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A review of potential use cases for measles-rubella, measles-mumps-rubella, and typhoid-conjugate vaccines presented on microarray patches

Adam Soble [a,*], Melissa Ko [a], Shawn Gilchrist [b], Stefano Malvolti [c], Mateusz Hasso-Agopsowicz [d], Birgitte Giersing [d], Jean-Pierre Amorij [e], Courtney Jarrahian [f], Fayad El Sheikh [g], Marion Menozzi-Arnaud [g], Tiziana Scarna [g]

[a] MMGH Consulting GmbH, Geneva, Switzerland
[b] MMGH Consulting GmbH, Toronto, Canada
[c] MMGH Consulting GmbH, Zürich, Switzerland
[d] Immunization, Vaccines and Biologicals, World Health Organization, Geneva, Switzerland
[e] Supply Division, Vaccine Centre, UNICEF, Copenhagen, Denmark
[f] PATH, Seattle, WA, United States
[g] Gavi, The Vaccine Alliance, Geneva, Switzerland

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ABSTRACT

As an innovative vaccine delivery technology, vaccine microarray patches could have a meaningful impact on routine immunization coverage in low- and middle-income countries, and vaccine deployment during epidemics and pandemics. This review of the potential use cases for a subset of vaccine microarray patches in various stages of clinical development, including measles-rubella, measles-mumps-rubella, and typhoid conjugate, highlights the breadth of their applicability to support immunization service delivery and their potential scope of utilization within national immunization programs. Definition and assessment of the use cases for this novel vaccine presentation provide important insights for vaccine developers and policymakers into the strengths of the public health and commercial value propositions, and the preparatory requirements for public health systems for the future rollout of vaccine microarray patches. An in-depth understanding of use cases for vaccine microarray patches serves as a foundational input to overcoming the remaining technical, regulatory, and financial challenges. Additional efforts will help to realize the potential of vaccine microarray patches as part of the global effort to improve the coverage and equity of national immunization programs.

1. Introduction

Following years of plateauing immunization coverage, the impact of the Coronavirus Disease 2019 (COVID-19) pandemic has caused backsliding of immunization coverage to levels last observed in 2008 [25,28]. While more children received three doses of diphtheria, tetanus, and pertussis-containing vaccines (DTP) in 2021 than ever before, there remained an estimated 25 million children who were un- or under-immunized, a 32 % increase compared with 2019 [4,12]. The decline of global immunization coverage levels and the increasing number of zero-dose children, defined as children who do not receive a single dose of diphtheria, tetanus and pertussis-containing vaccine, emphasizes the critical need for novel approaches to enhance the coverage and reach of immunization programs, in order to achieve universal health coverage goals [23,28]. Immunization programs in lower-middle income countries (LMICs) in particular, face logistical and administration challenges with existing vaccine products and presentations, namely, the need for cold storage and transport, complex administration requirements, and multidose containers, which can lead to higher wastage, safety issues and missed opportunities for vaccination. World Health Organization's (WHO) Immunization Agenda 2030 has therefore underscored the critical need for research and development of novel vaccine product innovations to increase vaccine coverage and prevent further backsliding resulting from the COVID-19 pandemic

* Corresponding author at: MMGH Consulting, Kuerbergstrasse 1, 8049 Zurich, Switzerland.
E-mail addresses: soblea@mmglobalhealth.org (A. Soble), kom@mmglobalhealth.org (M. Ko), shawngilchrist@sympatico.ca (S. Gilchrist), malvoltis@mmglobalhealth.org (S. Malvolti), hassoagopsowiczm@who.int (M. Hasso-Agopsowicz), giersingb@who.int (B. Giersing), jamorij@unicef.org (J.-P. Amorij), cjarrahian@path.org (C. Jarrahian), felsheikh@gavi.org (F. El Sheikh), mmenozziarnaud@gavi.org (M. Menozzi-Arnaud), tscarna@gavi.org (T. Scarna).

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Vaccine microarray patches (MAPs) are a promising vaccine innovation currently in development with distinct advantages over available needle and syringe (N&S) vaccine presentations. MAPs are coin-sized flat patches comprised of micron-sized projections that can deliver a dose of a vaccine into the skin epidermis and dermis in a minimally invasive manner [19]. As of the end of 2022, vaccine MAPs for influenza, measles-rubella, and COVID-19 have entered early-stage human clinical trials, reaching Phase I and Phase II [20,1,3]. While progress is being made to overcome the technical challenges to ensure scalability and manufacturability of the technology, significant at-risk investments are still required to establish manufacturing lines or facilities in parallel to clinical development to accelerate access to vaccine MAPs following market authorization [21].

The potentially game-changing programmatic advantages offered by vaccine MAPs include being ready-to-deploy without reconstitution; potential for improved thermostability, potential to be administered by lower cadres of healthcare personnel; and potential reduction of missed opportunities for vaccination from multidose dose presentations may help to extend the reach of immunization programs. These advantages of MAPs may be most prominent through supporting vaccine delivery to reach zero-dose children in the most remote and challenging settings and in areas experiencing outbreaks of vaccine-preventable diseases [2,19,10,22]. Increased coverage of vaccines using MAP presentations compared to N&S may be achieved because of better acceptance by the public and health workers owing to the simplicity, ease of use, and mitigation of vaccine acceptance challenges such as needle phobia. [22].

Vaccine MAPs may also offer benefits for epidemic and pandemic preparedness and response through a simplified vaccine distribution process which would not require procurement, storage and transportation of separate administration devices and functions with reduced cold chain requirements, as well as their potential to be administered in a variety of community settings with the involvement of non-healthcare professionals. Vaccine MAPs could ease drug substance supply requirements with reduced quantities per dose, should vaccine MAPs be able to achieve dose sparing, and may alleviate pressure on fill and finish capacity requirements and ancillary supplies. MAPs for COVID-19 vaccines themselves have been undergoing rapid development to address the challenges encountered with global delivery, the scarcity of trained health workers in low resource settings, and the economic and logistical barriers to distribution and storage [5,3]. Further advancements in the development of MAPs could offer a new tool to support ongoing epidemic preparedness and response activities.

Given the potential of vaccine MAPs to address multiple vaccine delivery challenges, they were recognized by the Vaccine Innovation Prioritization Strategy (VIPS)[1] as the top priority vaccine product innovation amongst three prioritized innovations to address key public health needs, particularly to increase vaccine coverage and equitable delivery of vaccines in low resource settings [8,9,14,17].

While there is alignment among global immunization stakeholders calling for the acceleration of vaccine MAP development, vaccine MAPs are still early in the development process and few candidates have advanced beyond the pre-clinical evaluation stage into clinical trials. Significant obstacles thus remain before vaccine MAPs can be used by national immunization programs [9,7,21]. To incentivize investments to advance vaccine MAP development, different stakeholders in the immunization ecosystem require a more comprehensive understanding of the likely uses and potential uptake of this novel presentation, given their anticipated differences with existing N&S presentations.

To support the assessment of vaccine MAP value, it is critical to identify how vaccine MAPs can be used by national immunization programs or other primary health services, including the settings in which MAPs can be used, the health cadres that can administer MAPs, and the populations that could be vaccinated using MAPs, which can in turn help to quantify the potential market for the product. To better understand the potential for vaccine MAP use in different settings and the implications for policy and development decisions, we assessed a subset of vaccine MAPs currently in development by applying a user-centric framework to define the potential use cases of different vaccine MAPs. Use cases, which describe the situations where a product can be used to achieve a specific outcome, provide insights to critical attributes that must be included in a vaccine's target product profile (TPP), define the populations that can be reached through different channels of health systems, and are also a valuable input into vaccine demand forecasting and investment decisions on new product development, particularly if new vaccine products are likely to require a higher cost to produce than those already being used by national immunization programs.

This assessment includes a review of immunization stakeholder views on the programmatic viability of vaccine MAPs, specifically for measles-rubella (MR), measles-mumps-rubella (MMR), and typhoid conjugate vaccine (TCV) and investigates the implications of the broad potential uses of vaccine MAPs within immunization programs. These products were selected based on their potential for high public health impact and their potential for use in a variety of settings targeting different target populations.[2] The selected antigens also represent immunization programs at different stages of maturity, with MR and MMR broadly used globally, though use is differentiated by region and national income, while TCV is a new vaccine which as been introduced in a limited number of countries. Our findings identify commonalities between the use cases for different vaccine MAPs, which enable an improved understanding of the potential uses and viability of this novel vaccine presentation and help inform the development decision making and policy requirements necessary to advance the technology towards future use by national immunization programs.

2. Methods - Use cases for vaccine microarray patches

Use cases for MR-MAPs, MMR-MAPs and TCV-MAPs were systematically defined to evaluate the ways in which each vaccine MAP could be respectively used within a health system, to reach all target populations, and to maximize impact in support of disease control objectives. An iterative and consultative process with product experts and program users was conducted to identify the critical programmatic dimensions influencing the ways in which vaccine MAPs could be used within health systems. Mixed methods approaches were employed, which included a structured review of published and grey literature to understand disease epidemiology, key vaccine characteristics, the design of current vaccination programs, and the existing vaccine market. Desk review findings were used to inform the development of preliminary use cases which were subsequently revised and validated following quantitative analyses, online surveys, interviews, and focus groups with national immunization program stakeholders, decision makers and other stakeholders. The use cases for each product were developed separately using similar approaches.

2.1. MR-MAPs

A landscape review of public and semi-public technical documents related to MR-MAPs were reviewed to inform the development of the preliminary MR-MAPs use cases Detail about the documents included in the landscape review can be found in Annex 1. Using the findings from the landscape review, draft MR-MAP use cases were developed.

[1] VIPS is global partnership between Gavi, the WHO, UNICEF, BMGF and PATH to priorise and drive vaccine delivery innovations to increase equitable vaccine coverage in LMICs and contribute to pandemic preparedness and response.

[2] This was based on the feedback received from consulted stakeholders and found to be particularly relevant for MR and MMR vaccine MAPs.

Next, validation of the draft uses cases were conducted through the use of an online survey and interviews. For the survey, 111 individuals were sent personalized links through Qualtrics™. The survey was also made available to a global network of immunization professionals through the TechNet-21 website. The respondents were requested to answer a series of pre-defined questions related to a country's ability to achieve its MR control and elimination strategies focusing on (i) identifying key vaccine delivery challenges and influential factors; (ii) evaluating the importance of the draft MR-MAP use cases and where they could be utilized; and (iii) identifying where MR-MAPs would have the most contribution to achieving a country's goals. The respondents were asked to rate each survey question using a 5-point Likert scale and matrixed questions were used to evaluate the importance of MR-MAP use cases. Average scores were calculated for each of the questions and stratified analyses were conducted using Microsoft Excel to consider different in response trends by geographical location, technical expertise or organizational perspectives. There were a total of 70 survey respondents and key results from the survey can be found in Annex 2.

Additionally, we contacted 49 individual EPI managers for telephone interviews using a semi-structured guide. A total of 30 respondents answered a series of predefined questions related to: (i) their current technical MR vaccine delivery challenges; (ii) whether the proposed use cases would be appropriate for the country and why; (iii) additional use cases; (iv) how MR-MAPs would help resolve the previously identified technical vaccine delivery challenges and contribute to the achievement of their MR goals. Questions were sent in advance and, if needed, tailored to the participant. In the situation where EPI managers could not be reached, the WHO immunization focal point was contacted. Countries were identified for interviews based on factors which included population, size, the number of unimmunized children (using WUENIC MCV1 coverage), high priority countries for Gavi and the Measles & Rubella Partnership. Interview responses were documented verbatim in real time and all interview transcripts were reviewed by the project team to identify key themes and results. Sentiment analysis was also performed using Qualtrics™ to further explore identified themes, with the project team reviewing all assigned sentiments before finalizing the results. Annex 3 provides the key results of the interviews.

This approach taken to define and evaluate use cases for vaccine MAPs was endorsed by WHO's Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC) as being systematic and scientific, endorsing the 6 use cases identified for MR-MAPs [26].

2.2. MMR-MAPs

The methods employed to develop use cases for MR-MAPs were leveraged for the development and validation of the MMR-MAPs use cases. A rapid assessment of published and grey literature was first performed to identify factors affecting the use of MAPs, the delivery challenges for MMR vaccine, and potential self-administration of MAPs. The period for the literature search ranged from January 1st, 2000, to Sept 21st, 2021, and search PubMED and clinical trial registries in the United States, China, India, and South Korea. Additional searches and data from WHO, the European Centers for Disease Control (ECDC) and Google were incorporated. Structured search terms were developed and a total of 421 peer-reviewed articles were identified. Abstracts were first reviewed for relevance. If abstracts were deemed to lack relevance to the project, then they were excluded. If abstracts indicated possible relevance to the project, then the full article was reviewed. Results from the rapid literature assessment can be found in Annex 4.

138 individuals from countries using MMR vaccine were contacted to complete a survey regarding the relevance of the preliminary MMR-MAPs use cases. Similarly, to the MR-MAPs survey, a 5-point Likert scale questions were used to evaluate the importance of MR-MAP use cases. Average scores were calculated for each of the questions and stratified analyses were conducted using Microsoft Excel to consider different in response trends by geographical location. A total of 22 survey responses were received and an overview of the key results are summarized in Annex 5.

As MR-MAPs was widely consulted on, it was decided to take light-touch approach to consulting on MMR through the use of focus groups. Three focus groups were organized to target experts with specific knowledge in measles, rubella, and mumps epidemiology and vaccination as well as vaccine regulation. 17 individuals were invited to participate in the focus group. The focus groups were performed via teleconference using a semi-structured discussion guides focused on current MMR delivery challenges and the feasibility of MAPs use cases focused on self-administration and their capacity to address existing challenges. To complement the low participation in the focus groups, we also contacted 11 individuals for one-on-one telephone interviews with a selected group of individuals. Annex 6 provides additional information regarding the focus groups and interviews for MMR-MAPs.

2.3. TCV-MAPs

Methods consistent with those described for MR-MAP and MMR-MAP use cases were employed to develop the TCV-MAP use cases. A rapid assessment of published and unpublished literature and data to identify any potential factors affecting the future use of TCV-MAPs. The rapid assessment of literature consisted of the identification of peer-reviewed articles on PubMed based on structured search criteria as well as published or unpublished data from various online databases including the Institute for Heath Metrics and Evaluation (IHME), PathogenWatch, WHO/UNICEF Joint Reporting Form, WHO's Market Information for Access to Vaccines initiative, and WHO Immunization, Vaccines and Biologicals department (IVB) Data repository. The time period for the literature search ranged from March 2, 2016, to Nov 15, 2021, and was selected because the first Phase III data for TCV was not available until Q2 2015. A total of 277 articles were identified for review. If abstracts were deemed to lack relevance to the project, then they were excluded. Articles determined to be relevant were reviewed in full with key information extracted to support the development of TCV-MAPs use cases. The full details and results of the literature assessment are detailed in Annex 7. A survey was then developed and distributed to 629 individuals to explore viewpoints of immunization stakeholders regarding the key challenges that TCV-MAPs could address. The survey was distributed to targeted respondents with personalized links through Qualtrics™. Stratified analyses were conducted using Microsoft Excel to evaluate any difference in trends in responses stratified by the regional location of respondents, whether respondents identified themselves as implementers (e.g., working for CSOs, NGOs, UN agencies, or government representatives), and whether respondents were in LICs or LMICs. A total of 155 survey responses were received and key results from the survey are summarized in Annex 8. Semi structured focus groups were then organized with key country stakeholders to collect their feedback on the preliminary use cases for TCV-MAPs. Countries were selected based on their recent introduction of TCV, imminent plans to or active discussions regarding the introduction of TCV, or where typhoid disease burden is known to be high. The focus groups were organized as virtual discussions held on the Microsoft Teams platform and participants were provided with an overview of TCV-MAPs followed by 4 guiding questions for discussion regarding the relevance of the use cases. Consultations with global typhoid experts were also convened with a focus on the same guiding questions as those used in the focus groups. Focus group discussions and consultations were documented verbatim in real time and all transcripts were reviewed by the project team to identify key themes and results. A total of 23 country stakeholders and typhoid experts participated in the focus groups and consultations, for which key results are summarized in Annex 9.

The employed methods highlighted that use cases for each of the vaccine MAPs share notable features and can be applied to other vaccine

MAPs with minimal adjustment to account for vaccine and disease-specific considerations; 7 use cases were defined for MMR-MAPs in contrast to 6 for MR-MAPs, and 6 for TCV-MAPs.

3. Results - A. – MR-MAPs

Immunisation efforts have reduced the annual number of measles deaths by 94 % between 2000 and 2020 [18] and a similar impact on rubella and congenital rubella syndrome (CRS) incidence has been observed in countries that have introduced the rubella vaccine [16]. Despite tremendous progress between 2000 and 2010, when the estimated global MCV1 coverage increased from 72 % to 84 %, MCV1 coverage has since plateaued and decreased [6]. The COVID-19 pandemic exacerbated this trend, and in 2021 global coverage for MCV1 decreased by 5 percentage points, leaving 5 million additional children unvaccinated compared to 2019 [28]. Supplemental immunization activities including wide age-range (i.e., 9 months up to 15 years of age) catch-up campaigns are being conducted in many countries to increase population level coverage and reduce the number of individuals susceptible to measles. Current immunization programs face challenges to deliver MR vaccines including logistical failures and programmatic errors related to storage, reconstitution or administration. MR-MAPs have the potential to overcome many of these current logistical obstacles, reduce the number of zero-dose children and accelerate the elimination of measles and rubella [11].

Two primary dimensions have been identified, based on the results of the landscape analysis and input from consulted stakeholders which have the largest influence on the potential uses of MR-MAPs vaccines, which define the foundation of the MR-MAPs vaccine use cases; the location of delivery of the vaccine (e.g., fixed post health facility) and the type of health worker responsible for administering the vaccine (e.g., doctor, nurse, or community health worker). Based on the vaccine delivery locations and health workers within a health system relevant for MR-MAPs, six use cases were validated (Fig. 1) [15] and used to develop a global demand forecast for MR-MAPs [13].

Use case 1 (UC1) was defined as delivery by a health worker (HW) or a community health worker (CHW) in fixed health posts, whereas use case 2 (UC2) was defined as delivery by HWs in locations with limited or no cold chain capabilities or health services. Use case 3 (UC3) was defined as delivery by CHWs only in locations with limited cold chain capability or health services, and delivery by CHWs in home community with no cold chain was defined as use case 4 (UC4). Delivery by HWs and self-administration with HW or CHW assistance was defined as use case (UC5) and use case 6 (UC6) was defined as self-administration with no HWs assistance.

Consulted stakeholders indicated that MR-MAPs would increase programmatic efficiency, through the reduction in reconstitution errors and improved safety, reduced cold chain requirements increased immunization coverage, in particular linked to increased ease of administration and expansion of the types of individuals able to safely administer the vaccine.

Clear use cases for MR-MAPs were identified as stakeholders indicated these efficiencies could be realized in routine immunization delivered at both fixed health posts in the health system (UC1, 3, 5) as well as through community-based delivery strategies (UC2, 4, 6). MR-MAPs therefore have the potential to be used more broadly within immunization programs: in the same settings where N&S vaccine presentations are currently used, and, in addition, in community settings that are difficult to access with current vaccines. Most of the stakeholders thought that MR-MAPs could be delivered in community settings through outreach and mobile strategies and that vaccine administration could be performed by CHWs (UC3 and 4). In this way MR-MAPs could potentially expand the workforce capable of delivering vaccines, helping to address a key constraint of immunization programs in low resource settings. Many stakeholders also saw the potential benefits of MR-MAPs to increase vaccine access in hard-to-reach or security compromised areas, to the chronically unimmunized populations (UC 2, 3, 4). Stakeholders from countries utilizing MMR or MMRV in their routine immunization schedule highlighted a role for MR-MAPs, particularly in specific populations such as vaccine hesitant, those lacking health services such as asylum seekers and travelers, for older age catch-up immunization, and isolated communities, given the pain-free administration and programmatic benefits of MAPs. In higher resource settings, stakeholders also identified the possibility of self-administration of MR-MAPs through pharmacies for specific hard-to-reach populations (UC 5 & 6). Supervised self-administration of MR-MAPs, which stakeholders identified as more feasible than self-administration without assistance, could increase immunization program efficiency and broaden the potential locations where immunization services could be offered as part of routine and outreach delivery strategies. Stakeholders noted that use cases 5 and 6, which include self-administration, would require country-specific legal and regulatory changes regarding vaccination administration before MAPs could be considered for implementation.

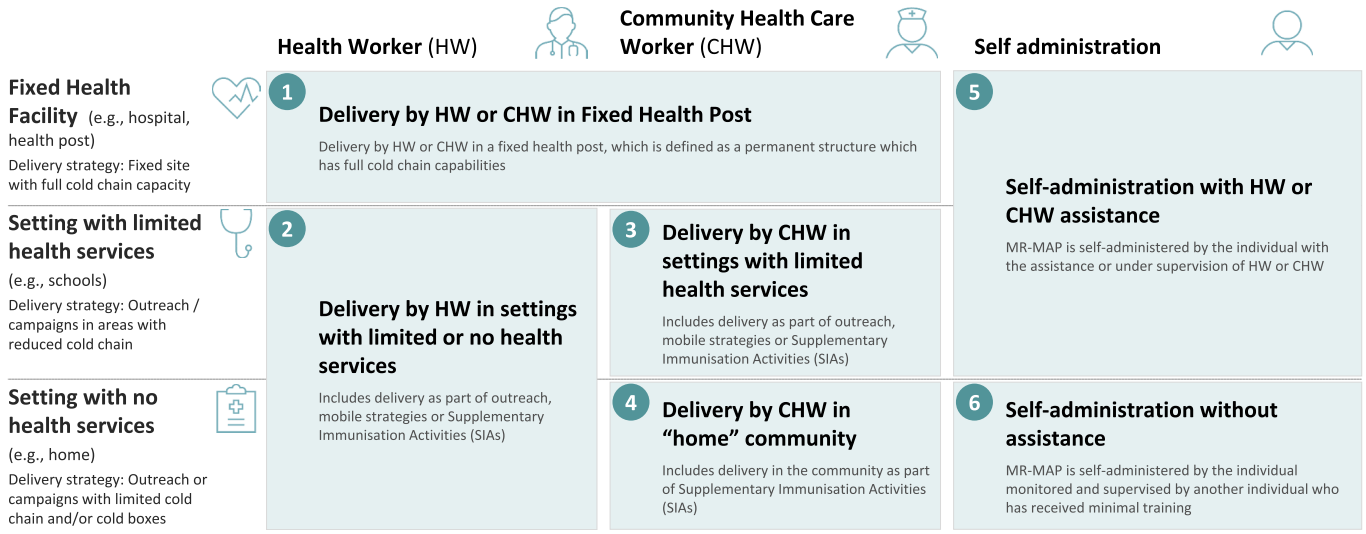

Fig. 1. Validated use cases for MR-MAPs.

4. Results - B. - MMR-MAPs

Measles-mumps-rubella (MMR) vaccines are typically delivered in high- and upper-middle-income countries targeting mumps control, because of their advantages over individual vaccines. The MMR vaccine is not widely used in low resource settings where mumps is currently considered to be a lower public health priority. In addition to the six use cases defined for MR-MAPs, a seventh use case was identified for MMR-MAPs. Use case 7 (UC7) was defined as delivery by non-health workers in settings with limited or no health services (Fig. 2).

Stakeholders consulted during the development and validation of the MMR-MAP use cases highlighted that settings with limited or no health services are the locations where MMR-MAPs could deliver the most potential benefit (UC 2, 3, 4, 6, 7) to reach special populations and reduce missed opportunities for vaccination. While delivery by trained health workers was identified as the most prominent delivery channel, delivery by non-health personnel within the primary health care system (e.g., teachers, community leaders) was also considered possible (UC7). A broader cadre of personnel capable of administering MMR-MAPs could help to improve access to the vaccine, particularly in settings with limited or no health services. With regards to the delivery locations of the MMR-MAP use cases, stakeholders indicated that use cases 1–4, delivery of MMR-MAPs by HWs and CHWs in fixed health facilities, and in settings with limited or no health services, were very important for MMR, with use case 5 potentially playing an important role in private healthcare settings. Vaccination of vulnerable and hard-to-reach populations and use in outbreak response were the areas where self-administration of MMR-MAPs was highlighted as most promising.

5. Results - C. TCV-MAPs

Typhoid conjugate vaccine (TCV) is recommended by WHO (Strategic Advisory Group of Experts on Immunization [24], in a single dose to infants and children aged ≥6 months in typhoid-endemic countries. Historically, large outbreaks of typhoid have been reported in south Asia, southeast Asia, and sub-Saharan Africa in areas with unsafe water, sanitation, and hygiene. Introduction of TCV into routine immunization programs is recommended to be prioritized in countries with high burden of disease or a growing burden of drug-resistant typhoid. Vaccination of special populations at increased risk for typhoid should be considered in countries with lower endemicity.

Given the broader set of populations that could potentially be vaccinated with TCV-MAPs, the selected dimensions for the TCV-MAP use cases were the vaccine delivery locations and the specific populations recommended by WHO for vaccination with existing TCVs. The type of health worker administering TCV-MAPs was also identified as an important factor and was incorporated into the delivery location dimension. This is a key difference compared to the use cases developed for MR-MAPs and MMR-MAPs, which are based on the different delivery locations and different health workers that could be mobilised to deliver MR-MAPs or MMR-MAPs. The differentiation for TCV-MAPs is driven by the populations recommended for TCV vaccination, which include infants and young children, like MR and MMR, but also include at-risk adolescent and adult populations including professional food handlers, travelers, and health workers. These populations are not routinely targeted by national immunization programs, likely more reliant on the delivery of vaccines through other PHC services across the life course and are therefore an important dimension in assessing how TCV-MAPs could be used.

Six use cases were developed for TCV-MAPs (Fig. 3). Use case 1 (UC1) is defined as delivery to a child less than 2 years of age in a health facility that has full cold chain capabilities with administration performed by a HW or non-HW, whereas use case 2 (UC2) is defined as delivery to a child less than 2 years of age in a setting with limited health services that has reduced cold chain capabilities by a HW or non-HW. These use cases were determined to be most relevant for the routine delivery of TCV-MAPs. Use case 3 (UC3) was defined as delivery to a child less than 2 years of age in a setting with no health services with no cold chain capabilities (e.g., mobile with cold boxes) by a HW or non-HW. This use case is likely to be relevant during outreach or periodic intensification of routine immunization, in addition to catch-up campaign activities at the time of TCV introduction. UC1, UC2, and UC3 overlap across the MR-MAPs and MMR-MAPs use cases for routine delivery but without the differentiation of the involved health workers.

Use case 4 (UC4) defined as delivery to a child older than 2 but younger than 15 years of age in any delivery location (full cold chain, reduced cold chain, or no cold chain) by a HW or non-HW. This use case is specifically relevant during wide-age range catch-up campaigns at the time of TCV introduction into a routine immunization program. Use case 5 (UC5) was defined as delivery to military personnel in a health facility with full cold chain capabilities by HW, whereas use case 6 (UC6) was defined as delivery to an adult traveler either in a health facility (e.g., travelers' clinic) or setting with reduced cold chain (e.g., pharmacy) by a HW or non-HW.

Surveys and focus groups of key country stakeholders were organized to collect feedback on the TCV-MAP use cases and to assist in understanding how different countries might use TCV-MAPs.

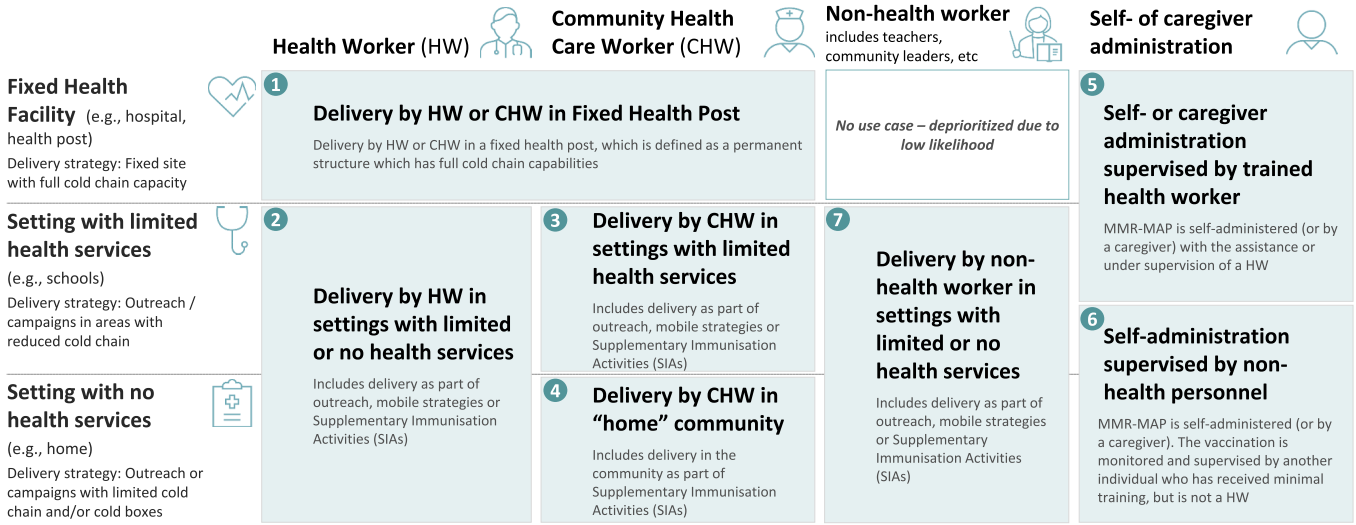

Fig. 2. Validated use cases for MMR-MAPs.

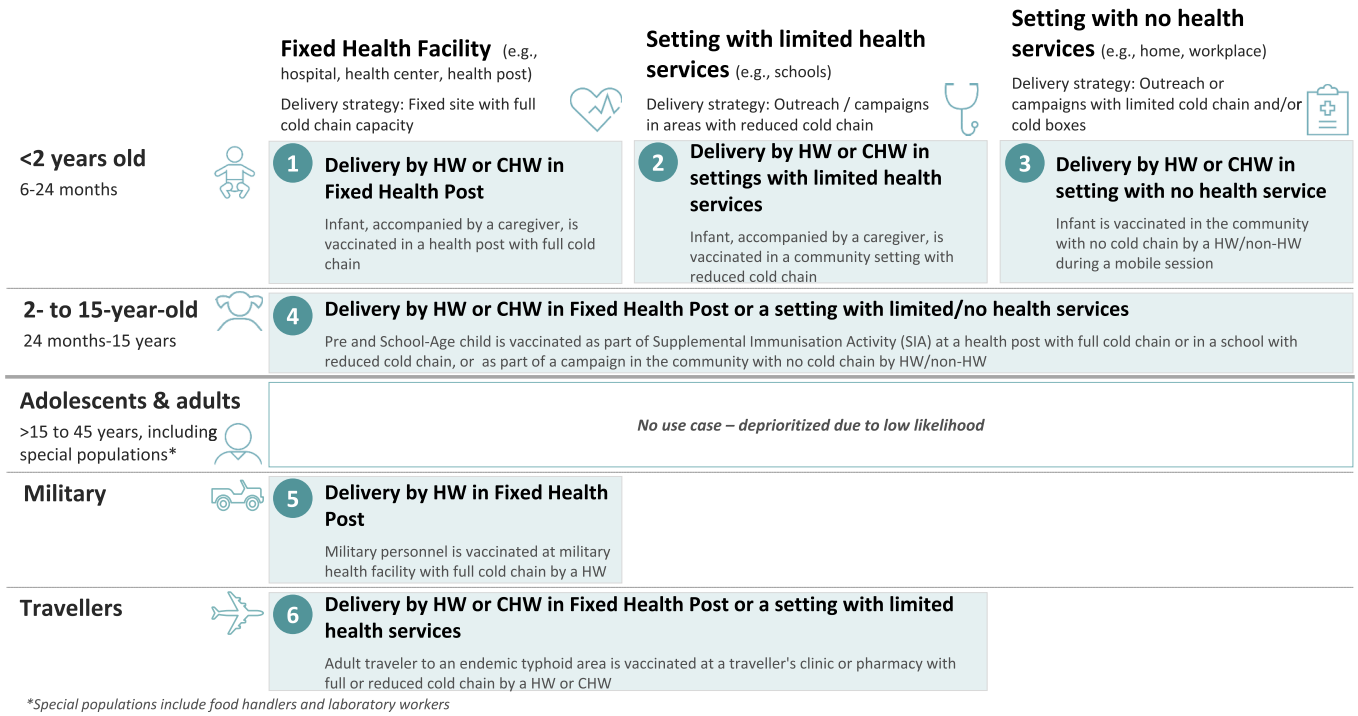

Fig. 3. Validated use cases for TCV-MAPs.

Stakeholders noted the potential utility of TCV-MAPs to reach <2-year-olds as well as 2–15-year-olds through fixed and mobile delivery locations, particularly in high typhoid endemicity settings, and many stakeholders thought TCV-MAPs could help support immunization programmes to reach other special populations. Stakeholders highlighted that TCV-MAPs could also help immunization programmes to effectively reach travellers, health workers, and military personnel, including in settings with low typhoid endemicity. Stakeholders therefore perceived a usefulness and value of TCV-MAPs to reach a range of potential target populations, not only a subset of target populations (e.g., hard-to-reach).

Stakeholders felt that TCV-MAPs would be programmatically valuable in all delivery locations and that health workers such as doctors, nurses, midwives, community health workers, and pharmacists, would be likely to safely deliver TCV-MAPs. TCV-MAPs could therefore be delivered in a variety of primary health care settings within the health system and administered by several different cadres of the health workforce. Similar to the stakeholder feedback on the MMR-MAP use cases, stakeholders noted that delivery by non-HWs would need to overcome important administrative, programmatic, and acceptability barriers, including changes to national immunization administrative and regulatory policies, as well as challenges to maintaining immunization data systems and robust pharmacovigilance, particularly for MAPs that are delivering newly introduced vaccines, and acceptance by targeted populations.

With WHO's recommendations for typhoid vaccination prioritizing routine use of TCV among infants and young children in high burden countries, with more targeted use in lower endemicity settings, there are different applications of the use cases for TCV-MAPs in different geographic settings. In countries with higher typhoid endemicity, UC1, UC2, UC3, and UC4 may be more relevant in their national efforts to reduce typhoid disease burden. In countries with lower typhoid endemicity seeking to protect at risk populations, use cases 5 and 6 may be more relevant. The relevance of different use cases for countries with varying typhoid endemicity suggests the potential for a dual market for TCV-MAPs in both high- and low-income countries, which may be an important factor in decisions to support investments required to develop TCV-MAPs and other vaccine MAPs. In settings with lower typhoid endemicity, vaccine policy recommendations will likely prioritize TCV-MAP use only among specific at-risk populations.

6. Discussion

Developing use cases for new vaccine products and presentations, such as vaccine MAPs, is critical for informing desired product attributes described in target product profiles and to support the estimation of future potential demand for vaccine MAPs, both of which are important in guiding developer decisions regarding investment in new product development. The methodology for developing use cases for vaccine MAPs is based on key elements that can inform the design of existing immunization programs. These elements include the epidemiology of the disease, program goals, program design, including the of type of health workers involved, vaccination strategies, and target populations. The use cases defined for MR-MAPs, MMR-MAPs, and TCV-MAPs share a number of commonalities despite being oriented around different dimensions.

Overall, consulted implementation and policy stakeholders generally had positive views about the utility of vaccine MAPs, their application in a variety of settings, and their administration by both health workers and non-health professionals. Stakeholders indicated that vaccine MAPs have the potential to be used broadly in settings providing routine, fixed post pediatric vaccination, as well as community vaccination settings reached through outreach or mobile strategies that target hard-to-reach populations and reduce missed opportunities for vaccination (Table 1). For MR and MMR specifically, the staff responsible for administering the vaccine (e.g., HCW or CHWs) was found to be especially important whereas for TCV-MAPs, stakeholders indicated that the broader potential target populations for the vaccine were more influential to its use cases.

The use cases provide a useful foundation to support the identification of priority populations, based on immunization program goals and policy recommendations, and support preparation activities for vaccine introduction through an improved understanding of the locations and administrators that can be used to optimally reach different populations.

Table 1
Applicability of UCs to MR, MMR and TCV.

Vaccine administrator and place of delivery	MR	MMR	TCV
Delivery by a HW (or a CHW) in a fixed post (e.g., hospital, health center, health post)	Yes	Yes	Yes (+ military / travellers)
Delivery by a HW in settings with limited or no health services (e.g., schools, community center)	Yes	Yes	Yes (+ travellers)
Delivery by a CHW in settings with limited health services (e.g., schools, community center)	Yes	Yes	Yes
Delivery by a CHW in their "home" community (i.e., home)	Yes	Yes	Yes
Self-administration with HW or CHW assistance in any setting	Yes	Yes (e.g., Private setting – pharmacy)	Yes (e.g., Private setting – pharmacy)
Self-administration without assistance in any setting	No	No	No
Delivery by non-HW in settings with limited or no health services (e.g., schools, community center)	NA	Yes (UC7)	Yes (UC3)

Note: Table assumes that all target populations for each vaccine can be vaccinated in all settings unless where specifically indicated.

However, to enable high uptake and coverage of vaccine MAPs, and ensure their suitability for the identified use cases, vaccine developed using the MAP presentation will need to realize minimal cold chain storage volume and improved thermostability (e.g., controlled temperature chain (CTC)) compared to existing N&S presentations and also have a manageable wear time to enable simple ease of use. These elements can help to enable higher coverage and uptake of vaccine MAPs compared to N&S, which are key foundational steps towards creating the commercially viable market required for manufacturers to sustainably develop and manufacture vaccine MAPs.

Although there was less consensus among stakeholders regarding the potential for self-administration with a vaccine MAP, some potential exists in private healthcare settings that legal and regulatory impediments can be overcome, such as delivery through pharmacies in high income countries. Key challenges to self-administration of vaccine MAPs include the inability to record immunization administration information and challenges to monitor and report AEFIs outside settings with health services.

The assessment of use cases across the different vaccine MAPs yielded two key findings related to vaccine administration by the health workers. Firstly, expanding the health workforce capable of administering vaccine MAPs, beyond doctors and nurses, could lead to an expansion in vaccine delivery; by increasing the staff capable of delivering vaccines, health systems can reach more communities and deliver vaccines more equitably to all members of a community. Secondly, stakeholders were in consistent agreement that the vaccine MAPs could be effectively used in settings with limited or no health services and no cold chain capacity.

7. Limitations

There are several important limitations to this work. Firstly, the feedback from stakeholders consulted on the use cases for MR-MAPs, MMR-MAPs, and TCV-MAPs was based on hypothetical product profiles which may not reflect the product attributes of vaccine MAPs that are successfully developed. Therefore, the collected feedback only represents stakeholder views on how vaccine MAPs could be used. Secondly, the potential use of vaccine MAPs will be significantly influenced by their procurement costs; however, country willingness-to-pay was not evaluated as part of the use case development process. Thirdly, there is limited data on the usability of vaccine MAPs in each use case, particularly self-administration, highlighting a key area of implementation research that will be required to inform national decisions regarding vaccine MAP adoption and their scope of use within national immunization programs. Thus, additional research is necessary to evaluate the usability of vaccine MAPs and willingness-to-pay for vaccine MAPs, given their respective importance in influencing how these products are ultimately used and the demand that arises for them.

8. Conclusion

The vaccine MAP use cases presented here are critical for evaluating their feasibility and potential benefit for immunization programs. They also help to determine the commercial opportunities required to accelerate vaccine MAP development for practical use, and shape policy considerations for program design and implementation. These use cases offer valuable insights into the delivery strategies for vaccine MAPs and their impact on health system delivery, as well as identify areas for further research and policy development. The next steps involve quantifying the potential populations reached in each of the use cases and forecasting of their potential demand to understand the potential health and economic impact of vaccine MAPs.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

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Appendix A

Annex 1. Key results from MR-MAP landscape review

A variety of documents (34 in total) were included in the MR-MAPs landscape review:
WHO documents and reports(N = 10)

- 2013 – WHO – MEASLES AEROSOL VACCINE PROJECT - REPORT TO SAGE
- 2015 – WHO – Microarray Patch (MAP) Product Development Workshop
- 2016 – WHO – Vaccine Presentation and Packaging Advisory Group – Delivery Technology Working Group, Preferred Product Characteristics: Measles-Rubella Microarray Patch – VERSION 1

- 2017 – WHO – Managing pain during vaccine administration - A training module
- for health workers
- 2019 – WHO – WHO Measles rubella (MR) microarray patch (MAP) Research & Development meeting – 13th June 2019 - Meeting summary
- 2019 – WHO – Update on MR MAP product development and proposal for country workshop/s
- 2019 – WHO – Measles-rubella microarray patch (MR–MAP) target product profile
- 2019 – WHO – Total Systems Effectiveness Evaluating all trade-offs to inform choice, presentation to Gavi
- 2020 – WHO – How, where and when are we going to use microarray patches to deliver measles and rubella vaccines?
- 2021 – WHO – Concept Note. Researching best practice for pandemic preparedness: capturing countries' perspectives and priorities to guide the development, introduction and use of measles and rubella microarray patches (MR-MAPs)

VIPS and other immunization partner grey literature documents (N = 15)

- 2016 – PATH – Global Vaccine Immunization Research Forum, Johannesburg, South Africa - Microarray patch case study: Measles-rubella vaccine
- 2016 – PATH – Global Vaccine Immunization Research Forum, Johannesburg, South Africa - Vaccine technology costs and health impact assessment tool
- 2016 – AMP – Microarray Patch Acceptability and Usability Evaluation in Low- and Middle-Income Countries
- 2017 – PATH – Evaluation of Microarray Patches for Human Factors – Considerations and Program Feasibility. Results of simulated-use testing in clinics in Ghana
- 2019 – JSI/Dose Per Container Partnership – Implementing 5-dose Measles-Rubella Vaccine Vials in Zambia Research Findings
- 2019 – PATH – PATH Vaccine Technology Impact Assessment model (VTIA): Application to measles rubella microarray patch assessment - World Health Organization MR MAP meeting, June 13, 2019
- 2019 – PATH – VIPS DTWG consultation: Microarray patches (MAPs) October 2019
- 2019 – VIPS – TECHNICAL NOTE – Microarray patches (MAPs)
- 2019 – William Davidson Institute at the University of Michigan – Total Systems Effectiveness: Health Investment Prioritization Coverage Tool
- 2020 – VIPS – Draft VIPS five-year action plan (AP) for MAPs
- 2020 – VIPS – Vaccine microarray patches (MAPs): VIPS Alliance Action Plan
- 2020 – VIPS – VIPS Phase II executive summary: Microarray patches (MAPs)
- 2020 – VIPS – PHASE 2 TECHNICAL NOTE - Microarray patches (MAPs)
- 2020 – VIPS – VIPS update to the Delivery Technologies Working Group
- 2021 – PATH – Measles-Rubella Microarray Patch Vaccines: A Business Case Analysis

Peer-reviewed and pre-print publications (N = 9)

- 2016 – Sarah Marshall, Laura J. Sahm & Anne C. Moore – The success of microneedle-mediated vaccine delivery into skin, Human Vaccines & Immunotherapeutics, 12:11, 2975–2983, https://doi.org/10.1080/21645515.2016.1171440
- 2017 – D. N. Durrheim and J. L. Goodson – Time for an immunisation paradigm shift, Trans R Soc Trop Med Hyg 2017; 111: 41–42, https://doi.org/10.1093/trstmh/trx018
- 2018 – Germain J.P. Fernando et al. – Safety, tolerability, acceptability and immunogenicity of an influenza vaccine delivered to human skin by a novel high-density microprojection array patch (Nanopatch™), Vaccine 36 (2018) 3779–3788
- 2019 – Elise Guillermet et al. – End-user acceptability study of the nanopatch™; a microarray patch (MAP) for child immunization in low and middle-income countries, Vaccine 37 (2019) 4435–4443
- 2019 – Nicolas Peyraud et al., Potential use of microarray patches for vaccine delivery in low- and middle- income countries, Vaccine 37 (2019) 4427–4434
- 2019 – Patrick T. Wedlock et al., The potential effects of introducing microneedle patch vaccines into routine vaccine supply chains, Vaccine 37 (2019) 645–651
- 2020 – Angus H. Foster et al., Safety, tolerability, and immunogenicity of influenza vaccination with a high-density microarray patch: Results from a randomized, controlled phase I clinical trial, PLOS Medicine - https://doi.org/10.1371/journal.pmed.1003024
- 2020 – Thomas J. Ellison et al., VaxiPatch™, a novel vaccination system comprised of subunit antigens, adjuvants and microneedle skin delivery: An application to influenza B/Colorado/06/2017, Vaccine, https://doi.org/10.1016/j.vaccine.2020.07.040
- 2021 – Christopher L.D. McMillan et al., Complete protection by a single dose skin patch delivered SARS-CoV-2 spike vaccine - bioRxiv preprint https://doi.org/10.1101/2021.05.30.446357

The review served as a basis for the identification of the key programmatic challenges faced during the administration of the MCVs and enabled the documentation of the different modalities and strategies used to deliver MCVs. More specifically, the review a supported the identification of the key users involved in the administration of MCVs, and the locations used to deliver MCVs under different delivery strategies. The outcome of this review informed the draft definition of the MR-MAPs use cases and the subsequent validation steps performed via the survey and the interviews.

Annex 2. Key results from the MR-MAP use case survey

Seventy individuals partially or fully completed the survey conducted to support the development of the MR-MAPs use cases. Table 1 provides an overview of the demographic characteristics of the 70 survey respondents for MR-MAPs.

Table 1
Demographics of 70 survey respondents for MR-MAPs.

Survey demographics	#	%
Organization type		
Agency of the United Nations	33	47 %
Implementation but not gov't or UN	9	13 %
Industry/Product Development/Design	13	19 %
Ministry of Health	5	7 %
Other[1]	10	14 %
Total	**70**	100 %
Respondent Role		
Development or Manufacturing	7	10 %
EPI manager	5	7 %
Epidemiologist	13	19 %
Immunisation	25	36 %
Researcher	8	11 %
Surveillance	6	9 %
Other[2]	6	9 %
Total	**70**	100 %
Geographical location (WHO region)		
AFR	15	21 %
AMR	22	31 %
EMR	6	9 %
EUR	6	9 %
SEAR	16	23 %
WPR	5	7 %
Total	**70**	100 %

[1] Others include: Donors (2), Independent (2), and CDC (4), and Academia (2).
[2] Others include: Health system specialist (2), vax logistics (1), health economist (1), public health specialist (1), trading (1).

The majority of the respondents agreed that contamination or wastage due to the multi-dose vials and cold chain requirements during outreach were the top two challenges with the highest agreement amongst the stakeholders (Fig. 1).

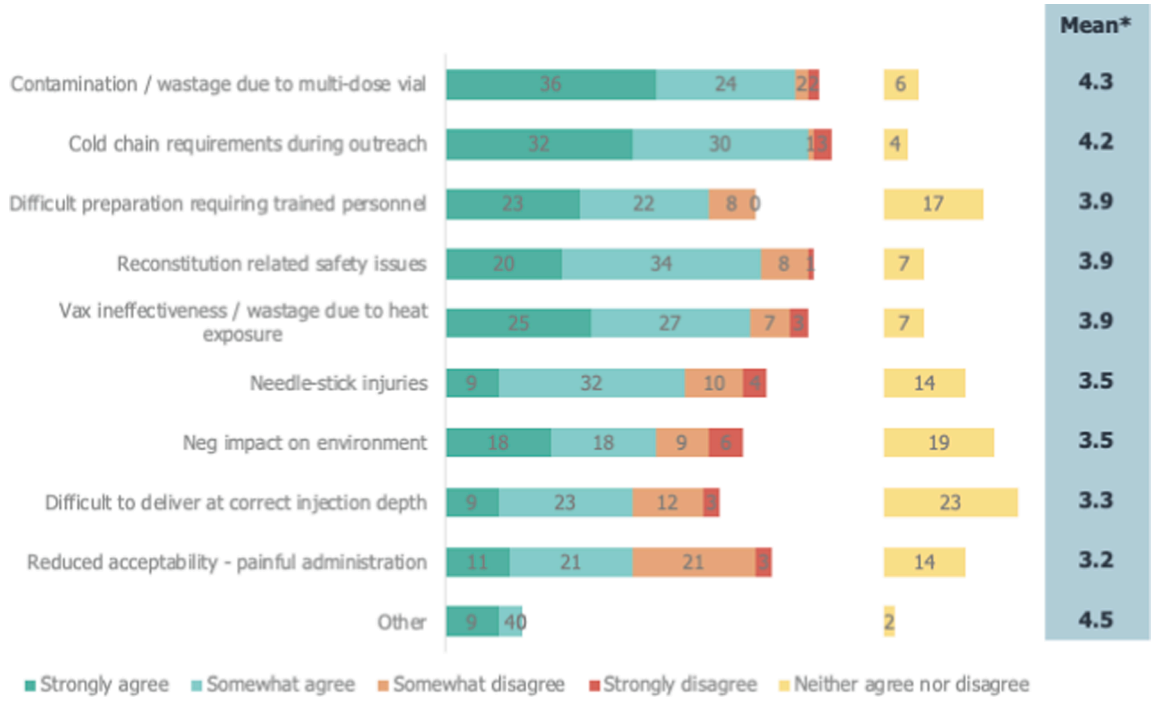


Fig. 1. MR vaccine delivery challenges.

The respondents were then asked to rate the importance of the predefined six UCs. UC3, UC4, and UC2 received the highest level of importance per the respondents. UC1 and UC5 received moderate importance and UC6 received the lowest level of importance with the highest level of discordant opinions where 47 % of respondents stated that UC6 was only slightly or not at all important. UC5 also had a relatively high number of individuals rating it as not important at all (25 %). Fig. 2 provides additional details on the level of importance the respondents assigned to MAPs as part of MR control efforts.

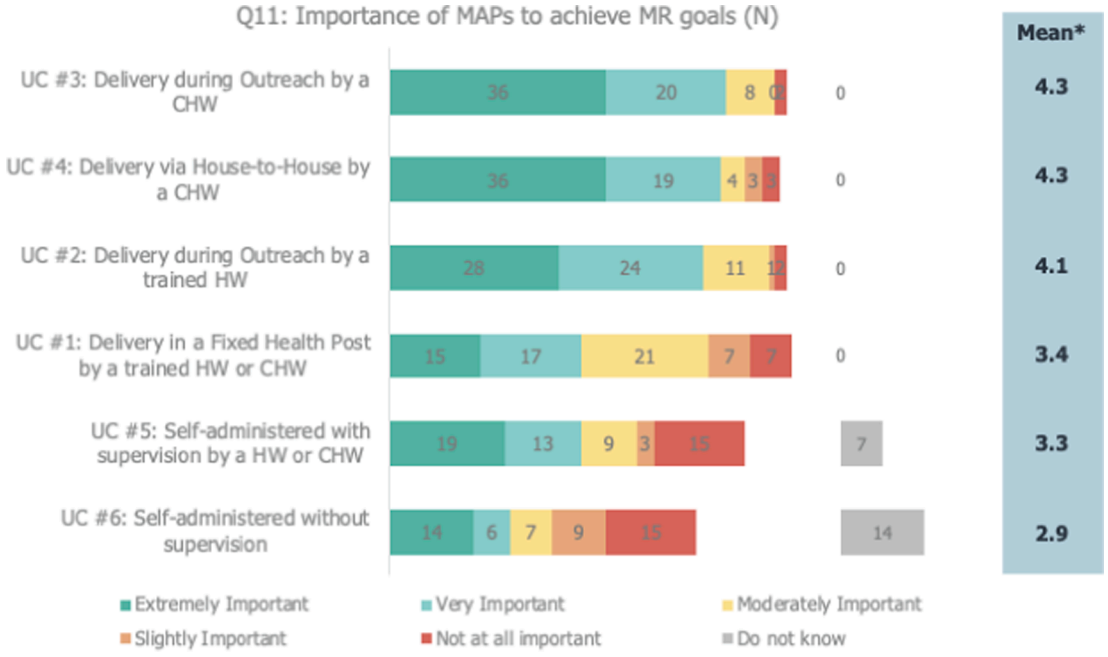


Fig. 2. The importance of MAPs to achieve a country's control and elimination goals by predefined UCs (Number of respondents).

When the results were stratified, there was general agreement amongst the different perspectives for UC2, UC3, and UC4. However, opinions differed particularly for the UCs utilising self-administration (UC5 and UC6) and for delivery in a fixed health post (UC1), with respondents with and industry background rating these UCs as more important than those representing the global and regional or national public health functions (Fig. 3).

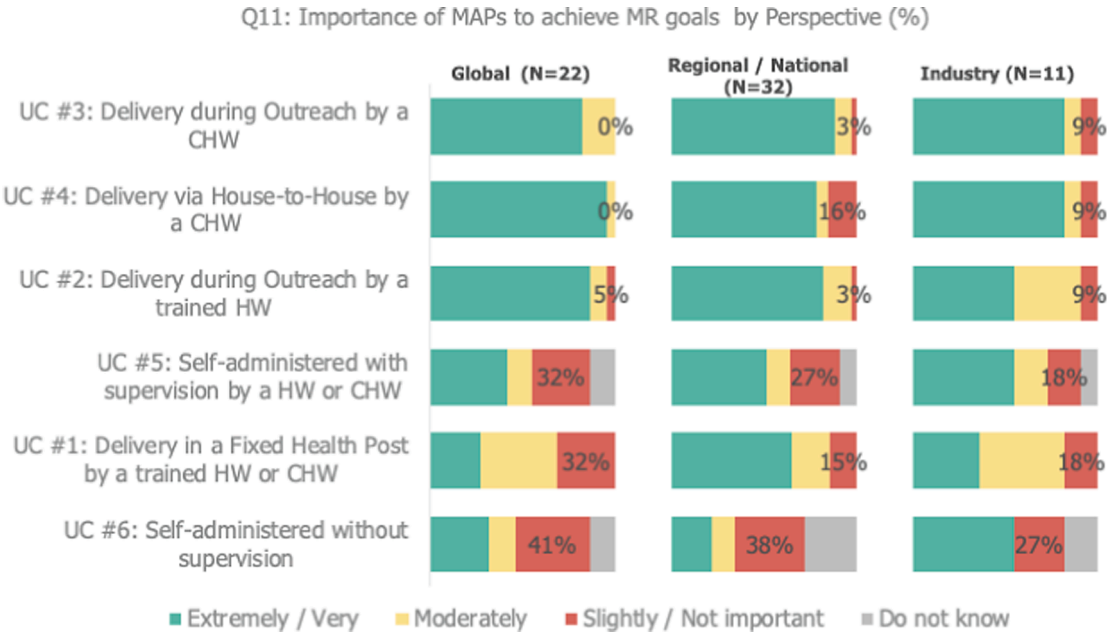


Fig. 3. The importance of MAPs to achieve a country's control and elimination goals by predefined UCs (percentage of respondents).

The respondents were asked to select the country income groups where MR-MAPs would contribute most to MR control and elimination goals. While the majority of respondents indicated that UC1 could be used by all countries, the opinions differed for the other UCs. There was overall high acceptability of UC2, UC3, and UC4, with only a limited number of respondents indicating that no countries would utilise these UCs. Conversely, UC5 and UC6 contained the highest percentage of respondents who felt that no countries would use these UCs at 22 % and 38 %, respectively.

Lastly, 65 respondents provided their feedback on whether MR-MAPs could contribute to MR control and elimination goals. In general, respondents agreed that MR-MAPs could have a positive effect and help to achieve MR control goals and objectives. Areas where respondents did not agree were largely related to self-administration where 62 % and 50 % agreed with allowing pharmacists to administer MR vaccines with allowing self-administration of MR vaccines, respectively (Fig. 4).

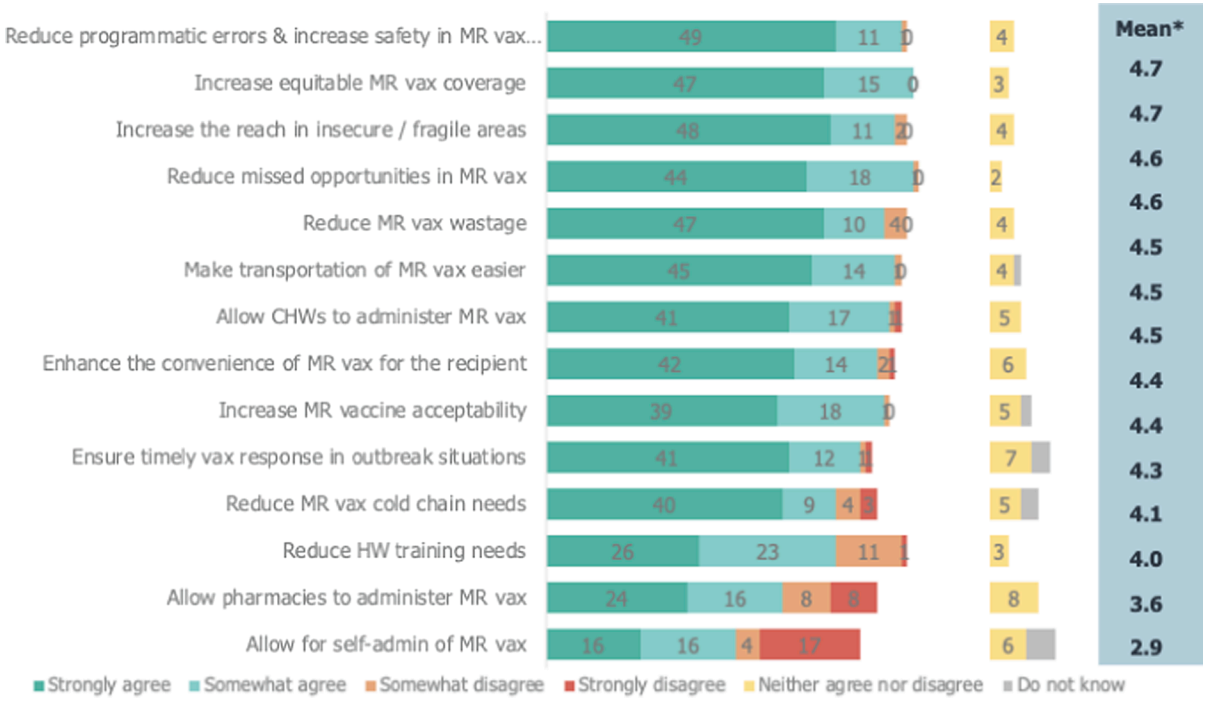


Fig. 4. MR-MAPs can contribute to the following programmatic challenges (number of respondents).

Annex 3. Key results from MR-MAP interviews

30 individuals across the WHO regions and World Bank Income Group classifications, were interviewed and the interviewees comprised of 16 EPI managers and 14 WHO immunization focal points at the country or regional levels.[3] The table below provides the demographic characteristics of the interviewees.

Table 2
Demographic characteristics of the interviewees.

Interview demographics	#	%
World Bank income group		
High income	3	10 %
Upper middle income	4	13 %
Lower middle income	11	37 %
Low income	11	37 %
Total	**30**	100 %
Geographical location (WHO region)		
AFR	12	40 %
AMR	3	10 %
EMR	5	17 %
EUR	2	7 %
SEAR	5	17 %
WPR	3	10 %
Total	**30**	100 %

The interviewees were asked to identify and discuss their top three technical vaccine delivery challenges. The majority of respondents (N = 22) cited logistics and transportation challenges e.g., difficulties in conducting outreach activities, inability to prepare vaccines in advance when conducting outreach, insufficient number of health facilities, lack of or insufficient cold chain, and the inability to access hard-to-reach or security compromised areas or vulnerable populations. The second most identified challenge related to vaccine acceptability, including challenges in communication, fear of needles/crying children, and overcrowded vaccination schedules. The third most identified challenge included human resources and administration. Respondents referred to human resources as either the lack of quality vaccinators or insufficient number of individuals to deliver the vaccines and to administration mainly as related to reconstitution and safety issues. Other challenges that were identified were low coverage or high drop-out rates, adverse events following immunization (AEFI), and high vaccine wastage or costs.

Respondents were provided an overview of the six use cases and asked to give their feedback on whether their country or region would utilise MR-MAPs, considering that MR-MAPs would become available around 2030 which many felt that the use cases could be relevant for their countries.

The majority of the individuals did believe that use case 3 (82 %) and use case 4 (70 %) could be utilised in their countries as they saw the benefits

[3] MR regional focal points for PAHO and AFRO were interviewed.

of an expanded workforce including CHWs to deliver vaccines, with a few respondents indicating that polio vaccines were delivered by volunteers and MR-MAPs could follow suit. Many also saw the benefits to improve access of hard-to-reach or security compromised areas, the chronically unimmunized, and to insecure areas. Some individuals indicated use cases where delivery was by CHWs would not be accepted as their countries had experienced serious AEFIs related to MR or due to legal constraints on who can administer vaccinations.

Some countries felt that use cases in the fixed health structures would not be relevant for their countries as they utilise MMR or MMRV in their routine schedule or already have strong systems in place and would not want to upset these, which could trigger additional implications for other vaccines.

Although the respondents were initially cautious towards UC5 and UC6, upon further discussion, it became clear that both of these UCs could have roles to play. The majority of respondents cited two key barriers to self-administration – the inability to record and report vaccination and the inability to monitor for AEFIs.

Use case 6 remained the most divisive with some countries indicating that it would be acceptable if appropriate advocacy and communications were conducted, and the community felt responsibility and pride in utilising a new innovative technology. Respondents indicated that MR-MAPs could be a powerful tool against hesitancy as the parents could be administering the vaccine themselves thus ultimately participating in the vaccination process and feeling more empowered. Other respondents indicated that this would not be possible given the linkages of vaccination with infant and child health checks.

As countries with MMR or MMRV in their routine programme were interviewed, a stratified analysis of the above was conducted to better understand the appropriateness of UC4, UC5, and UC6. UC1, UC2, and UC3 were not separately evaluated as many stated they would not want to replace MMR/MMRV with a MR vaccine. These countries saw a role for MR-MAPs, particularly in specific populations such as vaccine hesitant, asylum seekers and travellers, and for older age catch-up immunization or isolated communities. A few also indicated the possibility to conduct self-administration of MR-MAPs through pharmacies if there was an ongoing outbreak.

When asked how MR-MAPs could impact their MR programmes, all respondents responded in a positive manner. All of the individuals indicated that MR-MAPs would increase their efficiency, citing the reduction in reconstitution errors, increased ease of administration, and expansion of the types of individuals able to administer the vaccine. Further, ~30 % cited that MR-MAPs would help them save time either in delivering the vaccine faster or in reducing their preparation and planning time. Others also cited the reduction in waste management and vaccine wastage.

~80 % of the respondents stated that MR-MAPs would help to increase MR coverage and reduce inequities (e.g., reducing drop-out rates, increasing the ability to access hard-to-reach areas or migrant populations). Almost 60 % of the respondents cited decreased logistics and transportation (e.g., no cold chain requirements) as an important aspect of MR-MAPs. Lastly, 40 % of respondents indicated that MR-MAPs would increase vaccine acceptance by reducing the number of injections and reducing pain and fear.

Annex 4. Key results from MMR-MAP rapid literature assessment

Information from a total of 48 peer-reviewed articles were used to support the development of MMR-MAP use case. The literature assessment found that self-administration of MAPs or similar medical devices (e.g, pen devices for insulin) were possible and could be correctly and consistently administered as well as was preferred by the participants. The literature also indicated that the participants preferred MAPs over intramuscular administration. Further, the literature showed there could be potentially significant cost savings and provided potential estimates of cost-effective prices.

The literature also indicates two key barriers to the industrialization of MAPs related to the high costs of component production and challenges with aseptic product highlighting that MAPs may need multiple regulatory approvals prior to commercialization.

With regards to the use of MMR in outreach, the literature found outreach use largely related to measles outbreaks and could extend to all ages in a variety of delivery locations such as schools or universities, doctor's offices, shopping centers, workplaces, and military barracks. The only reported MMR campaigns are reported from HICs and most PAHO countries for the purpose of catching up immunization coverage with MMR or controlling outbreaks of either measles or mumps.

Finally, the literature looked to understand the prevalence of immunization in pharmacies indicating that community pharmacies may expand access to immunization, but the convenience of access did not appear to be sufficient to increase vaccination coverage rates.

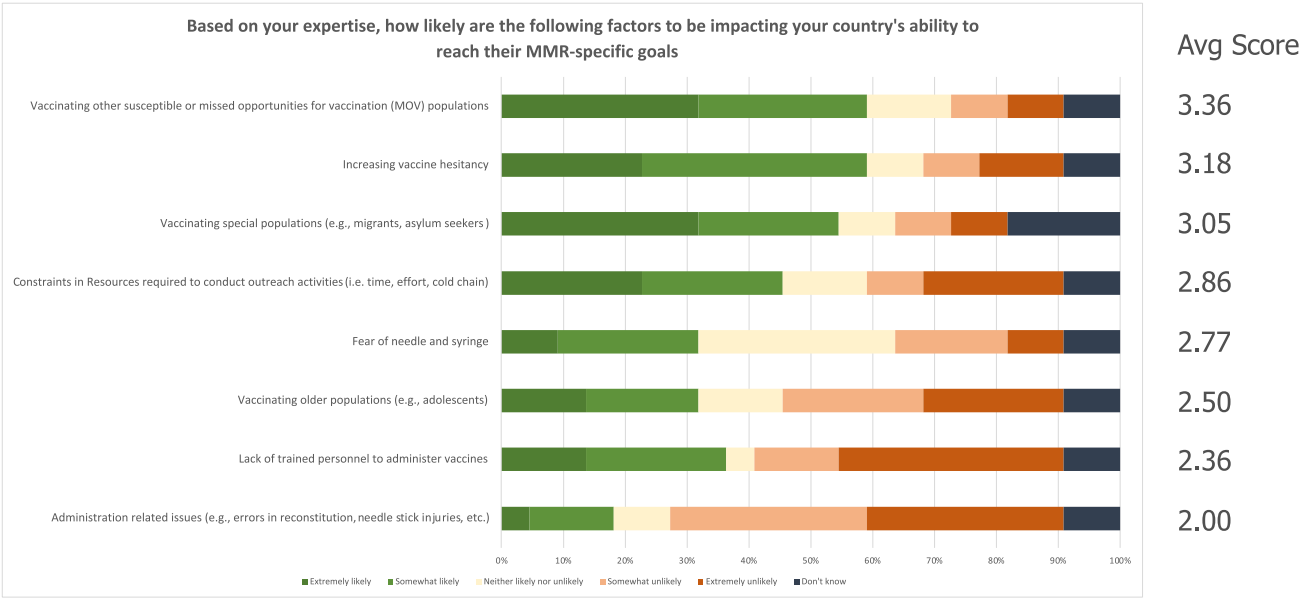
Annex 5. Key results from the MMR-MAPs survey

Twenty-two individuals provided full or partial responses to the survey. Table 3 provides an overview of the demographic characteristics of the survey respondents.

Table 3
Demographics of 22 survey respondents for MMR-MAPs.

Survey demographics	#	%
Organization type		
Academic or research institution	1	23 %
Agency of the United Nations	5	55 %
Implementation but not gov't or UN	1	5 %
Ministry of Health	12	5 %
Other	3	14 %
Total	**22**	100 %
Geographical location (WHO region)		
AFR	2	9 %
AMR	7	32 %
EMR	3	14 %
EUR	7	32 %
SEAR	0	0 %
WPR	3	14 %
Total	**22**	100 %

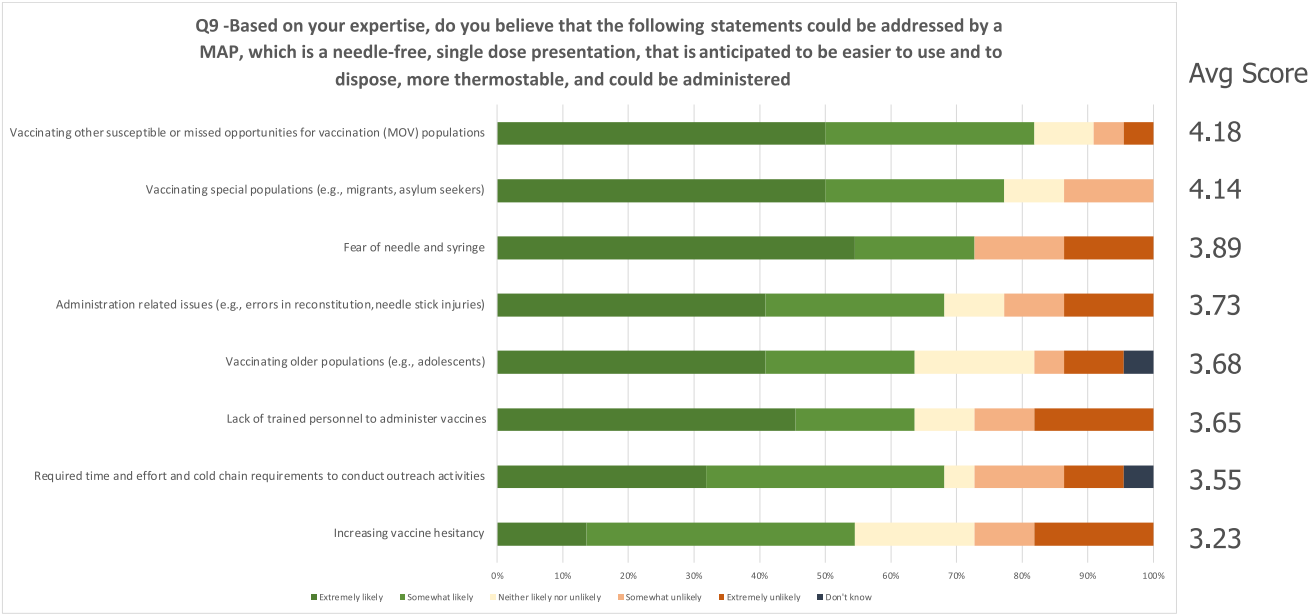
The respondents highlighted that vaccinating individuals that were previously missed opportunities (average of 3.36) and vaccine hesitancy (average of 3.18) as the most serious barriers to MMR vaccination (Fig. 5).



Average score based on weighted average of following scores: extremely likely = 5, somewhat likely = 4, neither likely nor unlikely = 3, somewhat unlikely = 2, unlikely = 1, do not know = 0

Fig. 5. Key factors impacting country's ability to reach their MMR-specific goals.

When asked if MAPS could address some of the identified barriers, the respondents felt that MAPs could on a whole address the identified barriers to some extend with its ability to reach missed opportunities and special populations as well as reducing needle-phobia as the top three barriers (Fig. 6).



Average score based on weighted average of following scores: extremely likely = 5, somewhat likely = 4, neither likely nor unlikely = 3, somewhat unlikely = 2, unlikely = 1, do not know = 0

Fig. 6. Key barriers to be addressed by MMR-MAPs.

The respondents confirmed that use cases 1 to 4 would be extremely important for MMR-MAPs, with use case 2 scoring the highest average at 3.82 followed by use case 1 at 3.68 (Fig. 7). While use cases 5 and 6 had more mixed feedback on their importance, scoring 2.50 and 2.45, respectively, highlighting the need for further discussion and exploration (Fig. 7).

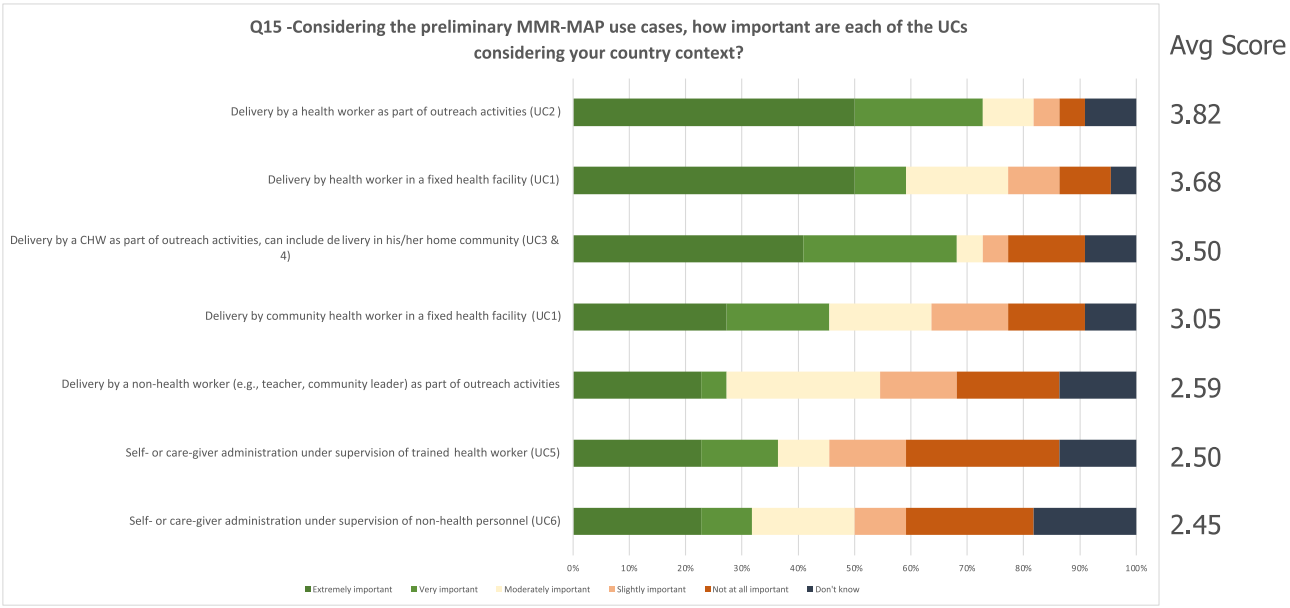


Fig. 7. Importance of proposed MMR-MAP use cases.

Annex 6. Key results from the MMR-MAPs focus groups

Through the virtual focus groups and the one-on-one telephone interviews, we consulted 9 individuals on the MMR-MAP use cases. One individual is a WHO regional focal point for measles, five individuals represented countries that currently utilize MMR vaccines, and three individuals are regulatory experts.

The overall sentiment towards MAPs was again positive with many highlighting its potential ability to address some of the barriers they regularly see as well as to potentially reduce some burden on health workers and the immunization system, particularly related to cold chain. However, in countries with high routine coverage, they did not necessarily view MAPs as needed to replace the needle and syringe in this setting but thought that it could be useful in a campaign or outreach activities.

The feedback received also showed hesitation towards use cases 5 and 6 related to self-administration with some respondents highlighting potential legal issues, lack of training, monitoring of AEFIs, fake vaccines, or rumors. Although there was hesitation on use cases 5 and 6, the potential self-administration was played out by some respondents, indicating potential during mass vaccination campaigns, if vaccinating adolescents or the elderly age group, or for use in pharmacies. Many highlighted the use of a gradual approach if self-administration were to be seriously considered.

The respondents generally agreed with the proposed use cases and did not offer many edits to change their definition.

Annex 7. Key results from the TCV-MAPs rapid literature assessment

Based on the search methodology employed, 277 articles were identified and the abstracts of each were reviewed for relevance to the definition of the TCV use cases. Based on the abstract review, 72 articles were identified as relevant and were reviewed in detail, with key information extracted from each article. The literature sought to understand 1) the distribution of typhoid disease burden at both national and sub-national levels, and which countries possessed data about drug-resistant typhoid; 2) the countries currently using TCV, how that corresponds to the distribution of typhoid disease burden, the evidence being used to inform introduction decisions, and to identify the countries and delivery strategies being used to for typhoid polysaccharide vaccines; and 3) the extent to which typhoid vaccines are recommended and used in military-serving populations. Due to the highly heterogenous nature of available data on typhoid both between countries and within countries due to incomparable diagnostic or epidemiological methods and covering different time periods, the rapid literature assessment was unable to identify information needed to answer the identified research questions.

Annex 8. Key results from the TCV-MAPs survey

One hundred and fifty-five individuals either partially or fully completed the survey. Table 4 provides an overview of the demographic characteristics of the survey respondents.

Table 4
Demographics of 155 survey respondents for TCV-MAPs.

Survey demographics	#	%
Organization type		
Academic or research institution	70	53 %
Agency of the United Nations	4	3 %

(*continued on next page*)

Table 4 (*continued*)

Survey demographics	#	%
Civil society or non-governmental organization	20	15 %
Government agency or department	15	11 %
Philanthropic organization	10	7 %
Vaccine manufacturer or developer	5	4 %
Other	9	7 %
Total	**133**	100 %
Geographical location (WHO region)		
AFR	48	36 %
AMR	23	17 %
EMR	4	2 %
EUR	23	19 %
SEAR	22	17 %
WPR	13	19 %
Total	**133**	100 %

When respondents were asked to rate the usefulness of a TCV-MAP to reach the different target populations, more than 70 % of the respondents indicated their potential utility to reach 2–15-year-olds and <2-year-olds (Fig. 8). While more than 50 % of the respondents thought TCV-MAPs would be useful to reach food handlers and 15–45-year-olds. ~45–49 % of the respondents felt that TCV-MAPs would be useful to reach Travellers, health workers, and military personnel.

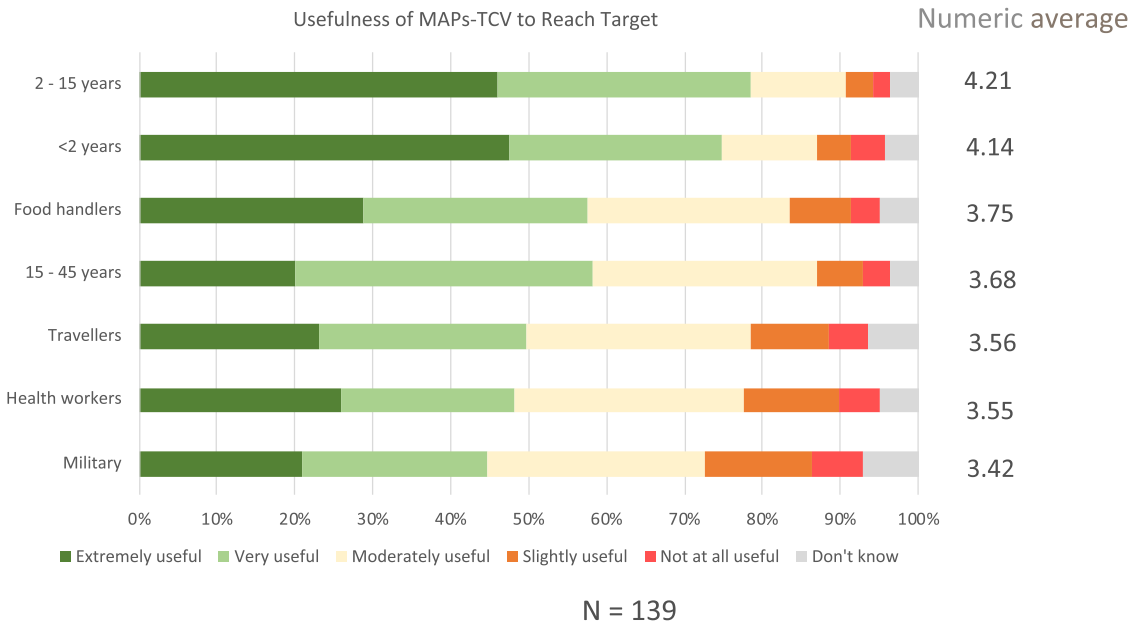


Fig. 8. Usefulness of TCV-MAPs to reach specific target populations.

Suitable delivery locations were also explored, and participants indicated that TCV-MAPs would be useful in all delivery locations with public settings with some health services being rated as the highest (Fig. 9). The stratified analysis indicated that those who were classified as "implementers" tended to have a higher perceived usefulness for TCV-MAPs in public settings rather than private settings.

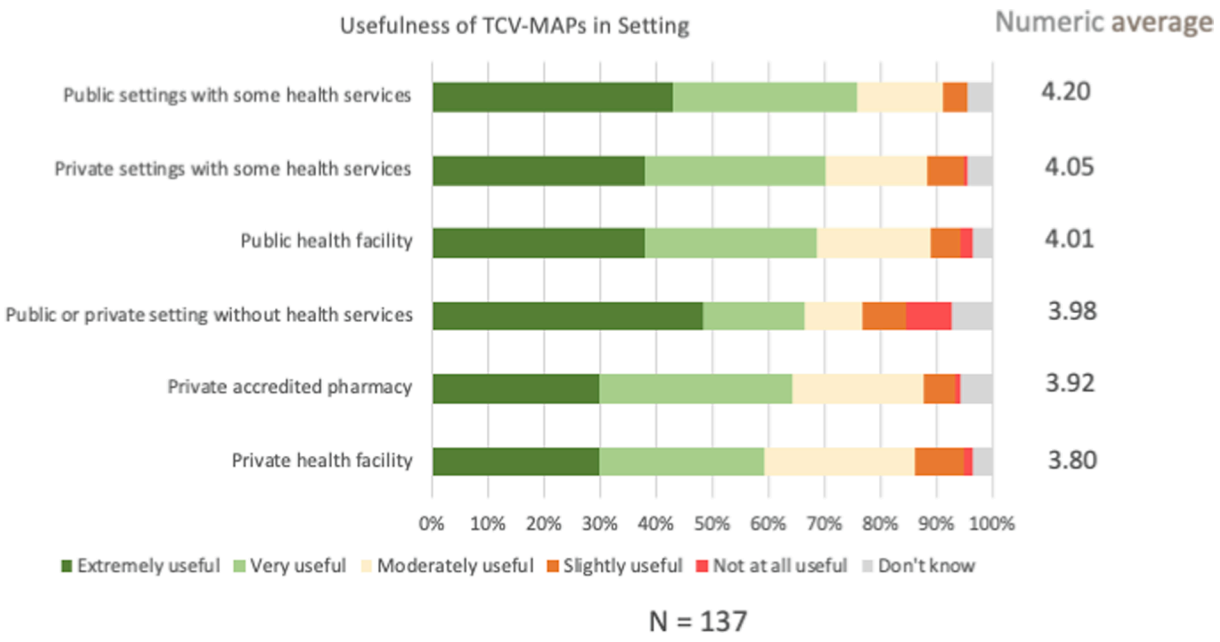


Fig. 9. Usefulness of TCV-MAPs in different delivery settings.

Finally, respondents were asked to rate the perceived likelihood of administration of TCV-MAP by different types of health and non-health workers. Over 65 % of the respondents felt that health workers such as doctors, nurses, midwives, community health workers, and pharmacists, would be extremely likely to deliver TCV-MAPs (Fig. 10).

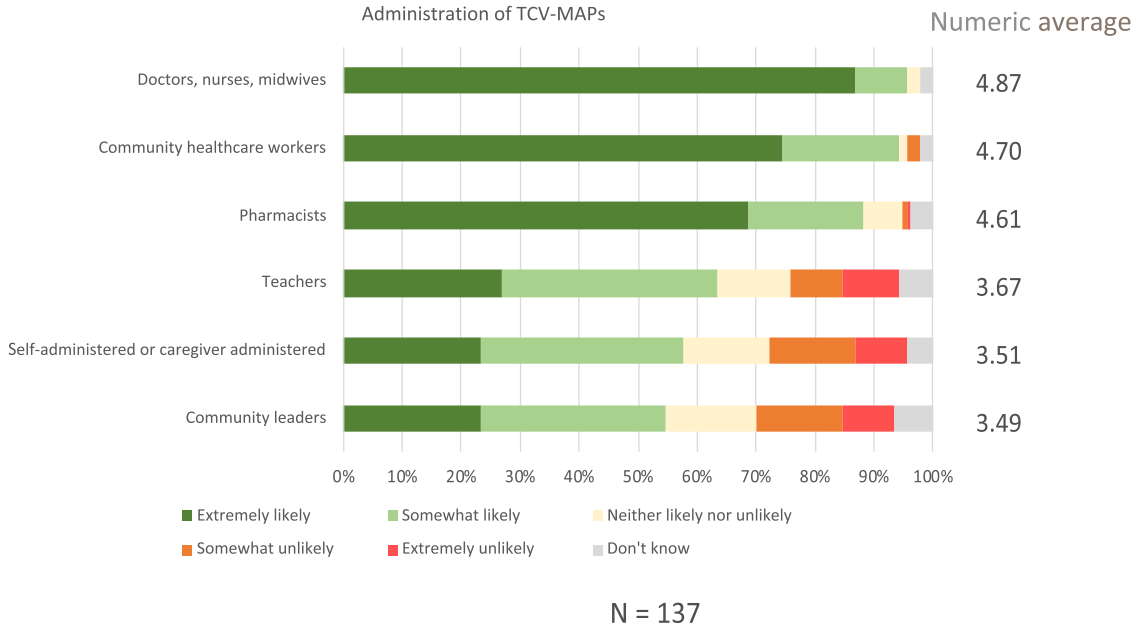


Fig. 10. Different types of TCV-MAPs administration by health and non-health workers.

Annex 9. Key results from the TCV-MAPs interviews and focus groups

Overall MMGH discussed the preliminary Use Cases and country archetypes with 23 experts and country representatives from India, Liberia, and Kenya. The feedback obtained from the experts and country representatives did not indicate a significant change would be needed in the proposed Use Cases and country archetypes. Several experts suggested calling out more clearly special populations such as refugees and travellers as well as certain delivery settings such as security risk areas or disaster settings.

Country stakeholders also highlighted that any new presentation should work within the delivery current systems and support the ongoing efforts to strengthen those systems. It was noted that MAPs could be used to help revitalize school-based vaccination by providing outreach or mobile services and that pharmacies do not play an important role in many national immunization programmes due to challenges related to quality control and supervision. The importance of understanding costs of the MAP presentation and how this may compare to other vaccines or other priorities was

flagged as a key consideration for country-level decisions.

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