REACHING ZERO-DOSE CHILDREN

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

PRODUCED BY: AZIE J, LALIKA M, INGLE E, SETH A, SHRESTHA P & PATEL R

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ENTERSTRATEGIC ANALYSIS,
RESEARCH & TRAINING CENTER
Department of Global Health | University of Washington

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1. Introduction

1.1 Project Overview

The Global Delivery Programs (GDP) team at BMGF aims to support prevention of 7-8M deaths from vaccine-preventable diseases and eradication of polio by 2025. GDP works with partners to ensure that low and middle-income countries (LMICs) can carry out high levels of routine and supplementary immunization activities that are effective, equitable, sustainable, and timely, focused on serving the most vulnerable.

In this context, one of the focus areas for GDP is to reach a greater portion of "zero-dose children", i.e., children who do not receive a single vaccine shot and are left entirely out of the immunization system. These children account for ~75% of under-vaccinated children. This means that most children who receive their first set of vaccines are highly likely to receive the remaining vaccines. Reaching these missed communities of zero-dose children is critical to both achieving equity and saving the greatest number of lives. In recent years (2016-2019), while Gavi countries have made some progress (~17-20%) on reducing the number of zero-dose children, this observed progress occurred in a few select countries.

In recent years, key global partners (such as Gavi, WHO and UNICEF among others), with support from the Foundation, have undertaken substantial work to understand *who* zero-dose children are, *where* they reside (characteristics, distribution) and <u>what</u> tools are needed to reach them. The challenge ahead is converting identification to immunization, including having a better understanding *why* these communities are underserved and generating appropriate programmatic strategies to reach them.

Given the Foundation's desire to better understand the barriers and potential interventions to reach zero-dose children, the GDP team has engaged University of Washington's Global Health Strategic Analysis and Research Training Program (START) team to conduct research on reaching zero-dose children. The findings from this research will help inform GDP team's strategic goals in immunization over the next five years, as well as help generate ideas for further investments, including gaps where further evidence generation and testing is needed.

1.2 Research Questions

The key research questions for this study are given below:

- Identify barriers to vaccination for communities with high rates of zero-dose children;
- Identify successful interventions to reach zero-dose children and learn from health and nonhealth programs on finding and serving these zero-dose children (e.g., "last mile" efforts); and
- To understand the cost effectiveness and sustainability of these interventions and identify any specific considerations, such as gender-related barriers, for these interventions.

1.3 Study Methodology

This study was conducted in two phases, with the first phase focused on identification of barriers to reach zero-dose children followed by the second phase of the research which included grey literature review and key informant interviews (KII) to gather insights on interventions to reach zero-dose children. Specific details on the literature review methodology and KIIs are described below.

1.3.1 SEARCH STRATEGY IN PUBMED

A search strategy was developed in PubMed to identify research articles on barriers to reach zerodose children. "Zero-dose" was used as the key concept for the search and terms such as "DTP-1", "undervaccinated" and "unvaccinated" were used as proxies for zero-dose children. Time period for the search strategy was limited to 2000-2021. A total of 1004 articles were extracted from PubMed for initial screening. After the initial screening and title and abstract review, 29 studies were selected for inclusion in this review.

("child"[MeSH] OR child* OR "pediatrics"[MeSH] OR pediatric* OR paediatric*)

AND

(challenges OR barriers OR obstacles OR disparity OR inequity OR coverage)

AND

(vaccination OR vaccines OR immunization OR immunisation OR vaccin* OR immuniz* OR immunis*)

AND

("zero dose" OR "zero-dose" OR "DTP1" OR "DTP-1" OR "DPT1" OR "DPT-1" OR unvaccinated OR undervaccinated)

AND

(2000:2021[pdat])

1.3.2 GREY LITERATURE REVIEW

To conduct the grey literature review, we searched the terms "zero-dose" and "unvaccinated" to find popular articles and organizations working in this field. Additionally, we referred to sources provided to us by The Foundation and other researchers studying this topic. We included all relevant articles and proceeded with a snowball approach where we followed links provided and sources used by the primary sites we were finding.

1.3.3 KEY INFORMANT INTERVIEWS

We followed a snowball approach to identify key experts to conduct KIIs on identifying barriers and interventions to reach zero-dose children. We contacted lead authors of research articles published on zero-dose children and also connected with implementing organizations working on last mile delivery efforts for immunization. The table below includes the names and affiliations of the key experts who provided valuable insights on reaching zero-dose children.

Table 1: Key Experts Interviewed

Name	Title	Group/Affiliation
Dr. Gagandeep Kang	Professor	Christian Medical College, Vellore, India
Dr. Mira Johri	Professor in the Department of Health Management, Evaluation and Policy	University of Montreal School of Public Health
Emily Lawrence	Senior Manager- Research, Evidence and Learning	Village Reach
Dr. Emmanuel Mugisha	Director- Typhoid Vaccine Acceleration Consortium & Senior Technical Advisor for Immunizations	PATH- Uganda
Dr. Alyssa B. Sharkey	Lecturer in Global Health and Senior Health Specialist, Implementation Research	Princeton University
Dr. Naveen Thacker	Leading IPA Vaccine Trust Project, ex-CSO representative on Gavi Board,	International Pediatric Association

2. Background on Zero-Dose Children

In this section, we provide a brief background on characteristics and distribution of zero-dose children, largely based on our grey literature review.

2.1 Who are Zero-Dose Children

Zero-dose children refers to those children who have failed to receive even one of the routine vaccinations (1–3). The diphtheria–tetanus–pertussis (DTP) containing vaccine is one of the few vaccines universally present in all national vaccination schedules for children under one year of age. Thus, it is a useful to measure the proportion of zero-dose children operationally by an indication of those who have not received the first dose of DPT (DTP-1) by 12 months of age.

2.2 Current State of Zero-Dose Children

Globally, the number of zero-dose children fell from 56.8 million in 1980 to 14.5 million in 2019 (4). According to the Global Burden of Disease (GBD) estimates, Southeast Asia, east Asia, and Oceania had the largest reductions in zero-dose children during this time. However, the absolute number of zero-dose children still remains high. This puts nearly 13 percent of the global children population at a very high risk of suffering and dying from vaccine-preventable diseases, since nearly half of these deaths is attributed to the unvaccinated status of these children (5–7).

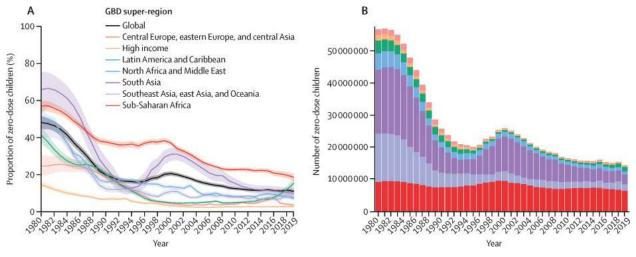


Figure 1: Proportion (A) and total number (B) of zero-dose children, globally and by GBD super-region, 1980–2019 (Source: GBD)

Most of the zero-dose children live in low- and middle-income countries (LMICs). In 2020, 16.6 of the 17 million zero-dose children lived in LMICs—with 71 percent of them living in middle-income countries (MICs) and 26 percent in low-income countries (LICs). Additionally, more than 65 percent of zero-dose children lived in 10 countries of India, Nigeria, Democratic Republic of the Congo, Pakistan, Ethiopia, Indonesia, Philippines, Angola, Mexico, and Brazil (8). Furthermore, evidence shows existence of

differential geographic distribution of zero-dose children across LMICs, with high prevalence observed in remote rural but also urban poor settings (9–12). For instance, in Ethiopia and the Democratic Republic of Congo, zero-dose children are concentrated in remote rural areas, but in Pakistan these children are concentrated in urban poor settings. Similarly, nearly 20 percent of zero-dose children live in conflict-afflicted areas, with the highest figures originating from Nigeria (2,13).

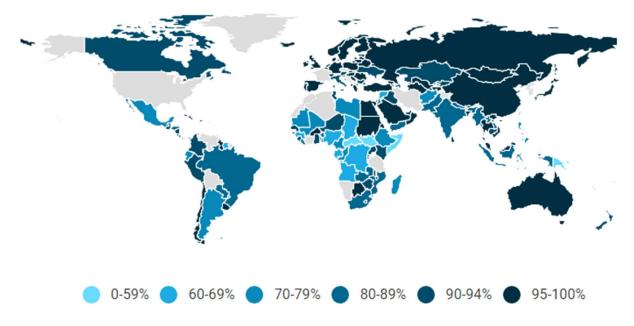


Figure 2: DTP-1 coverage unreached children by country, 2020 (Source: UNICEF)

The ongoing COVID-19 pandemic has also aggravated the zero-dose children issue, especially in LMICs (2,14). According to Gavi and Scaling Up Nutrition, in Gavi-eligible countries alone, the number of zero-dose children has soared by approximately 30 percent during the pandemic (15). This increase led to a 4-percentage point decline in vaccination coverage in 2020, with the most vulnerable populations being the most affected.

The next section discusses the key barriers to reaching zero-dose children across these settings.

3. Barriers for Zero-Dose Children

A systematic review conducted by Rainey et.al. identified 19 reasons for non-vaccination of children based 11 peer-reviewed articles published from 1999 to 2009. These reasons included factors related to immunization systems, parental attitudes and knowledge, family characteristics, and issues related to communication and information on vaccination (16). The study also noted that the factors related to under-vaccination (i.e., receiving at least one but not all recommended vaccinations) were similar to those for zero-dose children. Further, the authors identified several areas of improvement in immunization systems, such as improving vaccine supply, health worker training, and outreach services, to ultimately improve vaccination rates among children. However, they acknowledged that factors related to under-vaccination and non-vaccination due to parental knowledge and attitudes are more difficult to address and require contextualized interventions.

In this section, we elaborate on the specific barriers to reaching zero-dose children as they relate to immunization systems, parental knowledge and attitudes, and individual-level barriers.

3.1 Health Systems Barriers

3.1.1 PROGRAM COST TO REACH ZERO-DOSE CHILDREN

Gavi is one of the leading vaccine providers in the world, especially for reaching traditionally underserved populations. Since 2010, trends have shown that a large proportion of zero-dose children live in MICs that are not eligible for as much external funding as LICs. In 2019, it was found that 69% of zero-dose children live in MICs. Further, 21% of zero-dose children live in non-Gavi eligible MICs or Gavi-transitioned countries (17). As countries transition away from donor programs to rely more on domestic vaccination programs, some zero-dose children are left behind before they are targeted through programs and policies. Many MICs including Brazil, Mexico, and the Philippines have experienced a decline in DTP-1 coverage as their GDP increases and they shift from low to middle income status (18). The 2030 Immunization Agenda for MICs forecasts additional challenges in the next decade citing financing requirements, inequities, and the added burden of global pandemic (17).

Further, the cost to reach a zero-dose child is found to be three to four times higher than the cost to reach other children who are already being immunized (5,19). The program cost barrier is a large part of what is preventing routine immunizations specifically in MICs, who are less eligible for external funding for reaching zero-dose children on their own. As immunization systems in MICs increasingly become more independent, they are navigating delivering routine immunizations before zero-dose children can be made a priority.

3.1.2 ACCESS TO AFFORDABLE VACCINES AND RELATED EQUIPMENT

Related to program costs, access to affordable, quality vaccines, and vaccine-related equipment are also key barriers to most LMIC's ability to reach zero-dose children. Several factors associated with inadequate health systems seem to drive the prevalence of zero-dose children. For instance, evidence from Uganda point to vaccine stockouts, poor cold supply chains, lack of vaccination staff, and

underequipped vaccination facilities as barriers to zero-dose children vaccination (20). MICs especially are limited by financial and legal barriers that result in sub-optimal procurement practices. Their access to affordable products is limited by poor policy that further inhibits long-term planning and forecasting (17).

Further, there are additional incurred costs in resources to maintain the cold chain to store vaccines and the cost of delivery. Limited political will, inability to finance independent vaccination programs, and unaffordable vaccine prices are part of what is contributing to low vaccine coverage in general. These barriers are amplified with the additional costs of reaching zero-dose children as described above.

3.2 Parental Knowledge and Attitudes

3.2.1 AUTONOMY TO MAKE HEALTHCARE DECISIONS

Inter-generational influence plays a huge role on immunization decision-making of some families of zero-dose children. In many extended families, most mothers have limited autonomy over immunization decision-making for their children despite being their primary caregiver; instead, decisions are often driven by mothers-in-law or partners. In traditionally patriarchal societies, such as Nigeria for instance, women have stated concerns about going against wishes of their male partners or mothers-in-law to vaccinate their children for fear of being abandoned (21).

In another setting in Afghanistan, approximately 60% of children are under-vaccinated or non-vaccinated. One of the major barriers cited for non-vaccination and under-vaccination of children is lack of maternal autonomy to make decisions regarding vaccination of their children. Existing studies suggest that engagement with community and religious leaders to increase women's autonomy could lead to downstream increases in childhood vaccination coverage (22).

3.2.2 TRUST IN INSTITUTIONS

Members of communities with limited resources and poor healthcare infrastructure often have little trust in the healthcare system and therefore may be more hesitant to vaccinate their families. This is true of communities with poor health systems and also of migrant communities who do not have well established and consistent primary care. Trust is a crucial factor in the choice to vaccinate and to engage with the systems that make vaccination possible (23).

As an example, a study conducted by Stoop et.al. on mistrust of government institutions and child vaccination coverage in Africa found that institutional mistrust (including head of state, parliament, electoral system, courts and local government) was negatively associated with the likelihood that a child had received each of the eight basic vaccinations. A 1 SD increase in the institutional mistrust index was associated with a 10% increase in the likelihood that a child is non-vaccinated (24).

Further, factors that inhibit vaccine uptake can be seen on an organizational level where mothers are unable to access vaccination services. Attitude of healthcare workers can have a positive impact on childhood vaccination outcomes as well as the atmosphere of the centers. Centers with cooling systems, drinking water outlets, good places to sit and wait, incentives such as bed nets, vitamins and other incentives have been found to increase childhood immunization uptake (21).

3.2.3 MISCONCEPTIONS AND FEARS REGARDING VACCINES

More women also show disinterest in immunizing their children due to ignorance fueled mainly by fear of side effects of vaccination (25). According to existing literature, misconceptions that the children could become weak and riddled with fever after taking vaccination and that vaccination is a western culture introduced to make children weak are common myths that lead to non-vaccination of children.

3.3 Socio-economic Barriers

Bosch-Capblanch et.al. conducted a study to understand the individual-level barriers related to non-vaccination of children across 96 LMICs (26). The result from their analysis is presented in the chart below. Based on the study, the median likelihood of being non-vaccinated was greater among the poorest households as compared with the richest and children with less educated caregiver and caregiver' partners.

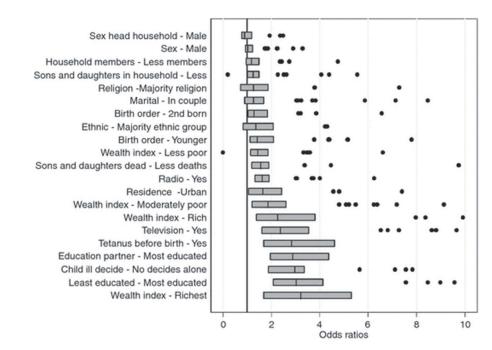


Figure 3: Odds Ratio by predictor. Mid-lines in boxes: median; lateral extremes in boxes: 20th and 75th percentiles; dots: individual surveys. Data from the unique or most recent survey in each country.

We discuss some of these individual-level barriers in detail below.

Religious Beliefs

Religious beliefs are another factor associated with non-vaccination in some LMICs (25,27). For example, in India, Muslim children are 2.2 times more likely to be non-vaccinated compared to Hindu children (28,29). Similarly, countries such as Pakistan, Afghanistan and Nigeria have particularly

experienced setback in vaccination due to mistrusts in vaccination attributed to western plots to reduce the population believed to be their greatest strength, a notion often stoked by religious leaders.

• Education Level

Across geographies, there is a direct correlation between level of education and immunization ratesthose with higher education are more immunized and the opposite is also true. When it comes to zerodose children, they frequently have the lowest education rates for the caregiver and caregiver's partner (31). Without vaccines, these communities face the compounded vulnerabilities of outbreaks of vaccine preventable diseases without the resources to respond. This feeds the cycle of poverty and impedes an individual and community's ability to improve as the resources they have must be used to pay for treatment.

• Poverty

Poverty is also a key barrier to receiving even one dose of a vaccine for many children when combined with other factors. According to the Deputy CEO of Gavi, Anuradha Gupta, "zero-dose children are the face of extreme poverty, with two-thirds of them living in households subsisting on less than \$1.90 per day" (32).

3.4 Barriers for Zero-Dose Children by Setting

3.4.1 URBAN-RURAL GEOGRAPHY

Evidence shows differential rate of vaccination among children depending on where they live. For instance, in a study conducted in India, children from urban areas are consistently less likely to be unvaccinated compared to those from rural areas (33). However, in some settings, relatively higher rates of non-vaccination are observed in peri-urban areas.

Related to this, the prevalence of zero-dose children is also be aggravated by poor road conditions in rural and peri-urban areas. These conditions make it difficult for the caretakers to bring their children to immunization centers. Similarly, healthcare workers are not able to travel for community immunization outreach programs aimed to be implemented in distant rural areas, which usually do not have access to health facilities (20).

While these barriers are similar for most zero-dose children, there is no generalizable criteria for whether a child will be missed by vaccination efforts. What is true in one area may not be true for another, even within the same country. For example, a study in Tanzania found that low paternal education, lack of antenatal care, and home births were significantly associated with low vaccination rates only in rural settings and not in urban settings of the same region. Wealth and mothers education were found to be factors in both urban and rural areas, but this finding suggests that practitioners should be wary of using evidence from one setting to infer barriers in another (34). Localized approaches will likely be the most successful in going the last mile to reach the zero-dose child.

3.4.2 REMOTE RURAL POPULATION

Existing research highlights the importance of targeting specific geographical locations for vaccination campaigns. A recent study found that 42.2% number of children who have never been vaccinated (i.e., zero-dose) and 24.1% severely under-vaccinated children in Massai nomadic pastoralist community in Kenya largely pointing to the frequent mobility of women and children as a key factor. Children in these geographic settings were also found to be nine times likely to be unvaccinated than children in settled homes (35).

Further, most remote villages and areas riddled with tribal wars and insurgencies suffer hugely from receiving regular and consistent services due to disruptions from conflict, violence towards healthcare workers, inciting fear, and making it difficult for governments to operate ideally in such places (21).

3.4.3 CONFLICT SETTINGS

According to the CDC, fragile or conflict-affected countries accounted for 44% of zero-dose children in 2019 (18). The risks of being unvaccinated in a conflict zone have greater consequences than risks elsewhere because of compounding factors like malnutrition, increased spread of infectious or communicable disease, and lesser access to care. In countries experiencing conflicts, vaccine preventable diseases significantly add to the existing death toll of the conflict itself.

Conflict adds a layer of multifaceted barriers to the process of vaccinating zero-dose children. Fear from donors and vaccine delivery teams may deter efforts to even reach children in conflict settings in the first place. Conflict zones also create barriers to the spread of information as communities in these setting are often susceptible to silo sources of information emanating from the dominating group's rhetoric. This is seen in Borno State, Nigeria, for example, where demand for vaccines, even when they are readily available, decreased due to suspicion, misinformation, and rumors circulating amongst the community. Mothers in this region were also scared of holding on to vaccine cards for fear of being labeled traitors by Boko Haram (36).

When vaccine efforts are undertaken, they must navigate the additional barriers of safety, negotiating access with leaders and military groups in certain territories, and transportation of vaccines through uncertain landscapes. Save the Children lists recommendations for overcoming additional barriers in conflict situations including additional surveillance and early warning systems, extensive planning and monitoring, stockpiling, extending age requirements for vaccines, mobilizing community demand, and civil society partnerships. They also note that vaccine campaigns in conflict areas tend to be more successful when integrated with other humanitarian activities (37).

4. Interventions to Reach Zero-Dose Children

Given the barriers highlighted in the previous section, zero-dose children may be subjected to different socio-cultural, economic, and political conditions that hamper efforts to vaccinate them than children who receive at least one vaccine. Data to date suggests that while innovative technological interventions may ensure that vaccines reach remote areas or clusters of zero-dose children based on their location, they do not guarantee an increase in vaccine uptake. Therefore, for these interventions to be effective and sustainable, there is a need for combining interventions that help the vaccines reach these communities with those aimed to improve vaccine acceptance in the community and integrate these solutions into the existing primary health care structures.

In this section, we elaborate on the specific interventions for reaching zero-dose children in three different specific types of settings where zero-dose children are commonly found: urban areas, remote rural population, and conflict settings. Based on our research, the proposed solutions to reach zero-dose children are in line with Gavi's IRMMA (Identify-Reach-Monitor and Measure- Advocate) Framework, particularly around integration with primary health care services across the life course (38). These interventions are described below in detail.



Using zero-dose strategy to strengthen equitable Primary Health Care across the life course

Figure 4: Using a Primary Health Care strategy across the life course to reach zero-dose children (Source: Gavi)

4.1 Urban Slums

Large urban slum areas are characterized by limited access to quality healthcare services generally, and certainly include zero-dose children (39,40). In some settings, children may never receive any vaccines despite having access to immunizations services. As discussed in the previous section, this may be due to lack of caretaker's knowledge, mother's lack of autonomy, mistrust of the government, or public health authorities among other factors. Therefore, cross-cutting approaches geared towards

improving immunization service delivery and building demand and trust among the people are vital to ensure an increase in vaccine coverage among zero-dose children in urban areas, with particular emphasis on slum areas.

4.1.1 HEALTH SECTOR INTERVENTIONS

In the following section, we describe different interventions that can help address this challenging issue in the urban setting.

• Building Trust in the Community

Community's cultural norms must be explored to tailor appropriate and culturally sensitive messages to address this issue. Additionally, the immunization advocates should be those whom the community trusts. For example, in Afghanistan, community-based outreach immunization programs have leveraged *Ulema*, religious leaders, to promote immunization. The same strategy is documented in urban settings in Chad, Nigeria, Pakistan, and India. In Chad, village chiefs and community registers were involved in promoting vaccination. India is leveraging Accredited Social Health Activists (ASHA), who receive performance-based incentives for promoting vaccination in urban areas (41). In Nigeria, religious and traditional leaders receive non-monetary incentives to recognize them for good performance in immunization-related promotional activities (42). Lastly, Pakistan is leveraging slum health committees—formed by the residents of slums —to reach zero-dose children in urban areas (43).

Leveraging Community Assets

As discussed previously, zero-dose children are likely to be residing in areas with other hesitant families also living in the same community. Therefore, apart from attaining community buy-in, community members should be directly involved in interventions to reach these children. For instance, Ethiopia formed a network of informants and influential community members and tailored crucial components of the immunization services, such as where and when to hold the services. In Kenya, polio survivors were leveraged to advocate for immunization. Similarly, India implemented a Mother Meeting strategy to facilitate information sharing, promote healthy behavior adoption, and establish trust through women-support groups (44).

Strengthening Health Monitoring Systems

Incomplete and incorrect data makes it challenging to assess immunization coverage in LMICs and identify zero-dose children living in urban areas. Additionally, the lack of data disaggregation from urban areas masks the immunization inequities between slum and non-slum areas (45). Consequently, to address this issue, innovative health monitoring initiatives are paramount. For instance, India has developed an urban immunization dashboard using health management information systems, which is leveraged to reach unimmunized children (46).

Similarly, failure to detect adverse events post vaccination may fuel the existing misinformation regarding vaccines, thus leading to parents of unimmunized children refusing to vaccinate their children. Leveraging information systems to identify the events and manage them appropriately may help reduce misinformation, improving parents' trust. For instance, Uganda has developed the Vaccine Adverse Events Information Management System (VAEIMS) to detect adverse events after vaccination and manage them in a timely fashion.

• Tailoring Location and Timing of Immunization Services to Community Needs

When both parents tend to work outside the urban slum areas, it becomes difficult to take their children to the vaccination centers during the traditional working hours (32). Therefore, proper timing of vaccination services or extending vaccination hours is crucial to reach zero-dose children in urban slums. For example, Uganda moved vaccination outreach activities to weekends to improve vaccine uptake. Similarly, in Nairobi, Kenya, opening hours of immunization centers were extended to increase vaccination coverage. Kyrgyzstan leveraged mobile vaccination sessions organized by civil society organizations (46). A study conducted in Bangladesh showed that offering evening vaccination services in slum areas increased vaccine uptake significantly (47).

The distance of vaccination centers from the community also impacts vaccine uptake in urban areas. Therefore, strategic positioning of vaccination centers near the pockets of families with zero-dose children may help address the existing inequity. Innovative technology such as GIS can also be leveraged to map the existing distribution of vaccination sites and redistribute them. For example, GIS technology was utilized in Karachi, Pakistan, to map the distribution of vaccination centers and vaccinators (40). This strategy unmasked the inequity in the utilization of immunization services—which would not be revealed if the data were to be presented in tabular form alone. These findings informed the development of subsequent interventions to reach unvaccinated children. Similarly, Pakistan leveraged transit points such as bus stops and transit areas between districts—deploying vaccinators around these areas. In Afghanistan, permanent transit teams and cross-border vaccination centers were established, supplemented by GIS monitoring.

• Integrating Strategies

A disconnect in micro-planning activities and several departments serving the slums may harm immunization coverage. Therefore, joint micro-planning and integration of fieldwork from all departments can be beneficial to increase the quality of outreach services. For instance, Myanmar successfully combined microplanning and an open-source GIS application, the QGIS project, to develop strong micro-plans when implementing its urban immunization strategy. Nigeria included outreach and mobile sessions for urban slums in its immunization session plans in line with the Reaching Every Ward (REW) micro-plan. In Uganda, vaccination outreach in slum areas is combined with village health team (VHT) systems—a national community health worker program aimed to deliver essential health services and education—in urban areas (46,48).

Linking Services to Improve Vaccine Uptake

Some zero-dose children in urban areas may already have access to other health services. Establishing a referral system between these services providers and immunization centers would help reach them. For instance, in its Roadmap for Achieving Universal Immunization Coverage in Karachi, Pakistan is building a referral system to ensure that unvaccinated children attended in pediatric departments are referred to immunization centers. Additionally, immunization services will be offered daily in those facilities known to receive a high load of pediatric patients (40,49).

4.1.2 NON-HEALTH SECTOR INTERVENTIONS

In this section, we highlight some non-health interventions which can influence immunization strategies to reach zero-dose children.

Leveraging Art to Increase Vaccine Uptake

One element that differentiates vaccines from commodities that reach every corner of the world, such as Coca-cola or Heineken, is advertisements. Advertisements influencing social acceptance of vaccines are scarce. In many LMICs, every bodega or shack is painted with graffiti or intentional advertising for commercial products. This approach is used by many phone service providers, making the likes of Airtel, Safaricom, and Vodacom household names in Sub-Saharan Africa. These images work because everyone sees them. The use of art for public health promotion has been shown to be effective and is widely supported, especially for campaigns against HIV, COVID-19, and stigma around mental health (50,51).

Bunn et al. conducted a review and found that art-based approaches are enough to *"facilitate inquiry, achieve significant reach and in some instances support demonstrable health-related change"* (52). Art can take many forms, but the most notable, accessible, and common is simple street art. The impact of arts-based approaches for public health messaging is seen in Zimbabwe, where UNICEF, in partnership with GOAL Zimbabwe, initiated an outdoor campaign to promote healthy practices to limit the spread of COVID-19. This project reached an estimated 2.5 million people, including 400,000 children and almost 200,000 pregnant and lactating women in three predominantly rural provinces (51). Since this approach has the potential to reach people regardless of access to technology, literacy, or language barriers, it can be leveraged to improve vaccine uptake for zero-dose children in urban areas.



Figure 5: Outdoor media campaign using art murals in Zimbabwe (Source: UNICEF Zimbabwe)

• Engaging the Community in the Decision-Making Process

The top-down approach to immunization limits engagement and ownership of the stakeholders, which, in turn, impacts vaccine uptake (53). One way to improve vaccine uptake is to engage the community directly in identifying and prioritizing their challenges (54,55). In case the challenges are non-vaccine ones, immunization strategies may be integrated to offer solutions to both. Urban slums tend to face many challenges, and slum dwellers are potentially the best people to identify them. For example, In India, *Humara Bachpan* has been organizing campaigns led by children to map their neighborhoods and identify, among other things, where play spaces should be located (56). Similar initiatives may be taken to engage the slum communities in identifying, for example, the ideal location or conditions of the immunization center or time to offer the services. Similarly, the communities may be engaged to map the services needed the most in the community, which can be leveraged to increase vaccine uptake.



Figure 6: Hand-drawn maps from Humara Bachpan project in India

4.2 Remote Rural Population

Remote and rural populations are often characterized by their remoteness in geographic accessibility and infrastructural development. Globally, there are 3.4 billion rural population (57) and unique health system challenges exist in these communities. Issues of geographic access, poverty, weak infrastructure for data and human resource, and lack of structural power are some reasons that define equitable vaccine coverage in remote and rural areas (58). Interventions that are particularly targeted to reach zero-dose children within these populations also need to consider these social, economic, and cultural determinants that shape health system deliveries in these areas. Some of the interventions to reach zero-dose children in remote and rural areas are described below.

4.2.1 HEALTH SECTOR INTERVENTIONS

In the following section, we describe different health sector interventions that can help reach zerodose children in the remote and rural setting.

• Innovation in Vaccine Delivery

Due to the difficult geographical terrain and isolated settings of the rural areas, vaccine accessibility and quality is one of the main challenges. As explained by Dr. Kang during a KII, delivering the vaccines on time is important, but having a competent person to use them correctly is equally vital. Therefore, innovations in delivery mechanisms such as making vaccines safe, less wasteful and low resource-intensive could also potentially help in improving coverage and reaching zero-dose children. Some examples of such interventions are highlighted below:

> Remote temperature monitoring device: ColdTrace 5, a remote temperature monitoring (RTM) device, allows real-time monitoring of vaccine fridge temperature and power availability and uploads that data continuously. These RTM devices also send SMS to health officers to alert about any potential damage to vaccines. The data on the cold chain equipment on several health facilities can be monitored remotely via a dashboard helping to prevent any equipment failure and vaccine wastage. JSI in

partnership with Nexleaf Analytics has installed it in 120 immunization sites in Tanzania and 36 sites in Kenya which has helped in improving supply chain and storage of vaccines.

- Thermostable and durable vaccines: Rural areas are geographically difficult to reach, and vaccines need to withstand long days and harsh weather conditions. Therefore, microarrays that ensures stability of vaccines in high temperatures and solar direct-drive refrigerators that provides enabling conditions to store vaccines in electricity-deprived rural areas are examples of such alternative modes of delivery (59) (60). Solar-powered fridges have been used in Vietnam and reported to be appropriate for remote areas lacking electricity (61). Similarly, using lightweight and sustainable single-dose vials to prevent waste are also encouraged (62).
- Drones: Drones are a common discussion in the vaccine community, and routine immunization service delivery through drones have already made news in Ghana (63). However, many are wary of the lack of trained human deliverers and the "jab and leave" mentality this creates, thus, leaving people vaccinated but with no other health resources.

Improving Robust Data Collection

Before attempting to reach zero-dose children, understanding the actual size of population to target is also necessary. In an absence of a robust and timely data on this population, it becomes hard to conceptualize an estimated number of zero-dose children, thus, creating a fundamental issue of enumeration in developing and evaluating any intervention to reach them. Hence, interventions such as geospatial information mapping (GIS) have been used to map houses to get population targets and augment mass vaccination campaigns. For example, **Reveal**, a geospatial modeling platform is used in a pilot study in Zambia, where aerial satellite maps were used to identify built structures and locate zero-dose children (64) Another intervention that (65). could potentially be used in optimizing data

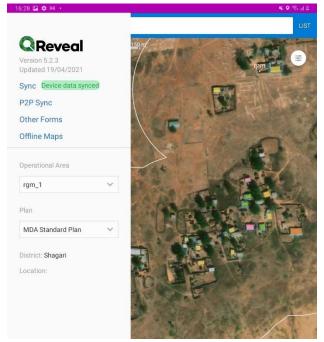


Figure 7: Reveal platform to locate zero-dose children

collection are the electronic immunization registries which allows using disaggregated data of the registered children to understand the population size and resource tracking (58). Besides, using digital and analytical approach, a simple and engaging way to record timely data in a rural health clinic is "Family folders" in Ethiopia (66). The healthcare workers get comprehensive data on both patients and their family through which they can monitor their health needs and easily reach them in case there are losses to follow up.

Health Systems and Workforce Integrated Solutions

Some of the popular interventions such as My village My Home and Reach Every District have been used for routine immunizations that target different health system levels and incentivize health workers. However, a strong emphasis on integrating other health services, particularly enhancing trust in immunization and health system among rural communities, can help amplify reaching zero-dose children through an already existing strong immunization platform. Some of these examples are elaborated below:

 My Village My Home (MVMH) is a community level tool funded by the USAID and led by JSI in India, Malawi and Timor Leste to record the births and vaccination dates of every infant in a community (67). This poster-sized material helps community-level workers, e.g., ANMs, ASHAs, and AWWs to visually assess the immunization status of all infants born within a year, the tool allows the community as a whole to monitor the immunization coverage of all the target infants in their village.



Figure 8: My Village My Home tool to track immunization status of children in India

Reach Every District (RED) 0 strategy has been adopted by the World Health Organization and UNICEF since 2002 (68). RED is a health micro-planning strategy to improve access to immunization and hard-to-reach beyond for populations by encouraging districts and health facilities to make micro plans to map barriers and identify solutions. The planning methodology operates through five operational strategies: re-establishing outreach services, supportive supervision, linking services with communities, monitoring & using data, and planning and managing resources.

Put these R.E.D tools into action

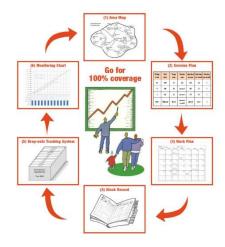


Figure 9: RED strategy tools for micro-planning

 Integrated Maternal and Child Health MCH program: Posyandu program is a community volunteer-led health post in Indonesia that offers an integrated MCH service including family planning, nutrition, and immunization at the village level (69). Since the mid-wives and community members run this program, it also provides a

sense of empowerment and inclusion into the community, thereby developing trust among the village members. Similarly, MomConnect South African in Department of Health uses a mechanism of registering births and provides information on when appointments are due. Vaccine messages be therefore can integrated into programs already reaching

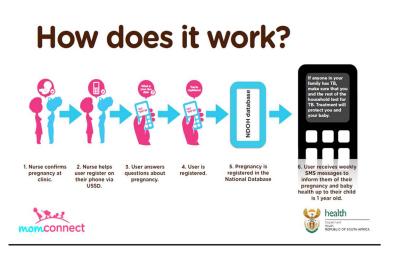


Figure 10: MomConnect platform to register births in South Africa

caregivers. Another example is the Vaccination Weeks Americas initiative, where at least 14 countries in the Latin America and Caribbean region have integrated other health services such as Vitamin A and deworming programs into the immunization services (70). This Pan-American initiative has also proven to advance equity in services and increasing coverage and access of vaccines.

 Integration with WASH services: WaterAid and RAVIN in collaboration with the Government of Nepal introduced hygiene behavior change practices into the national routine immunization services which showed a reinforcement in gaining trust in immunization services and improving immunization coverage.

• Community Engagement

Similar to urban geography, engaging communities is key in understanding where and how to reach zero-dose children in remote areas. Community members are the gatekeepers and most trusted individuals who can be leveraged to enter the community and ensure last mile populations are reached. As per Dr. Mira Johri, "*Trust barriers are often perpetuated if certain groups in the society do not receive health services like other advantaged groups*," and to target zero-dose children, diversification of services through more contextual representation of the caregivers helps to gain their trust. Therefore, immunization interventions should engage diverse community groups such as the women groups, religious leaders, traditional health workers, political chiefs, and tribal leaders. Particularly, soliciting community involvement generates demand and accountability for immunization and other health services (58).

Another approach to engaging communities is also about understanding that one size does not fit all, and interventions need to be contextual. This concept was exemplified in in two Indian states, where drumbeating was tested and considered as a culturally appropriate, low cost, and scalable method to aware community about the vaccination days and improve vaccination timelines among children in remote/rural populations (71). This initiative was accepted by the community and proven to be an effective intervention for mobilization and awareness.



Several other approaches have been Figure 11: Drumbeating initiative to improve immunization timeliness in India

outlined such as the Program Keluarga Harapan in Indonesia, offering direct cash transfers to mothers for participating in health and education services; and provision of food rations, medicine vouchers, motherhood kits, charm bracelets, and transport vouchers are non-monetary incentives that can be applicable to motivate families to vaccinate their children (58).

4.2.2 NON-HEALTH SECTOR INTERVENTIONS

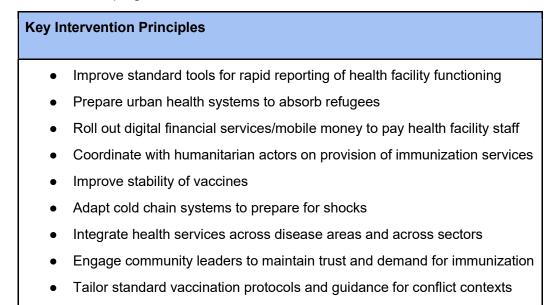
While health system-based interventions are vital and directly relevant to improving immunization efforts in remote and rural areas, issues and challenges to vaccinations are not only confined to health sector. According to Dr. Alyssa Sharkey, "Improving broader underlying issues like employment, education and trying to have better economy in these regions, [is] ultimately what's going to be needed to really change these families' lives." Therefore, examples in the non-health sector, largely based on integration with existing systems or structures, that can address broader structural determinants and influence the uptake of vaccines among hard-to-reach communities can also be explored. Some of these interventions include:

- Integration with animal health services: In Chad, vaccination services targeting both human and animal health achieved higher coverage among pastoralist communities (72). This integration of services among pastoralists was found to be more cost-effective, feasible and acceptable.
- Integration with agricultural services: Vaccine delivery in remote and rural populations can be pursued using agricultural supply chain vendors. Organizations such as the OneAcre Fund in Africa is reaching the last-mile communities with agricultural supplies and Digital Green in India is working towards increasing productivity and nutritional literacy among farmers (73). In some instances, such as COVID-19 pandemic, they also delivered health and hygiene products and vaccines (74). Digital Green, while targeting farmers and agricultural productivity, works with the community to develop educational videos on safe motherhood and family planning, which can also be extended to vaccine literacy and awareness to reach zero-dose children in remote and rural areas (75).
- Integration with communication channels: Communication platforms are often leveraged to reach large geographical areas and distant communities. Similarly, some of the efforts made to enhance vaccine literacy and acceptance involves radio broadcasts, SMS services, and community videos (58). For example, engaging radio station operators to spread knowledge around immunization and include a call-in option for community feedback to address their questions and concerns on immunization (76).
- Integration with the commercial sector: Public-private partnerships in the field of medicine and global health cannot be emphasized enough. The Project Last Mile is a collaboration between USAID, The Global Fund, BMGF, and Coca-Cola that leverages the network of the Coca-Cola System, pioneering public-private partnership to help improve uptake of life-saving health services and to enable medicines to go to the "last mile" and benefit communities in Africa. For example, Coca-Cola's supply chain has been successful in delivering lifesaving drugs in rural areas of Tanzania and is expanding in other African countries (77). The Project Last Mile has also become exemplary in using private sector market strategies for the uptake of public health services with its study in eSwatini for the engagement of young girls and adolescents in sexual and reproductive health services (78). Involving vaccines as a part of the private sector supply chain or market strategy to attract hard-to-reach communities can help in reaching zero-dose children. Another initiative that has gained growing attention in the wake of COVID-19 pandemic is the support of Tech Mahindra Ltd in last mile supply during the pandemic. The tech giant has now committed to improve the global supply chain of vaccines in order to control issues of vaccine counterfeit and stock-outs through the roll out of their "vaccine ledger" project (79). Rather than the siloed approaches, engaging with the private sector that are willing to commit to improving health services and delivery would be a win-win for both sectors.

4.3 Conflict Settings

According to the Equity Reference Group for Immunization (ERG), approximately 40% of zero-dose children live in fragile or conflict settings (80). Reaching these areas is therefore critical to vaccinating every child. Many of the interventions discussed previously for urban and rural settings

such as monitoring systems, cold chain enhancement, and drones can be adapted to conflict settings as well. Further, the ERG proposes the following key set of intervention principles to supplement vaccination programs in conflict zones:



While many zero-dose children are missed because of socio-cultural barriers, children living in conflict regions are unique in that the main barrier to their vaccination is physical access. This is shown in figure 12 by significant declines in vaccination during times of conflict where vaccination rates were previously higher. For example, DTP3 coverage in Syria went from 80% in 2010 to 47% in 2018 after conflict erupted (81).

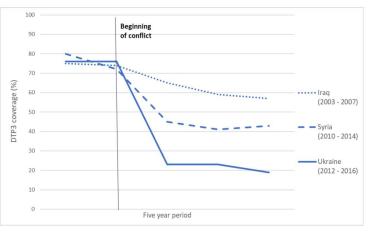


Figure 12: Decline in vaccination rates following conflicts in Iraq, Syria, and Ukraine

The previously higher rates of vaccination show that these people are not unvaccinated by choice, but because of the pervasive disruptions that conflicts cause to all areas of society. Though these children are less likely to be vaccinated, they are at higher risk of vaccine preventable diseases. Diseases spread rapidly in conflict affected regions because of lack of infrastructure, close living spaces for displaced peoples, and climate factors. Therefore, the interventions to reach zero-dose children in conflict are primarily those that will provide physical access. To address the disruptions in the supply chain, some form of political negotiation is necessary to guarantee the health and security of delivery teams and health care workers.

4.3.1 HEALTH SECTOR INTERVENTIONS

Specific examples of health interventions to reach zero-dose children in conflict settings are highlighted below:

• Monitoring and Data Sharing

One theme of this research is the "invisibility" of zero-dose children. Zero-dose children may not be registered with the health system and may not have a vaccination card or in many cases record of their birth. Therefore tracking, monitoring, and evaluation of zero-dose children is a barrier to implementers in this field especially in times of conflict and migration. To address this issue, some tested interventions could be Village Reach's Electronic Immunization Registries (EIR) program and the IRC's mReach tracing data platform that enables health workers to register children and track their immunization status (82) (83). This was used in settings including Somalia where mReach was further enhanced with Google Maps and along the Thai and Myanmar border where IRC used the Digital Health ID to trace migration and the vaccines received by migrants.

Another innovative form of monitoring and data tracking that has been shown to reduce fraud and save donor money is Biometrics (84). Biometrics uses fingerprints or iris scanning as a key for aid distribution and tracking migration. Biometrics such as iRespond have been used in various settings including Myanmar, Senegal, and Sierra Leone. Biometrics have also been used to require fingerprints or iris scans for food distribution by the WFP in refugee camps in Kenya and Jordan and can be utilized to track immunization status of zero-dose children (85,86).



Figure 13: Use of biometrics in refugee camps by WFP

In some cases where people are scared to have

vaccine cards for fear of retaliation or accusations of being government sympathizers. Vaccine cards may also be lost in migration. These technologies eliminate the need for a physical tracker of vaccination status like a vaccine card and may help overcome that fear as well.

• Monitoring Facilities

In addition to monitoring and data gathering for individuals, the data stream is disrupted, and misinformation is quick to take hold in conflict settings, hence monitoring of facilities is another necessary step that can facilitate supply chain demands and prevent escalation of stockouts. Health Resources and Services Availability Monitoring System (HeRAMS) is a system being used and developed by the WHO to monitor health systems and facilities functioning in various geographies (80,87).

• Engaging Health Care Workers

Vaccination is unique in that it requires a trained individual who is able to administer vaccines. Innovations in vaccines themselves like self-administrable vaccines are being discussed, but for now there is a human aspect of vaccine delivery. Part of what makes zero-dose children hard to reach in conflict zones is the added risk it poses to healthcare workers and the danger that often prevents many from being willing to take that risk. The loss of healthcare personnel in times of conflict can be drastic, though these health advocates have proven to be essential for successful vaccine delivery time and time again. An innovative approach to monitor safety of healthcare workers uses WhatsApp messages or anonymous online reports to a hub to regularly share real-time damage to health facilities and threats against staff with partners (88).

• Mobile Money Transfers

In addition to planning for safety and negotiations, incentivizing healthcare workers to provide compensation for the additional risk and fear may encourage them more to take the trip to less safe regions. We hypothesize this could be done with direct cash transfers as has been done in other sectors. Experts during key informant interviews shared that investing in the vaccine deliverers directly effects the number of children they vaccinate. We believe cash incentives will also push them to go the extra mile to reach more children in conflict zones. This can be an accessible intervention because mobile money networks work even in fragile settings. One such program was successfully implemented by the government of Liberia (89).

• Engaging Community Leaders and Change Agents

In cases of vaccine refusal or misinformation, engaging community leaders like religious leaders can change public opinion. In Afghanistan "mobile mullahs" travel by motorcycle to remote and fragile areas to explain that vaccination is permissible under Islamic religious law and help counter anti-vaccination rumors (90).

4.3.2 NON-HEALTH SECTOR INTERVENTIONS

In addition to strengthening the health system and adaptation to mitigate the consequences of conflict, non-vaccine specific initiatives and integration with other sectors can provide an extra push to reach zero dose children in conflict zones

Leveraging Existing Humanitarian Pathways

Vaccines have much in common with infant formula in that they are both heavily politicized by the international community, are needed by similar demographics, and in that need increases during times of conflict and instability. Some evidence suggests that increases in conflict-related casualties are associated with a significant decline in breastfeeding and an increase in breastfeeding substitutes like infant formula (91). Though there are obvious risks with the promotion of infant formula such as reducing the probability and duration of breastfeeding, when provided as temporary relief, the provision of infant formula has the potential to provide a route for the supply of other health interventions, and increase engagement with the health supply and support system (91). This report is not advocating for ignoring the tumultuous and exploitative nature of formula milk in the past, but recognizes that formula milk can be highly useful when supplementary in settings where undernutrition is increasing, like



Figure 14: Infant formula milk companies targeting mothers in Philippines (Source: Save the Children)

conflict zones (92). There is significant overlap in the demographic that would benefit from formula and vaccines in conflict zones and existing humanitarian infrastructure may be able to deliver both. If not used in tandem, the reach of infant formula is nevertheless a pathway that could be explored in vaccine delivery. Furthermore, access to infant formula may further incentivize a trip to receive an immunization.

5. Summary and Conclusion

Barriers to reach zero-dose children are multiple, heterogenous, and require understanding of local context. They can be broadly categorized into two groups. First, those that have very little access to primary care services as zero-dose children face systematic exclusion from most health services, and second, those who refuse to get vaccinated due to mistrust of the health system, religious beliefs, or other reasons. In conflict settings, additional barriers also include addressing damaged infrastructure, supply chain disruptions, difficulty retaining health workers, insecurity, mistrust between authorities and communities as well as population displacement and migration. Based on the review of existing literature and key informant interviews, some key lessons and recommendations are summarized below to reach zero-dose children:

5.1 Implementing Integrated Solutions

There are several existing as well as novel interventions that can be implemented to reach zero-dose children. While innovative technological interventions may ensure that vaccines reach remote areas or clusters of zero-dose children based on their location, they do not guarantee an increase in vaccine uptake consistently in the long term. In particular, for these interventions to be effective and sustainable, there is a need for combining interventions that help reach these communities with those aimed to improve vaccine acceptance in the community. For instance, initiatives to immunize communities that do not have access to other essential services may face resistance due to trust issues. Identifying zero-dose children using sophisticated technological tools coupled with leveraging existing or new non-vaccine initiatives to immunize the population may be more effective in such communities. Additionally, working with the community leaders and health workers would help mobilize community members and identify other issues that are a priority to the population, which, in turn, could be leveraged to improve vaccine uptake.

5.2 Contextualization of Interventions

Along with adopting an integrated approach, it is also important to consider adaptation of interventions to the local context to be more effective in reaching zero-dose children. The table below categorizes the interventions discussed in the previous chapters as broadly generalizable to context specific.

Broadly generalizable

Context-specific

- Application of GIS
- Use of drones
- Use of biometrics
- Cold chain innovations/vaccine design
- Electronic immunization registries
- Job aids for community health workers (e.g., My Village My Home)
- Microplanning tools
- Incentives [monetary and nonmonetary]
- Training vaccine deliverers
- Leveraging community assets and influential leaders
- Community mapping
- Radio broadcasts/SMS reminders
- Leveraging commercial sectors
 (Project Last Mile/Tech Mahindra)

Urban Slums

- Integrated service referrals
- Redistributing vaccination centers around transit points
- Art for public health messaging
- Drumbeating

Remote rural population

- Partnering with delivery of agricultural supplies
- Vaccination campaigns targeting both humans and animals
- Art for public health messaging
- Drumbeating

Conflict setting

- Emergency humanitarian response pathways
- HeRAMS monitoring facility stockouts and safety (could be scaled up in other settings too)

5.3 Monitoring and Evaluation

Monitoring and evaluating immunization programs can play a pivotal role in ensuring that zero-dose children are vaccinated. Evidence suggests that existing interventions to increase vaccine uptake among under-vaccinated children have been relatively successful. However, there is need to evaluate if these gains can be observed for reaching zero-dose children and assess their impact. Further, there is limited evidence on cost-effectiveness of scaling these interventions in specific contexts, particularly urban slums, remote rural, and conflict settings to support implementation of these programs. Thus, it is critical to include a cost-effectiveness component since the outset of designing and planning tailored interventions to inform the implementation to reach zero-dose children.

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