MEASLES INCIDENCE AND MEASLES VACCINE COVERAGE IN SOUTH EAST ASIA REGION

(2017-2021)

A thesis submitted for the degree of Master of Philosophy at

The Australian National University

National Centre of Epidemiology and Population Health

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February 2023

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Statement of authorship

I declare that the work contained in this thesis is my own work. To the best of my knowledge and belief, this thesis contains no material previously published by another person except where due acknowledgement has been made. This thesis contains no material that has been accepted for the award of any other degree or diploma in any university. Contributions made to the research by others have been acknowledged in the respective chapter preface.

Ei Ei Zar Nyi
February 24th, 2023

Acknowledgments

First and foremost, I would like to express my sincere gratitude to my academic supervisor Dr. Samantha Colquhoun for providing me an opportunity to complete this Master degree in a difficult situation and for giving me guidance and encouragement during the course and advice to get a job related to my career. I would like to extend my words of gratitude to my associate supervisor, Dr Amy Parry, for her invaluable support and guidance throughout this study while she was undertaking her PhD.

I would like to thank my former academic supervisor Dr. Phillipa Binns for her interest, kind support and close supervision during MAE program in 2020 and 2021. I never forget my former field placement supervisor Dr. Toe Thiri Aung for her kind support not only in my academic journey but also in my personal journey.

I owe my deepest gratitude to Australian Government, Department of Foreign Affairs and Trade, ASEAN MAE Fellowship for providing a scholarship to undertake this Masters degree and for bringing me Australia to complete the course block in 2020.

I really thank the program administrators and academic administrators: Ms Hayley Primrose, Ms Laura Vitler, Ms Sam Dissanayake**,** Ms Abigail Fang Fang for supporting me in administration and finance. I would like to thank Dr Tsheten Tsheten for assisting me with statistical and mapping support.

I also acknowledge Ministry of Health, Myanmar for permission to apply for this program. I also am grateful to staff from NCEPH and my field placement (Central Epidemiology Unit) and all the supporters for helping me to study in feasible environment.

I would like to thank my fellow MAE colleagues of the 2020 cohort for sharing knowledge, supports and laughs.

Last, but not the least, I would like express my special thanks to every single family member including my late husband for supporting me with everything I need throughout the program of study.

Abstract

Introduction

Measles is a highly contagious disease caused by the measles virus of the paramyxovirus family. Measles remains one of the leading causes of childhood morbidity and mortality worldwide, accounting for more than 140,000 deaths in 2018. There was global concern about the high risk of measles outbreaks occurring due to the disruption of immunisation services during the COVID-19 pandemic. This study aimed to describe the incidence and immunisation coverage of measles in South East Asia Region (SEAR) between 2017 and 2021.

Methods

A cross-sectional descriptive study was undertaken using publicly available data from WHO, UNICEF, World Bank, and Our World in Data. Analysis included measles cases, estimated measles vaccine coverage, supplementary immunisation activities. Statistical analysis was conducted using STATA17.

Results

During the study period, a global measles peak was seen in 2019; regional peaks varied between 2018-2019. Global and regional measles incidence fell during 2020-2021. Globally, measles incidence was reported to be >80% lower in 2020 and 2021 than in 2019, with regions ranging from 61% to 91.5% lower. A large decline in incidence was seen in SEAR with a 67.3% drop in 2020 and 78.2% in 2021.

Globally, measles vaccine coverage fell during the study period. Global MCV1 coverage reduced by 3.5% in 2020 and 5.8% in 2021, but global MCV2 coverage rose by 1.4% in 2020 and remained unchanged in 2021. In 2020, the estimated national immunisation coverage (MCV1) declined in six SEAR countries ranging from 3% in Sri Lanka to 13.6% in Indonesia, while MCV2 coverage dropped in five SEAR countries ranging from 2.5% to 15.5%. There was a statistically significant

negative correlation between country's population and elimination status ($p<0.006$). The association between incidence and MCV1 coverage was not significant.

Discussion

Although a drop in cases was detected in SEAR, India and Indonesia were included in top 10 countries globally with multiple reported measles outbreaks during June-November 2022. During a global pandemic, we would expect disruption to health systems including surveillance and access to routine health services, therefore the findings reported in this study could be under reporting and may not reflect the real situation.

Conclusion

This study found a decrease in measles incidence as well as reduced measles immunisation coverage in SEAR countries. This appears contradictory as low measles immunisation coverage may increase disease transmission causing large measles outbreaks in some SEAR countries. The findings are likely impacted by COVID-19 pandemic disruptions to measles surveillance and immunisation. The true situation may be clearer to see in the coming years as we emerge from the pandemic and reinstate health and data systems in countries. All countries need to focus on building stronger health systems and restoring immunisation and surveillance system for measles to allow progress to elimination to continue.

Prologue

Background journey to MAE

I commenced this degree as a Master of Philosophy in Applied Epidemiology (MAE) Scholar, supported by the Australian Government Department of Foreign Affairs and Trade (DFAT) ASEAN Australia Health Security Fellowship Program. I commenced the MAE program on 17th February 2020, and I completed course block 1 (CB1) at the National Centre for Epidemiology and Population Health (NCEPH) at the Australian National University (ANU). As a requirement of the MAE program, I was placed in a field placement at the Central Epidemiology Unit (CEU), Ministry of Health, Myanmar since 9th March 2020.

Summary of field placement activities

CEU was one of the units under the Department of Public Health, led by the Deputy Director General (DDG) (Epidemiology). CEU was mainly responsible for the communicable disease surveillance and response in collaboration with related ministries, departments and organisations. The National Surveillance System targets epidemic prone communicable diseases, Diseases Under National Surveillance (DUNS), emerging infectious diseases, climate-related communicable diseases and vaccine preventable diseases. The CEU was responsible for preparedness and response to emergence and re-emergence of infectious diseases including Ebola Virus Disease, Zika, influenza, avian influenza including Influenza AH7N9, and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and enhancing the international networking including animal health sector for information sharing and capacity building. CEU was also focal point for Point of Entry (POE) surveillance including international airports, seaports and ground crossing points.

When I worked in my field placement, the COVID-19 pandemic crisis was occurring all over the world. I was too busy with control and response activities of the pandemic working in COVID-19 Central Command Committee led by Union Minister for Ministry of Health. CEU colleagues and I worked together to conduct the disease surveillance to prevent, control and respond to the outbreaks. We worked on many different kinds of activities; such as establishing a reporting system, developing data collecting tools, collecting data, matching and cleaning data, analysing and interpreting data for policy makers for decision and community for awareness raising. I communicated and coordinated with focal points from all states and regions for sharing technical inputs in response activities and having quality data. I was also involved in rapid response team training as a facilitator and attending stakeholder meeting for prevention and control of COVID-19 in Myanmar.

After I had worked in the field placement for five months, there was a family health problem and I had to take leave in 2020. After my leave, I returned to work in the field placement at the MoH. Unfortunately, a military coup occurred in Myanmar leading to an unstable situation within the country, so I had to take some additional leave in 2021.

When I resumed my MAE program, I completed other course blocks (CB2 and CB3) online because there were lockdown procedures and international flight restrictions. To complete an MAE, completion of three course blocks and four core competencies are required. I had completed the course work, the outbreak investigation (COVID-19), data analysis, surveillance project (Measles and Acute Flaccid Paralysis). I had almost finished my epidemiology study, *Effect of non-pharmaceutical interventions (NPI) on transmission of COVID-19 among townships in Ayeyarwaddy region, Myanmar 2021*, it was submitted to the ANU Human Research Ethic Committee and received the feedback to revised it. This project remains incomplete.

For the outbreak requirement, I participated in COVID-19 outbreak investigation in Central Institute of Civil Service (Yangon) with Yangon Regional Outbreak Investigation Team in January, 2022. I had completed my data analysis project, *Comparing Epidemiology of COVID-19 in Myanmar between 2020 and 2021*. For my surveillance evaluation, I had reviewed and evaluated the surveillance system of measles and AFP, with a focus on timeliness and

completeness; I was assigned as a focal person in evaluation meetings of measles and AFP surveillance system with states and regions in 2020.

Changing to the Master of Philosophy coursework

In the period following the military takeover, I was not able to continue to work in the field placement. NCEPH and academic supervisors tried to connect with other organisations to help me continue the MAE for my field placement, but those organisations could not accept due to rules and regulations set by Myanmar Government. So, it was impossible to complete the MAE program without a field placement. I therefore changed my degree from the MAE to Master of Philosophy(M.Phil) program.

When I started the MPhil program, I completed most of MAE requirements including three course blocks, quizzes and oral presentation. As my initial MAE projects could not be completed, for circumstances beyond my control I had to conduct a Master of Philosophy (MPhil) thesis with publicly available data that did not need to get approval from the local ethical board. Now, I am submitting my MPhil thesis to my examiners with the help of my supervisors and all supporters. To satisfy the degree components I have completed the following MAE course work subjects in addition to this measles data analysis project:

- POPH8913 Analysis of Public Health Data
- POPH8914 Issues in Applied Epidemiology
- POPH8915 Research Design and Methods
- POPH8916 Outbreak Investigation
- POPH8917 Public Health Surveillance

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List of Abbreviations

AFR	Africa Region
AMR	Americas Region
ANU	Australian National University
ASR	Age Standardized Rate
CB	Course Block
CDC	Centers for Disease Control and Prevention
CEU	Central Epidemiology Unit
CFR	Case Fatality Rate
DPR	Democratic People's Republic of Korea
DPT3	Third dose of Diphtheria, Tetanus toxoid and Pertussis vaccine
EMR	Eastern Mediterranean Region
EPI	Expanded Program of Immunization
EUR	European Region
GBD	Global Burden of Disease
GMRLN	Global Measles and Rubella Laboratory Network
IEA	International Epidemiological Association
JRF	Joint Reporting Form
MAE	Master of Philosophy in Applied Epidemiology
MCV	Measles Containing Vaccine
MCV1	First dose of Measles Containing Vaccine
MCV2	Second dose of Measles Containing Vaccine
MMWR	Morbidity and Mortality Weekly Report
MPhil	Master of Philosophy
MR	Measles Rubella
NCEPH	National Centre of Epidemiology and Population Health
NPI	Non-Pharmaceutical Interventions
NVC	National Verification Committee
ORI	Outbreak Response Immunisation

PHEIC	Public Health Emergency of International Concern
R0	Reproductive number
RVC	Regional Verification Committee
SDI	Socio-Demographic Index
SEAR	South East Asia Region
SEA-RVC	South East Asia Regional Verification Committee
SIA	Supplementary Immunisation Activities
SSPE	Subacute Sclerosing Panencephalitis
UNICEF	United Nations Children's Fund
VPD	Vaccine Preventable Disease
WHO	World Health Organization
WPR	Western Pacific Region
WUENIC	WHO/UNICEF Estimates of National Immunization Coverage

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CHAPTER 1: INTRODUCTION

Background information

Measles is a highly contagious disease caused by the measles virus of the paramyxovirus family, but ≥ 95% coverage of 2 doses of measles-containing vaccine (the first dose of measles-containing vaccine (MCV1) and the second dose of measles-containing vaccine (MCV2) can protect children against measles. After the widespread measles vaccine globally in 1980, measles incidence and cases declined eventually, but measles remains one of the leading causes of childhood morbidity and mortality worldwide, accounting for more than 140,000 deaths from measles in 2018. High measles mortality was found in low-income countries and low health care settings and large measles outbreaks occurred in many developing countries, particularly in Africa and Asia (1, 2). Health consequences of measles infection include the economic impact on individuals, families and societies expensing the cost for public health response to the outbreaks, direct medical treatment and cost of lost productivity (3).

Problem statement

Annual reported measles cases decreased dramatically between 2000 and 2016, but a global measles resurgence occurred between 2017-2019 (4). In 2020 and 2021, global reported measles cases and incidence decreased abruptly with decreasing measles vaccine coverage. But reported measles cases increased by 79% in the first two months of 2022, compared to the same period in 2021 worldwide (5). In 2018, 86% of infants were immunised by measles vaccine reducing 73% measles deaths in 2018 compared to 2000. During 2000-2021, 56 million children were prevented from measles and measles related deaths by immunisation, but 40 million children missed their measles vaccine in 2021, increasing the risk of large outbreaks. Twenty-one countries had faced large and disruptive measles outbreak in 2021 (6) these outbreaks continued to occur in 2022.

South East Asia Region (SEAR) has one fourth of the world population and 25% of reported measles cases were reported from SEAR in 2018 (7). The South East Asia Region was accountable for about 18% of 22.3 million global unimmunised (MCV1) children, (3 million from India and

0.6 million from Indonesia) in 2020 (8). In 2020, India and Indonesia were two out of ten countries with the highest number of umimmunised children worldwide (4). SEAR has the third greatest measles burden region in 2021 and had a triple burden of diseases (communicable diseases, non-communicable diseases, injuries) (9). As of 13 January 2023, India had the most measles outbreaks globally during June 2022 – November 2022 (10).

All regions, not just the SEAR, are risk of measles outbreaks because of the disruption to immunisation services during pandemic. The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend the countries to make effort on prevention and control of measles and other vaccine preventable diseases (VPDs). There is also a global concern about the high risk of measles outbreaks occurring due to the disruption of immunisation services during the COVID-19 pandemic. The study aimed to describe the incidence and immunisation coverage of measles in SEAR between 2017 and 2021 which takes in the period prior to and during the global COVID-19 pandemic.

CHAPTER 2: LITERATURE REVIEW

In this section I reviewed the research articles related to my thesis including grey literature and meeting reports. These were summarised and then evaluated. Although the study area of this thesis is the WHO Region of South East Asia (SEAR), I reviewed previous knowledge and experience about other WHO regions and member states in all six WHO regions to provide context and a global picture. The WHO regions are Africa Region (AFR), Americas Region (AMR), South East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR) and Western Pacific Region (WPR).

2.1 Search Strategy

I searched PubMed and Scopus databases for published articles related to measles incidenceincluding "measles" and key words to find data on: reported cases, incidence and outbreaks, measles vaccine coverage, Supplementary Immunisation Activities (SIAs), progress towards measles elimination, impact of COVID-19 on measles incidence and immunisation. Most studies reviewed and/or evaluated progress towards measles elimination, measles incidence and measles vaccine coverage in WHO six regions and some were focused in specific countries. I searched the grey literature by browsing health related websites and online libraries (WHO, UNICEF etc). Articles were included if they were published in English and were from the period 1999-2022. This resulted in 74 articles included. I have undertaken a synthesis of the relevant literature published and grey literature and presented it in this Chapter.

2.2 Transmission of measles

There are three genera in the Paramyxoviridae family, and they are Paramyxovirus, Pneumovirus and Morbillivirus. Parainfluenza viruses and mumps viruses are species of Paramyxovirus, respiratory syncytial virus is species of Pneumovirus and measles virus is species of Morbillivirus (11). Measles is only found in humans and no animal reservoir is known. Measles is transmitted

by droplet, close personal contact or direct contact with nasal or throat secretions of virus infected person. The virus can survive and be communicable in the atmosphere or on contaminated surfaces until 2 hours. The incubation period, the period between inoculation of virus and appearance of first symptom, is 10-12 days (range 7-21 days). Measles can be transmitted by an infected person from 4 days before the onset of the rash to 4 days after the rash appears. The common symptoms are fever, runny nose, cough and rash. Measles rash may start as red macules on the face and then appear on the other part of the body. Measles virus infection may be fatal when complications occur. Measles related deaths were related to respiratory and neurologic complications. People who got complication of measles are commonly unimmunised young children, pregnant women and immunocompromised people. Measles related deaths are more common in resource poor countries. Complications of measles may be due to virus itself and secondary bacterial infection four weeks after the rash appears. Common acute complications of measles are otitis media, pneumonia, laryngo-tracheo-bronchitis, diarrhea, febrile convulsion, encephalitis and blindness (especially in malnourished children). Subacute Sclerosing Panencephalitis (SSPE) is a rare complication of measles and may occur a decade after measles infection (1, 11, 12).

2.3 Prevention of measles

Although measles is a highly infectious disease, it can be prevented by a measles vaccine. A measles vaccine was developed and introduced in some countries as early as 1960. The WHO recommended to initiate an Expanded Programme of Immunisation (EPI) with inclusion of measles vaccine with other antigens such as diphtheria, pertussis, tetanus, poliomyelitis and tuberculosis since 1974 (13, 14). The recommended age for the first dose of measles containing vaccine (MCV1) is at the age of 9-12 months depending on the endemic status, health care system and political conditions of the country. The second dose of measles containing vaccine (MCV2) is recommended at the age of 15-18 months. MCV1 was given at 9-15 months age and MCV2 is given at 15-36 months age in most countries and a booster at 4-9 years in some countries depending on the country's context. However, the actual ages at which these doses are given differs from recommendation, with MCV1 given at 9-15 months of age, some countries added the third dose for the school going children, adult and high-risk group (15, 16).

According to WHO (2019), before the pre-vaccine era and widespread use of vaccine, 2.6 million people died from measles and its complications annually. Large measles outbreaks occurred every 2-3 years. After worldwide use of measles vaccine, an estimated 23.2 million people were saved from dying of measles related death. Measles mortality was reduced by 73% globally when comparing 2000 and 2018. Despite a safe and cost-effective vaccine being widely available, there were noticeable measles deaths of more than 140,000 globally in 2018 (1). There were many challenges to get population immunity to prevent measles transmission and measles related deaths. Socially and geographically hard to reach areas are major causes of low immunisation gaps and natural disaster and conflictsituations are accountable for weak and fragile immunisation programme. And misinformation delivered by anti-vaccination groups and vaccine hesitancy can reduce the vaccine coverage.

High population immunisation coverage prevents epidemics and outbreaks in the community. There is no evidence that any vaccine can prevent a disease totally. The first dose of measles vaccine has 92% effectiveness in preventing measles virus infection while the second dose of measles vaccine has 95% (17). To obtain herd immunity, the critical prevalence of protected people (Ic) should be 94.4% for basic reproductive number of the disease (R0=18) and the prevalence of people protected by vaccine (Iv) should be higher than (Ic) (>94.4%). In 2019, there were epidemics and outbreaks in some countries because of low immunisation coverage of (MCV1 and MCV2) < 95% and it reflected the low herd immunity in population with 88.1% of (Ip) worldwide (18).

2.4 Global measles elimination goals

Because safe and effective measles vaccine is easily available and the reaching elimination targets were considered feasible, in 2012 World Health Assembly endorsed Global Action Plan set the goal of measles elimination in five out of six regions by 2020 (1). The Americas was certified as reaching measles elimination in 2016, but there were multiple reported outbreaks in countries in the Americas which led to the loss of elimination status in 2018 (19, 20). All WHO Regions have adopted measles elimination goals by developing strategic plans and frameworks for verification of measle elimination in line with the World Health Organization (WHO) global strategic plan

and framework (1). The WHO defines measles elimination as *"the absence of endemic measles virus transmission in a defined geographical area (e.g. region or country) for at least 12 months in the presence of a surveillance system that has been verified to be performing well. Verification of measles elimination takes place after 36 months of interrupted endemic measles virus transmission"* (21).

All member states are required to implement the strategic plan in accordance with their regional goals and organise the National Verification Committee (NVC) to monitor and evaluate the progress of measles elimination in the country. The Regional Verification Commission (RVC) was established to review the indicators for verification of measles elimination. RVC assesses the documents of standard indicators whether the country is certified in elimination or not. When all the countries in the region are verified for elimination, the region can be certified for regional elimination status (21-23). As of September 2019, 84 out of 194 Member States were verified to have measles elimination. Despite all six WHO regions having adopted the measles elimination goals and endorsed their own strategic framework for regional measles elimination, by the end of 2020, no WHO region had achieved elimination and sustained elimination and no new countries had verified elimination (4, 23). According to Measles and Rubella Global Update August 2022 updated by WHO, as of September 2022, 76 Member States were verified as having eliminated measles and more information is included in Annex 1 (24).

2.5 Surveillance

Surveillance has an essential role in measles elimination to evaluate the effectiveness of an immunisation program and find out the immunity gaps. All member states have established case-base surveillance. Measles surveillance is conducted through reporting of suspected cases and laboratory confirmation by a WHO accredited laboratory. Almost all member states had feasible systems to confirm measles cases through WHO Global Measles and Rubella Laboratory Network (GMRLN) in 2020. Measles surveillance is done with other vaccine preventable diseases (such as rubella, polio, neonatal tetanus) as an integrated surveillance system. According to the WHO case definition of suspected measles case, reporting units report the suspected measles cases to the country's health system. Then the countries report to WHO regional office and the regional office

reports to WHO Headquarter (HQ) through the WHO/UNICEF Joint Reporting Form on Immunization (JRF) (1, 4, 25). To verify elimination, surveillance systems should be sensitive to detect every suspected case and outbreak for early detection and response (21).

2.6 Immunisation

Immunisation of the eligible population is crucial to achieving and sustaining measles elimination and monitoring and evaluation of immunisation data is important at national, regional and global level. Immunisation data for all Expanded Program on Immunisation (EPI) antigens are reported monthly within Ministries of Health in a country. From late 1970 until 1998, the WHO and UNICEF collect national immunisation coverage data of all EPI antigens separately in different formats causing double reporting.0. The WHO and UNICEF established a reporting format, WHO/UNICEF Joint Reporting Form on Immunisation (JRF) for collection of some VPD surveillance data and immunisation data in 1998. All member states reported immunisation coverage annually to WHO and UNICEF through JRF since 2000. A country's official immunisation coverage is obtained from administrative coverage and survey coverage data.

Administrative coverage is calculated by using data reported by health facilities and it is the proportion of vaccinated children among the target children. Administrative coverage may be unreliable due to underreporting of vaccinated children and overreporting of children who are not included in target population. Survey coverage is based on household surveys of immunisation and is the proportion of vaccinated children among the target children in the sample. Surveys data include checking immunisation cards and asking questionaries and it may have recall bias of respondents. So, country's authorities need to estimate official coverage by using administrative and survey data to get actual coverage. WHO and UNICEF evaluate the national immunisation data and estimate national immunisation coverage annually. WHO/ UNICEF Estimates of National Immunisation Coverage (WUENIC) is defined as the percentage of surviving infants/children who received the 1st dose/2nd dose of measles containing vaccine. These data are released on WHO immunisation data portal and updated on July 15 every year (18, 26).

To achieve the elimination goal, two doses of MCV coverage should be demonstrated for ≥ 95% of the target population at regional, national level and district level. Identifying immunity gaps and

intensifying routine immunisation and conducting Supplementary Immunisation Activities (SIAs) and Outbreak Response Immunisation (ORI) were implemented by member states to get high population immunity.

Measles outbreaks reflect weakness of health services including low performance of an immunisation program. Detecting one confirmed case in an eliminated country is assumed as an outbreak (7). The WHO defines an outbreak as: *"two or more laboratory-confirmed cases that are temporally related (with dates of rash onset occurring 7–23 days apart) and epidemiologically or virologically linked, or both"* (25). Preparedness and response to outbreaks and outbreak investigation is the one of the strategies in progress toward measles elimination.

2.7 Global measles epidemiology and measles vaccine coverage

In 1989, the World Health Assembly set global goals for reduction in measles morbidity and mortality as 90% and 95% respectively, by 1995 (27). The target for the measles vaccine coverage was set in 1990 aiming to achieve 90% coverage by 2000. After setting these goals, measles morbidity and mortality dropped by 70% and 88% by the end of 1997 (28). This was the early step of measles prevention and control activities in global public health action plan.

During the pandemic, coverage with both the first and second doses of measles-containing vaccine (MCV1 and MCV2 respectively) has declined in many countries globally. As of 14 December 2020, 28 European region countries had delayed their measles immunization campaigns while 18 countries are currently battling measles outbreaks within their borders. Amid these concerning setbacks, it's worth highlighting that some determined countries have managed to move forward with vaccinations in spite of the daunting obstacles presented by the coronavirus crisis. (29).

2.8 Measles incidenceand measles containing vaccine (MCV) coverage in WHO regions

WHO African Region (AFR)

In 2011, the WHO African Region (AFR) adopted measles elimination goals and had set a strategy for the elimination of measles by 2020 in the African Region. Until now no African country has achieved verification of measles elimination. In the secretariat report of the Regional Office for Africa between 1980 and 1989, annual reported suspected measles cases were about one million in the whole region (30). The average annual reported measles cases were below 100,000 for the whole region in 2006 - 2009. The WHO/ UNICEF estimated (MCV1) coverage increased from 56% in 2001 to 69% in 2009 (31). A recent study identified that the quality of measles surveillance in 2020 reduced to the lowest level in the whole African region within 7 years due to impact of COVID-19 pandemic and sub-optimal immunization coverage was also exacerbated and considerable measles outbreaks may provoke across countries in the African region. The disruptions to immunization services during the pandemic have hindered efforts to sustain high vaccination coverage, enabling the unchecked spread of infectious diseases like measles (31). According to WHO and UNICEF joint news release (2022), during 2021 and 2022, most measles cases and outbreak occurred in Africa and the East Mediterranean region(5). In AFR, estimated 864,000 more children missed their MCV1 vaccine between January and July of 2020, compared to the same period in 2019 due to disruption of pandemic on routine health services (32).

WHO Region of Americas (AMR)

The WHO Region of the Americas (AMR) achieved verification of measles elimination in 2016; however, endemic measles transmission was reestablished in Venezuela (2016) and Brazil (2018). The Morbidity and Mortality Weekly Report (MMWR) (2021) of progress toward regional measles elimination – worldwide 2000-2020 (4) described that MCV1 coverage were 92%, 87% and 85% in 2016, 2019 and 2020 respectively, being 7.6% dropped of MCV1 coverage between 2016 and 2020 and only 33 countries achieved MCV1 coverage ≥ 90%, compared to 69 countries

in 2019 Annex 2. The reported number of measles cases were highest in 2019 which accounted for 21,971 and incidence per 1 million population was 37 in 2019. The Americas region also remains committed to measles elimination;according to Pan American Health Organization (WHO), in 2020 and 2021, 8,734 and 722 measles cases were reported through WHO/UNICEF joint report forms (33).

WHO Eastern Mediterranean Region (EMR)

The Eastern Mediterranean Region (EMR) initially set the goal for measles elimination by 2010 and then postponed to 2015. In 2012, The Eastern Mediterranean Region (EMR) aimed for measles and rubella elimination by 2020 and adapted the regional strategies for measles elimination (34). In EMR, there was an considerable progress to the interruption of measles virus transmission from 1998 to 2010 and reduced reported measles cases from 89,478 in 1998 to 10,072 in 2010 decreasing by 89% within 13 years (35). The regional office for the Eastern Mediterranean assumed that there was a slow progress in elimination targets since 2011 with the reason of geopolitical situation in EMR countries and significant reduction in donor funding. Reported measles cases increased by three times from 10,072 to 33,943 between 2010 and 2019. In 2020, reported measles cases decreased to 6,122 as measles surveillance systems, which are vital for detecting outbreaks and targeting interventions, also deteriorated significantly during COVID-19 pandemic. The estimated MCV1 coverage was 85% Annex 2 with 33 countries with ≥ 90% MCV1 coverage because large-scale supplementary immunization activities were postponed as countries battled the COVID-19 crisis in MMWR (2021) (4).

WHO European Region (EUR)

The European Region (EUR), 60th session of the Regional Committee endorsed the new target date for elimination of measles and rubella by 2015 in 2010 (36) and all member states reconfirmed elimination goals by 2020. In Datta et al (2018), reported measles cases dropped 86% in 2015 compared to reported number in 1990 and reduced 80% of reported cases in the first three quarter of 2016 compared to same period in 2015 even though notification by countries made significantly,

surveillance system in some countries needed to be strengthened to investigate every suspected measles case (37). In EUR Region, measles resurgence occurred since 2017 and peaked in 2019, with more than 100,000 cases were reported. During COVID-19 pandemic, there was a dramatic decrease in the reported measles cases and incidence in the early months of 2020 compared to 2018 and 2019 Annex 2 (29) and it was suggested that there may be underreporting due to disruptions in laboratory surveillance during the peak of COVID-19 outbreaks in the Region. But (MCV1) coverage was not much changed between 2019 and 2020 (96% and 94%) (4).

WHO Western Pacific region (WPR)

In 2005, the WHO Western Pacific Regional Committee set measles elimination target by 2012. Measles has resurged in 2013 and 2014 increasing of measles incidence from 5.9 cases per million population in 2012 to 17.7 in 2013 and 44.0 in 2014. This resurgence was mainly attributed by measles cases in endemic countries and imported cases in non-endemic countries (38) occurring outbreaks in previous verified measles-eliminated countries (39). There were 57,879 and 78,479 reported measles cases and incidences were 31 and 41 per million population in 2016 and 2019, and cases dropped to 6,601 and incidence decreased to 4 in 2020 Annex 2 (MMWR, 2021) (4). Estimated regional (MCV1) coverage remained to achieve≥ 95% during 2011 to 2019 and fell into 94% and 91 % in 2020 and 2021 (40). The widespread disruption caused by the COVID-19 pandemic in 2020 led to concerning setbacks in global measles vaccination coverage and surveillance efforts.

2.9 South East Asia Region measles incidenceand measles containing vaccine (MCV) coverage

Meeting measles elimination targets

The Regional Office for South East Asia (SEAR) adopted a measles control target in 1989 when the World Health Assembly endorsed the reduction of measles morbidity and mortality by 90% and 95% respectively, by 1995 compared to previous years (before widespread use of vaccine) (41, 42). Though these goals had not been met elsewhere either globally or regionally. SEAR have made positive progress towards measles control. Regional measles morbidity and mortality decreased by in a range of 70% - 88% by the end of 1997. At that time all member states of SEAR except Thailand and Democratic People's Republic of Korea (DPR Korea), administered a single dose of measles vaccine at the ninth month of age. Measles vaccine coverage increased dramatically from < 10 % in 1985 to > 80% in 1990 and vaccine coverage has remained stable > 80% in nine out of ten member states since 1997 (at that time there were ten member states in SEAR and Timor Leste included in SEAR countries in 2003). In the period 1990-1997, four out (Indonesia, Myanmar,Sri Lanka and Thailand) of 10 member states significantly declined reported measles cases meanwhile tow countries (Bhutan and India) decreased reported cases.Two member states (DPR Korea and Maldives) detected no measles cases while two member states (Bangladesh and Nepal) reported substantial increased number of measles cases. Measles cases rose by 50 times greater in 1997 compared to 1990 in Nepal, this was attributed not only to the incidence of multiple outbreaks but also to improved case detection rates. Nine countries demonstrated an increased change in the percentage of vaccine coverage, in Maldives, there was no change and India dropped by 10% vaccine coverage rate within eight years (43).

Measles mortality

In 2003, the SEA Regional Technical Advisory Group on Immunisation affirmed a Regional Strategic Plan for Measles Mortality Reduction (2003-2005) in line with a targeted reduction of measles deaths by 50% by the end of 2005 (44). The target was endorsed by World Health

Assembly. MMWR (2004) evaluated the progress toward sustainable measles mortality reduction in South East Asia (MCV1) coverage estimated by WHO/UNICEF rose by 70% in 2002 from 58% in 1999 Supplemental Immunisation Activities (SIAs) were conducted in 6 countries during 1999-2002, achieving coverage from 69-124% (43).

Elimination strategy for SEAR

In 2013, the sixty-sixth meeting of the Regional Committee for South East Asia adopted the regional goal of measles elimination and rubella control by 2020 and the goal was revised to 'measles and rubella elimination by 2023' in 2019 by the Seventy-Second Session of the Regional Committee for WHO South-East Asia Region. The Regional Committee also endorsed the "*Strategic plan for measles and rubella elimination in WHO South-East Asia Region: 2020–2024*" to provide a strategic framework for achieving the elimination goal (23). Sixth Meeting of the WHO South-East Asia Regional Verification Commission for measles and rubella (2021) made a conclusion that Bhutan, DPR Korea, Maldives, Sri Lanka, Timor-Leste were verified for their sustained measles elimination status (45).

Reported measles incidence and cases

The Centers for Disease Control and Prevention (CDC) updated the Progress Towards Measles Elimination-South East Asia Region 2003-2013 in 2015 and published in MMWR (Vol.64, 2015) (46). In that report, a significant reduction of reported cases and incidence were found in the region that reported cases decreased by 68% (from 94,598 in 2003 to 30,101 in 2013) and annual incidence per million population decreased by 73% (incidence per million population was 59 in 2003 and 16 in 2013) between 2003 and 2013, and five countries had an incidence of < 5 per million population. However, many suspected outbreaks (numbers of outbreaks=5,680) occurred in the region during 2003-2013 and 248 laboratory confirmed measles outbreak and 14 mixed measles and rubella outbreaks were reported in 2013. According to 2013 outbreak data, age group

of 1-4 years was 35%, 5-9 years (30%), < 1 year (13%), ≥ 15 years (13%). The author concluded that although measles morbidity and mortality reduced substantially in SEA during 2003-2013, the countries particularly India and Indonesia need to focus on routine immunisation and SIAs reaching 2-dose routine MCV coverage ≥ 95% and case-based surveillance and laboratory diagnosis (46).

Measles vaccine coverage estimates

During the period 1995-1997, Supplemental Immunisation Activities (SIAs) were conducted in seven countries. However, there was a difference between routine vaccination coverage and surveys results in the same year because countries only used routine administrative reports for estimation of vaccination coverage and overestimated true coverage rates (28). Nevertheless, SEA countries used surveys data in 1999 and national data and WHO/UNICEF estimates were not much different in 2002 as those two estimates relied on the survey data (43). Bangladesh, DPR Korea, India, Myanmar and Nepal have challenges to control measles and need to focus on measles morbidity and mortality by increasing immunisation coverage. Bhutan, Indonesia, Maldives, Sri Lanka and Thailand were in on the track of measles control (28).

A second dose of measles containing vaccine (MCV2) was introduced in many SEAR countries in the 2000s. Two countries introduced (MCV2) before 2003, this increased to nine countries during 2003-2013 (40) and all 11 member states had introduced (MCV2) in the period 2003-2020 (8). Modelling undertaken on measles elimination in SEAR for the period 2003-2020 in 2022 estimated that measles cases reduced 84% (from 16,225,870 in 2003 to 2,552,584 in 2020). According to WHO/UNICEF joint report, during 2003-2013, India, Indonesia, Nepal, Sri Lanka and Timor-Leste had significantly declined measles incidence per million population and nine countries increased (MCV1) coverage and Sri Lanka reduced (MCV1) coverage 3% (from 99% to 96%). Coverage in Thailand remained unchanged (8).

The coverage of first dose of measles containing vaccine (MCV1) had a significant reduction from 94% in 2019 to 88% in 2020 and the coverage for second dose of measles containing vaccine declined from 83% in 2019 to 78% in 2020. In the region, 32.7 million children were vaccinated (MCV1) and 29 million were vaccinated (MCV2) through routine immunisation in 2020 and more

50 million children got vaccination of measles vaccine through mass campaigns in 2020. Nevertheless, 4.3 million children were still unvaccinated and 3.6 million children were incompletely vaccinated. By achieving measles elimination goal, WHO estimated that at least 1.1 million measles cases are prevented every year in the region and 1.1 million measles related deaths will be halted by 2023 as well (47).

2.10 Influencing factors for achieving measles elimination target

To describe the mortality, morbidity, risk factors and social determinants of health associated with SEAR countries, a study was conducted by the International Epidemiological Association (IEA). Measles immunisation coverage was twice in the richest group in India, however, only 30% and 10% higher measles immunisation coverage was seen in the richest group in Sri Lanka and Bangladesh, respectively compared to poorest group. The author, however, described their report was limited to data from some countries and data variation between international reports and national reports (9).

One provocative hypothesis that emerged was that existing live-attenuated vaccines could provide nonspecific protection against severe COVID-19. With no approved treatments or vaccines initially available, researchers scrambled to identify existing tools that could potentially mitigate the impact of this novel coronavirus. In the previous study of correlation between measles immunisation coverage and overall morbidity and mortality for COVID-19, a correlation between the measles vaccine coverage and COVID-19 new cases per one million population was found to be significant. There was no correlation between vaccine coverage and COVID-19 related deaths and no significant association between MCV coverage and total COVID-19 cases and deaths per one million population. Though the researchers hypothesized there may be an inverse correlation, with higher measles vaccination rates associated with lower COVID-19 severity, the data did not bear this out. There was no evidence of a negative correlation between measles vaccination coverage and COVID-19 outcomes. This suggested that any claims of a protective effect of the measles vaccine against COVID-19 were not founded. However, there are important limitations

in the data that prevent to definitely rule out the possibility of other routine childhood vaccinations impacting COVID-19. (48).

Wariri Oghenebrume et al conducted a study in 2021 to determine health systems-related, familial, and cultural factors which influence the delivery and uptake of measles vaccination in Indonesia. A significant association between maternal age, maternal education, wealth, the number of children per household and uptake of measles vaccination after controlling all confounding. There was an association between first dose of measles vaccination at the age of 9 month and immunity against measles infection. However, other possible influencing factors of vaccination coverage, such as antenatal care that could not be accessed in their study was considered as a limitation (49).

During 2000-2019, decreasing geographic inequality was correlated with increased vaccine coverage which was obviously seen in India. MCV1 coverage was below 80% in certain rural areas with high geographical inequality in 2008. Additionally, during 2000-2010, there was a substantial increase in heterogeneity of measles vaccine coverage. However, from 2010 to 2019, vaccine coverage increased in rural areas, significantly reducing geographical inequality in India. The increase in coverage occurred not only at the national level but also at the subnational level over time, due to the implementation of a special mission that targeted pocket areas for immunization. The launch and expansion of MCV2 at all levels further improved vaccine coverage and promoted greater equality in India.(50). In the retrospective multi-country series analysis study was conducted in 15 west African countries in 2021 in which there was a negative association between the weighted mean MCV1 coverage and weighted mean incidence rate. The weighted mean MCV1 coverage rose during 2001-2019 meanwhile the weighted mean incidence rate per million population fell in these years. A reverse relationship between the number of children immunised through SIAs and the weighted mean measles incidence rate in west Africa was found as well. Cape Verde, The Gambia, and Ghana had made progress towards measles elimination by 2020 as less population was related to achieving measles elimination goals as Cape Verde and The Gambia have lower population than other countries in the study. It was considered that data limitation may be biased in interpretation of the results and the results might not reflect the real situation (51).

An analysis study of Global Burden of Disease (GBD) (Wang Ruitong et al, 2022) was conducted to better understanding the trends and risk factors of measles incidence in 204 countries in 1990-

2019 and countries were grouped into 5 regions (a high, high- middle, middle, low-middle, or low SDI) according to Socio-demographic Index (SDI) which was the composite indicator of income per capita, average years of schooling, and fertility rates. Higher SDI reflected the higher income, longer years of schooling and lower fertility rate. It was founded that there was an inverse relation between SDI and measles age standardized rate (ASR), higher SDI with lower measles (ASR). But there was a positive association between SDI and (MCV1) and (MCV2) coverage. Moreover, there was also a negative correlation between measles ASR and measles-containing vaccine coverage (MCV) rate in 204 countries and territories during the study period. In this regard, lower SDI was associated with higher ASR and lower MCV coverage attributing to high level of vaccine hesitancy, insufficient funding to support routine vaccination programs. But limitations such as inadequate reporting, missing data etc) in assessing the actual number of measles cases and measles vaccine coverage in analysis were found (52).

The reduction in vaccine coverage in March and April 2020, particularly in regions such as North Africa and the Middle East, South East Asia, had severe annual impacts according to the Global Burden of Disease (GBD) super-regions. The COVID-19 pandemic caused unprecedented disruptions in vaccine delivery, leading to a significant decrease in global coverage of DTP3 and MCV1 in 2020, reaching levels not witnessed in over a decade. While some signs of recovery appeared in the latter half of 2020, the pandemic and its disruptive effects persist. Even if vaccination rates were to return to pre-pandemic levels, millions of children would still remain under-vaccinated or unvaccinated, leaving them vulnerable to vaccine-preventable diseases (53). The COVID-19 pandemic has impacted immunisation and health services throughout SEAR. My research aims to provide an analysis of this by analysing publically available data and examining published and grey literature for the period 2017-2021.

CHAPTER 3: METHODS

3.1 Aim of the study

To describe the incidence and immunisation coverage of measles in South East Asia Region, 2017-2021.

3.2 Specific objectives

1. To describe the EPI history of 11 member states of SEAR
2. To examine the reported measles cases and incidence by SEAR countries
3. To examine the measles vaccination coverage (measles-containing vaccine first dose (MCV1) and measles-containing vaccine second dose (MCV2)) in all SEAR countries pre and post the COVID-19 pandemic
4. To identify the Supplementary Immunisation Activities (SIA) in SEAR countries
5. To find out the correlation between measles incidence and measles vaccine coverage (MCV1 and MCV2)
6. To describe the association between a country's population, income status, development status, introduction period of (MCV2) and measles elimination status

3.4 Research Question

What is the measles incidenceand measles containing vaccine coverage in 11 member states of WHO SEAR from 2017-2021?

3.5 Study Design

A cross sectional descriptive study using secondary data.

3.6 Study area

Data were collected for the World Health Organization (WHO) South East Asia Region (SEAR) by WHO, UNICEF, World Bank. I also retrieved data from Our Word in Datawhich is a third-party organization that has collated secondary data from various sources.

Study area was South East Asia Region of the WHO.

3.7 Study period

The collected data were within a five-year period of 2017-2021.

3.8 Study population

Data included reported measles cases, incidence and measles-containing vaccine coverage in WHO SEAR.

3.5.1 All confirmed measles cases reported by countries were included in study population.

Case definition of confirmed measles case are as follows according to WHO recommended cases definition (25);

(i) Laboratory confirmed case

A suspected case of measles that has been confirmed positive by testing in a proficient laboratory, and vaccine-associated illness has been ruled out.

A suspected measles case is defined as A suspected case is one in which a patient with fever and maculopapular (non-vesicular) rash, or in whom a health-care worker suspects measles.

(ii) Epidemiologically-linked confirmed measles case

A suspected case of measles that has not been confirmed by a laboratory, but was geographically and temporally related with dates of rash onset occurring 7–23 days apart from a laboratory-confirmed case or another epidemiologically linked measles case.

(iii) Clinically compatible measles case

A suspected case with fever and maculopapular (non-vesicular) rash and at least one of cough, coryza or conjunctivitis, but no adequate clinical specimen was taken and the case has not been linked epidemiologically to a laboratory-confirmed case of measles or other communicable disease.

(iv) Discarded case

A discarded case is a suspected case that has been investigated and discarded as a non-measles (and non-rubella) if the result is negative testing by accredited laboratory, epidemiological linkage to a laboratory-confirmed outbreak of non-measles disease, incompatible with confirmed measles case definition (25). Discarded rate is one of the main and sensitive indicators of measles surveillance performance and calculated by number of total discarded measles cases divided by total population per 100,000 population and the target is ≥2 discarded measles cases per 100,000 population.

3.5.2 Measles incidence is the number of measles cases per 1 million population in a defined area within a year period.

$$\text{Measles incidence in a year} = \frac{\text{Number of new measles cases in a population within a year}}{\text{Number of populations in which the cases occurred within a year}} \times 1{,}000{,}000$$

3.5.3 Measles Containing Vaccine (MCV) coverage

Measles containing vaccine coverage is the proportion of children who received the measles containing vaccine through routine immunisation.

$$\text{MCV coverage} = \frac{\text{Number of children who received measles containing vaccine (MCV1 or MCV2) within a given year}}{\text{Total number of children in the target group for MCV1 or MCV2 in a defined period}}$$

(i) **MCV1** coverage is the percentage in the target population who received one dose of measles containing vaccine in a given year. In most SEAR

countries, the 1st dose of measles containing vaccine (MCV1) is given at the age of 9 months so that the target population is surviving infants.

(ii) **MCV2** coverage is the percentage in the target population who have received two doses of measles-containing vaccine in a given year. The 2nd dose of measles containing vaccine (MCV2) is given within 15-36 months of age in SEAR countries.

3.9 Data sources

Secondary data extracted from the website of WHO, UNICEF, World Bank and Our World in Data were used in this study. Our World in Data is a third-party organization that has collated secondary data from various sources I retrieved data from this source to as well as WHO and UNICEF. Data for reported measles cases were extracted from WHO Global Health Observatory Data (54). Reported measles cases and incidence were available from WHO Immunisation data portal (55). Measles containing vaccine coverage data (global, regional and country level) were collected from WHO immunisation data portal (https://immunisationdata.who.int/) which is WHO/ UNICEF Estimates of National Immunisation Coverage (WUENIC) reported annually by member states by using WHO/UNICEF Joint Reporting Form on Immunisation (JRF). These data are updated annually and released on July 15 of each following year. JRF reports has limitation itself, there may be underreporting of measles cases due to weakness in surveillance system and lack of laboratory testing in some countries. In the process of conducting my research, I refrained from consulting other peer-reviewed literature or online reports, including serosurveys and reviews of immunization cards. These resources were specifically focused on examining the immunity levels in the SEAR countries. A limitation of the measles vaccine coverage is denominator of the target group in the countries which may be incomplete due to weakness in administrative reports. Countries were classified by World Bank income status (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups) and development status is referenced to United Nations World Economic Situation and Prospects 2021: https://www.un.org/development/desa/dpad/wp-content/uploads/sites/45/WESP2021_ANNEX.pdf). Country's measles immunisation schedule and introduction of 2nd dose

of measles containing vaccine (MCV2) were available from regional and country Expanded Programme of Immunisation (EPI) through WHO South East Asia Region (SEAR) website. Data for Supplementary Immunisation Activities was extracted from WHO Immunisation data portal (55). COVID-19 data of SEAR countries were collected from Coronavirus Pandemic (COVID-19) – Our World in Data; https://ourworldindata.org/coronavirus (56). Population data was 2020 population and collected from Worldometer https://www.worldometers.info/population/ (57) which was based on the data of United Nations, Department of Economic and Social Affairs, Population Division.

3.10 Statistical analysis

Data were checked for completeness, errors, and consistencies. Descriptive statistics was used for characterising and summarising the data set. Mean and standard deviation were used for normally distributed continuous variables, median and inter quartile range for non-normal continuous variables, and frequency and relative frequency for categorical variables. Statistical analysis was conducted by using Stata version 17. As the sample size was too small and more than 20 percent of cells with expected frequencies was less than 5, Spearman's rank test, Fisher's exact test and Wilcoxon rank sum tests were used to find association between country's income status/ development status and elimination status and to find the association between measles incidence and MCV coverage, morbidity and mortality of COVID-19. Statistically significant level was set a P- value of 0.05.

I compared measles incidence, cases and measles vaccine coverage before and after COVID-19 pandemic to examine the impact of the pandemic on countries' surveillance system and immunisation services. It was assumed that 2019 was before pandemic period. 2020 was a starting period of pandemic because the World Health Organization's first sharing of a cluster of unidentified pneumonia in Wuhan, China and the declaration of the novel coronavirus outbreak a public health emergency of international concern (PHEIC) was made in January, 2020 (58). During 2021, COVID-19 outbreaks occurred in almost all countries and the countries experienced the response, mitigation measures and lessons learned from previous outbreaks in 2020 and health

systems in many countries remained disrupted in 2021. Therefore, 2020-2021 was referred as the pandemic years.

3.11 Ethical considerations

The data used was secondary, non-identified data that was publicly available. All of information accessed was published by WHO, UNICEF, World Bank, Our World and member states website. According to Australian National Statement on Ethical Conduct in Human Research (2007), Section 5.1.22, the research can be exempt from ethical review if it involves the use of existing collections of data or records that contain only non-identifiable data about human beings (59).

CHAPTER 4: RESULTS

This study was conducted to describe the incidence and immunisation coverage of measles in South East Asia Region, 2017-2021. The data were secondary data and collected from the website of WHO, UNICEF, World Bank and Our World in Data. Measles incidence in 11 SEAR countries were included in this study. The findings were presented into two parts; first part was descriptive information using tables and graphs of estimated number and percent of variables, the second part I look at the association between dependent and independent variables using non-parametric tests. because the sample size was small and there was more than 20 percent of cells have expected frequencies of less than 5.

4.1 Measles incidence, reported cases and measles immunisation coverage in global and WHO regions

The data in Annex 3 shows a significant decrease in reported measles cases during the pandemic compared to the period before it, both globally and in most WHO regions. The mean reported measles cases peaked in 2019 at 145,504, which was 5 times higher than in 2020 and 7 times higher than in 2021.

The global mean percentage of MCV1 coverage was 88% in 2019, 86% in 2020, and 84% in 2021. MCV1 coverage in the SEAR region dropped below 90% after the COVID-19 pandemic, and MCV2 coverage did not exceed 90% from 2017 to 2021. The peak of reported measles cases occurred in 2019 globally and in the Africa, the Americas, European, and Western Pacific regions. More details was described in Annex 4. The Eastern Mediterranean and South East Asia regions had the highest number of reported cases in 2018. MCV1 and MCV2 coverage in the AFR, AMR, and EMR regions was consistently below 90% during 2017-2021, except for AMR achieving 91% MCV1 coverage in 2018. However, the EUR and WPR regions achieved over 90% coverage of both MCV1 and MCV2 within 5 years. Detail information can be seen in Annex 5.

The reported measles cases, incidence, and measles vaccine coverage decreased significantly during the COVID-19 pandemic years compared to before the pandemic. Globally, measles cases were over 80% lower in 2020 and 2021 than in 2019. Most regions experienced a drop in reported cases, with the most significant decrease in the Western Pacific Region (WPR) at 98.6%. However, the Eastern Mediterranean Region (EMR) saw an increase in cases by 41.3%. Additionally, the Southeast Asia Region (SEAR) experienced a large drop in cases, with a reduction of 68.1% and 77.8% from 2019 to 2020 and 2021, respectively. Detail information can be seen in Annex 6.

Global coverage for the first dose of MCV1 decreased worldwide from 86% in 2019 to 83% in 2020 and further to 81% in 2021. However, coverage for the second dose of MCV2 increased from 71% in 2019 to 72% in 2020 and remained the same in 2021. MCV1 coverage decreased in all regions during and after the pandemic, with changes ranging from 1.1% to 8.5%. MCV2 coverage increased in some regions and decreased in others during 2020 and 2021. In SEAR, MCV1 coverage notably dropped by 6.4% in 2020 and 8.5% in 2021, and MCV2 coverage also decreased by 3.6% in 2020 and 6.0% in 2021 (Annex 6).

4.2 SEAR countries measles elimination status and immunisation history

Elimination status, population, development status, income status in 11 SEAR countries is shown in Table 5.1. Five countries (Bhutan, DPR Korea, Maldives, Sri Lanka and Timor-Leste) had certified elimination of measles and 6 countries (Bangladesh, India, Indonesia, Myanmar, Nepal, Thailand) remain endemic status and they are ongoing towards measles elimination in 2023.

Table 5.1 Elimination status, population, development status, income status in 11 SEAR countries.

Country	Elimination status		Population (2020)*	Income status**	Development status***
	Verified§	Endemic			
Bangladesh			164,689,383	Middle	Least Developed
Bhutan	2017		771,608	Middle	Least Developed
DPR Korea	2018		25,778,816	Low	Developing
India			1,366,417,754	Middle	Developing
Indonesia			273,523,615	Middle	Developing
Maldives	2017		540,544	Middle	Developing
Myanmar			54,409,800	Middle	Least Developed
Nepal			29,136,808	Middle	Least Developed
Sri Lanka	2019		21,413,249	Middle	Developing
Thailand			69,799,978	Middle	Developing
Timor-Leste	2018		1,318,445	Middle	Least Developed

§Countries were verified measles elimination by Regional Verification Commission (NVC) and data as of September 2022: Year of verified elimination were described. *Population data was available from Worldometer population database and accessed on 28th September 2022: Note: Population data was 2020 population except India which was 2019 data. **Income status was based on United Nations World Economic Situation and Prospects 2021. ***Development status was World Bank Income status.

The 2nd dose of measles containing vaccine (MCV2) introduction year, age of administration (MCV1 and MCV2) in 11 SEAR countries was shown in Table 5.2. Since 2016, all SEAR countries had introduced 2nd dose of measles containing vaccine (MCV2) and added in National EPI schedule. Since 2016, all SEAR countries had introduced 2nd dose of measles containing vaccine (MCV2) and added in National EPI schedule. Thailand has included MCV2 immunisation since 1996 Table 5.2.

Table 5.2 The 2nd dose of measles containing vaccine (MCV2) introduction year, age of administration (MCV1 and MCV2) in 11 SEAR countries

Countries	EPI launched (Year)	MCV2 introduction (Year)	Age of administration (month)	
			MCV1	MCV2
Bangladesh	1979	2012	9	15
Bhutan	1979	2006	9	24
DPR Korea	1980	2008	9	15
India	1978	2010	9 - 12	16-24
Indonesia	1977	2004	9	18
Maldives	1976	2007	9	18
Myanmar	1978	2012	9	18
Nepal	1977	2015	9	15
Sri Lanka	1978	2001	9	36
Thailand	1977	1996	9	18
Timor-Leste	1978	2016	9	18

Data source from WHO immunisation data portal accessed on 12 July 2022 (Vaccination schedule for measles) https://immunisationdata.who.int/pages/schedule-by-disease/measles.html?ISO_3_CODE=&TARGETPOP_GENERAL= and
South East Asia Region (Vaccine preventable disease surveillance, country EPI factsheet) https://www.who.int/southeastasia/health-topics/immunisation/vaccine-preventable-disease-(vpd)-surveillance-data

4.3 Measles incidence, reported cases and immunisation coverage in 11 SEAR countries

Table 5.3 shows that during 2019-2021 in SEAR regional measles cases decreased 68% from 29,389 in 2019 to 9,389 in 2020 meanwhile reported cases reduced 78% from 29,389 in 2019 to 6,514 in 2021. The highest number of measles cases were reported by India and Thailand in 2018. In 2019, the reported cases were peak in Bangladesh, Myanmar, Nepal, Sri-Lanka and Timor-Leste. Incidence per 1 million population reduced during 2020-2021pandemic years in 10 SEAR

countries compared to 2019 before pandemic. In 2020, 15 measles cases were reported by Maldives compared to 0 case in 2019. There was no reported case in DPR Korea since 2017.

Table 5.3 Measles cases, incidence, and percentage change between before pandemic years and during 2020-2021 pandemic years in 11 countries

Countries	Measles	Before pandemic			2020-2021 pandemic years		% Change	% Change
		2017	2018	2019	2020	2021	(1) §	(2) §§
Bangladesh	Cases	4,001	2,263	5,827	2,410	203	-59%	-97%
	Incidence*	24.7	13.8	35.2	14.4	1.2	-59%	-97%
Bhutan	Cases	66^	18^	2^	0	0	-100%	-100%
	Incidence*	87.3	23.6	2.6	0	0	-100%	-100%
DPR Korea	Cases	0	0	0#	0	NA¶	0	NA¶
	Incidence*	0	0	0#	0	NA¶	0	NA¶
India	Cases	12,032	19,474	10,430	5,604	5,700	-46%	-45%
	Incidence*	8.9	14.2	7.5	4	4	-47%	-47%
Indonesia	Cases	9,035	5,300	1,965	524	394	-73%	-80%
	Incidence*	34.2	19.8	7.3	1.9	1.4	-74%	-81%
Maldives	Cases	1^	1^	0	15	0	1500%	0
	Incidence*	2.1	2	0	29.2	0	2920%	0
Myanmar	Cases	1,293	1,389	5,252	444	8	-92%	-100%
	Incidence*	24.7	26.4	99	8.3	0.1	-92%	-100%
Nepal	Cases	99	260	430	388	143	-10%	-67%
	Incidence*	3.5	9.1	14.9	13.2	4.8	-11%	-68%
Sri Lanka	Cases	1^	1^	49^	2	0	-96%	-100%
	Incidence*	0	0	2.3	0.1	0	-96%	-100%
Thailand	Cases	1,946	6,035	5,412	NA¶	66¶¶	NA¶	-99%

	Incidence*	27.4	84.8	75.9	NA¶	0.9¶¶	NA¶	-99%
Timor-Leste	Cases	0	0	22	2	NA¶	-91%	NA¶
	Incidence*	0	0	17.2	1.5	NA¶	-91%	NA¶
Regional	**Cases**	28,474	34,741	29,389	9,389	6,514	-68%	-78%
	Incidence*	14.4	17.4	14.7	4.8	3.2	-67%	-78%

Data were downloaded on 18 July and 19 October 2022. *Incidence per 1 million population. #This data was taken from DPR Korea EPI factsheet 2020 since it was missing in WHO immunisation data portal. ¶Data were not available in WHO immunisation data portal as Thailand did not report measles case data to the JRF in 2020 and Sri-Lanka did not report measles case data in 2021 and incidence could not be calculated. ¶¶These data were obtained by downloading on 18 July 2022, in early period of annual update, but they were not described in dataset downloaded in 19 October 2022. The denominator is 1 million per population. § % change (1) is % change of cases and incidence in SEAR and countries between before COVID-19 pandemic (2019) and during pandemic year (2020). §§ % change (2) is % change of cases and incidence in SEA region and countries between before COVID-19 pandemic (2019) and pandemic years (2021). In this study, 2020 and 2021 were assumed pandemic years because there was a more impact on health system because the epidemiology of virus was uncertain and vaccine was developed in early stage of pandemic and not widely used in all countries. Despite the widespread use of the effective COVID-19 vaccine worldwide and the implementation of more strategic preparedness, preventive, and control measures based on the experience in 2021, there were still lingering impacts on the health system. ^ import or import related measles cases in measles elimination countries

Figure 5.1 shows reported measles cases compared before pandemic and 2020-2021 pandemic years. Most countries reported a higher number of cases in 2019 and the highest number of cases was 10,430 in 2019 almost half of the cases were reported in 2020 (5,604 cases) and 2021 (5,700 cases). 11 countries reported to WHO in 2019, but some countries did not report to WHO during 2020-2021.

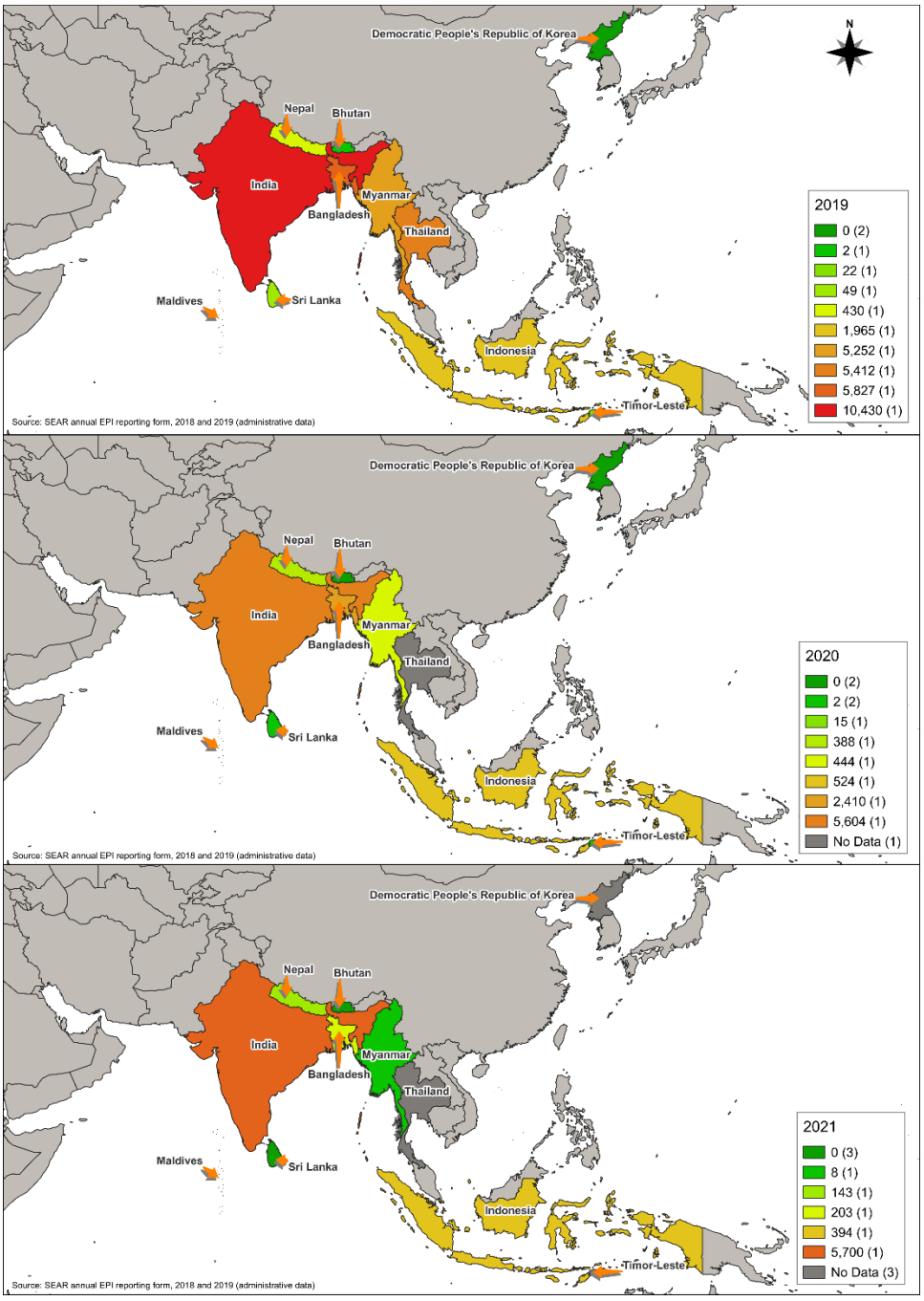


Figure 5.1 Comparison of reported measles cases in 2019 and 2020/2021 in SEAR countries

Figure 5.2 shows comparison of MCV1 coverage between before pandemic and 2020-2021 pandemic years. Seven out of 11 countries had achieved ≥ 95% MCV1 coverage in 2019 and five countries in 2020 and 2021.

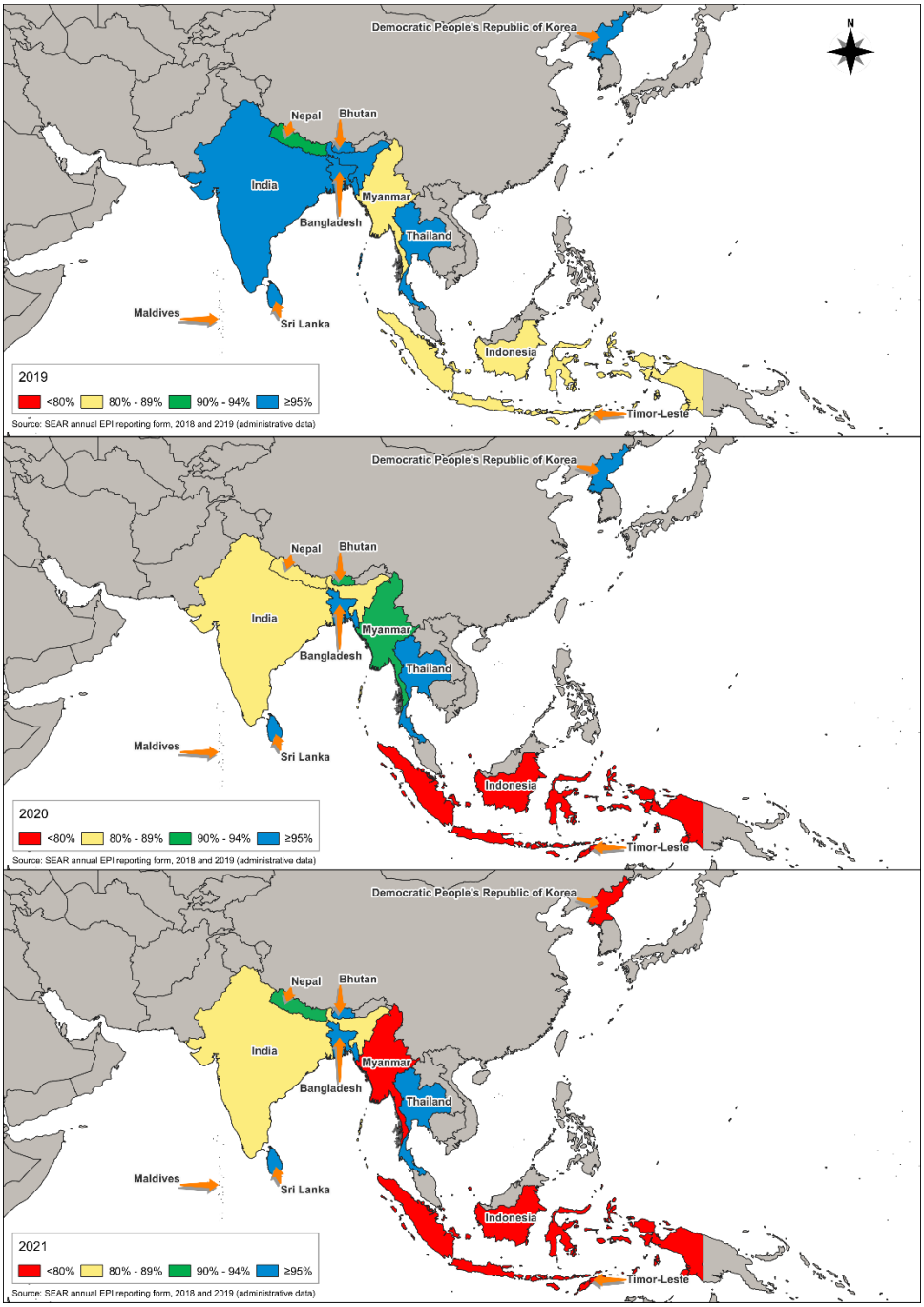


Figure 5.2 Comparison of MCV1 (WUENIC) coverage in 2019 and 2020/2021 in SEAR countries

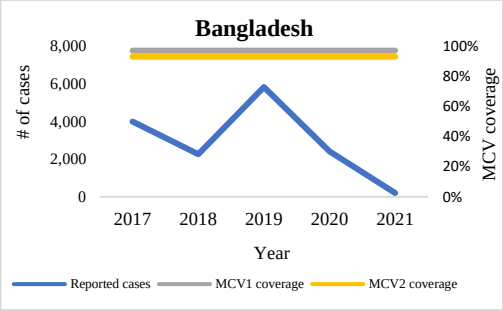
Nine out of 11 countries (82%) had achieved ≥ 90% MCV1 coverage in 2017 and 2018, eight countries (73%), seven countries (64%) and six countries (55%) had achieved ≥ 90% MCV1 coverage in 2019, 2020 and 2021. MCV1 coverage dropped in 6 countries (Bhutan, India, Indonesia, Nepal, Sri-Lanka, Timor-Leste) changing of 3.0% - 15.5% between 2019 and 2020. Bangladesh, Maldives and Thailand remained constant of MCV1 and MCV2 coverage before and 2020-2021 pandemic years Table 5.4.

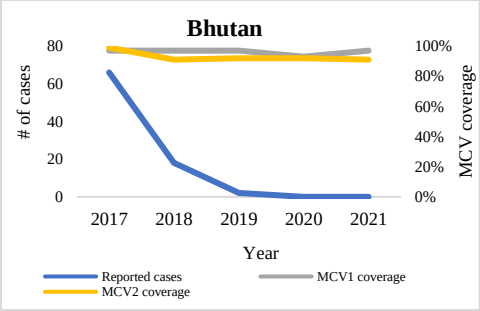
The peak of reported cases varied in SEAR countries during 2017-2020. DPR Korea. There was a rise of MCV1 and MCV2 coverage in 2020 compared to 2019 in DPR Korea and Myanmar, but there was a significant reduction of MCV1 and MCV2 coverage in 2021 in these two countries. Most countries maintained routine immunization for measles in 2020 and 2021, despite the challenges posed by COVID-19. Bhutan, India, and Sri Lanka did not experience significant declines, and Figure 5.5 illustrates that Timor Leste managed to stay close to 2019 levels without dropping back to 2017-2018. In 2021, MCV2 coverage increased nearly back to before the pandemic in Nepal. However, declines in three countries are noteworthy, particularly the decline in Indonesia over 2020 and 2021. The declines in DPR Korea and Myanmar in 2021 are also concerning. Please refer to Figure 5.3 for more details.

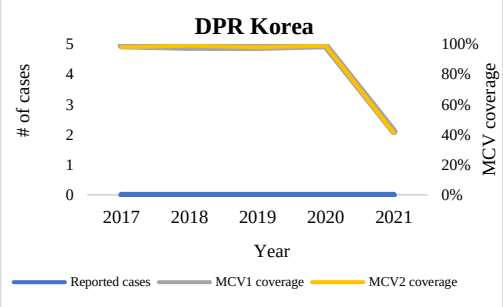
Table 5.4 MCV coverage and percentage change between before pandemic and 2020-2021 pandemic years in 11 SEAR countries

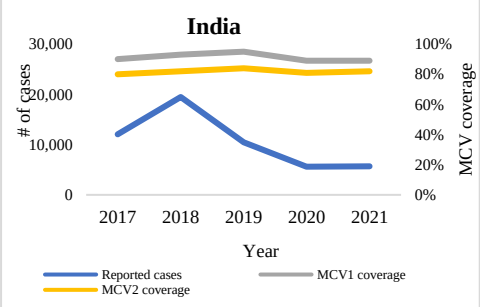
Countries	Coverage %	Before pandemic			Pandemic years		% Change (1) §	% Change (2) §§
		2017	2018	2019	2020	2021		
Bangladesh	MCV1	97%	97%	97%	97%	97%	0.0%	0.0%
	MCV2	93%	93%	93%	93%	93%	0.0%	0.0%
Bhutan	MCV1	97%	97%	97%	93%	97%	-4.1%	0.0%
	MCV2	99%	91%	92%	92%	91%	0.0%	-1.1%
DPR Korea	MCV1	99%	98%	98%	99%	42%	1.0%	-57.1%
	MCV2	98%	99%	98%	99%	41%	1.0%	-58.2%
India	MCV1	90%	93%	95%	89%	89%	-6.3%	-6.3%
	MCV2	80%	82%	84%	81%	82%	-3.6%	-2.4%
Indonesia	MCV1	90%	89%	88%	76%	72%	-13.6%	-18.2%
	MCV2	63%	67%	71%	60%	50%	-15.5%	-29.6%
Maldives	MCV1	99%	99%	99%	99%	99%	0.0%	0.0%
	MCV2	99%	99%	96%	96%	96%	0.0%	0.0%
Myanmar	MCV1	83%	93%	84%	91%	44%	8.3%	-47.6%
	MCV2	80%	87%	80%	90%	42%	12.5%	-47.5%
Nepal	MCV1	90%	91%	92%	87%	90%	-5.4%	-2.2%
	MCV2	59%	69%	76%	74%	87%	-2.6%	14.5%
Sri Lanka	MCV1	99%	99%	99%	96%	97%	-3.0%	-2.0%
	MCV2	99%	99%	99%	96%	97%	-3.0%	-2.0%
Thailand	MCV1	99%	96%	96%	96%	96%	0.0%	0.0%
	MCV2	95%	87%	87%	87%	87%	0.0%	0.0%
Timor-Leste	MCV1	77%	77%	85%	79%	79%	-7.1%	-7.1%
	MCV2	57%	54%	80%	78%	78%	-2.5%	-2.5%
Regional	**MCV1**	**91%**	**93%**	**94%**	**88%**	**86%**	**-6.4%**	**-8.5%**
	MCV2	**79%**	**81%**	**83%**	**80%**	**78%**	**-3.6%**	**-6.0%**

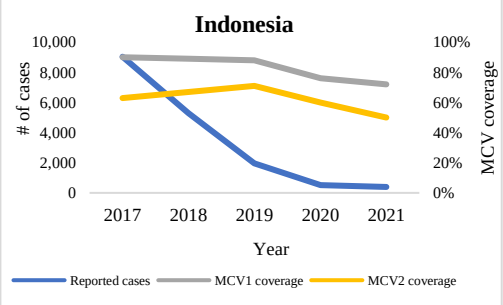
Data were downloaded on 18 July and 19 October 2022. § % change (1) is % change of MCV1 and MCV2 coverage in SEAR and 11 countries between before COVID-19 pandemic (2019) and during pandemic (2020). §§ % change (2) is % change of MCV1 and MCV2 coverage in SEA region and countries between before COVID-19 pandemic (2019) anpandemic year (2021). In this study, 2020 and 2021 were assumed pandemic years because there wa impact on the health system. After all, the epidemiology of the virus was uncertain and vaccine was developed in early stage of pandemic and not widely used in all countries. Despite the widespread use of the effective COVID-19 vaccine worldwide and the implementation of more strategic preparedness, preventive, and control measures based on the experience in 2021, there were still lingering impacts on the health system.

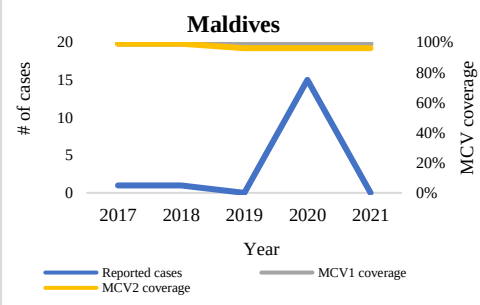

Bangladesh
8,000
6,000
4,000
2,000
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage

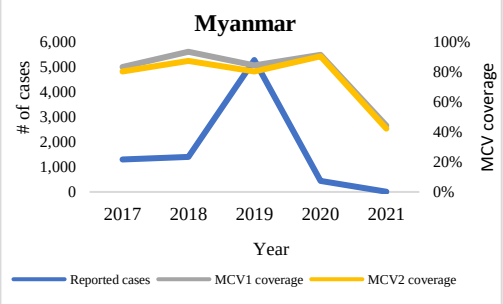

Bhutan
80
60
40
20
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage

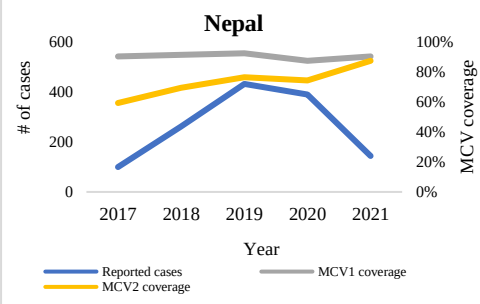

DPR Korea
5
4
3
2
1
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage

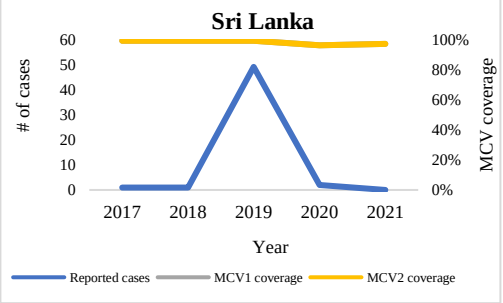

India
30,000
20,000
10,000
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage

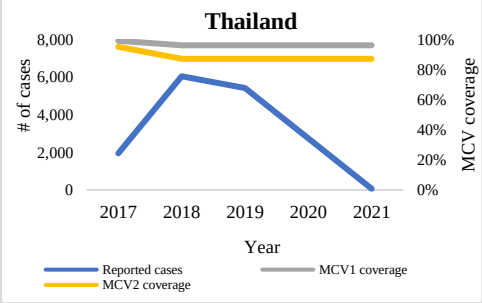

Indonesia
10,000
8,000
6,000
4,000
2,000
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage


Maldives
20
15
10
5
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage


Myanmar
6,000
5,000
4,000
3,000
2,000
1,000
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage


Nepal
600
400
200
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage


Sri Lanka
60
50
40
30
20
10
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage


Thailand
8,000
6,000
4,000
2,000
0
# of cases
100%
80%
60%
40%
20%
0%
MCV coverage
2017
2018
2019
2020
2021
Year
Reported cases
MCV1 coverage
MCV2 coverage

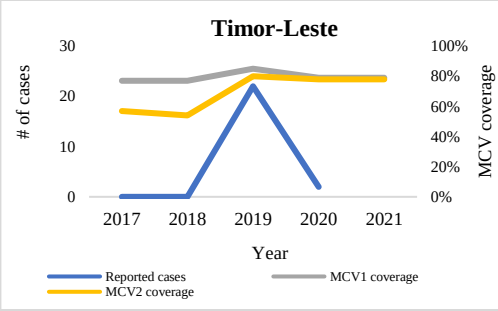


Figure 5.3 Reported measles cases and MCV1 and MCV2 (WUENIC) coverage in 11 SEAR countries 2017-2021

Supplementary Immunisation Activities (SIAs) for measles were undertaken in 11 SEAR countries (2017-2021). According to WHO data as of July 2022, all SEAR countries (except Sri Lanka) conducted planned SIA activities during 2017-2019, but only 4 countries conducted planned SIAs during 2020-2021 Table 5.5.

Table 5.5 Supplementary Immunisation Activities (SIAs) in 11 SEAR countries (2017-2021)

Countries	Year	# of SIAs	Target population	Immunised population	Coverage (%)
Bangladesh	2017	2	2,016,341	2,044,292	101
	2020	1	35,337,521	36,585,691	104
Bhutan	2017	2	534,560	526,674	99
	2018	1	100,000	14,698	15
DPR Korea	2019	3	6,864,815	6,555,347	95
	2020	1	491,217	488,502	99
India	2017	13	67,880,000	65,644,000	97
	2018	17	181,814,000	176,146,000	97
	2019	2	61,002,000	61,237,000	100
Indonesia	2017	1	34,964,384	35,307,148	101
	2018	1	31,963,154	23,453,882	73
Maldives	2017	2	64,001	48,480	76
Myanmar	2019	3	4,838,232	4,628,890	96
Nepal	2020	1	2,548,336	2,563,810	101
Sri Lanka[§]	-	-	-	-	-
Thailand	2018	3	750,794	351,343	47
	2021	1	384,457	57,602	15
Timor-Leste	2018	1	140,428	157,171	112

Data source – WHO immunisation data portal (as of 2022, July 11): Supplementary Immunisation Activities conducted during 2017-2021 in 11 countries were collected. [§] Conducting SIAs within 2017-2021 were not found in Sri Lanka.

4.4 Association between annual incidence and MCV1 coverage

Spearman's rank tests were used to analyse the association between annual incidence rate and 1st dose of measles containing vaccine (MCV1) coverage before pandemic and 2020-2021 pandemic years. There was a weak non-significant linear relationship between annual incidence and MCV1 coverage prior to the pandemic and there was no relationship in 2020-2021 pandemic years. Table 5.6.

Table 5.6 Correlation between annual incidence and MCV1 coverage before pandemic and 2020-2021 pandemic years

MCV1 coverage	Spearman's rho	P value
Incidence (Before Pandemic)	-0.400	0.223
Incidence (2020-2021 Pandemic year)	0.018	0.958

For the period "before pandemic", I used combined2017, 2018, and 2019 data.For " the pandemic year" I used the data combined data of 2020 and 2021 for all SEAR countries.

4.5 Association between elimination status and country's development status, economic status, 2nd dose of measles containing vaccine (MCV2) introduction year

The association between elimination status and country's development status, economic status, 2nd dose of measles containing vaccine (MCV2) introduction year were calculated by Fisher's exact test with p value ≤ 0.05. MCV2 introduction years were divided into two groups according to mean introduction year. Wilcoxon rank sum test was used to analyse the correlation between population and elimination status. The results presented in Table 5.7 state that there was a link between a country's population and elimination status ($p<0.006$). However, there could be many confounders

that might have an impact on the findings. For instance, younger age groups and low performance could be the confounding variables. It's important to recognized that this is a simplistic approach to a complex issue. However there was no association between elimination status and the country's development status, economy, and MCV2 introduction year.

Table 5.7 Association between elimination status and country's population, development status, economy, MCV2 introduction year in 11 SEAR countries

Country's status	Elimination status		Total	*Fisher's exact* value	P value
	Elimination	Endemic			
Population	5	6		-2.739[a]	0.006*
Rank sum	15.00	51.00			
Developing	3 (27.27)	3 (27.27)	6 (54.55)	1.000	0.608
Least Developed	2 (18.18)	3 (27.27)	5 (45.45)		
Low income	1 (9.09)	0 (0.00)	1 (9.09)	0.455	0.455
Middle income	4 (36.36)	6 (54.5)	10 (90.91)		
Before/During 2007	3 (27.27)	4 (36.36)	7 (63.64)	1.000	0.652
After 2007	2 (18.18)	2 (18.18)	4 (36.36)		

[a] Analysed by Wilcoxon rank-sum test with z value.
*Statistically significant at 0.05 level

CHAPTER 5: DISCUSSION

The highest measles incidence and number of cases were found in 2019 globally but regional variation can be seen between 2018 and 2019. Large outbreaks in Africa Region (Central African Republic, Democratic Republic of the Congo, Madagascar), in European Region (Georgia, Kazakhstan, North Macedonia, Ukraine) and in the Western Pacific Region (Samoa, Tonga) in 2019 caused a global measles r esurgence (60).

There was a steep fall in number of worldwide reported cases and incidence in 2020 and this drop continued in 2021. Global measles incidence decreased by 82.0% in 2020 compared to 2019 and this fall of incidence was found in all six regions decreasing ranging from 54.5% to 91.6%. Measles incidence decreased by 85.5% in 2021 which is more significant reduction because more outbreaks with high morbidity and mortality of COVID-19 occurred in most countries throughout 2021 impacting the country's health system comparing to early period of pandemic. The reduction of incidence and cases might be assumed to be linked to the interruption of measles transmission, but other possible factors should be considered. COVID-19 related response measures could influence the reporting system causing underreporting and underestimating. In 2021, 21% of countries did not report measles cases to WHO/UNOCEF in time and cases from these countries did not include in WHO/UNICEF dataset. Although there was a reduction in reported cases, large and disruptive measles outbreaks were reported by 21 countries during May 2021- April 2022. Reductions in notifiable diseases, including measles, may indicate that there was a weakness in national surveillance systems due to disruptions to health programs, competing and other workforce priorities during COVID-19 pandemic.

During the pandemic, MCV1 reported coverage decreased globally by 3.5% in 2020 and 5.8% in 2021 compared 2019. A reduction of vaccine coverage, including measles vaccine were found in most countries because health system and routine immunisation were likely to have been disrupted due to the utilisation of health infrastructure and workforce focusing mainly on the pandemic response, control and prevention all over the world. Only 39% of countries reached ≥ 90% MCV1 coverage in 2020 reducing from 61% of countries in 2019 (4). Interruption of immunisation

impacted millions of children who missed their childhood vaccination during pandemic and 73 million children were left unimmunised measles vaccine. In this regard, WHO/UNICEF predict increasing risk of vaccine preventable outbreaks particularly measles outbreaks in next coming years as seen during the pandemic.

Not only the SEAR countries but countries from other regions also did not achieve the target indicators of surveillance. Globally more than half of the countries (63%) did not meet measles surveillance indicators of discarded measles cases per 100,000 total population in 2020 (4). In the Africa region, there was a drop in numbers of suspected measles occurring since April 2020 with 23% of African countries achieving the target discarded rate in 2020. This was likely due to decreasing sensitivity of the surveillance systems which were impacted during pandemic in some African countries (61).

All SEAR countries were conducting case-based measles surveillance by laboratory confirmation through WHO accredited laboratory network by 2020. During the COVID-19 pandemic, communicable disease surveillance systems were disrupted, including measles surveillance. We found, five out (Bangladesh, Bhutan, Maldives, Napal, Timor-Leste) of 11 countries had achieved the discarded rate of ≥ 2 per non- measles case per 100,000 population in 2020 and 2021 and eight out of 11 SEAR countries had met the target indicator of discarded case (case definition for discarded cases was provided in CHAPTER 3) in 2019 (25).

The regional reported cases and incidence were highest in SEAR in 2018. A regional measles resurgence in 2018 and 2019, saw large outbreaks in some SEAR countries (India, Indonesia, Myanmar and Thailand) during these years. However, measles incidence and cases declined substantially in 2020 and 2021 which was the lowest number since 2011. We can see that the reduction of incidence and cases occurred simultaneously with low surveillance indicators in some countries during 2020-2021. This is most likely attributed to the disrupted, weak and not sensitive enough surveillance system's ability to detect early cases and outbreaks which, in turn, led to underreporting of cases and increasing risk of outbreaks. During 2020-2021, multiple measles

outbreaks occurred in Bangladesh, India, Indonesia, Nepal and Thailand. The Centers for Disease Control and Prevention (CDC) listed India and Indonesia in top 10 countries with global measles outbreaks between March 2022 – August 2022. So, consideration of decrease in measles incidence in these years may have some explanations. In this point, we have to consider if the decrease in incidence is real, or could it be attributed to the lack of data being collected and reported. We would expect an increase with the disruption of health systems including surveillance. We propose four possible considerations:

(1) Interruption of transmission may occur because following the outbreaks the SEAR regional MCV1 coverage has reached over 90% since 2017, with the highest coverage in 2019 (94%), which has helped prevent measles transmission due to high population immunity and the peaks in measles cases in 2018-2019, can be expected a large amount of naturally derived immunity to add to vaccine derived immunity. Drop of incidence was seen in almost all SEAR countries.

(2) Pandemic related response measures (lockdown procedures, restriction of public gathering, cancellation of festivals) may have led to reduction of cases, due to limited transmission

(3) Disruption of surveillance system during pandemic (perhaps, resources mobilisation, deployment of surveillance staff to pandemic response, unavailability of health facilities and lab testing) made under reporting of cases likely as only 50% of countries had achieved target indicators of surveillance in 2020 and 2022.

(4) Less utilisation and decreased availability of routine of health services (including outpatient care) because of panic related to COVID-19 may have delayed self-reporting, causing under-reporting.

Concerns on reporting cases and incidence

In SEAR there was a significant drop (50%) of reported measles cases in 2020 compared to 2019 possibly related to the interruption of disease transmission itself because preventive measures of

COVID-19 such as wearing mask, hand washing, social distancing and restriction of public gatherings also prevented measles, as it is also a respiratory infection (62). For example, the reported number of notifiable diseases including vaccine preventable diseases decreased during week 10-33, 2020 compared to the same period in 2016-2019 because of impact of pandemic and associated Non Pharmaceutical Interventions (NPI) and country's surveillance systems were the most impacted (63).

Among SEAR countries, Myanmar had a large drop of incidence in 2021 compared to 2019. Myanmar health system was disrupted by pandemic since 2020 and this was aggravated by withdrawal of health care providers during, which has worsened since the military coup in 2021. Routine health care services including surveillance and immunisation services were not conducted during 2021 resulting in large drop in reported incidence and vaccine coverage. In 2020-2021 pandemic year, Bangladesh, Indonesia, and India experienced a notable reduction in reported measles cases and incidence when compared to the period before the pandemic.

Despite Indonesia being ranked among the top 10 countries for measles outbreaks, the actual number of recorded cases during the COVID-19 pandemic was notably lower compared to pre-COVID years, despite reported low coverage of MCV1 and MCV2. It's possible that improvements in measles surveillance and reporting systems were implemented during the pandemic. Enhanced surveillance could lead to earlier detection and containment of measles outbreaks, even with lower overall case numbers reported.

The significant decrease in measles cases in India during the COVID-19 pandemic can be attributed to several proactive measures and innovations implemented by the measles and rubella (MR) elimination program including risk assessment tailored approach to identify vulnerable populations and areas at higher risk of measles outbreaks. Based on these assessments, tailored approaches were developed to target specific groups with intensified vaccination campaigns and other public health interventions. During 2020, telephonic delivery of ACS accounted for a

significant portion (19%) of all ACS provided. Other innovation, Telephonic Delivery of Acute Care Services (ACS), ensured that essential healthcare services, including those related to measles, continued to reach the population even during pandemic-related restrictions and lockdowns. The combined efforts of targeted vaccination campaigns, enhanced surveillance through the MR dashboard, improvements in case detection criteria, telephonic delivery of healthcare services, and strengthened laboratory capabilities played pivotal roles in reducing measles cases in India during the COVID-19 pandemic.

During the COVID-19 pandemic, Indonesia, despite being ranked among the top 10 countries for measles outbreaks historically, experienced a notable decrease in recorded cases compared to pre-COVID years. This decline occurred despite reported low coverage of MCV1 and MCV2 vaccinations. One plausible explanation for this discrepancy could be the implementation of enhanced measles surveillance and reporting systems during the pandemic. These improvements likely facilitated earlier detection and more effective containment of measles outbreaks, potentially masking the true impact of the virus with lower reported case numbers.

Furthermore, countries that had achieved measles elimination except DPR Korea also observed a decrease in cases, although the Maldives reported 15 cases in 2020 after recording none in 2019. Interestingly, Thailand's measles cases for 2020 and Sri Lanka's for 2021 were not available in the WHO's immunization data portal, hinting at potential underreporting. The reported reduction in measles cases may not reflect the true situation due to potential underreporting caused by the pandemic and the measures taken to control it. Meanwhile, there were multiple measles outbreaks in Bangladesh, India, Indonesia, Nepal, and Thailand during the years 2020-2021. In that point, Myanmar and Nepal had MCV1 and MCV2 coverage below 95% and experienced a peak in cases in 2019, with Nepal reporting almost as many cases in 2020. During pandemic years, Measles outbreaks occurred in Nepal with no outbreaks reports in Myanmar. It seems highly likely that the healthcare systems in Myanmar were disrupted to such an extent that outbreaks were missed or not reported. Therefore, the observed decrease in measles incidence during these years may be related to possible considerations.

The absence of reported cases or outbreaks does not necessarily indicate low transmission of the disease, especially in the context of Southeast Asia (SEAR) countries where underreporting or missed outbreaks can occur due to various factors including the sensitivity of the surveillance system, disease awareness and reporting practicing, diagnostic capabilities, etc. For example, there were concerns about the significant drop in sensitivity of MR surveillance at national and subnational levels in Thailand during 2020-2021 pandemic year with no reported cases in 2020. Based on the meeting reports of the WHO South-East Asia Regional Verification Commission for measles and rubella (SEA-RVC), the SEA-RVC could not determine the extent as well to which active surveillance was being conducted in Thailand. It was mentioned that there was confusion about whether "zero reporting" was an intentional strategy throughout Thailand or if it reflected gaps in surveillance. Furthermore, The extent and effectiveness of outbreak response measures in Thailand were also unclear. Effective outbreak response requires rapid detection of cases, prompt investigation, and implementation of control measures to prevent further spread.

Low incidence with large measles outbreaks

Prior to the COVID-19 pandemic in 2018, when large outbreaks occurred in some SEAR countries, health authorities addressed to strengthen surveillance and immunisation activities to have high population immunity to prevent further outbreaks. Regional MCV1 and MCV2 coverage were the highest in 2019 since 2011. However, both MCV1 and MCV2 coverage stagnated in 2020 and 2021, decreasing by 6.4% in 2020 and 8.5% in 2021. Immunisation activities were more interrupted in 2021 because COVID-19 situation when most of the countries in SEAR faced larger waves of coronavirus outbreaks.

Possible factors of low immunisation coverage

In 2020, estimated national immunisation coverage (MCV1) declined in six SEAR countries, compared to 2019 ranging from 3.0% in Sri Lanka to 13.6% in Indonesia while MCV2 coverage dropped in five SEAR countries ranging from 2.5% to 15.5%. In 2021, MCV1 and MCV2 coverage declined in 7 countries. As Indonesia faced the high transmission of coronavirus with high case fatality rate (CFR) during 2020-2021, the government and health authorities focused on public health and social measures of COVID-19 including wearing mask, social distancing, stay at home procedures, public holidays, restriction of public transports throughout the pandemic instead routine health services including routine immunisation. Estimated MCV1 and MCV2 coverage in Indonesia dropped significantly during pandemic. DPR Korea had an increase in both MCV1 and MCV2 in 2020, the highest decline in 2021 because of MR vaccine stock out in DPR Korea Similarly, Myanmar made an increase MCV1 and MCV2 coverage in 2020, but a significant drop in 2021 perhaps due to immunisation services deteriorating because of the conflict occurring across the country. Bangladesh and Thailand had made enhanced efforts focused on immunisation activities. Amid mitigation of pandemic. Bangladesh had maintained >90% of both MCV1 and MCV2 coverage throughout the pandemic. Thailand has remained constant with measles vaccine coverage during 2020-2021 comparing to 2019.

Vaccine hesitancy could be one of the causes of low immunisation coverage in some SEAR countries as South East Asia Regional Verification Committee (SEA-RVC) recommended Indonesia to address on vaccine hesitancy to achieve high population immunity (64). Low vaccine coverage was associated with low socio-demographic index like low income per capita, low average years of schooling and possible factors could be vaccine hesitancy and traditional beliefs (49, 52).

Immunisation services were devastated in most countries in all regions during pandemic and measles vaccine coverage were lower in 2020 than in 2018 and 2019 (65). Immunisation doses of

DPT3 and MCV1 notably reduced in 2020, the lowest in April 2020 because of disruption in supply of vaccines and reduction in vaccination demand in most countries in all regions (66). Millions of children missed their childhood immunisation during pandemic and those children are susceptible to vaccine preventable disease particularly measles. In some SEAR countries, low MCV1 coverage was likely found in socio-geographic inequalities such as urban/rural residency, wealth quintiles, maternal education (67).

Correlation between incidence and MCV1 coverage

We found that there was a weak non-significant linear relationship between annual incidence and MCV1 coverage prior to the pandemic. This suggests that while there was some observable trend between higher MCV1 coverage and lower measles incidence, it was not strong enough to be statistically significant. Factors other than vaccination coverage likely also influenced measles incidence before pandemic. There was no relationship in 2020-2021 pandemic year which indicates that factors related to the pandemic (such as disruptions in healthcare services, changes in population behavior, or altered disease transmission dynamics due to COVID-19 control measures) may have overridden any previous association. after pandemic

Correlation between country's population and elimination status

In our study, the correlation between country's population and elimination status was significant and this presents an interesting and important finding in public health and vaccination efforts. The result means that the eliminated countries had less population than non-eliminated countries. So, population has an important role in interruption of disease transmission especially in developing countries. need to cover the health services to all target population. There may be gaps and inequities in providing health services even though primary health services such as immunisation, maternal and child care in countries with high population. Inequity in health services could be

challenges in reduction morbidity and mortality of diseases and elimination strategies. Homogenous immunisation coverage in high populated SEAR countries particularly India and Indonesia may affect the regional measles elimination target (68). So, it is encouraging for supporting the most populous countries to ensure comprehensive coverage of measles-containing vaccines (MCV) involves a multifaceted approach that addresses both logistical challenges and healthcare system strengthening in collaboration with national governments, international partners, and local communities.

Supplementary Immunisation Activities (SIA)

Not only routine immunisation activities but also supplementary immunisation activities (SIA) were destroyed and/or postponed in most countries during 2020. Only four countries could conduct the planned SIAs during 2020-2021 and some MR campaigns have not been conducted till July 2022. Disruption of overall health system (lockdowns, deployment of staff), disruption in supply chain of childhood vaccines (transporting, stockout), avoidance of health facilities by community (panic of COVID-19) made stagnation of immunisation coverage during the pandemic. Although India and Indonesia planned to conduct Measles and Rubella (MR) campaign in 2020, these campaigns were postponed and have not been conducted until July 2022. Myanmar did not implement MR follow up campaign until July, 2022 despite it was planned to conduct in 2021.

Limitations

The findings may be subjective because there are some limitations in this study. The data used in this study was secondary data only. We relied on reporting mechanisms that were affected by COVID-19 pandemic- i.e. resources were likely focused elsewhere (vaccine logistics, cold chain, delivery systems, human resources, data systems all likely to have been adversely affected). The dataset was aggregated secondary data updating national data availability and three countries (27%) did not report measles cases to WHO during 2020-2021.. Vaccine coverage data were the WHO/UNICEF estimates of national administrative coverage in which there may be biases in

numerator (vaccinated children) and denominator (target population). Age distribution of cases, measles related deaths and outbreaks data in SEAR were limited to access ie. The dataset from WHO's Global Health Observatory data repository did not include sub-national data, outbreaks data and death data and so we cannot see the consequences of low immunisation. Limited time period as focus was to up to 2022 and the world is still affected by ongoing pandemic waves. Countries are at different levels of recovery from the pandemic. The time period may be too short to show the real emerging picture of measles incidence and mortality due to disruption in EPI and surveillance systems..

The decline in measles incidence observed during 2020-2021, as highlighted by this study, can be attributed to a combination of factors. While disruptions to immunization programs due to the COVID-19 pandemic likely played a significant role in some SEAR countries, it's essential to consider several contributing factors beyond just low immunization coverage during the pandemic. Pre-existing challenges such as low immunization coverage rates before the pandemic could have created a pool of susceptible individuals within the population. This buildup of susceptible is known to facilitate large outbreaks once routine immunization services are disrupted, underscoring the importance of sustained vaccination efforts even during crises.

Additionally, the effectiveness of surveillance systems in detecting and reporting measles cases during the pandemic may have been compromised in some countries. This potential for underreporting or delayed detection could influence the reported incidence rates and contribute to the perception of a decline in cases. While routine immunization efforts were generally maintained across many SEAR countries during 2020 and 2021, notable declines in measles incidence were observed in countries like Indonesia, DPR Korea, and Myanmar. These declines raise concerns about gaps in immunization coverage or other systemic factors that warrant further investigation and targeted intervention. In conclusion, the decline in measles incidence during the pandemic years reflects a complex interplay of factors, including disruptions to immunization services, age-specific vulnerabilities, pre-existing immunization gaps, and potential surveillance challenges. Addressing these factors through strengthened immunization programs, improved surveillance

capabilities, and targeted interventions is crucial to preventing future outbreaks and ensuring sustained progress towards measles elimination in SEAR countries. The results of this study may not reflect the real measles situation in SEAR.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

In conclusion, the drop in measles incidence with reported low measles immunisation coverage in SEAR countries is not expected to be likely to reduction in of measles transmission. It could be that the COVID-19 pandemic impacted significantly in measles surveillance and immunisation in all SEAR countries. Impairment of the surveillance system is likely to lead to under detection of early cases increasing spread of the disease. Low immunisation coverage is likely to produce immunity gaps with high risk of outbreaks in coming years affecting millions of children.

The true situation may appear over years as we emerge from the pandemic and reinstate health and data systems in countries. Therefore, these data suggest that all countries in SEAR need to focus on building stronger, more resilient health systems and support the restoration of immunisation and surveillance systems. This could be achieved by

- Making efforts to accelerate quality surveillance including cross border surveillance to better understand the current epidemiology of the disease
- Expanding laboratory testing capacity at all level to achieve and sustain the sensitive surveillance system
- Identifying and closing the immunity gaps to have high population immunity with ≥95% of 2 doses of measles containing vaccine by routine immunisation and SIA/Campaigns and building a robust immunisation programme based on lessons learnt in pandemic
- Modifying a national and subnational strategic plan for measles elimination in ongoing pandemic
- Risk assessment and preparedness of vaccine preventable diseases outbreak response plans
- Collaboration with partner organisations to implement the strategic plan for measles elimination by 2023 including intensifying immunisation system

Providing support to strengthen immunization systems, enhance vaccine supply and distribution, improve surveillance and monitoring to ensure that everyone in populous countries receives the protection afforded by measles-containing vaccines.

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ANNEX

Annex 1 **Verification status of measles elimination in Regions (as of 06/09/2022)**

Regions	# of Member States	Verification status	% of verification	Elimination status	Endemic status	Unclassified *
AFR	47	0	0	0	47	0
AMR	35	33	94	0	0	2
EMR	21	3	14	0	18	0
EUR	53	29	55	1	18	5
SEAR	11	5	45	0	5	1
WPR	27	6	22	0	21	0
GLOBAL	**194**	**76**	**39%**	**1**	**109**	**8**

Data source-WHO Head Quarter; AFR-Africa Region, AMR-Americas Region, EMR-Eastern Mediterranean Region, EUR-European Region, SEAR-South East Asia Region, WPR-Western Pacific Region; Verification Status-Elimination verified by Regional Verification Committee (RVC), Elimination Status-Just verified by National Verification Committee (NVC).

*Note : not all were classified , this table represents the data available for 194 countries

Annex 2 **Measles cases, incidence, MCV1 and MCV2 coverage and % countries with MCV1 coverage ≥ 90% in WHO regions between 2000 and 2015, 2016, 2017, 2018, 2019, 2020**

Region (# of countries)	Year	Reported measles cases	Measles incidence*	MCV1 coverage**	MCV2 coverage**	% Countries with ≥ 90% MCV1 coverage***
AFR(47[$])	2000	520,102	842	53	5	9
	2015	98,621	100	26	18	26
	2016	36,269	37	69	22	34
	2017	72,603	69	70	25	34
	2018	125,426	118	74	26	30
	2019	618,595	567	70	33	30
	2020	115,364	108	68	36	15
AMR(35)	2000	1,754	2	93	65	63
	2015	423	0.6	94	53	83
	2016	97	0.1	92	80	66
	2017	775	1.7	92	74	63
	2018	16,327	24	90	82	57
	2019	21,971	32	87	72	69
	2020	1,584	2	85	73	37
EMR(21)	2000	38,592	90	71	28	57
	2015	21,335	33	76	68	57

Region (# of countries)	Year	Reported measles cases	Measles incidence*	MCV1 coverage**	MCV2 coverage**	% Countries with ≥ 90% MCV1 coverage***
	2016	6,275	10	82	74	57
	2017	36,427	57	81	67	62
	2018	64,722	93	82	74	57
	2019	18,458	27	84	75	52
	2020	6,122	10	83	76	33
EUR(53[$])	2000	37,421	50	91	48	62
	2015	25,947	31	94	89	81
	2016	4,440	5	93	88	81
	2017	24,356	27	95	83	90
	2018	82,523	98	95	91	89
	2019	106,130	116	96	91	85
	2020	10,772	17	94	91	57
SEAR(11[$])	2000	78,558	51	63	3	30
	2015	29,109	17	85	71	46
	2016	27,530	14	89	75	64
	2017	28,474	14	87	77	64
	2018	34,741	18	89	80	82
	2019	29,389	15	94	83	73
	2020	9,389	5	88	78	55

Region (# of countries)	Year	Reported measles cases	Measles incidence*	MCV1 coverage**	MCV2 coverage**	% Countries with ≥ 90% MCV1 coverage***
WPR(27)	2000	177,052	104	85	2	48
	2015	65,176	35	96	93	67
	2016	57,879	31	96	93	63
	2017	10,695	6	97	94	59
	2018	29,497	15	95	91	59
	2019	78,479	41	95	93	67
	2020	6,601	4	95	94	44
Global	**2000**	**853,479**	**145**	**72**	**18**	**45**
	2015	**245,928**	**36**	**85**	**61**	**61**
	2016	**132,490**	**18**	**84**	**67**	**61**
	2017	**173,330**	**25**	**85**	**67**	**61**
	2018	**353,236**	**49**	**86**	**61**	**69**
	2019	**873,022**	**120**	**86**	**71**	**62**
	2020	**149,796**	**22**	**84**	**70**	**39**

Data source-Progress toward measles elimination worldwide (MMWR) (vol-65,66,67,68,69,70) in which measles cases, incidence and vaccine coverage were compared between 2000 and year of interest (2010,2016,2017,2018,2019,2020): In this table, information of 2010 was not described.

*Measles incidence per 1 million population

**MCV1 and MCV2 coverage-WHO/UNICEF estimates of national immunisation coverage

*** In 2013, Global Action Plan recommended to achieve MCV1 coverage ≥ 90% in all countries and ≥ 80% in district level:

$ In 2000, 46 member states in AFR, 52 member states in EUR and 10 member states in SEAR.

Annex 3 **Estimating the numbers of measles reported cases, incidence and MCV coverage in global and six WHO regions within five-year period**

Regions	Measles	Before pandemic			2020-2021pandemic years	
		2017	2018	2019	2020	2021
AFR	Cases	72,603	125,426	618,595	115,369	89,606
	Incidence*	69.2	116.6	559.8	106.3	82.9
	MCV1	70%	70%	70%	69%	68%
	MCV2	25%	26%	33%	40%	41%
AMR	Cases	895	16,714	21,971	9,996	682
	Incidence*	1.1	16.6	32.3	9.8	0.7
	MCV1**	88%	91%	87%	85%	84%
	MCV2**	76%	84%	72%	72%	75%
EMR	Cases	36,434	64,764	18,458	6,769	26,089
	Incidence*	54	89.6	26.4	10.3	39.8
	MCV1**	82%	83%	83%	83%	82%
	MCV2**	74%	74%	76%	77%	77%
EUR	Cases	24,356	89,148	106,130	10,945	89
	Incidence*	26.4	96.4	116.6	13.5	0.1
	MCV1**	95%	95%	96%	94%	94%
	MCV2**	91%	91%	92%	91%	91%
SEAR	Cases	28,474	34,741	29,389	9,389	6,514
	Incidence*	14.4	17.4	14.7	4.8	3.2
	MCV1**	91%	93%	94%	88%	86%
	MCV2**	79%	81%	83%	80%	78%
WPR	Cases	10,695	29,503	78,479	6,599	1,061
	Incidence*	5.6	15.5	41	3.5	0.6

	MCV1**	96%	95%	95%	94%	91%
	MCV2**	93%	93%	93%	94%	91%
Global	**Cases**	**173,457**	**360,296**	**873,022**	**159,067**	**124,041**
	Incidence*	**23.7**	**47.2**	**119.5**	**21.5**	**17.3**
	MCV1**	**85%**	**86%**	**86%**	**83%**	**81%**
	MCV2**	**68%**	**70%**	**71%**	**72%**	**71%**

Data source was WHO Immunisation data portal and downloaded on 19 October 2022. * Annual measles incidence per 1 million population. ** Measles containing vaccine (first dose of measles containing vaccine – MCV1 and second dose of measles containing vaccine – MCV2) coverage (%). Comparing cases, incidence and MCV1 and MCV2 coverage between the period before COVID-19 pandemic (2017-2019) and during (2020)/ after (2021) COVID-19 pandemic. In this study, 2020 and 2021 were assumed pandemic years because there was impact on health system because the epidemiology of virus was uncertain and vaccine was developed in early stage of pandemic and not widely used in all countries. Despite the widespread use of the effective COVID-19 vaccine worldwide and the implementation of more strategic preparedness, preventive, and control measures based on the experience in 2021, there were still lingering impacts on the health system.

Annex 4 Reported measles cases and MCV1 and MCV2 coverage in global 2017-2021

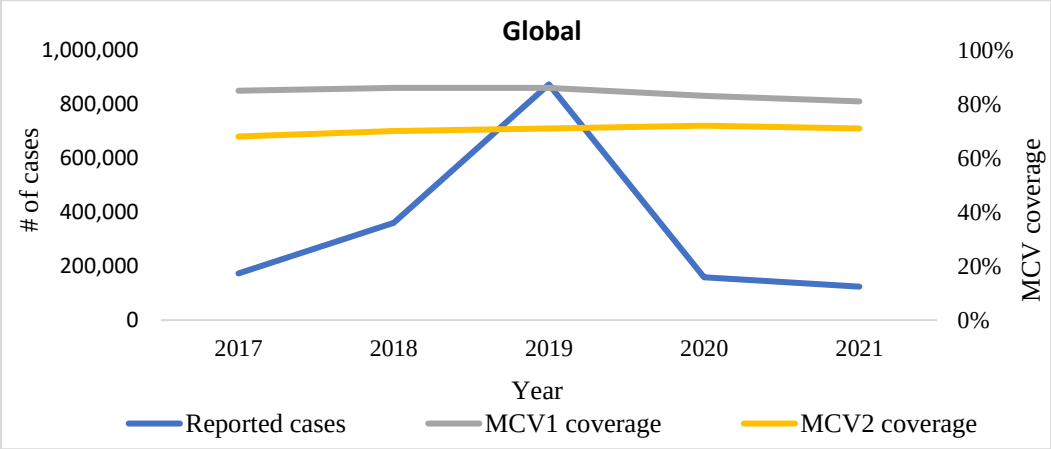

Figure: Reported measles cases and MCV1 and MCV2 coverage in global 2017-2021.
MCV1 and MCV2 coverage - WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC)

Annex 5 Reported measles cases and MCV1 and MCV2 coverage six WHO regions 2017-2021.

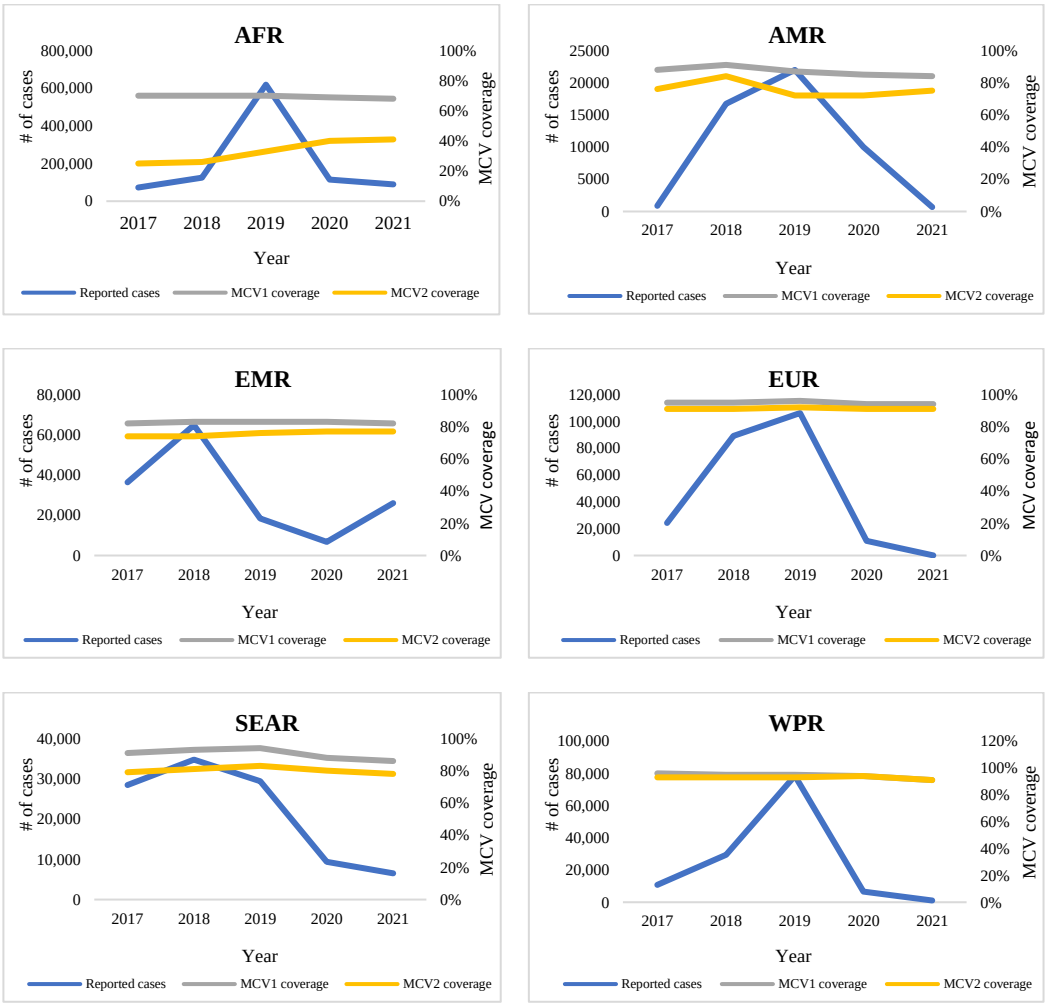

Figure: Reported measles cases and MCV1 and MCV2 coverage six WHO regions 2017-2021. MCV1 and MCV2 coverage - WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC)

Annex 6 **Percentage change of reported measles incidence and MCV coverage in global and six WHO regions between the period of before and during 2020-2021 COVID-19 pandemic year**

Regions	Measles	% Change period between before (2019) and (2020) COVID-19 pandemic year	% Change period between before (2019) and (2021) COVID-19 pandemic year
AFR	Cases	-81.3%	-85.5%
	Incidence*	-81.0%	-85.2%
	MCV1**	-1.4%	-2.9%
	MCV2**	21.2%	24.2%
AMR	Cases	-54.5%	-96.9%
	Incidence*	-69.7%	-97.8%
	MCV1**	-2.3%	-3.4%
	MCV2**	0.0%	4.2%
EMR	Cases	-63.3%	41.3%
	Incidence*	-61.0%	50.8%
	MCV1**	0.0%	-1.2%
	MCV2**	1.3%	1.3%
EUR	Cases	-89.7%	-99.9%
	Incidence*	-88.4%	-99.9%
	MCV1**	-2.1%	-2.1%
	MCV2**	-1.1%	-1.1%
SEAR	Cases	-68.1%	-77.8%
	Incidence*	-67.3%	-78.2%

	MCV1**	-6.4%	-8.5%
	MCV2**	-3.6%	-6.0%
WPR	Cases	-91.6%	-98.6%
	Incidence*	-91.5%	-98.5%
	MCV1**	-1.1%	-4.2%
	MCV2**	1.1%	-2.2%
Global	**Cases**	-81.8%	-85.8%
	Incidence*	-82.0%	-85.5%
	MCV1**	-3.5%	-5.8%
	MCV2**	1.4%	0.0%

Data source was WHO Immunisation data portal and downloaded on 19 October 2022. *Incidence per 1 million population. **WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) annual measles containing vaccine (first dose of measles containing vaccine – MCV1 and second dose of measles containing vaccine – MCV2) coverage (%). In this study, 2020 and 2021 were assumed pandemic years because there was impact on health system because the epidemiology of virus was uncertain and vaccine was developed in early stage of pandemic and not widely used in all countries. Despite the widespread use of the effective COVID-19 vaccine worldwide and the implementation of more strategic preparedness, preventive, and control measures based on the experience in 2021, there were still lingering impacts on the health system.