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Barriers to uptake and implementation of malaria chemoprevention in school-aged children: a stakeholder engagement meeting report

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Malaria is a leading cause of death in school-aged children in sub-Saharan Africa, and non-fatal chronic malaria infections are associated with anaemia, school absence and decreased learning, preventing children from reaching their full potential. Malaria chemoprevention has led to substantial reductions in malaria in younger children in sub-Saharan Africa. In 2022, the WHO updated its recommendations for chemoprevention to older, school-aged children where epidemiologically indicated. To date, there has been limited uptake of these policies which include both extending the age of seasonal malaria chemoprevention in seasonal transmission settings and providing intermittent preventive treatment to school-aged children in perennial transmission settings. In April 2024, a stakeholder meeting was convened in Kigali, Rwanda, to analyse barriers to implementation of malaria chemoprevention targeting school-aged children. Key evidence gaps were identified and needs for coordination and advocacy were highlighted.

KEYWORDS

malaria, school - aged children, transmission, education, chemoprevention, intermittent preventive treatment

Background

Despite widespread implementation of malaria control interventions over the last several decades, progress towards malaria elimination has stalled. The burden of malaria remains high in areas of sub-Saharan Africa, and additional strategies are required to strengthen malaria control (1). While the majority of malaria related mortality occurs in young children, the burden of malaria in older, school-aged children (5–15 years old) is increasingly recognized, negatively impacting children's health and educational attainment, but also perpetuating malaria transmission within communities and threatening malaria elimination goals (1–3).

Malaria, the disease resulting from infection with *Plasmodium* parasites, may manifest as severe disease leading to malaria-related mortality, uncomplicated clinical malaria prompting outpatient treatment, or chronic, sub-clinical infections (4, 5). Among school-aged children in Sub-Saharan Africa, malaria is the leading cause of death in (6). In addition to loss of life, frequent episodes of uncomplicated clinical malaria in this age group are associated with anaemia and school absences contributing to negative impacts on education, as well as increased caring duties for family members and additional costs to health systems (7, 8). Chronic, sub-clinical infections are the most common manifestation of malaria in school-aged children, with community surveys in high burden countries revealing that more than 40% of 'asymptomatic' school-aged children are infected with malaria parasites (9–12). In fact across the region, prevalence of infection is higher in school-aged children compared to younger children and adults group (9, 10, 13–16). With regard to the health and education of school-aged children themselves, these chronic infections are associated with anaemia, decreased cognitive function, and poor educational outcomes (4, 17–

21). This constraint on children's education ultimately limits them from reaching their full potential and decreases human capital (22). Furthermore, school-aged children have been identified as a primary reservoir for community transmission, contributing to continued risk of infection and mortality in other vulnerable groups (23–26).

Chemoprevention, which is the routine administration of antimalarial drugs at regular intervals to both clear existing infections and prevent new ones, has been a long-standing tool for malaria control and is proposed as a strategy to reduce the burden of malaria in school-aged children 5–15 year olds. First adopted by the World Health Organization (WHO) in 2002 as supplementary antenatal care to decrease adverse effects of malaria in pregnancy, the use of chemoprevention was then expanded to protect younger children through intermittent preventive treatment in infants (IPTi) – now termed perennial malaria chemoprevention (PMC), and seasonal malaria chemoprevention (SMC). Since its adoption as policy in 2012, SMC, which targets children 3–59 months old, now reaches an estimated 53 million children annually and has substantially reduced malaria related morbidity and mortality in younger children (1, 27, 28). In 2022, the WHO updated the guidelines for malaria chemoprevention strategies to broaden their use and support more country-driven, tailored approaches to malaria control (29). These recommendations expanded the age range for provision for chemoprevention through either intermittent preventative treatment of school-aged children (IPTsc) or extending the target age of SMC (ext-age SMC) to older children where epidemiologically indicated.

Since the expansion of the WHO recommendations, however, implementation of chemoprevention in older children has been limited. This slow introduction may be due to many factors. Under the current Global Malaria Technical Strategy, National Malaria Control/Elimination Programs (NMCPs) are supported to develop

bespoke approaches to optimize malaria control for their country utilizing national burden stratification and sub-national tailoring of intervention mixes constrained by domestic and donor funding (30, 31). In this context, we sought to bring together key stakeholders from NMCPs, program implementation partners, and researchers in malaria, school health, and education to review the status of malaria chemoprevention targeting school-aged children in sub-Saharan Africa.

Stakeholder meeting proceedings

A group of stakeholders and experts representing eight sub-Saharan African countries and 30 organisations met in Kigali, Rwanda on the sidelines of the Multilateral Initiative on Malaria Conference (MIM) in April 2024 to:

1. Determine the barriers faced by interested National Malaria Control/Elimination Programmes (NMCPs) in implementing IPTsc or ext-age SMC and identify potential solutions.
2. Identify knowledge and research gaps which remain to support program development and prioritization.
3. Enhance knowledge exchange between country programs, implementing partners, and researchers.

Lauren Cohee (LSTM, UK) and Chris Drakeley (LSHTM, UK) began the meeting by providing an overview of malaria in school-aged children, highlighting, as described above, the direct impacts malaria on the health of school-aged children as well as the indirect impacts of malaria in school-aged children on education of school-aged children themselves, community level malaria transmission, and, ultimately human capital.

Suzanne van Hulle (CRS, US/Switzerland) reviewed the 2022 WHO updated guidelines for malaria chemoprevention and

summarised key strategy considerations for both IPTsc and ext-age SMC. The similarities and differences between these two approaches to malaria chemoprevention are summarized in Table 1. The key difference in the approaches is that ext-age SMC applies in areas where SMC is already being conducted. If programs are developed to target school-aged children in areas *without* SMC in younger children, the approach is defined as IPTsc.

Key considerations for both strategies fall into four core categories: prioritization, timing, delivery point, and drug selection (Figure 1).

Local epidemiology, intervention layering, cost and budget constraints inform prioritisation of chemoprevention for school-aged children. In addition, WHO guidelines emphasize that implementation should not compromise interventions targeting younger children who are at highest risk of severe malaria. Optimal delivery strategy, including both delivery point and timing, should be guided by alignment of the school calendar and the seasonality of local malaria transmission, as well as social acceptability and operational feasibility.

For next-age SMC, guidance for drug selection, dosing schedule, and frequency is based on general SMC guidelines. There is limited data on SMC drug regimens other than sulfadoxine-pyrimethamine + amodiaquine (SPAQ), which is widely used across West Africa. Based on the half-life of SPAQ, SMC is recommended every 28 days, with current evidence supporting 3–4 cycles in areas with short transmission seasons, and up to six cycles in settings with longer transmission seasons. In contrast to SMC, no guidance on drug choice for IPTsc is provided. Over 20 years of IPTsc trials, multiple drug regimens have been evaluated, including SPAQ, SP + piperaquine, SP + artesunate, artesunate + amodiaquine and dihydroartemisinin-piperaquine (DP) (32, 33). The IPTsc dosing schedule will depend on the half-life of the drug used and should be informed by local malaria epidemiology with timing to ensure protection at the period of greatest malaria risk (34, 35). For both approaches, it is recommended that first- and second-line malaria treatments are avoided, if safe and effective alternatives are available. Special consideration should be given to treatment of girls post menarche, as data on the safety, efficacy and pharmacokinetics of most antimalarial agents in the first trimester of pregnancy is limited; and potential interactions with other drugs delivered through school-health, or other child-health programmes should be examined (36, 37). All of these considerations present a significant challenge to programs aiming to select the appropriate regimen.

Mahamoudou Touré (University of Sciences, Techniques, and Technologies of Bamako, Mali), Geoffrey Makenga (National Institute for Medical Research, Tanzania; University of Antwerp, Belgium), and Lauren Cohee (LSTM, UK) presented progress towards and outcomes of recent, ongoing and planned trials in 5 countries, summarised in Table 2.

Defining barriers, knowledge gaps and research priorities

Following introductory presentations and review of recent studies, meeting attendees split into breakout groups to discuss barriers, knowledge gaps and pathways forward to enable effective

TABLE 1 Definition, setting and target audience of Intermittent Preventive Treatment of malaria in school-aged children (IPTsc) and extended-age Seasonal Malaria Chemoprevention (ext-age SMC), adapted from WHO guidelines and meeting presentation.

Definition	IPTsc		ext-age SMC
What?	Preventative chemotherapy is the use of medicines, either alone or in combination, to prevent malaria infection and its consequences. It requires giving a full treatment course of an antimalarial medicine to vulnerable populations at designated time points during the period of greatest malarial risk, regardless of whether the recipient is infected.		
Where?	Malaria-endemic settings with moderate to high perennial or seasonal transmission		Areas of seasonal transmission
Who?	Age groups* should be identified using local data on the age distribution of malaria admissions and severe disease.		
How?	May be delivered via fixed point (e.g. school-based) or community-based (e.g. door-to-door)		

*While ext-age SMC has typically be considered up to 10 years of age and IPTsc has generally referred to 5–15 year olds, the current guidelines do not stipulate age restrictions and advise use of local data to determine the target population.

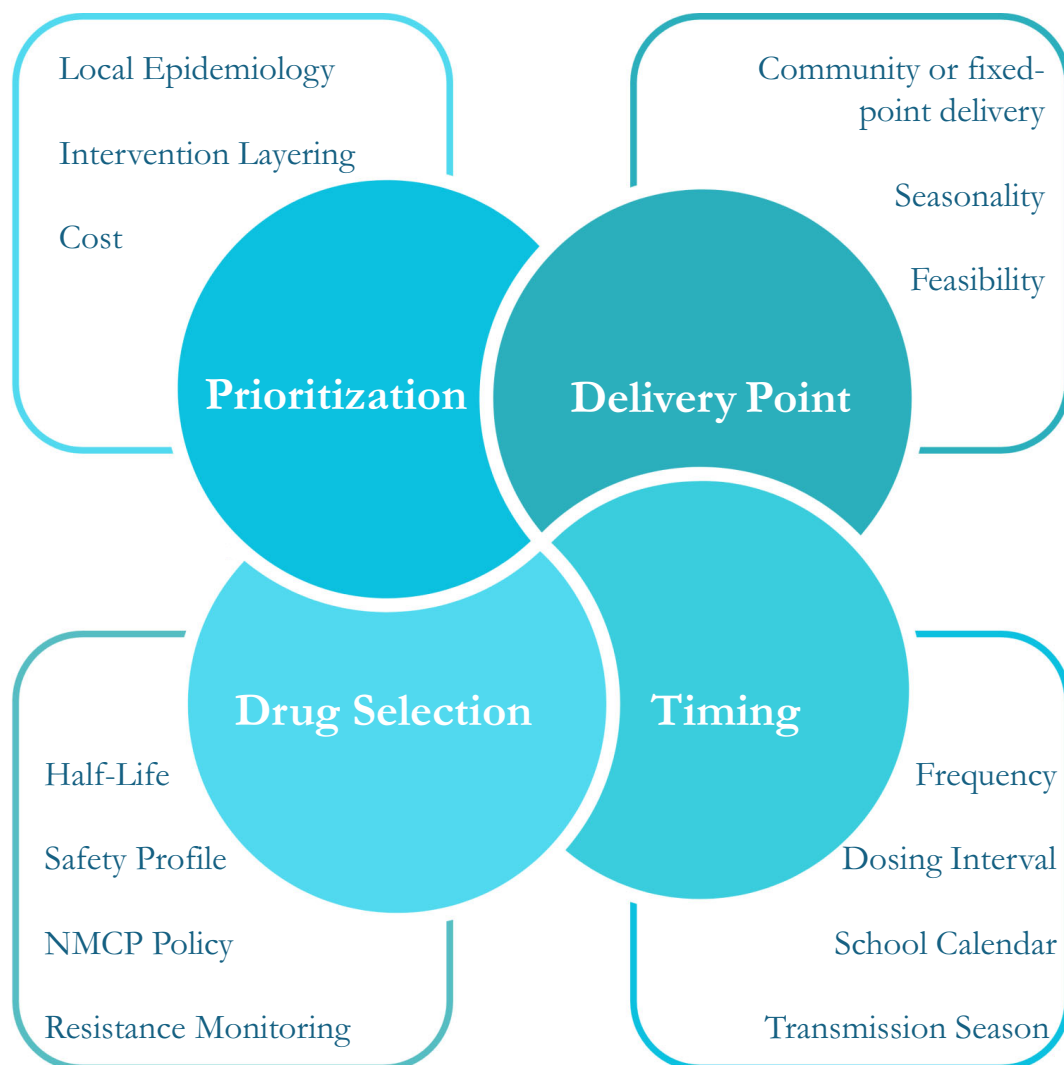


FIGURE 1
Core decision-making components for chemoprevention in school-aged children.

implementation of chemoprevention in school-aged children. Each group then fed back to the larger group for discussion and consensus building. The main themes that arose are summarized below and in [Figure 2](#).

Generating additional evidence of the burden of malaria in school-aged children and the direct and indirect impacts of chemoprevention

Access to more granular, age-disaggregated data is required to determine when/where countries should prioritize targeting school-aged children and for monitoring the impact of programs post-implementation

The WHO guidelines emphasise “using local data on the age distribution of malaria admissions and severe disease” to determine

when chemoprevention should target older children (29). However, data on the relative burden of malaria in school-aged children is not widely available, as routine surveillance reporting on hospitalisations, severe and uncomplicated malaria is often dichotomized as “under 5 years old” or “over 5 years old”. Consistent access to disaggregated data will also be important for monitoring the impact of chemoprevention programs targeting school-aged children.

Further exploration of the indirect benefits of chemoprevention in school-aged children on education and community-level malaria transmission could reveal substantial dividends

School-aged children have been shown to be the largest infectious reservoir in many settings. The community protective effects of ext-age SMC have already been demonstrated in multiple sites in West Africa (40, 41) and dynamic transmission models suggest IPTsc would reduce clinical malaria in younger children and adults across multiple transmission settings (42). Additional

TABLE 2 Summary of trials which are planned, ongoing, or completed after the most recent systematic review of preventive treatment targeting school-aged children. (Cohee et al., 2020).

Country	Intervention	Study type	Study population	Drug	Frequency	Outcomes			Status and source
						Malaria	Education	Acceptance	
Mali	Ext-age SMC	Pilot non- inferiority randomised clinical trial	Children >3 months and <9 years	SP+AQ vs DP	4 monthly rounds during transmission season	Yes	No	No	Complete Mali ICEMR
Mali	Ext-age SMC	District-wide non-inferiority randomised clinical trial	Children >3 months and <9 years	SP+AQ vs DP	4 monthly rounds during transmission season	Yes	No	No	Complete - Mali ICEMR (protocol published (38))
Burkina Faso	IPTsc	Village-level cluster randomised controlled trial	Children >5 and <15 years	SP+AQ vs DP IVM vs Standard of Care	4 monthly rounds during transmission season	Yes	No	Yes	Ongoing - MoH, MoE Malaria Consortium (39)
Nigeria	IPTsc	Individually randomised controlled trial	Children >5 and <12 years	SP AQ vs DP vs Standard of Care	Seasonal: SP+AQ: every 4 weeks for 4 rounds DP: every 8 weeks for 2 rounds Perennial: SP+AQ: every 4 weeks for 6 rounds DP: every 8 weeks for 4 rounds	Yes	Yes	No	On-going- Nigeria NMEP, Fosun Pharmaceuticals. Evidence Action
Tanzania	IPTsc	Clinical trial	Children >5 and <15 years	DP and ASAQ	3 Rounds, 4 months apart (once per school term)	Yes	Yes	No	Complete, published (Makenga Baraka, et al., 2023) (32)
Tanzania	IPTsc	Implementation study- school- level cluster randomised controlled trial	Children >5 and <15 years	DP	3 Rounds, 4 months apart	Yes	Yes	Yes	Complete. Methods published (Makenga Seth, et al., 2023) (37)
Malawi	IPTsc	Individually randomized, controlled trial	Children in primary grades 1-8	DP vs SP+CQ (females >10 years old received CQ only) vs Standard of Care	3 rounds, every 6 weeks, during transmission season	Yes	Yes	No	Complete, unpublished Clinicaltrials.gov NCT05980156
Malawi	IPTsc	Household randomized, controlled trial	Children in primary grades 1-8	DP vs SP+AQ (females >=13	3 rounds, every 6 weeks, during	Yes	Yes	No	On-going Clinicaltrials.gov NCT05980156

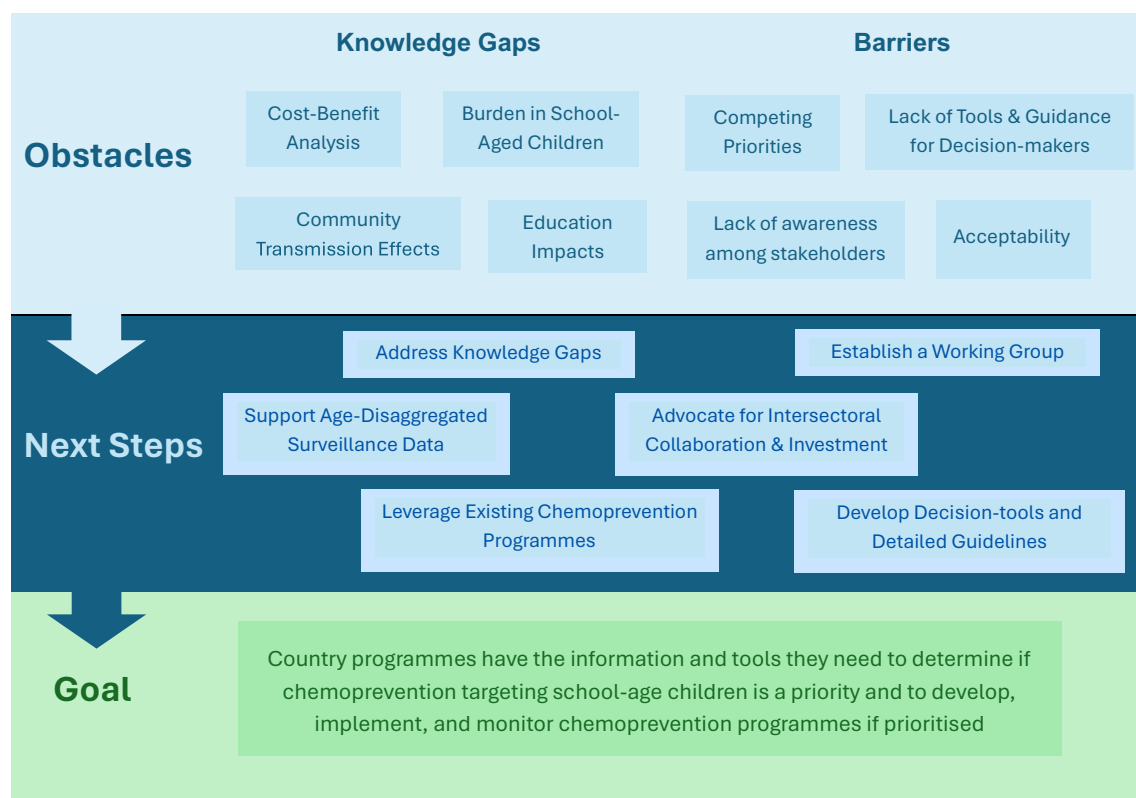


FIGURE 2
Summary of meeting findings.

studies in diverse transmission settings would further characterise the extent of transmission reduction potential. Similarly, previously demonstrated positive effects on cognitive function, learning, and educational attainment warrant further evaluation.

Common metrics across diverse study sites could clarify efficacy and strengthen evidence based for policy recommendations

There is some consensus on metrics for malaria-related individual-level outcome measures in studies evaluating impact chemoprevention in school-aged children, e.g. prevalence of infection, anaemia, and incidence of clinical malaria. No consensus exists on metrics for measuring impact on transmission or education. Harmonized metrics for these outcomes is critical in building the evidence base for these indirect, but crucial, outcomes. While these outcomes would be most rigorously evaluated in cluster randomised trials, implementation and pilot studies should not be missed as opportunities to generate evidence. Agreement on optimal study designs for these settings is needed, with input from key decision-makers and funders on outcomes of highest priority. For example, impact on cognition, learning, and education are often measured as secondary outcomes using heterogeneous metrics that limit evidence synthesis. Engaging with colleagues in the education sector to identify meaningful metrics and measuring them may be a key advocacy tool influential in garnering investment from education and broader development sectors.

Improve understanding of the cost-effectiveness of chemoprevention in school-aged children

Limited evidence on the cost-effectiveness and broader economic impacts of chemoprevention targeting school-aged children is a barrier to funding for and prioritization of IPTsc and ext-age SMC

While some costing and cost-effectiveness evidence is available from trials in Kenya and Mali, variations on drug choice, delivery mode, expected coverage and frequency of administration within each country make these data difficult to generalize (43, 44). Additionally, the potential indirect benefits for communities through transmission reduction and improved education are important factors in cost-benefit evaluations and budgetary decision making. For example, by reducing clinical incidence, chemoprevention decreases health system costs in terms of case-management costs and burden on health facilities. Chemoprevention can also better target difficult-to-reach populations, and directly observed therapy improves adherence and may reduce risk of antimalarial resistance. Improved education outcomes and reduced burden on caregivers can also increase individual earning potential, with lifelong benefits (45). It is important that decision-makers and funders consider the myriad knock-on savings benefits of chemoprevention when configuring programme budgets. Further research applying appropriate cost-

evaluation methods is needed to support decision-makers to present sufficient justification to prioritise school-aged children within constrained budgets.

Combining malaria chemoprevention with other interventions targeting school-aged children could improve cost efficiency and sustainability

This could include malaria-specific approaches, such as new vector control tools and vaccine strategies in the longer-term. Integration with other established health interventions which target school-aged, such as nutrition, deworming and human papillomavirus (HPV) vaccination programs, may also increase uptake and efficiency.

Barriers and knowledge gaps for effective implementation

Intersectoral collaboration and investment are needed to ensure success in targeting school-aged children

Integration with school systems, Ministries of Education, and national and sub-national school health programs is imperative particularly when schools serve as the primary delivery channel. Similarly, for community-based delivery, integration with community health worker networks, routine adolescent health services, and surveillance systems is important for feasibility, acceptability, and uptake.

Choice of anti-malarial drugs for chemoprevention in school-aged children requires careful consideration

Drug selection for IPTsc or ext-age SMC should be in alignment with national drug policies and resistance mitigation strategies, as well as safe, affordable, and acceptable for the target population. All the identified on-going or planned implementation, pilots, and research studies discussed in the meeting will use either dihydroartemisinin-piperaquine (DP) or sulfadoxine-pyrimethamine plus amodiaquine (SPAQ). These drugs have demonstrated protective efficacy in reducing clinical incidence and parasite carriage in chemoprevention in school-aged children. Addition of single-dose primaquine for gametocytocidal action may be of further interest particular when considering application of chemoprevention targeting school-aged children as a population-level transmission reduction strategy or as an approach to mitigate the potential spread of drug resistant parasites.

In the context of the emergence of artemisinin resistance in Africa and existing wide-spread antifolate resistance, the degree of drug resistance in different contexts as well as the impact of chemoprevention as a potential driver of drug resistance should be considered and monitored. Additional consideration should be taken regarding the safety of drugs administered to adolescents who have begun menstruation and may become pregnant. However, high-risk pregnant adolescents are also a group that may benefit from interventions which clear parasites and decrease anaemia pre-pregnancy. Future drug candidates specifically for use in chemoprevention are also in development (46).

Funding structures and limited resources can hinder introduction of new interventions

Malaria control is a complex and costly endeavour, with many factors influencing the allocation of limited funds. While there is considerable interest among national malaria programs in addressing the burden of malaria in school-aged children, resource allocation remains a critical barrier as the majority of malaria funding comes from external donors, who are currently limited in the ability to meet the funding needs for interventions targeting younger children and malaria case management. Thus, further evidence is needed on the benefits and cost-effectiveness of targeting this age group among competing priorities. In the absence of additional funds, funders and national decision-makers may be limited to budget restructuring, particularly cost-shifting from treatment to prevention. Stronger age-disaggregated surveillance, quantification of community transmission reduction, and evidence of cost-savings or cost-neutrality of chemoprevention are needed to justify allocation of limited funds for school-aged children. Equally, funders must be open to act swiftly in response to growing evidence.

Decision-tools and implementation guidelines are needed to support countries as approaches to target school-aged children with chemoprevention are not 'one-size fits all' and require context specific design

Introducing chemoprevention in school-aged children requires consideration of several factors, including timing and frequency of drug administration according to transmission seasons and school calendars, drug choice and alignment with national treatment policies, and combination with other existing interventions (Figure 1). Data gaps in surveillance, delivery cost, projected implementation coverage and performance prevent effective decision-making. Tools and implementation guidance for ext-age SMC are/can be adapted from general guidance for SMC. However, no tools or additional guidance for implementation is currently available for IPTsc. Additional support is needed for implementation and evaluation of school-based delivery in particular.

Attendees also highlighted the vital role of community engagement and social science studies to assess, understand and adapt implementation strategies to different settings. Attention will also need to be paid to reaching out-of-school children when school-based delivery is used.

Looking forward, attendees supported the following next steps:

1. Utilise programmatic implementation, pilot studies, and, if required, clinical trials to generate knowledge in the areas outlined above (indirect benefits on transmission and education, feasibility, acceptability, and cost-benefits). Develop replicable evaluation designs with indicators that support quality impact monitoring and evidence generation to facilitate data sharing across sites.
2. Establish a Working Group to enhance knowledge exchange, amplify existing work, develop consensus on indicators and metrics, and streamline information sharing channels between researchers, funders, and key decision-makers.

- Advocate at all levels to: communicate the burden of malaria in school-aged children to make the case for investment; enhance collaboration with the education sector, including empowering “champions” in health and education sectors with messaging on positive school outcomes; work with decision-makers to ensure malaria in school-aged children is on the agenda; and highlight the role of interventions targeting school-aged children to accelerate elimination goals.

Conclusions and outcomes

Malaria infection in school-aged children is an important but perhaps under-recognized challenge to malaria control. Program managers, policymakers and researchers in attendance agreed that when combined with accurate age-stratified data on the local burden of disease, the current evidence on the direct impacts of chemoprevention on malaria prevalence and death in school-aged children may be sufficiently compelling for implementation or programmatic consideration. Attendees generally agreed that quantifying and communicating the indirect benefits of chemoprevention on education and community transmission reduction could also heavily influence prioritization. Amidst competing priorities for malaria control, the education sector and school health specialists must play a leading role in advocating for interventions in school-aged children. Vitality, the evidence to support uptake must be compelling to funders and budget-holders for malaria control programmes. Additional tools and more detailed guidance for developing programs, supporting implementation, and evaluating programs are critical for progress. The meeting’s momentum and the report’s outlined next steps are expected to help overcome obstacles and promote broader adoption of chemoprevention in school-aged children. Although delivery of chemoprevention to school-aged children presents challenges, the potential benefits to individual children and communities are likely to be substantial.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

CMo: Writing – original draft, Writing – review & editing, Visualization. IB: Writing – original draft, Writing – review &

editing, Visualization. JA: Writing – review & editing. VB: Writing – review & editing. AB: Writing – review & editing. TB: Writing – review & editing. AC: Writing – review & editing. FC: Writing – review & editing. RC: Writing – review & editing. SC: Writing – review & editing. KC: Writing – review & editing. SD: Writing – review & editing. OD: Writing – review & editing. SD: Writing – review & editing. JG: Writing – review & editing. AL: Writing – review & editing. CMa: Writing – review & editing. GM: Writing – review & editing. OM: Writing – review & editing. IM: Writing – review & editing. JN: Writing – review & editing. NO: Writing – review & editing. MP: Writing – review & editing. AS: Writing – review & editing. SS: Writing – review & editing. AT: Writing – review & editing. AT: Writing – review & editing. MT: Writing – review & editing. JV: Writing – review & editing. SV: Writing – review & editing. EW: Writing – review & editing. CD: Conceptualization, Funding acquisition, Writing – original draft, Writing – review & editing. LC: Conceptualization, Funding acquisition, Writing – original draft, Writing – review & editing. DH: Conceptualization, Writing – review & editing. JBY: Conceptualization, Writing – review & editing.

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