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Title Page

Title: Missed Opportunities for Vaccination in Médecins Sans Frontières supported health facilities: eldest children urge for a second chance.

Running Title: MOV in MSF supported health facilities

Key words: MOV, vaccination, children, immunization program, survey, low-income countries, Expanded Program of Immunization, missed opportunities

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Title: Missed Opportunities for Vaccination in Médecins Sans Frontières supported health facilities: eldest children urge for a second chance.

Abstract

Objective

To describe Missed Opportunities for Vaccination (MOV) among children visiting MSF-supported facilities and its related factors, and to identify reasons for non-vaccination.

Methods

We conducted a cross-sectional survey in 19 MSF-supported facilities between 2011 and 2015 in Mauritania, Niger, South Sudan, Democratic Republic of Congo, Pakistan, and Afghanistan, including children 0-59 months of age whose caregivers presented their vaccination card at consultation exit. We describe MOV prevalence and assess the association of MOV with age, type of facility and reason for visit.

Findings

Among 5055 children's caregivers interviewed, 2738 presented a vaccination card. Of them, 62.8% were eligible for vaccination and of those, 64.6% had a MOV. Presence of MOV was more likely in children visiting a hospital or visiting a health facility for a reason other than vaccination. MOV occurrence was significantly higher among children aged 12-23 months (84.4%) and 24-59 months (88.3%) compared with children below 12 months (56.2%), $p \leq 0.001$. Main reasons reported by caregivers for MOV were lack of vaccines (40.3%), reason unknown (31.2%), and not being informed (17.6%).

Conclusion

MOV remains an important problem in low resource settings. Children beyond the Expanded Program of Immunization target are particularly vulnerable for MOV; therefore, assessments should include children above 23 months of age to better estimate MOV. We strongly recommend assessment of eligibility for vaccination in all children in health care settings regardless of the visit reason and strengthening implementation of "Second year of life" visits to reduce MOV.

Strengths and limitations of this study

- The major strength of the study is that only children with a valid vaccination card were included, so not relying on self-reported data helped to avoid potential recall bias
- Differences by gender on Missed Opportunities for Vaccination were not explored
- Reasons related with Missed Opportunities for Vaccination were limited to those included at the questionnaire and declared by caregivers.

Introduction

Since 1983, the Global Advisory Group of the Expanded Program of Immunization (EPI) has recommended using every opportunity to immunize each eligible child, regardless of the reason for consultation. If that occasion does not result in receiving all the vaccines for which the child is eligible, it is defined as a Missed Opportunity for Vaccination (MOV). Among the causes for under-vaccination in low and middle-income countries, 44% are for reasons related to health systems, including MOV and lack of access to health care (1). In 1993, the first systematic review, including 45 countries, found a median MOV prevalence of 67% (2). Since then, the World Health Organization (WHO) has promoted the use of MOV surveys to measure the performance of health services in vaccination (3),(4). In order to improve immunization coverage, in 2017 WHO recommended a revised methodology to assess MOV, targeting children aged 0-23 months (5). However, data is scarce on MOV prevalence in children above 23 months of age (6). Through its medical humanitarian programs in low and middle-income countries, Médecins Sans Frontières (MSF) strengthens routine vaccination services regardless the age of the child following WHO recommendations in order to reduce the number of under and unvaccinated children. Therefore, we took the opportunity to systematically assess MOV in children up to five years of age within MSF programs.

Our objective was to describe the MOV prevalence and characteristics, and to identify reasons for non-vaccination among children up to five years of age visiting MSF-supported health facilities in six different countries.

Methods

Study design and settings

A cross-sectional exit survey of caregivers was performed in 19 health facilities (four hospitals and 15 primary health care centers [PHCC]) between 2011 and 2015 in six countries: Mauritania, Niger, South Sudan, Democratic Republic of Congo, Pakistan and Afghanistan.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study population and participant selection

The study population consisted of children up to five years of age accompanied by a caregiver, visiting an MSF-supported facility. Health facilities and time to perform the assessment were selected on a convenience basis during the study period. A convenient sample of all caregivers accompanying a child under five years of age on the specific day of the survey in each facility were approached. Caregivers were invited to participate at the facility exit, regardless of the reason for the visit, and those who provided oral consent were interviewed. If several children were present per caregiver, the interviewer included them all. Children whose caregivers did not present the respective vaccination card were excluded from the analysis.

Data collection

MSF developed a standardized methodology to assess MOV based on the 1988 WHO tool. Interviews were conducted in local languages. In preparation for the survey, local staff received a two-day training focusing on conducting the interview and identification of eligible children for vaccination according to national vaccination schedules.

A structured questionnaire was used (Supplementary material). Information on type of facility (hospital or primary health care center [PHCC]), age of the child, presentation of vaccination card, reason for visiting the facility and vaccination history were collected. Surveyors

determined if the child was eligible that day for at least one vaccine dose according to age and the national vaccination schedule, whether he/she had received all the recommended vaccines during the visit, and the presence of a contraindication for vaccination (defined as fever above 38,5 °C). For those who had not received each of the recommended vaccines during the visit, surveyors asked for reasons why the child was not vaccinated, caregivers' acceptance of receiving the missing vaccines doses, and their awareness of next vaccination appointment.

Data analysis

We classified children as having a MOV as per standard WHO's definition (5) according to each national vaccination schedule. A MOV occurs when a child eligible for vaccination (without contraindication) remains unvaccinated or partially vaccinated (not up to date) at the end of any visit to a health facility (Figure 1).

We calculated the prevalence of MOV as the number of children with MOV divided by the number of children eligible for a vaccination - which excluded those already up to date at the start of the visit and those with a reported contraindication. Among children with MOV we calculated 1. vaccination acceptance (as the proportion of caregivers who would have accepted vaccination if it had been proposed on the day of the visit) and 2. vaccination appointments given (as the proportion of caregivers who knew their date of next vaccination appointment).

Proportions were used to describe the children and to estimate MOV. Significant differences in the distribution were assessed using the Pearson's two-sided Chi-square test or Fisher exact test. For the bivariate analysis, age was categorized in targeted by the EPI (below 12 months of age) or not targeted (≥12 months). Reason for visit to the facility was grouped into either vaccination or other reasons. We assessed the association of MOV with age, type of facility and reason for visit by calculating Odds Ratios. A logistic regression model was adjusted for age

(0-11,12-59 months), type of facility (hospital, PHCC), and reason for visit (vaccination, other reason). The level of statistical significance was set at $p < 0.05$.

In each facility, data entry officers inputted the paper questionnaire data into an Excel database, which was validated by two of the study investigators. The analysis was performed using STATA (version 16, College Station, Texas).

Ethic statement

Prior to each evaluation authorization from the local health authorities and from the director of each health facility was obtained. Oral consent was obtained from each caregiver. During the survey, children identified with MOV were sent back to the vaccination unit to receive the missing vaccine(s) if the caregiver agreed and if there was no shortage. All data from the questionnaires were anonymous and entered into a dedicated password-protected electronic database. This research fulfilled the exemption criteria set by the Médecins Sans Frontières Ethics Review Board.

Results

From 2011 to 2015, the caregivers of 5055 children were interviewed in 19 facilities (four hospitals and 15 PHCC). We report the results for the 2706 (53.5%) children who presented their vaccination card on the day of the survey: 1888 from Niger, 447 from South Sudan, 244 from Mauritania, 79 from Democratic Republic of Congo, 33 from Afghanistan and 15 from Pakistan.

Characteristics of the study population

Among the 2706 children included, 995 (36.7%) where already up to date before the visit, and 1711 (63.2%) where eligible for vaccination. Twenty three caregivers (1.3%) reported a contraindication (Figure 1). Among eligible children, 609 (36.1%) were vaccinated during the visit, whereas 1079 (63.9%) had a MOV at exit from the health facility.

Children's baseline characteristics are presented in Table 1. Their mean age was 10.1 months (Standard Deviation - 9). The majority (2213, 81.8%) were interviewed at exit of a PHCC. The most common reason for visiting the health facility was curative consultation (831, 30.7%).

Characteristics of children with MOV

Most of the children who were eligible for vaccination and consulting for a reason other than vaccination, had a MOV (960, 71.9%), while a third of the children coming to the facility for vaccination also had a MOV (119, 33.7%). More than 80% children aged 12-23 months and almost 90% of children aged 23-59 had a MOV, compared to 55% of children below 12 months. MOV occurrence was significantly more likely among older children than younger ones (Table 1).

Only four caregivers of children with MOV would have refused vaccination if it had been proposed during the visit. About one fifth (21%) of caregivers of children with MOV were aware of the date of the next vaccination appointment.

The most common reason declared for having a MOV was lack of vaccines (40.1%), followed by reason unknown (32%), not being informed (17.3%), lack of staff (3.3%), waiting time too long (1.7%) and other unclassified reasons (5.6%).

Factors related with presence of MOV

Children above 12 months of age (not targeted by the EPI) and those accessing the health facility for a reason other than vaccination, had an almost five times higher risk of having a MOV (Table 2), compared to children below 12 months of age and those visiting for vaccination. Those children visiting a hospital had 2.7 times higher risk for having a MOV than children visiting a PHCC. After adjusting by type of facility and reason for visit, children above 12 months still had a significantly higher risk of having a MOV (adjusted OR: 1.7, 95%CI 1.1-2.5).

Table 1. Characteristics of children who visited MSF-supported health facilities and the presence of Missed Opportunities for Vaccination (MOV), 2011-2015

	Total children n=2706 n (%)	Eligible for vaccination [a] n=1688 n (%) [b]	MOV No n (%) [c]	MOV Yes n (%) [c]	*p* value
Age groups					
<12 m	1805 (66.7)	1203 (66.5)	540 (44.9)	663 (55.1)	<0,001 [e]
12-23 m	597 (22.1)	314 (52.6)	49 (15.6)	265 (84.4)	
24-59 m	304 (11.2)	171 (56.3)	20 (11.7)	151 (88.3)	
Facility type					
Hospital	493 (18.2)	336 (68.2)	67 (20)	269 (80.1)	<0,001 [e]
PHCC[d]	2213 (81.8)	1352 (61.1)	542 (40.1)	810 (59.9)	
Reason of the visit					
Curative	831 (30.7)	513 (61.7)	40 (7.8)	473 (92.2)	<0,001 [f]
Other	706 (26.1)	311 (44.1)	281 (90.4)	30 (9.7)	
Vaccination	436 (16.1)	353 (81.0)	234 (64.3)	119 (33.7)	
Nutrition	430 (15.9)	275 (64.0)	23 (8,4)	252 (91.6)	
Mother Child Health visit	265 (9.8)	214 (80.8)	29 (13.6)	185 (86.5)	
Accompanying	38 (1.4)	22 (57.9)	2 (9.0)	20 (90.9)	

[a] Without contraindication for vaccination
[b] Row percentage over the total children
[c] Row percentage over the eligible children without contraindication for vaccination
[d] PHCC: Primary Health Care Center
[e] Chi square test
[f] Fisher exact test

Table 2. Factors related to Missed Opportunities for Vaccination (MOV) in eligible children who visited MSF-supported health facilities, 2011-2015

	MOV children n= 1079 n (%)	Odds Ratio (95%CI)	Adjusted Odds Ratio (95%CI)
Age in months			
0-11 m	663 (55.1)		
12-59 m	416 (85.8)	4.91 (3.67-6.57)	3.79 (2.84-5.07)
Reason for visiting			
Vaccination	119 (33.7)		
Other	960 (89.0)	5.03 (3.86-6.56)	3.52 (2.70-4.58)
Facility type			
PHCC [a]	810 (59.9)		
Hospital	269 (80.1)	2.69 (2.00-3.60)	2.75 (2.02-3.73)

[a] PHCC: Primary Health Care Center
Odds ratio adjusted for age, reason for visiting, facility type (two categories each)

Discussion

This study summarizes MSF experience and lessons learned assessing MOV from 2011 to 2015 in six low-income countries. To our knowledge, this is one of the few studies that assess MOV in children beyond the EPI target. Our results highlight that, despite MSF's efforts, most children had a MOV after visiting one of the facilities. Of those children who specifically visited for vaccination, one third still missed at least one dose of vaccine for which eligible during the visit. The proportion of children with MOV increased with age, with children above one year of age being at higher risk.

MOV prevalence in our study (63.9%) was higher than the last systematic review conducted in low income countries in 2014, which found a prevalence of 32% (26.8–37.7) (6). An explanation could be that the majority of studies in this meta-analysis only included children below two years of age resulting in a lower estimation of MOV. As our data show, MOV was nearly 90% in children above 23 months of age. One of the few studies including older children also reported that MOV prevalence was higher in children aged 1-5 years (56.6%), compared to those below one year (31.4%) (7). Thus, we believe that overall MOV prevalence is being seriously underestimated, as assessments do not include children beyond the EPI target, that is, above 23 months of age.

Consistent with recent studies in low income countries (8), we found a higher MOV prevalence in children above 12 months. In a recent study that assessed MOV with WHO methodology in Chad and Malawi (9), Ogbuano et al. found a MOV prevalence of 86% in Chad and 94% in Malawi among children above one year of age, compared to 49% and 61% below one year respectively.

Age as a risk for having MOV may be explained by older children having been perceived as "too old" to be eligible (10), as most of EPI programs only target children below one year of

age. In a WHO review about factors related with under-vaccination (11), false contraindications like age were found to be one of the main reasons for having a MOV. This was reflected in our study, where only 4% (n=14) of children visiting specifically for vaccination were above 12 months of age. A "second year of life healthy child visit" is already recommended by WHO (12) increasing the number of opportunities for vaccination in children above 12 months of age, especially in those who might have missed vaccination in their first year of life. This strategy, together with complementary catch-up activities to continue screening children at any contact with health services should be strengthened in low-resource settings (13)(14)(15). The latest WHO update of recommendations for routine immunization (16) emphasizes that measles vaccine should not be limited only to children up to 12 months of age. We believe this approach must be extended to all vaccines included in the vaccination schedule, in order to increase individual protection and improve population vaccine coverage.

Our data draw attention to the high proportion of children missing the opportunity to get vaccinated at hospital level. A similar proportion has been found in a recent study performed in northern Indian hospitals (17). This could be explained by the belief of false contraindications for vaccination in a sick child, both among caregivers and health care workers. For example, a study in Haiti reported that up to 13% of reasons for under vaccination was child illness, despite the fact that mild infections should not prevent vaccination (18). In the last MOV assessments using WHO methodology, Anyie J. Li et al. (10) found that only 24% of health care workers were able to identify true contraindications, and L. Kaboré et al. (8) reported that 83% of health workers failed to correctly identify valid contraindications for vaccination. Promoting training on true contraindications for vaccination among health care workers could be an effective strategy to reduce MOV (19).

We identified that one third of children actually visiting for vaccination were still not up to date at the end of the visit despite being vaccinated with one or more doses. Similar estimates were

found in four recent MOV assessments in East Timor, Chad, Malawi, and Burkina Faso (8)(9)(10). This could be explained by supply shortages of specific vaccines, but also by health workers potentially failing to identify eligibility for certain vaccines. Failure to administer simultaneous vaccines due to fear of wasting doses from multi-vial vaccines has been also suggested as an explanation for remaining MOV after vaccination visits (20)(21).

Over three-quarters of eligible children consulting for reasons other than vaccination (mother-and-child health visits, nutrition, curative) had a MOV. Integrating vaccination into other preventive services could represent a significant reduction on MOV (22). Also, strengthening routine screening of vaccination status irrespectively of reason visit, could be an opportunity to improve vaccine uptake (23).

Our survey allowed us to identify and address the two main reasons related to MOV. More than a third of caregivers reported lack of vaccines as the reason for MOV, and almost 20% reported not been informed about the eligibility of the child. This is consistent with recent MOV assessments (9), where approximately 30% of health care workers reported insufficient vaccine supply or logistics issues. Inadequate vaccine supply has already been pointed out as one of the main reasons for under vaccination in low income countries (1). Ministries of Health and their partners must work to ensure adequate vaccine supply at facility level in order be able to vaccinate any children who had already accessed health care services (24). Lack of information on vaccine eligibility has also been reported elsewhere (25); therefore, promotion strategies should address the lack of information causing MOV.

This study has three main limitations. First, gender was not collected, missing the opportunity to uncover gender differences. Nevertheless, no gender differences in the distribution of MOV have been reported in the latest studies (6)(9). Second, our survey didn't allow us to explore health care providers' practices and perceptions, identified as one of the main reasons related

with MOV in the last systematic review (6). In 2015, WHO launched a revised MOV strategy which included Knowledge, Attitudes and Practices (KAP) questionnaires, to better guide the implementation of interventions to reduce MOV (9), which is generating new evidence (26). Third, we excluded from the analysis almost half of the children, as they were not able to present a vaccination card. This may mean that we underestimated MOV prevalence in our target population, since not presenting a vaccination card has been associated with MOV (1)(6)(27). However, not relying on self-reported data helped avoid potential recall bias, which is a limitation in vaccine coverage studies in low resource settings(28).

Conclusions

Despite progress in vaccine coverage through the Global Vaccine Action Plan, MOV remain an important problem in low-resource settings. Avoiding MOV should remain a priority where access to health care is limited, especially considering also the negative impact COVID-19 pandemic is having on routine immunization programs, especially in low and middle income countries (29).

We recommend integrating routine vaccination screening in health care settings regardless of visit reason as a main strategy to identify eligible children and reduce MOV, together with addressing caregiver's lack of information and knowledge gaps in health care workers.

We identified that children above 23 months of age as particularly vulnerable for MOV. At the moment of our report, WHO methodology for MOV assessments only targets children below 23 months, which according to our findings leads to underestimation of MOV. Therefore, we recommend that MOV assessments should include children up to 5 years of age. Strengthening the implementation of second year of life visits, as recommend by WHO, and catch-up vaccination activities would provide missed vaccine doses to those who urge for a second chance.

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Contributorship Statement

Bachy C. and Panunzi I. designed the study and contributed to the development on the field. Bachy C., Panunzi I., Gil-Cuesta J. and Borras-Bermejo B. carried out the data analysis. Borras-Bermejo B. drafted the manuscript that was critically reviewed and approved by all authors.

Competing interests

None declared

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Data Availability Statement

Questionnaire dataset is available in a public, open access repository.

[dataset] (30) Borras-Bermejo B. Data from: Missed Opportunities for Vaccination in MSF-Supported Health Facilities. Open Science Framework. December 6, 2021.

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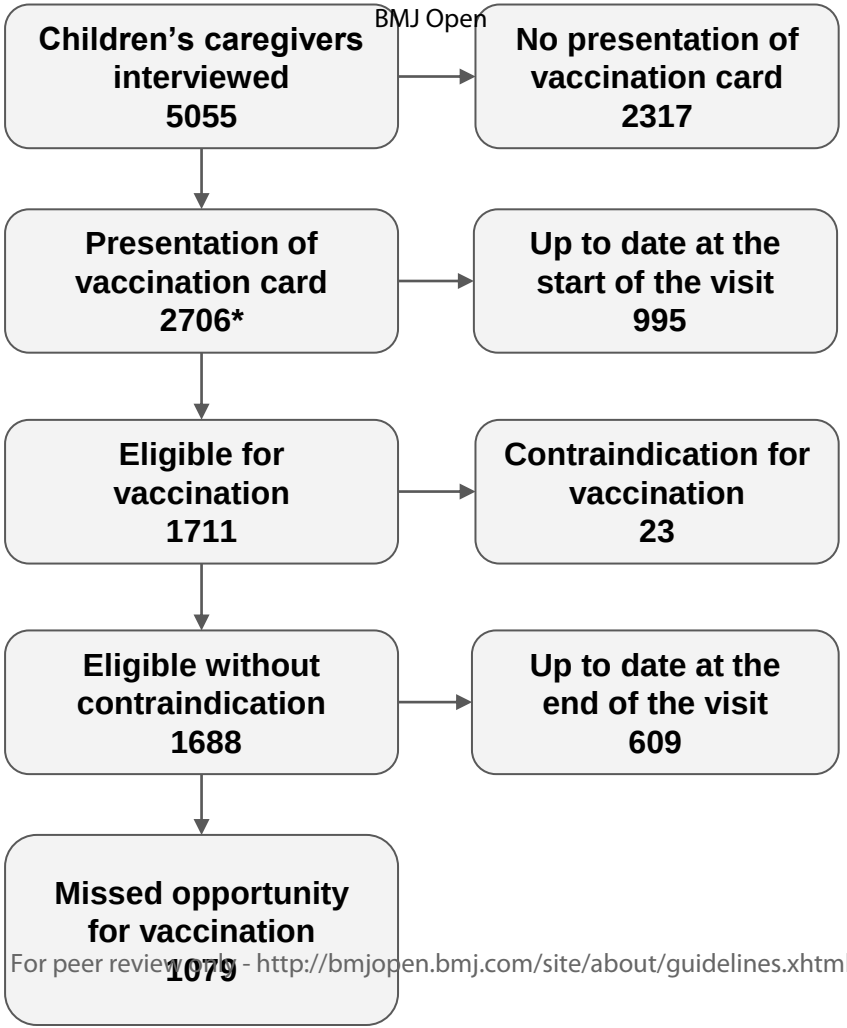
Figure 1. Flow chart of participants' inclusion and for determining Missed Opportunities for Vaccination (MOV), MSF-supported health facilities, 2011-2015

**32 children were not included due to data inconsistencies.*



DO NOT fill in (for encoding purpose only) Rec :

Evaluation of missed vaccination opportunities: child questionnaire

District: ..... **Team:** ……..…… **N° child:** ☐

Center: ..... **Date:** ..... / ..... / ..... **Age of the child:** ..... years …… months

1) Do you have a vaccination card or a health book for the child?

☐ **No** ☐ **Yes** → Did you bring it today? ☐ **No** ☐ **Yes**

2) What was the <u>main</u> purpose of your visit to the health center today? (One answer only)

☐ Curative consultation
☐ MCH consultation
☐ Accompanying an adult
☐ Vaccination
☐ Feeding program
☐ Other: .....

3) Vaccination status:

*Write the **<u>dates</u>** (dd/mm/yy) mentioned in the health book **<u>and circle it</u>** if vaccine given today.*
*If the history of vaccination is only confirmed orally by the caretaker, write **<u>H</u>**.*
***<u>Cross</u>** the box (X) for the missing dose of vaccine that could have been given today.*

	Dose 0	Dose 1	Dose 2	Dose 3
BCG	X		X	X
HepB birth dose		X	X	X
Polio				
DTP - HepB - Hib	X			
PCV 13	X			
Rota	X			X
Measles	X			X
Yellow fever	X		X	X

4) Was the child eligible for a vaccine today?

☐ **No** → **Do you know the date of your next vaccination?** ☐ **No** ☐ **Yes** → ***END***

☐ **Yes** → **Did the child present with a true contra-indication to the vaccination today?**

☐ **No** ☐ **Yes** → ***<u>GO TO QUESTION 6</u>***

5) Did the child receive <u>all</u> vaccines required today?

☐ **Yes**

(If X in box) ☐ **No** → **Would you have accepted the vaccination today if proposed?**

☐ **Yes** ☐ **No** → Why? .....

→ **Reason(s) for not receiving all vaccines today? (One answer only)**

☐ Out of stock
☐ Waiting time too long
☐ Don't know the reason
☐ No vaccinator
☐ Not enough information
☐ Other: .....

6) Did you get an appointment for your next vaccination? ☐ **No** ☐ **Yes**

THANK YOU FOR YOUR PARTICIPATION!

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-6*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9

		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	NA
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Missed Opportunities for Vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low resource countries.

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Title Page

Title: Missed Opportunities for Vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low resource countries.

Running Title: MOV in MSF supported health facilities

Key words: vaccine, vaccination, children, immunization program, health policy, process assessment, survey, low-income countries, Expanded Program of Immunization, missed opportunities, MOV, catch-up

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Title: Missed Opportunities for Vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low resource countries.

Abstract

Objective

To describe Missed Opportunities for Vaccination (MOV) among children visiting MSF-supported facilities, their related factors, and to identify reasons for non-vaccination.

Design: Cross-sectional surveys conducted between 2011 and 2015.

Setting and participants: children up to 59 months of age visiting 19 MSF-supported facilities (15 primary health care centers and 4 hospitals) in Afghanistan, Democratic Republic of the Congo, Mauritania, Niger, Pakistan and South Sudan. Only children whose caregivers presented their vaccination card were included.

Outcome measures: We describe MOV prevalence and reasons for no vaccination. We also assess the association of MOV with age, type of facility and reason for visit**.**

Results: Among 5055 children's caregivers interviewed, 2738 presented a vaccination card of whom 62.8% were eligible for vaccination and of those, 64.6% had a MOV. Presence of MOV was more likely in children visiting a hospital or a health facility for a reason other than vaccination. MOV occurrence was significantly higher among children aged 12-23 months (84.4%) and 24-59 months (88.3%) compared with children below 12 months (56.2%, $p \leq 0.001$). Main reasons reported by caregivers for MOV were lack of vaccines (40.3%), reason unknown (31.2%), and not being informed (17.6%).

Conclusions

Avoiding MOV should remain a priority in low-resource settings, in line with the new 2030 Immunization Agenda. Children beyond the Expanded Program of Immunization are particularly vulnerable for MOV. We strongly recommend assessment of eligibility for vaccination as routine health care practice regardless of the reason for the visit by screening vaccination card. Strengthening implementation of "Second year of life" visits and catch-up activities are proposed strategies to reduce MOV.

Strengths and limitations of this study

- The major strength of the study is that only children with a valid vaccination card were included, so not relying on self-reported data helped to avoid potential recall bias
- Differences by gender on Missed Opportunities for Vaccination were not explored
- Reasons related with Missed Opportunities for Vaccination were limited to those included at the questionnaire and declared by caregivers.

INTRODUCTION

Since 1983, the Expanded Program of Immunization (EPI) has recommended using every health care visit as an opportunity to immunize each eligible child, regardless of the reason for consultation. A Missed Opportunity for Vaccination (MOV) occurs when a child eligible for vaccination (without contraindication) remains unvaccinated or partially vaccinated (not up-to-date) at the end of the visit, so the consultation does not result in the children receiving all the vaccine doses for which he or she was eligible. Among the causes for under-vaccination in low and middle-income countries, 44% are for reasons related to health systems, including MOV and lack of access to health care (1). In 1993, the first systematic review including 45 countries found a median MOV prevalence of 67% (2), and despite increases in routine vaccination coverage since then, MOV remain as high as 32% in the last systematic review performed in 2014 (3). Since then, the World Health Organization (WHO) has promoted the use of MOV assessments to measure the performance of health services in vaccination (4)(5). In order to improve immunization coverage, in 2017 WHO recommended a revised methodology to assess MOV, targeting children aged 0-23 months (6). However, data is scarce on MOV prevalence in children above 23 months of age (3). Through its medical humanitarian programs in low and middle-income countries, Médecins Sans Frontières (MSF) strengthens routine vaccination services regardless the age of the child, following WHO recommendations (7), in order to reduce the number of under and unvaccinated children. Therefore, we took the opportunity to systematically assess MOV in children up to five years of age within MSF programs.

Our objective was to describe MOV prevalence and its characteristics, and to identify reasons for non-vaccination among children up to five years of age visiting MSF-supported health facilities in six different countries.

METHODS

Study design and settings

A cross-sectional exit survey of caregivers was performed in 19 health facilities. They included four hospitals and 15 primary health care centers (PHCC) between 2011 and 2015 in six countries: Afghanistan, Democratic Republic of the Congo, Mauritania, Niger, Pakistan and South Sudan. Countries, health facilities and time of the assessments were chosen on a convenient basis following operational reasons. Facilities included were chosen because MSF was already supporting routine vaccination and where MOV training to local staff was feasible in those health facilities.

Patient and Public Involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Study population and participant selection

The study population consisted of children up to five years of age accompanied by a caregiver, visiting an MSF-supported facility. A convenience sample of all caregivers accompanying a child under five years of age was approached on the day of the survey at each facility. Caregivers were invited to participate when exiting the facility, regardless of the reason for their visit, and those who provided oral consent were interviewed. If several children were present with one caregiver, all were included. Children whose caregivers could not present a vaccination card were excluded from the analysis.

Data collection

MSF developed a standardized methodology to assess MOV based on the 1988 WHO tool (8). Interviews were conducted in local languages. In preparation for the survey, surveyors

locally recruited received two days of training focusing on conducting the interview and identifying eligible children for vaccination according to national vaccination schedules, age of the child and minimum interval between doses.

A structured questionnaire was created (Annex 1) and used in all assessments. Information on type of facility (hospital or PHCC), age of the child, presentation of a vaccination card, reason for visiting the facility and vaccination history were collected, as well as whether there was a contraindication for vaccination. We considered as contraindications, fever above 38,5 °C and a severe allergic reaction to a previous dose of DTP-containing or measles-containing vaccines. For those who had not received any of the recommended vaccines during the visit, surveyors asked for reasons why the child was not vaccinated, whether caregivers accepted receiving the missing vaccines doses, and about their awareness of the next vaccination appointment.

We classified children as having a MOV as per standard WHO's definition (6): a MOV occurs when a child eligible for vaccination (without contraindication) remains unvaccinated or partially vaccinated (not up to date) at the end of any visit to a health facility (Figure 1).

Surveyors determined if the child was eligible that day of the assessment for at least one vaccine dose according to age and National immunization schedules (Figure 2), and whether the child had received all the recommended vaccines during that visit. Most of National immunization programs allowed vaccination until 12 months of age by the time of the assessments. Nevertheless, MSF supported vaccination of children up to 5 years of age in each of these facilities. In our study, surveyors considered a MOV if a child did not receive the indicated vaccines even if they were above the recommended age to receive them according to the country policy, to the exception of BCG and Rotavirus (Figure 2). Only

widely introduced vaccines in each country were considered to ascertain MOV. Year of vaccine introduction in each country can be consulted here (9).

For those having a MOV, surveyors asked for reasons why the child was not vaccinated, whether caregivers would have accepted receiving the missing vaccines doses, and about their awareness of the next vaccination appointment.

Data analysis

We calculated the prevalence of MOV among children eligible for a vaccination, excluding those with a reported contraindication. Among children with a MOV we calculated the proportion of caregivers who would have accepted vaccination if it had been proposed on the day of the visit and the proportion of caregivers who knew their date of next vaccination appointment.

Proportions were used to describe the children and to estimate MOV. Significant differences in the distribution were assessed using the Pearson's two-sided Chi-square test or Fisher exact test. For the bivariate analysis, age was categorized as below and above 12 months of age as this was the main target of the National program schedules in countries included at the time the survey was performed. Reasons for visit to the facility were grouped into either vaccination or others. We assessed the association of MOV with age, type of facility and reason for visit by calculating Odds Ratios. A logistic regression model was adjusted for age (0-11,12-59 months), type of facility (hospital, PHCC), and reason for visit (vaccination, other reason). The level of statistical significance was set at $p < 0.05$.

In each facility, data entry officers inputted the paper questionnaire data into an Excel database, which was validated by two of the study investigators. The analysis was performed using STATA (version 16, College Station, Texas).

Ethics issues

Prior to each evaluation, authorization from the local health authorities and from the director of each health facility was obtained. Oral consent was received from each caregiver. During the survey, children <12 months identified with MOV were sent back to the vaccination unit to receive the missing vaccine(s) if the caregiver agreed and if there was no shortage. All data from the questionnaires were anonymous and entered into a dedicated password-protected electronic database. This research fulfilled the exemption criteria by Médecins sans Frontières Ethics Review Board (MSF ERB) for a posteriori analysis of routinely collected clinical data and thus did not require MSF ERB review. It was conducted with permission from the Medical Director, Operational Centre Brussels Médecins sans Frontières.

RESULTS

From 2011 to 2015, the caregivers of 5055 children were interviewed in 19 facilities (four hospitals and 15 PHCCs). We report the results for the 2706 (53.5%) children who presented their vaccination card on the day of the survey: 33 from Afghanistan, 79 from Democratic Republic of the Congo, 244 from Mauritania, 1888 from Niger, 15 from Pakistan and 447 from South Sudan. Characteristics of children not presenting vaccination cards can be consulted at Supplementary table 1.

Characteristics of the study population

Among the 2706 children included, 995 (36.7%) were already up to date before the visit, and 1711 (63.2%) were eligible for vaccination. Twenty-three caregivers (1.3%) reported a contraindication (Figure 1). Among eligible children, 609 (36.1%) were vaccinated during the visit, whereas 1079 (63.9%) experienced a MOV during their health facility visit.

Children's baseline characteristics are presented in Table 1. Their mean age was 10.1 months (Standard Deviation - 9). The majority (2213, 81.8%) were interviewed at exit of a PHCC. Reasons for visiting the health facility were distributed among curative consultation (31%),

followed by unspecified reason (26%), vaccination (16%), nutrition (16%), mother and child health visit (10%) and accompanying an adult (1%).

Characteristics of children with MOV

Most children who were eligible for vaccination and consulting for a reason other than vaccination, had a MOV (n=960, 71.9%), while a third of the children coming to the facility for vaccination also had a MOV (n=119, 33.7%). More than 80% of children aged 12-23 months (265/314) and almost 90% of children aged 23-59 (151/171) had a MOV, compared to 55% of children below 12 months (663/1203). MOV occurrence was significantly more likely among older children than younger ones (Table 1). Differences in MOV by country can be consulted at Supplementary table 3.

Only four caregivers of children with MOV would have refused vaccination if it had been proposed during the visit. About one fifth (21%) of caregivers of children with MOV were aware of the date of the next vaccination appointment.

The commonest reason declared for having a MOV was lack of vaccines (40.1%), followed by reason unknown (32%), not being informed (17.3%), lack of staff (3.3%), waiting time too long (1.7%) and other unclassified reasons (5.6%).

Factors related with presence of MOV

Children above 12 months of age and those accessing the health facility for a reason other than vaccination, had an almost five times higher risk of having a MOV (Table 2), compared to children below 12 months of age and those visiting for vaccination. Children visiting a hospital had a 2.7 times higher risk of having a MOV compared to children visiting a PHCC. After adjusting by type of facility and reason for visit, children above 12 months still had a significantly higher risk of having a MOV (adjusted OR: 1.7, 95% CI 1.1-2.5).

Table 1. Characteristics of children who visited MSF-supported health facilities and the presence of Missed Opportunities for Vaccination (MOV), 2011-2015

	Total children n=2706 n (%)	Eligible for vaccination [a] n=1688 n (%) [b]	MOV No n (%) [c]	MOV Yes n (%) [c]	*p* value
Age groups					
<12 m	1805 (66.7)	1203 (66.5)	540 (44.9)	663 (55.1)	<0,001 [e]
12-23 m	597 (22.1)	314 (52.6)	49 (15.6)	265 (84.4)	
24-59 m	304 (11.2)	171 (56.3)	20 (11.7)	151 (88.3)	
Facility type					
Hospital	493 (18.2)	336 (68.2)	67 (20)	269 (80.1)	<0,001 [e]
PHCC[d]	2213 (81.8)	1352 (61.1)	542 (40.1)	810 (59.9)	
Reason of the visit					
Curative	831 (30.7)	513 (61.7)	40 (7.8)	473 (92.2)	<0,001 [f]
Other	706 (26.1)	311 (44.1)	281 (90.4)	30 (9.7)	
Vaccination	436 (16.1)	353 (81.0)	234 (64.3)	119 (33.7)	
Nutrition	430 (15.9)	275 (64.0)	23 (8,4)	252 (91.6)	
Mother Child Health visit	265 (9.8)	214 (80.8)	29 (13.6)	185 (86.5)	
Accompanying	38 (1.4)	22 (57.9)	2 (9.0)	20 (90.9)	

[a] Without contraindication for vaccination
[b] Row percentage over the total children
[c] Row percentage over the eligible children without contraindication for vaccination
[d] PHCC: Primary Health Care Center
[e] Chi square test
[f] Fisher exact test

Table 2. Factors related to Missed Opportunities for Vaccination (MOV) in eligible children who visited MSF-supported health facilities, 2011-2015

	MOV children n= 1079 n (%)	Odds Ratio (95%CI)	Adjusted Odds Ratio (95%CI)
Age in months			
0-11 m	663 (55.1)		
12-59 m	416 (85.8)	4.91 (3.67-6.57)	3.79 (2.84-5.07)
Reason for visiting			
Vaccination	119 (33.7)		
Other	960 (89.0)	5.03 (3.86-6.56)	3.52 (2.70-4.58)
Facility type			
PHCC [a]	810 (59.9)		
Hospital	269 (80.1)	2.69 (2.00-3.60)	2.75 (2.02-3.73)

[a] PHCC: Primary Health Care Center
Odds ratio adjusted for age, reason for visiting, facility type (two categories each)

DISCUSSION

This study summarizes the MSF experience and lessons learned assessing MOV from 2011 to 2015 in six low-income countries. To our knowledge, this is one of the few studies that assessed MOV in children beyond 23 months of age. Our results highlight that, despite MSF's efforts, most children had a MOV after visiting one of the facilities. Even among those children who specifically visited for vaccination, one third still missed at least one dose of a vaccine for which they were eligible during the visit. The proportion of children with MOV increased with age, with children above one year of age being at higher risk.

MOV prevalence in our study (64%) was higher than the last systematic review conducted in low income countries in 2014, which found a prevalence of 32% (26.8–37.7) (3). An explanation could be that the majority of studies in this meta-analysis only included children below two years of age resulting in a lower estimation of MOV. As our data show, MOV was nearly 90% in children above 23 months of age. One of the few studies to include older children also reported that MOV prevalence was higher in children aged 1-5 years (56.6%), compared to those below one year (31.4%) (10). Thus, we believe that overall MOV prevalence is being seriously underestimated, as assessments do not include children beyond the EPI age target for most vaccines, that is, above 23 months of age.

Consistent with recent studies in low-income countries (11), we found a higher MOV prevalence in children above 12 months. In a recent study that assessed MOV with WHO methodology in Chad and Malawi (12), Ogbuano et al. found a MOV prevalence of 86% in Chad and 94% in Malawi among children above one year of age, compared to 49% and 61% below one year, respectively.

Age as a risk for having MOV may be explained by older children having been perceived as "too old" to be eligible (13), as most National immunization programs only target children

below one year of age. Age as a false contraindication was found to be one of the main reasons for having a MOV in a WHO review about factors related with under-vaccination (14). But efforts are being made to 'Leave No One Behind' (15)**:** the latest WHO update of recommendations for routine immunization (16) emphasizes that measles vaccine should not be limited to children up to 12 months of age. Actually, there are no age limits to vaccinate children (with rotavirus exception). In line with that, a "second year of life healthy child visit" is already recommended by WHO (17)(7) increasing the opportunity to vaccinate children, especially in those who might have missed vaccination in their first year of life. This strategy, together with complementary catch-up activities to continue screening children at any contact with health services, should be strengthened in low-resource settings (7)(18)(19)(20). We believe this 'never too old' policy should be adopted by all national immunization programs in order to ensure children do not miss the opportunity to be fully vaccinated at any age.

Our data draw attention to the high proportion of children missing an opportunity to get vaccinated at hospital level. A similar proportion has been found in a recent study performed in northern Indian hospitals (21). This could be explained by vaccine shortage at hospital level but also by the belief in the false contraindication for vaccination in a sick child among caregivers and health care workers. For example, a study in Haiti reported that up to 13% of reasons for under-vaccination was child illness, despite the fact that mild infections should not prevent vaccination (22). A similar finding is highlighted in a MOV assessment in East Timor (13) were Anyie J. Li et al. found that only 24% of health care workers were able to identify true contraindications, and L. Kaboré et al. (11) reported that 83% of health workers failed to correctly identify valid contraindications for vaccination. This could be avoided through the proper adherence to the Integrated Management of Newborn and Childhood Illnesses (IMNCI) guidelines (19), already in place in these countries (23).

We identified that one third of children actually visiting for vaccination were still not up to date at the end of the visit despite being vaccinated with one or more doses. Similar estimates were found in four recent MOV assessments in East Timor, Chad, Malawi, and Burkina Faso (11)(12)(13). This could be explained by supply shortages of specific vaccines, but also by health workers potentially failing to identify eligibility for certain vaccines. Failure to administer simultaneous vaccines due to fear of wasting doses from multi-vial vaccines has been also suggested as an explanation for remaining MOV after vaccination visits (24)(25). Among reasons for MOV in our study, almost 20% reported not being informed by health care workers about the eligibility of the child for vaccination. This lack of information on vaccine eligibility has also been reported elsewhere (26). Therefore, promoting training on eligibility assessment and true contraindications for vaccination among health care workers could be an effective strategy to reduce MOV (27).

Over three-quarters of eligible children consulting for reasons other than vaccination (mother-and-child health visits, nutrition, curative) had a MOV. This highlights the need of strengthening routine screening of vaccination status that must be done irrespective of reason visit. Caregivers should be encouraged to bring the vaccination card to every contact with health services, to facilitate and ensure that the child can be properly screened for vaccination eligibility. So, integrating vaccination into other preventive or curative services at hospital and at primary health care level, could facilitate a significant reduction on MOV (28)(29).

In our study, caregivers reported lack of vaccines as the main reason for MOV. This is consistent with recent MOV assessments (12), where approximately 30% of health care workers reported insufficient vaccine supply or logistics issues. Inadequate vaccine supply has already been pointed out as one of the main reasons for under vaccination in low income countries (1). Ministries of Health and their partners must work to ensure adequate vaccine

supply at facility level in order be able to vaccinate any children who have accessed health care services (30).

This study has three main limitations. First, gender was not collected, losing the opportunity to uncover gender differences. Nevertheless, no gender differences in the distribution of MOV have been reported in the latest studies (3)(12). Second, our survey didn't allow us to explore health care providers' practices and perceptions, identified as one of the main reasons related to MOV in the last systematic review (3). In 2015, WHO launched a revised MOV strategy, which included Knowledge, Attitudes and Practices (KAP) questionnaires, to better guide the implementation of interventions to reduce MOV (12); it is generating new evidence (31). Also, we could not explore other factors that have been previously related to MOV such as maternal education, living in rural areas, number of children and other economic inequalities (32).

Third, we excluded from the analysis almost half of the children whose caregivers could not present a vaccination card. This may mean that we underestimated MOV prevalence in our target population, since not presenting a vaccination card has shown to be associated with MOV (1)(3)(33). On one hand, not relying on self-reported data helped avoid potential recall bias, which is a limitation in vaccine coverage studies in low-resource settings (34). On the other hand, possession of vaccination card declines with age (10) (a relation also observed in our study, Supplementary table 1); what could result in an overestimated prevalence of MOV in older children. Nevertheless, when assessing the relation between MOV and age including those with and without vaccination card, we obtain similar results (Supplementary table 2).

Finally, as children with identified MOV were sent back for vaccination when possible, it could have introduced a bias in MOV prevalence if these children were inadvertently

interviewed again. Also, MOV prevalence estimates may have improved over the last ten years, as WHO has lately reinforced EPI vaccination during the second year of life.

CONCLUSIONS

Despite progress in vaccine coverage, MOV remains an important problem in low-resource settings. Avoiding MOV should remain a priority where access to health care is limited, in line with the new 2030 Immunization Agenda (15). This is particularly important considering the negative impact COVID-19 pandemic is having on routine immunization programs in low and middle-income countries (35)(36).

We recommend integrating systematic vaccination screening into routine health care services, regardless of the reason for the visit, the type of facility and the age of the child. To promote maintaining and providing vaccination cards at every health care visit will help to reinforce vaccination screening and better identification of eligible children.

We identified that children above 23 months of age are particularly vulnerable for MOV. Thus, we would recommend including children beyond 23 months of age in the current WHO methodology for MOV assessments in order to avoid underestimation of MOV. National immunization programs should allow to administer missing doses regardless the age of the child, as the EPI has expanded its vaccination recommendations during second year of life and beyond. Strengthening the implementation of second-year-of-life visits, as recommended by WHO, with catch-up vaccination strategies (7) would provide additional opportunities to receive missed vaccine doses and *leave no one behind*.

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Contributorship Statement

Bachy C. and Panunzi I. designed the study and contributed to conduct it in the six countries. Bachy C., Panunzi I., Gil-Cuesta J. and Borras-Bermejo B. carried out the data analysis. Borras-Bermejo B. drafted the manuscript that was critically reviewed and approved by all authors.

Competing interests

None declared

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The study was carried out by MSF staff as part of their routine activities. No extra funding was required.

Data Availability Statement

Questionnaire dataset is available in a public, open access repository.

[dataset] Borras-Bermejo B. Data from: Missed Opportunities for Vaccination in MSF-Supported Health Facilities. Open Science Framework. December 6, 2021.

https://doi.org/10.17605/OSF.IO/SFXDK

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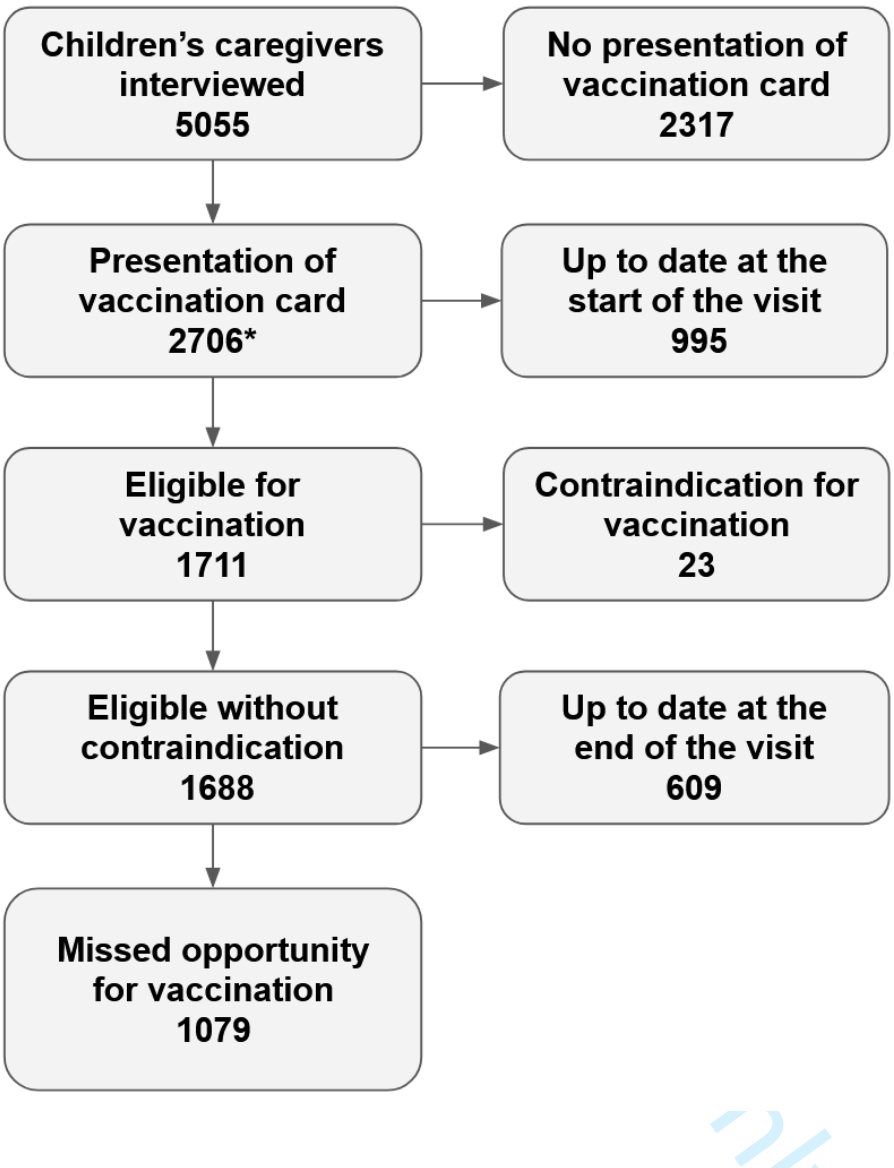
Figure 1. Flow chart of participants' inclusion and for determining Missed Opportunities for Vaccination (MOV), MSF-supported health facilities, 2011-2015.

32 children were not included due to data inconsistencies.

Figure 2. Immunization schedule to ascertain MOV

BCG: Bacille Calmette-Guerin vaccine.
OPV: Oral Polio vaccine. Inactivated Polio Vaccine was not considered for MOV.
Pentavalent vaccine: Diphtheria-tetanus-pertussis-hepatitis B- Haemophilus influenza type b.
PCV: Pneumococcal conjugate vaccine. Only considered for MOV in countries where it was introduced.
Measles containing vaccine: only one dose was considered for MOV.
Yellow Fever: it was considered for MOV only in endemic countries.

Figure 1. Flow chart of participants' inclusion and for determining Missed Opportunities for Vaccination (MOV), MSF-supported health facilities, 2011-2015



**32 children were not included due to data inconsistencies.*

Figure 2. Immunization schedule to ascertain MOV

Vaccine	Recommended age
Birth dose	
BCG	At birth – up to 12 months
OPV	At birth – up to 2 weeks
Hepatitis B vaccine	At birth – up to 2 weeks
First dose	
OPV	From 6 weeks - up to 12 months
Pentavalent vaccine	From 6 weeks
PCV	From 6 weeks
Rotavirus	From 6 weeks - up to 12 months
Minimum interval of 4 weeks between First and Second dose	
Second dose	
OPV	From 10 weeks - up to 12 months
Pentavalent vaccine	From 10 weeks
PCV	From 10 weeks
Rotavirus	From 10 weeks - up to 12 months
Minimum interval of 4 weeks between Second and Third dose	
Third dose	
OPV	From 14 weeks - up to 12 months
Pentavalent vaccine	From 14 weeks
PCV	From 14 weeks
Measles-containing vaccine	From 9 months
Yellow Fever	From 9 months

BCG: Bacille Calmette-Guerin vaccine.
OPV: Oral Polio vaccine. Inactivated Polio Vaccine was not considered for MOV.
Pentavalent vaccine: Diphtheria-tetanus-pertussis-hepatitis B- Haemophilus influenza type b.
PCV: Pneumococcal conjugate vaccine. Only considered for MOV in countries where it was introduced.
Measles containing vaccine: only one dose was considered for MOV.
Yellow Fever: it was considered for MOV only in endemic countries.

Supplementary Table 1. Characteristics of interviewed children by presentation of vaccination card. MSF-supported health facilities (2011-2015)

		Presentation of vaccination card				
	Total	No		Yes		
	N	N	%	N	%	*p* value
Age groups						
<12 m	2742	906	33.0	1836	67.0	
12-23 m	1263	665	52.7	598	47.4	
24-59 m	1050	746	71.1	304	29.0	<0.001 [a]
Eligible						
No	2276	1258	55.3	1018	44.7	
Yes	2779	1059	38.1	1720	61.9	<0.001 [b]
MOV [c]						
No	2985	1358	45.5	1627	54.5	
Yes	2070	959	46.3	1111	53.7	0.558 [b]
Total	5055	2317	45.8	2738	54.2	

% Row percentages
[a] Fisher exact test
[b] Chi square test
[c] MOV over the eligible children without contraindication for vaccination

Supplementary Table 2. Characteristics of children with MOV irrespective of the possession of vaccination card. MSF-supported health facilities (2011-2015)

	MOV [a]				
	No		Yes		
	N	%	N	%	*p* value
Age groups					
<12 m	588	33.2	1182	66.8	
12-23 m	66	11.6	504	88.4	
24-59 m	55	12.5	384	87.5	0.001 [b]
Total	709	25.5	2070	74.5	

[a] MOV over the eligible children without contraindication for vaccination
[b] Fisher exact test

Supplementary Table 3. Children who visited MSF-supported health facilities by country (2011-2015)

	Children with vaccination card		Eligible with no contraindication		MOV	
Country	n	%[a]	n	%[b]	n	%[c]
Afghanistan	33	1.2	11	33.3	8	72.7
Democratic Republic of the Congo	79	2.9	41	51.9	26	63.4
Mauritania	244	9.0	158	64.8	118	74.7
Niger	1888	69.8	1073	56.8	851	79.3
Pakistan	15	0.6	8	53.3	1	12.5
South Sudan	447	16.5	397	88.8	75	18.9
Total	2706	100.0	1688	62.4	1079	63.9

[a] Column percentage
[b] Row percentage among children with vaccination card
[c] Row percentage among eligible children without contraindication

DO NOT fill in (for encoding purpose only) Rec :

Evaluation of missed vaccination opportunities: child questionnaire

District: ..... **Team:** ..... **N° child:** ☐

Center: ..... **Date:** ..... / ..... / ..... **Age of the child:** ..... years …… months

1) Do you have a vaccination card or a health book for the child?

☐ **No** ☐ **Yes** → Did you bring it today? ☐ **No** ☐ **Yes**

2) What was the <u>main</u> purpose of your visit to the health center today? (One answer only)

☐ Curative consultation
☐ MCH consultation
☐ Accompanying an adult
☐ Vaccination
☐ Feeding program
☐ Other: .....

3) Vaccination status:

*Write the **<u>dates</u>** (dd/mm/yy) mentioned in the health book **<u>and circle it</u>** if vaccine given today.*
*If the history of vaccination is only confirmed orally by the caretaker, write **<u>H</u>**.*
***<u>Cross</u>** the box (X) for the missing dose of vaccine that could have been given today.*

	Dose 0	Dose 1	Dose 2	Dose 3
BCG	X		X	X
HepB birth dose		X	X	X
Polio				
DTP - HepB - Hib	X			
PCV 13	X			
Rota	X			X
Measles	X			X
Yellow fever	X		X	X

4) Was the child eligible for a vaccine today?

☐ **No** → **Do you know the date of your next vaccination?** ☐ **No** ☐ **Yes** → ***END***

☐ **Yes** → **Did the child present with a true contra-indication to the vaccination today?**

☐ **No** ☐ **Yes** → ***<u>GO TO QUESTION 6</u>***

5) Did the child receive <u>all</u> vaccines required today?

☐ **Yes**

(If X in box) ☐ **No** → **Would you have accepted the vaccination today if proposed?**

☐ **Yes** ☐ **No** → Why? .....

→ **Reason(s) for not receiving all vaccines today? (One answer only)**

☐ Out of stock
☐ Waiting time too long
☐ Don't know the reason
☐ No vaccinator
☐ Not enough information
☐ Other: .....

6) Did you get an appointment for your next vaccination? ☐ **No** ☐ **Yes**

THANK YOU FOR YOUR PARTICIPATION!

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10

		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	NA
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Title Page

Title: Missed Opportunities for Vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low resource countries.

Running Title: MOV in MSF supported health facilities

Key words: vaccine, vaccination, children, immunization program, health policy, process assessment, survey, low-income countries, Expanded Program of Immunization, missed opportunities, MOV, catch-up

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Title: Missed Opportunities for Vaccination (MOV) in children up to 5 years old in 19 Médecins Sans Frontières-supported health facilities: a cross-sectional survey in six low resource countries.

Abstract

Objective

To describe Missed Opportunities for Vaccination (MOV) among children visiting MSF-supported facilities, their related factors, and to identify reasons for non-vaccination.

Design: Cross-sectional surveys conducted between 2011 and 2015.

Setting and participants: children up to 59 months of age visiting 19 MSF-supported facilities (15 primary health care centers and 4 hospitals) in Afghanistan, Democratic Republic of the Congo, Mauritania, Niger, Pakistan and South Sudan. Only children whose caregivers presented their vaccination card were included.

Outcome measures: We describe MOV prevalence and reasons for no vaccination. We also assess the association of MOV with age, type of facility and reason for visit**.**

Results: Among 5055 children's caregivers interviewed, 2738 presented a vaccination card of whom 62.8% were eligible for vaccination and of those, 64.6% had a MOV. Presence of MOV was more likely in children visiting a hospital or a health facility for a reason other than vaccination. MOV occurrence was significantly higher among children aged 12-23 months (84.4%) and 24-59 months (88.3%) compared with children below 12 months (56.2%, $p \leq 0.001$). Main reasons reported by caregivers for MOV were lack of vaccines (40.3%), reason unknown (31.2%), and not being informed (17.6%).

Conclusions

Avoiding MOV should remain a priority in low-resource settings, in line with the new "Immunization Agenda 2030". Children beyond their second year of life are particularly vulnerable for MOV. We strongly recommend assessment of eligibility for vaccination as routine health care practice regardless of the reason for the visit by screening vaccination card. Strengthening implementation of "Second year of life" visits and catch-up activities are proposed strategies to reduce MOV.

Strengths and limitations of this study

- The major strength of the study is that only children with a valid vaccination card were included, so not relying on self-reported data helped to avoid potential recall bias
- Differences by gender on Missed Opportunities for Vaccination were not explored
- Reasons related with Missed Opportunities for Vaccination were limited to those included at the questionnaire and declared by caregivers.

INTRODUCTION

Since 1983, the Expanded Program of Immunization (EPI) has recommended using every health care visit as an opportunity to immunize each eligible child, regardless of the reason for consultation. A Missed Opportunity for Vaccination (MOV) occurs when a child eligible for vaccination (without contraindication) remains unvaccinated or partially vaccinated (not up-to-date) at the end of the visit, so the consultation does not result in the children receiving all the vaccine doses for which he or she was eligible. Among the causes for under-vaccination in low and middle-income countries, 44% are for reasons related to health systems, including MOV and lack of access to health care (1). In 1993, the first systematic review including 45 countries found a median MOV prevalence of 67% (2), and despite increases in routine vaccination coverage since then, MOV remain as high as 32% in the last systematic review performed in 2014 (3). Since then, the World Health Organization (WHO) has promoted the use of MOV assessments to measure the performance of health services in vaccination (4)(5). In order to improve immunization coverage, in 2017 WHO recommended a revised methodology to assess MOV, targeting children aged 0-23 months (6). However, data is scarce on MOV prevalence in children above 23 months of age (3). Through its medical humanitarian programs in low and middle-income countries, Médecins Sans Frontières (MSF) strengthens routine vaccination services regardless the age of the child, following WHO recommendations (7), in order to reduce the number of under and unvaccinated children. Therefore, we took the opportunity to systematically assess MOV in children up to five years of age within MSF programs.

Our objective was to describe MOV prevalence and its characteristics, and to identify reasons for non-vaccination among children up to five years of age visiting MSF-supported health facilities in six different countries.

METHODS

Study design and settings

A cross-sectional exit survey of caregivers was performed in 19 health facilities. They included four hospitals and 15 primary health care centers (PHCC) between 2011 and 2015 in six countries: Afghanistan, Democratic Republic of the Congo, Mauritania, Niger, Pakistan and South Sudan. Countries, health facilities and time of the assessments were chosen on a convenient basis following operational reasons. Facilities included were chosen because MSF was already supporting routine vaccination and where MOV training to local staff was feasible in those health facilities.

Patient and Public Involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Study population and participant selection

The study population consisted of children up to five years of age accompanied by a caregiver, visiting an MSF-supported facility. A convenience sample of all caregivers accompanying a child under five years of age was approached on the day of the survey at each facility. Caregivers were invited to participate when exiting the facility, regardless of the reason for their visit, and those who provided oral consent were interviewed. If several children were present with one caregiver, all were included. Children whose caregivers could not present a vaccination card were excluded from the analysis.

Data collection

MSF developed a standardized methodology to assess MOV based on the 1988 WHO tool (8). Interviews were conducted in local languages. In preparation for the survey, surveyors

locally recruited received two days of training focusing on conducting the interview and identifying eligible children for vaccination according to national vaccination schedules, age of the child and minimum interval between doses.

A structured questionnaire was created (Annex 1) and used in all assessments. Information on type of facility (hospital or PHCC), age of the child, presentation of a vaccination card, reason for visiting the facility and vaccination history were collected, as well as whether there was a contraindication for vaccination. We considered as contraindications, fever above 38,5 °C and a severe allergic reaction to a previous dose of DTP-containing or measles-containing vaccines. For those who had not received any of the recommended vaccines during the visit, surveyors asked for reasons why the child was not vaccinated, whether caregivers accepted receiving the missing vaccines doses, and about their awareness of the next vaccination appointment.

We classified children as having a MOV as per standard WHO's definition (6): a MOV occurs when a child eligible for vaccination (without contraindication) remains unvaccinated or partially vaccinated (not up to date) at the end of any visit to a health facility (Figure 1).

Surveyors determined if the child was eligible that day of the assessment for at least one vaccine dose according to age and National immunization schedules (Figure 2), and whether the child had received all the recommended vaccines during that visit. Most of National immunization programs allowed vaccination until 12 months of age by the time of the assessments. Nevertheless, MSF supported vaccination of children up to 5 years of age in each of these facilities. In our study, surveyors considered a MOV if a child did not receive the indicated vaccines even if they were above the recommended age to receive them according to the country policy, to the exception of BCG and Rotavirus (Figure 2). Only

widely introduced vaccines in each country were considered to ascertain MOV. Year of vaccine introduction in each country can be consulted here (9).

For those having a MOV, surveyors asked for reasons why the child was not vaccinated, whether caregivers would have accepted receiving the missing vaccines doses, and about their awareness of the next vaccination appointment.

Data analysis

We calculated the prevalence of MOV among children eligible for a vaccination, excluding those with a reported contraindication. Among children with a MOV we calculated the proportion of caregivers who would have accepted vaccination if it had been proposed on the day of the visit and the proportion of caregivers who knew their date of next vaccination appointment.

Proportions were used to describe the children and to estimate MOV. Significant differences in the distribution were assessed using the Pearson's two-sided Chi-square test or Fisher exact test. For the bivariate analysis, age was categorized as below and above 12 months of age as this was the main target of the National program schedules in countries included at the time the survey was performed. Reasons for visit to the facility were grouped into either vaccination or others. We assessed the association of MOV with age, type of facility and reason for visit by calculating Odds Ratios. A logistic regression model was adjusted for age (0-11,12-59 months), type of facility (hospital, PHCC), and reason for visit (vaccination, other reason). The level of statistical significance was set at $p < 0.05$.

In each facility, data entry officers inputted the paper questionnaire data into an Excel database, which was validated by two of the study investigators (10). The analysis was performed using STATA (version 16, College Station, Texas).

Ethics issues

Prior to each evaluation, authorization from the local health authorities and from the director of each health facility was obtained. Oral consent was received from each caregiver. During the survey, children identified with MOV were sent back to the vaccination unit to receive the missing vaccine(s) if the caregiver agreed and if there was no shortage. All data from the questionnaires were anonymous and entered into a dedicated password-protected electronic database. This research fulfilled the exemption criteria by Médecins sans Frontières Ethics Review Board (MSF ERB) for a posteriori analysis of routinely collected clinical data and thus did not require MSF ERB review. It was conducted with permission from the Medical Director, Operational Centre Brussels Médecins sans Frontières.

RESULTS

From 2011 to 2015, the caregivers of 5055 children were interviewed in 19 facilities (four hospitals and 15 PHCCs). We report the results for the 2706 (53.5%) children who presented their vaccination card on the day of the survey: 33 from Afghanistan, 79 from Democratic Republic of the Congo, 244 from Mauritania, 1888 from Niger, 15 from Pakistan and 447 from South Sudan. Characteristics of children not presenting vaccination cards can be consulted at Supplementary table 1.

Characteristics of the study population

Among the 2706 children included, 995 (36.7%) were already up to date before the visit, and 1711 (63.2%) were eligible for vaccination. Twenty-three caregivers (1.3%) reported a contraindication (Figure 1). Among eligible children, 609 (36.1%) were vaccinated during the visit, whereas 1079 (63.9%) experienced a MOV during their health facility visit.

Children's baseline characteristics are presented in Table 1. Their mean age was 10.1 months (Standard Deviation - 9). The majority (2213, 81.8%) were interviewed at exit of a PHCC. Reasons for visiting the health facility were distributed among curative consultation (31%),

followed by unspecified reason (26%), vaccination (16%), nutrition (16%), mother and child health visit (10%) and accompanying an adult (1%).

Characteristics of children with MOV

Most children who were eligible for vaccination and consulting for a reason other than vaccination, had a MOV (n=960, 71.9%), while a third of the children coming to the facility for vaccination also had a MOV (n=119, 33.7%). More than 80% of children aged 12-23 months (265/314) and almost 90% of children aged 23-59 (151/171) had a MOV, compared to 55% of children below 12 months (663/1203). MOV occurrence was significantly more likely among older children than younger ones (Table 1). Differences in MOV by country can be consulted at Supplementary table 2.

Only four caregivers of children with MOV would have refused vaccination if it had been proposed during the visit. About one fifth (21%) of caregivers of children with MOV were aware of the date of the next vaccination appointment.

The commonest reason declared for having a MOV was lack of vaccines (40.1%), followed by reason unknown (32%), not being informed (17.3%), lack of staff (3.3%), waiting time too long (1.7%) and other unclassified reasons (5.6%).

Factors related with presence of MOV

Children above 12 months of age and those accessing the health facility for a reason other than vaccination, had an almost five times higher risk of having a MOV (Table 2), compared to children below 12 months of age and those visiting for vaccination. Children visiting a hospital had a 2.7 times higher risk of having a MOV compared to children visiting a PHCC. After adjusting by type of facility and reason for visit, children above 12 months still had a significantly higher risk of having a MOV (adjusted OR: 1.7, 95% CI 1.1-2.5).

Table 1. Characteristics of children who visited MSF-supported health facilities and the presence of Missed Opportunities for Vaccination (MOV), 2011-2015

	Total children n=2706 n (%)	Eligible for vaccination [a] n=1688 n (%) [b]	MOV No n (%) [c]	MOV Yes n (%) [c]	*p* value
Age groups					
<12 m	1805 (66.7)	1203 (66.5)	540 (44.9)	663 (55.1)	<0,001 [e]
12-23 m	597 (22.1)	314 (52.6)	49 (15.6)	265 (84.4)	
24-59 m	304 (11.2)	171 (56.3)	20 (11.7)	151 (88.3)	
Facility type					
Hospital	493 (18.2)	336 (68.2)	67 (20)	269 (80.1)	<0,001 [e]
PHCC[d]	2213 (81.8)	1352 (61.1)	542 (40.1)	810 (59.9)	
Reason of the visit					
Curative	831 (30.7)	513 (61.7)	40 (7.8)	473 (92.2)	<0,001 [f]
Other	706 (26.1)	311 (44.1)	281 (90.4)	30 (9.7)	
Vaccination	436 (16.1)	353 (81.0)	234 (64.3)	119 (33.7)	
Nutrition	430 (15.9)	275 (64.0)	23 (8,4)	252 (91.6)	
Mother Child Health visit	265 (9.8)	214 (80.8)	29 (13.6)	185 (86.5)	
Accompanying	38 (1.4)	22 (57.9)	2 (9.0)	20 (90.9)	

[a] Without contraindication for vaccination
[b] Row percentage over the total children
[c] Row percentage over the eligible children without contraindication for vaccination
[d] PHCC: Primary Health Care Center
[e] Chi square test
[f] Fisher exact test

Table 2. Factors related to Missed Opportunities for Vaccination (MOV) in eligible children who visited MSF-supported health facilities, 2011-2015

	MOV children n= 1079 n (%)	Odds Ratio (95%CI)	Adjusted Odds Ratio (95%CI)
Age in months			
0-11 m	663 (55.1)		
12-59 m	416 (85.8)	4.91 (3.67-6.57)	3.79 (2.84-5.07)
Reason for visiting			
Vaccination	119 (33.7)		
Other	960 (89.0)	5.03 (3.86-6.56)	3.52 (2.70-4.58)
Facility type			
PHCC [a]	810 (59.9)		
Hospital	269 (80.1)	2.69 (2.00-3.60)	2.75 (2.02-3.73)

[a] PHCC: Primary Health Care Center
Odds ratio adjusted for age, reason for visiting, facility type (two categories each)

DISCUSSION

This study summarizes the MSF experience and lessons learned assessing MOV from 2011 to 2015 in six low-income countries. To our knowledge, this is one of the few studies that assessed MOV in children beyond 23 months of age. Our results highlight that, despite MSF's efforts, most children had a MOV after visiting one of the facilities. Even among those children who specifically visited for vaccination, one third still missed at least one dose of a vaccine for which they were eligible during the visit. The proportion of children with MOV increased with age, with children above one year of age being at higher risk.

MOV prevalence in our study (64%) was higher than the last systematic review conducted in low income countries in 2014, which found a prevalence of 32% (26.8–37.7) (3). An explanation could be that the majority of studies in this meta-analysis only included children below two years of age resulting in a lower estimation of MOV. As our data show, MOV was nearly 90% in children above 23 months of age. One of the few studies to include older children also reported that MOV prevalence was higher in children aged 1-5 years (56.6%), compared to those below one year (31.4%) (11). Thus, we believe that overall MOV prevalence is being seriously underestimated, as assessments do not include children beyond the EPI age target for most vaccines, that is, above 23 months of age.

Consistent with recent studies in low-income countries (12), we found a higher MOV prevalence in children above 12 months. In a recent study that assessed MOV with WHO methodology in Chad and Malawi (13), Ogbuano et al. found a MOV prevalence of 86% in Chad and 94% in Malawi among children above one year of age, compared to 49% and 61% below one year, respectively.

Age as a risk for having MOV may be explained by older children having been perceived as "too old" to be eligible (14), as many National immunization programs only target children

below one year of age. Age as a false contraindication was found to be one of the main reasons for having a MOV in a WHO review about factors related with under-vaccination (15). For example, even if 2013 WHO removed age restriction for rotavirus vaccine in the WHO African region, nevertheless it is not implemented in many countries (16)(17). But efforts are being made to 'Leave No One Behind' (18)**:** the latest WHO update of recommendations for routine immunization (19) emphasizes that measles vaccine should not be limited to children up to 12 months of age. In line with that, a "second year of life healthy child visit" is already recommended by WHO (20)(7) increasing the opportunity to vaccinate children, especially in those who might have missed vaccination in their first year of life. This strategy, together with complementary catch-up activities to continue screening children at any contact with health services, should be strengthened in low-resource settings (7)(21)(22)(23). We believe this 'never too old' policy should be adopted by all national immunization programs in order to ensure children do not miss the opportunity to be fully vaccinated at any age.

Our data draw attention to the high proportion of children missing an opportunity to get vaccinated at hospital level. A similar proportion has been found in a recent study performed in northern Indian hospitals (24). This could be explained by vaccine shortage at hospital level but also by the belief in the false contraindication for vaccination in a sick child among caregivers and health care workers. For example, a study in Haiti reported that up to 13% of reasons for under-vaccination was child illness, despite the fact that mild infections should not prevent vaccination (25). A similar finding is highlighted in a MOV assessment in Timor Leste (14) were Li et al. found that only 24% of health care workers were able to identify true contraindications, and Kaboré et al. (12) reported that 83% of health workers failed to correctly identify valid contraindications for vaccination. This could be avoided through the

proper adherence to the Integrated Management of Newborn and Childhood Illnesses (IMNCI) guidelines (22), already in place in these countries (26).

We identified that one third of children actually visiting for vaccination were still not up to date at the end of the visit despite being vaccinated with one or more doses. Similar estimates were found in four recent MOV assessments in Timor Leste, Chad, Malawi, and Burkina Faso (12)(13)(14). This could be explained by supply shortages of specific vaccines, but also by health workers potentially failing to identify eligibility for certain vaccines. Failure to administer simultaneous vaccines due to fear of wasting doses from multi-vial vaccines has been also suggested as an explanation for remaining MOV after vaccination visits (27)(28). Among reasons for MOV in our study, almost 20% reported not being informed by health care workers about the eligibility of the child for vaccination. This lack of information on vaccine eligibility has also been reported elsewhere (29). Therefore, promoting training on eligibility assessment and true contraindications for vaccination among health care workers could be an effective strategy to reduce MOV (30).

Over three-quarters of eligible children consulting for reasons other than vaccination (mother-and-child health visits, nutrition, curative) had a MOV. This highlights the need of strengthening routine screening of vaccination status that must be done irrespective of reason visit. Caregivers should be encouraged to bring the vaccination card to every contact with health services, to facilitate and ensure that the child can be properly screened for vaccination eligibility. So, integrating vaccination into other preventive or curative services at hospital and at primary health care level, could facilitate a significant reduction on MOV (31)(32).

In our study, caregivers reported lack of vaccines as the main reason for MOV. This is consistent with recent MOV assessments (13), where approximately 30% of health care workers reported insufficient vaccine supply or logistics issues. Inadequate vaccine supply

has already been pointed out as one of the main reasons for under vaccination in low income countries (1). Ministries of Health and their partners must work to ensure adequate vaccine supply at facility level in order be able to vaccinate any children who have accessed health care services (33).

This study is not from a representative sample, and very few children were eligible in two of the six countries included (Supplementary table 2). It has three main limitations. First, gender was not collected, losing the opportunity to uncover gender differences. Nevertheless, no gender differences in the distribution of MOV have been reported in the latest studies (3)(13). Second, our survey didn't allow us to explore health care providers' practices and perceptions, identified as one of the main reasons related to MOV in the last systematic review (3). In 2015, WHO launched a revised MOV strategy, which included Knowledge, Attitudes and Practices (KAP) questionnaires, to better guide the implementation of interventions to reduce MOV (13) which is generating new evidence (34). Also, we could not explore other factors that have been previously related to MOV such as maternal education, living in rural areas, number of children and other economic inequalities, as information on contacted caregivers was not kept(35) and unfortunately, we do not have information to estimate the participation rate.

Third, we excluded from the analysis almost half of the children whose caregivers could not present a vaccination card. This may mean that we underestimated MOV prevalence in our target population, since not presenting a vaccination card has shown to be associated with MOV (1)(3)(36). On one hand, not relying on self-reported data helped avoid potential recall bias, which is a limitation in vaccine coverage studies in low-resource settings (37). On the other hand, possession of vaccination card declines with age (11) (a relation also observed in our study, Supplementary table 1); what could result in an overestimated prevalence of MOV

in older children. Nevertheless, when assessing the relation between MOV and age including those with and without vaccination card, we obtain similar results (Supplementary table 3).

Finally, as children with identified MOV were sent back for vaccination when possible, it could have introduced a bias in MOV prevalence if these children were inadvertently interviewed again. Also, MOV prevalence estimates may have improved over the last ten years, as WHO has lately reinforced EPI vaccination during the second year of life.

CONCLUSIONS

Despite progress in vaccine coverage, MOV remains an important problem in low-resource settings. Avoiding MOV should remain a priority where access to health care is limited, in line with the new "Immunization Agenda 2030" (18). This is particularly important considering the negative impact COVID-19 pandemic is having on routine immunization programs in low and middle-income countries (38)(39).

We recommend integrating systematic vaccination screening into routine health care services, regardless of the reason for the visit, the type of facility and the age of the child. To promote maintaining and providing vaccination cards at every health care visit will help to reinforce vaccination screening and better identification of eligible children.

We identified that children above 23 months of age are particularly vulnerable for MOV. Thus, we would recommend including children beyond 23 months of age in the current WHO methodology for MOV assessments in order to avoid underestimation of MOV. National immunization programs should allow administration of missing doses, regardless of the age of the child, as the EPI has expanded its vaccination recommendations during the second year of life and beyond.

Strengthening the implementation of second-year-of-life visits, as recommended by WHO, with catch-up vaccination strategies (7) would provide additional opportunities to receive missed vaccine doses and *leave no one behind*.

Data Availability Statement

Questionnaire dataset is available in a public, open access repository.

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Contributorship Statement

Bachy C. and Panunzi I. designed the study and contributed to conduct it in the six countries. Bachy C., Panunzi I., Gil-Cuesta J. and Borras-Bermejo B. carried out the data analysis. Borras-Bermejo B. drafted the manuscript that was critically reviewed and approved by all authors.

Competing interests

None declared

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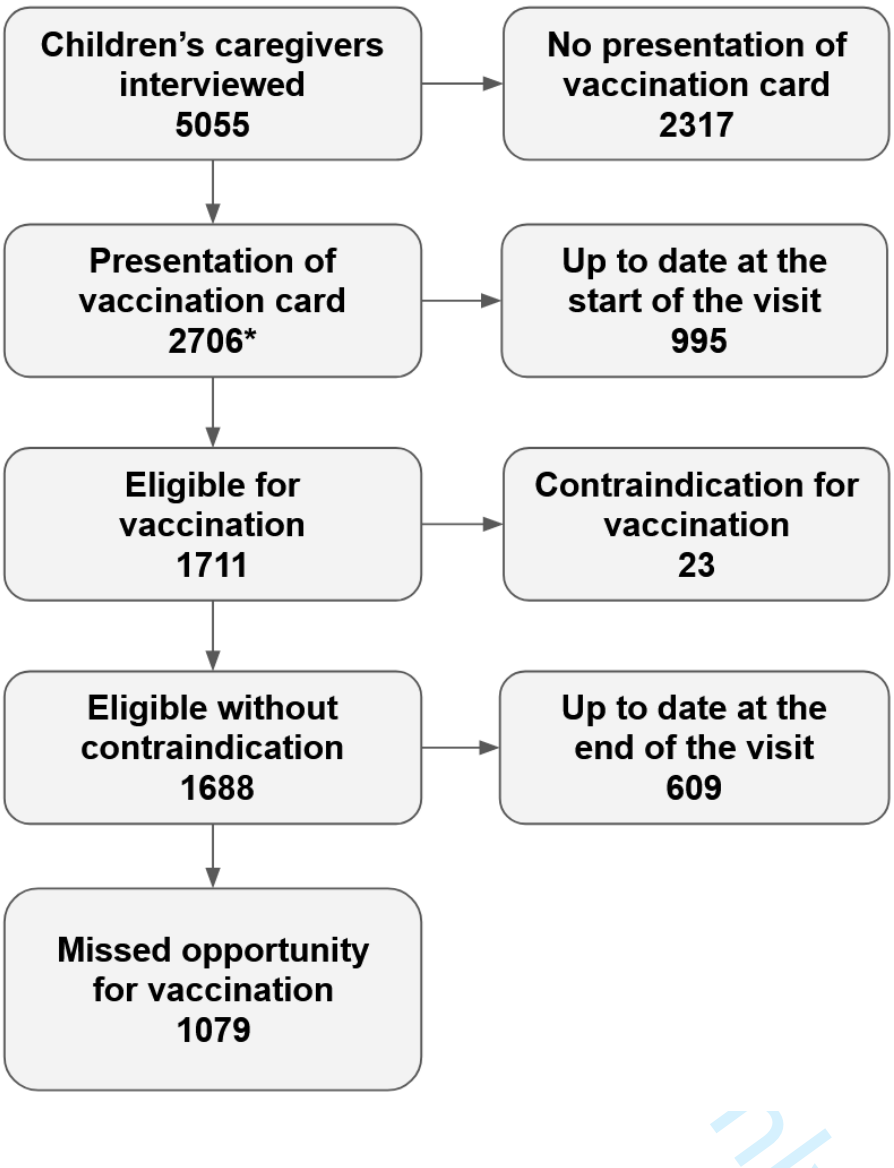
Figure 1. Flow chart of participants' inclusion and for determining Missed Opportunities for Vaccination (MOV), MSF-supported health facilities, 2011-2015

Figure 2. Immunization schedule to ascertain MOV

Figure 1. Flow chart of participants' inclusion and for determining Missed Opportunities for Vaccination (MOV), MSF-supported health facilities, 2011-2015



**32 children were not included due to data inconsistencies.*

Figure 2. Immunization schedule to ascertain MOV

Vaccine	Recommended age
Birth dose	
BCG[1]	At birth – up to 12 months
OPV[2]	At birth – up to 2 weeks
Hepatitis B vaccine	At birth – up to 2 weeks
First dose	
OPV	From 6 weeks
Pentavalent vaccine[3]	From 6 weeks
PCV[4]	From 6 weeks
Rotavirus	From 6 weeks - up to 12 months
Minimum interval of 4 weeks between First and Second dose	
Second dose	
OPV	From 10 weeks
Pentavalent vaccine	From 10 weeks
PCV	From 10 weeks
Rotavirus	From 10 weeks - up to 12 months
Minimum interval of 4 weeks between Second and Third dose	
Third dose	
OPV	From 14 weeks
Pentavalent vaccine	From 14 weeks
PCV	From 14 weeks
Measles-containing vaccine[5]	From 9 months
Yellow Fever[6]	From 9 months

[1]BCG: bacille Calmette-Guerin vaccine.

[2]OPV: Oral poliovirus vaccine. Inactivated poliovirus vaccine was not considered for MOV.

[3]Pentavalent vaccine: Diphtheria-tetanus-pertussis-hepatitis B- *Haemophilus influenzae* type b vaccine.

[4]PCV: Pneumococcal conjugate vaccine.

[5]Only one dose of Measles containing vaccine was considered for MOV.

[6]Yellow Fever was considered for MOV only in endemic countries.

DO NOT fill in (for encoding purpose only) Rec :

Evaluation of missed vaccination opportunities: child questionnaire

District: ..... **Team:** ..... **N° child:** ☐

Center: ..... **Date:** ..... / ..... / ..... **Age of the child:** ..... years …… months

1) Do you have a vaccination card or a health book for the child?

☐ **No** ☐ **Yes** → Did you bring it today? ☐ **No** ☐ **Yes**

2) What was the <u>main</u> purpose of your visit to the health center today? (One answer only)

☐ Curative consultation
☐ MCH consultation
☐ Accompanying an adult
☐ Vaccination
☐ Feeding program
☐ Other: .....

3) Vaccination status:

*Write the **<u>dates</u>** (dd/mm/yy) mentioned in the health book **<u>and circle it</u>** if vaccine given today.*
*If the history of vaccination is only confirmed orally by the caretaker, write **<u>H</u>**.*
***<u>Cross</u>** the box (X) for the missing dose of vaccine that could have been given today.*

	Dose 0	Dose 1	Dose 2	Dose 3
BCG	X		X	X
HepB birth dose		X	X	X
Polio				
DTP - HepB - Hib	X			
PCV 13	X			
Rota	X			X
Measles	X			X
Yellow fever	X		X	X

4) Was the child eligible for a vaccine today?

☐ **No** → **Do you know the date of your next vaccination?** ☐ **No** ☐ **Yes** → ***END***

☐ **Yes** → **Did the child present with a true contra-indication to the vaccination today?**

☐ **No** ☐ **Yes** → ***<u>GO TO QUESTION 6</u>***

5) Did the child receive <u>all</u> vaccines required today?

☐ **Yes**

(If X in box) ☐ **No** → **Would you have accepted the vaccination today if proposed?**

☐ **Yes** ☐ **No** → Why? .....

→ **Reason(s) for not receiving all vaccines today? (One answer only)**

☐ Out of stock
☐ Waiting time too long
☐ Don't know the reason
☐ No vaccinator
☐ Not enough information
☐ Other: .....

6) Did you get an appointment for your next vaccination? ☐ **No** ☐ **Yes**

THANK YOU FOR YOUR PARTICIPATION!

Supplementary Table 1. Characteristics of interviewed children by presentation of vaccination card. MSF-supported health facilities (2011-2015)

		Presentation of vaccination card [d]				
	Total	No		Yes		
	N	N	%	N	%	*p* value
Age groups						
<12 m	2742	906	33.0	1836	67.0	
12-23 m	1263	665	52.7	598	47.4	
24-59 m	1050	746	71.1	304	29.0	<0.001 [a]
Eligible						
No	2276	1258	55.3	1018	44.7	
Yes	2779	1059	38.1	1720	61.9	<0.001 [b]
MOV [c]						
No	2985	1358	45.5	1627	54.5	
Yes	2070	959	46.3	1111	53.7	0.558 [b]
Total	5055	2317	45.8	2738	54.2	

% Row percentages
[a] Fisher exact test
[b] Chi square test
[c] MOV over the eligible children without contraindication for vaccination
[d] Vaccination history was obtained by presentation of vaccination card or oral history.

Supplementary Table2. Children who visited MSF-supported health facilities by country (2011-2015)

	Children with vaccination card		Eligible with no contraindication		MOV	
Country	n	%[a]	n	%[b]	n	%[c]
Afghanistan	33	1.2	11	33.3	8	72.7
Democratic Republic of the Congo	79	2.9	41	51.9	26	63.4
Mauritania	244	9.0	158	64.8	118	74.7
Niger	1888	69.8	1073	56.8	851	79.3
Pakistan	15	0.6	8	53.3	1	12.5
South Sudan	447	16.5	397	88.8	75	18.9
Total	2706	100.0	1688	62.4	1079	63.9

[a] Column percentage
[b] Row percentage among children with vaccination card
[c] Row percentage among eligible children without contraindication

Supplementary Table 3. Characteristics of children with MOV irrespective of the possession of vaccination card. MSF-supported health facilities (2011-2015)

	MOV [a]				
	No		Yes		
	N	%	N	%	*p* value
Age groups					
<12 m	588	33.2	1182	66.8	
12-23 m	66	11.6	504	88.4	
24-59 m	55	12.5	384	87.5	0.001[b]
Total	709	25.5	2070	74.5	

[a] MOV over the eligible children without contraindication for vaccination
[b] Fisher

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10

		(*b*) Report category boundaries when continuous variables were categorized	10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	NA
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.