

# Perception of Malaria Chemoprevention Interventions in Infants and Children in Eight Sub-Saharan African Countries: an End-User Perspective Study

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## Research

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# Abstract

**Background:** Preventive chemotherapy interventions have been identified as key tools for malaria prevention and control. Seasonal malaria chemoprevention (SMC) and intermittent preventive treatment of infants (IPTi) represent the two major chemoprevention measures recommended by the WHO since 2012. A large number of publications of clinical trials have reported on the efficacy and safety profile of these interventions. However, little literature exists on end-user experience. The objective of this study was to provide insights on the perceptions and attitudes towards SMC and IPTi to identify drivers of and barriers to acceptance.

**Methods:** a total of 179 in-depth qualitative interviews were conducted with community health workers (CHWs), health center managers, parents of children receiving chemoprevention, and national decision-makers across eight countries in sub-Saharan Africa. Questionnaires were adapted to the malaria chemoprevention intervention in place in each country. The transcribed verbatim responses were coded and analyzed using a thematic approach.

**Results:** Study data indicate that SMC is largely well perceived and accepted by end-users, mainly due to its generally favorable efficacy and safety profile. Despite this largely positive perception, coverage remained below 100%, with health-center managers and CHWs who participated in our survey estimating, respectively, that 88% and 92% of eligible children received the first dose each month. The main causes mentioned for missing doses were children's absenteeism, children being sick, parents' reluctance, and lack of staff. Regarding IPTi, results from participants based in Sierra Leone showed that the intervention was generally well accepted and integrated into the Expanded Programme on Immunization (EPI) program. High infant mortality rate due to malaria and supportive efficacy data led Sierra Leone to implement IPTi, although these arguments were not sufficient for respondents from other countries. At the field level, parents and CHWs from Sierra Leone recognized the efficacy of the intervention in protecting their infants from malaria. The main challenges encountered were access to water, crushing the tablets, and high staff turnover.

**Conclusions:** SMC and IPTi are perceived as valuable interventions. Our study identified the key elements that need to be considered to facilitate the expansion of these two interventions to different geographies or age groups.

## Background

Since 2000, tremendous gains have been made in reducing the burden of malaria thanks to global control efforts. However, since 2016, this progress plateaued and malaria remains one of the most devastating infectious diseases with an estimated 228 million infections and 405 000 deaths in 2018, mainly children under the age of five in sub-Saharan Africa [1]. To reduce the burden of malaria, preventive chemotherapies have been identified as key elements of malaria prevention and control toolbox [2]. WHO-recommended preventive therapies include intermittent preventive treatment of pregnant women (IPTp),

intermittent preventive treatment of infants (IPTi) and seasonal malaria chemoprevention (SMC) [3]. This article focuses on the latter two chemoprevention interventions targeting children and infants.

SMC is defined as the intermittent administration of full treatment courses of an antimalarial medicine to children aged 3 to 59 months in areas of highly seasonal transmission during the rainy season. The objective is to prevent malarial illness by maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk. WHO recommends SMC with a combination of two antimalarial medicines, sulfadoxine-pyrimethamine + amodiaquine (SPAQ), in areas with highly seasonal malaria transmission in the Sahel sub-region of Africa, where *P. falciparum* is sensitive to both these medicines. SMC was first recommended by the WHO in 2012, followed by development of regional and national plans for its implementation [4]. SMC has been shown to prevent approximately 75% of all clinical malaria episodes and a similar proportion of severe malaria episodes, even where insecticide treated net usage is high [5]. In addition, a recent retrospective study from Issiaka *et al* demonstrated that the implementation of SMC was associated with a substantial reduction in hospital admissions and all-cause mortality in the health district of Ouelessebouyou, Mali [6]. In Senegal, SMC has been used in children up to 10 years old based on the findings that the malaria burden was also high in the 5 to 10 years old group [7]. According to the WHO 2019 World Malaria Report, 31 million children in 12 countries in Africa's Sahel sub-region were protected through SMC programmes in 2018 Africa [1]. However, about 12 million children who could have benefited from this intervention were not covered.

IPTi is a course of antimalarial medicine delivered to infants using routine immunization services. Treatment is given three times during the first year of life at approximately 8 to 10 weeks, 12 to 14 weeks, and 9 months of age, corresponding to the routine vaccination schedule of the Expanded Programme on Immunization (EPI). WHO recommends IPTi with sulfadoxine-pyrimethamine (SP) in areas with moderate to high malaria transmission in sub-Saharan Africa that have less than 50% prevalence of Pfdhps 540 mutation in the *P. falciparum* parasite [8]. Administration is associated with a favorable safety and tolerability profile, is simple, cost-effective and it was well accepted by health workers and communities, as indicated during the initial pilots in the early evaluation periods [9]. It has been confirmed that IPTi-SP has no negative effect on the protective efficacy of EPI vaccines [10, 11]. A recent Cochrane review of IPTi by Esu *et al* found that although the effect varied over time and between drugs, the overall impact of IPTi was a 27% reduction of clinical malaria [12]. They concluded that IPTi with SP probably made little or no difference to all-cause mortality, but resulted in fewer episodes of clinical malaria, anemia, parasitemia and fewer hospital admissions. To date, Sierra Leone is the only country that has fully implemented the IPTi intervention.

Other preventive interventions have been trialed or piloted, including intermittent preventive treatment in school children (IPTsc), mass drug administration (MDA) and post-discharge malaria chemoprevention (PMC) [13, 14]. PMC being one of the most recently investigated interventions, we sought to better understand how it could be implemented. PMC is the intermittent administration of full treatment courses of antimalarials to children recovering from severe anemia. In Malawi, a randomized clinical trial of PMC evaluated the effect of artemether lumefantrine (AL) administered one and two months after discharge to

children under 5 years of age who had been admitted with severe anemia [15]. The intervention decreased the composite endpoint of death, severe anemia or severe malaria by 31%. Similarly, a study in Kenya and Uganda demonstrated that the administration of dihydroartemisinin-piperazine (DHA-PPQ) to children admitted for all-cause severe anemia at 2, 6, and 10 weeks after discharge reduced all-cause readmission or death by 35% [16].

Because adoption and implementation of SMC has been fragmented and IPTi limited to Sierra Leone, we designed a survey to better understand how SMC and IPTi interventions are perceived in a selection of countries. In addition, as IPTi is delivered via the EPI program, we investigated the hurdles facing this program that could impact the potential implementation of IPTi. Lastly, as clinical trials are currently investigating the impact of providing intermittent administration of full courses of treatment of antimalarials to children recovering from severe anemia, we sought to better understand the management of children under 5 years of age hospitalized for severe anemia.

## Method

### Study setting

To understand in-country approaches to malaria chemoprevention in children, eight countries in Africa were selected based on their past and current experiences with various malaria chemoprevention strategies, as well as some countries that did not implement any intervention. Table 1 summarizes which interventions have been implemented or trialed in each country.

**Table 1.** Chemoprevention intervention per country:

Country	SMC	Ext SMC*	IPTi	PMC
Cameroon	✓			
DRC			Pilot	
Ghana	✓		Pilot	
Nigeria	✓			
Senegal	✓	✓	Pilot	
Sierra Leone			✓	
Tanzania			Pilot	
Uganda				Trial

\*: *Ext SMC: extended seasonal chemoprevention to the 5 to 10 years age group*

These countries were also selected because of their geographic diversity within Africa and their varying population size. Participants from all countries were asked questions about their vaccination programs,

and how they manage severe anemia patients.

## Study design

### *Key informant interviews*

Research participants were selected based on their involvement in malaria management and included National Malaria Control Programme (NMCP) coordinators or staff members, key opinion leaders (KOLs) such as clinicians or professors, and in-country malaria organization representatives. Personalized introduction emails were sent by Medicines for Malaria Venture (MMV) to 32 potential key informant participants, outlining the scope of the project. Seven (21%) contacts declined to participate in the survey either because they were not involved in malaria chemoprevention, but provided references and introductions to other key informants. Eleven (32%) contacts did not respond or were not able to participate in the timeframe allocated to that research. A total of 14 contacts accepted the invitation and were interviewed, including six NMCP coordinators, two NMCP staff members, four Professors from academic or research centers, and two local UNICEF representatives. Participation in the survey was voluntary, and no incentive or compensation was offered to participants. Note that no one from Tanzania was interviewed as it was not possible to schedule a time for the interviews during the period allocated to the study. Number of participants per country is shown in Table 2.

**Table 2.** Number of respondents per specialty per country

<b>Country</b>	<b>Health center managers</b>	<b>CHWs</b>	<b>Parents</b>	<b>Key informants</b>	<b>Total</b>
Cameroon	8	10	5	2	25
DRC*	16			2	18
Ghana	8	10	5	2	25
Nigeria	13	16	5	3	37
Senegal	8	10	5	2	25
Sierra Leone	15		5	2	22
Tanzania	15				15
Uganda	11			1	12
<i>Total</i>	<i>94</i>	<i>46</i>	<i>25</i>	<i>14</i>	<i>179</i>

\*: Democratic Republic of Congo

Five discussion guides were produced by MMV. The list of questions in each guide was adapted to the country's past and current experience with malaria chemoprevention strategies. All interviews were conducted in French or in English by phone by a single moderator. The interviews took place from 19

June to 25 July 2019. One respondent in DRC provided feedback by email. Interviews lasted from 15 to 60 minutes, with an average of 33 min.

### ***Health center managers, community health workers and parents' interviews***

Seven discussion guides were generated by MMV and shared its field partner, Sanisphere. Each discussion guide was tailored to the target respondent (health center manager, CHWs, parents) and the type of intervention (IPTi, SMC, extended SMC, vaccination campaign, management of severe anemia). Separate local ethics clearance was obtained for each country and each site by the field partner. The objective of the study was described before each interview and written informed consent was sought from each participant. Confidentiality was assured at all stages of the study and permission was asked for tape-recording. The study did not involve patients, and data on patient characteristics were provided only in the aggregate. As such, there was no institutional review board involved in approving the research as per the European pharmaceutical Market Research Association (EphMRA) code of conduct and the British Health Business Intelligence Association (BHBIA) guidelines [17, 18].

At field level, recruitment and interview of health center managers, community health workers (CHWs) and parents were undertaken by Sanisphere. Respondents were recruited in districts and health centers where children receive SMC and/or participate in IPTi. Screening questions were used to either qualify or disqualify respondents from participating in the interview. These questions were adapted to each country's policy regarding SMC and IPTi implementation status as specified in Table 1. The final sample for the field survey consisted of 94 health center managers, 46 CHWs and 25 parents. The total number of respondents per type per country is shown in Table 2. Detailed sample composition description of each target can be found in the appendix. All interviews were conducted face-to-face, in French or English. Interviews took place from 9 August 2019 to 28 September and lasted 45 min on average for health center managers and CHWs, and 25 minutes on average with parents. The interviews were audio recorded and transcribed into English. Transcripts from the first 4 interviews in Nigeria and DRC were shared with MMV to serve as a pilot and provide further guidance to interviewers. Transcripts were then received on a bi-weekly basis.

### **Data analysis**

For the key informant interviews, debriefing notes were generated by the moderator for each call/meeting. The 14 debriefing notes were structurally coded and entered in Excel to facilitate the analysis. Analysis was performed by the moderator who conducted the interviews to ensure consistency in the analysis.

The analysis of the transcripts from the interviews with health center managers, CHWs and parent was performed by one researcher who systematically reviewed the 165 transcripts, entered, and coded the data into Excel to facilitate the analysis. A second researcher independently coded a random sample of 27 transcripts (10 health center managers, 10 CHWs and seven parents). To judge coding reliability, Cohen's kappa was used to examine the consistency between both coders. Findings of this analysis indicate that coefficients for each variable examined were 0.72 for health center managers, 0.61 for

CHWs and 0.73 for parents, with an aggregated score of 0.69. Given that attaining a kappa value of 0.6 or higher is considered a substantial level of mutual agreement, we determined that our coding was reliable [19]. Cohen's kappa score was not calculated for the key informant because of the low number of interviews.

## Results

### Seasonal Malaria Chemoprevention:

Understanding of current SMC practices was investigated by interviewing a total of nine NMCP representatives, KOLs and in country partners from Cameroon, Ghana, Senegal, and Nigeria. According to the nine key informants the SMC intervention implementation was facilitated by the fact that good results were obtained during trials and local pilots. Engagement of policy makers and community leaders was mentioned as the key driver of implementation and acceptance of the intervention. The hurdles encountered were mainly linked to adherence to the program and administration of the second and third dose of SPAQ, as well as limited funding in Nigeria. In Senegal, extension of SMC to children 5 to 10 years of age was triggered by the early SMC trials which demonstrated that children in this older age group were just as affected by malaria as the younger children. According to the key informants from other SMC-implementing countries interviewed for this survey, a similar extension to 5 to 10 years old did not occur mainly because of limited funding, and the absence of a pilot study in their countries to demonstrate the same benefit in the older age category.

Results from the interviews with 37 health center managers, 46 CHWs and 20 parents in Cameroon, Ghana, Nigeria and Senegal showed that SMC was generally positively perceived by the survey participants thanks to its efficacy in preventing malaria (figure 1).

### **Efficiency:**

*"The drug is very effective. The reason I said this is because before the start of this chemoprevention, during raining season, facilities are usually congested with sick people. All of the beds for admission would have been occupied. But due to the effectiveness of the chemoprevention such congestion is now a thing of the past." Health center manager, Nigeria.*

### **Cost:**

*"SMC reduces expenses for us parents. There are too many mosquitoes here, without prevention it would be too expensive to treat children. Malaria access requires spending in health centers, yet prevention is free." Mother of 2 children, Cameroon.*

The main barriers to SMC implementation mentioned by health care professionals were the side effects, driven by respondents from Senegal; a number of staffing issues including lack of staff, transportation to households, and absence or delay in payment of incentives to staff; and poor acceptance from parents (figure 2).

**Adverse effects:**

*“During the first day we had less problems but on the second day, third day we had all the problems in the world because it was at that moment that the side effects started and we had many cases of refusal because the parents could not bear these effects in the children and they said that the drugs are not good. In the second passage, it was even worse, we had many cases of refusal; when we went to discuss with the parents, they said downright “no, all the children were sick”, we tried to talk to them but there was nothing to do” Health center manager, Senegal*

The three main ways to improve SMC delivery, according to health care professionals who participated in the survey were: 1) Better education of parents to increase their acceptance of SMC (Senegal), 2) In time payment of incentives, (Cameroon), offering a better incentive plan to cover the transportation fee, or offering a small incentive to parents (Nigeria and Ghana), and 3) Improvement of side effects associated with the treatment (Senegal). For parents involved in the survey, the main improvements were extension of SMC (to older children and even adults, and to regions that are not currently covered and extended duration (coverage for a longer period than the current 4 months) (figure 3).

Several potential barriers to SMC were specifically investigated during the survey. These included issues around drug stocks; staffing and workload; inadequate coverage; and potential conflicts with other public health campaigns.

***Availability of drug:***

Health center managers and CHWs who participated in this study anecdotally reported SPAQ out-of-stock situations. Most of these situations were corrected within 24 hours and had no impact on children’s malaria protection.

***Staffing and workload:***

Health center managers with the lowest number of CHWs were those most in need of an increase in staff, requesting on average 36% more CHWs. Half of the CHWs who had participated in the survey said the workload associated with SMC was fine, while the other half thought it was too much. In terms of turnover, most parents who participated in the survey in Nigeria and Cameroon mentioned that CHWs varied frequently, while parents from Senegal and Ghana reported that it was steadier.

***Coverage:***

According to health center managers and CHWs who participated in the survey, 88% and 92% of eligible children received the first dose of SMC each month, respectively. In terms of second and third dose, an estimated 11% of children did not receive it according to one health center manager. This number increased to 22% of children according to CHWs. Respondents from Cameroon, Ghana and Nigeria indicated that the main reasons for not providing SMC to children was absence or illness, while in Senegal it was parental refusal. A number of measures have been put in place by respondents to ensure

that children in Cameroon, Ghana and Nigeria receive the second and third doses of SMC, including providing advice to mothers, collecting empty blisters as proof of administration, and the use of recording cards to keep track of administration.

*“... without lying to you, officially almost all the children received. But unofficially, those who have actually received are few, given the demotivation of CHWs on the field. Hence, it can be estimated that 25% of children have not received their SPAQ dose.” Health center manager, Cameroon.*

### ***Conflicting campaigns:***

Lastly, although conflicting interventions were mentioned as a potential barrier, it was noted that SMC campaigns tend to run in isolation, according to most health center managers and CHWs interviewed. On the rare occasions when other interventions took place at the same time as SMC, these caused no conflict. Some anecdotal comments pointed to possible benefits of running net distribution, nutrition education programs or vaccination campaigns at the same time as SMC.

### **Intermittent preventive treatment of infants (IPTi):**

IPTi was investigated by interviewing two key informant respondents from Sierra Leone, the only country where IPTi is currently routinely performed. In addition, experience with IPTi was investigated in the three countries that piloted IPTi, namely DRC, Ghana and Senegal, by interviewing two key informants per country. Finally, the general perception of IPTi was obtained from three key informant respondents from Cameroon and Uganda. In Sierra Leone, the main drivers to implementing IPTi were the very high mortality rate in infants and the absence of seasonal transmission that made SMC unsuitable. IPTi adoption was facilitated by the good perception of SP thanks to the malaria prevention in pregnancy program and the important role played by CHWs in sensitizing the community to the intervention. The main hurdles related largely to logistic issues such as availability of clean water, drug shortage, nurse turnover, and poor attendance to EPI visits.

DRC, Ghana and Senegal piloted IPTi but decided not to implement it for the following reasons: lack of involvement of policy makers from the start of the process, logistics issues around synchronization with other programs, the belief of some health care professionals that infants are protected by their mothers' antibodies at the beginning of life, unconvincing results at the end of the trial, fear of SP side effects, overexposure to SP in infants due to their mother receiving SP during pregnancy, absence of solutions past the age of one, and the gap between two vaccination programs leading to a gap in coverage. Cameroon and Uganda did not pilot IPTi and do not plan to implement it because they are concerned about resistance to SP, they foresee difficulties in integrating it into the EPI program, the acceptance of parents is expected to be low, and the gap between two administrations does not provide full coverage. Nigeria is the only country that envisages implementing IPTi to reduce malaria burden in infants.

In addition to key informant interviews, IPTi was investigated by interviewing 15 health-center managers and five parents in Sierra Leone. According to the former, the advantages of IPTi were its effectiveness in

reducing the number of malaria cases, the absence of side effects, and the good supply of SP. The main barriers were the difficulties in preparing the drug, with crushing the tablets being the hardest and most time consuming step of the treatment; the limited access to commodities such as clean water and cups; and the lack of training of staff/nurses due to high turnover rates. Participating parents were largely satisfied with IPTi because they perceived it as efficacious in protecting infants from malaria, and having no side effects. The main areas for improvements highlighted were increase in drug stocks to avoid having to return to the facility, access to clean water, and availability of a pediatric formulation.

### **Expanded Programme on Immunization (EPI):**

Perception, drivers, and barriers of EPI program were investigated by interviewing 91 health center managers involved in the EPI program in all eight countries: Cameroon, DRC, Ghana, Nigeria, Senegal, Sierra Leone, Tanzania, and Uganda. The EPI program was largely well perceived by communities and parents according to health-center managers who participated in the survey. The stated main hurdles fell into five broad categories: logistics-related issues such as out-of-stock or inadequate storage of product; lack of knowledge or understanding of the program by parents and lack of endorsement by community leaders; children not showing; staffing issues such as lack of staff and high staff turnover; and transportation difficulties both for parents to come to the EPI center, and for staff to travel to communities (figure 4).

Reported attendance to vaccination visits ranged from 66% to 93% of eligible children at 10 weeks, 68% to 90% of eligible children at 14 weeks and 54% to 88% at 9 months. The measures put in place to increase attendance to EPI visits by survey participants included having a system that tracks the no-shows, raising awareness amongst parents, developing outreach services, and providing an incentive to parents.

### **Post-discharge malaria chemoprevention (PMC):**

Post-discharge malaria chemoprevention is currently being investigated in several clinical trials in Uganda, Kenya and Malawi. We evaluated the degree of knowledge and interest in this intervention amongst the 14 NMCPs, KOLs and in-country malaria organizations included in our survey. Very little knowledge about this intervention was observed amongst all 14 participants, even in Uganda where it has been evaluated in a clinical trial.

In addition, our evaluation shows that of the 94 health-center managers who participated in the research were largely unfamiliar with PMC. Therefore, the focus was on capturing some basic information about the management of patients under 5 years of age presenting with severe anemia who required hospitalization. Forty-three percent of health-center managers we interviewed said they either do not see or do not manage these patients. The remaining 57% who do take care of these patients claimed they performed malaria tests in 94% of children with 66% coming back positive. Transfusion was needed for 77% of children with 86% of them receiving it as reported by our sample. The biggest issues faced by interviewed health-center managers regarding treatment of children under 5 years of age with severe

anemia were parents' financial difficulties, lack of blood for transfusion, artesunate out of stock, delay in seeking treatment and poor adherence with treatment.

## Discussion

The efficacy and safety of malaria chemoprevention interventions in children and infants have largely been documented, and numerous publications of clinical trials results are available. There is however little literature on end-users' experience outside of clinical trials. This qualitative study provides novel and valuable insights on the perceptions and attitudes towards SMC and IPTi from those who implement it in the field – health-center managers, CHWs, and parents – as well as national representatives who are involved in setting up malaria elimination policy in their country.

Regarding SMC, the results from this study indicates that it is largely well perceived by end users. The good efficacy and generally favorable safety profile, as well as the growing experience with this intervention drove the positive perception. Similar findings have been reported by other researchers, including a recent publication of a qualitative study among parents and CHWs in the upper West region of Ghana which demonstrated that the high acceptability of the SMC intervention was driven by the perception that SMC had helped reduce the prevalence of malaria [20]. The success of SMC at the end-user level could not have been achieved without the early endorsement of the intervention by national stakeholders. Feedback obtained from key informant participants identified that robust clinical trial data at country level as well as involvement of local policy makers as early as possible in the exploration of the intervention facilitated its adoption. These are important findings for countries where SMC is not yet implemented. National programs willing to implement SMC in a country should make sure that key national stakeholders and policy makers are involved at the beginning of the project, and should leverage the good results obtained in other countries if local trials have not been conducted. Although investigation of funding was not part of the scope of this survey, it must be noted that it is a critical element that impacts the uptake and roll out of any intervention. Finally, several countries are in the process of redefining their malaria epidemiological stratification. This exercise is important to define which areas are eligible for SMC implementation. Efficacy and cost effectiveness of SMC is highly linked to the seasonality of malaria transmission in the targeted areas.

Despite SMC's high acceptability at the central and field level, coverage remained below 100%, meaning that not all eligible children received chemoprotection, and not all who received it completed the full seasonal course. In our survey health center managers and CHWs reported that 90% of eligible children received the first dose each month at best. The consequences of poor adherence to the SMC program can be dramatic as it raises the risk of resistance emergence to the drugs used and impairs the efficacy of the intervention [21]. Although numerous studies tried to estimate adherence to SMC, it must be emphasized that, to date, there is little objective, quantitative data that confirm adherence (such as plasma drug levels) from areas where SMC is implemented as a routine program [20–23]. In the absence of such a standardized systematic measure of adherence, we investigated the causes for reduced adherence in order to identify measures that could increase access to SMC. Participants in our survey indicated that

the main reasons for low coverage were child absenteeism, ailing children, or parental reluctance to allow their children to receive a drug. CHWs participating in our survey mention the latter as the biggest hurdle. Work from other groups identified further causes for low coverage [22, 23] including insufficient training of community distributors, inadequate supply of commodities and insufficient financial resources for remuneration, advocacy and supervision, and parents forgetting to administer the second and third dose. There were anecdotal mentions of the drug being given to another child, or saved for later, and parental reluctance to allow their children to receive the drug [20, 23]. These findings illustrate the breadth of reasons that can prevent all eligible children from receiving SMC and must be taken into consideration by policy makers and program heads who want to start or optimize SMC in their country.

The potential hurdles to SMC implementation are not limited to uptake or adherence issues. In their 2017 publication Coldiron *et al*/identified logistical burdens, the use of preventive medication requiring a 3-day course of therapy, and geographical difficulties as potential challenges to full SMC implementation [21]. Our survey also investigated stocking issues; staffing and workload issues; and conflicts with other campaigns as potential barriers to SMC. Stocking and potential conflicts with other campaigns were not reported as having an impact on SMC implementation, positive or negative. Most of the out-of-stock situations lasted one day and were quickly resolved, and there was little overlap of SMC campaigns with other interventions. Staffing issues, on the contrary, were mentioned as an important barrier to SMC implementation, mainly, not enough CHWs to perform the campaign, resulting in a heavier workload for those on the ground. Delay in payment of CHWs incentive was also mentioned as a demotivating factor and increases staff turnover. These hurdles are important to take into consideration when implementation or extension of SMC is planned.

Regarding IPTi, results from participants based in Sierra Leone indicate that the intervention is largely well accepted and integrated in the EPI program. Drivers of adoption of IPTi at the national level were the high mortality rate in infants, good efficacy data shown in early clinical trials and the absence of a significant rainy season that prevented Sierra Leone from implementing SMC. These arguments were not sufficient for decision makers from the other countries included in our survey to decide to implement IPTi. The reasons for their reluctance ranged from fear of the emergence of resistance to SP, expected difficulties to synchronize with EPI programs, unconvincing efficacy results, and gaps in coverage. These concerns are in line with the potential challenges identified and discussed in 2005 by O'Meara *et al* [24]. Several potential adaptations can be envisaged to make IPTi more attractive to decision makers including: extending IPTi beyond the 3rd vaccination up until children reach 2 years of age; use a drug other than SP in areas where SP resistance is a concern; synchronize IPTi with interventions other than EPI to increase the number of exposures to the drug. These adaptations will need to be trialed and endorsed by regulatory authorities before they can be rolled out. At the policy level, it is important to engage with local decision makers as early as possible in the process and to allow them to tailor the approach to their country's needs. At the field level, parents and CHWs from Sierra Leone recognized the efficacy of the intervention in protecting their infants from malaria. The main difficulties at this level related to logistics issues such as access to water and crushing the tablets, and staffing issues related to high staff turnover and training needs.

Lastly, our survey provided some high-level information about potential hurdles to the implementation of PMC. Participants in our survey indicated that financial difficulties experienced by parents and poor adherence to treatments were two of the biggest issues they faced when treating patients under 5 years of age presenting with severe anemia. These two potential barriers will have to be addressed should PMC be implemented at a large scale, in addition to raising awareness about this intervention.

## Limitations

The main limitation of the interviews with key informants was the small number of participants. Caution should be used when generalizing results of this subset of respondents to the whole malaria prevention field. To mitigate the impact of small sample size, we targeted participants who were the most influential and knowledgeable. The survey with field-level participants also presents a number of limitations. Regarding the sample size and composition, the total number of respondents per country was limited, and not all regions or districts were represented. Although we interviewed respondents from a mix of regions and settings to mitigate geographical bias, caution should be used when generalizing results of this subset of respondents to the entire malaria-endemic region of sub-Saharan Africa. In terms of methodology, as with any survey, our findings reflect the answers and views of participants that may be influenced by their recall and response bias. To mitigate this risk, all key informants were interviewed by one person to achieve greater uniformity in interpretation. As for the interviews with field-level participants, clear guidance was provided to interviewers to ensure they obtained the most accurate information. Several interviewers were used to administer the questionnaire in the different countries, which could result in some interviewer-based country variation. Importantly, all respondents answered the same questionnaire, and interviewers were trained to avoid this type of bias. Despite these limitations, we believe the data presented here are valuable as they provide some qualitative input on experience with and perception of malaria chemoprevention interventions and they represent real-life data typically not obtainable on a large scale.

## Conclusion

This end-user perspective study has provided new insights about the drivers and barriers for the adoption of various malaria chemoprevention interventions from the point of view of a select group of target respondents, key stakeholders and end users. Wherever implemented, the chemoprevention interventions explored in our survey were perceived as valuable and efficacious in preventing malaria by survey participants. Logistical issues, such as staff shortages and out-of-stock situations, were identified as the biggest barrier to a full use of these interventions, highlighting the need for health system strengthening measures. Further expansions of these interventions, either to eligible geographies or broader age groups, could be envisaged providing that health systems are able to absorb the increased workload and provision of sufficient drug is secured, that country generated data on the positive impact of these interventions are available, and that the expansions are endorsed by normative bodies.

# Abbreviations

AL: artemether lumefantrine; BHBIA: British Health Business Intelligence Association; CHWs: community health workers; DHA-PPQ: dihydroartemisinin-piperaquine; DRC: Democratic Republic of Congo; EphMRA: European pharmaceutical Market Research Association; EPI: Expanded Programme on Immunization; IPTi: intermittent preventive treatment of infants ; IPTp: Intermittent preventive treatment of pregnant women; IPTsc: intermittent preventive treatment in school children; KOLs: key opinion leaders; MDA: mass drug administration; MMV: Medicines for Malaria Venture; NMCP: National Malaria Control Program; PMC: post-discharge malaria chemoprevention; SMC: seasonal malaria chemoprevention; SP: sulfadoxine-pyrimethamine; SPAQ: sulfadoxine-pyrimethamine + amodiaquine; WHO : World Health Organization

# Declarations

## **Ethics approval and consent to participate:**

Separate local ethics clearance was obtained for each country and each site by the field partner. The objective of the study was described before each interview and written informed consent sought from each participant. Confidentiality was assured at all stages of the study and permission asked for tape-recording. The study did not involve patients, and data on patient characteristics were provided only in the aggregate. As such, there was no institutional review board involved in approving the research as per the European pharmaceutical Market Research Association (EphMRA) code of conduct and the British Health Business Intelligence Association (BHBIA) guideline

## **Consent for publication**

Not required.

## **Availability of data and materials**

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

## **Competing interests**

The authors declare that they have no competing interests

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## **Authors' contributions**

CA contributed to the development of the study protocol, performed interviews with key informant respondents, and made supervisory field visit in Kenya for the interviews of field based participants, ran the analysis and wrote the finale reports and the manuscript. AMT provided introductory emails to key informant, reviewed the questionnaires, final reports and the manuscript.

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## Figures

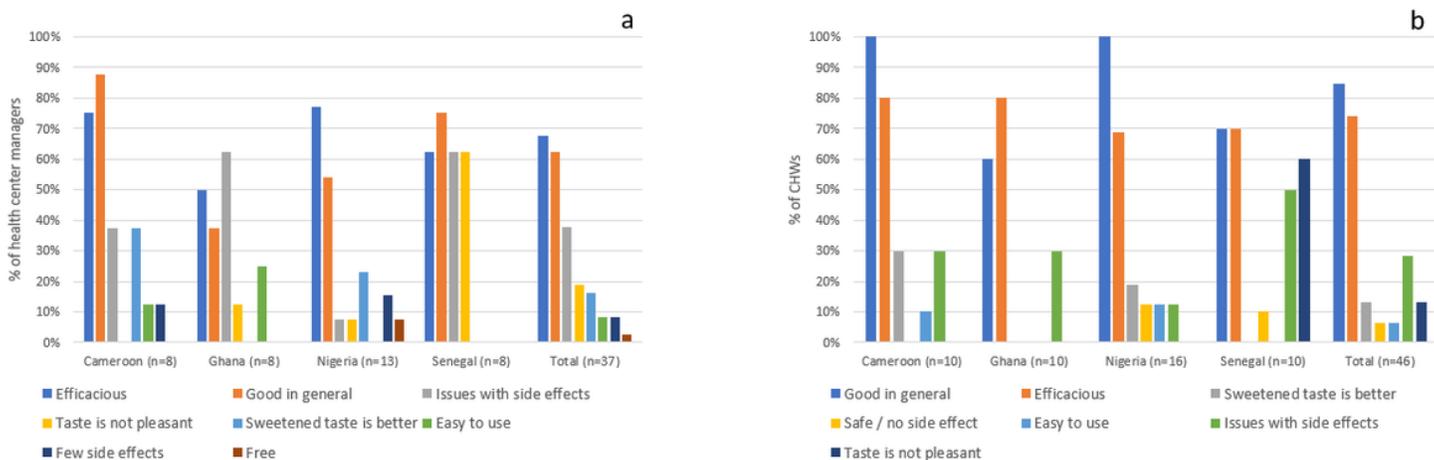


Figure 1

SPAQ perception by health center managers (a) and CHWs (b).

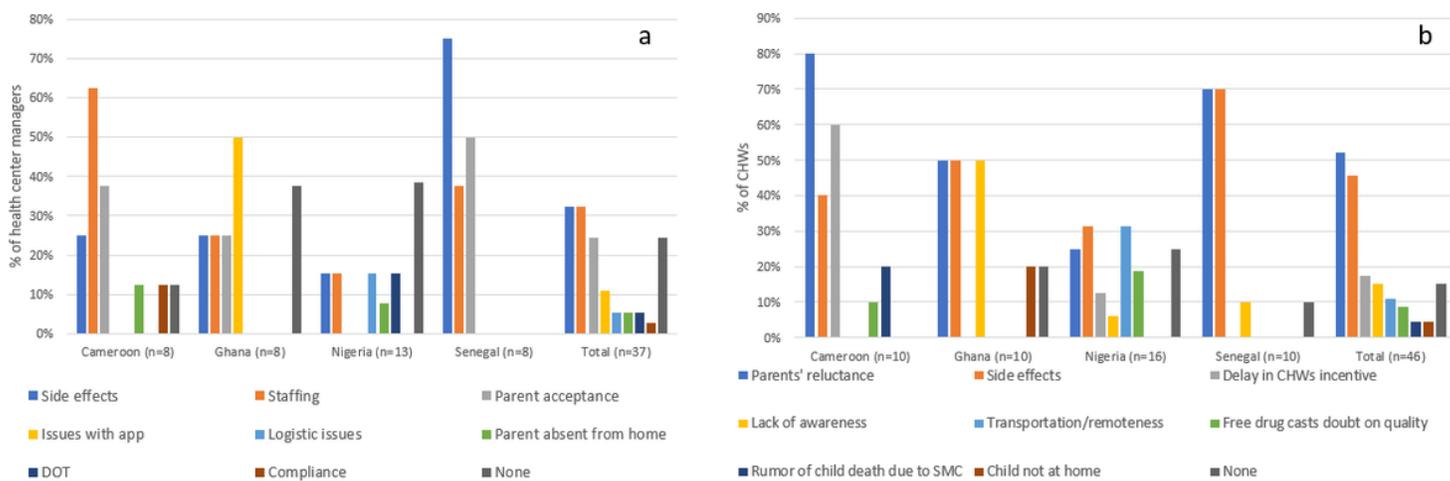


Figure 2

Barriers to SMC implementation at the health center level (a) and at the CHWs level (b).

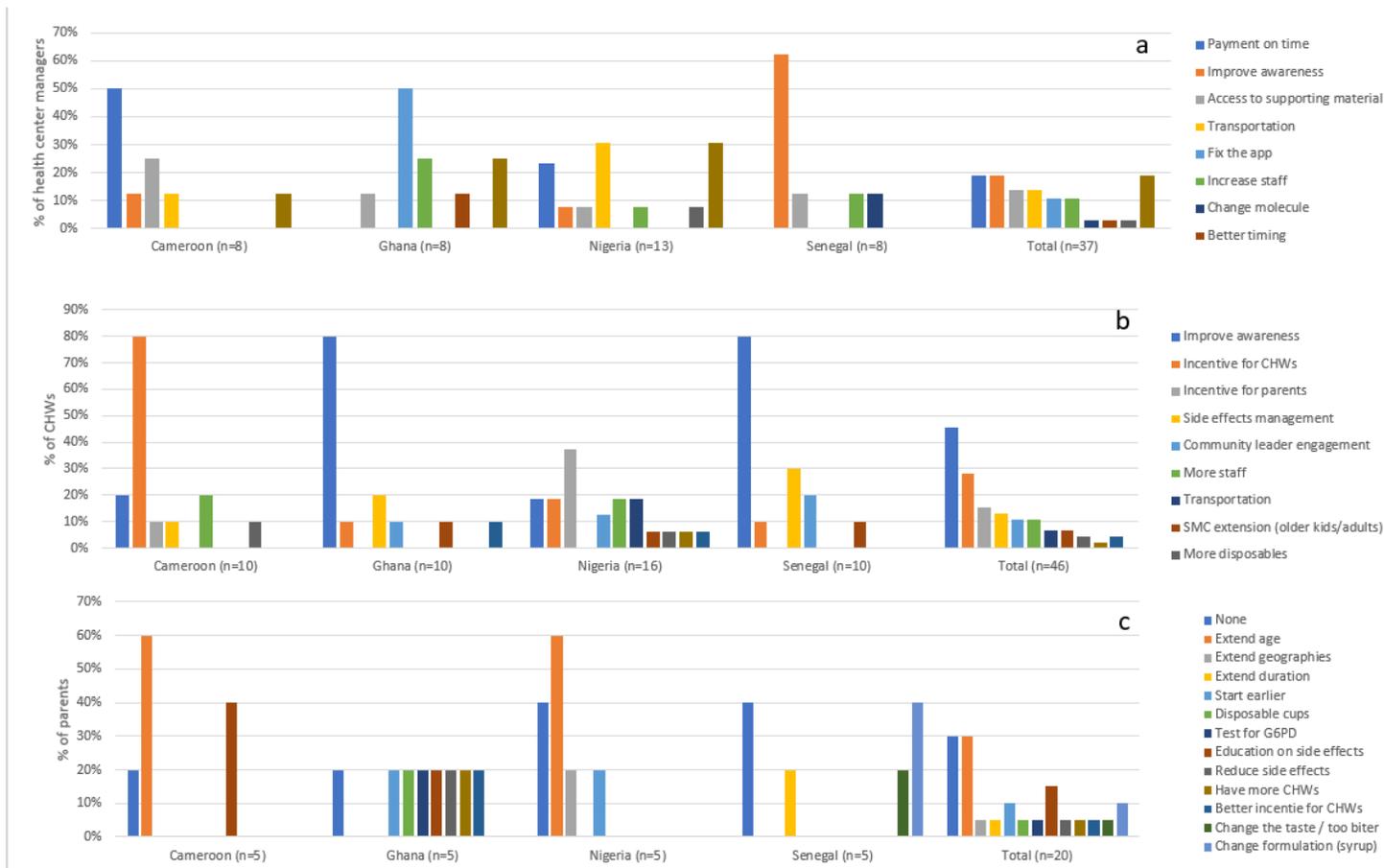


Figure 3

SMC improvement at health center manager (a), CHWs (b) and parents' level (c).

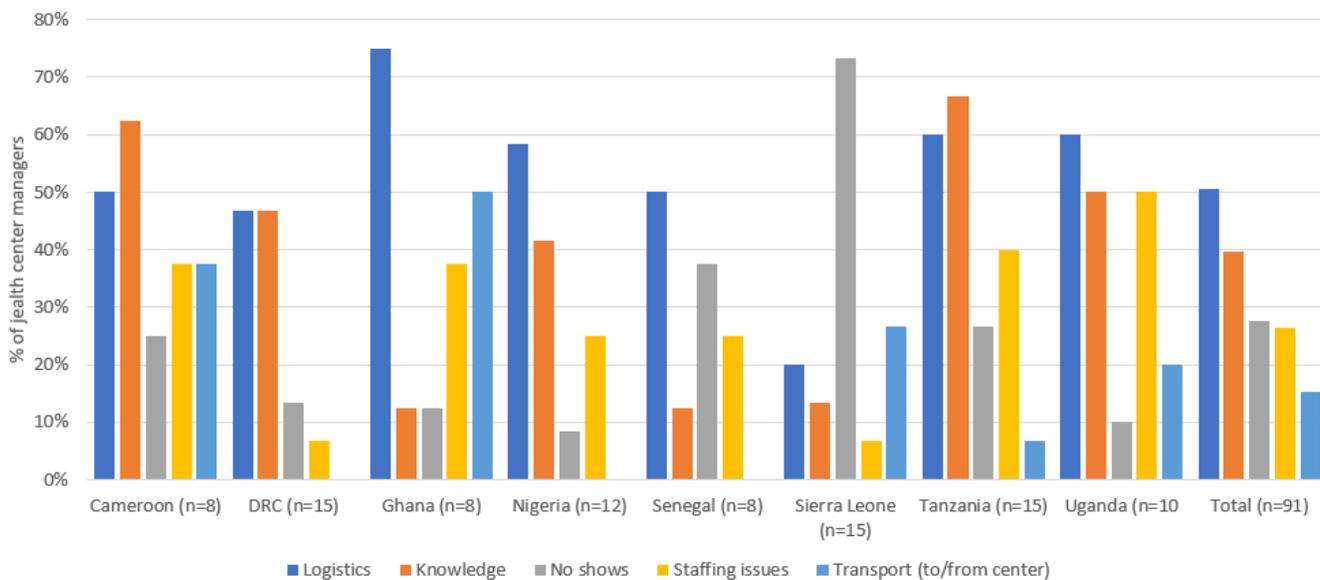


Figure 4

Main issues reported about EPI program.

## Supplementary Files

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- [Appendix.docx](#)