The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 5, 2025

GLOBAL VACCINATION INITIATIVES AND THEIR LONG-TERM OUTCOMES IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

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DOI: https://doi.org/10.5281/zenodo.15495077

Keywords
Vaccination Programs, Disease Outbreaks, Global Health, Low-middle Income Countries.

Article History
Received on 15 April 2025
Accepted on 15 May 2025
Published on 22 May 2025

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Abstract

Background: *Vaccination programs are critical in preventing disease outbreaks, particularly in low- and middle-income countries with limited healthcare infrastructure. Evaluating the effectiveness of these programs helps assess their impact on public health, guiding future interventions and resource allocation.*

Methodology: *- This systematic review assesses the effectiveness of vaccination programs in low- and middle-income countries (LMICs), focusing on coverage, disease reduction, and barriers to uptake. A total of 25 published original articles between the years 2010 and 2024 were finally chosen on the vaccination program. Studies included in the work encompassed different types of designs primarily RCTs, cohort studies, and case-control studies. The studies were retrieved from scholarly databases such as PUBMED, Medline, WHO Global Research on COVID-19, and Google Scholar using key terms; vaccination programs and vaccination-preventable diseases. Several factors including vaccine hesitancy and access to vaccines are highlighted as major challenges impeding progress towards the implementation of the Global Immunization Agenda 2030 goals.*

Results: *- The use of vaccines in disease prevention is a key intervention essential for disease control interacting positively with health status in LMIC countries. Research has proved that vaccines greatly minimize diseases such as rotavirus, measles, influenza as well as dengue. Mobile conditional cash transfers, for instance, have been effective in the case of immunization while there has been protection for mothers as well as their children through maternal vaccination. Vaccination also adds credence to health systems as it relieves health services. Efforts such as HPV vaccination have boosted health equity whereas, economic assessment has reflected the cost effectivity. Disease eradication provides Long-*

term benefits, as seen with polio, measles, and rotavirus vaccines, enhancing global health security.

Conclusion: *- Routine immunization and expanded program of immunization guarantee control of communicable diseases, and enhance health systems and life courses in low and middle-income countries; logistical barriers and vaccine hesitancy are some of the barriers that may limit the success of the program; however, there are some proven solutions like mobile health solutions and the act of providing incentives like cash to those who accept to be vaccinated.*

INTRODUCTION

Immunization programs are considered one of the safest and most efficient interventional strategies to control communicable diseases and diseases that could otherwise have been prevented worldwide. Vaccines have played significant roles in improving human health, reducing the death rates of millions of people, and even eradicating some diseases every year. Vaccination campaigns have been remarkably effective in the developed world and the proportion of children suffering from measles, polio, and diphtheria stands robustly testament to that success. Nevertheless, the efficacy of these programs remains questionable in LIMCs due to the scarcity of health facilities, inadequate finance, and the instability of the political environment that complicates successful vaccination programs (Rémy et al., 2015).

According to the estimation made by the World Health Organization (WHO), up to 3 million deaths are prevented from diseases like diphtheria, tetanus, and pertussis each year by vaccines (Montero et al., 2024). In high-income countries, local immunization systems have already achieved great progress in combating the outbreaks. Nevertheless, in LMICs, vaccination over the past few decades has risen, though it remains low, and several barriers persist to hinder these programs.(Sinuraya et al., 2024). Vaccination outcomes may be affected by factors such as the capacity of health systems, access to vaccines, and the quality of immunization services. In addition, socio-demographic factors like poverty, education, and awareness also are important predictors in influencing the success of a vaccination program in LMICs (Ekezie et al., 2022).

The World Bank uses the gross national income (GNI) per capita to categorize countries, through the atlas method. Low-income countries are those with a GNIP per capita of less than $1085 while the lower middle-income countries have a GNIP per capita between $1085 and $4255 (Dutta & Hazarika, 2023). Tan MM, et al. (2024) describe LMICs as having a high incidence of the disease and low life expectancy due to the key determinants, which exclude them from using public services, including health services (Tan et al., 2024).

The need to reinforce the campaigns on vaccination is underlined by the ability of these interventions to check on epidemics as well as endemics. For instance, the campaign to eliminate smallpox in the twentieth century is one of the most successful vaccinations that have been undertaken in time and shows that vaccines can wipe out total diseases (Stewart & Devlin, 2006). Similarly, in countries of West Africa like Guinea, Sierra Leone, and Liberia, the introduction of the Ebola vaccine recently has facilitated the control of outbreaks of the virus and saved countless lives (Ajelli et al., 2016). However, several challenges have continued to persist especially in resource-constrained environments as follows: There is an equal and even greater concern on the issue of accessibility and affordability of vaccines especially to the many LMICs as procurement and other related costs, lack of proper storage, inadequate and often nonexistent primary healthcare structures are added barriers to vaccination coverage (Keith et al., 2013).

One more important aspect that affects the efficacy of vaccination programs in LMICs is the concern of vaccine hesitancy, which has been an evolving challenge worldwide. In developing countries, their health sector is not very strong and people doubt the information they get, they doubt their healthcare system, and some of the cultural beliefs create problems when it comes to vaccines making it even harder for people to get the vaccines needed for the creation of the herd immunity. A cross-sectional study conducted in Nigeria in 2019 revealed that vaccine hesitancy played a major role in the circulation of

vaccine-preventable diseases such as poliomyelitis and measles (Sato & Takasaki, 2021). Misconceptions regarding vaccines and general knowledge regarding the need to be immunized have also become part of the campaign to effect change in these areas through the provision of correct information regarding the same.

Unlike high-income countries, mass vaccination programs in LMICs are a component of health systems strengthening. Implementation of scale-up immunization, despite coming across challenges whereby; enhancing the logistics of immunization, adequate training of health care providers, and enhancing storage mechanism for the vaccines are among the negative impacts of immunization. It has also been an experience with other countries like India and Nigeria, where political campaigns and mobile vaccination stations have been effective in enhancing vaccination coverage in compound rural areas (Decouttere et al., 2021).

The vaccine impact deals with the level to which vaccination campaigns reduce the incidence and spread of vaccine-preventable diseases in LMICs. This can be done by comparing the number of cases of contracting diseases, hospitalization, or deaths due to diseases that could have been administrated with the help of vaccination or extension of such programs (Rodrigues & Plotkin, 2020). Vaccination in the LMICs depends on the collaboration and donations received from other countries and agencies. Multilateral agencies like Gavi, the Vaccine Alliance, and the Global Fund have played vital roles in supporting financial, advisory and vaccine needs so that children in even the poorest countries of the world can receive vital vaccines. Nevertheless, as it has been indicated results such as geopolitical tensions and uneven distribution of resources may slow down these efforts in some geographic locations (Nunes et al., 2024).

Problem statement: -

Despite vaccination campaigns, LMICs are periodically witnessing outbreaks of another disease Listing few; inadequate or weak state health systems, inadequate or no access to vaccines, and low compliance levels. Although various vaccination programs have been implemented and are still being implemented in high-income countries, their effects on LMICs and most particularly the long-term effects have not been fully researched. This deficit of knowledge prevents the formulation of strategies geared at narrowing the vaccination gap and ultimately reducing the potential of disease outbreaks. Therefore, this systematic review will assess the impact of vaccination in LMICs, establish key success factors of immunization, and offer a conclusion that would help boost strategic immunization in the mentioned regions.

Rationale: -

Nevertheless, with the growth of globally focused initiatives, LMICs continue to grapple with issues such as inadequate health services provision, and low rates of clients' acceptance of vaccines which hampers vaccination campaigns. It will be the goal of this review to give worthwhile insights into the uptake of the strategies in particular and the lessons enjoined towards the formulation of appropriate policies for the advancement of public health in general. Such knowledge will enhance coverage levels and decrease morbidity and mortality from preventable diseases, as well as improve global health objectives and more sustainable vaccinations aligned to contexts of limited-resource settings.

Research question: -

How effective are vaccination programs in preventing disease outbreaks and improving long-term health outcomes in low- and middle-income countries?

Objective: -

To evaluate the effectiveness of vaccination programs in preventing disease outbreaks in low- and middle-income countries.

METHODOLOGY: -

This systematic review was done to evaluate the effectiveness and impact of vaccination programs across different regions and settings, with a particular emphasis on improving vaccine coverage, reducing vaccine-preventable diseases, and addressing barriers to vaccination uptake. The inclusion criteria concentrated on studies published between 2010 and 2024, warranting significance to the present state of knowledge on vaccination programs. Out of these, 25 papers were included in the review with a diverse

methodological base that includes RCT, cohort, case-control studies, modeling studies, economic evaluation studies, and more. These studies were mainly conducted in LMICs of South Asia (Pakistan, Nepal), Sub-Saharan Africa (South Africa, Malawi) Central America (El Salvador), South America (Brazil) the Middle East (Qatar). Discussed studies included immunization in childhood, rotavirus, influenza, varicella, MMR, maternal vaccine knowledge, and vaccination dengue ranging from small groups to population one, which yielded millions of population samples.

These studies were obtained from reputable sources, including PUBMED, Medline, Cochrane database, and Google Scholar by using the keywords, vaccination programs, immunization strategies, and vaccine-preventable diseases with a special emphasis on their ability to prevent disease outbreaks in low and middle-income countries. Thus, only the articles published in peer-reviewed scientific journals in English, and the studies of human subjects were selected. Excluded were research that has involved animal models, in-vitro experimentation, or any study that does not present adequate information on the impact of vaccination programs. The review also pointed out the research gap primarily toward works identifying obstacles to vaccination, including those involving low-resource countries and investigations targeting policy intervention approaches, including mandatory vaccination legislation and incentive systems.

A common theme evident in most of the studies was the fact that vaccination programs helped increase immunization coverage and reduce several diseases such as rotavirus, influenza, and measles and hospitalizations. Several works revealed multiple barriers to vaccination, for example, misinformation and doubts concerning the necessity to be vaccinated, no access to vaccination services, and no means of transportation to the centers where vaccinations are carried out. It was common to call for targeted interventions to extend coverage to hitherto unserved or poorly served groups, especially those residing in rural and other disadvantaged areas. Another study also recommends increasing efforts in education and communication to address the problem of vaccine hesitancy and increase public understanding of the benefits of vaccination.

The review also highlighted the economic impacts of vaccination interventions as key to economic development through the reduction of cost burden on health care systems and improvement of workforce productivity particularly in LMICs. For example, mandatory conditions including vaccination laws and intention-based policies were perceived to improve vaccination coverage. The data analysis shows the patterns and dynamics of immunization programs across the world: the permanent investment in vaccination systems, the necessity of continuous improvements of the communication approaches to increase public confidence, and the necessity of further international collaboration to increase access to vaccines. Such attempts are important to help reduce the impact of vaccine-preventable diseases, especially in the areas where vaccination rates remain low and immune-mediated diseases remain a major issue.

Specific recommendations arising from the review were encouraging investment in vaccination programs to enhance their support structures, vertical communication, and community reassurance. The review also noted the necessity to implement the commitment within the framework of the GA 2030 which is the Global Immunization Strategic Agenda whose goal is to protect against vaccine-preventable diseases for every individual in each country. Hence, confirmation made from this review stresses the effectiveness of large-scale vaccination programs to enhance the health condition of the entire world population, especially countries that are frequently affected by diseases causing infections.

RESULTS: -

Characteristics of included studies:

In this systematic review on vaccine effectiveness in preventing outbreaks of diseases, 25 papers were included. These studies included original researches (19) such as RCTs (10), cohort designs (5), case-control designs (4), as well as modeling studies (3), and economic evaluation studies (3) respectively. All the studies were based on global vaccination programs, especially in LMICs, and assessed the impact regarding disease's incidence, vaccination rates, and health systems enhancement from a long-term perspective. Most of the studies ranged between the years 2010 and 2024, more especially from 2015 to

2023; and offered relevant information concerning vaccine effectiveness in various settings (Figure-1).

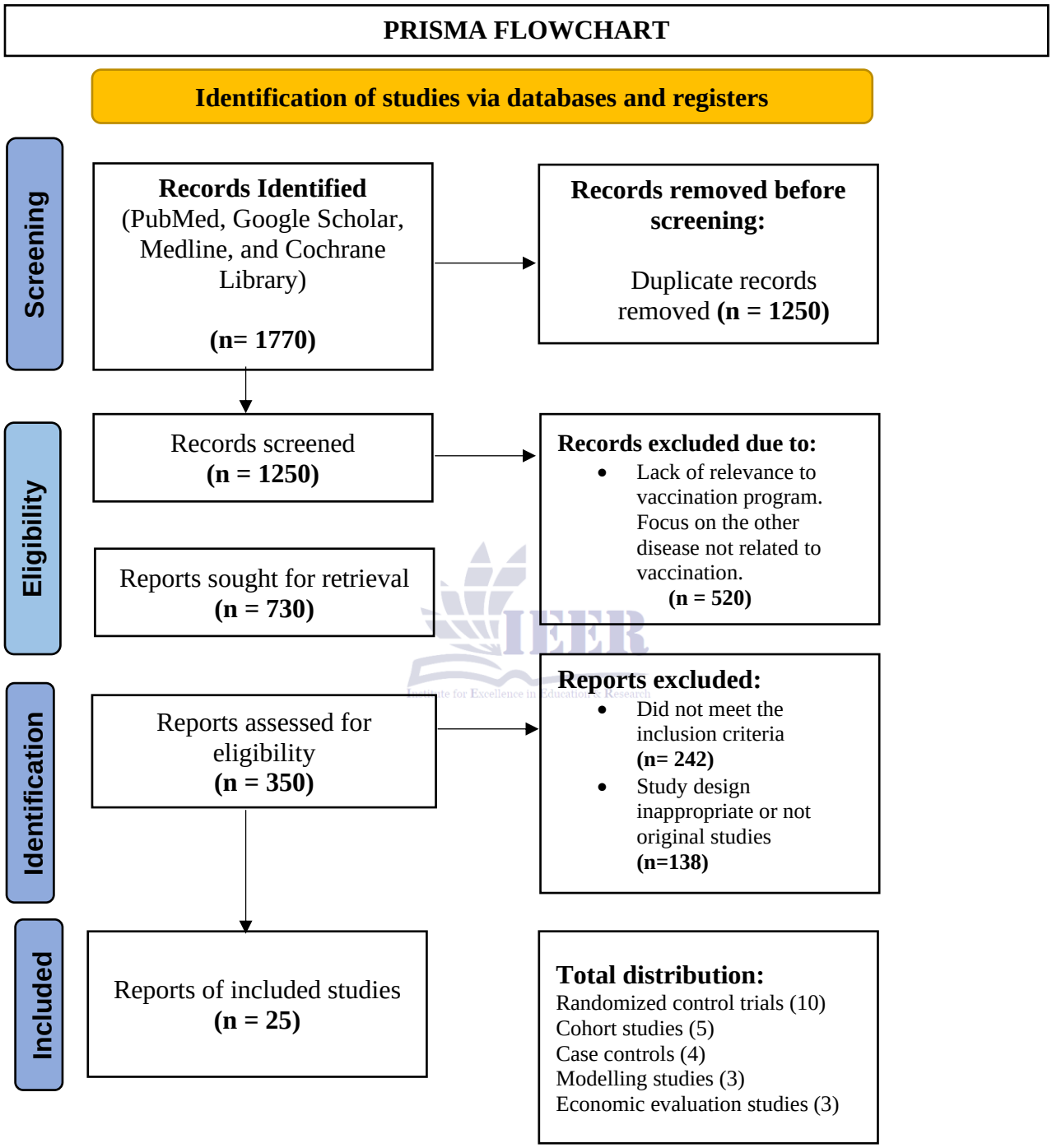

Figure-1: PRISMA FLOW CHART

I. Global Vaccine Coverage and Disease Control

Immunization campaigns are one of the keys to preventing the spread of communicable diseases in the world. Other research has also proved that immunization can substantially decrease rates of outbreaks of diseases such as rotavirus, measles, influenza, and dengue. For instance, mobile conditional cash transfer (mCCTs) was learned to have enhanced immunization coverage for children in Pakistan for $23 per fully immunized child(Chandir et al., 2022). This means that the use of financial incentives can increase vaccine demand even in a situation where resources are limited. Furthermore, the efficacy of the monovalent rotavirus vaccine was also established in El Salvador, where the rate of severe disease among children under two was significantly reduced the efficiency of which was higher among the younger children (de Palma et al., 2010). An intentional immunization against dengue in Brazil showed initially somewhat poor results because of a lack of targeting the right population, where the vaccine was only about 60% effective in people with no prior exposure to the virus (Diaz-Quijano et al., 2024).

Vaccination also plays a central role in preventing influenza, especially through maternal immunization. This systematic review that aggregated three RCTs revealed a 35% protection of maternal influenza immunization towards generalized infant influenza, with protection rising after 29 weeks of pregnancy (Omer et al., 2020). This underlines the need to give vaccines during pregnancy on time to help both the mother and her baby. Moreover, the MMR vaccine has been proven to be effective in poverty reduction of pediatric hospitalizations and prevention of not only the targeted diseases but also of other untargeted infections as evidence showed (La Torre et al., 2017).

II. Health System Strengthening

Vaccine interventions remain an important aspect of health system strengthening especially in developing countries. Modern developments in vaccines like the human papillomavirus (HPV) vaccine have played a big role in creating increased capacity in population health. In nations India, Peru, Uganda, and Vietnam, the school-based campaigns to provide HPV vaccine achieved community population coverage, indicating the acceptable approaches to fitting into the Systems of Health services (LaMontagne et al., 2011).

Other immunization interventions enhance health system coping as it shifts the load on the health organizations. The cases in South Africa and Malawi provide evidence that rotavirus vaccination reduces healthcare utilization for illnesses associated with it thus offloading pressures on health facilities to attend to other functions (Bar-Zeev et al., 2018). Nevertheless, there are still difficulties in delivering vaccines, especially in the regions that are far from large urban centers and where the population uses transportation limited to automobiles, in addition to the low coverage of vaccines. A study in New York indicates that mobile health interventions including text message maternal vaccine reminders increase vaccination rates amongst low-income populations (Stockwell et al., 2014).

III. Impact on Health Equity

Vaccination activities affect health equity in that they influence LMICs more than any other population. In different research, the benefits of vaccines for decreasing the disease incidence rate among deprived people have been indicated. mCCTs implemented in Pakistan for rural and low-income families also used financial incentives as a means through which the developing world increased immunization for its children (Chandir et al., 2022). Susceptible pregnant women immunization like in Nepal, Mali, South Africa, and other developing countries safeguards the mom and the kid hence prejudice minimal health by expanding access to preventive services in communities that often lack adequate health care (Omer et al., 2020).

HPV vaccination programs in India, Peru, Uganda, and Vietnam have further helped in eradicating disparities between gender and social classes by preventing those diseases that can be controlled and which manifest themselves in adolescent female genital organ cancers, a group that is rarely noticed in most health-oriented programs (LaMontagne et al., 2011). In this case, although vaccination programs enhance health equity the current challenges encountered include vaccination hesitance, vaccination myths, and disparities. To eliminate these obstacles, support is required, especially in rural and

underserved regions where access is lower than the average for the country.

IV. Economic Benefits and Cost-Effectiveness

Anti-infectious vaccination is very effective in prevention and has a very low cost/effectiveness ratio, especially in LMICs. In Pakistan for example, previous evaluations have shown that mCCTs raised rates of immunization at a cost of only $23 for each additional fully vaccinated child a price considered reasonable given the overall effectiveness to public health (Chandir et al., 2022). Cost-effectiveness analysis of tuberculosis vaccines also yields reasonable values where tuberculosis vaccines can potentially prevent millions of cases of illness and save billions of dollars in healthcare expenditure by 2050 (Knight et al., 2014). This confirms the long-term gains of supporting the manufacture of vaccines and discouraging illness outbreaks that could in turn affect the productivity of the workforce.

Other immunization campaigns also have a wider economic advantage since they help cut the number of people who spend time away from work whenever there are epidemics. For instance, the varicella vaccine has decreased the rate of school absenteeism and hospitalization in Qatar thus an economic reason to have mass vaccination. These indirect benefits enhance national output and lessen the general disease-caused burden on the economy (Bibi et al., 2023).

V. Long-Term Health Outcomes and Disease Eradication

Immunization does have overall long-term health benefits, which in due course may lead to the elimination of specific illnesses. For instance, the MMR vaccine has been very effective in the prevention of measles and the related complications which are hospitalizations and deaths in the world. MMR and rotavirus which are common vaccines have helped prevent infectious diseases globally but especially in more sensitive children (La Torre et al., 2017).

It turns out that the polio vaccine has helped lower the cases of polio cases all over the world, putting the world within reach of eradicating polio (Lohiniva et al., 2023). In the same way, regular immunization campaigns against such diseases as malaria and rubella are important for the prolonged control and even elimination of the diseases (La Torre et al., 2017). New vaccines like those targeting tuberculosis identified earlier can greatly minimize or eradicate some of the conditions that are still potentially deadly particularly in low-income countries hence protecting universal health security (Knight et al., 2014).

DISCUSSION: -

The studies discussed above span a wide range of vaccination and immunization-related research, from evaluating the effectiveness of different vaccines in preventing several infectious diseases to exploring innovative methods to increase vaccination uptake in low-resource settings. The findings jointly highlight the difficulties and challenges related to vaccination efforts in diverse global settings, highlighting the significance of tailored, context-specific strategies to maximize vaccine coverage, effectiveness, and public health impact.

Among these, the important focus is made on the considerable differentiation in vaccines' efficacy according to such parameters as age, the presence of chronic diseases, geographical location, and the type of vaccine. For instance, the efficacy of the monovalent rotavirus vaccines that was conducted in El Salvador in the year 2010 revealed that it gave a protective efficacy of 76% in children below the age of two years but was only 59% in children the age of 12 months or older (de Palma et al., 2010). In simple terms, this means that as the children grow older, the effectiveness of rotavirus vaccines reduces, probably because the children acquire different strains of rotavirus, or there are other immune system-related factors at play. Similarly in Botswana, a survey done to evaluate the efficacy of the monovalent rotavirus vaccine (2016) demonstrated that the vaccine was half effective in preventing rotavirus hospitalization, half of the result may be attained in well-nourished children (Gastañaduy et al., 2016). This is an indication therefore that nutritional status interacts with the performance of the vaccine, as such the socio-economic determinants such as nutrition should also be taken into consideration in the implementation of the vaccine. Studies of this sort remind us that when using vaccination, the demographic characteristics and conditions of the population should be taken into

consideration as certain factors can affect the outcome of the vaccine application.

Another crucial issue evolving from the studies is the need for effective communication tactics to advance vaccine uptake, mainly in low-income or underserved populations. The study that concerned text message communication and Influenza vaccine for pregnant women in New York City (2014) showed that an increase in early third trimester, vaccination increased up to 30% among women who received the text reminders (Stockwell et al., 2014). This helps to demonstrate how even basic, cost-effective measures such as text messages can boost vaccine rates in patient groups with possible challenges reaching, including those on lower incomes or other minorities. On the other hand, the study done in Karachi Pakistani on knowledge of maternal vaccine, in the year 2011 revealed that the intervention which was focused on the educational session for enhancing the immunization knowledge of the mothers resulted in the addition of 39 % increase in vaccine rates among the children (Owais et al., 2011). This verdict supports the notion that educational interventions, particularly those targeting women in low-literacy settings, can be extremely crucial in cultivating vaccine uptake, mostly in regions with restricted healthcare infrastructure.

In this context, more widespread studies on HPV vaccine delivery programs at numerous LMICs (2011) show that school-based vaccination programs are specifically effective in increasing coverage rates of the vaccines between 68.4 % to 96.1 % (LaMontagne et al., 2011). This finding is important for two reasons: firstly, to stress the significance of school-based interventions; secondly, to discuss overcoming programmatic barriers as a factor in increasing vaccine uptake. The study suggested the organization of more discussion strategies with the ultimate aim of focusing on approaches to overcoming logistic obstacles and enhancing positive motivational factors as the way to boost HPV vaccination coverage rates; all of the aforementioned strategies could potentially be used for other vaccines in similar conditions. Moreover, the qualitative systematic review on enhancing demand for polio vaccines in Ghana (2023) presented that the reasons concerning polio vaccine receiving among caregivers of children under five are social norms, perceived safety, and access (Lohiniva et al., 2023). Immunization program planning and implementation should, therefore, consider local contexts, social relations, and access constraints as we noted in this research. For example, social campaigns on untruths about the vaccine and social marketing of the safe benefits of the vaccine could be very effective when implemented in societies that display low acceptance of vaccines.

Therefore, the strategies for enhancing the uptake of vaccines were important and highlighted; this research also shows policymakers and the government's part in vaccine coverage and efficacy. For example, regarding the outcomes of the effectiveness of dengue vaccination with CYD-TDV (Dengvaxia) in Brazil (2024), the authors revealed that usage of the vaccine depended on the individual history of the dengue virus, so in the case of prior exposure to the virus, efficacy was considerably higher (71%) (Diaz-Quijano et al., 2024). The study recommended vaccination was given to those with a previous history of dengue infection which could be a policy implication of the study in endemic regions. The study of new tuberculosis vaccines also supported the call for investment in adolescent and adult vaccines by underlining the fact that Tube vaccines are more effective and less expensive in L&MICs (Knight et al., 2014). Urgent calls for strategic policymaking and investing in the development of vaccines, particularly for TB are threats to mankind were also highlighted by this study.

Arguably, just as crucial is the issue of cost-utility of vaccination campaigns which several studies show. Chandir et al., 2022, using data from a study on small mobile conditional cash transfers (mCCTs) in Pakistan also arrived at a similar conclusion, and reported that mCCTs, led to improved immunization coverage for $23 per additional fully immunized child (Chandir et al., 2022). This study presents the possibility of using monetary rewards to promote immunization effectively, given the effect of costs when immunization services are inaccessible in resource-constrained settings. Similarly, the study done on maternal influenza vaccination (2020) revealed that maternal vaccination was 35% effective in preventing infant influenza the higher being 71% when vaccination was done after 29 weeks (Omer et al., 2020). This discovery stresses the fact that the gains of vaccination should plan for necessary periodic

vaccinations, which can prevail. Moreover, there is a study reviewing the effectiveness of COVID-19 vaccines in Iran (2023) which demonstrates the high efficacy of vaccines like BBIBP-CorV, ChAdOx1-S, and BIV1-CovIran in preventing hospitalization and death due to COVID-19 over a certain period (Heidarzadeh et al., 2023). These findings are relevant for ongoing vaccine distribution and promote the continuing use of vaccines to combat the effects of the pandemic, especially in areas with high cases.

The studies also point to the continuation of surveillance to determine vaccine efficacy over time and across groups. The test-negative case-control study on SARS-CoV-2 vaccine effectiveness in India (2022) showed that BBV152 had the effectiveness of fifty percent against symptomatic covid, with higher efficacy if a longer gap between the two doses was considered (Oliveira et al., 2023). This study therefore encourages further surveillance and follow-up of the vaccine, especially with the new strains of the virus arising from time to time. In the same manner, a study done by La Torre et al (2017) on the efficacy of MMR vaccination in Rome, Italy also showed that not only did the vaccination against measles, mumps, and rubella was effective against the diseases targeted it was also protection against other types of infectious diseases as well as respiratory diseases; this goes to show that vaccination has got beyond health benefits against the targeted diseases, it has wider benefits (La Torre et al., 2017). Finally, these results stress the importance of continuous monitoring and investigation of vaccine efficacy, considering that new strains of pathogens appear and the range of demands in the healthcare system expands.

At last, the investigations also indicate that the rates indicating vaccine effectiveness and coverage are primarily related to issues of social contextual factors like availableness of healthcare facilities, socio-economic status, and educational levels. For example, the actual investigation of the rotavirus vaccine in the province of Quebec (2016) only established that the vaccine highly protected children against severe gastroenteritis in higher-income groups and that socioeconomic determinants of health were crucial in the effectiveness of the intervention (Gosselin et al., 2016). Likewise, in the study on cholera vaccination in Haiti (2015) the vaccine had 63% effect when self-reported and only 58% when verified, again indicating that the vaccine remains important in managing cholera in endemic nations (Ivers et al., 2015). This remains as an indication that there is a need to enforce healthcare structures and access especially in endemic regions, and the need to enhance vaccination strategies to prevent sporadic occurrences of the diseases.

Combined, these studies provide a rich portrait of immunization work as well as the kinds of difficulties that have been encountered in the global drive to enhance vaccine availability and efficacy. Regardless of the questions asked, ranging from evaluating the effectiveness of the vaccines in various environments to estimating the effectiveness of various strategies to promote immunization, the results suggest that further context-specific efforts, effective communication, and constant surveillance are crucial for immunization programs. That's why these and other similar studies remain highly relevant as the world calls for solutions to both new and old infections that continue to threaten and kill millions of people worldwide, especially in low-income and high-vulnerability populations.

CONCLUSION

In low and middle-income countries vaccination are highly beneficial in preventing disease outbreaks, enhancing health systems, and improving lifetime health. This study demonstrates how vaccines are important tools in controlling the spread of infections, eliminating health inequalities, and making big economic gains, especially in the developing world. As a result of the above barriers like logistical barriers and vaccine hesitancy, there is evidence that when targeted interventions like mobile health solutions and/or financial incentives are put in place then the barrier is likely to be overcome. The future of vaccination goals must focus on sustained investment in vaccination strategies plus innovation and related strategies that will help to maintain the existing progress towards effectively combating diseases around the world.

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Table-1: Systematic Review Analysis

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
1.	Small mobile conditional cash transfers (mCCTs) of different amounts, schedules, and design to improve routine childhood immunization coverage and timeliness of children aged 0-23 months in Pakistan: An open label multi-arm randomized controlled trial. 2022	To evaluate the impact of small mobile conditional cash transfers (mCCTs) on childhood immunization coverage and timeliness in Pakistan, comparing different amounts, schedules, and design of mCCTs, and to understand the cost-effectiveness of such interventions for improving immunization rates.	Karachi, Pakistan	11,197 caregiver-child pairs, randomly assigned to 7 arms: 5 mCCT arms, 1 reminder (SMS) arm, and 1 control arm (1598-1600 caregiver-child pairs per arm)	mCCTs increased full immunization coverage (OR: 1.18, p = 0.005) and were also cost efficient with an additional expenditure of USA $23 to immunize an additional immunologically fully protected child. This paper has established that increased payments and airtime enhanced FIC.

2.	Rotavirus vaccine effectiveness in low-income settings: An evaluation of the test-negative design. Randomized controlled trial (RCT). 2017	To evaluate the use of the test-negative design (TND) for measuring rotavirus vaccine (RV) effectiveness in low-income settings, comparing TND estimates with original RCT vaccine efficacy estimates, and assessing the core assumption that rotavirus vaccine has no effect on rotavirus-negative diarrhea.	South Africa and Malawi	4939 healthy infants aged 5–10 weeks, randomly assigned in a 1:1:1 ratio to receive two doses of RV1, three doses of RV1, or three doses of placebo	TND vaccine effectiveness (VE-TND) estimates were similar to original RCT vaccine efficacy (VE-RCT) estimates. Neither RV1 nor RV5 significantly affected rotavirus-negative diarrhea. The TND method is suitable for evaluating rotavirus vaccines.

S.NO	**Title, Study Type, and Publication Year**	**Research Objective**	**Research Setting**	**Sample and Sample Size**	**Results and Recommendations**
3.	Efficacy, duration of protection, birth outcomes, and infant growth associated with influenza vaccination in pregnancy: a pooled analysis of three randomised controlled trials. Pooled analysis of three randomized controlled trials (RCTs). 2020	To determine the vaccine efficacy of maternal influenza immunization against maternal and infant PCR-confirmed influenza, the duration of protection, and the effect of gestational age at vaccination on vaccine efficacy, birth outcomes, and infant growth up to 6 months of age.	Nepal (2011–2014), Mali (2011–2014), South Africa (2011–2013)	10,002 women and 9,800 liveborn infants across three trials	Maternal vaccination had 35% efficacy against infant influenza, higher after 29 weeks (71%). No impact on birth outcomes or infant growth. Further evaluation is needed for early vaccination.
4.	Real-World Effectiveness of the Varicella Vaccine among Children and Adolescents in Qatar: A Case–Control Study.	To evaluate the real-world effectiveness of varicella vaccination among children aged 1–18 years in Qatar during the period 2017 to 2019.	Primary healthcare system in Qatar, including the Primary Health Care	862 varicella cases and 5454 matched controls	The study found a 56% reduction in infection with one varicella dose and 86% with two. It recommended promoting the two-dose vaccine for better protection, especially in multicultural settings.

	2023		Corporation (PHCC)		
5	Effectiveness of rotavirus vaccination against childhood diarrhoea in El Salvador: case-control study. 2010	To evaluate the effectiveness of a monovalent rotavirus vaccine against severe rotavirus disease and its impact on diarrhoea in children under 2 years old in El Salvador.	Seven hospitals in cities across El Salvador (Central America), January 2007 to June 2009	323 children under 2 years old were admitted with laboratory-confirmed rotavirus diarrhea and 969 healthy controls matched for age and neighborhood	The rotavirus vaccine was 76% effective in children under 2, but only 59% in those 12 months and older. It reduced hospital admissions by 40% in 2008 and 51% in 2009. The study recommends further focus on its impact in older children.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
6.	The effectiveness of measles-mumps-rubella (MMR) vaccination in the prevention of pediatric hospitalizations for targeted and untargeted infections: A retrospective cohort study. 2017	To evaluate the effectiveness of the measles-mumps-rubella (MMR) vaccine in reducing hospitalizations for infectious diseases (both targeted and untargeted), as well as for respiratory diseases in children in Rome.	Rome	11,004 children	The MMR vaccine was highly protective against measles, mumps, and other infectious and respiratory diseases. The study concludes it is effective for primary prevention of both targeted and untargeted diseases.
7.	Influenza Vaccine Text Message Reminders for Urban, Low-Income Pregnant Women: A Randomized Controlled Trial. 2014	To evaluate the impact of influenza vaccine text message reminders on vaccination rates among low-income obstetric patients in New York City.	Community-based clinics in New York City	1187 obstetric patients enrolled from 5 community-based clinics	Text message reminders increased vaccination rates by 30%, particularly in the early third trimester. This strategy effectively boosts influenza vaccination in pregnant women.
8.	Does improving maternal knowledge of vaccines impact infant immunization rates? A community-based randomized-controlled trial in Karachi, Pakistan. 2011	To assess the impact of a low-literacy immunization promotion educational intervention for mothers in low-income communities of Karachi on infant immunization completion rates.	Low-income communities in Karachi, Pakistan	366 mother-infant pairs, with infants aged ≤ 6 weeks, randomized into intervention and control groups	The intervention group had a 39% higher vaccine completion rate (72.1% vs. 51.7%). A simple educational intervention can significantly improve vaccine completion, crucial for routine

					immunization in Pakistan.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
9.	Effectiveness of mass dengue vaccination with CYD-TDV (Dengvaxia®) in the state of Paraná, Brazil: integrating case-cohort and case-control designs. 2024	To estimate the effectiveness of CYD-TDV (Dengvaxia®) in preventing symptomatic dengue cases during a vaccination campaign targeting individuals aged 15–27 years in selected municipalities in Paraná, Brazil.	Selected municipalities in Paraná, Brazil	1869 dengue cases identified from 2019-2020, with vaccination coverage compared to the target population.	Overall vaccine effectiveness (VE) was 21.3%. VE was 71% in those with prior dengue, but only 12% in those without. The study suggests using dengue history to prioritize CYD-TDV vaccination in endemic regions.
10.	Impact and cost-effectiveness of new tuberculosis vaccines in low- and middle-income countries. Modeling study. 2014	To estimate the impact and cost-effectiveness of potential new tuberculosis vaccines in low- and middle-income countries, focusing on vaccines targeted at infants and adolescents/adults.	Low- and middle-income countries	The study used a transmission model rather than human subjects. Estimates were made based on the projected impact of vaccines in various income groups and countries.	An adolescent/adult-targeted TB vaccine is more impactful and cost-effective ($149 per DALY averted), preventing 17 million cases by 2050. Investment in such vaccines is recommended, even with lower efficacy, focusing on adults in trials.
11.	Human papillomavirus vaccine delivery strategies that achieved high coverage in low- and middle-income countries. Observational study. 2011	To assess HPV vaccination coverage after demonstration projects conducted in India, Peru, Uganda, and Viet Nam, and to explore the reasons for vaccine acceptance or refusal.	India, Peru, Uganda, and Viet Nam	Over 7,000 parents or guardians of adolescent girls from households in demonstration project areas, with HPV vaccination coverage data collected from school-based programs, health centers, and campaigns.	HPV vaccination coverage ranged from 68.4% to 96.1%, with school-based programs achieving high rates. Addressing programmatic barriers and reinforcing positive motivators can improve uptake, enhancing vaccine coverage across

					different delivery strategies.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
12.	A Cluster-Randomized Controlled Trial to Reduce Diarrheal Disease and Dengue Entomological Risk Factors in Rural Primary Schools in Colombia. Cluster-randomized controlled trial. 2016	To investigate whether interventions targeting diarrhea and dengue risk factors would reduce school absenteeism due to diarrheal disease and decrease dengue entomological risk factors in rural primary schools.	34 rural primary schools in La Mesa and Anapoima municipalities, Cundinamarca, Colombia	34 schools with 1,301 pupils	Interventions did not reduce school absenteeism or mosquito density but decreased the Breteau Index by 78% and improved water quality by 78%. Future approaches should target effective, acceptable, and affordable interventions in schools and communities.
13.	Strengthening polio vaccine demand in Ghana: Understanding the factors influencing uptake of the vaccine and the effectiveness of different message frames. Cross-sectional study. 2023	To understand the factors influencing the uptake of the polio vaccine in Ghana and assess the effectiveness of different message frames (e.g., social norms) in encouraging vaccination among mothers of children under five years old.	Ghana	708 caregivers of children under the age of 5, surveyed via an interactive mobile phone platform	35% of caregivers hadn't vaccinated their children, with lower uptake linked to access issues. Knowledge, safety perceptions, and social norms influenced uptake. More research is needed on message frames and strategies to address barriers.
14.	Effectiveness of an inactivated virus-based SARS-CoV-2 vaccine, BBV152, in India: a test-negative, case-control study. 2022	To evaluate the effectiveness of BBV152, an inactivated virus-based SARS-CoV-2 vaccine, against symptomatic RT-PCR-confirmed COVID-19 infection in India.	All India Institute of Medical Sciences (AIIMS), New Delhi, India	2714 symptomatic employees from AIIMS who had an RT-PCR test for COVID-19. The final analysis was based on 1068 matched case-control pairs (cases: test-	BBV152 showed 50% effectiveness against symptomatic COVID-19, with higher efficacy after longer dose intervals. The vaccine remains effective, especially against the delta variant, and should be

				positives, controls: test-negatives)	used alongside non-pharmacological measures.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
15.	Effectiveness of COVID-19 vaccines on hospitalization and death in Guilan, Iran: a test-negative case-control study. 2023	To estimate the effectiveness of COVID-19 vaccines (BBIBP-CorV, ChAdOx1-S/nCoV-19, rAd26-rAd5, BIV1-CovIran, and BBV152) against hospitalization and death due to COVID-19 in Guilan Province, Iran, between May 22 and December 21, 2021.	Guilan Province, Iran	42,084 participants: 19,500 COVID-19 cases (hospitalized with positive RT-PCR tests) and 22,586 controls (negative RT-PCR tests)	BBIBP-CorV, ChAdOx1-S, and BIV1-CovIran vaccines showed high effectiveness over time, particularly against hospitalization and death. Ongoing monitoring of vaccine effectiveness is crucial for ensuring sustained protection long after vaccination.
16.	Effectiveness of Vaccination During Pregnancy to Prevent Infant Pertussis. Retrospective cohort study. 2017	To estimate the effectiveness of maternal Tdap vaccination in preventing pertussis in infants during the first 2 months of life and the first year of life, accounting for infant DTaP doses.	Kaiser Permanente Northern California, USA	148,981 newborns born between 2010 and 2015	Maternal Tdap vaccination was 91.4% effective in preventing infant pertussis in the first 2 months and 69.0% during the first year. The study supports the U.S. recommendation for Tdap vaccination during each pregnancy.
17.	Effectiveness of reactive oral cholera vaccination in rural Haiti: a case-control study and bias-indicator analysis. 2015	To assess the effectiveness of the reactive cholera vaccination in Haiti and to evaluate the likelihood of bias in the study through a bias-indicator study.North-East Nigeria.	Bocozel and Grand Saline, Haiti	47 cholera cases and 188 controls in the primary case-control study; 42 cases and 188 controls in the bias-indicator study	The bivalent oral cholera vaccine showed 63% effectiveness based on self-report and 58% when verified. It provided protection for 4-24 months and remains crucial for controlling cholera in endemic areas like Haiti.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
18.	Effectiveness of Monovalent Rotavirus Vaccine After Programmatic Implementation in Botswana: A Multisite Prospective Case-Control Study. 2016	To determine the effectiveness of the monovalent G1P[8] rotavirus vaccine (RV1) against rotavirus diarrhea hospitalization in Botswana after its routine programmatic implementation.	Four hospitals in Botswana	242 case patients (children with laboratory-confirmed rotavirus diarrhea) and 368 controls (non-rotavirus "test-negative" diarrhea cases)	RV1 vaccination showed 54% effectiveness against rotavirus hospitalization, with higher effectiveness in well-nourished children (75%). Undernutrition may reduce effectiveness. The study supports continued use and monitoring of RV1, especially in low-income settings.
19.	Vaccine Effectiveness against SARS-CoV-2 Variants in Adolescents from 15 to 90 Days after Second Dose: A Population-Based Test-Negative Case-Control Study. 2023	To estimate the vaccine effectiveness (VE) against hospitalization and severe illness in adolescents due to infection with SARS-CoV-2 variants (gamma, delta, and omicron).	Brazil	8458 eligible adolescents (12-19 years of age), including 3075 cases with laboratory-proven COVID-19 and 4753 controls with negative tests for COVID-19	Vaccine effectiveness against COVID-19 hospitalization dropped from 88% to 59% during Omicron. Effectiveness against severe outcomes also decreased, emphasizing the need for updated vaccines to improve protection in adolescents..
20.	Effectiveness of Poliovirus Vaccines against Circulating Vaccine-Derived Type 2 Poliomyelitis in Nigeria between 2017 and 2022: A Case-Control Study. 2024	To estimate the effectiveness of novel type 2 oral poliovirus vaccine (nOPV2) against circulating vaccine-derived poliovirus type 2 (cVDPV2) paralysis and compare nOPV2 effectiveness with that of monovalent type 2 oral poliovirus vaccine (mOPV2) and inactivated poliovirus vaccine (IPV) in Nigeria.	Nigeria	- **Retrospective Study**: 509 cVDPV2 poliomyelitis cases, 1303 matched test-negative controls. - **Prospective Study**: 181 of 392 cases matched to 1557 community controls.	nOPV2 and mOPV2 showed low effectiveness against cVDPV2 (12%-17%), while IPV demonstrated strong effectiveness (43%-89%). Routine IPV immunization is crucial, and nOPV2 is supported for cVDPV2 outbreak response due to genetic stability.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
21.	Impact of Monovalent Rotavirus Vaccine on Diarrhoea-Associated Post-Neonatal Infant Mortality in Rural Communities in Malawi: A Population-Based Birth Cohort Study. 2018	To investigate the impact and effectiveness of the monovalent rotavirus vaccine (RV1) in reducing diarrhoea-associated mortality in infants aged 10–51 weeks in rural Malawi.	Rural communities in Mchinji, Central Malawi	**Total live births recruited**: 48,672	RV1 introduction reduced diarrhoea-associated mortality by 31%. Despite a non-significant effect on mortality (34%), these findings support rotavirus vaccination programs in rural sub-Saharan Africa to reduce infant mortality.
22.	Efficacy of a Single-Dose Regimen of Inactivated Whole-Cell Oral Cholera Vaccine: Results from 2 Years of Follow-Up of a Randomized Trial. 2018	To assess the protective efficacy of a single-dose inactivated whole-cell oral cholera vaccine (OCV) over a 2-year period, focusing on both all episodes of cholera and severe cholera episodes.	Dhaka, Bangladesh	A total of 205,513 participants were randomized, with 204,700 included in the per-protocol analysis (102,552 vaccine recipients and 102,148 placebo recipients).	The inactivated OCV showed 39% overall efficacy and 50% against severe cholera, with higher protection in older children and adults. No significant protection was observed for children under 5. A single-dose regimen provides lasting protection for older age groups.
23.	Effectiveness of Rotavirus Vaccine in Preventing Severe Gastroenteritis in Young Children According to Socioeconomic Status. Retrospective cohort study. 2016	To assess the effectiveness (VE) of the monovalent rotavirus vaccine in preventing acute gastroenteritis (AGE) and rotavirus gastroenteritis (RVGE) hospitalizations in young children based on socioeconomic status (SES) in Quebec, Canada.	Quebec Eastern Townships, Canada	- Vaccinated children (2011–2013): 5,033 - Unvaccinated children (2011–2013): 1,239 - Unvaccinated children (2008–2010): 6,436	The rotavirus vaccine showed 62% effectiveness against AGE hospitalization and 94% against RVGE. Effectiveness was lower in low-income children, highlighting the need for addressing socio-economic disparities in vaccine impact.

S.NO	Title, Study Type, and Publication Year	Research Objective	Research Setting	Sample and Sample Size	Results and Recommendations
24.	Measuring the Effectiveness of Catch-up MMR Delivered by School Nurses Compared to Signposting to General Practice on Improving MMR Coverage. Retrospective cohort study. 2020	To assess whether increased coverage of the measles, mumps, and rubella (MMR) vaccination differs between areas where school nurses deliver catch-up MMR doses to adolescents in school settings, compared to signposting to general practice.	NHS England South (South Central) commissioning boundary, UK	27, 527 Children born between 1 September 2000–31 August 2001, in school year 9 during the 2014–15 academic year	School nurse delivery increased catch-up MMR coverage by 1.6%, significantly more than the 0.2% increase with general practice ($P < 0.0001$). Contract school nurses, prioritizing minority and deprived children.
25.	Tracking Demographic Movements and Immunization Status to Improve Children's Access to Immunization: Field-Based Randomized Controlled Trial Study Type: Randomized Controlled Trial Publication Year: 2024	To assess if community volunteers tracking vaccination status and demographic movements improves timeliness, completeness, and coverage through catch-up sessions.	Foumban health district in West Cameroon.	**Intervention Group**: 633 households at midline and 729 at endline; **Control Group**: 507 households at midline and 651 at endline. **Total Sample**: 1,484 households across both groups.	The study showed significant improvements in vaccination timeliness for the 0-23 months' group, and in coverage and completeness for DPT-Hi+Hb vaccines. It recommends using community volunteers to track vaccination status and organize catch-up sessions, especially in low-resource settings, with further validation needed in other contexts.