



Role of MR vaccine in eliminating measles and rubella (vaccine efficacy, effectiveness, current schedule, target groups, immunological issues of MR vaccine in infancy versus in second year of life)

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Background

Children in the Asia-Pacific area continue to suffer from vaccine-preventable illnesses

The measles virus is a highly contagious respiratory human infection

Measles virus infection typically causes a fever systemic disease with viremia and rash that may progress to encephalitis or pneumonia

Around 7 million otherwise healthy children die annually from measles before the advent of live attenuated measles vaccinations

Even though there is a cheap and effective vaccine for measles, measles still kills about 360 children every day around the world

Measles is believed to be the most common cause of death in children, and rubella can cause fetal death or birth defects

Source: WHO

Bangladesh MR History

1979: Bangladesh introduced first dose of Measles Vaccine at 9 month

2003: Laboratory supported measles Surveillance initiated

2005/2006,2010: Conducted nationwide measles catch up & follow up campaign

2012: Introduced MR vaccine at 9 months & Measles 2nd dose at 15 months

2014: Conducted MR catch up campaign nationwide, the first time launched its largest ever MR vaccination campaign to reach 52 million children aged nine months to <15 years

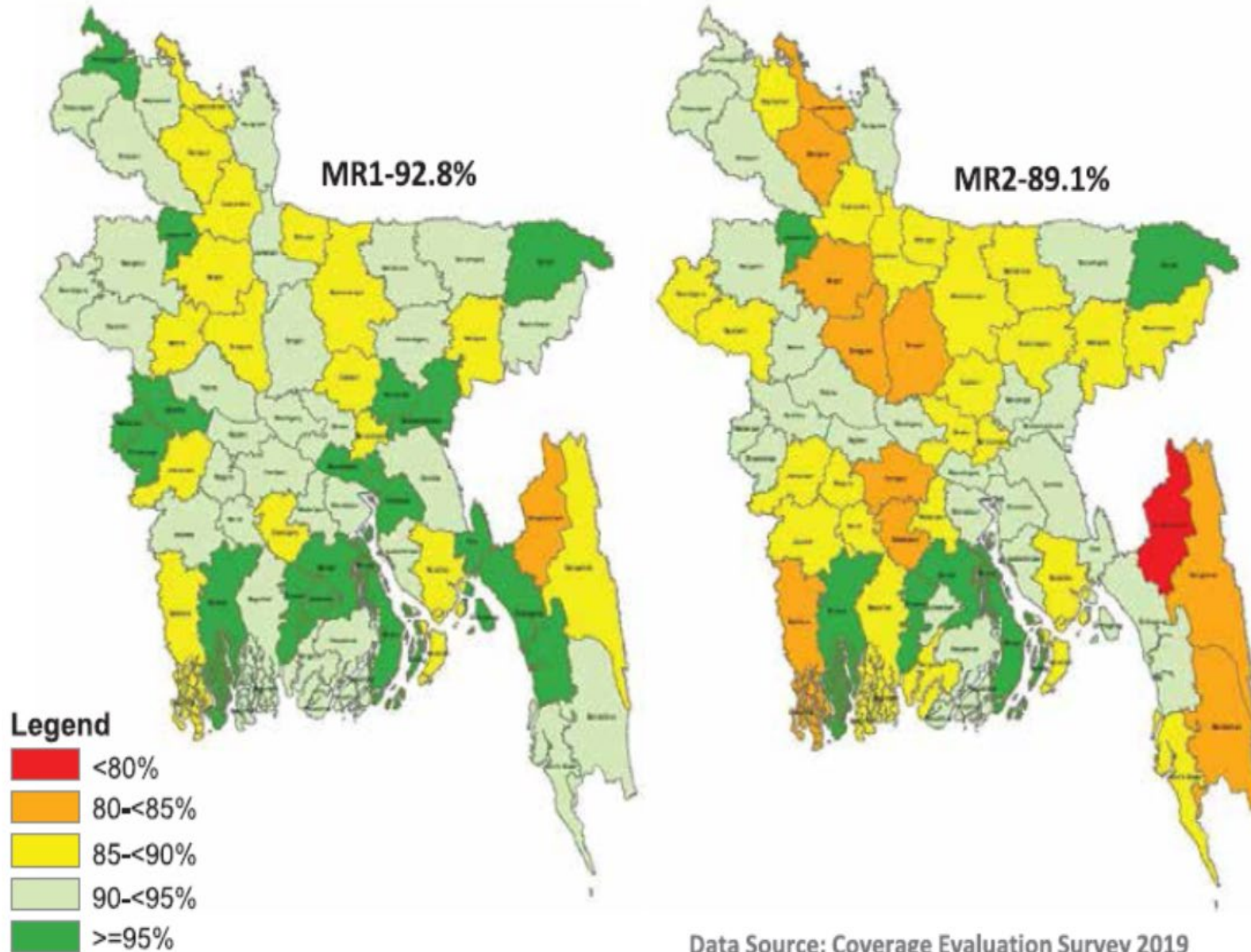
2015: Switch from Measles 2nd dose to MR vaccine at 15 months & National Verification Committee (NVC) for measles , Rubella & CRS elimination formed

2017: Strategic Plan for elimination of Measles, Rubella & CRS

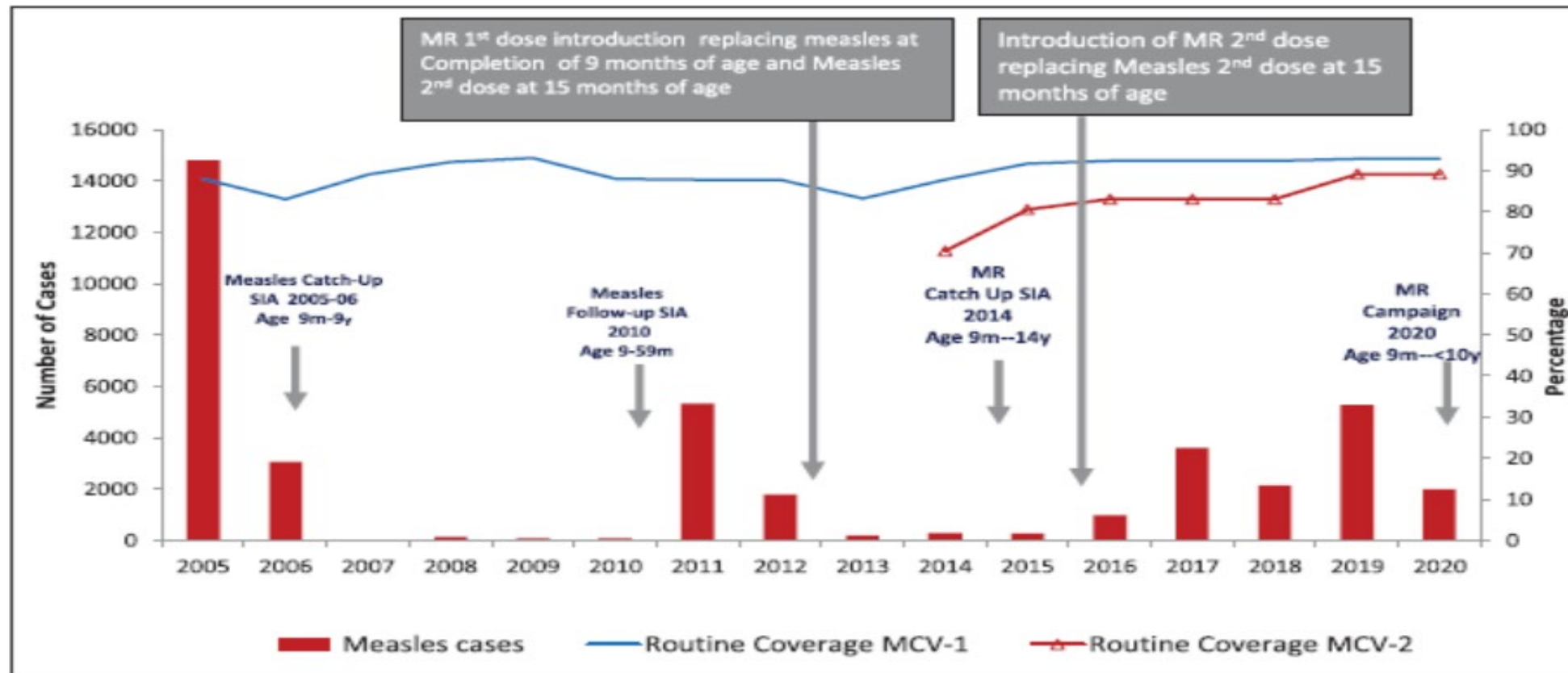
2018: Rubella & CRS control certification by SEAR

2021/2021: MR follow up campaign nationwide conducted

MR Coverage in Bangladesh



Impact of routine and supplementary vaccination on reporting of measles cases, 2005-2020



Data as of 30 June 2021

MR bulletin, July 21

Data source: National EPI Surveillance

Zero-dose and partially vaccinated children –2020 cohort

Under one year population: 3,293,482

MCV Zero dose Children: 98,804; 3% of under one year population

MCV partially vaccinated children: 131,739; 4% of under one year population

RCV Zero dose Children: 98,804; 3% of under one year population

Estimated Measles cases and deaths in Bangladesh & modelling exercise

2021: Estimated measles cases-46,345 & deaths-566

2014 to 2021: % of reduction in measles cases-58% & % of reduction in deaths-68%

2014 to 2021: Cumulative measles cases averted due to vaccination-19,965,665 & deaths-352,201

2021: Bangladesh was estimated to have >95% coverage for MCV1 & MCV2-78% & continued to perform & maintain high coverage in during pandemic

2022-2040 (Time frame of Interest): A modelling exercise was supported by VIMC to assess the impact of various vaccination scenarios on the probability of MR elimination

Post 2022: MCV1 & MCV2 coverage stagnant from 2022 onwards at highest coverage achieved in last three years as per WUNIC estimates

Post 2022: The country proposed MR SIA in 2024 among age 09-59 months & every 04 years until 2040 to achieve 95% coverage

Post 2022: Routine immunization annual coverage improvement- MCV1-1% & MCV2-1%

2028: Achieve Measles & Rubella elimination by 2028 to verify the SEAR region free by 2030

Immunological issues of giving Measles vaccine

- A systematic study was conducted to investigate the effect of MCV1 administration on babies under the age of 9 months on the immunogenicity and vaccination efficacy of subsequent MCV doses. It shows of signs of humoral and cellular immunity, such as seropositivity, geometric mean titers, avidity, T-cell activation, and vaccine efficacy. It showed that a two-dose MCV schedule commencing before 9 months of age resulted in high seropositivity (98%) and vaccine effectiveness (95%), with no evidence of lower protection than a two-dose MCV schedule starting at 9 months of age or later
- WHO recommendations say that when MCV is given to infants younger than 9 months in high-risk settings, the first dose should be followed by two more doses of MCV. It is also important to compare the immunogenicity of a three-dose MCV schedule starting before 9 months of age with a regular two-dose MCV schedule starting at 9 months of age or later. After an early three-dose MCV schedule, there were no differences in seropositivity, cellular immunity, or antibody titres

Co-administration of MR with other vaccine

- It is suggested that vaccines be given at the same time to cut down on the number of vaccination sessions, increase compliance, and make sure the best coverage
- Between the ages of 13 and 15, children all across the world receive vaccinations for a variety of infectious diseases, including tetravalent measles, mumps, rubella, and varicella (MMRV) and meningococcal C (Men C or Men ACWY) conjugate vaccines. Co-administration of MMRV with tetravalent meningococcal conjugate vaccination has been the primary focus of the vast majority of research
- Children in Burkina Faso between the ages of 15 and 23 months who received a single dose of TCV along with their normal MCV-A
- In China, both the measles-rubella vaccine and the live attenuated SA 14–14–2 Japanese encephalitis vaccine (LJEV) was given at the same time when a child is 8 months old
- In Germany, The administration of the MMRV vaccine in combination with a booster dose of the DTPa-HBV-IPV/Hib vaccination was safe and did not result in an increase in the reactogenicity profile of either vaccine
- Since 2006, the measles and rubella combination (MR) vaccine and two-dose immunization have been administered in Japan. Children who receive the monovalent measles and rubella immunization are the only ones who receive a second vaccination
- Vaccines have typically been purchased by low and medium-income countries (LMICs) in multi-dose vials to lessen the burden of cold chain storage and delivery

Studies on Co-administration of MR vaccines with cholera and typhoid vaccines

A Co-administration study of oral cholera vaccine (OCV), typhoid conjugate vaccine (TCV), measles and rubella (MR) vaccines in Bangladesh will be started soon in Dhaka

We will assess whether seroconversion following co-administration of MR vaccine, OCV and TCV are non-inferior to seroconversion when the vaccines are administered as the first individual vaccines

Children will be randomly assigned to one of the following six study arms:

Arm A: OCV only

Arm B: TCV only

Arm C: MR only

Arm D: Co-administration of MR and TCV

Arm E: Co-administration of MR and OCV

Arm F: Co-administration of TCV and OCV

Arm		Time (days)						
		0	28	56	84	180	208	236
A	OCV only (n=413)	OCV	OCV	MR			MR (2 nd dose)	
B	TCV only (n=314)	TCV		MR			MR (2 nd dose)	
C	MR only (n=250)	MR				MR (2 nd dose)		
D	MR + TCV (n=314)	MR + TCV				MR (2 nd dose)		
E	MR + OCV (n=413)	MR + OCV	OCV			MR (2 nd dose)		
F	TCV + OCV (n=413)	OCV + TCV	OCV	MR			MR (2 nd dose)	

Blood collection point

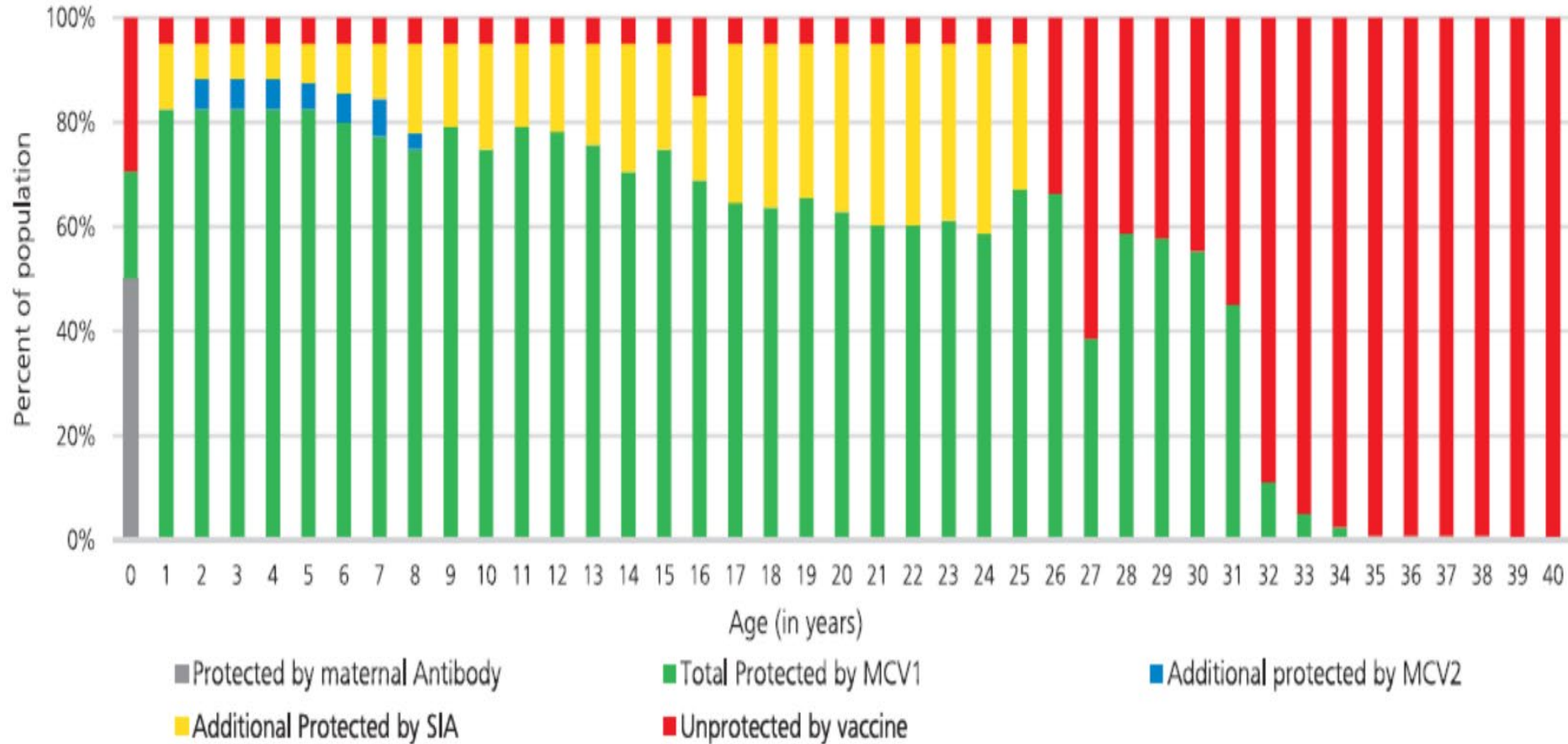
MR Vaccine- In the Forcibly Displaced Myanmar National (2020-2023)

There was a sustained high number of measles cases from September to November 2019. More than 1,510 measles cases have been reported in 2019

MR Coverage in Routine Immunization				
Year	Administered number of MR1	Coverage percentage of MR1	Administered number of MR2	Coverage percentage of MR2
2020	26,623	87%	18,261	60%
2021	38,442	126%	27,340	90%
2022	38,885	128%	32,330	106%
Note: Coverage percentage is not accurate (more than hundred), because denominator was not confirmed by registration agencies				

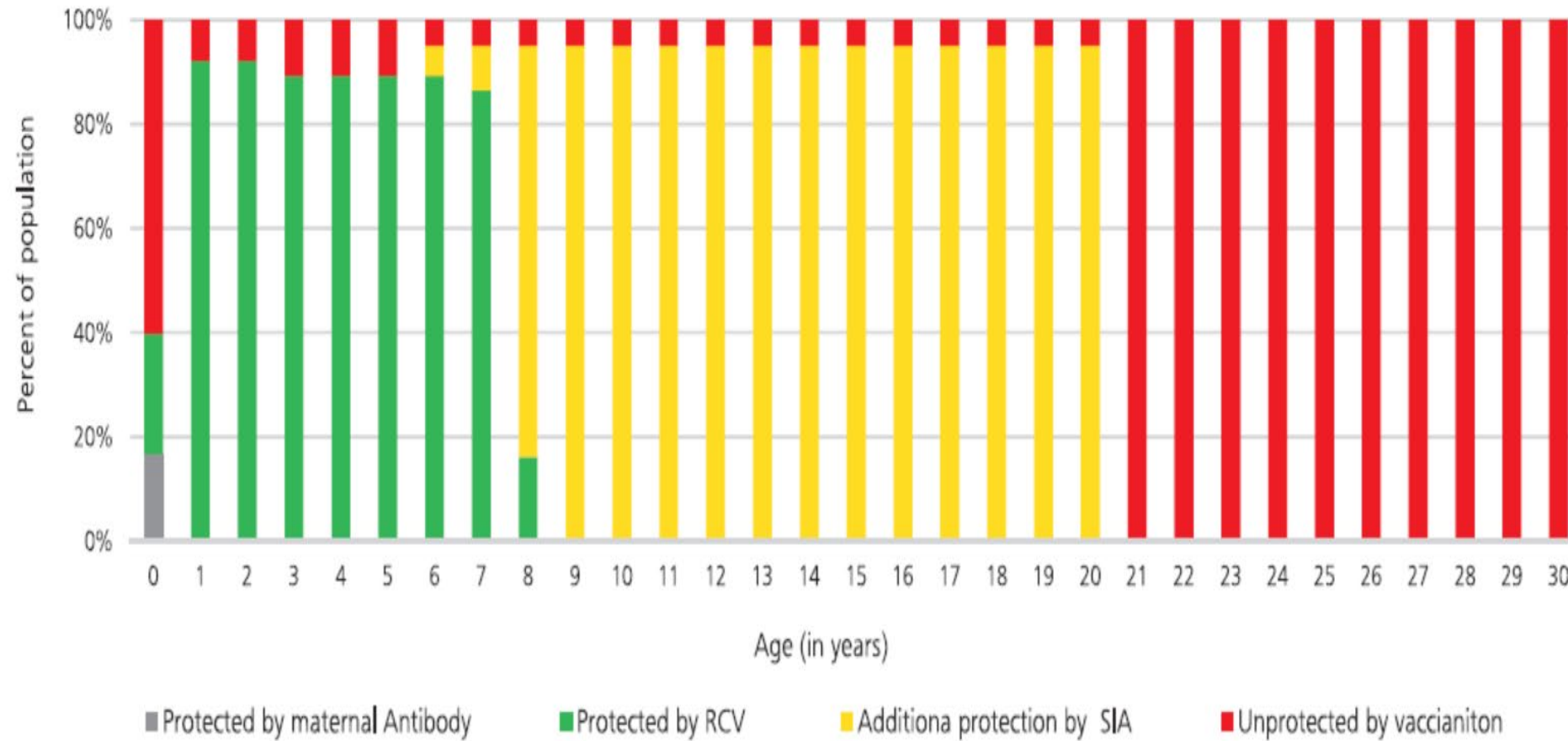
MR Coverage in Special Campaign in 2023					
2 nd Round (1 st Round of MR) = 18 th January to 5 th February, 2023, MR1 given					
3 rd Round (2 nd Round of MR) = 4 th March to 25 th March, 2023, both MR1 and MR2 given					
Year	Target	Achievement		Percentage	
MR1	185,566	1 st Round	135,977	73%	Total 99%
		2 nd Round	47,820	26%	
MR2	135,977	102,471		75%	

Immunity against measles - immunity profile by age in 2020



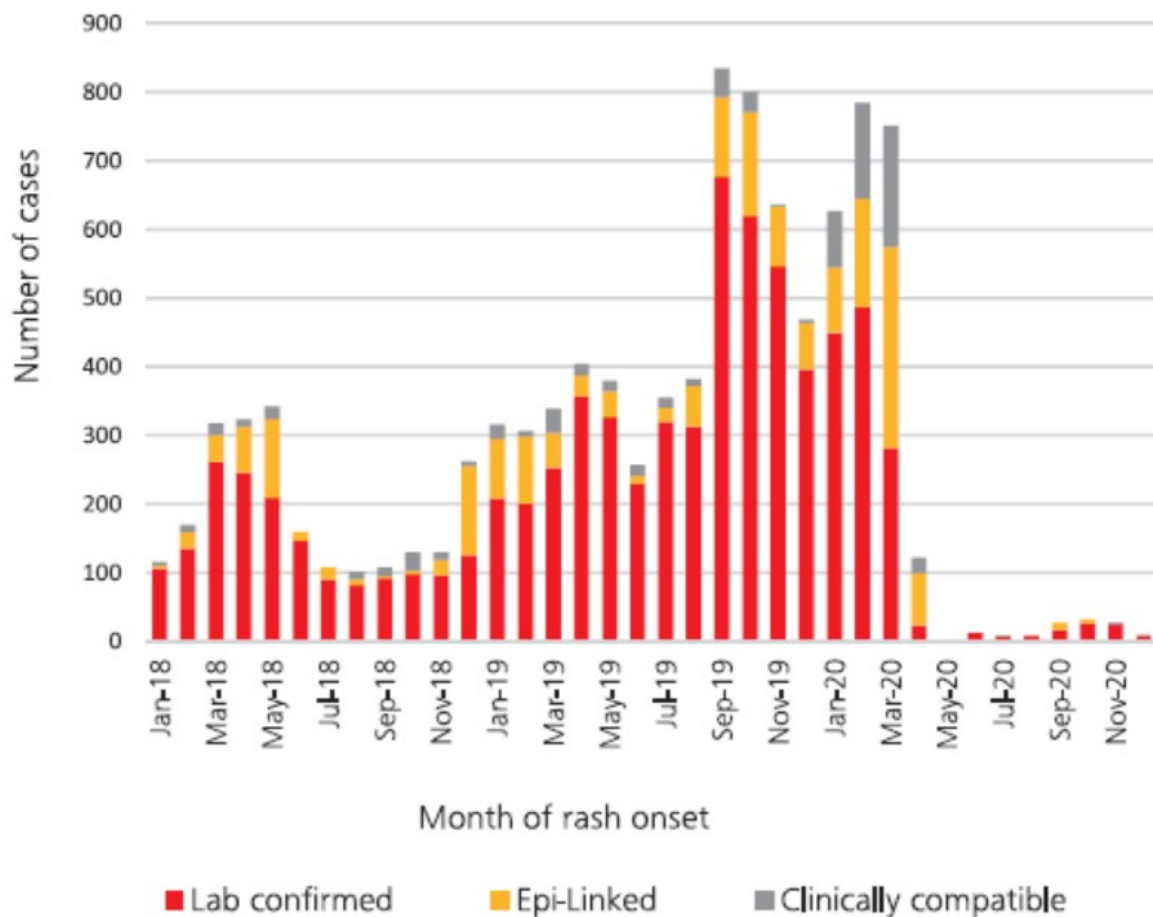
A total of 60% of the population was MCV/1 protected from birth to age 25, and from ages 35 to 40, 100% of people were unprotected. Under 26 years of age showed extra protection from SIA, while infants under 1 had 50% maternal antibody protection.

Immunity against rubella through vaccination - immunity profile by age in 2020

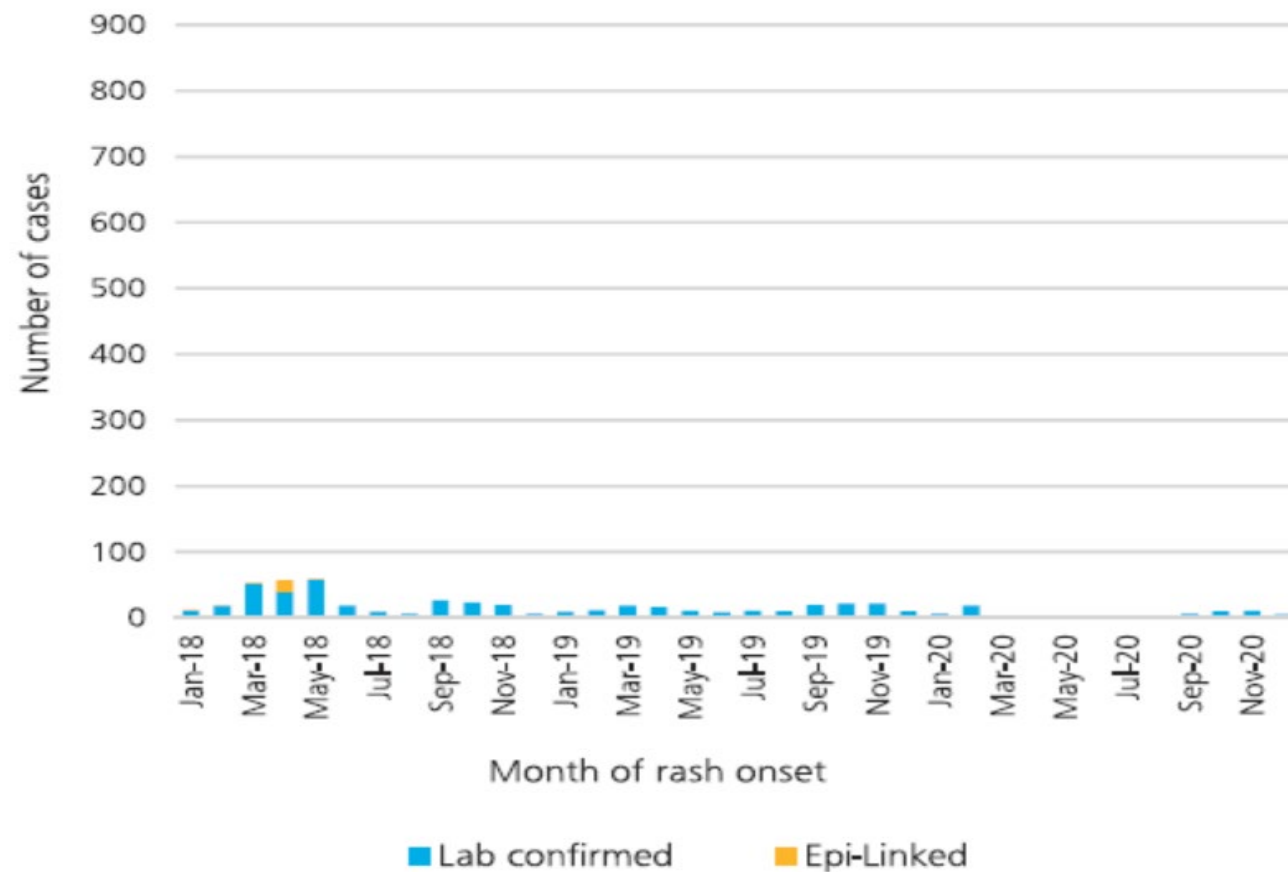


RCV protected children aged 0 to 8 years, the majority of whom were between 1 and 7 years old (80% of the total population). Additional protection was provided by SIA between the ages of 6 and 20 and between 21 and 30, who were not protected by immunization.

Confirmed measles cases by month 2018-2020

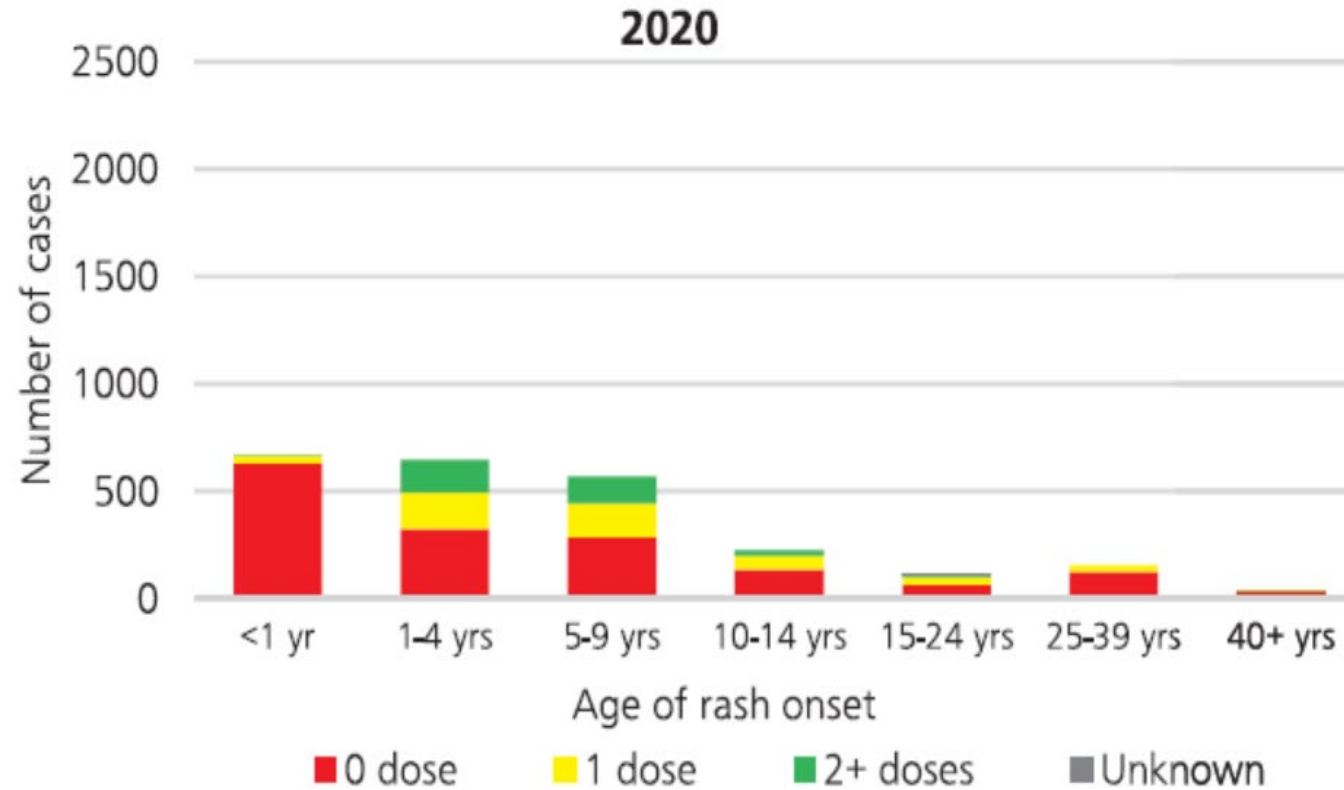


Confirmed rubella cases by month 2018-2020

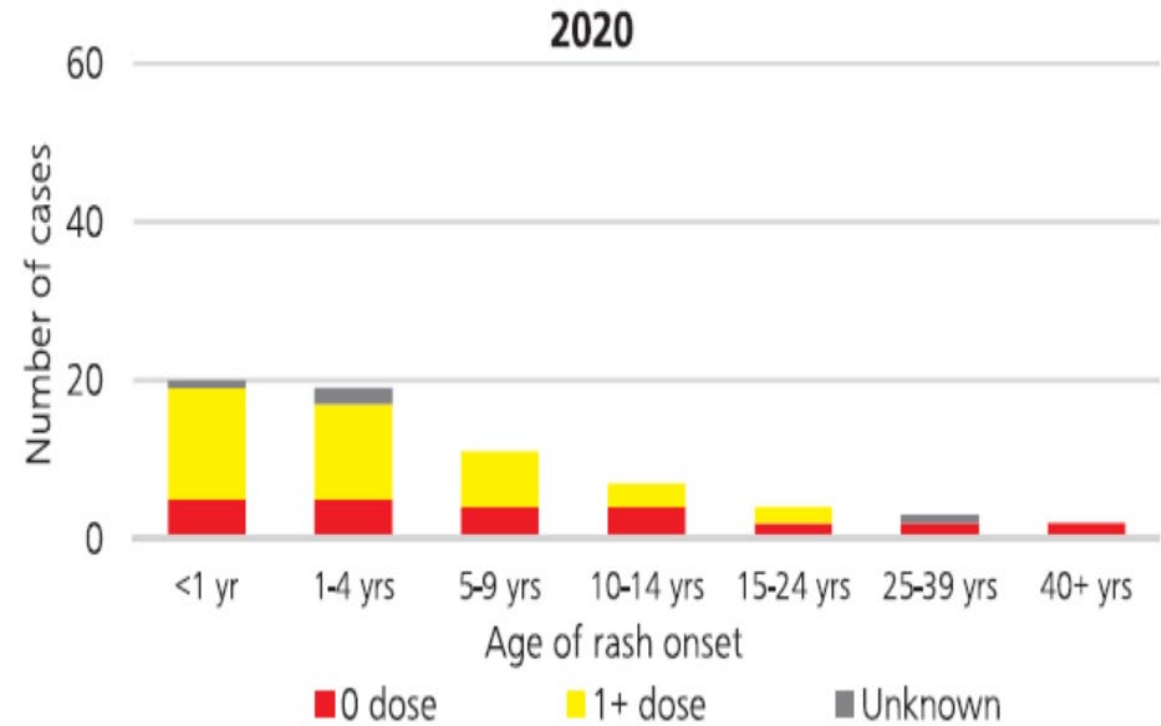


The case of measles was lab-confirmed throughout 2018-2020, but it reached its maximum point (800-750 number of cases) between September 2019 and May 2020. The number of epi-linked cases was likewise at its highest point during that time period. In the case of rubella, the number of laboratory-confirmed cases was below 100 from January 18 through November 20, and they were only epi-linked to April 18.

Vaccination status of confirmed (laboratory, Epi linked and clinically compatible) measles cases, by age in 2020



Vaccination status of confirmed (laboratory, Epi linked and clinically compatible) rubella cases, by age in 2020



Vaccination status of confirmed measles cases in 2020 revealed that no dose (0 doses) was present across all age groups, with 1 to 9-year-olds having the highest prevalence. This number was identical to that of the 1st dose. Two plus (2+ dosage) prevalence among children aged 1 to 9 was greater than 500.

Vaccination status of confirmed rubella cases in 2020 revealed that no dose (0 doses) was present across all age groups and one plus (1+ dose) was highest among those <1 year to 4 years (around 20 cases)

Conclusion

- Recent years have seen a dramatic increase in the number of recommended childhood immunizations, resulting in more complicated immunization schedules during the first years of life
- Since the introduction and subsequent widespread use of measles and rubella vaccines, the prevalence of both diseases has decreased dramatically. All six WHO regions have declared measles elimination goals, but no worldwide objective has been created. Large measles outbreaks between 2017 and 2019 illustrate, however, that there is still a gap between current control levels and elimination targets
- Measles cases have decreased by 62 percent and 25.5 million deaths have been prevented since 2000. Measles has been eradicated in 81 countries as of January 2021.
- The elimination of rubella has been confirmed in 93 countries as of January 2021, with vaccinations having been introduced in 173 of 194 WHO member countries.
- **In Bangladesh currently increasing number Mumps cases reported by Pediatricians during their day-to-day practice**
- **The country needs to incorporate Mumps vaccine in the current EPI schedule**