

Chapter 14

Malaria in Middle Childhood and Adolescence

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INTRODUCTION

The age distribution of cases of malaria is influenced by the intensity of transmission. In areas where the population has low exposure to infection, malaria occurs in all age groups. In high transmission areas, in contrast, the main burden of malaria, including nearly all malaria-related deaths, is borne by young children (figure 14.1). These different age patterns are seen because exposure to repeated malaria infections induces some protection against subsequent attacks; but protection is rarely complete.

The age pattern of clinical malaria is determined by the level of transmission and the consequent level of acquired immunity, so it is sensitive to changes in the level of transmission (Carneiro and others 2010; Snow and others 1997). In many malaria-endemic areas, successful control programs have reduced the level of transmission substantially (Noor and others 2014; O'Meara and others 2010; WHO 2015). Consequently, in such communities, the peak age of clinical attacks of malaria is shifting from very young to older children. In The Gambia, the peak age of hospital admission for severe malaria increased from 3.9 years in 1999–2003 to 5.6 years in 2005–07 (Ceesay and others 2008); similar changes have been seen in Kenya (O'Meara and others 2008).

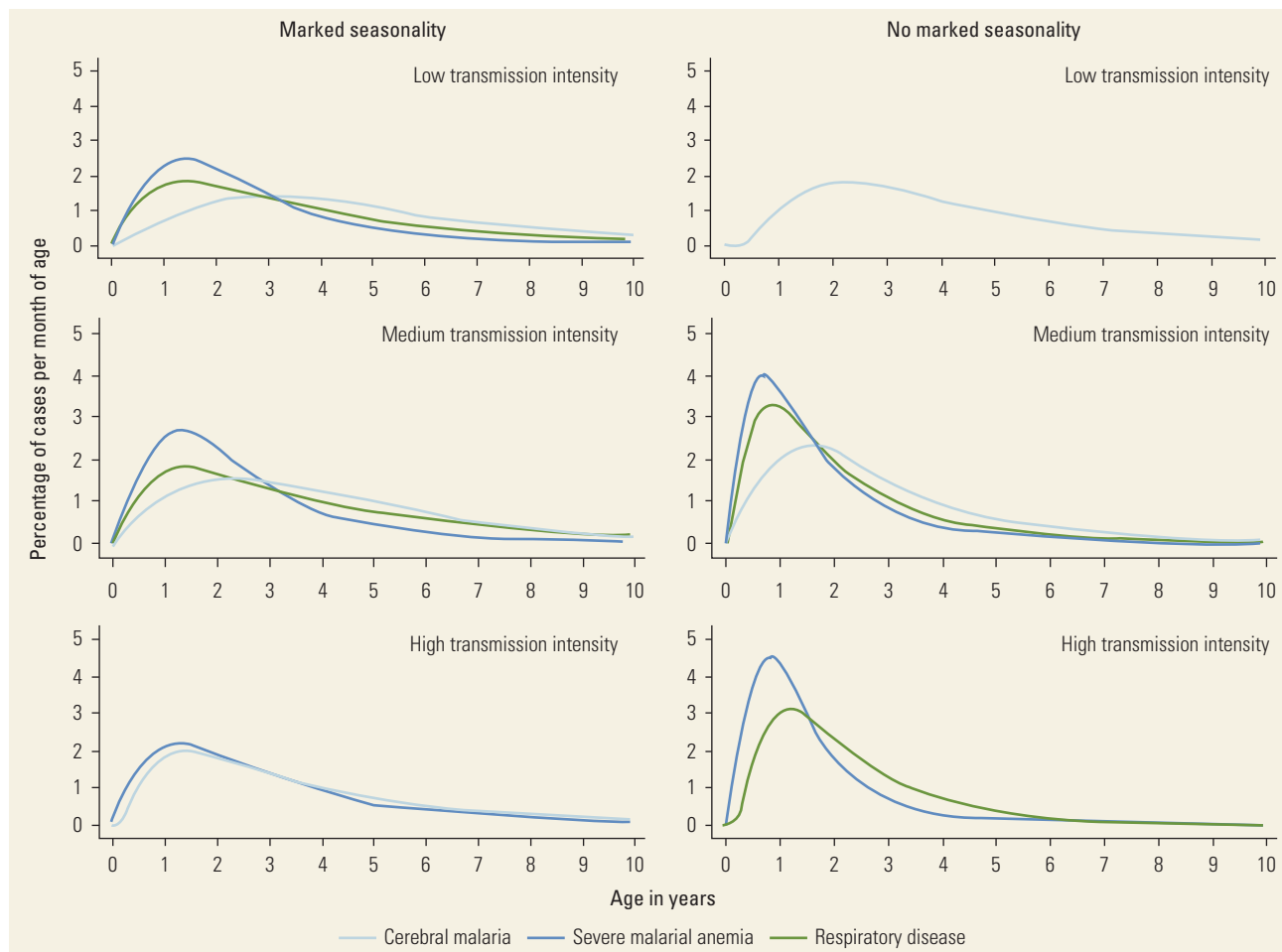
If the financial support for malaria control continues, further decreases in the intensity of transmission can be anticipated in many highly endemic areas; these decreases

will increase the incidence of clinical attacks of malaria, including severe attacks, in school-age children (ages 5–14 years). However, the epidemiology and management of malaria in school-age children has, until recently, received little attention. This chapter reviews the current burden of malaria in school-age children, its clinical consequences, and approaches to controlling the disease in this increasingly vulnerable group. The review focuses largely on Sub-Saharan Africa, in part because this region has the greatest burden of malaria in school-age children, but also because of the lack of information on the impact of malaria in school-age children in other parts of the world, including those where *Plasmodium vivax* is the dominant malaria parasite. An earlier version of the review has been published (Nankabirwa, Brooker, and others 2014). Definitions of age groupings and age-specific terminology used in this volume can be found in chapter 1 (Bundy, de Silva, and others 2017).

PREVALENCE OF MALARIA PARASITEMIA IN SCHOOL-AGE CHILDREN

The burden of malaria in school-age children is poorly defined because this age group is not routinely included in household-based cluster surveys. Information on the prevalence of malaria in this group is derived mainly from school-based surveys and from World Health Organization (WHO) estimates (WHO 2015).

Figure 14.1 Age Distribution of Cases of Severe Malaria by Intensity of Malaria



Source: Roca-Feltrre and others 2010.

Note: The figure shows the percentage distribution of each severe malaria syndrome by age for children under age 10 years according to seasonality and transmission intensity, such that the integral of the curve is equal to 100 percent of expected cases.

Understanding the burden of malaria among school-age children is essential to justify investment in school-based malaria control interventions (Bundy and others 2000) and to identify delivery mechanisms to help control malaria in this underserved population.

More than 500 million school-age children worldwide are at risk of malaria infection; 200 million of those at risk live in Sub-Saharan Africa (table 14.1) (Gething and others 2011). Annex 14A, table 14.1 summarizes the results of studies on the prevalence of asymptomatic malaria parasitemia in this population. Map 14.1 shows the frequency with which malaria surveys have been undertaken in school-age children, with an increase in recent years in East Africa. Map 14.2 shows the prevalence observed in school-age children by geographical area.

The majority of malariometric surveys are conducted in children ages 2–10 years. Relatively few

studies have been undertaken in older school-age children in Sub-Saharan Africa, and many of those are out of date following improvements in malaria control. In general, higher prevalence rates have been observed in West and Central Africa than in East Africa, but a great deal of heterogeneity has been observed with rates ranging from less than 5 percent to greater than 50 percent in different surveys. Recent studies in Malawi have emphasized the burden of malaria in school-age children and the role that those children play in acting as a reservoir of infection (Mathanga and others 2015; Walldorf and others 2015).

Few reports on the prevalence of asymptomatic malaria in school-age children outside of Sub-Saharan Africa are available (annex 14A, table 14.1). In the Republic of Yemen, Bin Mohanna, Bin Ghouth, and

Table 14.1 Estimated School-Age (5–14 Years) Population at Risk of *Plasmodium falciparum* Malaria in Millions by Region,^a 2010

Region	Unstable risk	Stable risk	Total
Andean Latin America	1.0	0.6	1.7
Caribbean	2.4	1.8	4.2
Central Asia	0.2	–	0.2
Central Latin America	3.9	2.3	6.2
Central Sub-Saharan Africa	<0.1	26.1	26.1
East Asia	1.6	0.6	2.2
Eastern Sub-Saharan Africa	3.3	80.7	84.0
Middle East and North Africa	4.0	2.5	6.5
Oceania	<0.1	1.4	1.4
South Asia	165.6	98.6	264.3
South-East Asia	37.8	31.6	69.4
Southern Sub-Saharan Africa	2.3	4.8	7.1
Tropical Latin America	4.6	1.7	6.3
Western Sub-Saharan Africa	1.6	86.8	88.4
World	228.5	339.5	568.0

Source: Adapted from Gething and others 2011; data provided by the Malaria Atlas Project (www.map.ox.ac.uk), with thanks to Pete Gething and Zhi Huang, University of Oxford.
Note: – = not applicable. Rows may not add precisely due to rounding.

a. Based on the Global Burden of Disease study, http://www.healthdata.org/sites/default/files/files/GBD_GBD2010_Regions_countries.pdf.

Rajaa (2007) find a prevalence of 13 percent in children ages 6–11 years in the Hajr valley. In Latin America, malaria transmission is restricted to Amazonian areas and is uniformly low. In Brazil, Vitor-Silva and others (2009) find that *P. vivax* was more common than *P. falciparum* among schoolchildren. On the Thai-Burma border, Luxemburger and others (1994) find that 10 percent of school-age children were infected, mainly with *P. falciparum*.

IMPACT OF MALARIA ON THE HEALTH AND DEVELOPMENT OF SCHOOL-AGE CHILDREN

Most school-age children with malaria parasitemia do not have any symptoms because they have acquired some immunity. However, asymptomatic infections can contribute to anemia and impairment of cognitive development. School-age children may be infected with a malaria parasite that expresses antigens to which they have not been exposed and to which they have little or no immunity; the result is the development of symptoms such as fever and, more rarely, severe diseases such as cerebral malaria, life-threatening anemia, and death.

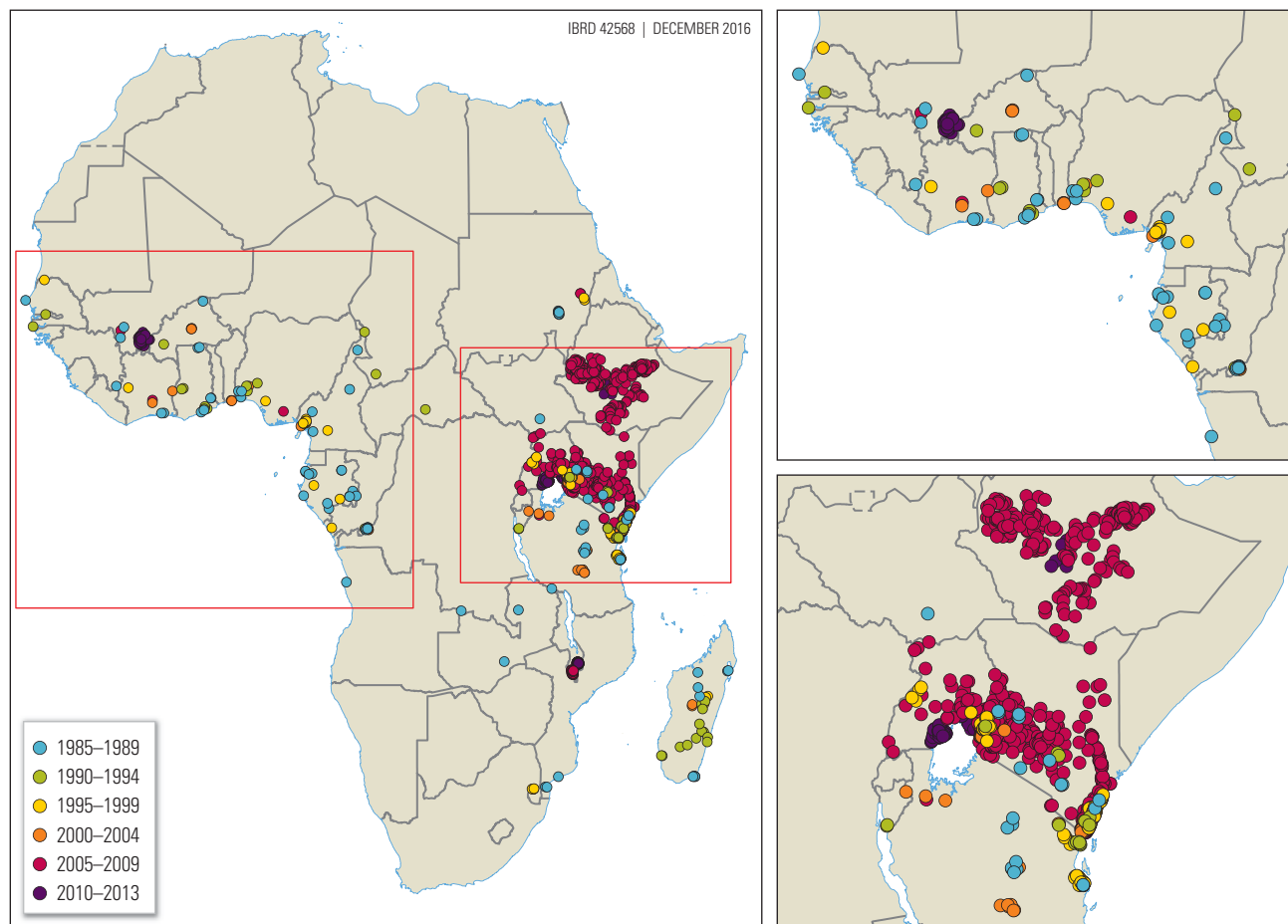
Mortality

The WHO estimates that there were approximately 438,000 (range 236,000–635,000) deaths from malaria in 2015; 90 percent of those deaths occurred in Sub-Saharan Africa (WHO 2015). A comprehensive review of malaria-related deaths between 1980 and 2010 (Murray and others 2012) reports many more deaths than the WHO; the review estimates that 6 percent to 9 percent of malaria deaths occur in children ages 5–14 years, corresponding to an annual figure in the range of 70,000–110,000 deaths. A lower malaria mortality rate was found in school-age children compared with younger children in Bangladesh and Sub-Saharan Africa (Adjuik and others 2006). A similar age pattern was found in India, with an estimated malaria-related death rate of 29 per 1,000 in children ages 5–14 years, compared with 55 per 1,000 in children under age 5 years in 2005 (Dhingra and others 2010).

Incidence of Clinical Malaria in School-Age Children

An estimated 214 million (range 149 million to 303 million) cases of malaria occurred worldwide in 2015; more than 80 percent were in Sub-Saharan Africa (WHO 2015). However, data on the incidence of clinical malaria in school-age children are scarce. Review of the limited

Map 14.1 Location of Malaria Parasite Surveys in School-Age Children, 1985–2013



Source: Malaria Atlas Project (MAP), <http://www.map.ox.ac.uk>.

information published indicates that annual incidence can vary from 0.03 to 2.7 cases per child per year, depending on the transmission setting (annex 14A, table 14.2). The limited data available suggest that it is not unusual for school-age children to experience one clinical attack of malaria severe enough to warrant treatment once every one to two years (Barger and others 2009; Clarke and others 2004; Nankabirwa and others 2010; Rohner and others 2010).

Malaria as a Cause of Anemia in School-Age Children

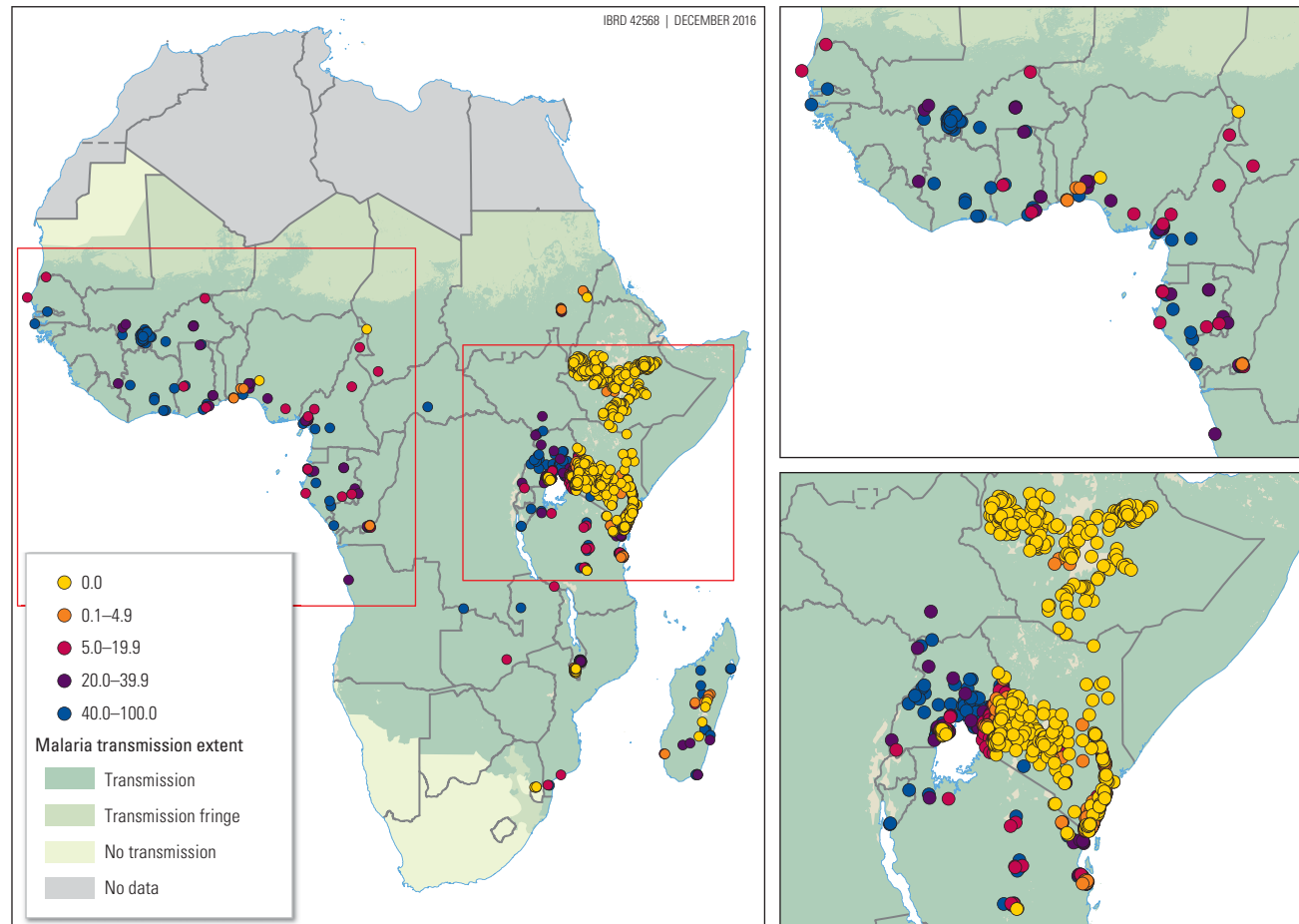
Anemia is a common problem among school-age children in the tropics. Its etiology is usually multifactorial, and the relative importance of different causes varies from area to area. It is difficult to separate malaria as a causative agent from other factors, such as nutritional deficiencies, helminth infections, and HIV/AIDS, which often coexist in the same communities (Stephenson and others 1985). Many other cross-sectional surveys carried out in highly endemic areas have found a significant

association between the prevalence of anemia and parasitemia, but these studies were conducted mainly among preschool-age children.

The strongest evidence for the role of malaria as a cause of anemia in school-age children comes from the results of intervention studies with trials of intermittent preventive treatment (IPT) in school-age children showing improvement in hemoglobin concentration in both East Africa (Clarke and others 2008; Nankabirwa and others 2010) and West Africa (Barger and others 2009; Clarke and others 2013; Tine and others 2011).

Overall, differentiating the effect of malaria on anemia in school-age children from other confounding factors is difficult; the limited evidence available suggests that it has a significant role. Although administration of supplementary iron can increase the incidence of clinical attacks of malaria in some circumstances, most studies have shown only a modest effect (Ojukwu and others 2009). The WHO and other health authorities (Raiten, Namasté, and Brabin 2011) recommend that iron supplementation is indicated in areas in which iron

Map 14.2 Prevalence of Malaria Parasitemia in School-Age Children in Sub-Saharan Africa
Percent



Source: Malaria Atlas Project (MAP), <http://www.map.ox.ac.uk>.

deficiency is a major problem, even if these areas are endemic for malaria, provided that malaria control measures, such as distribution of insecticide-treated bednets (ITNs), are put in place at the same time.

Malaria as a Cause of School Absenteeism

The estimated annual loss of school time in Kenya attributable to malaria in 2000 was 4 million to 10 million school days (Brooker and others 2000). Because malaria is an important cause of school absenteeism, preventive efforts should significantly improve school attendance. In a randomized clinical trial in Sri Lanka, Fernando and others (2006) report a 55 percent reduction in malaria incidence and a 62.5 percent reduction in school absenteeism among children who received chloroquine prophylaxis.

Despite the limited number of studies, the available evidence suggests that the cumulative effect of school absenteeism attributable to malaria for children in endemic areas is considerable, preventing children from

achieving their full academic potential and causing a loss to the state with respect to its investment in education.

Impact of Malaria on Cognitive Function

Studies in Africa and Asia provide strong evidence that malaria can impair the cognitive function of school-age children (Fernando, Rodrigo, and Rajapakse 2010; Kihara, Carter, and Newton 2006). Descriptive studies have evaluated the impact of severe malaria, uncomplicated malaria, and asymptomatic parasitemia on various aspects of cognition.

In Kenya, a retrospective assessment of children ages six to nine years who had had an episode of cerebral malaria found significant differences in speech and language and cognition, compared with the healthy control group (Carter, Mung'ala-Odera, and others 2005; Carter, Ross, and others 2005; Carter and others 2006); in Uganda, cerebral malaria was associated with persistent impairment of one or more cognitive domains

Table 14.2 Summary of the Results of Recent Trials of Chemoprevention in School-Age Children

Study setting	Population	Type	Treatment regimen	Study drug	Protective efficacy			Source
					Clinical malaria Percent (95% CI)	Malaria parasitemia Percent (95% CI)	Anemia Percent (95% CI)	
Year-round transmission								
Western Kenya	6,735 children ages 5–18 years; 30 schools	IPCs	Treatment once every school term (3 treatments per year)	SP + AQ	Not examined	89 (73–95)	48 (8–71)	Clarke and others 2008
Sierra Leone	591 children ages 6–14 years; 1 school	IPCs	Treatment at month 0 and month 3 (2 treatments per year)	SP	Not examined	No impact	No impact	Rohner and others 2010
Uganda	780 children; 3 schools	IPCs	Single course of treatment; protective efficacy measured after 42 days	SP	Not examined	No impact	No impact	Nankabirwa and others 2010
				SP + AQ	Not examined	48.0 (38.4–51.2)	Mean change Hb +0.37 (0.18–0.56)	
				DP	Not examined	86.1 (79.5–90.6)	Mean change Hb +0.34 (0.15–0.53)	
Uganda	740 children; 1 school	IPCs	Treatment once a school term (4 treatments per year)	DP	No impact	54 (47–60)	No impact	Nankabirwa, Wandera, and others 2014
		IPCs	Treatment once every month (12 treatments per year)	DP	96 (88–99)	94 (92–98)	40 (19–56)	
Highly seasonal transmission								
Mali	262 children ages 5–10 years; 1 village	SMC	Two treatments 8 weeks apart during the malaria season (2 treatments per year)	SP	36 (12–53)	Not examined	Not examined	Dicko and others 2008
Mali	296 children ages 6–13 years; 1 village	SMC	Two treatments 8 weeks apart during the malaria season (2 treatments per year)	SP + AS	66.6	80.7	59.8	Barger and others 2009
				AQ + AS	46.5	75.5	54.1	
Mali	1,815 children ages 6–14 years; 38 schools	IPCs	Single treatment at end of the malaria season (1 treatment per year)	SP + AS	Not examined	99 (98–100)	38 (9–58)	Clarke and others 2013
Senegal	1,000 children under age 10 years; 8 villages	SMC	Two treatments given monthly toward end of malaria season (2 treatments per year)	SP + AQ	79 (10–96)	57 (5–81)	41 (18–58)	Tine and others 2011

Note: AQ = amodiaquine; AS = artesunate; CI = confidence interval; DP = dihydroartemisinin-piperaquine; Hb = hemoglobin; IPCs = intermittent parasite clearance in schools; IST = intermittent screening and treatment; SMC = seasonal malaria chemoprevention; SP = sulphadoxine-pyrimethamine.

(John and others 2008). Similar findings were recorded in Malawian children with retinopathy-positive cerebral malaria (Boivin and others 2011).

Cerebral malaria is not a prerequisite for cognitive impairment as a consequence of malaria infection; studies have suggested that uncomplicated episodes of malaria can adversely affect cognition. Studies in Sri Lanka show that school-age children scored significantly lower on tests of mathematics and language during an episode of clinical malaria than children in the control group (Fernando, de Silva, and Wickremasinghe 2003). In a study in Sri Lanka, Fernando and others (2003) find a negative correlation between mathematical and language skills and a past history of repeated attacks of malaria during the preceding six years among children ages 6–14 years, even after correcting for socioeconomic factors. A history of one or more malaria attacks was associated with poor performance in mathematics and language in a cohort of 198 schoolchildren studied in Brazil (Vitor-Silva and others 2009). A study of school-age children in Mali, where *P. falciparum* malaria predominates, reaches similar conclusions (Thuilliez and others 2010).

Many of the studies considered were primarily descriptive, and their results are open to potential confounding by social or economic factors not included in the analysis. Accordingly, the strongest evidence to support the view that malaria impairs cognitive function comes from intervention trials. In Sri Lanka, a randomized, placebo-controlled, double-blind trial of chloroquine prophylaxis in children ages 6–12 years showed that educational attainment improved and that school absenteeism was reduced significantly ($p < 0.0001$) in children who took chloroquine prophylaxis (Fernando and others 2006). Children in The Gambia ages 3–59 months who were randomized to receive malaria prophylaxis with dapsone-pyrimethamine or placebo during the malaria transmission season for three successive years (Greenwood and others 1988) were reassessed when their mean age was 17 years (Jukes and others 2006). Educational attainment was better in children who had received prophylactic treatment than in the placebo group, but the scores for the cognitive tests were not significantly different between groups. Prophylaxis substantially increased the school enrollment of girls. The intervention also reduced school drop out for students in government schools (Zuilkowski and Jukes 2014).

In a large, stratified, cluster-randomized, double-blind, placebo-controlled trial conducted in schools in Kenya, IPT with sulphadoxine-pyrimethamine plus amodiaquine (SP + AQ) significantly improved sustained attention of schoolchildren ages 10–12 years (Clarke and others 2008). Significant effects on sustained

attention are also reported from a trial in schools in southern Mali (Clarke and others 2013).

Overall, these studies strongly suggest that both clinical malaria and asymptomatic parasitemia can adversely affect the cognitive skills of school-age children, but the mechanism by which this occurs remains uncertain.

APPROACHES TO THE CONTROL OF MALARIA IN SCHOOL-AGE CHILDREN

A range of strategies is available for the control of malaria in this age group, delivered through schools or communities. The optimal approach to delivering interventions, including frequency and timing, and their ultimate effectiveness will vary according to the local intensity of malaria transmission. Malaria interventions are best delivered as part of an integrated package, for example, as part of a school health program that also delivers deworming (see chapter 13, Bundy, Appleby, and others [2017]) or school feeding (chapter 12, Drake and others [2017]).

Treatment of Clinical Attacks

Ease of access of school-age children to effective treatment for clinical attacks of malaria is an essential component of any effective national malaria control program. However, in many parts of Sub-Saharan Africa, geographic and financial barriers prevent children from obtaining rapid access to diagnosis and treatment (see volume 6, chapter 14, Babigumira and others 2017).

Schools can play a vital role in ensuring that their pupils obtain rapid access to diagnosis and treatment by providing appropriate health education activities in school, but information about the treatment of malaria is rarely part of the curriculum. A content analysis of school textbooks in nine endemic countries found that most included information on modes of transmission, mosquitoes, and signs and symptoms of malaria, but little about ITNs or the need for prompt and appropriate treatment (Nonaka and others 2012). These findings suggest that improving textbook content in accordance with the national malaria control strategy should become a priority.

Access to prompt treatment can be improved by providing antimalarials to schools and by training teachers to administer antimalarial treatments correctly. In the past, when first-line treatment was either chloroquine or SP given presumptively, training teachers to provide treatment was shown to be feasible and to reduce school absenteeism and malaria deaths (Afenyadu and others 2005; Pasha and others 2003). However, the WHO now recommends diagnosis before any antimalarial

treatment is given (WHO 2015). Building on recent efforts to expand diagnosis and treatment of malaria outside of the formal health sector (Ansah and others 2015), an ongoing study in Malawi is evaluating the impact on school attendance and health outcomes of training teachers to use rapid diagnostic tests (RDTs) (Witek-McManus and others 2015). If this approach is effective, operational issues, including supply chains, blood safety, and teacher attrition, will require careful consideration before the strategy is scaled up.

Vector Control

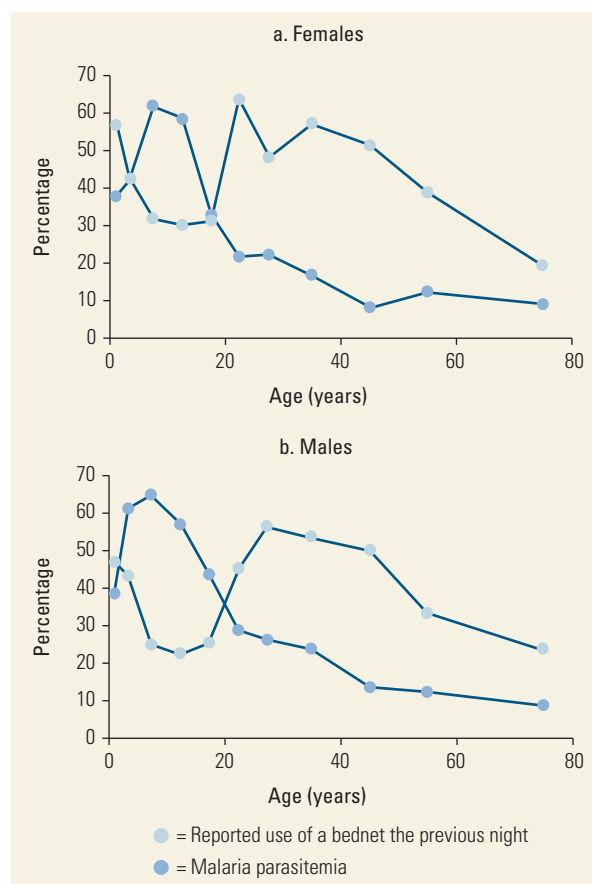
The main methods of vector control of malaria are ITNs, indoor residual spraying (IRS), and reduction of mosquito breeding sites.

Insecticide-Treated Nets

Strong evidence indicates that regular use of ITNs substantially lowers the risks of clinical malaria and all-cause mortality in children under age five years and reduces the burden of malaria among pregnant women (Lengeler 2004; Lim and others 2011). For these reasons, large-scale ITN distribution programs initially focused on these two vulnerable groups. However, following appreciation of the indirect herd effect of a high level of ITN coverage in a community, the development of long-lasting ITNs, and an increase in the financial and political support for ITN programs, there has been a shift from prioritizing vulnerable populations to protecting everyone with an ITN, including school-age children. However, an analysis of household surveys undertaken between 2005 and 2009 in 18 African countries found that school-age children were the group least likely to sleep under an ITN the previous night; between 38 percent and 42 percent of school-age children were unprotected (Noor and others 2009). Similar low ITN usage has been observed among school-age children in Cameroon (Tchinda and others 2012), Kenya (Atieli and others 2011), and Uganda (Pullan and others 2010) (figure 14.2). Substantial progress in population coverage with ITNs has been made since 2000, with more than 50 percent of the population of Sub-Saharan Africa sleeping under ITNs in 2015; nevertheless, ITN use among those ages 5–19 years remains lower than among the population as a whole (WHO 2015). Thus, even in countries with existing national policies of universal access to ITNs, school-based distribution of nets could have a complementary short-term role in addressing this gap.

Few studies have investigated the efficacy of ITNs in school-age children. An early trial among children in a rural boarding school in central Kenya showed that sleeping under an untreated mosquito net following a

Figure 14.2 Age Patterns in the Prevalence of Malaria Parasitemia and of Reported Use of a Bednet on the Previous Night in Uganda.



Source: Pullan and others 2010.

round of effective antimalarial treatment reduced the incidence of clinical malaria by 97 percent, but it did not reduce anemia (Nevill and others 1988). A reduction in the incidence of malaria was shown in a randomized trial of children ages 4–15 years in an area of low and unstable transmission on the Thai-Burmese border (Luxemburger and others 1994). In a rural area of western Kenya, where malaria transmission is perennial and high, a community-based trial showed that ITNs halved the prevalence of anemia in girls ages 12–13 years; ITNs were less effective in preventing anemia among girls ages 6–10 years (Leenstra and others 2003). Additional evidence provided by cross-sectional survey data suggests that net use among school-age children is associated with a 71 percent and 43 percent lower risk of *P. falciparum* infection in Somalia (Noor and others 2008) and Uganda (Pullan and others 2010), respectively. An analysis of country-wide data from school surveys in Kenya (Gitonga and others 2012) shows that ITN use was associated with a

reduction in the odds of malaria infection and anemia in coastal areas, where malaria transmission is low to moderate, and among boys in western lakeshore Kenya, where transmission is high. In addition, ITN use reduced the risk of parasitemia in the western highland epidemic zones and the risk of anemia in coastal areas where transmission is low.

As children become more independent with increasing age, parents have less control over their bedtimes, where they sleep, and whether they use nets. Education targeted directly to older children, for example, through malaria education in schools, could increase regular use of ITNs among teenage children.

Indoor Residual Spraying

IRS, the application of long-acting insecticides to the walls and roofs of houses and, in some cases, public buildings and domestic animal shelters, is an effective method of malaria control. IRS implemented as a community-wide campaign can achieve substantial reductions in the incidence and prevalence of malaria infection in all age groups (Pluess and others 2010). Repeated IRS campaigns conducted between 1955 and 1959 in the Pare-Taveta area of Tanzania were associated with a reduction in malaria parasitemia from 73 percent to 7 percent in children ages 5–9 years, and from 62 percent to 4 percent in children ages 10–14 years (Draper 1960). Targeted IRS conducted over 12 months in the epidemic-prone Kenyan highlands halved the monthly prevalence of asymptomatic infection in school-age children and reduced the incidence of clinical disease (Zhou and others 2010). Studies that have investigated the impact of combining vector control with ITNs and IRS have produced mixed results, with some showing a benefit and others no added effect.

Reduction of Breeding Sites

Breeding sites of malaria anopheline vector mosquitoes can be controlled in some epidemiological situations through application of larvicides, introduction of predator species, and habitat destruction and drainage (Tusting and others 2013). However, achieving a significant reduction in malaria transmission in many parts of Sub-Saharan Africa is difficult because of the multiplicity and changing nature of breeding sites of the main vector species, such as *Anopheles gambiae* (Fillinger and Lindsay 2011). It is unlikely that encouraging schoolchildren to destroy potential breeding sites of *An. gambiae* in school grounds will have any impact on the prevalence of malaria, although it could help reduce the numbers of other mosquito species, including those that transmit dengue.

Malaria Chemoprevention

The two main approaches to the use of antimalarial drugs to prevent malaria infection are chemoprophylaxis and IPT.

Chemoprophylaxis

Chemoprophylaxis involves the regular administration of antimalarial drugs to those at risk over a sustained period to provide persistent, protective blood levels. Compelling evidence indicates the benefits of chemoprophylaxis in school-age children. A review of trials of malaria chemoprophylaxis in the population of malaria-endemic areas reports significant health impacts in nearly all studies (Prinsens Geerligs, Brabin, and Eggelete 2003). Most of these studies focus on young children, but in 30 of the 36 trials that examined infection rates in children over age five years, reductions in malaria parasitemia ranged from 21 percent to 100 percent (Prinsens Geerligs, Brabin, and Eggelete 2003). A 2008 review confirms these findings (Meremikwu, Donegan, and Esu 2008). Chemoprophylaxis with chloroquine not only reduced the incidence of clinical malaria and absenteeism in Sri Lankan schoolchildren, it also significantly improved educational attainment (Fernando and others 2006).

Intermittent Preventive Treatment

An alternative to chemoprophylaxis is IPT, the periodic administration of a full therapeutic dose of an antimalarial or antimalarial combination to groups at increased risk of malaria. IPT clears existing asymptomatic infections and prevents new infections during the period immediately after treatment when protective blood levels are present. IPT is being evaluated in schoolchildren in two ways: intermittent parasite clearance in schools (IPCs) and seasonal malaria chemoprevention (SMC).

IPCs involves the administration of IPT on a periodic basis to schoolchildren, with the aim of clearing asymptomatic malaria infections and aiding hematologic recovery during the ensuing malaria-free period. Studies that have evaluated IPCs in school-age children are summarized in table 14.2. The first study of IPCs (called IPT in that study), conducted in schools in western Kenya, shows that IPCs with SP + AQ given once a term significantly reduced malaria parasitemia and anemia and significantly improved sustained attention (Clarke and others 2008). However, the spread of parasites resistant to SP, and the consequent withdrawal of SP and AQ in many East African countries, precluded further investigation of IPCs using these drugs in this area. Studies using alternative drugs, including dihydroartemisinin-piperaquine, conducted in a range of settings, show

effects on parasitemia, anemia, and clinical malaria similar to those obtained with SP + AQ, with a protective efficacy ranging between 54 percent and 99 percent reduction in malaria infection, and 38 percent to 60 percent reduction in anemia (Barger and others 2009; Clarke and others 2013; Nankabirwa and others 2010).

Several conclusions can be drawn from these studies.

- First, IPCs is highly effective in reducing the burden of malaria among school-age children.
- Second, the medication used for IPCs, and the timing of treatments, needs to be adapted to the local epidemiology.
- Third, IPCs is likely to be most effective in settings where a high proportion of children harbor asymptomatic infections, where malaria is a major cause of anemia, or both.

Seasonal Malaria Chemoprevention

SMC involves administration of treatment on a monthly basis to coincide with the annual peak in malaria transmission. This intervention is highly effective in reducing the incidence of clinical malaria and anemia in young children (Wilson 2011). In 2012, the WHO recommended implementation of SMC for children under age five years in areas of the Sahel subregion of Africa with highly seasonal transmission. This recommendation is being implemented increasingly widely in countries of the Sahel. Although less extensively researched, and not yet recommended by the WHO, evidence suggests that SMC is as effective in school-age children as in children under age five years (Barger and others 2009; Dicko and others 2008; Tine and others 2011, 2014), and Senegal provides SMC to children up to age 10 years.

Intermittent Screening and Treatment

An alternative to IPCs or SMC is intermittent screening and treatment (IST), an intervention in which individuals are screened periodically for malaria infection using an RDT, and those infected (whether symptomatic or not) are treated with a full course of an effective antimalarial agent or combination of agents. A population-based study of IST in Burkina Faso shows no impact on the incidence of clinical malaria in children under age five years or on malaria transmission (Tiono and others 2013); a cluster randomized trial in schools on the coast of Kenya, where transmission is low to moderate, finds no impact on health or cognition (Halliday and others 2014). Possible reasons for the absence of an impact in these studies are the inability of some of the currently available RDTs to detect low-density parasitemia, and the rapid rate of reinfection following treatment in the areas

in which these studies were done. The potential of this approach to control malaria in school-age children needs further investigation.

Vaccination

Development of an effective malaria vaccine has proved to be a major challenge, despite the exploration of many innovative approaches. One vaccine (RTS,S/AS01) has shown partial efficacy in a large-scale Phase 3 clinical trial and was given a positive opinion by the European Medicines Agency in July 2015 (RTS,S Clinical Trials Partnership 2015). However, the duration of protection provided by RTS,S/AS01 is relatively short, and vaccination in early life is unlikely to provide protection that lasts into school age. Only very limited data are available on the safety and immunogenicity of RTS,S/AS01 in school-age children (Bojang and others 2005). RTS,S/AS01 is the most advanced malaria vaccine, but several other vaccines are making steady progress (Schwartz and others 2012); in the longer term, vaccination may have an important role in the prevention of malaria in school-age children.

ECONOMICS OF MALARIA CONTROL IN SCHOOLS

Few economic analyses have evaluated malaria control among school-age children. A 2011 systematic review identified 48 studies that evaluated the cost-effectiveness of malaria interventions (White and others 2011), of which only two were conducted among school-age populations. The first study evaluated the cost-effectiveness of community-wide IRS programs among children ages 2–15 years in southern Mozambique (Conteh and others 2004). The financial costs per person covered in the rural area and peri-urban areas were US\$3.86 and US\$2.41, respectively. Using health facility records to estimate the number of infections averted, the economic cost per case of malaria parasitemia averted among those ages 2–15 years was US\$21.23.

The second study evaluated the cost-effectiveness of IPCs (Temperley and others 2008). The study estimated that the cost of IPCs delivered by teachers was US\$1.88 per child per year, with drug and teacher training constituting the largest cost components. The estimated cost per anemia case averted through IPCs was US\$29.84, and the estimated cost per case of malaria parasitemia averted was US\$5.36 (Temperley and others 2008). Another study investigates the cost of IST delivered through schools and estimates the cost of IST per child screened to be US\$6.61 (Drake and others 2011). These estimates

of cost and cost-effectiveness fall within the range of per capita costs of other malaria control strategies (White and others 2011), but they are more expensive than school-based deworming programs. However, the simultaneous delivery by teachers of both IPCs and deworming as part of an integrated school health package may yield economies of scope and increase cost-effectiveness. More studies are required on the cost-effectiveness of malaria control in schoolchildren.

It is also important to consider the effect of other ongoing malaria control measures because they will reduce malaria transmission in the wider community. In this situation, mathematical models of malaria can provide insight because they can simultaneously model multiple interventions and take into account the dynamics of malaria transmission, especially the mass effects of community interventions. For example, modeling of the cost-effectiveness of community-wide IST highlighted its value in medium-high transmission settings among school-age children, but only if it was continued indefinitely (Crowell and others 2013). The combined use of mathematical modeling and economic evaluation can help identify which interventions should be targeted specifically toward school-age children and which interventions should be delivered as part of community-wide malaria control.

CONCLUSIONS

On the basis of the available data, some recommendations can be made about the management of malaria in school-age children (box 14.1), but much more needs to be learned about the effectiveness of different approaches (box 14.2).

Better data are needed on the burden of malaria in school-age children. A standardized approach to data collection would improve the ability to monitor progress in this at-risk group. Systems to capture episodes of clinical and fatal malaria in school-age children do not need to be school based, but they should summarize data for this specific risk group.

The potential of serological tests to help in evaluating the burden of malaria in school-age children needs to be studied further. Improved information on the extent of the burden of malaria and on the socioeconomic consequences of malaria in this age group would enhance awareness at multiple levels.

- **Global level:** Policy makers and multilateral funding organizations would pay more attention to this issue.
- **National level:** Interactions among education, health, and potentially other sectors would be catalyzed.

Box 14.1

Policy Recommendations for the Control of Malaria in School-Age Children

National malaria control programs need to pay increasing attention to the problem of malaria in school-age children, as the proportion of cases of malaria in older children increases. Education about causes of malaria; its clinical features; and ways of diagnosing, treating, and preventing the infection should be an integral part of the curriculum of all schools in areas where the school-age population is at risk of malaria infection. All school-age children in high-transmission areas need to sleep under insecticide-treated bednets. School-age children who develop clinical malaria need to be able to recognize the nature of their illness and have easy and rapid access to reliable diagnosis and effective treatment, either in their schools or at nearby health facilities.

- **Local and individual levels:** Families that include schoolchildren would be better able to take the necessary steps to prevent and treat malaria.

Operational research is needed to determine how best to raise awareness of the importance of malaria, how to manage it, and how to improve the use of established control measures in this group. Improving the malaria-relevant content of school curricula will help children help themselves and equip them with the understanding needed to accept new approaches to the control of malaria, such as the value of blood testing for parasitological diagnosis to guide appropriate treatment. School-age children can become an important route for disseminating information on malaria control to the rest of the family.

Further studies are needed to understand the potential role of medications in preventing malaria in school-age children. Chemoprophylaxis, SMC, IPCs, and IST may all be beneficial, but it is not clear yet in which settings each might be most effective or cost-effective. Some chemoprevention is likely to be useful in high transmission settings. The cost-effectiveness of chemoprevention is likely to be lower in low transmission settings, where most recipients are unlikely to have malaria. However, the transmission threshold at which to introduce, or withdraw, chemoprevention will only become clear through the modeling of empirical data. The optimal characteristics of drugs for SMC, IPCs, and IST are likely to include low cost, a very good safety profile, exceptional tolerability, long

Box 14.2

Key Research Priorities for Malaria in School-Age Children

Epidemiology

- Acquisition of better knowledge of the magnitude and features of malaria in school-age children, especially in areas in which the overall incidence of malaria is declining

Pathogenesis

- Investigation both of the importance of malaria as a cause of anemia in school-age children and of how anemia is caused by the malaria parasite
- Investigation of the mechanisms by which severe, uncomplicated, and asymptomatic malaria impair cognition

Treatment

- Investigation of how malaria can be diagnosed using a rapid diagnostic test and treated effectively by school staff in different settings

Prevention

- Exploration of ways to improve coverage with insecticide-treated bednets among school-age children
- Investigation of the comparative advantages and cost-effectiveness of screening and treatment programs and of intermittent preventive treatment in the prevention of malaria in school-age children in high-risk areas, and investigation of the circumstances that favor either approach
- Exploration of the potential for vaccination to prevent malaria in school-age children

Economic and social consequences

- Acquisition of better knowledge of the socioeconomic consequences of malaria in school-age children, and the costs and benefits of individual malaria control measures in this age group

half-life, and single-dose treatment. The development of a rigorous target product profile would help guide the development of drugs suitable for use in the prevention of malaria in school-age children. The potential of IST programs to identify and help not only individuals but also communities at elevated risk of malaria warrants further exploration.

More effective control of malaria is only one part of the drive to improve the health and potential of school-age children. More work is needed to determine how and when to integrate malaria control strategies with other school-based programs at the local and national levels.

ANNEX

The annex to this chapter is as follows. It is available at <http://www.dcp-3.org/CAHD>.

- Annex 14A. Estimates of Parasitemia and Clinical Disease among School-Aged Children in Africa

NOTES

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World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - a) lower-middle-income = US\$1,046–US\$4,125
 - b) upper-middle-income (UMICs) = US\$4,126–US\$12,745
- High-income countries (HICs) = US\$12,746 or more

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