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Review

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Global Health Initiatives to Reduce Malaria Morbidity in School-aged Children

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ABSTRACT

Background: To review global initiatives to reduce the burden of disease from malaria on school-aged children. The focus is on approaches with potential to reduce mortality and morbidity, improve the health and ability of children to attend school, avoid malaria impacting their potential academic achievement, and minimize the risk of short- and long-term cognitive impairment.

Methods: Literature searches using defined terms related to malaria and education, and a scoping review of the key literature selected, to provide a narrative summary of the challenges and potential solutions identified.

Results: There is robust evidence that school-aged children are particularly vulnerable to malaria, and need special measures to protect them; calls are widespread for better diagnostic approaches and program innovation because of current levels of malaria-related morbidity and mortality. School-based programs that educate children broadly on causation, prevention and care required can improve access to timely diagnosis and treatment; however, currently national malaria control interventions do not specifically target school-age children. The literature describes intervention strategies that include seasonal chemoprophylaxis, intermittent protective treatment and antimalarial therapy linked to mass drug administration for neglected tropical diseases. Recently, a community participatory intervention model based on WHO-endorsed diagnostic and treatment principles has taught teachers to screen all children sick at school using rapid point-of-care diagnostic testing and treat promptly with Artemisinin combination therapy; morbidity and absenteeism are significantly reduced. There is no consensus on the optimal intervention strategy; approaches will need to vary, but evidence of 'what works and why' exists to guide constructive implementation measures in each endemic region.

Conclusion: Malaria exemplifies how health inequity negatively impacts a child's health and ability to benefit from education, yet simple and effective school-based approaches exist that positively impact morbidity, provide access to WHO-endorsed diagnosis and treatment, are applicable worldwide and can increase the capacity of children to learn.

Keywords: Absenteeism; Artemisinin Combination Therapy; Cognitive Impairment; Intermittent Protective Treatment; Rapid Diagnostic Testing; Seasonal Malaria Chemoprophylaxis; Teachers

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1. Introduction

Globally, malaria kills more than 1 million people a year, and perhaps closer to 3 million when the role of malaria in deaths related to other disease is included. Much of the mortality in endemic areas is concentrated among children under the age of five years; the number between 5 and 14 years (school-aged children) who die from malaria is not known, but in many low- and middle-income countries (LMICs) worldwide malaria is reported to be the main reason a school-aged child will die; in parallel, an important measure of the morbidity malaria causes is the fact that infection is cited as the principal reason why a child will be absent from school.

Teachers recognize the negative impact of malaria on pupil's health and the adverse effects of infection on their capacity to learn. The duration of malaria-related absence, frequency of absence due to repeated infection, residual malaise from sub-optimal treatment and temporary or permanent neurological complications of falciparum malaria are all known to compromise a child's potential to learn, yet school-age children have attracted relatively little attention as a group in need of special measures to protect them against malaria.

There are now widespread calls for innovation and implementation of programs to address malaria mortality and morbidity in school-age children.

2. Method

Searches were undertaken of the published literature on malaria in children using the following search terms, singly, or in combination: malaria, children, school, school children, school-based, teachers, teacher-based, rapid diagnostic testing (RDT), artemisinin combination therapy (ACT), chemoprevention, Africa, sub-Saharan Africa. Search results were supplemented by papers identified from the reference lists published in these papers and material familiar to the author. Review was limited to the English language and focused predominantly on Africa and research published in the last 20 years, except where prior work had historic relevance.

3. Background

"School-age children have attracted relatively little attention as a group in need of special measures to protect them against malaria."
(Nankabirwa et al., 2014a)

New and better diagnostic approaches are required to address malaria in children because of the current levels of morbidity and mortality (Bell et al., 2016). Schools present an obvious and logical opportunity to improve the access of school children to timely diagnosis and treatment, (Temperley et al., 2008; Macnab et al., 2016), however, currently national malaria control interventions do not specifically target school-age children despite increasing evidence that this age group bears the highest burden of infection (Cohee et al., 2018). Awareness of the impact of malaria among school-age children has stimulated investigation into interventions that can be delivered through schools, but currently there remains no consensus as to the optimal intervention strategy (Drake et al., 2011).

Despite being preventable, detectable and curable, malaria remains one of the main causes of mortality due to infectious disease (World Health Organization, 2015). In school-aged children the burden of disease and prevalence of infection varies widely depending on the level of transmission, setting and season, but, 7 out of 10 in Côte d'Ivoire were found to be infected with *Plasmodium falciparum* in a national, cross-sectional study (Houngbedji et al., 2015); 14–64% in Uganda are parasitemic at any one time (Nankabirwa et al., 2014a), and in Mali, malaria accounts for 36% of medical consultations in school children during peak transmission season (Barger et al., 2009). There is broad agreement that school-age children represent an underappreciated reservoir of malaria infection, have less exposure to antimalarial interventions, and malaria control and elimination strategies need to expand to include this age group (Walldorf et al., 2015).

Delay in the treatment of fever is a potent obstacle to the goal of achieving a reduction in malaria mortality (White, 2005). Failure to obtain WHO recommended diagnosis and therapy leads to poor disease management, which in turn contributes to a cycle of poverty in affected communities (Amexo et al., 2004; Sachs and Malaney, 2002). Lack of access to early and accurate diagnosis is common; studies indicate that in sub-Saharan Africa <50% of sick, febrile children receive artemisinin combination therapy (ACT) within 24 hours (Macnab et al., 2016; Simba et al., 2010; Tipke et al., 2009) Barriers to care include those of (Mutabingwa, 2005; Rutebemberwa et al., 2009):

- access (distance to a clinic and a lack of parental awareness of need)
- cost (of prescribed medication, time away from livelihood, and transport)
- uncertain availability of diagnostics and therapy at government clinics
- inadequate numbers of skilled staff
- variations in the quality of health care services and prescribing habits
- preference for traditional practices or use of unreliable treatment sources, and
- school-age children being brought less often for treatment compared to younger children

In 2014 a structured review summarized the negative impact of malaria on pupil's health and the adverse effects of infection on their ability to learn (Nankabirwa et al., 2014a); School teachers recognize these problems as they see first-hand the impact on school-age children's performance. They know infection robs children of the ability to attend school, that sub-optimal treatment leaves residual malaise which negatively impacts the capacity to be fully present in class, and repeated infection can permanently compromise a child's academic potential due to neurological complications (Fernando et al., 2010; Holding and Snow, 2001; Kihara et al., 2006; Jukes et al., 2006). The review emphasizes that school children need special measures to protect them against malaria, with more program implementation and innovative measures both being important. Ongoing research and evaluation are also called for to build the evidence base of 'what works and why,' and where such interventions are most effective.

A factor relevant to school-based health promotion in most LMICs, is that teachers generally send home children found to be sick at school (Macnab et al., 2014b). This devolves key care decisions to parents, which is problematic in malaria endemic areas, as many families lack the knowledge and/or resources necessary to provide what a child with probable malaria requires. This situation often contributes to morbidity, as in many cases appropriate diagnosis and treatment do not occur, or at best are delayed (Rutebemberwa et al., 2009).

The World Health Organization (WHO) advocates early, accurate diagnosis of malaria and prompt, effective and affordable treatment within 24 hours of the onset of illness (World Health Organization, 2015). Validated measures to do this exist, but in most LMICs the health resources necessary are limited, and are especially scarce in rural and low resource communities. The fact that malaria symptoms are not specific is an additional factor, as a reliable diagnosis cannot be made based on history and examination alone. Even using a WHO-derived diagnostic algorithm designed for Community Health Workers (World Health Organization, 1992), trained teachers in Ghana lacked the ability to match all presumptive malaria to the case definition (Afenyadu et al., 2005). This difficulty with diagnosing malaria on clinical grounds, also contributes to morbidity and mortality. Hence, simple, accurate and inexpensive diagnostic tools wider availability of effective therapy and health education are needed to reduce the impact of malaria on children.

Malaria education and health promotion initiatives centered on schools are an example of the type of innovative intervention called for by the WHO Commission on Social Determinants of Health to promote health behaviors and empower young people to take control of their lives (WHO Commission on Social Determinants of Health and World Health Organization, 2008). Such 'task shifting' to school-based programs can also increase provision of other essential health services (Agyepong et al., 2017). Robust, successful, valuable and cost-effective teacher-administered health programs in schools in LMICs include provision of intermittent anti-malarial therapy in Kenya (Temperley et al., 2008; Okello et al., 2012) prophylactic chloroquine in Sri Lanka (Fernando et al., 2006), and nationwide anti-helminth treatment in Uganda, and in Ghana (Brooker et al., 2008; Opoku et al., 2016). Cost-benefit analysis shows that health program delivery costs can be reduced by having teachers implement such programs (Drake et al., 2011; Laxminarayan et al., 2006).

4. Burden of Disease in School-age Children

While the overall incidence and number of deaths from malaria are decreasing worldwide the disease is still a major cause of mortality and morbidity among children (World Health Organization, 2015). **Mortality:** Fifty percent of deaths in school-aged children (defined as children aged between 5 and 14 years) are estimated to be due to malaria in Africa (Nankabirwa et al., 2014a). Cerebral malaria, (defined as: severe *P. falciparum* malaria presenting with neurological symptoms, including coma (Glasgow coma scale <11, or a Blantyre coma scale <3), or with coma that lasts >30 minutes after a seizure), affects more than half a million children per year in Africa, and kills between 10-40% of those infected (Holding and Snow, 2001). Poor health, poverty, lack of knowledge at a community level and limited access to care are contributory factors that increase a child's risk (Houngbedji et al., 2015; Mutabingwa, 2005). **Morbidity:** Studies in Africa and Thailand indicate that malaria causes 5-8% of all school absenteeism. Reports from Kenya indicate primary school students miss 11% of school days per year because of malaria, and secondary students can miss 4.3% of school days (Leighton and Foster, 1993). Such data equate with malaria being the cause of approximately 50% of all preventable absenteeism (Fernando et al., 2003b). Hence, reducing morbidity offers real potential for school children to gain increased educational benefits just from improved attendance.

However, the adverse effects on schooling clearly go far beyond compromised attendance. Even an attack of uncomplicated malaria can cause significant short-term impairment of cognitive performance; the impairment a child experiences often persists for around two weeks; and, adverse effects appear to be cumulative with repeated attacks (Kihara et al., 2006). In addition, where the principal infecting agent is *P. falciparum*, infection can be associated with permanent loss of cognitive and fine motor function from complications, especially where diagnosis is delayed and/or treatment is sub-optimal (Boivin et al., 2007; Fernando et al., 2010; Birbeck et al., 2010; Thuilliez et al., 2010). In the Brazilian Amazon (where infection is predominantly with *P. vivax*) multivariate analysis indicates that presenting with at least one episode of malaria independently predicts a poor performance at school (Vitor-Silva et al., 2009). In Asian studies in low transmission areas, most indices of performance tested at school entry in a cross-sectional study were poorer as the number of malaria infections experienced by the child increased (Fernando et al., 2003a); school performance of 6-14 year old children was related to the number of previous episodes of malaria; acute uncomplicated attacks caused short term learning difficulty for a week or more, and the effects were compounded by subsequent attacks. Thus, the combined effects of absence, sub-optimal convalescent health and long-term neurological compromise can adversely affect performance in class and pass rates, lead to the need for a child to repeat grades, and even cause children to drop out of school altogether.

The exact mechanisms causing long-term detriment to cognitive development and learning ability are debated. There is a clear relationship between infection intensity and the magnitude of the adverse cognitive effect (i.e. the higher the parasitemia, the higher the impact on cognitive score). Thuilliez et al. (2010) provide an excellent schematic that illustrates the probable effects and pathways depending on *falciparum* and *vivax* malaria.

Those children who survive 'cerebral' malaria frequently show clear evidence of neurological sequelae, including impaired ability to carry out executive functions (e.g. planning, initiating and executing executive tasks), and behavioral disorders that compromise their ability to engage fully in class. Kenyan school children hospitalized for cerebral malaria were 4.5 times more likely to have mild-to-severe learning difficulties 3-4 years later, even though half of them had no neurological problems at the time of admission (Holding and Snow, 2001). The risk of impaired intellectual function is increased where seizures accompany clinical malaria.

Thus, prolonged, severe and repeated illness can reduce both the opportunity and the ability of a school-age child to learn. Consequently, there is great potential worldwide for health and educational benefits to be accrued where a reduction in child morbidity due to malaria can be achieved.

5. School-based Intervention

5.1 Health education

WHO has always placed community participation at the centre of its 'health for all' strategies (Lasker and Weiss, 2003). It is often teachers who identify health issues that warrant attention, and seek to initiate education or skills teaching in school to address them, and teachers have collaborated in programs addressing a range of health issues. This evidence of cooperation and long-term commitment by teachers is important in the necessary dialogue about whether teachers will be motivated enough to invest the time required to initiate and then sustain any school-based intervention.

Globally more than 1 billion children have the potential to benefit from school-based health delivery (World Health Organization, 2013b; Macnab et al., 2014a). The WHO 'Health Promoting School' (HPS) model is an innovative approach to health promotion which employs multi-disciplinary strategies to engage a school community; children readily assimilate 'knowledge' and 'skills;' and WHO's overarching objective is to generate life-long learning that positively influences the social determinants of health (Viner et al., 2012; Tang et al., 2009). WHO now endorses school programs as a way to address specific health challenges worldwide (Airhihenbuwa et al., 2014).

In my opinion, inclusion of education on malaria in all schools in endemic areas should be the norm. Educational and protective strategies can be delivered in parallel and are potentially synergistic. Schools can play a vital role in ensuring that pupils understand key facts about malaria, transmission, prevention, diagnosis and treatment. I agree with other authors that such knowledge must be regarded as essential, and that there are many simple, effective and inexpensive ways to give children this knowledge through additions to the curriculum. However, for these messages to have impact, the facts shared and how they are taught must have 'resonance' and 'relevance' for the learner if there is to be any chance that what is learned will lead to a change in behavior. The incentive to educate effectively is research showing that adolescents tend to retain knowledge that they perceive to be personally and socially relevant; that effective learning can translate into positive behaviors, and many of these persist into adult life (Viner et al., 2012). Motivated teachers seek out novel approaches to engage their pupils; for example, implementing a clean-up program around the school where pupils collect discarded plastic bottles, bags and bottle caps, provides evidence-based learning when pupils understand these items offer a breeding habitat for mosquito larvae, and a way to encourage effective prevention practices (De Silva and Marshall, 2012).

Worldwide it is still commonplace to find children lack even the most basic knowledge about malaria. In a recent survey in Ugandan primary schools only 1 in 5 children knew what caused malaria or if it can be prevented, what signs and symptoms suggest infection, and what can be done to treat an infection (Macnab et al., 2016). Evidence that the broader community also lacks essential knowledge comes from data showing how small a proportion of sick, febrile children with presumptive malaria are taken for appropriate care. Simba et al. identified that < half (44.8%) were taken to government facilities and only 37.6% had prompt access to ACT (Tipke et al., 2009). My experience is similar; only 1 in 4 children (26%) sent home from schools with febrile illness compatible with malaria received management that met WHO criteria; the majority (42%) were only given an anti-pyretic, and care of the remainder included local herbal remedies (19%), being taken to church (8%), or visiting a traditional healer (6%).

There is also growing evidence that where children are taught about health effectively, they can act as agents for change in both the school and their local community (Simovska and Carlsson, 2012); knowledge and skills learned from school-based health education that engages children "ripple" out to involve siblings and parents (Macnab, 2020). Such willingness to share learned concepts and practices indicates acquisition of higher levels of health literacy (St Leger, 2001). A Ghanaian study evaluated the impact of malaria related participatory health education activities designed and led by teachers. Comparing communities with and without the school-based intervention: knowledge on malaria causation was significantly more accurate among pupils in the participating schools and adults in

their communities; the prevalence of parasitemia in pupils decreased from 31% to 10%, and the number of adults who had treated a bed net with insecticide in the past six months doubled (Ayi et al., 2010). Similar findings come from Lao PDR, where school-based education improved knowledge, attitudes, and practices towards malaria control in the community (Nonaka et al., 2008).

In keeping with other authors, in my opinion the following are key components where interventions to reduce morbidity from malaria among school children are to be offered:

1. **Education:** aim for all children to have 'health literacy' about malaria. include key facts in the curriculum of all schools in endemic areas about the cause, prevention and clinical features of malaria, and how and why diagnosis and prompt treatment are necessary.
2. **Prevention:** promote the use of insecticide treated nets, with the aim that all school-age children in malarial areas sleep under one. Children should understand vector control and contribute to local measures to clean-up garbage providing habitat.
3. **Accurate diagnosis and prompt treatment:** advocate for the use of WHO approved methods, for example RDT and ACT. Facilitate effective intervention; in rural areas or where access to clinics and/or alternative points of care providing such services are limited 'task shifting' is valid, by training teachers to provide RDT/ADT as a school-based health service.
4. **Policy:** establish local and national programs, inter-sectorial collaboration and leadership. These are needed to highlight current epidemiological findings and research data on malaria in school-age children, and give communities specific recommendations and direction on how to address the problems faced.

5.2 Prophylaxis: regular administration of preventive drugs

Chemoprophylaxis involves the administration of antimalarial drugs to those at risk of infection with the aim of maintaining protective levels within the blood stream (Temperley et al., 2008). Prophylaxis is generally not recommended for children in malaria endemic areas for multiple reasons; these include problems with adherence to prescribed regimens, compliance due to cost, and the significant risk of emergence, or increased risk of drug resistance. Over time, side-effects also preclude the use of chemoprophylactic drugs in children, particularly chloroquine.

5.3 Intermittent protective treatment (IPT)

IPT involves the periodic administration of a full therapeutic dose of an antimalarial drug or combination of drugs at predefined intervals to those at high risk of malaria, regardless of their infection status (White, 2005; Greenwood, 2006).

IPT is one of a number of possible malaria control strategies which could be delivered through schools; the study reported by Fernando et al. (2006) in Sri Lanka is an example of a comprehensive school-based intervention. In a randomized double-blind placebo-controlled trial weekly chloroquine or placebo was given to school children (6-12 years) for 9 months. In addition to a reduction in the incidence of malaria in the treated group, this study also documented a significant difference in absenteeism between those receiving chloroquine versus placebo, and a marked improvement in school performance. For children, IPT is now considered a preferable alternative to chemoprophylaxis. Trials have involved 2 main approaches:

- seasonal malaria chemoprevention (SMC), and
- intermittent parasite clearance (IPC).

SMC is a control strategy recommended by WHO that targets children living in areas of seasonal malaria transmission. SMC is recommended for children under five years of age in countries where >60% of the burden of malaria occurs in the months of the rainy season (which coincide with peak malaria transmission (?); an example is use of a single curative dose of sulfadoxine-pyrimethamine (SP) administered with a three-day course of amodiaquine (AQ). A number of alternative approaches are reported (Chandramohan et al., 2007; Cairns et al., 2012; Thera et al., 2018); evidence from several African countries has also shown that SMC is highly effective, eradicating most severe malaria,

and leading to strong reduction in *P. falciparum* prevalence, the incidence of clinical uncomplicated malaria, and malaria anemia. However, concerns with SMC, include that it does not provide complete protection and is demanding to deliver for families and healthcare providers.

Trials data on IPT generally indicate IPT regimens provide significant benefit for school-age children, providing reduced rates of infection, improved health, a decrease in absence from school, enhanced academic achievement, and improved cognitive ability (Dicko et al., 2008; Clarke et al., 2008; Nankabirwa et al., 2014b). The consensus is that IPT is a safe, simple strategy offering remarkable protection in schoolchildren in high-malarial-transmission settings, that also appears to have a substantial protective effect against all-cause mortality. Clarke et al. (2017) concluded that effective malaria IPT interventions could be a valuable addition to school health programs. Two systematic reviews and meta-analysis on efficacy and safety summarize the pros and cons of specific drug regimens (Wilson et al., 2011; Matangila et al., 2015).

However, in cluster randomized trial, Halliday et al. failed to show benefit from an intermittent screening and treatment program (IST) (Halliday et al., 2014). In a review examining why, Von Seidlein (2014) emphasized the results cannot be attributed to methodological uncertainty as the trial was conducted in a large sample of schools, to the highest procedural standards, with excellent adherence and follow-up. Instead, the author concluded that children found to be parasitemic most likely did benefit from early treatment; however, this was not an outcome the investigators measured.

5.4 Mass drug administration (MDA)

MDA is a WHO endorsed strategy to control Neglected Tropical Diseases (NTDs). The NTDs are a group of 13 major disabling conditions that are among the most common chronic infections in the world's poorest people; 7 of these are now targeted using MDA - ascariasis, trichuriasis, hookworm infection, schistosomiasis, lymphatic filariasis, trachoma, and onchocerciasis (Hotez et al., 2007). A key component of current NTD control policy is at least annual preventive chemotherapy distributed through school-based MDA initiatives (World Health Organization, 2013a); hence, MDA offers the opportunity to deliver school-based malaria strategies conjointly. A Ghanaian intervention combining IPT of malaria with MDA to control intestinal soil-transmitted helminths (STH) is a positive example; measures of anemia, sustained attention, and recall in the schoolchildren improved (Opoku et al., 2016). The addition of antimalarials to routine annual MDA programs has been shown in Malawi to be well-tolerated, safe for teachers to administer, beneficial and well-received by parents (Cohee et al., 2018). Hence, this is an appealing model, and adding malaria treatment to already established platforms for NTD control may also increase the cost-effectiveness of both interventions, leading to increased sustainability.

5.5 Rapid diagnostic testing (RDT) and Artemisinin combination therapy (ACT)

RDT kits provide point-of care diagnosis from a drop of blood; the major advantage is that this makes immediate treatment feasible. RDTs are especially useful where health facilities are scarce and/or operate using staff with minimal skill levels. Overall, research confirms that RDTs represent a cheap diagnostic approach in school malariometric surveys, and can be used to reliably estimate infection in low and high prevalence categories (World Health Organization, 2015).

The sensitivity and specificity of RDTs are good enough for them to replace conventional testing for malaria, and are more cost effective than diagnostic microscopy (Wongsrichanalai et al., 2007; World Health Organization and others, 2011; Abba et al., 2011). However, in the context of employing school-based diagnosis, minimizing mistakes is crucial; it has been shown that job aids (step-by-step instructions) that supplement manufacturer's instructions can improve performance (Rennie et al., 2007).

The positive impact of RDTs on malaria management has been widely demonstrated, and effective roll-out and use is achievable on a national scale through well planned implementation (Thiam et al., 2011). Proof of the relevance for scale up of use by appropriately trained teachers in schools includes:

1) kits can be stocked and used correctly outside formal health facilities, (Kyabayinze et al., 2010) and, 2) basic training programs enable teachers and other individuals without a formal health care background to use RDT reliably and effectively (Counihan et al., 2012; Witek-McManus et al., 2015).

ACT is the first-line treatment for *P. falciparum* malaria recommended by WHO for use worldwide since 2001 in all countries with endemic disease (Group et al., 2004; Benjamin et al., 2012) Benefits of genuine ACTs include high efficiency, fast action, few adverse effects, low cost and the potential to lower the rate at which resistance emerges and spreads. But care must be taken in LMICs over the choice of the preparation used, as sub-standard and counterfeit products with little or no efficacy are unfortunately widespread which pose severe threats to human health. Estimates in 2013 indicated that > 100,000 deaths in sub-Saharan Africa in children < 5 years of age were associated with poor quality antimalarials. In addition to risking patient health because of limited or absent efficacy, falsified medicines also contribute significantly to the risk of drug resistance developing; for example, the efficacy of ACT has declined on the Thai–Cambodian border, a site of emerging antimalarial-drug resistance historically (Dondorp et al., 2009).

Since the efficacy of ACTs is high, more could be achieved through increased availability; the major challenge is finding effective ways to deliver these drugs to those who need them most (Whitty et al., 2008). Exploratory avenues trialed include: a community case management approach, where a variety of trained providers deliver ACT (Akweongo et al., 2011), deployment through trained agents in drug stores, pharmacies and private medical clinics, and via teachers in school programs (Mbonye et al., 2015; Mphwatiwa et al., 2017).

6. Developing a Model for Teacher-driven School-based Care

“If teachers could be trained to promptly detect and adequately treat uncomplicated malaria and promptly refer severe forms of the disease, improved access to this critical service would be achieved. For example, school absenteeism and man hours lost to the disease would be reduced, especially in these rural communities.”
(Afenyadu et al., 2005)

These words, written in a 2005 review on how to improve access to early treatment, introduced the concept that teachers should be trained to intervene, and were followed by calls for innovative solutions to the health burden of malaria in school-children from WHO, (Agyepong et al., 2017) and other experts. The authors also identified that decentralization to the district level, and collaboration between health and education sectors, were required in order to improve the health status of school children.

In an early exploratory trial, 12 Ghanaian schools trained teachers to diagnose and treat uncomplicated malaria using an adaptation of a WHO diagnostic algorithm and recognize and refer severe forms of the disease for appropriate treatment. The authors concluded that primary school teachers in rural communities are willing partners in bringing early case detection and adequate management closer to the people (Afenyadu et al., 2005). Findings were similar in a contemporaneous study in Tanzania where the clinical diagnostic algorithm included measurement of body temperature, although training in diagnosis and treatment only involved head teachers and selected ‘health’ teachers (Magnussen et al., 2001).

In Malawi, teachers were taught to use pupil-treatment kits containing drugs dispensed according to national guidelines. The authors concluded school-based interventions could play a part in mitigating malaria based on comparison of overall and malaria-specific mortality rates (Pasha et al., 2003). In a second Malawian study significant reductions in general absenteeism and grade repetition by students were noted (Simwaka et al., 2009).

The first model for teacher-administered RDT/ACT was developed as a community outreach health education project by a local NGO after teachers had identified the unacceptable health bur-

den malaria was creating among their pupils (Macnab et al., 2016; Macnab, 2020); the decision to introduce school-based RDT/ACT was made collaboratively during community-based dialogue.

Macnab reported evaluation of this 2-year trial. Four rural schools in Uganda were involved. All teachers were trained broadly on malaria causation, prevention and treatment; two volunteer teachers in each school were specifically trained to collect the required data, conduct RDT and administer ACT in children falling sick at school (Macnab et al., 2016; Macnab, 2020). The effect on absenteeism was evaluated as a surrogate for morbidity. A baseline 'pre-intervention' year's data were compared to a subsequent treatment year when all sick children had a teacher-administered RDT and prompt ACT if they tested positive. A single dose ACT preparation was used to ensure a full course of treatment was completed. Pre-intervention 953/1764 pupils were sent home due to presumed infectious illness, parental management only approached WHO standards for malaria diagnosis and treatment in 1:4 children, and the mean duration of absence from school was 6.5 school days. During school-based teacher-administered RDT/ACT 1066/1774 pupils were identified as sick, 765/1066 were RDT positive and received ACT, and duration of absence fell to 0.6 school days. After being promptly treated many children felt well enough to ask to return to class within hours, and consequently had no days when they were absent from school.

Overall, absence from school was reduced by 60.8% by this intervention. If the same percentage of children sent home in the 'pre-intervention' year had malaria as were diagnosed using RDTs in the 'treatment' year this would equate to 1358 cases in 1775 children over the 2 years - a malaria incidence rate of 79% across the 4 schools. No children died from malaria during the intervention year. Delivery was readily implemented Subsequently Mphwatiwa et al. (2017) reported on a similar approach in Malawi. An impressive element was that this trial was established following intersectoral collaboration between the Ministry of Health and Ministry of Education Science and Technology. Findings included:

- *Positive outcomes:* trained teachers were trusted providers of malaria testing and treatment; access to treatment by children increased; absenteeism decreased.
- *Potential barriers:* increased teacher workloads and need for supervision from health workers.
- *Concerns:* lack of incentives and concerns for sustainability of drug supply.

Both Macnab and Mphwatiwa concluded that training teachers to "test and treat" was well received, supported national health and education policies and was seen to be a worthwhile intervention. Importantly, sustainability is demonstrated by ongoing data from Uganda; for 3 years post intervention the target schools have independently continued RDT/ACT and the significant reduction in malaria morbidity has been sustained, and there is also robust evidence of greater knowledge about many aspects of malaria among the school-children and in the broader community (Macnab, 2020).

6.1 Training

A key question is can teachers be trained to provide appropriate diagnostic and treatment services for school children in the context of malaria? Importantly, trials show that teachers can be trained to correctly perform safe blood collection, accurate interpretation of RDT, correct dispensing of ACT, and sustain this competency (Witek-McManus et al., 2015; Macnab et al., 2016). Evaluative literature describes how to provide effective training and how to minimize common errors; comprehensive instructions on RDT/ACT are essential; periodic performance appraisals to monitor user RDT/ACT behavior should be basic component of implementation; common challenges described were how to dispose of medical waste and refer complicated patients to public facilities.

6.2 Cost

The cost and cost-benefit of RDT/ACT are relevant to their deployment. In 2008, studies comparing presumptive treatment and RDT use in rural health facilities in sub-Saharan Africa deemed the intervention cost-effective (Shillcutt et al., 2008). In the same year, cost of teacher-delivered IPT in Kenya was estimated to be US\$ 1.88 per child treated per year. The largest components were drug

and teacher training costs. Cost benefit analysis equated each anemia case averted to US\$ 29.84 and each *P. falciparum* parasitemia case averted to US\$ 5.36 (Temperley et al., 2008). In 2009 benefits far outweighed costs where teachers were trained to identify and treat children with malaria in Malawi; cost benefit accrued from significant reductions in both general absenteeism and grade repetition by students (Simwaka et al., 2009).

In 2011 the estimated cost of school-based IST from Kenya was US\$ 6.61 per child screened. Key components were: RDT kits 22%, salaries 36%, and 47% redeployment of resources including (health worker time and use of hospital vehicles), but costs would likely reduce by 40% with changes in delivery (alternative RDTs and removal of supervised treatment) (Drake et al., 2011). In the 2016 Ugandan trials, cost for RDT kits and ACT were US\$ 0.50 and US\$ 2.20 respectively; for every 3 sick/febrile children tested 2 were RDT positive (Macnab, 2013). Cost savings were made subsequently when the single dose ACT formulation used to eliminate any partial treatment bias was replaced with a conventional 3-day 6 dose preparation costing US\$ 1.0. Training and supervision costs were not included as the program was delivered as part of aid provided by a medical charity.

A key element of the affordability, cost-effectiveness and long-term sustainability of school-based treatment will be drug choice. Drugs best suited to mass treatment programs should be inexpensive, easy to administer (preferably as a single dose), and well-tolerated with minimal side-effects; for IPT, a long half-life is also advantageous. A global ACT subsidy would significantly increase usage of ACTs and reduce retail price; in rural Tanzania, a 90% subsidy increased the proportion of consumers purchasing ACTs from 1% to 44.2% one year later, and purchasing for children rose considerably (Sabot et al., 2009).

Importantly, effective program rollout offers potential overall savings; in Senegal a major reduction in anti-malarial drug consumption occurred after nation-wide introduction of RDT, and considerable cost-savings were achieved through centralized ACT procurement (Thiam et al., 2011); half of global demand for antimalarials has been estimated to be due to overuse in patients without malaria (Cohen et al., 2012). Substantial long-term cost-benefit will also accrue from improving the health of school-aged children in ways that aid cognitive development and promote educational achievement; future research is needed for this to be established.

7. Future Directions

"In Africa, there is increasing evidence of the dramatic reductions in malaria mortality and morbidity in early childhood due to recent up-scaling of malaria control efforts."
(Temperley et al., 2008)

In this report of epidemiologic change, the authors provide evidence from many useful trials of 'what works and why' that can be used to guide future directions. Increased recognition of the consequences of malaria has prompted growing interest and calls for innovative concepts in its control in children who attend school (Bundy et al., 2000; Jukes et al., 2006). The detrimental effects on hemoglobin levels (Koukounari et al., 2008), and then on learning and educational achievement (Lal-loo et al., 2006), led to models that provide school-children with access to accurate diagnosis and treatment in endemic areas, reduce morbidity, and increase the capacity of children to benefit from their education. The argument for universal, parasite-based diagnosis is clear. A broad selection of literature now describes the rationale, therapeutic options, design, delivery, training, effectiveness, cost, challenges and future research priorities for interventions applicable to school-based delivery.

What school-based malaria testing and treatment is undertaken in future will depend on priorities set nationally, which in turn requires vision beyond the conventional political time frame, but it is now clear that big benefits are there to be achieved. While funding agencies tend to call for bold, novel and disruptive thinking, there are strong grounds to argue that substantive investment in proven school-based models is needed in parallel. The efforts of major agencies made RDT and ACT more affordable

and hence more available; the benefits of now making teacher-driven diagnosis and treatment broadly available in endemic areas would be considerable. Arguably there is still no consensus as to the optimal intervention approach, and more evidence on the costs and cost-effectiveness for school-based malaria control are still needed. But individual region-specific programs can be tailored from the evidence now available to provide viable interventions for at risk populations.

Many malaria-endemic countries are considering scaling up RDT use in a variety of locations; it is not overstated to say that when well used, RDTs can transform fever management, reform understanding of malaria transmission, and have even made malaria elimination look achievable (Thiam et al., 2011). There is need for intersectoral collaboration at a national level, and only when this is realized is it likely that the effective upscaling of RDT/ACT availability will be achieved (Akweongo et al., 2011); legislative changes and investment in support programs and infrastructure will be required in parallel (Visser et al., 2017).

Use of RDT/ACT in school-based programs warrants special consideration, because, in addition to being simple to implement and low cost, this model uses WHO-endorsed testing and treatment methods, has broad relevance and is applicable to low-resource settings worldwide where the school-age population is at risk. Innovative ways are called for to make WHO endorsed entities more available to those in need, globally schools offer more than 1 billion children the potential to benefit from school-based healthcare delivery, and teachers can be effective agents for change, through innovative school-based models that engage and train them to deliver health education and elements of care endorsed by WHO.

Such models already meet the WHO Commission on Social Determinants of Health call to adopt a 'community empowerment approach', use 'non-traditional outlets' and 'improved tools' to address health challenges faced by young people, and seek longer and healthier lives for Africans (?). Future models that use novel ways to engage and train teachers to deliver health education and care, will also meet recommendations from the Lancet Commission on the future of health in sub-Saharan Africa to extend population access to services, by using 'people-centered approaches' and 'innovative education and training of personnel that correspond to local needs.' (Agyepong et al., 2017)

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Conflict of Interest

There is no conflict of interest.

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