



# Building evidence for improving vaccine adoption and uptake of childhood vaccinations in low- and middle-income countries: a systematic review

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## Abstract

Vaccine coverage for children is an important indicator of the performance of national health and immunization systems. Most of the existing literature has targeted mothers' low educational level, living in underserved districts and/or remote rural areas and economic poverty that are correlated with low immunization coverage but the supply- and demand-side constraints to immunization in low- and middle- income countries (LMICs) are not well understood. The reliability of claimed administrative immunization coverage in these contexts is questionable. To address these barriers within the present Expanded Programme on Immunization (EPI), the difficulties related to inadequate vaccination uptake must be addressed in more depth. Building on already produced literature, this study aims to determine the extent of immunization coverage among children in LMICs, as well as to fill in the gaps in awareness about system-level obstacles that currently hinder the effective delivery and uptake of immunization services through EPI. By two reviewers, a literature search using PubMed and Google Scholar along with targeted grey literature was conducted on the 2nd of June 2021 by following PRISMA guidelines. The search techniques for electronic databases used both Medical Subject Headings (Mesh) and free-text words were tailored to each database's specific needs using a controlled vocabulary that was limited to the English language from 2000 and 2020. Of the 689 records, eleven articles were included in this review meeting the inclusion criteria. In total, five articles related to vaccination coverage, four studies on components of the routine immunization system, one article on the implementation of new and under-utilized vaccines and one were on vaccines financing. We evaluated the quality of the included studies and extracted into tables created by one investigator and double-checked by another. Review findings suggest that specific strategies to reduce inequality may be required. Vaccine procurement and pricing strategies, as well as vaccine customization to meet the needs of LMICs, are all critical components in strengthening immunization systems. Our findings could be used to establish practical strategies for countries and development partners to address coverage gaps and improve vaccination system effectiveness.

## Introduction

Vaccine coverage for children is an important indicator of the performance of national health and immunization systems that is the proportion of the target population being vaccinated [1, 2]. Expanding coverage is a key goal of immunization initiatives since it increases the extent of health benefits from vaccination while also reducing inequalities in results among underserved communities. Immunization is one of the most cost-effective public health strategies for lowering infant morbidity and mortality globally [3, 4]. When the World Health Organization (WHO) initiated the Expanded Programme on Immunization (EPI) in 1974, it was the beginning of a worldwide movement to use vaccination as a public health intervention [5]. Vaccines are estimated to

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prevent 2.5 million deaths of children annually. If 90% of the global population under the age of five received existing vaccines, a further 2 million lives would be saved [6].

The WHO Global Vaccine Action Plan (GVAP) 2011–2020 has as one of its overarching goals to ensure that all people in the world have equitable access to the required immunization [7, 8]. Certain vaccines have been readily available, such as the Hib and hepatitis B vaccines, which have been adopted by over 98% of countries worldwide, while other essential vaccines, have been less widely adopted [9]. By October 2016, the national vaccination schedule of 86 states had HPV vaccines, but only 14% of low-/low middle-income countries had national programs, compared to 55% of high-income/high-middle-income countries [10]. There are still challenges that exist in achieving targeted vaccination coverage and inequalities in countries' access to immunization [7]. Low and middle-income countries (LMICs) have been prioritized for ongoing initiatives to boost immunization efforts due to the noticeable remaining gaps [11].

In low-resource countries, improvement or extension of health services is a major concern for initiatives to increase childhood vaccine coverage [12, 13]. Although the global vaccination coverage has increased significantly, many countries of Africa and Southeast Asia have experienced a decline, partly because of reduced funding, in the national vaccination coverage [14]. The broader framework of the health system is closely linked, and without a supporting health system, an immunization program would not achieve its objectives [15, 16]. In areas with underdeveloped health systems, there can be inequities with high variability in immunization coverage when accessing immunizations between individuals in the same country [17]. Although a mother's low educational level, living in underserved districts and/or remote rural areas and economic poverty is correlated with low immunization coverage [18], vaccination is characterized by many more complex and interrelated variables that affect its uptake.

The supply- and demand-side constraints to immunization in LMICs are not well understood. The reliability of claimed administrative immunization coverage in these contexts is questionable. To address these barriers within the present EPI, the difficulties related to inadequate vaccination uptake must be detailed and thoroughly addressed. Adoption of policy-backed measures is especially important in LMICs, where childhood death rates are still high. Therefore, building on already produced literature, this systematic review aims to determine the extent of immunization coverage among children in LMICs, as well as to fill in the gaps in awareness of system-level obstacles that currently hinder the effective delivery and uptake of immunization services through EPI.

An up-to-date systematic analysis to provide an evidence-based approach was needed that would improve the efficiency and fairness of immunization policies in LMICs and lead countries to reach the objectives, by using the best available evidence in the research field in the making of health decisions conscientiously, explicitly and judiciously. Also, appropriate corrective measures should be identified and implemented to address the challenges observed such as raising awareness of system-level barriers that currently obstruct the effective delivery and uptake of vaccination services through EPI.

## Methods

### Design

A systematic review methodology by following the principles of the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) was conducted for vaccination coverage in LMICs [19].

### Protocol registration

This review was not registered.

### Search strategies

The search techniques for electronic databases used both Medical Subject Headings (Mesh) and free-text words and were tailored to each database's specific needs using a controlled vocabulary. The reference list of all qualifying articles also searched the relevant study. A database-specific search syntax file regarding the complete search terms and strategies for each database is provided (Supp. file 1).

Two reviewers (F.A., and I.A) conducted a literature search in the electronic databases PubMed and Google Scholar on the 2nd of June 2021. The search was limited to the last two decades: 2000 and 2020. The following search keywords were used: vaccination, vaccination coverage, immunization programs, child, Hesitancy, vaccines regulators and lower-middle-income countries. The operators "OR" and "AND" were used in the search string when they were appropriate, yielding the following search string: ("Vaccination"[Mesh] OR "immunization" OR "immunization" AND "Vaccination Coverage"[Mesh] OR "reportage" OR "description" AND "child"[MeSh] OR "Children" AND "Developing Countries"[Mesh] OR "average income countries" OR "lower-middle-income countries" AND "Refusals" OR "Hesitancy" OR "Resistance" AND "Vaccine politics" OR "vaccine regulators" )

## Inclusion/exclusion criteria

This review adopted the following inclusion criteria to screen references: (a) only human vaccination was a priority; (b) only peer-reviewed papers written in English were considered; (c) only studies with data on immunization coverage, components of the routine immunization system, accelerated monitoring of priority vaccine-preventable diseases, and implementation of new and under-utilized vaccines were selected; and (d) studies that focused LMICs from 2000–2020 were chosen. In contrast, this review employed exclusion criteria. It did not consider those articles, which were carried out outside the LMICs; and studies that did not focus on human vaccination.

## Study selection and data extraction

The bibliographic search involved the following steps: document analysis with the extraction of the most relevant information; synthesis of the material that was sorted, integrated, and compared; and lastly, the end of the search, where we received the selected articles for review.

The articles were chosen based on predetermined inclusion and exclusion criteria after screening titles, abstracts, and reading full-text articles. Looking at studies that used data from LMICs, the researchers considered the following characters: immunization coverage, components of the routine immunization system, accelerated monitoring of priority vaccine-preventable diseases, and implementation of new and under-utilized vaccines selected.

Three separate researchers carried out all search and selection stages, and the results were compared and reviewed. An investigator with knowledge in the field of vaccination research double-checked all registries (including articles that raised questions). Figure 1 depicts the outline of the review.

Data from selected research were extracted into tables created by one investigator and double-checked by another. The tables included the following details on the study's characteristics: author, year of publication, country, type of the study, vaccine studied, methodology for obtaining results (serology, questionnaire, database), and type of vaccination carried out (systematic, update of the vaccination program, vaccination of risk groups, results and conclusion).

## Quality assessment of included studies

The final set of the included studies passed through an independent quality review by using the JBI-developed (Joanna Briggs Institute) standardized critical assessment checklists according to the type of study [20]. Additionally, the Mixed Methods Appraisal Tool (MMAT) V.2018 was used to

process one study [21]. Each paper was given a score based on the design category, and full score sheets were created. Two reviewers made decisions on research quality, and any disputes were handled through discussion.

## Data analysis

The findings were organized and reported using a qualitative methodological technique. We extracted data in this respect and examined each article accordingly. Finally, to better understand the results, the final remarks from the document have been included.

## Results

We searched from 2000 to 2020 and found 689 articles (Fig. 1). After eliminating 650 titles that were inappropriate to the study's goal, the titles and abstracts of 39 papers were evaluated, with 16 being selected for full-text screening, resulting in the elimination of another 23 articles. Finally, 11 articles were included in this systematic review to assess and analyze based on inclusion/exclusion criteria.

## Study characteristics

Table 1 summarizes the characteristics of individual studies. There were five articles related to vaccination coverage [1, 22–25], four studies on components of the routine immunization system [26–29], one article on the implementation of new and under-utilized vaccines [30] and one were on vaccines financing [31].

## Risk of bias

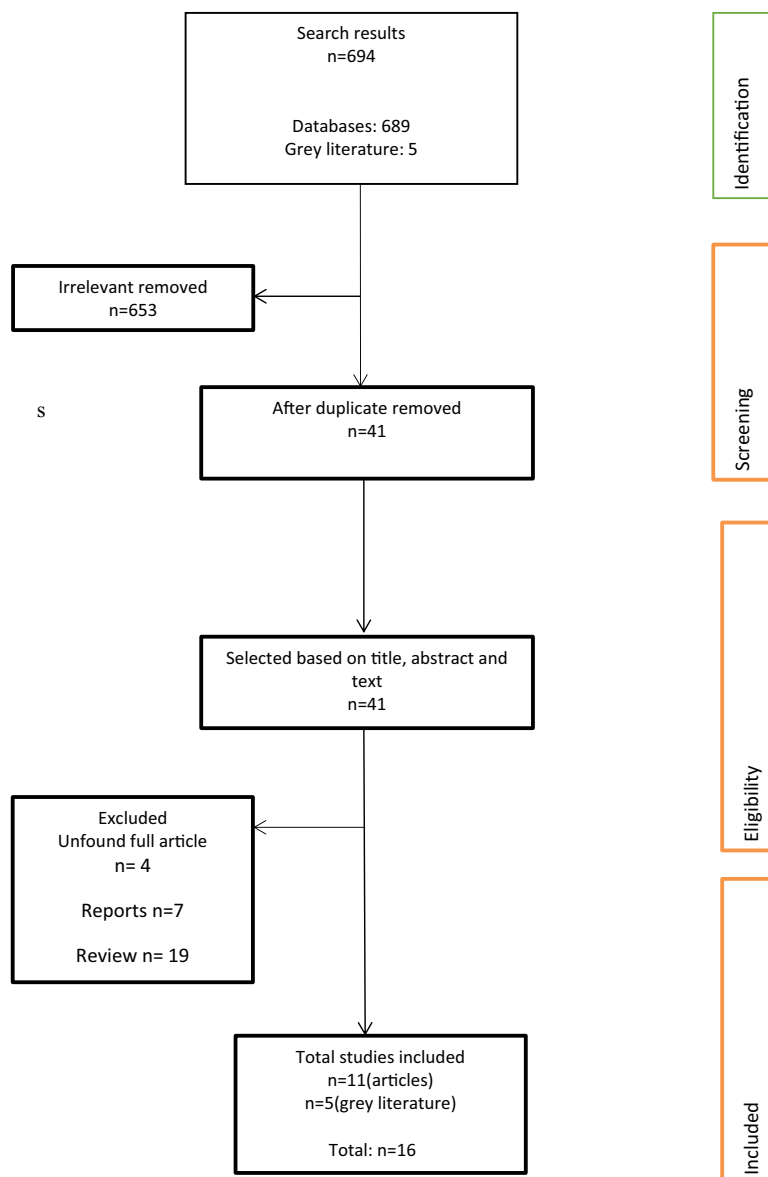
According to the JBI checklist and MMT (Supplemental Tables 1–7), all included studies had clear research questions, data collection procedures, and a study design suitable to achieve the aims and objectives. The target checklist's scores varied from nine to ten out of a possible eleven, with an average of nine. Due to a low score, no study was eliminated. Individual study scores are included in the supplemental Tables 1–7.

During our reading and analysis of the literature, we found various key themes that we mention below one by one.

## Childhood immunization coverage

According to the most recent survey data available in May 2015, more than 60% of all eligible children in LMICs had obtained complete vaccinations [24]. Table 2 illustrates the mean full vaccination coverage rates in LMICs in each WHO Region, ranging from 55.5% in the Eastern Mediterranean

**Fig. 1** Flow chart selection process (PRISMA)



Region to 68.9% in the Americas Region. Moreover, according to GAVI-supported countries, there is a lot of variation in immunization coverage. Coverage of DTP3 ranged from 37.4% in Ethiopia to 97.1% in Rwanda, with an average of 77.1% across all 45 countries participating in GAVI. MCV coverage was similar (77.5%, 95% CI 73.3, 81.7) on average [25].

Globally, although vaccination coverage has continued, around 20 million children remained unvaccinated, particularly 12.2 million (62%) of them were living in LMICs [32]. The African continent and conflict-affected countries have a disproportionate number of zero-dose children. They are also likely to be deprived of other health and welfare services [32]. There are many zero-dose children in middle-income nations such as the Philippines, Brazil, Mexico, and Angola.

In addition to this, disruptions to normal immunization programs associated with the COVID-19 pandemic and response actions were prevalent in 2020, affecting almost every country [33]. According to preliminary and fragmentary statistics received from numerous nations, the number of provided dosages in March and notably April 2020 was significantly lower than the previous year as depicted in Table 3 [32].

### Uptake of immunization challenges

Eight obstacles have been found that affect immunization coverage related to both demand and supply sides: (a) greater land area; (b) linguistic fractionalization; (c) gender inequality; (d) conflict areas (urban/rural residence);

Table 1 Characteristics of studies

References	Study design	Type of vaccination carried out	Country	Target group	Study Period	Vaccine	Study outcome
Arsenault et al. [25]	Survey	Coverage	Gavi-supported countries	Children 12–23 months	2005–14	DTP3 and MCV	The coverage of DTP3 and the magnitude of inequalities among nations were found to be highly variable, with results for MCV being similar to those for DTP3. Political stability, gender equality, and a ↓ land surface area were all found to be significant predictors of ↑ and more equitable DTP3 coverage. DTP3 coverage disparities were also ↓ in nations with more external health resources, ↓ rates of out-of-pocket spending, and better national coverage. Better vaccination outcomes were associated with ↑ government health investment and reduced linguistic fractionalization. In order to improve vaccination coverage and reduce inequities, policies and programmes must address major social determinants of health, such as geographic and social exclusion, gender disparity, and the availability of financial health protection. More investigation into the mechanisms that contribute to these relationships is needed
Hajizadeh [26]	Survey	Coverage	LMICs	children aged ≤ 59 months	2010–15	BCG, DTP, Polio and measles vaccines	The findings revealed that vaccination coverage was pro-rich in most countries, with children from higher socioeconomic status groups less likely than their lower socioeconomic status counterparts to receive all four basic vaccines. The concentration of antenatal care visits among wealthier mothers was positively associated with the concentration of vaccination coverage among wealthier children, according to meta-regression studies (coefficient=0.606, 95% CI 0.301 to 0.911). In most LMICs, pro-rich vaccination distribution remains a major public health concern. Policies targeted at improving prenatal care visits among women from lower socioeconomic categories may help to ↓ socioeconomic inequalities in vaccine coverage
Hanvoravongchai et al. [27]	Cross-sectional	Impact of AMEAs on Immunization services & Health system	Bangladesh, Brazil, Cameroon, Ethiopia, Tajikistan, and Vietnam	Key informants and health staff	2009–10	Measles vaccines	The influence of AMEAs was shown to vary, with good and negative implications in certain immunization and health-care system functions Overall, good effects on vaccination services were seen in Bangladesh, Brazil, Tajikistan, and Vietnam, while negative effects were seen in Cameroon and Ethiopia. While weaker health systems may not be able to profit adequately from AMEAs, disruptions to health care delivery are rare in more developed health systems. Opportunities to strengthen the routine vaccination service and health system should be actively pursued in order to alleviate system bottlenecks and reap advantages for both the eradication effort and other health priorities
Hoest et al. [22]	Observational	EPI schedule adherence and coverage	South Asia, Africa, and South America	Children (birth-24 months)	2009–14	EPI schedule	EPI vaccine coverage rates varied between sites and by kind of vaccine; overall, coverage was highest in Nepal and Bangladesh and lowest in Tanzania and Brazil. BCG coverage ranged from 87–100% across all sites, but measles vaccination rates varied from 73–100%. In all sites, there were significant delays between the intended administration age and the actual vaccination date, especially for the measles vaccine, when less than 40% of doses were given on time. A variety of socioeconomic characteristics were shown to be strongly linked to vaccination status in study children, however the findings were mostly site-specific. These findings underline the importance of increasing measles vaccination rates and reducing delayed vaccination in order to meet EPI targets for herd immunity and disease transmission reduction

Table 1 (continued)

References	Study design	Type of vaccination carried out	Country	Target group	Study Period	Vaccine	Study outcome
Ikilezi et al. [23]	Survey	Coverage	LMICs	Children aged < 2 years	1996–2016	DTP3, PCV3, pentavalent3, MCV2and rotavirus2	This study found that aid had considerable positive impacts in this study, especially among the newer vaccinations. Using 2016 country-specific disbursements and coverage levels as a baseline, it was estimated that additional donor assistance for health (DAH) per capita required to reach 90% ranged from 0.01USD to 4.33USD for PCV, 0.03USD to 9.06USD for pentavalent vaccine, and 0.01USD to 2.57USD for rotavirus vaccine among recipient countries below the universal target. For PCV, pentavalent, and rotavirus vaccines, the expected number of children vaccinated due to Gavi support was 46.6 million, 75.2 million, and 12.3 million, respectively. This analysis indicates that global immunization campaigns have been implemented successfully in the past, both historically and in the future. In order to attain universal vaccination coverage, methods for fiscal sustainability and efficiency must be reinforced as more vaccines are introduced and countries migrate away from foreign help. The final judgement on a prospective change in the NIP cannot be based on a simple algorithm. Because the relevant information contains components of varying kinds and magnitudes, to which different value judgments may be added, and which may have varying degrees of uncertainty. Every NIP should be supported by an active surveillance effort because any alteration could result in unanticipated changes in the vaccine's efficacy, evolutionary consequences, such as the pathogen's antigenic composition, and safety profile. Clinical–epidemiological surveillance, vaccine coverage surveillance, immunological surveillance, microbial population dynamics surveillance, and adverse event and safety issue surveillance are all part of the process. The decision to include a vaccination in the NIP should be treated as seriously as the decision to exclude a vaccine from the NIP, both scientifically and ethically.
Kimman et al. [28]	Survey	Updating of Immunization program	Global	Health staff, and health economists	2006	NIP	
Ladner [29]	Survey	Aiding program	LMICs	Program manager	2009–14	HPV	There were 29 initiatives in total, implemented by 23 institutions in 19 LMICs. Prior to the start of the vaccine campaign, twenty programme managers (97.7%) reported that their institution used vaccination sensitization techniques. The most commonly mentioned roadblocks were erroneous public perceptions about the vaccine's safety and efficacy. Significant health system constraints were found as insufficient infrastructure, human resource funding, and vaccination distribution technique. HPV vaccination and cervical cancer screening rates ↑ by combining HPV vaccination with other health interventions for mothers of targeted girls. The majority of programme directors said their initiatives had a favorable impact on national HPV vaccination policies. The majority of institutions have national and international partners who helped with human resources, technical aid, health professional training, and financial support. For such achievement, adequate and tailored planning and resources that support information sharing, sensitization, and mobilization are required. These findings can help inform the development of HPV vaccination programmes and policy in LMICs



Table 1 (continued)

References	Study design	Type of vaccination carried out	Country	Target group	Study Period	Vaccine	Study outcome
Makinen et al. [30]	Interview	Adoption of new vaccines	LMICs and UMICs	Participants in decision making	2010	New vaccine adoption	The most important criteria for acceptance were WHO guidelines, the availability of local epidemiological data, and a set of parameters including affordability, cost-effectiveness, and overall cost of the new vaccination for the programme. Although their resources and capacity differ, NITAG play an important role in advising decision-makers. Pooled procurement arrangements for vaccine procurement have advantages for both country decision-makers and manufacturers. Assistance with making epidemiological data and vaccine market information accessible to countries, building and reinforcing related analysis capacity, and assisting with purchasing mechanisms and practices such as pooled procurement are among the recommendations for countries and the international community
Ortega et al. [31]	Survey	Coverage	LMICs	Children (less than 1 year)	2002–2013	DTP, MCV, Polio	The main result of the empirical analysis was that the relative level of IFFs to total trade negatively impacted vaccination coverage but only in the case of countries with very high levels of perceived corruption. Given that there was an annual average of 18 million infants in this cluster of 25 countries, this result suggests that at least 34,000 children may not receive this basic health care intervention in the future as a consequence of ↑ in IFFs in any particular year. The main focus has been the urgent need to ↓ IFFs as part of development policy
Restrepo-Méndez et al. [24]	Survey	Coverage	LMICs	Children (any age) <sup>b</sup>	2000–2015	BCG, MCV1, DTP3, Polio vaccine	Around 56–69% of eligible children in LMICs appeared to have had full immunization in each of the WHO areas. However, the average amount of such coverage within each region varied substantially. It ranged from 11.4% in Chad to 90.3% in Rwanda in the African region. Madagascar and Mozambique looked to have made the most progress in enhancing full vaccination coverage over the last two decades, especially among the poorest quintiles of their populations, among the countries in which the coverage patterns analyzed. When just national mean values of full vaccination coverage are provided, most LMICs are influenced by pro-rich and pro-urban inequality
Utazi et al. [1]	Survey	Coverage	LMICs	Children aged < 5 years	2011, 2013–14	MCV	In geo-statistical models, only 4–5 covariates were found to be substantially predictive of measles vaccine coverage, with distance repeatedly picked as a crucial predictor. Significant heterogeneities within the three nations were highlighted by the output 1 km maps, which were not reflected by province-level summaries. When combined with demographic statistics, it was discovered that just a few districts had achieved the WHO Global Vaccine Action Plan 2020 target of 80% coverage at the time of the surveys. To eliminate vaccine-preventable diseases, a solid evidence base is needed to guide policies and make optimal use of limited resources

AMEAs accelerated measles elimination activities, IFFs illicit financial flow, LMICs low- and middle-income countries, NITAG national immunization program, NITAG National Immunization Technical Advisory Groups, UMICs upper middle income countries, ↑ increase(s/d), ↓ decrease (s/d)

<sup>a</sup>Included microbiologists, immunologists, epidemiologists and experts on vaccine safety

<sup>b</sup>For 20 study countries 18–29 months for MCV, 3 study countries 15–26 for MCV and 12–23 months formed the denominator group in all of the other study countries

**Table 2** Immunization coverage in low- and middle-income countries, by WHO division, 2001–2012 [24]

Region name	Mean coverage (%)
African region	56.7
American regions	68.9
South East Asian Regions	74.0
European Region	68.2
Eastern Mediterranean Region	55.5
Western Pacific Regions	63.2

(e) population displacement; (f) security; (g) wealth; and (h) socioeconomic status (e.g., multidimensional poverty) [24, 25]. Large countries may confront significant logistical challenges in providing healthcare in rural areas; thus, boosting the capacity of health services to offer immunization to rural communities is critical for improving coverage and equity. Linguistic fractionalization is frequently associated with increased social fragmentation between linguistic and ethnic groups. Hence, health and immunization systems should be tailored to the demands of various linguistic and ethnic groups in order to address established socioeconomic disparities [25].

Moreover, vaccination uptake is also influenced by a number of other factors: inadequate record-keeping, concerns about bad outcomes of immunization, shortage of a competent primary care system, complexity of immunization schedule, vaccine charges, issues with access to health care facilities, carelessness of parents, lack of parental knowledge, conflicting parents interests as well as requirement for many injections in a single visit are some of the issues. The other issues are time-consumption in the public clinics, reliable transportation shortage, a lack of reminders, and an incorrect interpretation of contraindications are all issues that need to be addressed [25]. Inequalities in vaccination coverage were linked to increased out-of-pocket costs. The elimination of user fees for immunization services has been frequently recommended [34]. For low-income families,

user fees are a significant obstacle to vaccination. Despite this, they are frequently charged for vaccines in LMICs, both legally and illegally (Table 4).

Inequality in childhood immunization can significantly depend on other factors, such as a woman's economic and socio-cultural empowerment that substantially affect her education. There are several factors that affect the education of a woman, such as the family's economic position and the area of living. Those women who belong to economically wealthier families and live in urban areas do have more formal education than those who are economically poor and live in rural areas. Particularly, the Americas region and the European region appeared to be more equal than the other regions in terms of the effects of urban/rural residency on full vaccination coverage [24, 26]. The Eastern Mediterranean Region has the most pro-urban inequities, with mean levels of full vaccination coverage for urban children being around 60% higher than for rural children as shown in Table 3.

Hence, education played a vital role to avail the healthcare provision [25]. Although it cannot be the sole factor, higher vaccination rates among children from economically wealthier homes may be due to the formal education of mothers. Higher educational attainment (as a means to minimize gender inequalities) helps mothers to take an active role in the public and private spheres, allowing them to seek better healthcare (e.g., vaccine coverage) for their newborns [26]. Immunization services may be unavailable to people irrespective of gender who lack financial or general autonomy. Furthermore, women who are younger, less educated, or uneducated were more likely to lack practical understanding about vaccination services and were less likely to grasp vaccination cards, return dates, and the need for repeat visits [25]. Overall, boys had greater percentages of full vaccination coverage than girls in LMICs. The absolute levels of gender disparity were relatively high in the South-East Asia and Western Pacific regions. Specifically, in the Western Pacific Region, boys had a 10% lower rate of full vaccination coverage than girls [24]. These socio-cultural factors highlight the importance of clear and accurate information regarding the vaccine's health advantages, as well as proper

**Table 3** Worldwide Immunization affected by the COVID-19 pandemic 2020 preliminary DTP coverage data compared to equivalent 2019 period [33]

Regions	Countries reported (% surviving infants) relative difference 2019–20(%)			
	January	February	March	April
African (AFR)	42 (94)	41 (84)	41 (84)	34 (75)
Regions of America (AMR)	20 (23)	20 (23)	20 (23)	0 (0)
Eastern Mediterranean region (EMR)	5 (54)	5 (54)	5 (54)	0 (0)
South-East Asia Region (SEAR)	9 (99)	9 (99)	9 (99)	5 (24)
Western Pacific Region (WPR)	5 (13)	5 (13)	5 (13)	4 (11)



sensitization and lobbying among parents and other key community stakeholders [29].

### Financing of childhood immunization services

Based on statistics on vaccine expenses and vaccine coverage, there does not appear to be an association between higher coverage and higher spending per surviving infant [35]. Nonetheless, GAVI's vaccination donor support, which is specifically focusing on vaccination, has helped to enhance the vaccination coverage in its portfolio, including pentavalent, pneumococcal, measles, and rotavirus vaccinations. The vaccine-specific impacts expressly point to progress toward a potential reduction in the burden of vaccination-preventable diseases, as suggested by the GAVI 2016–2020 strategy, which includes hepatitis B, rotavirus, and measles among the disease dashboard indicators [36].

With the help of DAH (donor assistance for health), coverage has significantly improved [23]. While there have been significant advances in coverage, with the majority of nations meeting the previous global aim of 80% by 2015 and 42 countries met the current Global Vaccine Action Plan GVAP target of 90% [23].

### Introducing new and underutilized vaccines

Between 2010 and 2017, 116 countries with low and middle economic resources introduced at least one new vaccine. A small margin probably missed GVAP's objective of introducing at least one new vaccine in all 139 low and medium-run countries by 2020. Nevertheless, new vaccines have been introduced faster than ever in the last decade. In LMICs, over 470 vaccinations have been introduced since 2011, and a number of these countries have implemented up to six or seven vaccines [8].

There are some factors that affect the new vaccine uptake in LMICs, such as the burden of disease, cost-related drivers, and other decision-making factors [30].

LMICs' decisions on whether or not to adopt a new vaccine were predictably, influenced by financial considerations. This

is not, however, a straightforward question of cost per dosage or cost per fully immunized child. There are several unknowns in decision-making, such as the new vaccine's affordability, the vaccination program's overall cost and financial requirements, the uncertainty about future price levels, and the price available dependent on different procurement arrangements. Thus, countries require direction and greater information on how to appropriately address these concerns [30].

### Accelerated control of vaccine-preventable diseases

#### Eradication of poliomyelitis

Despite enormous advances (Fig. 2), efforts to eradicate polio face major security challenges and community acceptance in the last wild polio transmission sites. In 2015 eradication certified Wild Poliovirus Type 2 and since 2012 Wild Poliovirus Type 3 has not been identified. Currently, only in Afghanistan and Pakistan do wild polioviruses like 1 appears to circulate. In a number of countries, poliovirus derived from vaccines continues to circulate [28]. These cases stress the need for high vaccine coverage in national immunization programs [8].

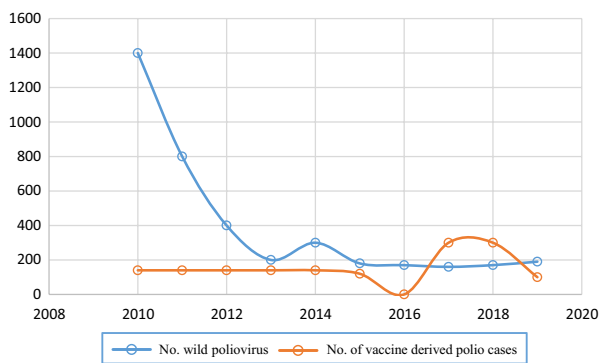
#### Measles elimination

The incidence of measles reported since 2000 was cut by 83% and, 21.1 million deaths have been prevented [27]. However, the cases of measles across the world have recently increased, with a doubling worldwide incidence from 2017 to 2018. Although all six WHO regions have pledged to eliminate measles by 2020, a global coverage of around 86% of the first dose of measles vaccine was too low to achieve elimination with significant variations in the overall and internal coverage [8].

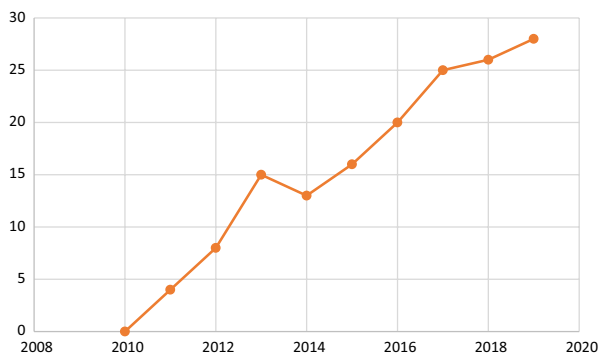
In national immunization programs, the global coverage of second-dose measles vaccine steadily increased from 42% in 2010 to 69% in 2018. Yet, numerous children still do not receive the two doses required to maximize protection. There are several factors behind it such as overall health system, immunization and vaccine hesitancy [8, 27].

**Table 4** Inequalities in vaccination due to residency in low and middle income nations by World Health Organization area, 2001–2012 [24]

Regions name	Mean urban/rural inequality	
	Urban coverage– rural coverage, percentage points	Urban coverage/ rural coverage
African Region	7.0	1.2
Region of the Americas	– 1.0	1.0
South-East Asia Region	2.6	1.1
European Region	3.4	1.1
Eastern Mediterranean Region	11.2	1.6
Western Pacific Region	9.0	1.2



**Fig. 2** Cases of wild poliovirus and circulating vaccine derived poliovirus around the world 2010–2019 [1]



**Fig. 3** Number of priority countries having validated maternal and neonatal tetanus elimination [1]

### Maternal and neonatal tetanus elimination

Some progress has been made, as in 2017, around 30,000 newborns died from infections with tetanus that represents a reduction of 85% since 2000. Nonetheless, the global target of eliminating maternal and neonatal tetanus in 40 priority countries by 2020 (Fig. 3) remained unachieved [8]. By July 2019, the disease was eliminated only in 28 countries.

## Discussion

The study findings showed that there were several factors associated with vaccination coverage across LMICs such as greater land area; linguistic fractionalization; gender inequality; conflict areas (urban/rural residence); population displacement; security; wealth; and socioeconomic status (e.g., multidimensional poverty). According to previous study, the impact of these factors on survey coverage varies by geography and time period, as well as the conceptual, methodological, and operational tactics used [37].

The current research found a robust link between greater socioeconomic position and full immunization coverage. Other well-known determinants of complete vaccination coverage, such as maternal education or literacy, location of residence (urban or rural) and child sex. We observed that sex, wealth or urban/rural residence, inequalities in full immunization coverage varied substantially. Inequalities related to wealth and urban/rural residence appeared to be ubiquitous and persistent and to be larger in general, than the corresponding sex-related inequalities [26]. Similar to previous studies where younger, less educated, and uneducated women are more likely to be unaware of vaccination services and to be unable to understand vaccination cards, return dates, and the need for multiple visits [38–40].

Well-educated women are more likely to have socially valued general abilities, which elevate their social position. This cultural capital can lead to improved communication between mothers and medical professionals, allowing them to use more healthcare services like immunization [41]. Moreover, we found that in LMICs, boys had somewhat higher rates of full immunization coverage than girls by less than three percentage points [24]. Similar to a previous study in Myanmar slightly greater rates of full immunization coverage among male children [42].

Land areas and issues with access to health care facilities were also well-known predictors of vaccination coverage. In providing healthcare such as immunization in rural areas, large countries may face major logistical obstacles. Other investigations in Sudan, Kenya, Eastern and Southern Ethiopia found similar results [43].

Moreover, workload due to staff shortage and inadequate workspace, shortage of vaccine, and noncompliance of a mother for the next scheduled date and high out-of-pocket cost was being all issues that need to be addressed. This is almost similar to a study conducted in Arebegona district, Southern Ethiopia [24]. In addition to this, accelerated control of vaccine-preventable diseases such as poliomyelitis, measles and maternal and neonatal tetanus elimination also need to be considered.

However, the papers included in this review looked at the general ideas of immunization services finance and vaccine coverage. While one study found no apparent link, others found that vaccination coverage improved with the help of GAVI and other assistance channels. Previous studies also indicated that the DAH for each health target area has also increased. Particularly, the importance of DAH for maternal, neonatal, and child health has greatly expanded [44]. In addition, although the implementation of new vaccines improved as indicated between 2010 and 2017, 116 countries with low and middle economic resources have introduced at least one new vaccine. However, it affected by the burden of disease, cost-related drivers, and other decision-making factors. A previous study also indicate the same results such

as introducing a new vaccine in a developing country may face several financial and logistical challenges [45].

## Practical suggestions

Since the case of vaccination is complex, context-specific strategies are required to increase the vaccine uptake and acceptance in LMICs. One strategy is to use immunization programmes and “outreach” methods to reach out to underserved populations. The Reaching Every District (RED) micro-planning process strategy, established by the WHO, UNICEF, and other partners in 2002 and successfully implemented in Africa, India, and other Asian countries are one example [46–48]. Supplementary Immunization Activities (SIAs), often known as mass-immunization programs, have been shown to be effective in minimizing inequity inside populations [17, 49]. They are used to enhance population health by expanding coverage, meeting global elimination targets, or containing outbreaks [49–51]. Although SIAs have been shown to improve uptake, such as in childhood polio vaccination, a percentage of children may still be left out of such practices [52]. Integrating health strategies can also aid in coverage improvement. As part of the Missed Opportunities for Vaccination Strategy, immunization program managers and field-based health workers should regularly use each and every encounter with a child to check their (and mother’s) immunization status, with adequate vaccination as required [53, 54].

The need for effective and accurate communication of the vaccine’s preventive health benefits and the appropriate build-up of awareness and advocacy between parents and key community players in conjunction with rumors and social and cultural barriers [8]. Since a virus can cross any geographical border, as we have seen in the case of COVID-19, there is a need for regional and global cross-border coordination.

## Conclusion

Immunization is widely regarded as an essential measure to prevent infectious disease and improve human health. Administering a vaccine helps the immune system to protect against infection. To have what can be called a large-scale protection, a large number of the population must be vaccinated as it creates herd immunity. The magnitude of COVID-19 has made it clear how important it is to vaccinate in any possible way to improve immunization that can protect people from morbidity and mortality. Following these lines, childhood vaccines are an important public health strategy for preventing serious diseases in young children, and they must be administered according to the EPI schedule for maximum effectiveness.

The ability of LMICs to achieve high and equal levels of coverage is necessary to obtain herd immunity. Critical socioeconomic determinants of health, such as geographic and social exclusion, gender inequality, and the unavailability of financial protection for health, must be considered in creating policies and programs to improve vaccination coverage and equity. Opportunities to strengthen immunization services and the health system should be actively pursued in order to alleviate system bottlenecks and incur advantages for other health priorities. National EPI are gradually including a variety of under-utilized vaccinations, newly available vaccinations, and innovative immunization methods with the help of international donors, political will, as well as financial planning and commitment.

Vaccine procurement and pricing strategies, as well as vaccine customization to meet the needs of LMICs are all critical components in strengthening immunization systems. Our findings could be used to establish practical strategies for countries and development partners to address coverage gaps and improve vaccination system effectiveness.

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**Availability of data and materials** The data set used and/or analyzed during the current study is available from the corresponding author on reasonable request.

**Author’s contributions** The authors of this manuscript are FA, IA, ZB and YY. FA is the main investigator of the study. FA made a considerable contribution for study design, cleaning the data, interpreting the analysis and drafting the manuscript along with IA. ZB and YY were involved in critically reviewed the manuscript. All authors read the final document and approved it.

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