Measles and rubella elimination: protecting children through immunization in South-East Asia Region (SEAR)

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Summary

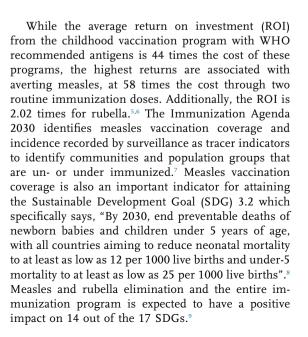
The South-East Asia Region (SEAR) adopted the goal of "measles and rubella elimination by 2023". The goal was revised in 2019 to 'measles and rubella elimination by 2023' The strategies adopted to reach the goal included achieving \geq 95% coverage with 2 doses of measles- and rubella-containing vaccine (MCV2; RCV2); establishing effective case-based surveillance supported by an accredited laboratory network; and implementing rapid response measures to control measles outbreaks. Of the 11 countries in the Region, to date five countries have eliminated measles and rubella and two more have controlled rubella. An estimated 242 million cases and 4.7 million deaths due to measles were averted between 2014 and 2022. The high-level political commitment, programmatic infrastructure and partnerships developed for the elimination of polio and maternal and neonatal tetanus played a critical role in this achievement. WHO, supported by key partners, provided technical support and strategic guidance for programmatic improvements, generated evidence to guide policy and strategic shifts, strengthened capacity of health workforce and conducted periodic programmatic reviews. However, unexpected occurrence of COVID-19 pandemic impacted vaccine coverage and quality of surveillance, thereby delaying achievement of the goal, and necessitating a revision of the target date of elimination.

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Introduction

Measles, a single-stranded, RNA respiratory tract virus commonly found in children, is one of the most contagious disease of humans, especially in children.² Before the introduction of measles vaccine in 1963, major epidemics occurred every 2–3 years with an estimated 30 million cases and more than 2 million deaths occurring globally each year due to measles, and more than 95% of individuals had been infected with measles virus by the age of 15 years.³ Similarly, Rubella virus is generally recognized as the most common infectious cause of birth defects, accounting for an estimated 100,000 infants born with congenital rubella syndrome (CRS) each year worldwide.⁴ For both these diseases, the primary strategy for prevention is vaccination.







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In 2013, following an extensive consultation and review of the benefits and the biologic, programmatic, and financial feasibility of measles and rubella elimination, the eleven Member States of the World Health Organization (WHO) South-East Asia Region (SEAR)^e adopted the goal of measles elimination (absence of endemic measles cases for a period of ≥ 12 months) and rubella and congenital rubella syndrome control (95% reduction in disease incidence from the 2013 level) by 2020.10 At that time, no global goal for measles and rubella elimination existed; a situation that has remained unchanged.¹¹ In 2014, to provide impetus toward achieving this goal, the South-East Asia Region declared measles elimination and rubella control as one of the Regional Flagship Priorities.12,13 In 2019, based on an in-depth independent review of the status of rubella control and a consultation with experts and Member States and taking the opportunity offered by measles elimination activities, the goal was revised to eliminating both measles and rubella (defined as for measles) by 2023.14 The strategies adopted to achieve the goal were:

- Achieving and maintaining ≥95% coverage with 2 doses of measles- and rubella-containing vaccine in every district through routine or supplementary immunization activities (SIAs)^f;
- Developing and sustaining a sensitive and timely case-based surveillance system that met recommended performance indicators;
- Developing and maintaining an accredited laboratory network;
- 4) Achieving timely identification, investigation and response to measles outbreaks; and
- 5) Linking with other public health initiatives to achieve the preceding four strategies.¹⁵

The purpose of this article is to review the progress achieved in the measles and rubella elimination efforts in WHO South-East Asia Region and identify key facilitators and barriers for the progress.

Progress in measles/rubella vaccination during the last decade

During the decade, access to two doses of measles containing vaccine and at least one dose of rubella containing vaccine was greatly enhanced (Table 1).

Country	MCV1	MCV2 ^a	RCV1 ^a	RCV2 ^a
Bangladesh	1979	2012	2012	2015
Bhutan	1979	2006	2006	2006
DPR Korea	1997	2008	2019	2019
India	1985	2010	2017	2017
Indonesia	1982	2003	2017	2017
Maldives	1983	2007	2007	2017
Myanmar	1987	2012	2015	2017
Nepal	1988	2015	2013	2015
Sri Lanka	1984	2001	1996	2001
Thailand	1984	1996	1986	1997
Timor-Leste	1982	2016	2016	2016

^aMCV1- first dose of measles containing vaccine; MCV2-second dose of measles containing vaccine; RCV1- first dose of rubella containing vaccine and RCV2second dose of rubella containing vaccine.

Table 1: Date of introduction of measles and rubella containing vaccines in SEAR Countries.

Between 2013 and 2022, approximately 314 million children have been vaccinated with the first dose of measles containing vaccine (MCV1), 265 million with the second dose of measles containing vaccine (MCV2) and 187 million children with the first dose of rubella containing vaccine (RCV1) as a part of routine immunization activities.¹⁶ All countries in the Region conducted supplementary immunization activities (SIAs) with measles and/ or rubella containing vaccine and more than 653 million children were vaccinated during these SIAs in various age groups.^{17,18}

Coverage with MCV1 increased from 85% in 2013 to an all-time high of 94% in 2019. Similarly, the coverage of MCV2 was reported at 83% in 2019 compared to 59% in 2013. The coverage of RCV1 in 2019 was estimated at 93% compared to 12% in 2013.16 The Region was however significantly hit by the COVID-19 pandemic in 2020 and 2021 and observed a significant decline in coverages of measles and rubella containing vaccine.19 (Figs. 1 and 2) The Region reported an 8% decline in MCV1, 11% decline in MCV2 and a 7% decline in RCV1 coverage in 2021 compared with 2019. This was followed by a sharp recovery of MCV1 and MCV2 coverage in the Region in 2022, with the MCV1 coverage only 2% below the 2019 level, and the MCV2 coverage 2% above the 2019 level.¹⁶ A total of 49,201 suspected measles cases were reported in 2022 compared with 31,091 in 2020 and 69,207 in 2019.

In 2013, all countries were conducting case-based surveillance which transformed to "Laboratory Supported Acute Fever and Rash Surveillance" by 2021. This effort was coupled with expansion of laboratory network from 23 laboratories in 2013 to 58 proficient laboratories in 2022 with at least 26 Measles-Rubella (MR) laboratories conducting both serology and Reverse Transcriptase - Polymerase Chain Reaction (RT-PCR) for measles and rubella and four laboratories including the Regional

^eThe WHO South-East Asia Region consists of Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste.

^fSIAs generally are carried out using two target age ranges. An initial, nationwide catch-up SIA focuses on all children aged 9 months–14 years, with the goal of eliminating susceptibility to measles in the general population. Follow-up SIAs generally are conducted nationwide every 2–4 years and target children aged 9–59 months; their goal is to eliminate any measles-rubella susceptibility that has developed in recent birth cohorts and to protect children who did not respond to the first measles-rubella vaccination.

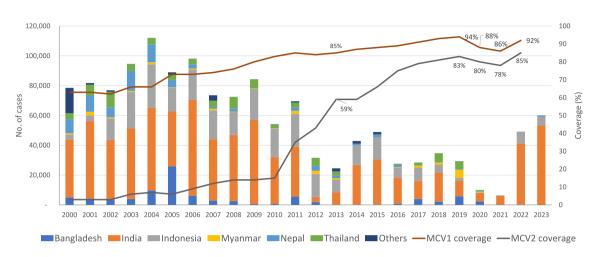


Fig. 1: Number of reported measles cases* and estimated percentage of children who received their first and second dose of measles-containing vaccine (MCV),[†] by country — World Health Organization (WHO) South-East Asia Region (SEAR), 2000–2023. Abbreviations: MCV1 = first dose of MCV in routine immunization; MCV2 = second dose of MCV in routine immunization. *Cases of measles reported to WHO and the United Nations Children's Fund (UNICEF) through the Joint Reporting Form from WHO-SEAR. [†]Data are from WHO and UNICEF estimates for SEAR, available at http://immunizationdata.who.int. ⁵Others include Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka, Timor-Leste.

Reference Laboratory (RRL) in Bangkok, Thailand, also conducting viral genome sequencing.²⁰ The sensitivity of measles and rubella surveillance as measured by the cardinal indicator of non-measles non-rubella discarded case^g rate per 100,000 population has increased from less than 0.5 is 2013 to around 3.79 in 2022—a more than seven-fold increase in the sensitivity of surveillance.²¹

By the end of 2021, the Region was no longer a major contributor to the global measles mortality burden. In 2014, the Region contributed to 40% (46,900 of total 114,900) of global measles deaths which reduced to 8% (10,230 of total 127,656) in 2021.^{22,23} The estimated annual number of deaths due to measles decreased by 78% (from 46,900 to 10,230 during the same period). Modeling data has estimated that cumulatively more than 242 million cases and more than 4.76 million deaths due to measles would have been averted due to vaccination during this period (Table 2).^{15,22,24-26}

All countries in the region were endemic (continuous transmission of indigenous or imported cases that persists for \geq 12 months in any defined geographical area) to measles and rubella in 2013. Following accelerated deployment of the elimination strategies, by October 2023, five countries—Bhutan, DPR Korea, Maldives, Sri Lanka and Timor-Leste were verified to have eliminated measles and rubella based on the verification framework developed by WHO.^{27,28} Two additional countries were verified to have controlled rubella and congenital rubella syndrome—Bangladesh and Nepal during this period.²⁹⁻³¹

We discuss below enabling factors and challenges faced in this effort, however, much more remains to be done in reaching the ultimate target of elimination.

Enabling factors

The Region's efforts over polio and maternal and neonatal tetanus elimination, and increases in routine immunization coverage, laid the foundations for establishing the goal of elimination of measles and rubella.^{32–36} The available infrastructure and capacity, especially for surveillance and vaccine deployment, were recalibrated for efficient implementation of regional strategy.^{37–39}

Political and programmatic commitment

The Region, through its various regional committee resolutions expressed ownership and highest level of political commitment to achieve the goal of measles and rubella elimination in the context where there was no global goal to guide the program.^{9,13} Declaring measles and rubella elimination as a flagship programme underscored the commitment and gave additional impetus.¹² This resulted in the development of a National Strategic Plan for measles and rubella elimination in each of the eleven Member States of the South-East Asia Region that provided the impetus for an accelerated implementation of activities as outlined in the results section.

^gA suspected case of measles/rubella that has been investigated and discarded is termed a non-measles, nonrubella case if any of the following is true: An adequate specimen collected during the proper time period after the onset of rash has tested negative in a proficient laboratory; there is an epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is not measles or rubella; another etiology has been confirmed, regardless of whether it meets the definition of an epidemiological linkage; and the case does not match the definition of a clinically compatible measles/rubella case.

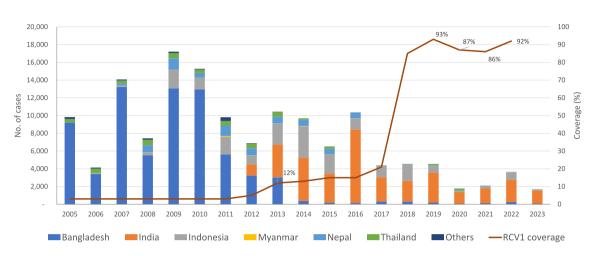


Fig. 2: Number of reported rubella cases* and estimated percentage of children who received their first dose of rubella vaccine (RCV),[†] by country — World Health Organization (WHO) South-East Asia Region (SEAR), 2005–2023. Abbreviations: MCV1 = first dose of MCV in routine immunization; MCV2 = second dose of MCV in routine immunization. *Cases of measles reported to WHO and the United Nations Children's Fund (UNICEF) through the Joint Reporting Form from WHO-SEAR. [†]Data are from WHO and UNICEF estimates for SEAR, available at http://immunizationdata.who.int. [§]Others include Bangladesh, Bhutan, DPR Korea, Maldives, Myanmar, Nepal, Sri Lanka, Timor-Leste.

Partnerships and collaborations

Much of the achievement of immunization in South-East Asia Region is a result of partnership that brought a range of stakeholders together – medical doctors, health workers, laboratory technicians, officials working in regulatory agencies, policymakers in health ministries, local partners, international agencies.^{37–40} The Immunization task forces, or the immunization coordination committees created at all levels of administration in larger countries were utilized as oversight

Country	2003						2022					% change, 2003-2022		
	WHO/ UNICEF estimated coverage ^a (%)		MCV schedule ^b			incidence ^{d,e}	WHO/ UNICEF estimated coverage ^a (%)		MCV schedule ^b		No. reported measles cases (JRF) ^c	Measles incidence ^{d,e}	MCV1 coverage	measles incidence ^e
	MCV1	MCV2	MCV1	MCV2			MCV1	MCV2	MCV1	MCV2				
Bangladesh	76	f	M-9 m	f	4067	30.2	97	93	MR-9 m	MR-15 m	311	1.8	28	-94
Bhutan	88	_f	M-9 m	f	0	0.0	97	97	MMR-9 m	MMR-24 m	7 ^j	0	10	0
DPR Korea	95	f	M-9 m	f	0	0.0	0 ^k	0 ^k	MR-9 m	MR-15 m	0	0	-100	0
India	60	f	M-9 m	f	47,147	42.4	95	90	MR-9 m	MR-16-24 m	40,967	28.9	58	-32
Indonesia	74	21 ^g	M-9 m	M-7 y ^g	24,457	111.0	84	67	MR-9 m	MR-18 m ^h	7704	28	14	-75
Maldives	96	f	M-9 m	f	75	247.8	98	98	MR-9 m	MMR-18 m	0	0	2	-100
Myanmar	80	f	M-9 m	f	830	17.2	75	90	MR-9 m	MR-18 m	10	0.2	-6	-99
Nepal	75	f	M-9 m	f	13,344	532.0	90	87	MR-9 m	MR-15 m	130	4.3	20	-99
Sri Lanka	99	90	M-9–12 m ⁱ	MR-3 y	65	3.4	99	98	MMR-9 m	MMR-3 y	0	0.0	0	-100
Thailand	96	92	M-9 m	MMR-6 y	4519	70.0	96	87	MMR-9 m	MMR-1.5 y	64	0.9	0	-99
Timor-Leste	55	_f	M-9 m	f	94	99.2	79	78	MR-9 m	MR-18 m	8 ^j	0	44	-94
Region overall	66	6			94,598	57.4	92	85			49,201	23.8	39	-59

JRF = joint reporting form; m = months; M = measles; MCV = measles-containing vaccine; MR = measles-rubella; MMR = measles-mumps-rubella; UNICEF = United Nations Children's Fund; y = years. ^aData were from WHO and UNICEF estimates, 2020 revision (as of July 2021). Data available at http://immunizationdata.who.int. ^bAs reported to WHO/UNICEF on JRFs for the year. ^cJRF was submitted to WHO and UNICEF by member states with the official immunization data and the number of measles cases in the country for the year. ^dMeasles incidence is calculated based on the reported measles cases and population by member states through WHO/UNICEF JRF. ^eCases per million population (excluding imported cases in countries verified to have eliminated measles). ^fMCV2 was not introduced into routine immunization. ^gSub-national introduction in schools of West Java at age 7 years. ^hMCV third dose given in schools at grade 1. ⁱChanged in 2011 from age 9 months to 9-12 months. ^JImported or import related bases. ^kNo vaccination conducted due to COVID-19 pandemic related barriers leading to vaccine stockout.

Table 2: Estimated coverage^a with the first and second dose of measles-containing vaccine (MCV), vaccination schedule,^b number of reported measles cases,^c and measles incidence,^{d,e} by country — World Health Organization South-East Asia Region, 2003 and 2022.

mechanisms for measles and rubella elimination. At subnational level, large countries activated or established multisectoral, intersectoral and cross-border collaborations created for previous elimination programs to enhance implementation of the strategies.^{41,42}

Clear articulation of strategies and directives

'The Strategic plan for measles elimination and rubella and congenital rubella syndrome control in the South-East Asia Region, 2014–2020' and a costed 'Strategic plan for measles and rubella elimination in WHO South-East Asia Region: 2020–2024' developed during the period provided the strategic framework to the program and identified five key areas of focus for program implementation viz-immunization, surveillance, laboratory support, outbreak response and creating enabling environment through advocacy, enhanced program oversight and better program governance.^{14,43} The first document focused more on developing the systems and the processes and the second document focused more on innovative approaches to accelerating progress.

Technical leadership

The Regional and National Immunization Technical Advisory Groups provided overall technical leadership to the immunization program while the Regional Verification Commission for measles and rubella elimination (SEA-RVC), established in 2016, monitored the implementation of norms and standards through the process of in-depth country program evaluation, site visits, as well as the intensive review of the annual progress report submitted by the national verification committees applying the standard criteria laid out in the "Framework for verification of measles and rubella elimination". This Framework was developed by WHO in 2016 and revised in 2020, in consultation with experts and Member States.^{27,28,44} The corresponding National Verification Committees (NVC) in the countries worked with respective governments to provide technical leadership and monitor progress towards the goal of measles and rubella elimination.29-31,45-47

A measles, rubella and congenital rubella syndrome surveillance guide was also developed in 2017 and updated in 2022 to support Member States to develop and implement elimination standard surveillance for measles and rubella.⁴⁸

High quality operations including monitoring, evaluation and course corrections

The country teams of WHO and partners provided support to ensure high quality operations. This included ensuring guidance on establishing high quality vaccine supply chain, cold chain, safe injection practices, and waste management among various other measures. Significant focus was maintained on monitoring evaluation and course correction. Programmatic risk assessment for measles and rubella transmission was conducted periodically in all countries on an annual basis since 2017 and reviewed jointly by the national immunization programs and national verification committees to prioritize geographical areas and develop further strategies to mitigate the risk of measles and rubella transmission as well as to close the immunity gaps through vaccination activities.³⁴

Periodic independent external evaluations were also conducted at regional and national level to inform timely course corrections.²⁴⁻²⁶ This included revising the goal of rubella control to rubella elimination; shifting the target date from 2019 to 2023; changing the case definition for suspected measles to a more sensitive syndromic approach of 'Acute fever and rash surveillance' and revision of the surveillance reporting sites in large countries involving more community informants.

Research and development

Several research studies to guide strategic interventions in the measles and rubella programme have been under implementation during the period. These include costing of measles and rubella elimination in the WHO South-East Asia Region; sero-surveys to assess the population immunity profile against measles and rubella for better targeting of SIAs in India and Nepal; assessment of other differential diagnoses of acute fever and rash to help determine if the current target of two non-measles, nonrubella fever and rash cases per 100,000 population needs revision; and development of rapid diagnostic test kit for measles and rubella.⁴⁹ Emerging technologies like microarray patches for vaccine administration appear promising for operations of the future.

Challenges

The COVID-19 pandemic impacted the delivery of immunization and surveillance activities, posing significant challenges to achieve the measles and rubella elimination goal by 2023.⁵⁰ Despite the challenges brought on by the pandemic, Bhutan, DPR Korea, Maldives, Sri Lanka and Timor-Leste sustained their measles elimination status while Maldives and Sri Lanka sustained their rubella elimination status.⁵¹

Significant challenges to achieve measles and rubella elimination in the Region remain irrespective of the pandemic, the greatest of which was to improve routine immunization programmes to 95% or more coverage with two doses of a measles-rubella containing vaccine in all districts of all countries. The un-evenness in vaccination coverage, due to operational issues as well as pockets of vaccine hesitancy remain a major challenge, especially in large countries of the Region. The accumulation of susceptible cohorts of children due to chronic gaps that further widened during the COVID-19 pandemic pose a risk of outbreaks of measles and rubella outbreaks. A root cause analysis of outbreaks conducted has demonstrated that these outbreaks have

Search strategy

This review draws from information already available with the WHO Offices as a part of this initiative. Additional sources of information were accessed through a literature search of available related articles, grey literature and library search on reports was conducted from publicly available sources. The primary databases employed were Medline through PubMed (https://pubmed.ncbi.nlm.nih.gov/), and World Health Organization (WHO) institutional repository for information sharing (IRIS) available online (https://apps.who.int/iris/). No attempt was made to obtain unpublished data, data unavailable in the public domain, or data available within specific institutions at the national, state or local level.

This study estimated measles deaths and cases averted during this period using the measles mortality model adopted by WHO-UNICEF. This model is rerun each year using the new and revised annual WHO-UNICEF estimates of national immunization coverage data as well as updated surveillance data. We used an updated (2021) data on case fatality from a recent systematic review and a suite of covariates with known relationships to case fatality in a Bayesian meta-regression modeling framework to produce estimates of measles case fatality ratios.¹

occurred because of failure to vaccinate due to either access issues or due to hesitancy to accept the vaccines by selected population groups, most of whom remain generally underserved for overall health services. Lack of awareness of benefits of vaccination campaigns is considered to have contributed to vaccine hesitancy. A similar approach to polio will be essential in the current situation for the special populations that remain hesitant to vaccination against measles and rubella.

Sensitivity of surveillance for measles and rubella remained sub-optimal in several endemic countries resulting in under reporting and underestimation of the disease burden. Of the measles outbreaks reported in the Region in 2022, only nearly half of these were responded with adequate immunization activities. Financial insufficiency and inadequate commitment for optimal implementation of key strategies at the subnational level were major hindrances to achieve the 2023 target of measles and rubella elimination.⁵²

Efforts were made to revive the coverage and surveillance through new and innovative ways including telephonic surveillance, virtual training and country-specific solutions were introduced to revitalize efforts.^{44,52} These efforts have resulted in a sharp recovery in immunization and surveillance performance, however an independent review commissioned to assess progress towards measles and rubella elimination by 2023 cautioned that the Region is off track to achieve the 2023 target and identified the need to revise the target date of measles and rubella elimination in consultation with global and regional experts, partners, and Member States.⁵²

Way forward

Ensuring optimal implementation of key elimination strategies at accelerated pace remains a challenge, more

so now with the COVID-19 pandemic and COVID-19 recovery phase that is likely to last for a couple of years. To accelerate progress and to sustain the gains, measles and rubella elimination activities should be optimally implemented through the primary health care (PHC) systems. Immunization programmes are an integral part of primary health care to achieve universal health coverage. Finally, the Region needs innovations to overcome vaccine delivery to areas with conflicts, migratory populations and specific populations with vaccine hesitancy. Measles and rubella elimination have their effect beyond immunization to overall child survival and development. Together we need to ensure that no child is left behind without the benefits of vaccination.

Contributors

Sunil Bahl and Sudhir Khanal were involved in the conceptualizing the paper and initial data analysis. Shahina Tabassum, Lucky Sangal, Jon Andrus, and Kumnuan Ungchusak were involved in the review of the draft manuscript, provide strategic comments and finalization of the manuscript.

Declaration of interests

SB, SK, LS are employees of WHO SEARO; ST, KU and JA are from South-East Asia Regional Verification Commission for Measles and Rubella Elimination. The views expressed in the submitted article are of the authors and not an official position of the institution to which they are affiliated. The authors were not precluded from accessing data in the study, and they accept responsibility to submit for publication. The authors declare no conflict of interest.

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