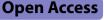
RESEARCH





Perceived barriers and opportunities for the introduction of post-discharge malaria chemoprevention (PDMC) in five sub-Saharan countries: a qualitative survey amongst malaria key stakeholders

Céline Audibert^{1*} and Hans Rietveld¹

Abstract

Background Post-discharge malaria chemoprevention (PDMC) is an intervention aimed at reducing morbidity and mortality in patients hospitalized with severe anaemia, with its effectiveness established in several clinical trials. The aim of this study was to better understand factors that would influence the scale up of this intervention, and to identify preferences for two delivery mechanisms, facility-based or community-based.

Methods Forty-six qualitative individual interviews were conducted in five sub-Saharan countries amongst malaria key opinion leaders and national decision makers. Findings were analysed following a thematic inductive approach.

Results Half of participants were familiar with PDMC, with a satisfactory understanding of the intervention. Although PDMC was perceived as beneficial by most respondents, there was some unclarity on the target population. Both delivery approaches were perceived as valuable and potentially complementary. From an adoption perspective, relevant evidence generation, favorable policy environment, and committed funding were identified as key elements for the scale up of PDMC.

Conclusions The findings suggest that although PDMC was perceived as a relevant tool to prevent malaria, further clarification was needed in terms of the relevant patient population, delivery mechanisms, and more evidence should be generated from implementation research to ensure policy adoption and funding.

Keywords Severe anaemia, Severe malaria, Post-discharge malaria chemoprevention, Sub-Saharan Africa

Background

Severe anaemia is a leading cause of paediatric hospital admission and mortality in sub-Saharan Africa [1-4]. Children under 5 years of age are most vulnerable with an in-hospital mortality rate ranging from 4 to 12% [5–7].

*Correspondence:

Céline Audibert

audibertc@mmv.org

It is increasingly recognized that children with severe anaemia remain at high risk after discharge from hospital, with up to 33% of the children dying or being readmitted within the first 6 months following discharge [5, 6, 8, 9]. Malaria infections in the post-discharge period have been shown to contribute to severe anaemia rebound, rehospitalization, and morbidity [3, 8].

Post-discharge malaria chemoprevention (PDMC) is the administration of a full anti-malarial treatment course at regular intervals to children who have recently



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

¹ Medicines for Malaria Venture (MMV), Route de Pre-Bois 20, 1215 Meyrin, Switzerland

been discharged from hospitals after being treated for severe anaemia [10]. Clinical trials conducted in The Gambia, Malawi, Kenya and Uganda involving 3,663 children with severe anaemia demonstrated that three months of PDMC significantly reduced mortality during the intervention period, as well as all-cause readmissions, readmissions due to severe malaria, and readmissions due to severe anaemia [11–14]. However, these benefits were limited to the intervention period and disappeared as the drug levels waned [12]. Three drug regimens were employed in these trials, involving monthly sulfadoxinepyrimethamine (SP) delivery for an average duration of 3 months [13], monthly artemether-lumefantrine (AL) given at 4- and 8-weeks post-discharge [11], or monthly dihydroartemisinin-piperaquine (DHA-PQ) given at 2-, 6- and 10-weeks post-discharge [14]. Based on this evidence, the malaria prevention guidelines of the World Health Organization (WHO) include a conditional recommendation for the use of PDMC to prevent new malaria infections in children admitted with severe anaemia during the period after hospital discharge when they are at risk of readmission or death [10]. To date, PDMC has not been implemented at scale and has only been trialed in clinical studies and small-scale pilots [12].

Unlike other malaria prevention interventions, such as intermittent preventive treatment in pregnant women (IPTp), perennial malaria chemoprevention (PMC) or seasonal malaria chemoprevention (SMC), PDMC targets a smaller population of seriously ill patients with an estimated 57,000 to 314,000 children under 5 years of age hospitalized with severe malarial anaemia per year [15]. While PMC and IPTp are delivered through established health systems such as the Expanded Programme on Immunization (EPI) and Ante Natal Care (ANC) programs, there is no guidance on how to implement and deliver PDMC. One acceptability study conducted in Malawi showed that PDMC was highly accepted among caregivers of children under 5 years of age previously treated for severe anaemia [16]. This study also found that caregivers preferred community-based delivery of PDMC rather than collecting drugs for each treatment course at the hospital. Community-based delivery of PDMC to children recovering from severe anaemia also resulted in higher adherence compared to facility-based delivery in Malawi [17]. While these findings are important to identify how to best implement PDMC, they may not be applicable to the context of other countries. In addition, a community-based delivery strategy also presents with potential sustainability challenges caused by inadequate supervision, low remuneration, and irregular supplies [18]. It is, therefore, necessary to carefully consider how to implement PDMC and identify the most effective delivery mechanisms.

This work aimed to better understand factors influencing the adoption of PDMC in five sub-Saharan African countries. An important component of the survey was to identify the anticipated advantages, disadvantages, and preferences for various PDMC delivery strategies. The insights provided by the malaria key informants interviewed for this work may serve to guide policymakers in determining the most appropriate delivery strategy for their specific context.

Methods

Study setting

The study was conducted in five sub-Saharan African (SSA) countries. Countries were selected to offer a mix of geographical location, malaria burden, and level of experience with PDMC. Table 1 shows the characteristics of the selected countries. The malaria burden was determined based on the WHO's identification of countries with the highest malaria burden and included in the High Burden to High Impact initiative (HBHI) [19]. Out of the 10 HBHI African countries, Nigeria and Uganda were selected due to the important number of severe malaria cases in these countries, and the fact that Uganda was involved in a PDMC clinical trial at the time of the study. This selection allowed to include two high burden countries, one involved in PDMC and one not yet trialing the intervention. The sample was completed with Kenya and Malawi as these countries were also involved in PDMC clinical trials [20, 21]. Lastly, Senegal was selected as a representative of countries where PDMC was not trialed yet, and with a lower burden of malaria.

Research design

The study consisted in a series of one-on-one interviews with national malaria key informants. A qualitative approach was selected given the exploratory nature of the research question. The study consisted of semistructured discussion guides that were adapted to the respondents' familiarity with PDMC (Additional file 1). A short description of PDMC was provided to participants

| Table 1 | Characteristics | of selected | countries |
|---------|-----------------|-------------|-----------|
|---------|-----------------|-------------|-----------|

| Country | High burden country | Participation in PDMC clinical trials | | |
|---------|---------------------|---|--|--|
| Kenya | No | Yes | | |
| Malawi | No | Yes | | |
| Nigeria | Yes | No | | |
| Senegal | No | No | | |
| Uganda | Yes | Yes | | |

PDMC Post-Discharge Malaria Chemoprevention

who were not familiar with the intervention (Additional file 2).

Respondent selection

The key informants selected for this survey consisted of a mix of representatives of national malaria programmes (NMCPs), acadaemia, funding partners, and policy makers. Potential survey participants were recruited through a mix of purposive and snowball approach. For the purposive sampling, authors generated a list of potential contacts through desk research and previous interactions with local malaria experts. This list was shared with the field partner and was expanded through snowballing: each participant was asked to identify other potential key informants in their network. Screening questions were used to qualify participants and ensure that they had sufficient knowledge or involvement with malaria. They were selected based on their role in their country's malaria management pathway and were identified as individuals able to make decisions on policies, research, or resource allocations in the field of malaria. In order to be selected to participate in the survey, key informants had to be actively working in the field of malaria for at least 10 years and devoting at least 50% of their professional time on malaria. Their familiarity with PDMC was determined at the time of recruitment, based on selfreporting. Those who self-reported being unfamiliar with PDMC were given a short description of PDMC for them to review before the interview date (Additional file 2). Respondent selection was stopped when no new information was obtained from survey participants.

Quality insight collection

Two semi-structured discussion guides were prepared by the field partner and the authors to facilitate collection of qualitative insight, one for each familiarity level with PDMC (Additional file 1). The guides consisted of questions designed to capture information across five key learning dimensions: context, knowledge and awareness, attitudes and perceptions, implementation, and future state. The discussion guides were generated in English and translated in French for the interviews conducted in Senegal. The translation into French was executed by the field partner, and checked by the corresponding author who is a native French speaker. In each country, the field partner allocated a team of two moderators to conduct the interviews. They were trained during a three-day training session and any question that emerged during the session was discussed with the authors. The guides were piloted with a subset of respondents and a debrief workshop was organized with the authors. The guides were adapted to improve the interview flow and facilitate collection of information. The authors, field partner representatives and interviewers had no established relationship with study participants. Interviews were carried out either face to face or virtually depending on participant's preference. Interviews were carried out in the participant's preferred language, either English or French. Each interview lasted between 20 and 60 min and was audiorecorded to facilitate translation, transcription, and analysis. Interviews took place from August to December 2022.

Analysis

The interview recordings were transcribed, and where applicable, translated from French to English by the field partner. All respondent information was stored separately from personal identifier information. Qualitative analysis was conducted on Dedoose (9.0.62) by a team of three coders. Coders were involved from the beginning of the project, participated in the preparation of the discussion guide, and were experienced in qualitative research and public health topics. Each transcript was coded deductively using pre-established codes derived from the research guide, and inductively by applying codes that emerged from the data as described by Thomas & Harden [22]. Inductive coding enabled a more contextualized approach and identification of country specific themes. Codes where then grouped thematically following the five components of the study: context, knowledge and awareness, attitudes and perceptions, and implementation, and future state. The code book was shared, discussed and validated with the authors. Interpretation of the codes led to the identification of key learning and recommendations addressing the research questions, which were presented to the authors by the field partner's research team. Several review iterations took place in order to refine the analysis, and agree on a final report.

Ethical considerations

Ethical guidelines were followed by informing participants about the purpose of the research, how the information will be used, their right to withdraw at any stage of the interview process. Written informed consent was obtained 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 did not collect patient characteristics. The purpose of the study was to collect key informants' professional opinions and insights and did not collect personal data or sensitive information. As such, there was no institutional review board involved in approving the research.

Results

Sample description

A total of 46 national malaria key informants were selected and interviewed, including 14 implementation partners, 11 policy makers, 7 academic researchers, 7 funding partners, and 7 MoH representatives. Table 2 provides a country breakdown of the participants per affiliation and level of familiarity with PDMC.

Familiarity, knowledge, and perception of PDMC

Out of the 46 national malaria key informants who were interviewed, half of them reported being familiar with PDMC, and the other half having little knowledge about the intervention (Table 2). Familiarity with PDMC was highest in respondents from Kenya and Malawi (60% and 70%, respectively) where PDMC clinical trials were ongoing. Level of familiarity with PDMC was the lowest in Nigeria (2 out of 10 participants), and less than half of participants from Uganda (44%) were familiar with PDMC although a clinical trial was ongoing in their country. Lastly, a majority of participants from Senegal (4 out of 7) felt familiar with PDMC. For those who were familiar with PDMC, the sources of information varied and included WHO guidelines, scientific literature and publications, international conferences, and interaction with researchers involved in PDMC trials.

Amongst those who said they had knowledge about PDMC, there was a general understanding that PDMC refers to the prescription of an oral anti-malarial to children diagnosed with severe malaria and severe anaemia for a period of 3 to 6 months after they are discharged. There was however some unclarity about who the target beneficiary should be, with many respondents emphasizing the use in severe malaria rather than severe anaemia.

The anaemia was often perceived as a consequence of severe malaria. Survey participants from Malawi had the most accurate understanding of PDMC, and stated that the intervention aimed to prevent malaria infection in children who presented with severe anaemia.

"This is a treatment that is being provided to children who were once admitted due to severe anaemia, regardless of what the cause of anaemia, be it malaria or other causes." (Funding partner, Malawi)

In terms of age range, most survey participants identified the 3 to 59 months old children as the obvious beneficiary of the intervention. A few respondents mentioned that it could be used in older children, especially in Senegal and Kenya.

Overall, PDMC was perceived as a beneficial intervention by most respondents. A continuum of benefit from the micro (child, caregiver, community) to the macro (health system and country) environment was mentioned. At the child level, PDMC was expected to reduce malaria-related mortality, morbidity and improve child survival and, therefore, improve quality of life. At the caregiver level, PDMC could improve family's socioeconomic status by reducing the costs associated with hospital visits, reduce the amount of time spent caring for a sick child, and alleviate some of the emotional and mental burden associated with having to care for a sick child. PDMC's benefits at community level would be to reduce the number of malaria carriers and, therefore, protect the whole population. It could also improve the community economic status as caregivers would fully participate in the labour market, and provide the opportunity to perform further awareness and information campaigns about malaria prevention. At the health care level, survey

| | Kenya | Malawi | Nigeria | Senegal | Uganda | Total |
|-------------------------|-------|--------|---------|---------|--------|-------|
| Familiar with PDMC: | | | | | | |
| NMCP/MoH | 0 | 2 | 1 | 2 | 0 | 5 |
| Funding partners | 1 | 0 | 1 | 0 | 1 | 3 |
| Academia / Research | 2 | 0 | 0 | 2 | 0 | 4 |
| Policy makers | 3 | 3 | 0 | 0 | 1 | 7 |
| Implementation partners | 0 | 2 | 0 | 0 | 2 | 4 |
| Not familiar with PDMC: | | | | | | |
| NMCP/MoH | 0 | 0 | 1 | 1 | 0 | 2 |
| Funding partners | 1 | 1 | 1 | 1 | 0 | 4 |
| Academia / Research | 0 | 1 | 1 | 0 | 1 | 3 |
| Policy makers | 1 | 0 | 3 | 0 | 0 | 4 |
| Implementation partners | 2 | 1 | 2 | 1 | 4 | 10 |
| Total | 10 | 10 | 10 | 7 | 9 | 46 |

Table 2 Sample composition per country

PDMC Post-Discharge Malaria Chemoprevention, NMCP National Malaria Control Programme, MoH Ministry of Health

respondents expected PDMC to help optimize use of resources – financial, work force, and commodities – thanks to reduced readmissions. At the country level, the benefits would largely be linked to the macroenvironment through reduced malaria prevalence, and reduced financial burden associated to malaria.

Reactions to PDMC delivery approaches

Survey participants were asked to react to the two delivery approaches suggested by the WHO, namely the facility-based approach for which caregivers obtain PDMC drug from a health facility every month, and the community-based delivery where caregivers receive all courses of PDMC through community-based settings.

Respondents mentioned adherence, treatment continuity and trust as the main advantages of the facility-based approach. More specifically, a respondent in Malawi indicated that delivering PDMC through the health-facility would increase adherence by leveraging the trust that was built between caregivers and health care workers during the treatment of a child. Two respondents from Uganda felt that facility-delivery offers continuity in the treatment, stating that any accompanying treatment should be handled by the facility that took care of the child in the first place. Another indirect benefit is the fact that facility visits offer the opportunity to examine a child for other issues and conduct other health assessment on a monthly basis (respondents from Malawi and Uganda).

"...there is that constant interaction between service user and a healthcare worker. And I guess if you're coming to pick medicine for this child, you're coming with the child. So, I get a chance to look at this child. And I can look at other issues other than the malaria, we can track nutrition status." (Implementing partner, Uganda)

The main challenges reported with facility delivery include time, cost and geographical constraints for caregivers, which may impact adherence to the intervention. Caregivers would have to return to the facility, incurring transportation cost and time away from work. This would negatively impact their economic situation and could prevent them from returning to the health facility to renew the drug prescription. Given that the visits are for follow-up rather than curative treatment, many respondents believed caregivers would be less likely to return, further affecting adherence.

When discussing the community-based approach, survey respondents identified three different delivery mechanisms:

• Caregivers are given the entire PDMC treatment upon discharge, and community health workers

(CHWs) perform regular follow-up to ensure that the medication is taken as prescribed.

- Local CHWs are informed of the patient's needs for the intervention and are in charge of storing and delivering PDMC through monthly visits to the child.
- Caregivers visit fixed pre-determined locations that are close to their home, and where they can obtain the required treatment.

Regardless of the delivery mechanisms, the community-based approach was advocated by a majority of respondents primarily due to its cost effectiveness and expected increased adherence to treatment. Both benefits derived from the fact that the point of care would be close to the patients. Caregivers would not need to take time off work and pay travelling cost to go to the health care facility. In addition, CHWs in charge of the monthly follow-up would ensure that the treatment is taken as intended.

"Probably it would be best if you're having these community health workers monitoring these kids, and then delivering the drugs themselves and ensuring that they're being taken." (Implementing partner, Uganda)

Survey participants indicated that PDMC implementation through the community-based approach should be straightforward to put in place as it would benefit from the existing community healthcare system. Some respondents from Senegal and Nigeria indicated that they have a robust community level delivery system thanks to the Seasonal Malaria Chemoprevention intervention. In Kenya, some respondents reported the successful use of CHWs to deliver treatment for other diseases such as HIV and tuberculosis that could be leveraged for the delivery of PDMC.

"We have a good community fabric, we have a good system, we have thousands of community actors, especially in the remote areas." (Programme manager, Senegal)

One of the main challenges identified with community delivery was the absence of incentives for CHWs. Survey participants indicated that poor financial support could have a negative impact on CHWs engagement and motivation. CHWs level of understanding of the intervention was another potential challenge and would require significant amount of training to be addressed. Providing sufficient education was perceived as necessary by respondents to ensure that CHWs deliver the intervention appropriately, and to avoid risks of mis-dosing and error in administration. From an operational perspective, lack of proper patient management tools and records between facility and CHW, and inadequate drug storage and drug management mechanisms were identified as potential barriers to proper implementation of PDMC.

Several survey participants viewed the facility and community delivery approaches as complementary and believed these two delivery channels could be leveraged for the successful implementation of PDMC. In this hybrid approach, community delivery was seen as a supplement to the facility delivery, ensuring adherence and tracking of children enrolled in the intervention.

"You cannot do one over the other because then you have missed opportunities. If a child comes to the facility, you check if they have been discharged recently and if they are due for their PDMC dosage. If yes, you give at the facility. If you're doing the village clinical and outreach clinic, you also check. Therefore, I don't think that one is better than the other." (Programme manager, Malawi)

A few survey respondents also indicated that this hybrid approach should include the private sector, capitalizing on the presence of drug stores and pharmacies at community level. The exact mechanisms of how to engage with the private sector were not discussed.

"In Uganda 61% of the population seeks care from the private sector. You need to look at pharmacies and drug stores." (Programme Manager, Uganda)

Adoption of PDMC: from evidence generation to policymaking and funding

Recommendations from survey participants on what would be required to facilitate the adoption of PDMC were collected. The three key areas that emerged were the generation of evidence, the regulatory environment, and the funding landscape.

Evidence generation

Respondents indicated that the type of evidence required would depend on the stage of PDMC implementation. At inception, baseline data on incidence and prevalence, as well as information about epidemiological transitions would be needed to support government and donor buyin. Next, the roll-out phase of PDMC implementation would require the most diverse and complete set of data, including clinical indicators, intervention effectiveness studies, adverse events monitoring, drug use surveillance, and behavioural studies to monitor willingness to adopt, adherence and compliance. In terms of clinical indicators, survey participants expect to see data on readmissions due to severe malaria after PDMC, readmissions due to severe anaemia, level of parasitaemia in children receiving PDMC, degree of anaemia, mortality rates. As for intervention effectiveness studies, they should provide information about pre and post intervention evaluation, impact at household level, administrative evaluation and follow-up evaluation. These indicators would be used to inform PDMC scale up and to monitor its implementation. Lastly, data on drug resistance, pharmacovigilance, cost effectiveness, intervention effectiveness, impact on school attendance, changes in knowledge, awareness, attitude and practice regarding PDMC would be needed during the scale up phase to support the sustainability of the intervention.

Importantly, the list of evidence identified by survey participants were described as the ideal set of indicators. Respondents warned that a number of challenges typically limit the production of the required evidence. The difficulties mentioned include: (1) the data collection methods which remain paper based in many settings, limiting access to information at community level; (2) the administrative burden of adding a new intervention to an already long and demanding list of data collection tools, which could result in the confusion of similarly perceived intervention (SMC, PMC); (3) insufficient training or competencies in data collection, resulting in poor accuracy of the data collected; (4) transitioning a data collection tool designed for a clinical setting to a community setting, and (5) potential disconnect between the public and the private sector, with data from the private sector not being systematically integrated into the national health information system.

Policy environment

From a policy perspective, there was a consensus that PDMC should be embedded in the existing malaria management guidelines and should be in line with the national malaria strategic plan. The National Malaria Elimination/Control Programme (NME/CP) under the Ministry of Health was identified as the primary owner of the plan and should be in charge of producing PDMC implementation guidelines. Updating the guidelines was identified as a potential bottleneck since the process requires the involvement of different stakeholders, which can take time. The following stakeholders, in addition to NME/CP representatives, were identified by survey participants as playing a role in the policy making and implementation processes: political leaders, Ministry of Finance, WHO, division of child and adolescent health, division of community health, donor and implementing partners (PMI, Global Fund), state and local government in Nigeria, academic institutions. The exact role played by each stakeholder was not clearly outlined and would require a complete mapping.

At the time of the survey, none of the participating countries had included PDMC in their guidelines. Malawi appeared to be the most advanced in the process, but a survey participant indicated that progress had stopped due to lack of sufficient evidence:

"WHO approval does not mean we automatically implement, we still have to go through our country policy introduction stages. We still have to pick up from where we left. We need to go back to the Malaria Advisory Board, present the data that was missing then. Once we convince this team, we will proceed to senior management in the Ministry of Health. When they get convinced, they will approve the introduction of post-discharge chemoprevention." (Policy Maker, Malawi)

Some survey participants also indicated that the funding of the intervention could be a potential barrier to the adoption of new malaria policy. Countries who are dependent on donor funding need to comply with the requirement of the donors. Without the endorsement of donors to fund PDMC, it could be challenging to include this intervention in the guidelines.

Funding landscape

Across all countries, respondents agreed that a co-financing model between governments and interested partners would be the best way to fund and drive the adoption of PDMC, ideally under the overarching responsibility of governments. However, several respondents noted that countries still largely rely on donor funds, which limits governments' ability to lead the implementation of the intervention. Some respondents suggested that the initial intervention development phase should be financially supported by donors, with governments planning to cover the cost once the PDMC intervention is in place. Lack of political will from Ministries of Health to fund PDMC was seen as a barrier to implementation by respondents from all five countries. Donor buy-in was identified as another barrier to PDMC implementation, especially in Senegal and Uganda where most of malaria programmes are donor-funded according to survey participants. Defining funding priorities and ensuring sufficient financing were identified as potential issues for PDMC implementation by respondents in Malawi, Senegal and Uganda. Limited funds could make it difficult to secure resources for sufficient and sustainable drug procurement, health care professional training and community engagement. As with many preventive measures, PDMC will compete with malaria treatment, as well as treatment for other high priority diseases such as Covid-19. Lastly, some survey participants from Kenya and Uganda mentioned corruption and fund misappropriation as potential barriers to PDMC funding.

PDMC and risk of drug resistance

Overall, more than half of respondents expressed concerns about potential drug resistance as a result of PDMC, although there were some country disparities. Respondents from Nigeria were the most concerned about the potential emergence of drug resistance as a consequence of PDMC. This concern was driven by fear of inappropriate treatment administration, self-medication, and treatment noncompliance. Some respondents also attributed the emergence of drug resistance to the already widespread use of malaria drugs (SP and AL) in various interventions and as first-line therapy.

"...there is a whole lot of intervention using SP and then AL is what we are using for treatment, and you are using it for prevention, so we are prone to resistance faster." (Policy Maker, Nigeria)

Respondents from other countries than Nigeria expressed mixed views about the risk of drug resistance as a consequence of PDMC. Those concerned by resistance feared that prolonged exposure to malaria drugs, poor compliance and adherence to treatment, could result in selective pressure within the population and trigger drug resistance. Respondents from Malawi flagged that their country was shifting away from SP and AL to DHA-PQ for first line treatment of malaria because of emerging resistance to SP and AL. It will, therefore, not be possible to use DHA-PQ for PDMC as it is becoming their preferred drug for first-line treatment.

Survey participants who were less concerned by the potential emergence of drug resistance indicated that the target population for PDMC was too small to trigger resistance. Respondents from Senegal were the least concerned by this issue, and indicated that although the risk of resistance exists, they believed it could be managed and controlled through surveillance, protocols that are well designed and adhered to, and regular drug efficacy testing.

"We are not within the framework of a campaign where we distribute mass drugs to an entire population of children. [...] It is a distribution which obeys a precondition which is hospitalization! [...] But all in all, we cannot fail to do what is called pharmacovigilance for the molecules that we are going to use. We should at least be able to reinforce surveillance and vigilance." (Programme manager, Senegal) "I don't think the number of severe malaria cases being given chemoprophylaxis would significantly contribute to a rapid increase in drug resistance." (Implementing partner, Kenya)

Survey respondents made the following recommendations to prevent the emergence of drug resistance during PDMC implementation: a) Use different drugs for PDMC and treatment, and rotate them frequently. b) Develop strong behaviour change messaging to emphasize the importance of adherence and compliance. c) Regularly conduct drug efficacy and resistance testing. d) Increase usage monitoring. e) Ensure that health facilities and CHWs implement good follow-up practices and check that the treatment is administered correctly.

Discussion

This review investigated the perception of national malaria key opinion leaders and decision makers on PDMC, including participants from countries where PDMC was not undergoing pilot testing during the study period. Overall, all participants demonstrated a satisfactory level of comprehension regarding PDMC, even those coming from countries where the programme was not piloted. This positive outcome contrasts with a 2019 study, which revealed that key opinion leaders in Nigeria, Senegal, and Uganda possessed limited knowledge about PDMC and struggled to accurately describe the intervention at that time [23]. This increase in knowledge and understanding of PDMC can be attributed to several factors, including the updated WHO guidelines released in June 2022—shortly preceding the survey—and the dissemination of information through various clinical trials' publications and presentations. Moreover, key opinion leaders and decision-makers perceived PDMC as a beneficial intervention with the potential to positively impact the entire continuum of care, spanning from individual patients to the broader healthcare system. This positive perception from key decision-makers is a promising first step for the programme's adoption and scale-up.

Despite the generally good understanding of PDMC, some ambiguity surfaced regarding the intervention's target group. Many participants expressed uncertainty, with some intending to apply PDMC to patients hospitalized for severe malaria and severe anaemia, while others focused solely on severe anaemia cases. Since severe anaemia is a perceived consequence of severe malaria, some participants deemed PDMC suitable for patients with severe malaria. This raises potential challenges for PDMC adoption. The primary challenge lies in determining the right target for evidence generation. Key informants emphasized the necessity of generating sufficient evidence to support the adoption and scaling up of PDMC implementation. Without consensus on the target group, it becomes challenging to produce the required evidence for inclusion in treatment guidelines and accurately monitor intervention performance. Another challenge pertains to funding. The WHO recommendations specify that PDMC should be used in children under 5 years of age hospitalized with severe anaemia only [10]. Deviating from these recommendations by extending PDMC to severe malaria cases could jeopardize securing funding from donors. Participants from a recent stakeholder engagement meeting held by the PDMC Saves Lives consortium recommended expanding the target group to include children hospitalized with "severe anaemia or severe malaria" [12]. They also felt important to include cerebral malaria in the target group in order to not neglect this equally vulnerable group from the post discharge malaria chemoprevention as continuum of care. The consequences of these recommendations from a regulatory and funding perspectives remain to be seen.

Determining how to deliver PDMC is a pivotal question touching on various aspects of product adoption. Since PDMC is administered to severely ill patients, ensuring the timing and frequency of preventive treatment is crucial. Adherence emerged as a significant concern raised by survey participants. The two envisioned delivery mechanisms-facility-based and communitybased- come with concerns about treatment adherence. For facility-based delivery, concerns centered on caregivers not returning to the healthcare facility every month due to geographical distance and associated costs. Community-based delivery raised fears of mistakes in dosing or administration frequency by healthcare providers, potentially leading to incorrect treatment. While survey participants believed that community-based delivery would enhance adherence, citing proximity to patients and the simplicity of the procedure, potential challenges included the substantial training required for Community Health Workers (CHWs). This is consistent with a recent study indicating that community-based delivery of PDMC resulted in higher adherence than facilitybased delivery [17]. However, the amount and frequency of training must be considered, as training all CHWs at the national level could be more expensive than training health facility staff in delivering PDMC. In addition, in areas where cases of severe malaria and severe anaemia are not frequent, CHWs would require frequent refresher training to ensure that they maintain a sufficient level of knowledge about PDMC. These training considerations will have an impact on the cost-effectiveness of the intervention and need to be investigated further. It could be envisaged to have a hybrid approach were both facility and community-based deliveries is offered. Criteria such as robustness of the CHWs system, cost of training, distance from heath care facilities, will need to be taken into consideration when selecting where to set up a facility delivery or a community-based approach.

Choosing the appropriate drug for PDMC was another topic of discussion during the survey, constituting a critical aspect of the intervention. Several factors need consideration in this selection process. First, the growing

evidence of anti-malarial resistance prompted the use of different drugs for treatment and prevention. The three drugs that have been trialed for PDMC to date, namely SP, AL and DHA-PQ, all demonstrated efficacy in reducing mortality and readmissions during the intervention period [11, 13, 14]. Out of these, only AL and DHA-PQ are used in first-line treatment. The question arises whether it makes sense to use them for PDMC. The argument in favor is the small number of patients using PDMC, reducing the risk of resistance emergence. As the WHO guidelines do not provide recommendations on which drug to use for PDMC, it will be up to the countries to decide which drug class to use depending on their strategy to fight resistance to malaria drugs. Another consideration is the ease of training and supply chain management; if the drug selected for PDMC is the same as for treatment, training, procurement and distribution become simpler as dosing and administration methods are already known. This ties back to the earlier discussion on the delivery channel, especially if CHWs are involved, as using a familiar drug simplifies training and the need for refresher training.

Strengths and limitations

The main limitation of this study was the small number of participants and countries. Therefore, caution should be used when generalizing results of this subset of respondents to the entire malaria-endemic regions of SSA. However, this was mitigated by the fact that survey participants were selected for their knowledge and influential role in malaria management. In addition, not all subcategories were represented in each country, For example, no MoH representatives were interviewed in Kenya, and no policy makers in Senegal. This was largely due to the difficulty to schedule appointments with these representatives during the period allocated to the survey. Despite this limitation, the overall sample composition was well balanced, and no country-level analysis was performed. Absence of end users such as health care professionals, CHWs and caregivers, is a second limitation of the study. While the view of the end users is important to capture when considering the implementation of the intervention, the rationale for their exclusion was that their perceptions are better captured through feasibility studies, which was not the scope of this study. Lastly, the study relies on participants' self-reported familiarity and knowledge of PDMC which could introduce a recall bias. To address this limitation, a narrative was prepared to describe what PDMC was, and interviewers were instructed to use the showcard whenever they felt that survey participants did not have a clear understanding of PDMC. The information presented on the showcard could have influenced the perceptions and opinions expressed by those who read it.

Conclusions

This survey offers an updated view of the perception of key opinion leaders and decision-makers on PDMC as a way to prevent malaria in vulnerable children. Despite increased awareness and positive perception of the intervention, half of the participants were unfamiliar with the intervention. In addition, the study identified an ambiguity regarding the target population which could impact evidence generation and funding prospects. The study also highlighted the need to carefully investigate PDMC delivery mechanisms as it has a critical role on adherence and significant consequences on cost of implementation associated with training of healthcare providers and drug supply. Lastly, the emergence of anti-malarial drug resistance calls for a careful selection of the drug to be used for this intervention. Overall, the study provides valuable insights for policymakers navigating PDMC adoption, and stresses the need for country-specific cost effectiveness analysis to adapt the intervention to locally-relevant malaria endemicity and healthcare system context.

Abbreviations

| AL | Artemether-lumefantrine |
|--------|--|
| ANC | Ante natal care |
| CHWs | Community health workers |
| DHA-PQ | Dihydroartemisinin-piperaquine |
| EPI | Expanded programme on immunization |
| IPTp | Intermittent preventive treatment in pregnant women (IPTp) |
| МоН | Ministry of Health |
| NMCP | National Malaria Control Programme |
| NME/CP | National Malaria Elimination/Control Programme |
| PDMC | Post-discharge malaria chemoprevention |
| PMC | Perennial malaria chemoprevention |
| SMC | Seasonal malaria chemoprevention |
| SP | Sulfadoxime pyrimethamine |
| SSA | Sub-Saharan Africa |
| WHO | World Health Organization |

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12936-024-05100-z.

Additional file 1. Discussion guide, provided as Wordfile. Provides the list of questions that were used in the survey.

Additional file 2. Description of PDMC approach, provided as Wordfile. Showcard that was provided to survey participants not familiar with PDMC, as background information.

Acknowledgements

The authors thank Dalberg Research for their valuable contributions to the survey.

Author contributions

CA and HR were involved in the survey conceptualization, validation and analysis. CA supervised the field partner and prepared the original manuscript draft. CA and HR read and approved the final manuscript.

Funding

This research received no external funding.

Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The study did not involve patients and did not collect patient characteristics. The purpose of the study was to collect malaria key informants' professional opinions and insights and did not collect personal data or sensitive information. As such, there was no institutional review board involved in approving the research. Written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 31 July 2024 Accepted: 31 August 2024 Published online: 06 September 2024

References

- 1. Kiguli S, Maitland K, George EC, Olupot-Olupot P, Opoka RO, Engoru C, et al. Anaemia and blood transfusion in African children presenting to hospital with severe febrile illness. BMC Med. 2015;13:21.
- Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf S, Johns NE, Lozano R, A systematic analysis of global anemia burden from, et al. to 2010. Blood. 1990;123:615–24.
- Calis JCJ, Phiri KS, Faragher EB, Brabin B, Bates I, Cuevas LE, et al. Severe anemia in Malawian children. N Engl J Med. 2008;358:888–99.
- Maitland K, Olupot-Olupot P, Kiguli S, Chagaluka G, Alaroker F, Opoka RO, et al. Transfusion volume for children with severe anemia in Africa. N Engl J Med. 2019;381:420–31.
- Bojang K, Mb VH, Palmer A, Wa B, Jaffar S, Bm G. Predictors of mortality in Gambian children with severe malaria anaemia. Ann Trop Paediatr. 1997;17:355–9.
- Lackritz E, Hightower AW, Zucker JR, Ruebush TK, Onudi CO, Steketee RW, et al. Longitudinal evaluation of severely anemic children in Kenya. AIDS. 1997;11:1487–94.
- Obonyo C, Vulule J, Akhwale W, Grobbee DE. In-hospital morbidity and mortality due to severe malarial anemia in western Kenya. Am J Trop Med Hyg. 2007;77(6 Suppl):23–8.
- Phiri KS, Calis JCJ, Faragher B, Nkhoma E, Ng'oma K, Mangochi B, et al. Long term outcome of severe anaemia in Malawian children. PLoS ONE. 2008;3:e2903.
- Dhabangi A, Idro R, John CC, Dzik WH, Opoka RO, Ssenyonga R, et al. Risk factors for recurrent severe anemia among previously transfused children in Uganda: an age-matched case-control study. BMC Pediatr. 2019;19:27.
- WHO. Guidelines for malaria [Internet]. Geneva, World Health Organization; 2023. https://www.who.int/teams/global-malaria-programme/guide lines-for-malaria
- 11. Phiri KS, Esan M, Van Hensbroek MB, Khairallah C, Faragher B, ter Kuile FO. Intermittent preventive therapy for malaria with monthly artemether– lumefantrine for the post-discharge management of severe anaemia in children aged 4–59 months in southern Malawi: a multicentre, randomised, placebo-controlled trial. Lancet Infect Dis. 2012;12:191–200.
- Hill J, Accrombessi M, Briand V, Dhabangi A, Hill J, Hoyt J, et al. Implementation of post-discharge malaria chemoprevention (PDMC) in Benin, Kenya, Malawi, and Uganda: stakeholder engagement meeting report. Malar J. 2024;23:89.
- Bojang K, Milligan P, Conway DJ, Sisay-Joof F, Jallow M, Nwakanma D, et al. Prevention of the recurrence of anaemia in Gambian children following discharge from hospital. PLoS ONE. 2010;5: e11227.

- Kwambai TK, Dhabangi A, Idro R, Opoka RO, Watson V, Kariuki S, et al. Malaria chemoprevention in the postdischarge management of severe anemia. N Engl J Med. 2020;383:2242–54.
- Okell L, Kwambai TK, Dhabangi A, Khairallah C, Nkosi-Gondwe T, Winskill P, et al. Projected health impact of post-discharge malaria chemoprevention among children with severe malarial anaemia in Africa. Nat Commun. 2023;14:402.
- Svege S, Kaunda B, Robberstad B, Nkosi-Gondwe T, Phiri KS, Lange S. Postdischarge malaria chemoprevention (PMC) in Malawi: caregivers` acceptance and preferences with regard to delivery methods. BMC Health Serv Res. 2018;18:544.
- 17. Nkosi-Gondwe T, Robberstad B, Mukaka M, Idro R, Opoka RO, Banda S, et al. Adherence to community versus facility-based delivery of monthly malaria chemoprevention with dihydroartemisinin-piperaquine for the post-discharge management of severe anemia in Malawian children: a cluster randomized trial. PLoS ONE. 2021;16: e0255769.
- Pallas SW, Minhas D, Pérez-Escamilla R, Taylor LA, Curry L, Bradley EH. Community health workers in low- and middle-income countries: what do we know about scaling up and sustainability? Am J Public Health. 2013;103:e74-82.
- WHO. High burden to high impact: a targeted malaria response [Internet]. Geneva, World Health Organization, 2018. https://www.who.int/ publications/i/item/WHO-CDS-GMP-2018.25
- 20. Gondwe T, Robberstad B, Mukaka M, Lange S, Blomberg B, Phiri KS. Delivery strategies for malaria chemoprevention with monthly dihydroartemisinin-piperaquine for the post-discharge management of severe anaemia in children aged less than 5 years old in Malawi: a protocol for a cluster randomized trial. BMC Pediatr. 2018;18:238.
- Kwambai TK, Dhabangi A, Idro R, Opoka RO, Kariuki S, Samuels AM, et al. Malaria chemoprevention with monthly dihydroartemisinin-piperaquine for the post-discharge management of severe anaemia in children aged less than 5 years in Uganda and Kenya: study protocol for a multicentre, two-arm, randomised, placebo-controlled, superiority trial. Trials. 2018;19:610.
- Thomas JD, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med Res Methodol. 2008. https://doi. org/10.1186/1471-2288-8-45.
- 23. Audibert C, Tchouatieu AM. Perception of malaria chemoprevention interventions in infants and children in eight sub-Saharan African countries: an end user perspective study. Trop Med Infect Dis. 2021;6:75.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.