we did not account for changes in the reduction in the force of infection over time in our mathematical modeling. It is plausible that the reduction in the force of infection was higher soon after the introduction of the SIAs than several years later. In addition, our analyses used the data associated with people aged at least 22 and 27 years for the surveys in 2014 and 2019, respectively, given that the people aged under 22 and 27 years for these surveys, respectively, would have been vaccinated. In addition, when calculating the reproduction numbers for rubella, we used estimates of the amount of contact between different age groups, which were derived from contact studies conducted outside of Lao PDR (Appendix).

To the best of our knowledge, this is the first study to demonstrate the effective and strategic use of the nationwide seroprevalence surveys at two different points to assess the baseline population immunity, identify the immunity gaps, conduct SIAs to fulfill the gaps, and evaluate the immunity changes. Seroprevalence surveys could provide critical evidence to assess the effectiveness of past immunization activities, develop strategic and efficient immunization activity plans to fulfill the gaps identified by the survey, and operationalize the plans as evidence-based interventions. To maximize the impact of the immunization program and accelerate the way to achieve the elimination goals, seroprevalence surveys should be regularly implemented at the national, subnational, and/or subpopulation levels to monitor and evaluate the effectiveness of the immunization program directly by measuring the immunity in addition to tracking the reported coverage and cases in the national surveillance. It is critical to identify undervaccinated and unvaccinated pockets among vulnerable or unreached populations in some geographical locations and use a tailored immunization approach to prevent outbreaks of measles among those populations, which is also recommended as Tailoring Immunization Programmes by the WHO [32] and has been done in several countries [33,34].

Declaration of competing interest

The authors have no competing interests to declare.

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Ethical approval

Informed written consent was obtained from all selected participants. When the participants were aged <18 years, it was obtained from their parents or legal representatives. The participants' names were not recorded. The research proposal was approved by the Ministry of Health; Lao PDR (06/NECHR); NCGM, Japan (NCGM-3038); and National Institute of Infectious Diseases, Japan (NIID-1012).

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Author contributions

SM, CP, LF, TUY, and HR conceptualized the study. SM, CP, and MH secured research funding. SM, CP, YI, and MH contributed to the study design. PN, KP, CT, and BK coordinated the survey and data collection. TO, MF, KK, and MH supervised the survey implementation. YM and MT conducted the laboratory analysis. SM, EV, and YI conducted the data analysis. SM, EV, and CP drafted the initial manuscript, and all authors reviewed and revised the drafted manuscript and approved the final manuscript.

Data sharing

The data for deidentified individual participants in this study will be available after publication and will be shared with those who get approval from the ethics committees in the Ministry of Health, Lao PDR; NCGM, Japan; and NIID, Japan. For data access, please contact the corresponding author and the immunization program at the Ministry of Health in Lao PDR.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2023.01.044.

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