

The transition from MCV 10-dose to 5-dose in India:

Answers to key questions

Why did India transition from 10-dose to 5-dose?

Q1.

What was the process for changing vaccine presentations in India?

Q2.

How did India evaluate cost and cold chain capacity?

Q3.

What was the impact on wastage and coverage?

Q4.

Background

India has used 5-dose measles-containing vaccine (MCV) vials in its national immunization program for nearly three decades. Its experience may inform other countries planning to introduce smaller-dose vials to reduce vaccine wastage, accommodate healthcare worker (HCW) preferences, and improve measles immunization coverage overall.

India introduced the measles monovalent (M) vaccine into its Universal Immunization Programme (UIP) in 1985. The rollout began in 80 districts and was nationwide by 1990. Initially, the vaccine was imported and delivered in the 10-dose vial presentation.

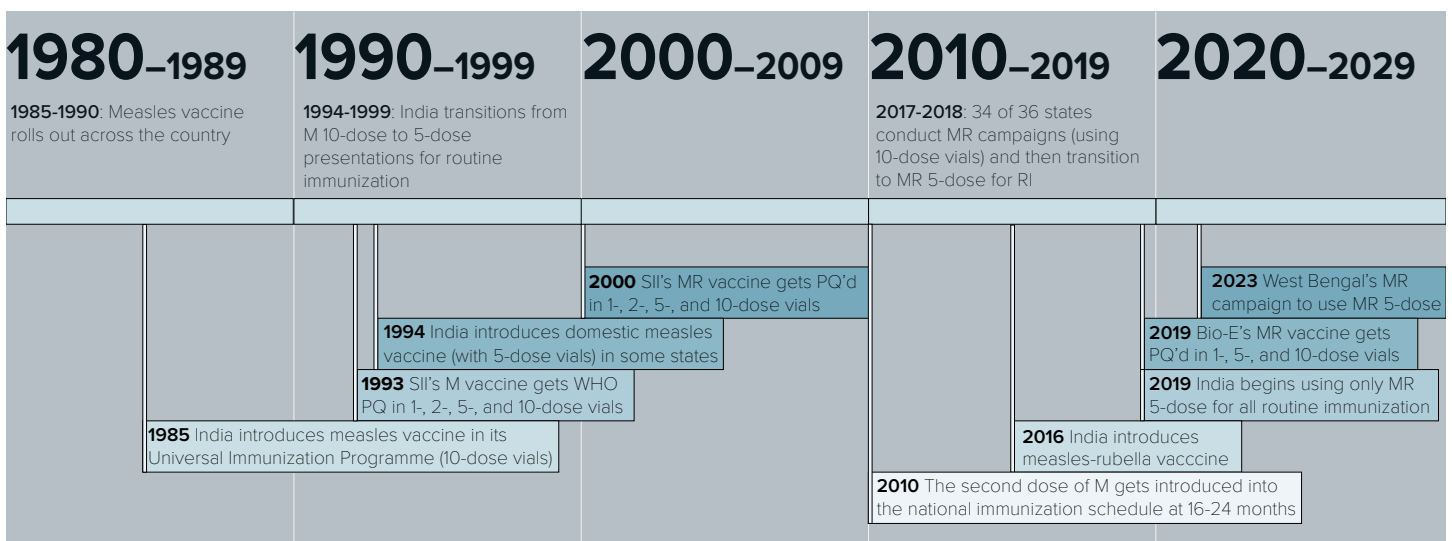
Over time, immunization experts saw high wastage of the measles vaccine in health center audits, heard reports of HCW hesitancy to open 10-dose vials for fear of wasting, and noted instances of adverse events due to improper handling of the vaccine. As a result, UIP managers eventually recommended that India switch to lower-dose vials for routine immunization (RI) in some settings.

By 1994, Serum Institute of India (SII) was domestically manufacturing its own measles vaccine. Based on field reports and UIP managers' recommendations, the government of India (GoI) directed SII to produce 5-dose vials for use in parts of the country with geographically hard-to-reach rural populations and smaller session sizes (e.g., in districts in northeastern and northwestern India, including Rajasthan). By 1999, GoI saw enough advantages to procure M 5-dose for routine immunization in all Indian states.

India introduced the measles-rubella (MR) vaccine in 2016 and launched rolling state campaigns the next year. During campaigns, HCWs used 10-dose vials to vaccinate large groups of infants and children up to 15 years old in schools and outreach sites. Once campaigns were complete, states got the MR vaccine in 5-dose vials for RI, given their proven potential to reduce wastage.

Today, HCWs follow the national immunization schedule, administering MR1 at 9-12 months and MR2 at 16-24 months. They use only 5-dose vials everywhere in the country. This use is extending to campaigns as well: West Bengal—India's fourth most populous state—will deploy 5-dose vials for its upcoming MR campaign, scheduled for 2023.

Despite having the largest birth cohort in the world, India has achieved high vaccination coverage against measles. In 2019, MCV1 coverage by age 12 months reached 95 percent and MCV2 coverage by 24 months was 84 percent.¹



¹ WHO/UNICEF estimates of national immunization coverage (WUENIC)

Why did India transition from 10-dose to 5-dose?

Q1.

Short answer: Goals driving India's transition to 5-dose MCV presentations included the country's need to reduce adverse events and wastage. UIP managers also considered HCW preference when they advocated fewer-dose vials at national planning sessions.

Investigating adverse events

In its first decade of measles immunization, India saw many disturbing instances of adverse events, including toxic shock syndrome and death after vaccination. Among other issues, many HCWs would keep a reconstituted vaccine for longer than advised—often to avoid throwing out unused doses.

In part, these events could be attributed to inadequate investment in HCW training, a lack of infrastructure and poor sanitation in some places, and other factors that might affect vaccine transportation and storage. But experts also pointed to the 10-dose vial: especially in hard-to-access, rural and resource-scarce settings, HCWs feared vaccine stockouts or reprimands from higher-ups if they tossed excess doses.

Risking wastage

Per India's Ministry of Health and Family Welfare (MoHFW) guidance, MCV should not be carried from one session site to another once reconstituted and must be used within four hours of reconstitution or else discarded.² Though the MoHFW recommends opening an MCV vial even when just one child is present for immunization, India does not have a formal Open Vial Policy for MCV—so HCWs exercise judgment. Every time an HCW chooses to open a 10-dose vial to vaccinate one child or just a few, they must weigh the risk of having to throw out the remaining doses. This diminishes vaccine stock that could be used to immunize more children another day and increases the possibility of running out of vaccine before the next resupply.

Thus, a supply-conscious health professional might opt not to open a vial outside of a scheduled vaccination day (when more children are present) to reduce the risk of wastage. HCWs are in a truly unenviable position when they must choose between throwing out needed vaccines, using doses beyond a safe timeframe, or refusing to vaccinate and turning people away—people who may not return.

Immunization program expert planning

Reflecting on the events that catalyzed India's transition to 5-dose—beginning with the measles monovalent vaccine (M) 5-dose in the mid-90s and then MR 5-dose in the late 2010s—one expert stressed the importance of UIP managers' participation in vaccine planning and procurement. During these sessions, managers with on-the-ground experience advocated for ordering smaller measles vaccine vials as one solution to limit adverse events and in response to HCW preference.

“When experienced immunization experts are included in planning processes, countries can make more informed vaccine procurement decisions with a greater understanding of needs on the ground.”

² Source: World Health Organization & Government of India Ministry of Health & Family Welfare. (2017). Introduction of Measles-Rubella Vaccine (Campaign and Routine Immunization). National Operational Guidelines 2017 (p. 79).

*Note: India's guidance on discarding the MCV is more conservative than WHO's—which recommends MCVs be discarded within six hours of opening or at the end of the immunization session, whichever comes first.

What was the process for changing vaccine presentations in India?

Q2.

Short answer: India has accomplished many switches in vaccine formulations and presentations. As one informant stated: “It’s all about clear messaging and SOPs.” This lesson can be taken for any country wanting to switch; however, as a case study, India is unique in many ways.

Clear SOPs and HCW training

The first presentation switch, from measles monovalent (M) 10-dose to M 5-dose, happened in stages. What began in 1994 as a targeted intervention for some states, ended with all states switching to 5-dose by 1999. To introduce the change in each state, the MoHFW disseminated a brief document that stated the date that the presentation change would occur and outlined essential information (with pictures) on how to reconstitute the vaccine with its diluent. A UIP manager that advocated for 5-dose vials in the 1990s said that the presentation switch was welcomed “with open arms” by state managers and field workers.

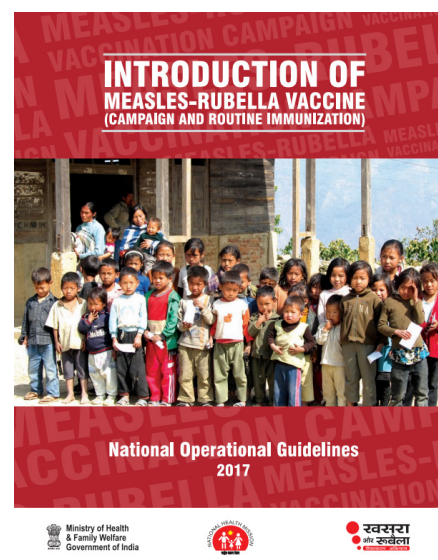
With MR, the 5-dose vial came immediately after campaign introductions due to HCW preference and its proven potential to reduce wastage in RI. The MoHFW developed detailed instructions to assist national, state and district level program managers to plan and implement MR introductions. As stated by one National Health Mission director in the 2017 operational guidelines for MR campaigns and subsequent routine programs: “The guidelines are extremely practical and have listed in detail the tasks and responsibilities to be completed by functionaries at all levels.”³

HCW training in India is conducted in a cascading fashion and is both centralized and dispersed. For vaccine and presentation changes, UIP managers call meetings with state and district managers to deliver the new guidance. District managers then hold sessions with primary HCWs to share the information. Primary HCWs then inform and train catchment officers, including auxiliary nurse midwives (ANMs) immunizing in the field and outreach sites. This system works well in India because HCWs visit district offices monthly to collect their salaries and expect to receive training and updates during these visits.

A unique procurement process

India is home to two of the world’s major vaccine makers: the Pune-headquartered Serum Institute of India and Hyderabad-based Biological E (Bio E)—both of which manufacture WHO-prequalified MCVs.

India does not go through UNICEF Supply Division for vaccine orders. Instead, it purchases MCVs directly from domestic manufacturers. One expert who helped facilitate the switch in the 90s indicated that the GoI worked directly with SII to fulfill measles 5-dose orders according to the country’s needs. A country has added flexibility and control when it manufactures its own vaccines locally.⁴



Source: WHO India & MoHFW (2017)

³ Source: (WHO India & MoHFW, 2017, p. V)

⁴ Countries that order vaccines through UNICEF will follow a more standardized process. The standard lead-time for ordering MCV 5-dose vials is 12-15 weeks (as compared to 6-8 weeks for 10-dose), per the M & MR Vaccine Five-Dose Vial Fact Sheet (UNICEF & WHO, 2022). The extra time accounts for the added complexity of filling and finishing smaller vials.

A cautionary note on mixed presentations and products

When asked whether a country might order different presentations for different regions (such as 10-dose in urban areas and 5-dose in rural areas), one former UIP manager responded, “That would be a logistic and management nightmare.” Nevertheless, India’s phased 5-dose rollout and the country’s continued use of 10-dose vials for campaigns prove that it is feasible to have both presentations circulating simultaneously—so long as training is sufficient, and instruction materials are clear. It’s especially important to illustrate the dimension differences between the 10-dose diluent vs. 5-dose diluent, and the 10-dose vial vs. the 5-dose vial—and ensure that HCWs can identify each. This is essential to prevent HCWs from reconstituting vaccines with the wrong amount of diluent, which has happened, according to anecdotal reports.

Similarly, because India currently uses both Bio E and SII’s MR vaccines, immunization supervisors emphasized the necessity to clearly delineate the different products.⁵ UIP experts noted that during immunization sessions, HCWs often do not double-check that the makers of a vaccine and a diluent match. Ideally, each state would receive only one of the two manufacturer’s products to avoid any possibility of confusing diluents.



Source: WHO India & MoHFW (2017, p. XVI)

⁵ Though both domestically produced vaccines are live attenuated, Bio E’s diluent contains 0.9 percent sodium chloride, whereas SII’s diluent is sterile water.

How did India evaluate cost and cold chain capacity?

Q3.

Short answer: Accounting for wasted doses is key for a cost-benefit analysis of 5-dose over 10-dose. In India, cold chain storage capacity was less of a factor than cost savings.

Cost considerations for 5-dose

India makes annual MR orders for RI based on the number of doses required to immunize every child in a birth cohort in each state, with a wastage factor and buffer in case of unexpected demand.

Some immunization managers have suggested that the GoI made a special arrangement with domestic manufacturers to close the “price-per-dose” gap between MCV 10-dose and 5-dose. Whether or not this was the case, the price difference between the two presentations has been described as “very negligible” and “marginal.”

Nevertheless, in price-per-dose terms, 10-dose vials are (marginally) cheaper. As such, UIP managers participating in procurement planning sessions needed to justify purchasing 5-dose instead. One former UIP manager who advocated for MCV 5-dose in planning meetings said that his job was to convince colleagues that “I’m saving by using 5-dose.”

One vial (at least) should be available at every immunization session. If the MoHFW elected to order doses in 10-dose vials, officials would have to order a significant excess to account for a large amount of wastage. So, while 10-dose vials may be cheaper per dose, they prove far less economical in wastage-adjusted terms. When looked at annually, the price difference between 5- and 10-dose vials is huge, as described by one key informant who showed the math.⁶

A 2010 Vaccine Wastage Assessment across five states in India found that 86 percent of MCV sessions required less than five doses.

MoHFW guidelines for immunization session sites



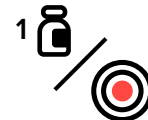
1 vial per available vaccine per session



Vial should be opened even for one child



~190,000
RI Sessions
Week



~9,880,000
RI Sessions
Year

There are approximately 190,000 RI sessions taking place across the country each week. That’s 9,880,000 sessions each year. Each session requires at least one vial.

Estimated price difference annually*

When looked at annually, the price difference between 5-dose vials versus 10-dose vials is huge. Under the simplifying assumptions that 1) there are 9.88 million RI sessions annually and 2) one vial is available per session, consider the vaccine procurement costs per vial of SII’s MR 5-dose versus 10-dose, based on UNICEF’s 2023 prices:

9,880,000 sessions per year x \$5.45

\$53,846,000

5-dose

9,880,000 sessions per year x \$8.73

\$86,252,400

10-dose

A total difference of **\$32.41 million**—or a savings of over **37 percent** with the **5-dose order**

⁶ India’s official wastage factor assumption for MR is 1.33 for RI.

* Calculations are based on figures cited in a key informant interview on August 16, 2022.

Cold chain requirements

Cold chain requirements and a country's capacity to accommodate added storage space for 5-dose vials are also important considerations when it comes to procurement planning. In India, these factors were not an issue, according to experts familiar with the planning process. That's in part because India expanded its cold chain capacity significantly in the 90s to accommodate the huge stocks of polio vaccines used in national campaigns.

In fact, when the state-by-state switch from measles monovalent 10-dose to 5-dose first began in 1994, SII's 10-dose and 5-dose vials were similar in size. Besides that, as one UIP manager who advocated for the switch said, "[India had] sufficient cold chain space to cater even to 10-dose vial containers" containing only 5 doses.

In addition, even though 5-dose vials have higher cold chain requirements per dose, the increase is partially offset by a reduction in total required supply (given lower wastage).

"India has a strong system for assessing cold chain. The country uses a digital platform and monitors 29,000 cold chain points storing vaccine."

SII and Bio E's 5- and 10-dose MCV cold chain capacity requirements (cf. UNICEF & WHO 2022)

Vaccine / Presentation	SII vial + diluent (cm ³ /dose)	Bio E vial + diluent (cm ³ /dose)
M 10-dose vial	3.30 + 3.14	2.11 + 2.53
M 5-dose vial	3.16 + 5.48	--
MR 10-dose vial	2.11 + 3.14	1.78 + 2.12
MR 5-dose vial	3.16 + 5.48	2.67 + 3.25

What was the impact on wastage and coverage?

Short answer: Since India has used 5-dose MCVs almost exclusively in routine measles immunization for nearly three decades, it's difficult to compare the programmatic impacts that this intervention alone had on wastage and coverage. However, some data clearly suggest the positive effects of using fewer-dose vials.

Vaccine wastage

In 2018 and 2019, India's MoHFW conducted a study with UNICEF to assess wastage for ten vaccines (including measles) in six regions, across 12 states and 24 districts. The average measles vaccine vial wastage rate at the service delivery point was 31 percent.

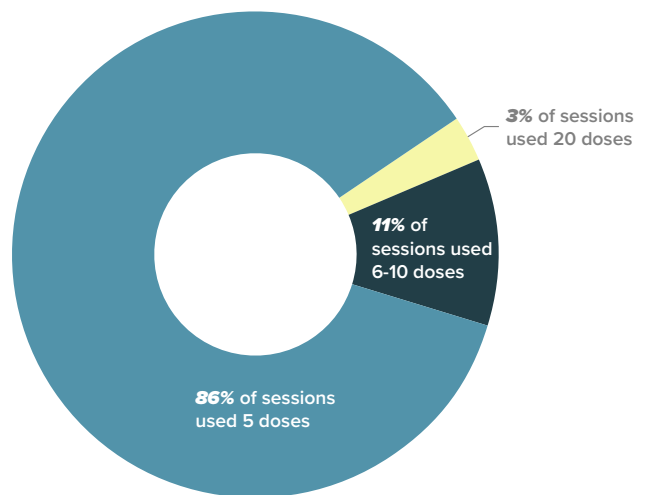
A similar wastage assessment was conducted in 2009 and 2010, which broke down wastage figures in five states (in descending order of population size: Uttar Pradesh, Himachal Pradesh, Maharashtra, Tamil Nadu, Assam). Wastage rates for the measles vaccine ranged from 26 percent in Uttar Pradesh (India's most populous state) to 58 percent in Himachal Pradesh. The average wastage rate for measles 5-dose across all the session sites was 35 percent.⁷

Both wastage assessments noted that lyophilized vaccines like measles and BCG had "substantially higher" wastage overall compared to liquid-formulated vaccines. However, the average wastage rate for the BCG vaccine was around twice that of measles (56 percent in 2019 and 61 percent in 2010). This is probably because BCG vaccines were presented in 10-dose vials.

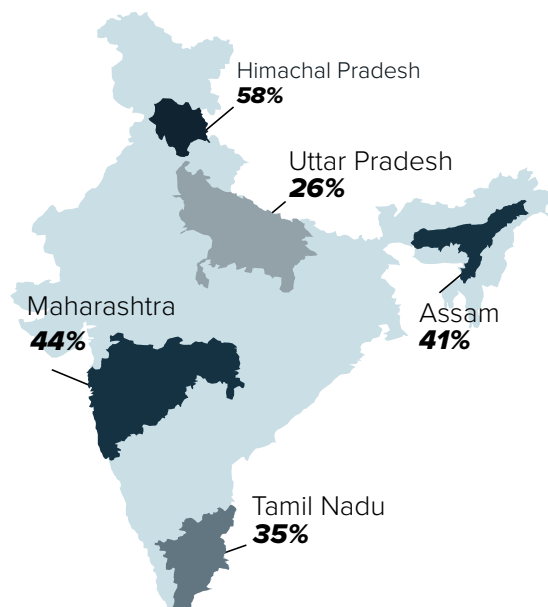
As the 2019 wastage assessment states simply: "Vaccines with higher vial presentation (10 doses or more per vial) have a higher wastage rate." Real-world details from the 2010 analysis help to illustrate why this is the case.

The analysis showed that 75 percent of BCG vaccination sessions required five or fewer doses—and only 25 percent required more than five. Findings were similar for measles: 86 percent of MCV immunization sessions required five doses or fewer. While some wastage is inevitable, the evidence suggests that 5-dose vials help considerably to reduce it.

MCV dose requirements for RI sessions, per 2010 Vaccine Wastage Assessment



Measles vaccine wastage rates per Vaccine Wastage Assessment (MoHFW & UNICEF, 2010)



⁷ According to the report: "Wastage of vaccines has a direct relationship with session size (number of beneficiaries per session) and vial size" (MoHFW & UNICEF 2010, p. 18).

Measles vaccination coverage

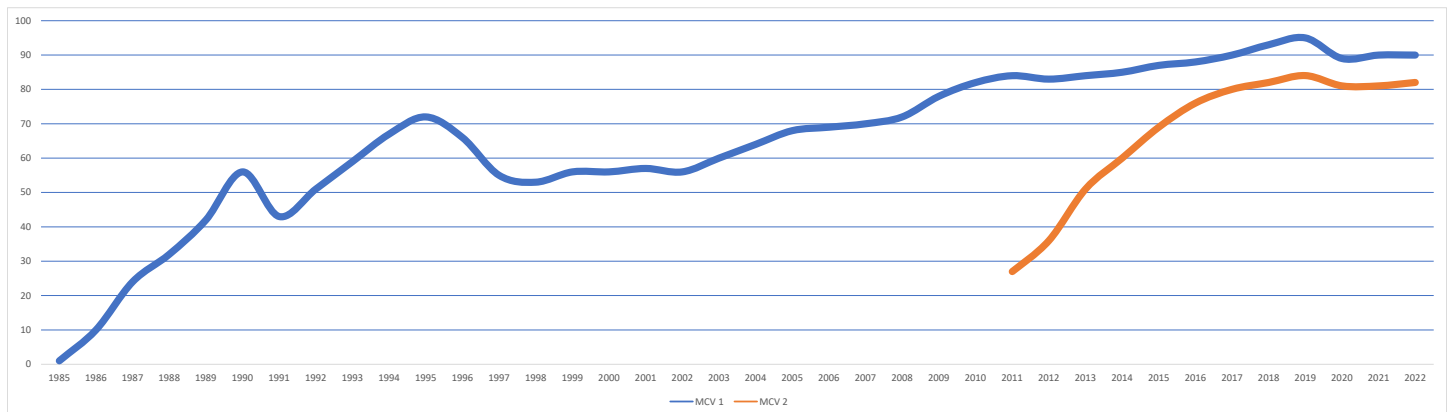
UIP experts in India point to high national vaccination coverage against measles as a clear indicator of the immunization program's success. Indeed, MCV1 coverage climbed from just 10 percent in 1986 to 88 percent in 2016, per WHO-UNICEF national estimates of immunization coverage (WUENIC) data.⁸

In 2017 and 2018, MCV1 coverage by age 12 months was 90 percent and above. Coverage peaked in 2019: at 95 percent for MCV1 and 84 percent for MCV2.

Like many countries, India experienced a dip in MCV coverage over the last two years, primarily due to Covid-19 disruptions to vaccination programs overall. Still, MCV1 coverage was 89 percent in 2021, while MCV2 was 82 percent.⁹

There are numerous and multifaceted reasons for success, and a more comprehensive review of India's MCV immunization program over time would give a more complete picture. Still, the fact that India has used primarily 5-dose vials for RI over nearly three decades is not insignificant. Other countries wanting to improve their MCV programs might also consider fewer-dose vials as a possible low-cost measure that enhances coverage while reducing wastage.

Increase in measles coverage (in percentage) from 1985-2022 (WUENIC)



⁸ According to WUENIC, the indicator for MCV1 is estimated as the percentage of children under age 1 who have received at least one dose of measles-containing vaccine in a given year.

⁹ According to WUENIC, the indicator for MCV2 is estimated as the percentage of children who received MCV2 according to the nationally recommended schedule. In India, MCV2 is administered between 16-24 months.

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