Prevalence and dynamics of missed opportunities for vaccination among children in Africa: applying systems thinking in a systematic review and meta-analysis of observational studies

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ABSTRACT

Objective: To estimate the prevalence of missed opportunities for vaccination (MOV) among children aged 0–23 months attending health-care facilities in Africa and explore the factors responsible for MOV using systems thinking.

Research design and methods: We conducted a systematic review and meta-analysis of studies reporting the proportion MOVs. Five electronic databases were searched. A random effects model was fitted to obtain pooled estimates of MOV and a causal loop diagram (CLD) was constructed to explore the dynamics of the causes of MOV. MOV was defined as any contact with health services in Africa, by an unvaccinated or under-vaccinated child, aged 0–23 months, who is eligible for vaccination and free of any contraindication, which does not result in vaccination.

Results: Four hundred and twenty-one publications were found, of which 20 studies from 14 countries were included. The pooled prevalence of MOV was estimated to be 27.26% (95% CI: 18.80–36.62). A CLD with seven reinforcing and two balancing loops were constructed.

Conclusion: Our findings suggest that about one in every four children under the age of two years who visited health facilities in 14 African countries missed the vaccination they were eligible to receive. To enable continent-wide estimates, more MOV assessments are required.

1. Introduction

According to the World Health Organization (WHO), a missed opportunity for vaccination (MOV) is defined as ‘any contact with health services by an individual (child or person of any age) who is eligible for vaccination (e.g. unvaccinated or partially vaccinated and free of any contraindications to vaccination) which does not result in the person receiving one or more of the vaccines doses for which he or she is eligible’ [1]. It can occur during clinic visits for preventive care such as immunization and growth monitoring or curative care for injuries and ailments [2]. Nevertheless, higher prevalence has been reported in curative care settings [2]. In a previous study, the median MOV prevalence in preventice health services was 32%, as compared to 42% in curative health services [2]. MOV has been identified as an important contributor to poor childhood immunization coverage level [2,3]. According to the WHO, MOV accounts for a fraction of its strategy on MOV to focus on children aged 0–23 months attending health-care facilities in Africa and explore the factors responsible for MOV.

The reasons for MOV are multifaceted, involving multiple stakeholders such as caregivers, health workers, and health system managers [4–8]. In a health facility survey conducted in Kenya, vaccine stockout, BCG syringe stockout, child illness, and underweight were reported as reasons for not vaccinating children during clinic visits [4]. Researchers in Eswatini (formerly Swaziland) reported that MOV occurred more frequently among children requiring the first dose of all vaccines antigens because they usually do not possess vaccination cards [5]. Surprisingly, they also found that MOV was higher in health-care facilities that offer integrated services [5].

With approximately 10 million children in Africa’s annual birth cohort remaining unvaccinated or partially vaccinated, the need to position MOV reduction as a cross-cutting health systems strengthening priority has become pertinent at district and national levels [9,10]. Encouragingly, the WHO has updated its strategy on MOV to focus on children aged 0–23 months in health service settings [11]. In addition, tools and protocols for assessments have been simplified and standardized for ease of use and applicability across diverse settings [11]. However,
existing literature on synthesized evidence of the prevalence of MOV, which is necessary for informed decision-making on the continent, has limitations.

Systematic reviews of health facility-based MOV assessment in Africa where the majority of unimmunized children live are scarce [12]. Previous reviews on MOV have, hitherto, combined estimates from population-based and health facility-based surveys [2,3]. Also, the age category of participants in individual studies that were considered in earlier reviews varies widely from newborns to adolescents, whereas the current focus is on children less than two years of age [2,3].

Furthermore, previous reviews have described the factors responsible for MOV using linear approaches [2,3]. Such approaches assume that factors interact with an outcome linearly to produce expected output [13]. Under real-world condition, the immunization subsystem can be described as a complex system both in design and in number of stakeholders which can include caregivers, health workers, health facility managers, and policymakers, among others [13,14]. All these components interact in a nonlinear and dynamic manner to produce unexpected output [13]. In addition, contextual factors such as resource availability and sociocultural beliefs that are at play where these systems are located can constantly influence the behavior of stakeholders [15,16]. Growing literature on complexity offers new insights on how to contextualize problems from a system-wide perspective [17–19].

Against this background, we aimed to estimate the prevalence of MOV among children aged 0–23 months attending health-care facilities in Africa and to explore the dynamics of factors responsible for it using systems thinking. This will provide relevant evidence for health policymakers and practitioners on the continent.

1.1. Theoretical underpinning of systems thinking approach

Several studies have proposed useful conceptual frameworks for exploring factors that are associated with non-vaccination or partial vaccination among children [20–22]. These studies have highlighted the multifaceted nature of the determinants of suboptimal vaccination [20–22]. In fact, one of the frameworks enumerated health worker-, health system-, and caregiver-related problems that can predict MOV [20]. Using a complex adaptive system (CAS) theory lens in this current study, we advanced existing conceptual frameworks by elucidating how these multiple factors that are associated with MOV potentially interact with each other [23]. CAS theory offers a way of making sense of the phenomena that are dependent upon the behavior of various stakeholders and their responses [24]. The advantage of viewing a problem through this lens is that it accounts for the variation in the degree of influence of stakeholders and the unpredictability of their behaviors [25]. In addition, it recognizes the dynamical interactions and synergies that occur continuously among multiple factors [25]. Applying this theory provides further insights into leverage points within the systems that can guide the prioritization of innovative solutions. To conceptualize the dynamic architecture of the factors that cause MOV among children within an Africa context, causal loop diagram (CLD) was employed [26]. This was to enable an explicit visual illustration of the relationship between these variables [26]. Some of the key elements of CLD include causality, delays, polarity, and feedback loop which can either be reinforcing or be balancing [27].

2. Methods

2.1. Protocol and registration

A protocol that prespecified the objectives and methodology including eligibility criteria was developed in advance and registered on PROSPERO with ID number CRD42018098736 (https://www.crd.york.ac.uk/PROSPERO/). This systematic review was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [28].

2.2. Eligibility criteria

We included surveys conducted in health facilities regardless of location characteristics (rural or urban) that reported the proportion of children aged 0–23 months who remained unvaccinated or under-vaccinated despite contact with health services in Africa. The eligibility criteria are summarized in Table 1.

2.3. Information sources

2.3.1. Electronic database

To identify relevant publications, a comprehensive and systematic search of electronic databases was performed. A total of five electronic databases were searched on the internet, and they include MEDLINE (via Pubmed), Scopus, Google Scholar, African Index Medicus, and WHO Institutional Repository for Information Sharing. No date, document format, or language restriction was specified. Search terms comprising of free text and medical subject headings were used in querying all the electronic databases. The search terms included ‘immunization,’ ‘vaccination,’ ‘missed opportunities,’ ‘children,’ ‘childhood,’ ‘prevalence,’ ‘burden,’ ‘epidemiology,’ ‘Africa,’ and ‘sub-Saharan Africa.’ A detailed search

| Characteristics       | Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|-----------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Population            | Children aged 0–23 months of age                                                   | Other populations such as adolescents                                               |
| Outcome               | Missed opportunities for vaccination: by vaccine and vaccine dose.                 | Missed opportunities for prophylactic antibiotics                                   |
|                       | Missed opportunities for vaccination is defined as ‘any contact with health services in Africa by an unvaccinated or under-vaccinated child aged 0–23 months who is eligible for vaccination and free of any contraindication which does not result in vaccination’ |
| Study type            | Facility-based surveys regardless of study design.                                 | Population-based surveys                                                             |
| Context               | Health care facilities (primary, secondary or tertiary) within Africa               |                                                                                     |
strategy was developed for Pubmed and adapted for the other databases. See Appendix 1 for a detailed search strategy. The last database search was conducted on 21 November 2018. Since Google yields high search volume, we limited the search to the first 250 results [29].

2.3.2. Other sources
Focal persons from WHO and MOV partner organizations including United Nations Children’s Fund, United States Centers for Disease Control and Prevention, Medicins Sans Frontieries, John Snow Inc, Agency de Medecine Preventive, Village Reach, Clinton Health Access Initiative, Gavi – the vaccine alliance, and Bill and Melinda Gates Foundation were contacted for any unpublished manuscripts or grey literature on MOV assessments in Africa. Finally, we searched the reference list of relevant articles to identify publications that were not indexed on the databases.

2.4. Study selection
Three authors (AAA, ABW, and AMS) screened the titles and abstracts of all the publications obtained from databases for relevance. Then, they independently assessed the full text of relevant studies against the eligibility criteria. During this process, disagreements were resolved through discussion. Reviewers were not blinded to the author or journal name.

2.5. Data collection process
A data extraction sheet was developed using Microsoft Excel 2016. The tool was pilot-tested with five randomly selected studies which informed some minor refinement. Data extraction was performed by two authors (ABW and AMS), and disagreement was resolved by discussion.

2.6. Data items
The data that were extracted from each included study are as follows: Study title, year of publication, surname of first author, affiliated institution(s) of first author, country of assessment, level of health-care (primary/secondary/tertiary), sample size of children aged 0–23 months, number of children who missed vaccines or vaccines doses among children aged 0–23 months during facility visit, proportion of MOV, sampling strategy, location characteristics of health facilities, means of assessing vaccination status, number of health facilities, and factors associated with MOV. Additional information about the geographical region (using United Nations ‘standard country or area codes for statistical use’) and WHO regions, Regional Office for Africa, and Regional Office for the Eastern Mediterranean were added.

2.7. Risk of bias in individual studies
The Risk of Bias Assessment tool for Non-randomized Studies and ACRIBAT-NRSI (‘A Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies’) (see Box 1) were adapted and used in this review [30,31]. The risk of bias was assessed by scoring (low risk = 1, unclear = 0, high risk = −1) each bias type for each publication and the total score was used as the summary assessment of the risk of bias.

2.8. Summary measure
The summary measure that was computed is the proportion of MOV. This was defined as the number of children aged 0–23 months who remained unvaccinated or under-vaccinated despite contact with health services divided by the total number of children aged 0–23 months attending health facility.

3. Data analysis
3.1. To estimate the prevalence of MOV among children aged 0–23 months attending health-care facilities in Africa
To compute the summary effect size, first, proportions that were extracted from individual studies were transformed using the Freeman–Tukey double arc sine transformation method [32]. This was to avoid skewness as the proportion of MOV was reported to be zero in one of the study [33]. The transformation serves to stabilize the variance thus enabling transformed proportions to approximate normal distribution [32]. Then, the normalized proportions and their asymptotic variances were used to compute the pooled estimate. Dersimonian and Laird random effect model was fitted using the number of children who missed vaccination (r) and total sample size of children (n) to obtain the pooled prevalence of MOV for each geographical region and Africa [34]. In the model, study-specific confidence limit for the pooled estimate was constructed using Clopper–Pearson method (exact method) [35]. Stata ‘metaprop’ package was used to perform this meta-analysis [36]. Heterogeneity across studies was calculated and I² was obtained [37]. To explore the heterogeneity, potential effect modifiers were considered in the univariable meta-regression analysis. These include study characteristics such as year of publication,
geographical region, WHO region, sampling strategy, sample size, number of health facilities, location characteristics, and means of assessing vaccination status. To check for bias, a funnel plot was constructed [38]. Then, Egger’s test was performed with included studies to explore for publication bias [39]. In addition, a contour-enhanced funnel plot was constructed [40]. Meta-analysis results were reported as pooled prevalence with 95% confidence intervals (CIs), while meta-regression results are reported as odds ratio with 95% CIs. All analyses were performed in Stata 14.2.

3.2. To identify factors associated with MOV among children aged 0–23 months attending health-care facilities in Africa

Factors were extracted from the included studies and then categorized into three themes as follows: health service–related factors, caregiver/parents–related factors, and health workers–related factors. The authors brainstormed on the identified factors before using them to build a CLD. AAA constructed the CLD, while CSW, OAU, MAG, ABW, ASM, and AAA validated the diagram. The validation was done by manually assessing the structure of the diagram and proposed linkages [41]. The linkages were assessed for clarity and plausibility. Disagreements were resolved through discussions.

3.3. To describe the dynamics of identified factors and their relationship with MOV

Variables were linked using arrows (→) to denote the direction of influence. If the influence is in the same direction, a positive (+) polarity is used, otherwise, a negative (−) polarity is indicated. In the diagram, we termed closed cycles as balancing feedback loop (denoted with B) if the effect of a change in the variables results in a counter change in the opposite direction, and reinforcing feedback loop (denoted with R) if the effect of a change in the variables within the loop will propagate more change in the same direction. CLD was built with Vensim PLE x32 [42].

4. Results

4.1. Characteristics of the included study

A total of 421 publications, 102 from Pubmed, 69 from Scopus, and 250 from Google Scholar, were retrieved. Upon removing duplicates, 366 studies were left. An additional 312 studies that were not relevant to our study were removed. A total of 54 full-text articles were selected for critical reading. Finally, 20 studies (three in French language) conducted across different levels of health care were included in this review [4,5,7,33,43–58]. The study selection process for this systematic review is presented on the PRISMA flow chart in Figure 1. No unpublished manuscript or reports were received. To avoid double counting, a thesis was excluded since it had also been published as a manuscript [51]. The included studies involved 6030 children under two years of age from 14 countries and were published between 1989 and 2017 as shown in Figure 2.

The countries are distributed across both WHO regions (EMR, 5; AFR, 15) on the continent. Sudan and Egypt are countries on the African continent that are in the EMR. The number of MOV assessments were highest in Sudan and Nigeria. Other characteristics of included studies are in Table 2.

4.2. Risk of bias of included studies

Based on sample selection, 4 out of 20 studies were assessed as having low risk, and risk was unclear in 8 studies thus yielding a score of −4. Participation rate was classified low risk in 17 studies and unclear in 3, hence, a score of 17. Analysis was appropriate for the type of sample across studies, thus yielding a score of 20. Detailed assessment of the risk of bias for each of the included studies is shown in Box 2.

4.3. Prevalence of MOV in Africa

The prevalence of MOV ranged from 0% (95%CI: 0.00–4.74) in Zimbabwe to 64.07% (95%CI: 58.04–69.80) in Sudan. Prevalence of MOV by geographical region are as follows: Western Africa [20.02% (95%CI: 15.87–24.53)], Eastern Africa [18.92% (95%CI: 4.43–40.16)], Southern Africa [39.38% (95%CI: 34.45–44.41)], and Northern Africa [46.99% (95%CI: 32.82–16.41)]. The overall random pooled prevalence on MOV among children aged 0–23 months in African health facility–based surveys is 27.26% (95%CI: 18.80–36.62). The variation in effect size that is attributable to heterogeneity (I²) is 98.36%. Figure 3 is a forest plot of the prevalence of MOV for 20 studies conducted in Africa.

Following univariable meta-regression analysis of study characteristics, it was found that the WHO region where the study was conducted had an unadjusted odds ratio (OR) of 3.12 (95% CI: 1.10–8.83) with a p-value of 0.03. The unadjusted OR and p-value for other study characteristics are presented in Table 3.

The funnel plot for estimates obtained in this study appeared asymmetrical. Following Egger’s test, the estimated bias coefficient was −9.66 (95%CI: −16.87 to −2.45) with a standard error of 3.42 and p-value of 0.012, thus providing evidence of small study effects. In the contour enhance funnel plot shown in Figure 4, studies appear to be missing in the area of low statistical significance, thus suggesting the presence of publication bias.

4.4. Dynamics of MOV

Of the 20 studies included in this review, 18 reported factors responsible for MOV. Using data extracted from individual studies, a CLD of these factors was constructed. We found seven reinforcing loops and two balancing loops. The first reinforcing loop (R1) depicts the direct relationship between health services and missed opportunities, while the second reinforcing loop (R2) shows the interplay between availability of commodities in health facilities and missed opportunities. Other loops are shown below in Figure 5.

5. Discussion

5.1. Main findings

This study advances current knowledge on MOV in Africa. The overall pooled prevalence of MOV was found to be...
27.26% (95%CI: 18.80–36.62). To the best of our knowledge, this is the first systematic review to compute the prevalence of MOV among children aged 0–23 months on the continent. In addition, this review focused on health facility–based surveys. The study also explored the regional difference in MOV prevalence. Furthermore, elements of complexity were innovatively used within the framework of a systematic review to explore the dynamics of MOV in Africa. CLD was used to illustrate the interrelationships between variables including feedbacks and delays. In our diagram, seven reinforcing loops and two balancing loops were identified.
### Definition of MOV

| S. no. | Study ID  | First author | Country | Geographic region (United Nations classification) | Number of health facilities | Year of MOV assessment | Location characteristics | Level of health care | Means of assessing vaccination status |
|--------|-----------|--------------|---------|--------------------------------------------------|-----------------------------|-----------------------|------------------------|-------------------|-------------------------------------|
| 1      | MOV001    | Borus (2004) | Kenya   | Eastern Africa                                   | 6                           | 2001                  | Urban                  | Mixed             | Combined vaccination cards and self-reporting |
| 2      | MOV002    | Brugh (1995) | Ghana   | Western Africa                                   | 3                           | Not clear             | Rural                  | Secondary         | Combined vaccination cards and self-reporting |
| 3      | MOV003    | Daly (2003)  | Eswatini | Southern Africa (Previously Switzerland)          | 34                          | 1997                  | Mixed                  | Primary           | Combined vaccination cards and self-reporting |
| 4      | MOV004    | Dawria (2017)| Sudan   | Northern Africa                                   | 1                           | 2016                  | Urban                  | Tertiary          | Combined vaccination cards and self-reporting |
| 5      | MOV005    | Dyer (1993)  | South Africa | Southern Africa                               | 24                          | 1991                  | Mixed                  | Mixed             | Combined vaccination cards and self-reporting |
| 6      | MOV006    | Hipgrave (1992)| Malawi | Eastern Africa                                   | 12                          | Not clear             | Rural                  | Mixed             | Combined vaccination cards and self-reporting |
| 7      | MOV007    | Loevinsohn (1989)| Sudan | Northern Africa                                   | 11                          | Not clear             | Urban                  | Mixed             | Combined vaccination cards and self-reporting |
| 8      | MOV008    | Loevinsohn (1992)| Sudan | Northern Africa                                   | 12                          | Not clear             | Urban                  | Mixed             | Combined vaccination cards and self-reporting |
| 9      | MOV009    | McCormick (1996)| Zimbabwe | Eastern Africa                             | 4                           | 1995                  | Urban                  | Mixed             | Combined vaccination cards and self-reporting |
| 10     | MOV010    | Tagbo (2005) | Nigeria | Western Africa                                   | 1                           | Not clear             | Urban                  | Tertiary          | Combined vaccination cards and self-reporting |
| 11     | MOV011    | Ubajaka (2012)| Nigeria | Western Africa                                   | 1                           | 2010                  | Urban                  | Tertiary          | Combined vaccination cards and self-reporting |
| 12     | MOV012    | WHO (1989)   | Egypt   | Northern Africa                                   | 1                           | 1988                  | Rural                  | Secondary         | Combined vaccination cards and self-reporting |
| 13     | MOV013    | WHO (1990)   | Ethiopia| Eastern Africa                                   | 9                           | 1988                  | Mixed                  | Combined vaccination cards and self-reporting |
| 14     | MOV014    | WHO (1989)   | Zimbabwe| Eastern Africa                                   | 2                           | 1987                  | Mixed                  | Not indicated     | Combined vaccination cards and self-reporting |
| 15     | MOV015    | Malual (2017)| South Sudan | Eastern Africa                        | 1                           | 2012                  | Urban                  | Tertiary          | Combined vaccination cards and self-reporting |
| 16     | MOV016    | Talani (2000)| Congo   | Middle Africa                                   | 10                          | 1998                  | Not Indicated          | Not clear         | Vaccination card |
| 17     | MOV017    | Josse (1989) | Benin   | Western Africa                                   | 7                           | 1989                  | Urban                  | Not clear         | Vaccination card |
| 18     | MOV018    | Fermon (1995)| Republic of the Niger | Western Africa | 5                          | 1992                  | Urban                  | Not stated        | |
| 19     | MOV019    | Himat (2003) | Sudan   | Northern Africa                                   | 11                          | 2003                  | Mixed                  | Combined vaccination cards and self-reporting |
| 20     | MOV020    | Onyiriuka (2005)| Nigeria | Western Africa                                   | 1                           | 2003                  | Urban                  | Secondary         | Combined vaccination cards and self-reporting |
5.2. Limitations and strengths of the study

Our findings should be interpreted bearing in mind the limitations and strengths of this study. The included studies span over two decades, from 1989 to 2017, which we consider to be a limitation. There would have been several changes to national immunization policies between those years. Although we would have conducted a subgroup analysis to stratify by time period, only 20 studies were included. The included studies span over two decades, from 1989 to 2017, which we consider to be a limitation. There would have been several changes to national immunization policies between those years. Although we would have conducted a subgroup analysis to stratify by time period, only 20 studies were
Due to this paucity of data, we had to be cautious so as not to produce estimates that might be misleading. In this study, we use a comprehensive and systematic search strategy, but we cannot conclude that all relevant publications were retrieved. Only 20 studies covering 14 out of the 54 countries in Africa were found. Even though subregions within the continent were represented, the findings should still be interpreted with caution.

Also, we observed high heterogeneity ($I^2$ of 98.36%) that was in part explained by the variation in WHO regions (Africa and Eastern Mediterranean). As a systematic review of observational studies that included surveys from multiple countries, heterogeneity is to be expected. It is likely that some factors or links might be missing in the CLD. This is especially important as we relied on published literature as our source of information. Also, as a conceptual tool, the direction of causality, and polarity are mostly based on the experiences of the authors. As a result, authors from different contexts might not necessarily replicate the same diagram.

A key strength of this study is that it was conducted in accordance with a standardized systematic review guideline. Our search included both published and unpublished literature. Also, five electronic databases were searched with no date or language restrictions. We predefined our eligibility criteria and three reviewers used it to rigorously assess included studies. In addition, we transformed the proportions that were extracted from individual studies to avoid skewing our estimates. Another key strength of this study is that we used CAS lens to enhance the description of the factors that are associated with MOV. This guided our interpretation of how the variables interrelate, thus accounting for underlying

| Study characteristics | Odds ratio | 95%CI | p-Value |
|-----------------------|-----------|------|---------|
| Year of publication   | 0.99      | 0.93–1.05 | 0.69 |
| Geographical region   | 1.32      | 0.91–1.92 | 0.14 |
| WHO region            | 3.12      | 1.10–8.83 | 0.03 |
| Sampling strategy     | 1.03      | 0.48–2.14 | 0.93 |
| Number of health facilities | 1.04 | 0.98–1.10 | 0.22 |
| Characteristics of location | 1.32 | 0.67–2.59 | 0.40 |
| Means of assessing vaccination status | 1.67 | 0.86–3.22 | 0.12 |
| Sample size           | 1.00      | 0.99–1.00 | 0.71 |

Figure 4. Contour-enhanced funnel plot of individual studies.

Figure 5. Causal loop diagram of factors associated with missed opportunities for vaccination.
complexity. Primary studies that are included in systematic reviews are a good source of data on moderators. Using CLDs to explicitly describe these factors within the context of a systematic review is a novel approach, which further broadens the applications of systems thinking.

5.3. MOV in Africa

African states, alongside other WHO member countries in 2012, endorsed the Global Vaccine Action Plan (GVAP) which aims to achieve 90% national immunization coverage and 80% immunization coverage at the district level, among other targets, by 2020 [59]. To support implementation efforts within the African region, a Regional Strategic Plan for Immunization 2014–2020 was developed [60]. Furthermore, in 2016, African countries reiterated their commitment to universal access to immunization within the framework of the sustainable development goals. However, the performance of immunization systems on the continent remained suboptimal [61]. So far, only 18 countries have met the GVAP target of 90% national immunization target [9]. According to the 2017 assessment report of GVAP, immunization coverage in the African region, at 74%, was lowest in the world [61].

Although several activities to improve immunization coverage are being implemented in various countries across the continent, health facility-based efforts receive less attention. Therefore, children who are eligible for vaccination often make contact with health services and exit without receiving the vaccine(s) or vaccine dose(s) for which they are due, thus resulting in MOV. Our study confirmed this, as we found that about 1 in 4 children aged 0–23 months in 14 African countries were missed for vaccination in health-care settings. The estimate we obtained in our study is lesser than MOV estimates for low- and middle-income countries [32.2% 95%CI (26.8–37.7)] most likely because we limited our age group to only children less than two years as recommended in the updated MOV methodology [1,3].

Home-based records (HBR) play an important role in MOV assessments [1]. It enables accurate quantification of the number of children who missed vaccination, as opposed to caregiver recall. Accordingly, in the updated MOV assessment methodology, immunization history that is obtained from HBR or any temporary immunization document is recommended [1]. In this review, we found that the majority of the studies assessed vaccination status using a combination of HBR and recall. To further improve the accuracy of assessments, there is a need to adhere to the updated MOV methodology.

This study presented a conceptual diagram that proposed the direction of relationship for several caregiver, health worker, and health systems factors that cause MOV. Loop R1 indicates that an increase in health service delivery will decrease MOV, and in turn, an increase in the number of children being immunized upon contact with health services will impact on health services as this can constraint resources. In loop R2, we postulate that an increase in health services delivery will increase the utilization of vaccines and syringes in clinics, and thus lead to stock-out of these consumables, thereby increasing MOV. Loop R3 shows that increased literacy level among caregivers is likely to increase knowledge of expanded programme on immunization which can in turn improve caregiver possession of vaccination cards to enable routine screening during clinic or hospital visits.

Reluctance to open new vials of vaccines stemming from poor attitude and practices among health workers can increase MOV as shown in loop R4. In addition, information about MOV in a clinic can improve health workers attitude and practice toward immunization. Targeted training and capacity building in clinics and hospitals can reduce the level at which health workers fail to vaccinate as a result of false contraindication, which can then reduce MOV as shown in loop R5. An increase in health service delivery can result in MOV through clinic delays and increase in time spent by caregivers in the clinic as shown in loop R6. Loop R7 show that poor attitude and practice of health workers toward immunization can decrease the level of attention given to vaccination history among children, which will further decrease the frequency of routine vaccination card screening in clinics, thereby worsening MOV.

Loop B1 indicates that increased health service delivery will result in better confidence in the system, thus increasing caregiver utilization and subsequently reducing MOV. Training and capacity building programmes can improve the attitude and practice of health workers involved in immunization services, and this can reduce non-vaccination due to false contraindication in loop B2. Some leverage points for interventions include routine screening of vaccination cards (R7), addressing false contraindication to vaccinate (R5), preventing reluctance to open new vial (R4), preventing consumable stock-out (R2), and reducing clinic delay (R6) among others were identified.

Several factors that can influence the caregiver utilization of immunization services were depicted. Those that improve utilization include literacy level of caregivers, low parity, and previous immunization in the child. While factors such as illness in the child, older child, fever or illness following last immunization, cost (transportation to health facility or service charges), when a caregiver was previously denied immunization, first immunization, language barrier with health workers, forgot about child’s immunization, fear of adverse effects, when the caregiver is ill, low socioeconomic status, fear of vaccinating an ill child, distance to health facilities, having an underweight child, and traditional beliefs and customs can all reduce utilization. Also, the dynamics of factors that affect the level of health service delivery were shown. Those that can increase the level of health service delivery include integration of services, emphasizing preventive care in clinics, provision of preventive services. While those that can reduce service delivery include curative services, workload, manpower, and vaccination clinic scheduling.

This research has implications for policy and practice. The study provided additional evidence regarding the magnitude of MOV among children aged 0–23 months in Africa. However, only 20 studies met the inclusion criteria. Considering the diverse settings on the continent, more context-specific surveys that focus on this age group are required. The occurrence of MOV in health services setting within Africa is unacceptable given the low immunization coverage in the general population. Decision-makers at the regional and national levels need to emphasize tailored strategies to address MOV in broader health sector plans so as to maximize the use of existing health facilities for the provision of immunization services.
The CLD illustrated the dynamics of factors responsible for MOV. The diagram shows potential leverage points that can be useful for designing facility-based interventions including quality improvement interventions. Given that multiple stakeholders were identified, innovative, facility-generated solutions that target them concurrently might be useful.

Our research recommendations are presented in Box 3 using the evidence, population, intervention, comparison, outcome, and time stamp EPICOT+ format [62].

**Box 3. Use of EPICOT+ framework to recommend future primary studies on MOV assessment in Africa.**

| Element | Core elements | Recommendation(s) |
|---------|---------------|-------------------|
| Evidence (state of evidence) | Only systematic review included 20 studies from 14 African countries were found | MOV assessments using WHO’s updated methodology should be used across multiple contexts in Africa as follows: |
| a. Children aged 0–23 months (with analysis disaggregated by age group: 0–11 and 12–23 months) | |
| b. Children attending specialized clinics for HIV, sickle cell disease, etc. | |
| c. Children in conflict affected areas | |
| d. Children living in slum and non-slum urban areas | |
| Population (Population of interest) | MOV assessments using WHO’s updated methodology should be used across multiple contexts in Africa as follows: | |
| Interventions | Based on our findings we recommend small tests of change that focus on some of the leverage points identified in our CLD through: | |
| a. Facility-based quality improvement projects for addressing MOV | |
| b. Collaborative quality improvement projects with multiple facilities to address MOV | |
| Comparisons | Control health facilities | |
| Outcomes | Proportion of MOV defined as the number of eligible children aged 0–23 months who missed vaccination (by vaccines and vaccine doses) divided by total number of children aged 0–23 months attending health facility | |
| Time stamp | January 2018 | |
| Optional element | For MOV Assessments: cross-sectional studies employing multilevel analysis approach to account for the independent influence of individual and contextual factors that can determine MOV | |
| Study type | For interventions: quasi-experimental studies | |

6. Conclusion

In conclusion, this study provided an estimate of the prevalence of MOV among children aged 0–23 months based on primary studies from 14 African countries. The findings suggest that about one in every four children under the age of two years who visit health facilities miss the opportunity to receive immunization services in these countries. This indicates that efforts to address MOV within health service settings in these countries can considerably improve immunization coverage. To enable continent-wide estimates, more MOV assessments are required. In addition, the interrelationships depicted in the CLD enhanced the understanding of factors and revealed leverage points for interventions.

Funding

The research reported in this publication was supported by the South African Medical Research Council with funds received from the National Research Foundation of South Africa through its competitive programme for rated researchers. This work is based on research supported wholly/in part by the National Research Foundation of South Africa (Grant Number: 106035).

Declaration of interest

A. Adamu and C. Wiysonge are supported by the South African Medical Research Council and the National Research Foundation of South Africa. O Uthman receives support from the National Institute of Health’s Official Development Assistance (ODA). A Wiyeh is supported by the South African Medical Research Council. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

Authors contribution

AAA conceptualized the study, developed the protocol, performed literature search, conducted data analysis and interpretation of results, wrote the first draft, reviewed and edited subsequent drafts. AMS and ABW participated in screening, data extraction, data analysis and manuscript review. CSW, OAU, MAG supervised the study, reviewed and contributed to protocol development, manuscript draft, interpretation of results, and were responsible for the final approval of the manuscript. All authors read and approved this manuscript.

Acknowledgement

We are grateful to the information specialist and librarians that supported this review with technical assistance. Joy Oliver of Cochrane South Africa, South African Research Council, Tygerberg, assisted with the development of the search strategy that was used in this review. Ingrid van der Westhuizen, Tracey Louw and Pamela Nyokwana, of the Medicine and Health Science Library of Stellenbosch University, South Africa assisted with retrieving published manuscript through inter library loan.

Reviewer declaration

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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