Title: Factors affecting poor measles vaccination coverage in Sub-Saharan Africa with a special focus on Nigeria: A Systematic Review

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Abstract

Measles is a highly contagious infection that can cause severe illness in children. Vaccination is the primary means of controlling the infection with elimination a possibility. However, the Measles-containing vaccine coverage in Sub-Saharan Africa is 70% while for Nigeria, it is 54% according to official estimates and 64.7% from household surveys [1–3]. This review aimed to identify factors that contribute to the poor coverage rate and propose appropriate recommendations to address these factors. A comprehensive search of five databases was done – MEDLINE, EMBASE, GLOBAL HEALTH, CINAHL Plus, and PUBMED. The search was conducted in accordance with the PRISMA guidelines and inclusion criteria for studies were conducted in sub-Saharan Africa, evaluated measles vaccine coverage gaps, evaluated strategies for improving measles vaccination coverage and published in English.

The database search yielded 23 publications. Several different factors influencing measles vaccine coverage were identified and were grouped into four main areas: immunization system; information and communication; family characteristics; and parental attitudes and knowledge. Fears and misconceptions were common reasons for non-vaccination. Activities to improve vaccination coverage were identified and these include structural reforms such as siting health centres within or proximal to target communities, improving female literacy and conducting measles vaccination campaigns.

In conclusion, multiple reasons for poor measles vaccination coverage were identified. Factors influencing the immunization system and information and communication factors can be fixed at country level, but challenges relating to family characteristics and parental attitudes and knowledge require solutions adapted to the community of concern.

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Introduction

Measles is an exanthematous viral infection that affects only humans [4]. In susceptible populations, measles attack rates can be >90%. Measles mortality was 2.6 million deaths per year before the availability of widespread vaccination. Measles remains one of the leading causes of death among children under five years of age globally and approximately 140,000 people died from measles in 2018 – mostly children under the age of five years[5]. There has been a resurgence of measles epidemic in the USA and Western Europe with international travel and vaccine hesitancy identified as major contributors [6].

Vaccination is the primary means of preventing measles in individuals and interrupting transmission within a population. Measles vaccine is available as either a single antigen or in combination with other viral antigens, commonly mumps and rubella. These vaccines are safe, effective and cost-effective [7–10]. Different vaccination strategies have been adopted that include campaigns and routine immunization and both of these approaches are cost effective [11–13].

The World Health Organization (WHO) target was measles elimination across its six regions by 2020 [14], which was an achievable goal as measles meets the criteria for elimination [15]. In order to ensure induction of herd immunity, necessary to attain this target, WHO recommended that measles containing vaccine (MCV) immunization coverage rates should be 93-95%[7,8]. Some studies have shown declining antibody titers to measles following a single vaccination which may necessitate a second dose of measles vaccine to ensure elimination [16,17].

MCV is one of the routine vaccines administered in Nigeria as a component of the National Program on Immunization. However, a second MCV dose is not routinely administered. MCV1 coverage is also suboptimal, at 54% according to official estimates and 64.7% from household surveys [1,2]. Out of the estimated 19.2 million infants not vaccinated with at least one dose of MCV through routine immunization in 2018, about 6.1 million were in 3 countries: India, Nigeria and Pakistan[5]. From January to April 2019, 20127 measles cases with 50 deaths were reported in Nigeria[18]. Following from the successful campaign against polio, the impact of measles on under-5 mortality[19], and the

feasibility of elimination, this review was conducted to synthesize the factors contributing to measles vaccination under-coverage in Nigeria and Sub-Saharan Africa, and propose appropriate activities to improve coverage, focusing on Nigeria.

Methods

Search Strategy and study Selection

An initial comprehensive search of the following databases was done – MEDLINE, EMBASE, GLOBAL HEALTH, CINAHL Plus, and PUBMED. The search was conducted electronically via the LSHTM library on the 5th of August 2017. Reference lists were also utilized as sources for potential articles, but this yielded few useful results as papers were either duplicates of results from database searches or older than 2000. Two revised searches were conducted electronically on the PUBMED database on 8th August 2020 and 5th May 2021. The search conducted on 8th August yielded 89 articles out of which six were selected for inclusion in the review, while the search of 5th May yielded 42 articles with 4 selected for inclusion in the review.

The study questions were broken down into component keywords. Synonyms for each keyword were incorporated into the search strategy. Free text and subject heading searches were conducted. Various tools were used including truncation and wild cards. Boolean operators were also deployed. The keyword search strategy is shown in Supplement Table S1. The various keywords were combined to produce relevant articles. We restricted to published studies in English Language, conducted in Sub-Saharan Africa from January 2000 till May 2021 that focused on measles vaccination coverage gaps and how to improve the gaps. Studies were excluded if they were not specific to measles vaccination, conducted outside Sub-Saharan Africa, published in language other than English, abstracts from conferences, editorials, reports and published before January 2000.

Reference Management

OM and EO did the initial screening and reviewed full texts of articles based on the inclusion and exclusion criteria. Disagreements were resolved by BG. A table was formulated to capture descriptive information and data for each included study; Setting, Year, Author, Objectives, Study design, target

population and final number of subjects studied for outcome, description of measurement of exposure and outcome (e.g., instrument, protocol, reliability) and key findings. Supplement S1 illustrates the PRISMA flow diagram.

Quality appraisal

Quality appraisal of the selected studies was conducted using the Mixed Methods Appraisal Tool (MMAT)-version 2011 [20]. OM and EO assessed the articles for methodological quality and where ratings differed, BG broke the tie. The studies were of varied quality when assessed using the mixed methods approach. The potential for selection bias or misclassification bias was a reason for relatively lower grades. A summary of quality appraisal is presented in supplement S4.

Results

Study selection

A total of 2145 papers were found through the database searches. 2014 were from the original search in 2017 and 89 and 42 papers from the updated PUBMED search in 2020 and 2021, respectively. 23 papers were included in the final review. Among the selected studies, twelve explored reasons for measles non-vaccination by surveying populations [21–34], one article reviewed country level immunization data in order to outline strategies to improve vaccine uptake and document progress [35], one article utilized a before and after approach to assess the impact of communication strategies on vaccine uptake [36] and one article assessed the impact of Supplemental Immunization Activities (SIA) on vaccine coverage and equity [37]. Five articles relied on dataset analysis to explore the effect of Ebola virus outbreak[38], female literacy [39] maternal HIV infection[40] and inequalities [41,42] on measles vaccination respectively. One article explored the effect of vial adjustments on vaccine coverage[43].

Study characteristics

Study design and setting

The 23 studies selected were conducted in 10 Sub-Saharan Africa countries. One study involved ten African Countries. Eighteen of the selected studies were quantitative studies, one was a qualitative study, one was a case report, and three studies utilized a mixed method approach. A breakdown of the

quantitative studies reveals one case control study, one cohort study and sixteen cross-sectional studies. Supplement S3 displays the characteristics of the studies included in the review.

Factors responsible for poor vaccination uptake

The factors responsible for poor vaccine uptake can be categorized using the "Classification of Factors Affecting Receipt of Vaccines"[44] framework. There are four classes in this framework: immunization system, communication and information, family characteristics and parental attitudes and knowledge.

Immunization system: challenges in this category were found in twelve of the articles [22,24–30,32,38,43,45]. These included distance to health facilities for routine immunization and to vaccination sites for measles campaigns, stock out of vaccines, a sick child, absent vaccinators, child either too young or too old, Ebola Virus Disease (EVD) outbreak, 10-dose MCV vials, abuse at health centers from staff and no mobile clinics. Immunization system challenges were also mentioned in the qualitative surveys [24,26,27,43]. Themes emerging from the focus group discussions include distance to health facilities, lack of vaccines and charges by healthcare workers. Participants' views include:

"The health facility is very far away. That is why we only go once or twice". (Female, Nigeria)

"It is because immunisation workers collect money from our wives. Since we don't have money to give to the health workers at the immunisation centres, our wives don't go for immunisation". (Male, Nigeria)

'It is needed that they [health professionals] are able to explain the diseases which they vaccinate for, which would help mothers decide to vaccinate their children. But if they do not know why they vaccinate, caregivers will not want to accept the vaccine.' (32-y-old female care- giver, Guinea)

Communication and information: seven of the articles had themes relating to lack of information and communication [22,24,27–31]. Problems identified that relate to communication and information included lack of knowledge about time or place for routine immunization and mass campaigns, lack of awareness of the need to return for immunization when a dose has been missed and vaccination is only for children who have birth certificates. This was a finding from the focus group discussions[27]:

"We think that when we deliver at home the child cannot be immunized in the hospital". (Female, Nigeria)

Family characteristics: Fourteen articles [22,24,27,28,30–33,39–41,45–47] had themes relating to family characteristics. Such challenges include being strangers in a community, discussion of immunization in the household, either parent lacking formal education, absence of family from the community on the days of a campaign, migration, sick parent, caregiver/parent absence on immunization days, birth order (later births) and lower socioeconomic quintile. One of the studies also demonstrated an association between improving female literacy rates and vaccination coverage for the country [39].

Parental attitudes and knowledge: Nine articles covered themes relating to this aspect [21,22,24,26–31]. The different reasons given include father's will to not have a child vaccinated; side effects of vaccines including pain and excessive crying; fears, misconceptions and conspiracy theories including future sterility, paralysis, delay in walking, ineffectiveness and/or no benefits from vaccines; either parent thinking that immunization is not worthwhile, religious beliefs, parents believe access to vaccines is via door to door campaigns only, caregiver too busy/other priorities and, wrong beliefs about measles causation including ignorance about the cause, result of acts of God and witchcraft. Participants' views from the focus group discussion [27] corroborated findings from the surveys.

"Our women don't have the time to stand in a queue and wait for their turn to immunise their children. They have to go to the farm and attend to other household activities" (Nigeria, male group)

"It is due to negligence that some women don't take their children for immunisation or they don't complete the course." (Nigeria, male group)

"There is no difference seen between those children that are immunised and those that are not immunised." (Nigeria, female group)

"Some people are afraid of the side-effects. When they see another child with any side-effects, they become afraid and don't take their own children for immunisation" (Nigeria, female group). This sentiment was also echoed by mothers in Guinea with reference made to Ebola Virus disease.

Improving vaccine uptake

Six articles [26,27,35,37,40,43] explored possible ways of improving measles vaccination uptake. The focus group discussion participants discussed ways to improve uptake and suggestions include better access to services with relation to distance and fees (no charges).

"Health facilities should be brought closer to the people". (Nigeria, male Group)

"If the vaccines are always available, people can go at any time and receive the immunisation for their children". (Nigeria female group)

"Government should make sure that immunisation is free". (Nigeria, female group)

Other suggestions focused on improving communication via the use of suitable channels including community and religious leaders, female leaders, health workers and mass media campaigns.

"The Chief will tell them and they will hear" (Nigeria, female group)

"Religious leaders (Imam) can convince people to immunise their children". (Nigeria, female group)

Participants from Northern Nigeria also stated the importance of convincing husbands first so that the husband would then convince his wife or allow her to take the child for vaccination.

"The Sarki should educate husbands on the importance of it, so that our husbands in turn will allow us to immunise our children". (Nigeria, female group)

"A husband can enlighten and convince his wife on the importance of vaccination". (Nigeria, male group)

Improvements in Ghanaian measles immunization coverage rates were associated with structural reforms to healthcare delivery [35]. These reforms increased district autonomy, improved financial and managerial capacity, increased spending on health, increased the number of health posts, transport availability, payment of travel claims, greater community involvement, reduced patient waiting times and use of client active feedback. There was a reduction in number of unvaccinated children from 18% in 1993 to 9% in 1998 according to Ghanaian DHS estimates.

Equity and uptake impact of Supplemental Immunization Activities (SIA) was assessed in Kenya [37]. This study showed that SIAs improve both uptake and equity of measles immunization. Routine immunization activities had an estimated measles vaccination coverage of 77% which improved after the SIA to 90% nationally. Regional measles immunization coverage rates also improved with five different regions improving from ranges of 64%-79% with routine immunization to 88%-94% coverage rates following the SIA. Socioeconomic inequalities in immunization rates also improved with rates in the poorest wealth quintile improving from 65% (95% CI: 59%-70%) to 86% (95% CI: 82%-90%) and the 2nd poorest quintile improving from 71% (95% CI: 66%-77%) to 92% (95% CI: 88%-95%).

Adoption of 5-dose vials may also improve vaccination coverage s demonstrated in Guinea. In interviews with healthcare workers, they revealed they were less concerned about vaccine wastage and felt more comfortable opening vials to vaccinate children. 38 of 42 (90%) HCWs using 5-dose MR vials reported offering MR vaccines at every fixed session regardless of the number of eligible children presenting. The use of community health workers[40] can also improve vaccination rates as CHWs can provide health education, monitor attainment of milestones, and encourage parents to visit health facilities and access immunization services.

Discussion

Based on the findings of this review, the factors responsible for measles under-vaccination in sub-Saharan Africa and in Nigeria are multifaceted. Some of the challenges fit into distinct categories while some are cross cutting.

Weaknesses in the immunization system can undermine client confidence in the health system and they may seek alternative forms of healthcare. Studies have shown that the “sick child” argument as a reason for non-vaccination should be used with caution as children with mild illnesses can be administered MCV [48]. However, none of the studies tried to discuss the severity of illness for which the children were not immunized. This would have been relevant because the children may have had moderate to severe acute illness, which is a contraindication to vaccination [49]. The corollary is that a

child presenting for vaccination may be mildly ill since the primary reason for presenting at the clinic that day is for immunization and not for treatment. Clarifying this situation would help in framing possible solutions.

Fees also constituted an important barrier especially for the lower socioeconomic classes [27] thus worsening the patterns of socioeconomic inequalities associated with immunization uptake. A dimension of the fees challenge is that participants who asserted that it was a problem also mentioned that the services were by policy, supposed to be free. The implication is that free health policies do not always translate to charge-free services and assessing the effect of removal of user fees on immunization services uptake may yield inaccurate effect estimates. People may not have a problem with paying for immunization services if the charges are legal and transparent and the problem with paying charges may be because the charges are perceived as illegal.

Distance to health facilities was commonly mentioned as a challenge to low uptake of vaccination. However, one of the studies [32] identified a paradoxical relationship where people living relatively far from the health facilities had higher immunization rates than sites proximal to the health facilities. A possible explanation, mentioned in the study, was the presence of mobile teams that delivered vaccination to the remote areas while people more proximal to the health facilities did not have access to mobile vaccination services.

Within contemporary Nigeria, a major challenge with immunization systems is the humanitarian situations occurring in different regions of the country and a similar situation prevails in other parts of sub-Saharan Africa. The boko haram crisis resulted in destruction of health facilities and displacement of health workers from three states (Borno, Adamawa and Yobe states)[50]. In African countries affected by Ebola Virus Disease, there was a significant reduction in Measles vaccination rates. A reduction has also been observed for all vaccinations following the SARS-CoV-2 outbreak across multiple countries[51]. Maternal HIV infection, however, had no effect on timeliness and coverage of measles vaccine[40].

Inadequate information and communication also contribute to poor uptake of immunization services. Poor information and communication can compound the problem of immunization systems because even if the services are available, lack of awareness about them means those services will not be accessed. The multilingual population of Nigeria presents a challenge to communication since it requires more resources to effectively reach people who speak uncommon languages. There are more than 520 languages in Nigeria [52] though empirical evidence suggests a majority speak at least one of 5 languages (English, pidgin English, Hausa, Yoruba or Ibo). The low literacy level in parts of Nigeria, which is especially marked in the rural communities [53] that are underserved by immunization, compounds the multilingual problem..

Adoption of different communication formats may improve uptake of measles vaccine. One of the reviewed studies [36], which was conducted in Kenya, showed that house to house visits can improve vaccination uptake as it can address personal misconceptions. The use of scheduled Short Message Service reminders for vaccination appointments can also be helpful and this has shown promise in Kenya [54,55]; 88.6% and 64.8% of urban and rural residents in Nigeria, respectively, possess mobile phones and the use of SMS may help [53] to improve coverage. The use of community stakeholders and authority figures in the communities may also improve measles vaccination uptake as community members may be more receptive to messages coming from a familiar person.

A group of factors related to family characteristics were found to constitute demand side barriers to immunization uptake. Birth between April and June in Malawi results in a child reaching 9 months of age during the rainy season, which in Malawi is between January and March. Bad and flooded roads during this period may account for the lower coverage[32]. In the more conservative regions of Nigeria, the critical role played by fathers in improving child immunization was recognized and participants encouraged educating husbands to improve children immunization [27]. Birth order was mentioned in an article exploring contributors to wealth-related inequality in measles immunization[41] and a possible explanation may be confounding as lower socio-economic classes tend to have more children and low immunization coverage.

Migration may also play a role in measles vaccination under-coverage in Nigeria as communities of pastoralists may be in transit during periods of immunization campaigns, hence not accessing services during such campaigns. A study [39] found that urban residence was associated with lower immunization coverage than rural residence. A possible explanation was proposed which stated that the high risk of contracting measles in the rural areas may make parents seek out vaccination as a precautionary measure. While this may be case, further studies would be required to explore this situation.

The second group of demand-side barriers are those that relate to parental attitudes and knowledge. Fears and misconceptions still account for low measles immunization uptake in sub-Saharan Africa.

A common misconception across countries pertains to ineffectiveness of vaccination [22,27,28,56]. There was no reference to this in the focus group discussion though the interview format may have provided a more convenient method for exploring the reasons for this belief.

The challenge in addressing parental knowledge and attitudes and family characteristics is that they require specific strategies tailored to the different communities where they may be holding back immunization uptake. As shown by the Nigerian example, in the north, strategies to promote male involvement may be more critical than in the south where ensuring that services are provided free of charge may be of higher priority [27]. The importance of religious leaders cannot be overstated. Focus group discussion participants mentioned that approaching the local ruler (Sarki) may be helpful. Religious rulers played a critical role in reducing vaccine skepticism and improving uptake of services during the polio vaccine immunization crisis [57].

Finally, the discussion of findings from this review considered published strategies that may improve measles immunization uptake. Improving vaccine uptake can be achieved by improving routine immunization and implementing supplementary immunization activities. In Ghana [35], improvement in measles vaccine uptake coincided with reforms that strengthened the health systems. These include increased district autonomy with increased financial and managerial capacity, increased budgetary allocation to the health sector in general and to the districts as well. The number of outreach posts per

health facility in Ghana increased from 7 in 1997 to 8.3 in 1999[35]. Other steps focused on improving quality of healthcare with the production and distribution of guidelines and an increase in technical supervision. Part of the challenges identified under the immunization system framework above is the distance of vaccination points from homes. Increasing health posts per health facility would potentially reduce this distance and improve access. Token fees were also charged however, and this may hamper the reduction of wealth-associated inequality in measles vaccination uptake. It is also instructive that technical oversight was weak despite this being one of the aims of the reform and the immunization dropout rates were high.

Supplementary Immunization Activities (SIA) improve measles uptake. This was demonstrated in the study in Kenya [37]. Regional discrepancies and socio-demographic inequalities in measles immunization were also reduced following the SIA. This is very important concerning Nigeria due to the high regional and socio-demographic inequalities in measles vaccine uptake. Implementing SIAs to improve coverage would not be novel in Nigeria as SIAs were a major strategy in improving polio vaccination coverage [58] and contributed to the eradication of the wild polio virus in the WHO Africa region[59]. SIAs can also form part of a comprehensive strategy during outbreaks; the 2019 outbreak in Nigeria included the deployment of Rapid Response Teams[18] that supported the outbreak response including vaccination, and case management among others. Within the context of pandemics, when facility visits reduce, adopting 5-dose vials can improve coverage as healthcare workers may be reluctant to open 10-dose vials to prevent wastage[43]. Deployment of community health workers to conduct home vaccinations may also be considered as this reduces crowding at facilities.

Participants in the focus group discussions [27] also suggested some ways of improving vaccination uptake. End user suggestions are a way of assessing the felt needs of the community and implementing them may improve community adoption of vaccination and improve uptake.

Another measure that may improve vaccination uptake is improvement in female literacy as evidenced by a study in Ghana [39]. However, this requires more long-term activities to improve girl child education, improving household economic situations and strengthening female empowerment initiatives. A summary of factors and recommendations is presented in table 1.

This study had some limitations. Some of the papers did not fully explain the meaning of their factors or lumped two factors together. The search criteria may also have excluded some important contributors to low vaccination coverage rates and ways to improve them. However, other reviews[60] that looked at general childhood immunization, corroborate the findings from this review reflecting the cross-cutting nature of poor vaccination coverage.

All the papers that assessed measles immunization coverage utilized mental recall, which is a subjective means of assessing the presence or absence of a condition. Multiple interventions, including vaccination programs, are delivered to communities and parents/caregivers may not be fully aware of the differences in interventions which can increase the likelihood of a misclassification error.

The selection of only English language papers for the review may also introduce some publication bias as papers in English language may have more significant results than papers in other languages. The recruitment of participants for some of the studies were not conducted in a random manner which may also introduce bias into the results.

Declarations

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