Impact of malaria control and enhanced literacy instruction on educational outcomes among Kenyan school children: a multi-sectoral, prospective, randomised evaluation

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Note to readers

This impact evaluation has been submitted to 3ie in partial fulfilment of the requirements of grant OW2.065 issued under Open window 2. 3ie has accepted the draft final report version as being technically sound, and no substantive changes are expected in the data or findings. At this stage, 3ie is continuing to work with the grantee to complete a final version. The authors retain sole responsibility for the content of their draft report and for any errors or omissions. It does not reflect the views of 3ie, its donors or its Board of Commissioners. Any comments or queries should be directed to the corresponding author, Simon Brooker: sbrooker@nairobi.kemri-wellcome.org

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List of Acronyms

AL	Artemether lumefantrine
AS	Artesunate
CHW	Community health worker
DMC	Data monitoring committee
DOMC	Division of Malaria Control
FGDs	Focus group discussions
FU1	Follow-up 1
FU2	Follow-up 2
GEE	Generalised estimating equations
IDI	In depth interview
IPT	Intermittent preventive treatment
IST	Intermittent screening and treatment
HALI	Health and Literacy Intervention
Hb	Haemoglobin
KEMRI	Kenya Medical Research Institute
KES	Kenyan shillings
KESSP	Kenya Education Sector Support Programme
LLIN	Long-lasting Insecticide-treated net
MoPHS	Ministry of Public Health and Sanitation
NAC	National Assessment Centre
NMS	National Malaria Strategy
RDT	Rapid diagnostic test
SACMEQ II	Southern African Consortium for Monitoring Educational Quality
SES	Socioeconomic status
SP-AQ	Sulfadoxine-Pyrimethamine and Amodiaquine
SSA	sub-Saharan Africa
TAC	Teacher Advisory Centre
TEA-Ch	Tests of everyday attention for children
WHO CHOICE	CHOosing Interventions that are Cost-Effective

Abstract

Background: Improving the health of school-aged children can yield substantial benefits for cognitive development and educational achievement. However, there is limited experimental evidence on the benefits of school-based malaria prevention or how health interventions interact with other efforts to improve education quality. This impact evaluation aimed to evaluate the impact of school-based malaria prevention and enhanced literacy instruction on the health and educational achievement of school children in Kenya.

Methods: A factorial, cluster randomised trial was implemented in 101 government primary schools on the south coast of Kenya, 2010-2012. The interventions were (i) intermittent screening and treatment (IST) of malaria in schools by public health workers using rapid diagnostic tests (RDTs), once a school term; and (ii) training workshops and support for teachers to promote explicit and systematic literacy instruction. Schools were randomised to one of four groups: (i) receiving either the malaria intervention alone; (ii) the literacy intervention alone; (iii) both interventions combined; or (iv) control group where neither intervention will be implemented. A total of 5233 children from Classes 1 and 5 were randomly selected and followed up for 24 months. The primary outcomes are educational achievement and anaemia, the hypothesised mediating variables through which education is affected. Secondary outcomes include malaria parasitaemia, school attendance and school performance. Data were analysed on an intention to treat basis. A nested qualitative evaluation investigated the community acceptability, feasibility and cost-effectiveness of the interventions. The study is registered with ClinicalTrials.gov, NCT00878007.

Results: During the intervention period, an average of 88.3% children in intervention schools were screened for malaria at each round, of whom 17.5% were RDT-positive. 80.3% of children in the control and 80.2% in the intervention group were followed-up at 24 months. No impact of the malaria IST intervention was observed for prevalence of anaemia or *P. falciparum* at either 12 or 24 months or on scores of classroom attention. No effect of IST was observed on educational achievement in the older class, but an apparent negative effect was seen on spelling scores in the younger class at 9 and 24 months and on arithmetic scores at 24 months.

In contrast, there was a significant impact of the literacy intervention on key educational outcomes. Significant improvements were observed in the intervention group compared with the control group at 9 months for two of the three literacy assessments, with a mean adjusted difference in spelling scores of 1.43 (95% CI 0.86, 2.00; p<0·001) and in Swahili sounds scores of 5.28 (95% CI 3.18, 7.39; p<0·001) between study groups. The significant impact of the literacy intervention on these outcomes was sustained at 24 months and was also observed in Swahili word reading, with a mean difference of 2.30 (95% CI 0.03, 4.58; p=0.047) observed between intervention and control groups. The positive impact of the literacy intervention appears to be primarily mediated through two key factors observed in the intervention schools, the increased time children spent reading in class and the increased print displayed in the classrooms.

Conclusion: We conducted the first cluster-randomised trial of the impact of school-based intermittent screening and treatment (IST) of malaria. We failed to detect any overall benefit of IST using AL on the health, attention or educational achievement of school children in this low-moderate malaria transmission setting. However, school screenings using RDTs could provide an operationally efficient method to identify transmission hotspots for targeted community control. The literacy intervention had a significant impact on literacy outcomes specifically knowledge of Swahili sounds, words and English spelling in this setting. Teachers in the intervention group had an increased focus on oral language development through letters and sounds, with increased student time spent reading and exposure to text shown to be key contributors to improved literacy performance. Thus simple measures such as displaying more text in the classrooms with which children can interact can significantly improve educational performance.

Interventions, evaluation questions, and policy relevance

Two interventions are being delivered through schools: (i) a malaria control strategy based on intermittent screening and treatment; and (ii) a literacy intervention based on a programme of training and support for class 1 teachers. Both interventions were developed within the context of current government strategies and guidelines and were designed to be affordable and replicable on a large scale, within existing programmes.

Malaria control

This intervention is based on intermittent screening and treatment (IST) for malaria and builds on a previous study evaluating the impact of intermittent preventive treatment (IPT) of malaria [1]. In that study, all children received a full course of the anti-malarials sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) once a school term, irrespective of whether children are infected, which resulted in a 48% reduction in the rates of anaemia and large improvements in children's sustained attention in class. However, changes in Kenya drug policy in 2009 led to the withdrawal of both AQ mono-therapy, because of future plans to combine the drug with artesunate for combination therapy, and SP, for which there are high levels of drug resistance in East Africa [2]. No other anti-malarials were identified as suitable for IPT in schools. Therefore, following extensive consultations with Kenyan policy makers and national and international malaria experts, the alternative of IST was identified. This intervention had previously been identified in the Kenya National Malaria Strategy, 2009-2017, under a newly launched *Malaria-free schools initiative* [3].

In IST, all children are screened for malaria using a rapid diagnostic test (RDT) once a school term. The RDT used is a ParaCheck-*Pf* device (Orchid Biomedical Systems, Goa, India) which is able to detect *P. falciparum* and other (unspecified) *Plasmodium* species. Children (with or without malaria symptoms) found to be RDT-positive are treated with artemether-lumefantrine, AL (Coartem®, Novartis), an artemisinin-based combination therapy. Screening and treatment is administered by district health workers and supported by the Division of Malaria Control (DoMC), Ministry of Public Health and Sanitation (MoPHS).

On day 1, children are screened by a laboratory technician using a RDT (Figure 1). Those children found to be RDT-positive are given milk and biscuits and then given the first dose of AL. Parents or older siblings of children are called and a nurse explains that their child is infected with malaria parasites and requires treatment (assuming they are not already taking medication). The parents/older siblings are given the second dose of AL and told that this should be taken in the evening with food. On day 2, the nurse returns to the school, gives the third AL dose to children and provides the parent/older sibling with the fourth dose. Children absent from school are followed up at their home and provided with the doses. On day 3, the procedures are the same as day 2. During follow-up visits, nurses monitor for potential side effects of treatment.

Figure 1. School children being screened for *Plamodium falciparum* infection by laboratory technicians from the district hospital and health centres.

The first round of screening and treatment was conducted in March 2010, the second round in June/July 2010, the third in September 2010, the fourth in March 2011 and the final round in September 2011.

Enhanced literacy instruction

The second component of our study is concerned with evaluating a low cost sustainable intervention to improve literacy instruction. An additional aim was to obtain causal data on two key questions to inform policy making:

1. Which instructional practices are most effective at improving early literacy skills? This is addressed through the development and analysis of a theory-based instructional intervention driven by observations of teacher behaviors before the intervention began.

2. What is the best way to ensure that teachers conduct the most effective practices in classrooms? The HALI project involves two different strategies for achieving this goal: (i) a teacher manual, which includes a set of lessons plans for class 1 teachers in English and Swahali, and which is introduced through in-service training workshops; and (ii) weekly text messages to support teachers' practice.

The final design of the literacy intervention was based on a comprehensive survey of existing literacy instruction practices in the study area [4] and an analysis of how these practices can be developed to align more closely with current evidence on how best to promote successful literacy acquisition [5-6]. The lessons included in the teacher manual are designed to be used on a daily basis and are appropriate for developing beginning reading skills in an alphabetic language. They include letter-sound relationships, blending, spelling, connected text, developing a concept of word in text, phonological awareness, vocabulary, and reading comprehension. The 140 sequential lessons are structured to guide the teacher in what to say, what to do (i.e. with their hands or materials), which instructional materials to use, and the estimated time of the lesson. The plans build from existing teaching methods (e.g. choral repetition, use of song) and show teachers how these methods can be modified slightly to promote successful beginning reading instruction.

The literacy intervention was conceptualized to be compatible with successful models of literacy acquisition in an alphabetic language while taking into account the current teaching practices we had observed in the area [4] as well as the perceived barriers to successful instruction. Importantly, the literacy intervention was not intended to be an independent curriculum for teaching reading in English and Swahili. Instead, the goal was to supplement the existing curriculum with methods to develop foundational literacy skills that did not have adequate attention previously.

Teachers implemented the literacy intervention as part of their routine teaching activities. Training workshops and weekly text message exchanges were implemented by the HALI team. The initial training workshops were held between February and March 2010 and sought to provide Class 1 teachers with background information about how children learn to read, to explain how to use the provided teacher manual and to give them the opportunity to customize materials for use in their classroom.

Following the workshop, the study teams communicate weekly with teachers using text messages providing brief instructional tips and motivation to implement lesson plans. A response is required in order to receive a small amount of credit for their mobile phones which facilitates and provides an incentive for further communication. The average response rate averaged 87% for the 37 weeks that we asked a question in year 1 and 84% in year 2. Each week teachers are requested to complete a Weekly Summary Sheet that documents which lessons they used, what worked well, and suggestions for improvement. Two day-long follow-up workshops were conducted, one in June 2010 when teachers learnt additional instructional methods, received and shared feedback and another in February 2011 as the students entered class 2.

Evaluation questions

Our evaluation is called the Health and Literacy Intervention (HALI) project. The main aim of the HALI project was to evaluate the impact and causal pathways for effects of the two interventions on the learning and education of school children in Kenya. The main questions that were examined are detailed in Box 1 below.

BOX 1: Key evaluation for the HALI project

1. quantify the impact of the malaria programme in improving classroom attention, school attendance, and educational achievement of children in school;
2. quantify the impact of the literacy programme in improving early grade reading;
3. determine whether health and education interventions work synergistically together, such that learning is improved only when teaching is effective and children are healthy enough to benefit from it;
4. identify the causal mechanisms by which malaria prevention and improved instruction may help develop literacy skills, using a developmental model of stages of competence in literacy;
5. analyse the costs and cost-effectiveness of the programmes;
6. assess the extent to which programmes are acceptable, feasible, affordable and can be easily implemented in order to inform the scaling-up of programs across Kenya.

Policy relevance

There are two key policy landscapes that relevant to our study – the health sector and the education sector - and we sought to provide the most relevant information to policy makers in the health and education constituencies in Kenya and elsewhere.

Malaria control policy and implementation in Kenya is guided by the National Malaria Strategy (NMS) [7]. In 2009, Kenya launched its second NMS, for the period 2009-2017. This plan details the key strategic objectives and targets that the national malaria control programme should achieve during the implementation period. The main objectives of NMS strategy are:

- To have at least 80 per cent of people living in malaria risk areas using appropriate malaria preventive interventions by 2013 through universal LLIN coverage for populations at risk, indoor residual spraying in targeted areas for disease burden reduction, and prevention of malaria in pregnancy.
- To have 80 per cent of all self-managed fever cases receive prompt and effective treatment and 100 per cent of all fever cases who present to health facilities receive parasitological diagnosis and effective treatment by 2013 by strengthening capacity for malaria diagnosis and treatment, increasing access to affordable malaria medicines through the private sector, and strengthening home management of malaria.
- To ensure that all malaria epidemic prone districts have the capacity to detect and the preparedness to respond to malaria epidemics annually by 2010.
- To strengthen surveillance, monitoring and evaluation systems so that key malaria indicators are routinely monitored and evaluated by 2011 through capacity strengthening for malaria surveillance, routine monitoring and operational research.

Priority is given to decentralizing malaria control operations to the implementation level and strengthening malaria control performance monitoring and evaluation. A new key component of the 2009-2017 NMS was a *Malaria-free Schools Initiative* which has the explicit goal of reducing the burden of malaria among Kenyan school children. Identified among possible prevention strategies that could be implemented through schools was intermittent screening and treatment of asymptomatic school children. It was this intervention that our study sought to evaluate.

Any malaria intervention implemented through Kenyan schools would need to be mainstreamed into current school health activities undertaken by the Ministry of Education and its school feeding, nutrition and health programme. The goal of this programme is to “enhance the quality of health in school communities by creating a healthy and child friendly environment for teaching and learning”. The programme currently implements a package of deworming and school feeding across Kenya and has expressed demand to integrate malaria control into its activities.

At the international level, the World Bank and WHO’s Global Malaria Programme recognises the important role of malaria control in schools and wishes to obtain a stronger evidence base to inform policy recommendations.

The commitment of the Kenya government to helping school children do well at school and to stay healthy is indicated by its implementation of the Kenya Education Sector Support Programme (KESSP), whose overarching goal is of enhancing access, equity, and quality at all levels of education and training. The Ministry of Education welcomes an emphasis on in-service training and seeks evidence that systematic instruction is essential for progress in early grading reading and educational achievement overall. In-service training at the local level is supported by a zonal-based teacher advisory system of over 1000 Teacher Advisory Centre (TAC) tutors who provide an effective group-based support service to teachers. The training workshops and on-going support of the literacy intervention is implemented with full support of the TAC tutors and this helps enhance policy relevance at the local level.

A key educational sector partner in ensuring the policy relevance of our study work at the national level is the Ministry’s National Assessment Centre (NAC), which is responsible for managing partnerships with external researchers. Technical input on project design was sought primarily from the technical committee of the NAC including representatives from the Directorate of Quality Assurance and Standards, the Department of Primary Education, the Department of Policy and Planning, Kenya National Exams Council, the National Assessment Center and the Kenyan Institute of Education. Our study has also collaborated directly with the Director of Quality Assurance and Standards which supports the Ministry’s key strategy “to identify, assess and test promising and relevant alternative teaching and learning methods to support more equitable, high quality and/or more efficient practices in the education.”

On a global stage, improving early grade literacy is at the top of the policy agenda as evidenced by two recent global meetings. (i) The All Children Reading Workshop organized for policy makers in sub-Saharan Africa (SSA) by the Global Partnership for Education was held in Kigali in March 2012. (ii) The World Literacy Summit, held in Oxford April 2012, led to the Oxford declaration which called for action on five fronts, one of which was the need for ‘A strong evidence base for why universal literacy is fundamental to an individual’s and country’s success and evidence on strategies and best practices that are having the greatest effect’. The declaration highlights the importance of teaching training programmes and in-service teacher training on effective teaching strategies. The report notes that “Commitment to research authenticated strategies will be our standard and application of these strategies our mantra. An example of such an instructional strategy would be phonics …. rather than rote recitation.” This statement illustrates that the questions addressed by our project are consistent with the global consensus on policies for improving literacy instruction.

Literature review

Malaria among school children and school-based control

Globally, malaria poses an enormous public health burden, with the majority of clinical episodes due to *Plasmodium falciparum* occurring in sub-Saharan Africa [8]. In areas of moderate or high malaria transmission, mortality is greatest among young children. Older children and adults, who have been regularly exposed to malaria, typically acquire immunity to clinical malaria and most malaria infections generally remain clinically asymptomatic. However, though mortality and morbidity may be low in areas of high malaria transmission, it is not insignificant, and is of potential importance for the health and education of schoolchildren. For example, chronic asymptomatic *Plasmodium* infection is a known contributor to anaemia [1,9-11]. The mechanisms by which malaria causes anaemia are still not fully understood but include haemolysis of infected and non-infected red blood cells and bone marrow suppression. Malaria can also contribute to iron deficiency by increasing demands for iron, as a result of enhanced erythropoiesis to compensate for haemolysis, and through interference with hepcidin regulation of iron uptake by erythrocytes.

Infection may have additional consequences for children's cognitive performance and ultimately educational achievement [12-19]. For instance, malaria has been related to increased absenteeism [20-22], grade repetition [23], and poorer educational achievement [20,24]. Again, the precise mechanisms are unclear, but among children who have experienced cerebral malaria, it is likely that some physical damage to the brain occurred during the acute episode. Possible pathways for how symptomatic malaria affects cognitive and education are assumed to be indirect, through the effect of anaemia, direct, possibly involving an immunological pathway [25], or a combination of both pathways.

Historically, school-based delivery of malaria chemoprophylaxis was associated with significant reductions in malaria-related morbidity and mortality, and improvements in educational outcomes [26-27], but fell out of use in Africa due to financing problems [28] and with the emergence of malaria drug resistance [29]. More recent evidence suggests that weekly chemoprophylaxis can improve school examination scores [30], but tends to be compromised by declining compliance and coverage over time.

An alternative strategy, which is currently recommended for young children and pregnant women, is intermittent preventive treatment (IPT) – the periodic mass administration of a full therapeutic course of antimalarial drugs, regardless of infection status. In a cluster randomised trial in western Kenya, we previously evaluated the impact of IPT with sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) and found a 48% reduction in the rates of anaemia and a large effect size of 0.48 standard deviations (SD) on children's sustained attention in class [1]. These findings highlight the adverse effect of asymptomatic malaria. Other researchers found that IPT using SP and artesunate (AS) in an area of moderate seasonal malaria transmission in Mali not only reduced rates of anaemia and parasitaemia among school-aged children but also rates of clinical attacks [11].

Recent changes in national drug policies in many African countries, especially in East Africa where SP resistance is widespread [2], preclude the current use of SP and AQ, some of the drugs previously used in IPT, thereby limiting its potential implementation. An alternative school-based malaria control strategy is intermittent screening and treatment (IST), using rapid diagnostic tests (RDTs) to screen and treat asymptomatic children. Recent studies in Ghana found IST in pregnant women to be equally efficacious as IPT [31] and acceptable to patients [32]. The current study therefore aimed to evaluate the impact of school-based IST on both the health and education of school children.

Interestingly, whilst the Kenya evaluation found a positive impact on cognition, no effect of IPT on educational achievement was observed. Possible explanations for such a finding are that children were not given the educational resources (such as quality instruction) or a sufficient period of prolonged instruction to learn effectively during the time course of the evaluation. To achieve a measurable impact on education, it may also be necessary to improve teaching methods in order to capitalise on any improvements in health status of school children following malaria control. Thus, a second aim of our evaluation was to evaluate the impact of an education intervention and its possible interaction with malaria prevention.

Improving literacy levels

Our study focused on literacy as poor early literacy achievement is a global problem, especially in SSA [33]. A complexity of contextual factors, including poverty and limited access to print, contribute to delayed reading acquisition [34-37], and it is not possible for schools to readily change such contextual factors.

One factor that schools can influence is the way in which classroom teachers teach reading [38-39], with evidence suggesting that students do best when literacy skills are taught in an explicit, systematic and appropriate way [6]. *Explicit* means that the concept is directly taught and modeled so the student does not have to infer what the teacher means. *Systematic* instruction progresses in a sequence moving from easiest to more difficult. Among other skills, teaching sound-to-symbol relationships, phonological awareness, and comprehension have been shown to reduce reading difficulties [5,40] and increase reading achievement in the United States [41]. Learning to read any alphabetic system depends on understanding the relationship between sounds and the letters that represent them. Regardless of context, students who do not have this insight are likely to struggle with reading.

Despite the growing consensus that promotes the development of literacy skills in an explicit and systematic manner, educators in some developing countries are only just beginning to teach skills that are known to improve literacy levels [42-43] and this contributes to the observed poor literacy levels. The Southern African Consortium for Monitoring Educational Quality (SACMEQ II) assessment project provides some information about Kenyan students' reading abilities. It found that 21% of sixth grade students reached a *desirable level* of reading (i.e. guaranteed to cope with the next year of schooling) and 66 percent reach the designated *minimum level* (i.e. would barely survive during the next year of schooling) [44].

The Kenyan national education policy specifies the use of the *mother tongue* (i.e., the local language spoken in a student's home) as the language of instruction in classes 1 through 3. After three years of instruction in the mother tongue, national policy states that English should be used in class 4 and thereafter. Swahili (also known as Kiswahili) is Kenya's national language and the lingua franca of the region and is taught as a subject to all students starting in grade 1. Although the language-of-instruction policy appears to be clear, practical implementation is less straightforward. A lack of instructional materials in mother tongue and a concern that students who do not begin instruction in English upon school entry will be disadvantaged when they take exit exams combine to increase the use of English in the early primary grades [44-45]. Our own analysis [4] found that attention to developing oral language skills is prioritized over teaching the relationships between sounds and symbols in our study site. Based on this analysis of current practices in Kenya, a training intervention for improved literacy instruction was developed that was rooted in the current strengths of Kenyan teachers (oral language development) but that would encourage the explicit and systematic teaching of letter-sound relationships.

Theory of change

The theory of change for this project is illustrated in Figure 2 with mechanisms for the two interventions, and the interaction between them, described below. Figure 3 presents a conceptual framework on how the quantitative and qualitative evaluation methods assess the impact of the malaria intervention and the literacy intervention.

Malaria intervention

Intermittent screening and treatment is hypothesized to improve educational achievement through two pathways. Treatment may prevent clinical attacks of malaria which leads to school absenteeism [20-22]. A growing literature demonstrates that children in most resource-poor settings spend only a small proportion of the allocated school time present in classrooms learning from the teacher. Pupil absenteeism is clearly a contributor to missed opportunities to learn and to poor academic achievement. Malaria treatment may also reduce anemia and consequently levels of fatigue. Evidence suggests that the cognitive functions most affected by such fatigue are the executive functions of attention and control [1]. Other research [46] suggests that these executive function skills are important for early achievement. The ability to pay sustained attention to the teacher and to reading material is a key component of learning and is hypothesized to play a role in the direct impact of malaria treatment on educational achievement and also in the interaction between the two interventions: children who can sustain attention for longer periods will benefit more from the enhanced instruction provided in the literacy intervention.

The relative contribution of the two pathways depends on the epidemiological context of the intervention. In areas where acquired immunity to malaria is limited clinical attacks will be more prevalent and we would expect to see more malaria-related school absenteeism. Where school children have partial immunity to the disease we would expect fewer clinical attacks and fewer instances of school absenteeism but we would hypothesize that children will be less able to concentrate in class due to malaria-related anemia.

Literacy instruction intervention

The literacy instruction intervention is characterized as a sequence of causally related behaviour changes. In the first instance teachers attend a training workshop where they are given new knowledge and skills as well as practical guides and lessons plans. The expectation is that teachers' instructional methods will consequently change as a result of the training, through the use of the scripted lesson plans and with text-message support. The instruction is targeted at developing children's skills through distinct, predictable phases of literacy acquisition from emergent reader, to beginning reader, to instructional reader. In this process of development children first acquire knowledge of letters and sounds and the relationship between them, they then improve decoding skills and word recognition before increasing their ability to read and understand connected text. Once comprehension is developed children can read to learn and the gateway to educational achievement is opened across all subjects.

Figure 2. The hypothesised causal pathways through which the malaria and literacy interventions are assumed to improve educational achievement. Open rectangular boxes indicate secondary and mediating outcomes; the incidence of clinical attacks is not measured. Circle boxes indicate contextual variables measured at household and school levels.

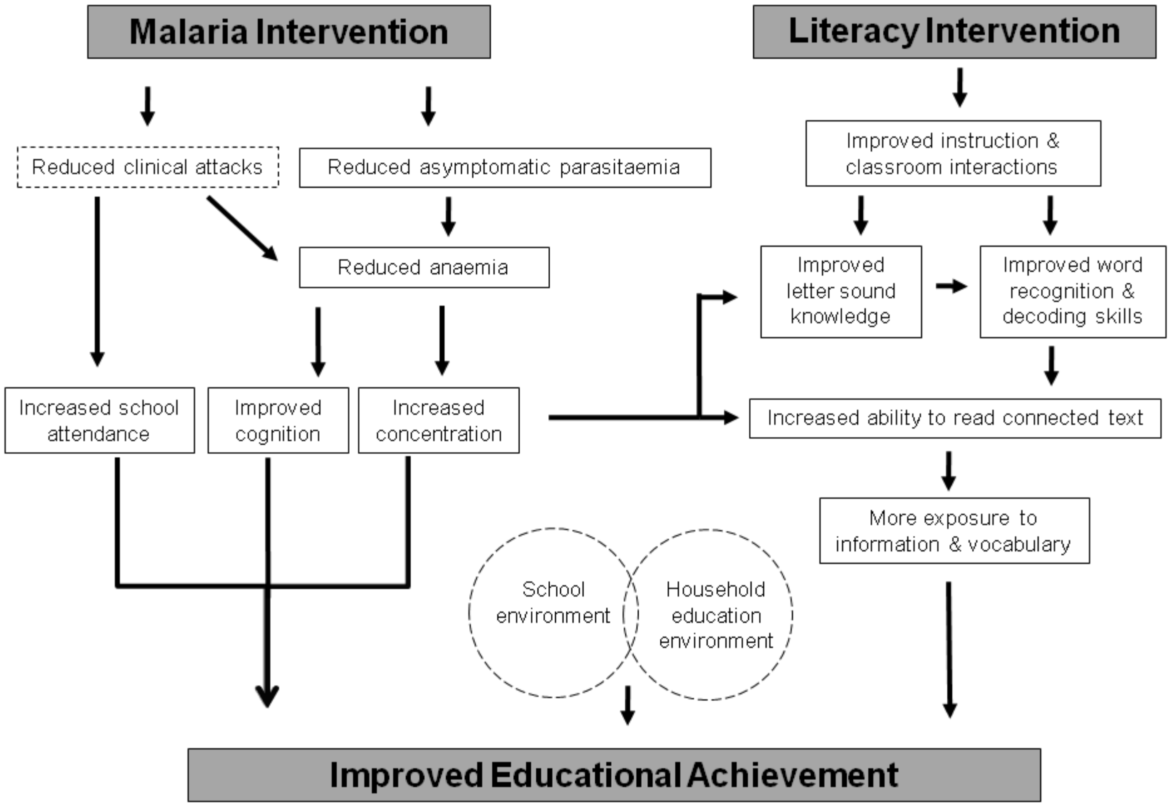
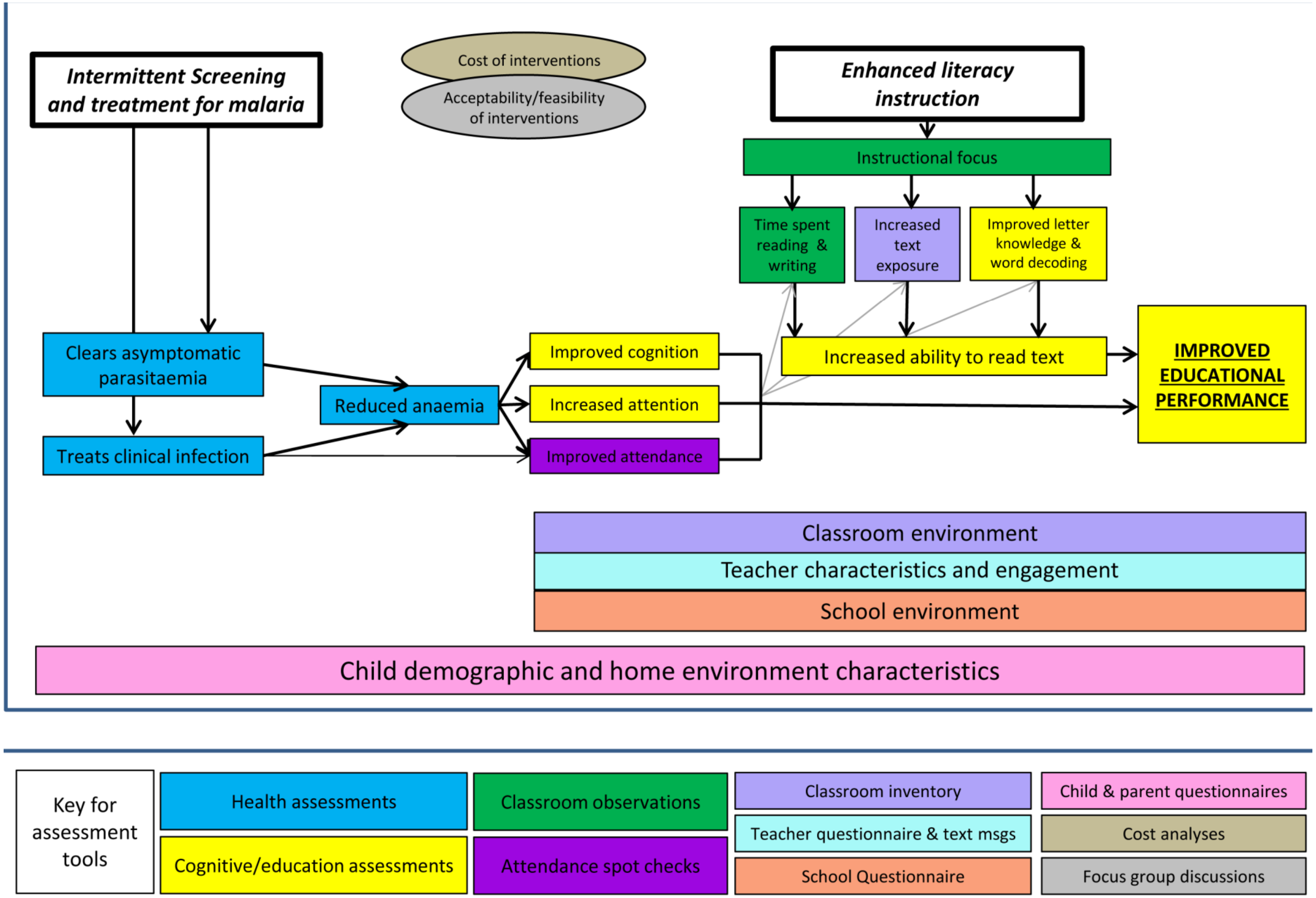


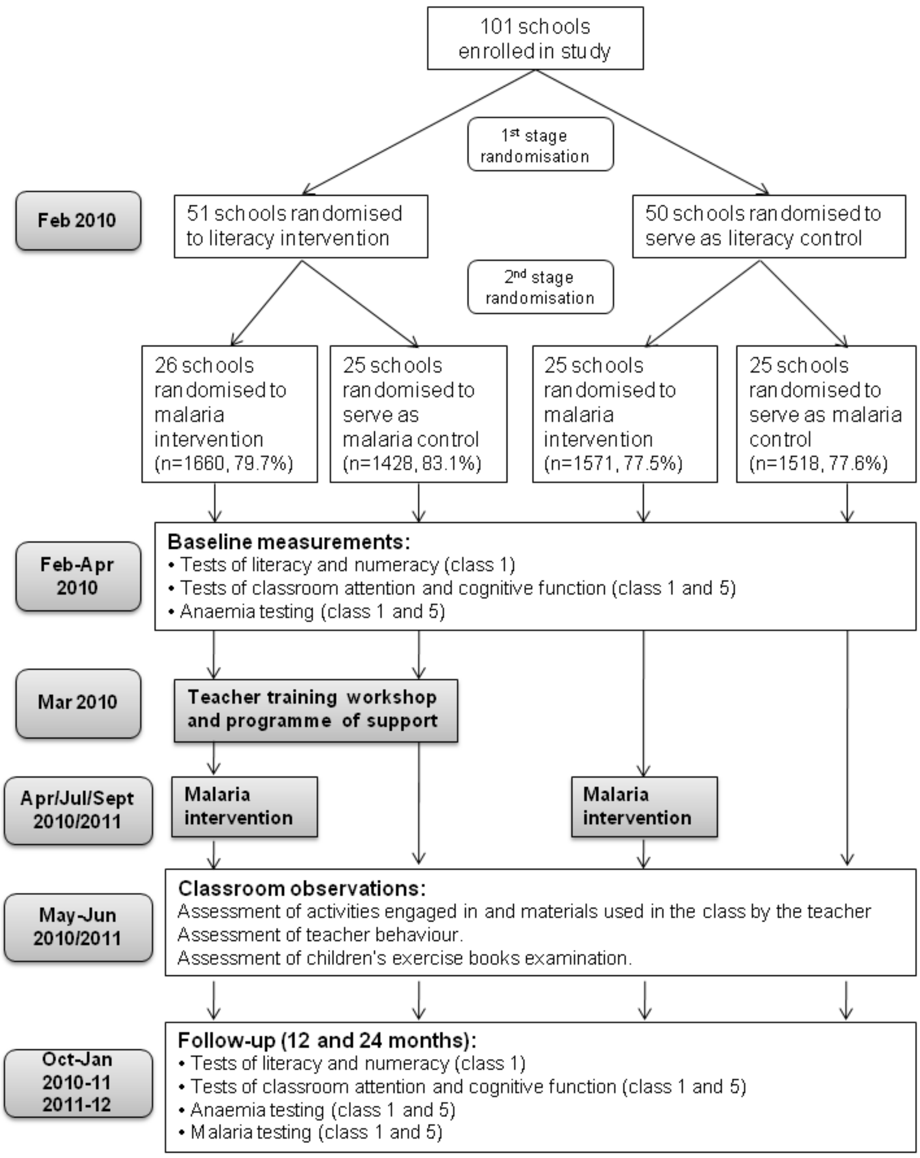
Figure 3. Conceptual framework on how the quantitative and qualitative evaluations assess the impact of the malaria intervention and the literacy intervention.



Evaluation design

The impact of the two interventions was evaluated through a cluster randomised trial, in which 101 schools were randomised to one of four groups: (i) receiving either the malaria intervention alone; (ii) the literacy intervention alone; (iii) both interventions combined; or (iv) control group where neither intervention was implemented. Children from classes 1 and 5 were randomly selected and followed up for 24 months to assess the impact of the two interventions. Both classes received the malaria intervention, but the literacy intervention was targeted only towards Class 1 as this is when children learn to read. This was an unblinded study as, following randomization, schools were aware of whether or not they received the malaria or literacy interventions. The timeline and flowchart of the study design is shown in figure 4.

Figure 4. Flowchart of randomisation and study design. The percentages refer to the percentage of children who were invited to participate in the study that provided informed consent and enrolled in the trial.

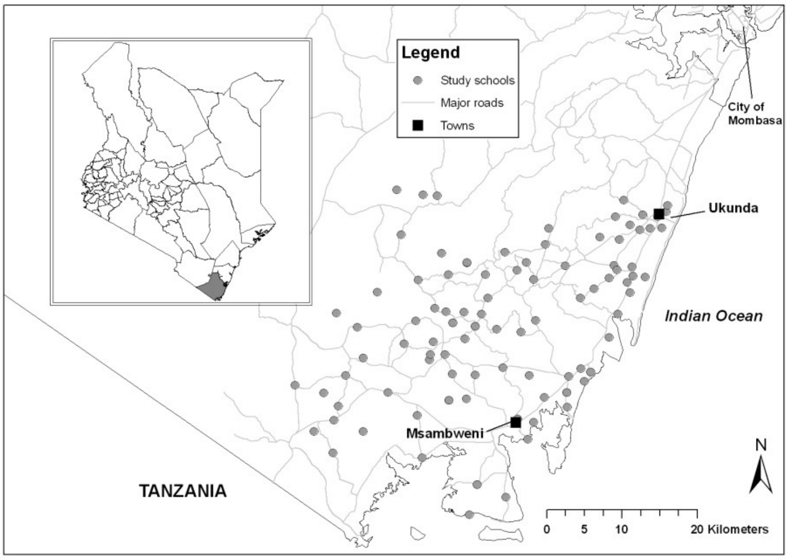


Sampling design and power calculations

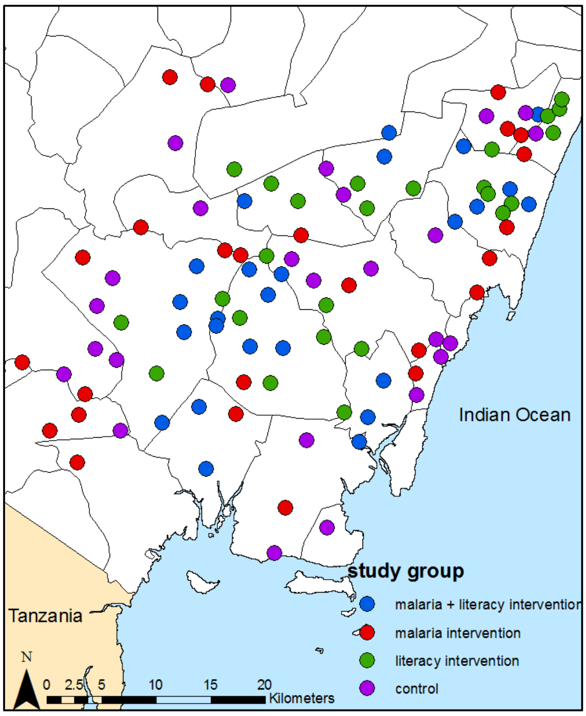
The study was conducted in rural government primary schools in Kwale and Msambweni districts, situated approximately 50 km south from Mombasa on the Kenyan coast (Figure 5). There are 85 schools in Kwale District and 112 schools in Msambweni District. In Kwale District, a different study was evaluating the impact of an alternative literacy intervention in two of the four zones; therefore only 20 schools in Mkongani and Shimba Hills zones were included in our study allowing the two interventions to proceed without leakage. In Msambweni District, we selected 81 of 112 schools; schools in Lunga Lunga and Mwereni zones about 70 km away from the project office, were excluded because of time and costs involve in travelling to them.

Figure 5. Map of (a) study areas in Kwale and Msambweni districts, Coastal Kenya. Insert: Map of Kenya with Kwale and Msambweni districts shaded in grey and (b) study schools in Kwale and Msambweni districts, Coastal Kenya showing the geographic distribution of schools to study groups.

(a)



(b)



Allocation of schools

Random allocation of the 101 schools to study group was conducted in two stages, each involving public randomisation ceremonies. These ceremonies were considered important in assuring participating schools and stakeholders of the fairness and transparency of the allocation and represented a simple way of allocating schools to the four different groups.

In stage one, groups of schools were randomised either to receive the literacy intervention or to serve as a literacy control school. In Kenya, schools are grouped by the District Education Office into so-called *school clusters* of between 3 and 6 schools, which regularly meet and share information, supported by a Teacher Advisory Centre (TAC) tutor. The 101 schools are grouped into 26 clusters. Randomisation was stratified by (i) cluster size, to ensure equal numbers of schools in the experimental groups; and (ii) average primary school leaving exam scores across the cluster, to balance the two groups for school achievement. The randomisation procedure was designed to minimize contamination across clusters. It is still nonetheless possible that following the training workshop, teachers from the intervention schools will have discussed their training with teachers from control schools. This is often unavoidable in studies evaluating education interventions but it is unlikely that teachers from control schools will obtain the complete set of training materials.

In stage two, the malaria intervention was randomly allocated amongst the 51 schools allocated to the literacy intervention and the 50 schools allocated to serve as literacy control schools during the first randomisation. Schools were stratified by average primary school leaving exam scores into 5 quintiles and by literacy intervention group, producing 10 strata overall. Prior the randomization ceremony, computer simulations were conducted to investigate the probability that all schools in a cluster could randomly receive the same malaria group allocation, thereby limiting the potential for independent analysis of the effects of literacy and malaria interventions. Contamination of the malaria intervention was unlikely since only children in the malaria intervention schools will be visited by district health workers and screened, and treated if found positive. Randomisation resulted in only one cluster where all schools received the same malaria group allocation.

Sample size estimation

Based on discussions with the Division of Malaria Control, Kenya Ministry of Public Health and Sanitation and previous studies on malaria and anaemia in school children (Clarke et al. 2008), the malaria intervention was considered to have public health value if a reduction of at least 25% in anaemia was achieved. Such a reduction can be achieved with a sample size of 27 schools in each malaria intervention arm with 50 children sampled per school for an assumed baseline prevalence of 20%, coefficient of variation of 0.2, power of 80% and significance level of 5%.

Sample size calculations for educational outcomes were calculated separately for classes 1 and 5 based on mean differences in test scores between the intervention and control schools for the malaria and literacy intervention separately. A sample size of 100 schools with 25 children per class per school was assumed for each calculation. For achievement tests, this is sufficient to detect an effect size of 0.192 standard deviation (SD) with 80% power at the 5% significance level assuming an intra-class correlation (ICC) of 0.2 (ICC varied from 0.1 to 0.2 with mathematics and literacy tests in class 2 in a previous impact evaluation in western Kenya [1]) and a correlation between baseline and final outcomes of 0.7. Under the same conditions, except for a change in ICC this sample size is sufficient to detect an effect size of 0.15 SD for tests of sustained attention, which have a lower ICC of 0.1.

Data collection

Sensitization and recruitment

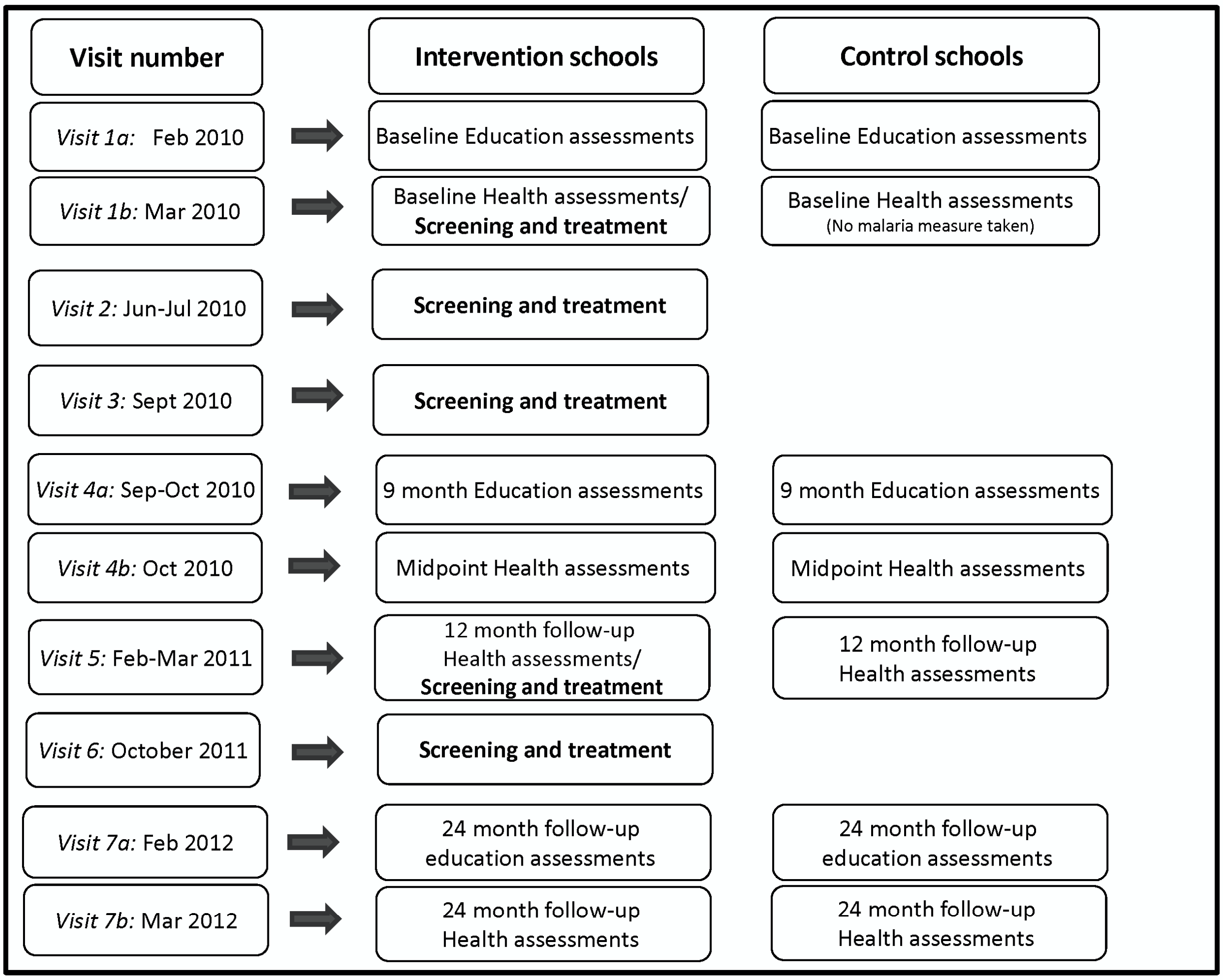
Sensitization took place at national, provincial and district levels before visiting the schools. At the national level, the study was approved by the Division of Malaria Control, Ministry of Public Health and Sanitation and the Director of Basic Education, Ministry of Education. At provincial and district levels, meetings were held with the Provincial Medical Officer and the Provincial Director of Education in Mombasa, as well as district health and education officials in Kwale and Msambweni. Finally, school head teachers and Teachers' Advisory Centres (TAC) tutors were informed of the study.

Prior to randomisation, enumeration of children in all schools was carried out through school visits in January and February 2010. Subsequently, school meetings were held with parents and guardians of children to explain all aspects of the study, emphasizing that the participation of their children in the study was voluntary and they had the opportunity to opt out of the study at any time. There was an opportunity to ask questions. Written informed consent was sought from parents or guardians. If parents failed to attend these meeting, home visits were undertaken to obtain consent. The eligibility criteria for inclusion into the study were as follows: enrolled at participating schools in Classes 1 and 5; provision of informed consent from parent or guardian; and willingness of the child to participant. Exclusion criteria include parents or guardians unwilling to provide informed consent; an unwillingness of the child to participant; known allergy or history of adverse reaction to study medications; and known or suspected sickle-cell trait (these children were referred to testing and/or clinical management as per national guidelines).

Timeline

Following recruitment, baseline health and education surveys were undertaken in January-February 2010, which were followed by the first round of IST and the teacher training workshop. Classroom observations occurred in May 2010, followed by the second round of IST in June-July 2010. The third round of IST occurred in September 2010. The first follow-up education surveys occurred in November 2010 and the first health surveys in February and March 20111, followed by a round of IST as well as refresher teacher training for the literacy intervention. The final round of IST was conducted in September 2011 with the 24 months follow-up health and education survey in February-March 2012. Figure 6 shows the timing of rounds of screening and treatment in relation to baseline and follow-up surveys. In the study area, the malaria transmission is seasonal following the two rainy seasons, April-July and September-November. Thus, the screenings covered both seasonal peaks of malaria.

Figure 6. The timings of screening and treatment and follow-up surveys.



*Screening and treatment - finger prick obtained for screening with Paracheck rapid diagnostic test and treated with Artemether Lumefantrine if infected (asymptomatic or symptomatic)

*Health assessments - finger prick obtained for measurement of heamoglobin using a Hemocue machine and for preparation of a bloodslide to be read by expert microscopists in the KEMRI laboratory in Nairobi.

Evaluation outcomes

The primary outcomes were educational achievement and anaemia, the hypothesised mediating variable through which education is affected by health (Figure 2). These outcomes were measured in a cohort of approximately 6,000 children, comprising a random sample of 25 children in Class 1 and 30 children in Class 5 from each school, selected at baseline. A full range of educational outcomes was assessed in Class 1 to evaluate the impact of both interventions, whereas a subset of educational outcomes was assessed in Class 5 to evaluate the impact of the malaria intervention alone.

Secondary outcomes occurring along the hypothesized causal pathway (Figure 2) were also assessed, including malaria parasitaemia, school attendance and school performance, and will identify the channels through which the interventions are expected to operate. Intermediate variables, such as teacher knowledge, methods of instruction and classroom interactions, were assessed during unannounced classroom observations. Important contextual factors, including school and household education environments, were assessed.

All enrolled children were surveyed and for children absent on the day of the survey, follow-up visits were made. The incidence of clinical malaria was not assessed, as this would have required prohibitively expensive and time-consuming active-case detection.

Anaemia and malaria parasitaemia

Anaemia is assumed to be microcytic and hypochromic, assessed by mean haemoglobin concentration. Among all children, haemoglobin concentration was assessed at baseline, 12 months (FU1) and 24 (FU2) months follow-up, based on a finger-prick blood sample using a portable photometer (Hemocue, Ängelholm, Sweden).

Malaria parasitaemia in the control schools was only assessed at 12 and 24 follow-up due to the ethical constraints of testing for malaria but not treating children found to be infected in the control schools. A finger-prick blood sample was used to prepare thin and thick film for confirmation and quantification of malaria parasites on the basis of expert microscopy. Slides were labeled and air-dried horizontally in a covered slide tray in the school. Slides were stained with 3% Giemsa for 45 minutes at the nearest health facility at the end of each day and transported to the KEMRI laboratory in Nairobi for reading. Parasite densities were determined from thick blood smears by counting the number of asexual parasites per 200 white blood cells (or per 500 if the count was less than 10 parasites/200 white cells), assuming a white blood cell count of 8,000/µL. A smear was considered negative after reviewing 100 high-powered fields. Thin blood smears were reviewed for species identification. Two independent microscopists read the slides, with a third microscopist resolving any discordant results.

Educational achievement and cognitive abilities

Children's competence in three main educational domains was assessed at baseline, and 9 months (FU1) and 24 months (FU2) follow-up. Assessments were administered either as individual or group tasks.

Among children in Class 1, literacy and numeracy tests were conducted in individualized and small-group settings. The literacy tasks focused on early literacy skills that are highly predictive of later reading acquisition [47], and included measures of oral vocabulary (receptive language), phonological awareness (matching beginning sound), letter knowledge, word recognition, passage reading, comprehension and spelling. The numeracy assessments measure foundational skills necessary for future understanding of mathematics, including numbers, operations, and geometry knowledge. In Class 5, achievement tests were administered in groups of 15 or less and involved word recognition, sentence reading comprehension tests, and a written arithmetic test.

Among all children in both classes, sustained attention and non verbal reasoning were assessed. Among children in Class 5, the sustained attention measure was the 'code transmission' adapted from the TEA-Ch (Tests of everyday attention for children) battery [48]. In the code transmission tasks, a list of digits is read out aloud at the speed of one every two seconds and children are required to listen out for a 'code' – two consecutive occurrences of the number 5 – and then record the 2 numbers that preceded the code. Children are tested in groups of 15 or less, and given a warm-up exercise to familiarize them with the recorded voice and 3 practice exercises before each test. For children in Class 1, floor effects were found to be common in the code transmission test Instead, sustained attention was measured using a pencil tapping task in which children are required to tap a pencil on the desk a predetermined number of times in response to the assessor's taps. This task is conducted with predetermined delays between items and assesses both sustained attention and executive control. Finally, non verbal reasoning was assessed in Class 1 by the Raven's Progressive Matrices task [49].

In total, 13 tasks were assessed in Class 1: receptive language, spelling, beginning sounds, letter knowledge, word recognition, passage reading with comprehension, non-verbal reasoning, sustained attention, and five math tasks. Five tasks were assessed in Class 5: word recognition, sentence reading comprehension, spelling, arithmetic and sustained attention.

All instruments were adapted to the Kenyan context to ensure face validity and appropriate stimuli over a period of 5 months (June-November, 2009). The provisional battery of tests was administered in 5 schools to provide pilot data to assess (i) properties of individual test items; (ii) internal reliability of individual tests; (iii) test-retest reliability of individual tests; and (iv) relationships between individual tests assessing related concepts. On the basis of these data, final changes were made to test items and a final battery of tests selected.

School attendance

Attendance at school was assessed through unannounced school visits and during scheduled data collection visits. Reasons for absence (e.g. illness, sent for fees, family emergencies, long-term absenteeism) were recorded.

Teacher interviews and classroom observations

During the second school term, two unannounced visits to each school were carried out to conduct teacher interviews and classroom observations. The teacher interview is based on a questionnaire developed in previous work in Western Kenya [50] and on scenario-based questions adapted from the *Authentic Pedagogy* classroom observation tool [51]. The classroom observation involved an assessor observing Class 1 English and Swahili lessons on two separate days and integrated two approaches to classroom observation. First, every 90 seconds a 'snapshot' of the classroom is taken, based in part on the Stallings snapshot instrument [52] and our adaptation of the instrument in previous work in western Kenya. The instrument codes the activities engaged in and materials used by the teacher and all students at one time point.

Second, specific literacy instruction practices are recorded at each time point based on established categories of effective pedagogy. This assessment is derived from the *CLASSIC* observation schedule designed to assess pedagogy for language instruction [53]. The instrument additionally includes teacher behaviours that are encouraged both during training and in the teachers' manual. The different aspects observed included:

1. The materials the teacher use (e.g. text book, letter cards, chalkboard);
2. The teachers specific instructional focus (e.g. letter names, meaning of words)
3. The teachers instructional activity (e.g. gaining student attention, reading to children)
4. The students' response or activity (i.e. listening, thinking, writing, choral reading).

The observation system uses a time sampling procedure. This means that only "slices" of the class are coded and not the entire 30 minute class. The "slices" are ten second intervals in which the coder (a) wrote a short narrative of what is occurring in the class; and (b) codes that narrative using the coding scheme. These slices occur every 90 seconds (e.g. 1:30, 3:00, 4:30, 6:00 minutes). The narrative allows the observer to complete coding each slice after the class has ended.

Household and school questionnaire data

During consent, parents and guardian were asked to complete a parental questionnaire, which contained questions designed to assess the educational and socio-economic environment of children's households. Thirteen questions asked parents and guardians about the main languages they spoke in the household and to their children, their own reading ability and habits, their schooling, and involvement in their children's school. Nine questions asked parents about the ownership and use of mosquito nets by themselves and their children. Five questions asked parents about household construction and ownership of key assets, in order to provide proxy information on socio-economic status [54].

During school meetings interviews with the head teacher collected information on the number of boys and girls enrolled in each class; examination results in English, mathematics and Swahili for the previous five years; indicators of the quality of infrastructure of the school, such as presence of toilets and hand washing facilities; whether the school had been in school health activities in the last year, such as school feeding, deworming and water and sanitation programmes; and the presence of health education material, including those for malaria.

Data analysis

The statistical analysis plan is presented in Appendix 1 and is summarized here. Primary analyses were conducted using the intention-to-treat principle whereby child and class-level data were analysed irrespective of whether they participated in either intervention.

Sets of primary and secondary outcomes were prespecified and approved by an independent Data Monitoring Committee (DMC) (Appendix 2) for follow-up 1 (FU1) and follow-up 2 (FU2) analyses (see Table 1).

Table 1. Predefined primary (shaded black) and secondary (shaded grey) outcomes for each intervention and their interaction for FU1 and FU2 analyses. Hatching indicates secondary outcome for a single intervention.

		1st year follow-up (FU1)			2nd year follow-up (FU2)		
Type of outcome	Outcome	Malaria	Literacy	Malaria x literacy	Malaria	Literacy	Malaria x literacy
Primary outcomes							
Health outcome (Classes 1 & 5)	Age- sex specific anaemia	■			■		
Class 1 educational outcomes							
Attention	Single digit code transmission$^{\Delta}$ (score 0-20)	■			≡		
Literacy	Spelling (score 0-20)	≡	■	■	■	■	■
	Swahili letter sounds (lpm) †	≡	■	■	≡	■	■
	English letter knowledge (lpm)	≡	■	■	≡	■	■
	Swahili word identification (wpm)	≡	≡	≡	≡	■	■
Numeracy	Written Numeracy (score 0-30)				■	≡	≡
Class 5 educational outcomes							
Attention	Double digit code transmission (score 0-20)	■			≡		
Literacy	Spelling (score 0-53)	≡					
Numeracy	Arithmetic (score 0-38)	≡			■		
Secondary outcomes							
Health outcomes (Classes 1 & 5)	Haemoglobin concentration (Hb) Moderate-Severe anaemia	▒			▒		
	Plasmodium falciparum infection	▒			▒		
Class 1 educational outcomes							
Non-verbal reasoning	Ravens (score 0-22)	▒	▒	▒			
	Ravens (score 0-12)				▒	▒	▒
Literacy	Beginning sounds (score 0-10)	▒	▒	▒			
	Receptive language (score 0-25)	▒	▒	▒			
	English word identification (wpm)				▒	▒	▒
	Swahili passage reading fluency (wpm)				▒	▒	▒
	English passage reading fluency (wpm)				▒	▒	▒
	Swahili passage comprehension (0-5)				▒	▒	▒
	English passage comprehension (0-5)				▒	▒	▒
Numeracy	Number Identification (score 0-20) †† Quantity Discrimination (score 0-10) ††	▒			▒	▒	▒
Arithmetic	Addition (score 0-30)	▒			▒	▒	▒
Class 5 educational outcomes							
Literacy	Comprehension - Silly sentences English (score 0-40)	▒			▒		
	Comprehension - Silly Sentences Swahili (score 0-40)				▒		

The literacy intervention and its interaction with the malaria intervention will be assessed in Class 1 children only.
wpm – words per minute, lpm – letters per minute; Note: All educational outcomes were measured at baseline except those indicated
$^{\Delta}$ Not measured at baseline as test was not anticipated to be appropriate for such young children. Thus, no adjustment for baseline measurements can be made.
† Baseline distributions indicated floor effects with a large spike at 0 words. It is anticipated that a dichotomised version of this variable will be used as the primary measure. However, the planned analysis of covariance may demonstrate that dichotomisation is not necessary.
†† The sum of these two variables will be analysed to provide an overall measure of numeracy.

Outcome definitions

Anaemia is defined according to WHO age-specific cut-offs for haemoglobin (g/l): <110 for <5 yrs; <115 for 5yrs- <12yrs; <120 for girls 12+yrs; <120 for boys 12-<15yrs and <130 for boys 15+). Since this primary health outcome is age-specific, all efforts were made to identify correct and complete age data. A definitive age variable was derived using baseline-reported information. Approximately 15 educational outcomes (including the primary outcome and excluding secondary outcomes for which floor effects are anticipated whereby the distribution of the outcome shows a heavy-left tail i.e. clumping at 0) were considered for formal statistical testing at the 5% level for each of the two interventions in each class.

Descriptive statistics

Tabulation of demographic and other characteristics was performed for the intention-to-treat study population. No significance tests were performed to test for differences at baseline. Descriptive statistics for continuous variables included the mean, standard deviation, median, range and the number of observations. Categorical variables were presented as numbers and percentages. School-level characteristics were tabulated by treatment arm both by the four treatment arms and separately for the treatment assignment of the 101 schools by education intervention arm and malaria intervention arm, respectively. Such tables help to differentiate between features of the two-stage randomisation process.

Impact analysis

Primary analyses of the outcome(s) followed the intention-to-treat principle, performed separately for the malaria and literacy interventions. All analyses were performed at the child-level and accounted for clustering (by school-cluster for the literacy intervention and by school for the malaria intervention) and for stratification (by mean school-cluster exam score and mean school exam score, respectively). Data from all children (both classes 1 and 5) enrolled in the 101 schools were used to evaluate effectiveness of the malaria intervention whereas only data from class 1 children in the 101 schools were used to evaluate effectiveness of the literacy intervention. All analyses accounted for the nature of the distribution of the outcome and report appropriate measures of effect and 95% confidence intervals (CIs). Continuous outcomes are reported on standard deviation (SD) scales for comparability of effect estimates.

Statistical analysis was conducted at the child level with clustering accounted for using generalised estimating equations (GEE), with an exchangeable correlation structure accounting for clustering by school or school-cluster for the malaria intervention and literacy intervention respectively. Robust standard errors were used. The primary analyses of each outcome included adjustment for baseline measures of that outcome (i.e. analysis of covariance) except for those of *P.falciparum*, as such data were not available in malaria control schools. Likewise, all primary analyses were adjusted for age and sex. Age was treated as a continuous variable since no material change in results was observed when age was treated as a categorical variable (results not shown). For both interventions, adjustment for age was deemed important since age is a strong predictor of anaemia and *P. falciparum* infection as well as of educational achievement. Adjustment for school-performance score or for school-cluster performance score (proxy for stratification factor) for the malaria intervention and literacy intervention respectively was performed. Binary outcomes were analysed using the log link to obtain risk ratios as the measure of effectiveness.

Given the design of the trial, whereby the literacy intervention was implemented in Class 1 children only whereas the malaria intervention was implemented in both classes 1 and 5, separate analyses of the two interventions forms the basis of the primary analyses.

Unadjusted and adjusted results are presented for all analyses. Adjustment for age and gender was pre-specified as the main adjusted analysis for each outcome. A second, 'fully' adjusted analysis was conducted for each outcome with additional adjustment for baseline nutritional status (measured by height-for-age), school-feeding, number of other children in the household, mother's education, wealth (measured by type of walls at home and whether the household owns a radio), time of baseline and time since baseline (to account for seasonality).

As a consequence of the randomisation scheme, details of the analysis of the literacy and malaria interventions differ and are described here. In the first stage of randomisation in which the literacy intervention was allocated, school-clusters were the unit of randomisation and therefore clustering was at that level in all these analyses. Furthermore, since stratification based on tertiles of mean school-cluster exam score for each group of school-cluster size used in the randomisation procedure, this was accounted for by inclusion of that mean exam score as a covariate in the GEE model. In the second stage of randomisation in which the malaria intervention was allocated, schools (i.e. not school-clusters) were the unit of randomisation and therefore clustering was at that level in these analyses. Furthermore, since stratification was used based on quintiles of mean school exam score (i.e. not mean school-cluster exam score) within the allocated treatment for the literacy intervention, a similar pragmatic approach to account for stratification was used, but this time the mean school exam score was used (i.e. rather than the mean school-cluster exam score).

An important secondary analysis was conducted in class 1 children only whereby the malaria and literacy interventions were analysed at the same time to assess sensitivity of the estimated effectiveness of the literacy intervention accounting for the malaria intervention. Clustering was accounted for at the school level.

Economic analysis

We sought to estimate the costs of the two interventions. Details of the costing of the malaria intervention are provided in Drake et al. [55]. Analysis was undertaken from the perspective of the Government of Kenya, as a public service provider. Only costs to the provider are included as costs to children accessing the intervention are likely to be low since it is delivered in schools and there is no fee to receive the intervention.

The estimated costs were calculated based on an initial 5 year programme implementation. The decreased value placed on future costs and annualization of capital costs is calculated using a 3% discount rate, in line with WHO recommendations [56]. The financial costs are the unadjusted funds required to finance the intervention and the economic cost reflects the total resource burden, taking into account the value of donated goods or unpaid workers. Costing was guided by a three-step process: resource identification, resource measurement and resource valuation. In this process, relevant unit costs were collected according to an ingredients based approach [57], the quantity or usage of each ingredient was determined and combined with cost information to produce a monetary valuation of total resources used, or economic cost. Costs were separated into those that required new funds, such as the purchase of additional RDTs and antimalarials, and those that involved the redeployment of existing resources, including use of health workers and teachers.

Cost data were collected in 2010, with unit costs established from the project accounting system and from interviews with purchasing officers. Where information was unavailable or unrepresentative, unit costs were sourced from the Ministry of Public Health and Sanitation, Ministry of Education or wholesale market prices. Ingredient usage was established from direct observation of the intervention, interviews with study coordinators, from health worker time sheets and driver mileage survey. The majority of costs were collected in Kenyan Shillings (KES) and then converted to US$ using the average exchange rate from the preceding 12 months (01.08.09 to 31.07.10): US$ 1 = KES 79.9 [58]. Costs derived from other years were inflated or deflated to 2010, using a compound inflation factor based on the year by year consumer price index [59]. The World Health Organization CHOosing Interventions that are Cost-Effective (WHO CHOICE) [60] was used to determine the country specific item lifespan of capital items: vehicle 8 years, personal computer 10 years, printer 10 years. Costs relating to activities solely for research purposes were excluded. To account for resource waste through faulty goods, mishandling or accidents, a wastage factor of 10% was applied to all relevant items.

Costing the malaria intervention

Intervention costs were grouped by resource type including: personnel; transport; field equipment; and health facility costs. In addition, costs were broken down by the various components or activities of the intervention including: community sensitisation; screening day; treatment days; administration; training and monitoring. Community sensitisation involves a meeting with parents and teachers at every school to describe the intervention and answer questions. It occurs once and comprises the set-up costs of the intervention, thus costs were annualized across the five-year programme. Screening day is the first day of the intervention, children are screened and treatment is started. Days two and three are treatment days where a nurse returns to the school to supervise the morning treatment and deliver the evening dose. Administration includes coordinator time, office use and the cost of distributing significant extra quantities of RDTs and anti-malarials to district hospitals. Training on the intervention delivery and a refresher of relevant clinical practice is given to all staff at every screening round. Monitoring of intervention delivery is undertaken by supervising health officers joining two intervention teams for observation at every round.

Univariate sensitivity analysis was conducted to determine how sensitive costs are to variation in input parameters, including commodity prices, the design of the delivery strategy, and evaluation methodology. Results are displayed graphically using a tornado diagram. For anti-malarials and RDTs, the highest and lowest prices of equivalents available in Kenya were chosen. Other variables examined include salary levels (±20%); discount rate (0%, 5%), and wastage factor (0%, 20%). To investigate the marginal cost of supervising treatment, health worker attendance on days 2 and 3 were removed, with parents/older siblings being given a full treatment course and instructions on how to administer treatment on the screening day. The second intervention change was the removal of technicians from the screening teams, with nurses from local health facilities carrying out RDT testing. The current estimates for the time spent at schools include preparation of bloodslides and collection of research information. For the sensitivity analysis is it estimated that nurses could carry implement IST without a technician under non-research conditions. A final parameter investigated was the prevalence of *Plasmodium falciparum* in the target population, a factor that will determine the quantity of anti-malarial treatments used.

Costing the literacy intervention

As with the malaria intervention, costs were grouped by resource type and intervention activity including: training workshops (initial and follow-up); teacher materials; training manual; and SMS support. No sensitivity analysis was conducted.

Qualitative evaluation: acceptability study of the malaria intervention

Six malaria intervention schools were purposively selected on the basis of the prevalence of *P. falciparum* infection, as determined in the 2012 baseline survey [61]. Two schools each with the highest, medium and lowest prevalence were chosen. The rationale for selecting schools with varying levels of infection prevalence was to allow for a range of responses from participants in areas of different malaria transmission intensities. Three of the six selected schools were located within a radius of 10kms of Ukunda town, where the project office is located; the other three schools were remote rural schools. Data were collected through in-depth interviews (IDIs) and focus group discussions (FGDs).

Focus group discussions

Parents were recruited into the study with the help of village elders and school management committee leaders. They were provided with a list of names of those parents whose children were enrolled in the study and were asked to identify and approach those who came from nearby villages with information about the qualitative study and invite them to attend the FGDs. In total, 12 FGDs were conducted with parents of children enrolled in the study, two from each school. Separate FGDs were conducted with teachers (5), health workers working for the trial (1), and community health workers (4). FGDs were of mixed gender and had between 5-12 participants. FGDs were moderated by a team of two trained field workers fluent in the local language working under the supervision of the lead investigator (GO). They were provided with a pretested flexible topic guide to direct the discussions. Discussion topics included: perceptions of the problem of malaria in school children, malaria testing and treatment, knowledge and experiences with IST in school children, perceptions of IST delivered by teachers, community health workers (CHWs) and health workers and opinions on school health programmes. Field workers carried a sample RDT to all the FGDs and used it to explain the procedure for malaria testing. At the end of each day of field work, the lead investigator met with the two field workers to discuss emerging themes and issues that required further probing in subsequent FGDs.

In-depth interviews

A total of 17 in depth interviews (IDIs) were conducted with head teachers of the selected schools and members of the district school health coordinating committee, comprising of representatives from both the ministries of education and health responsible for the implementation of school health programmes locally. Participants were initially contacted by telephone to identify a suitable date and time for the interview. Interviews were conducted, usually in participants' offices, by either the lead investigator or the senior social scientist (CJ). Interview topics included: participants' experiences of implementing school health programmes in the districts, knowledge and perceptions of school based health programmes and IST, and opinions on options for delivering IST in schools.

Data analysis

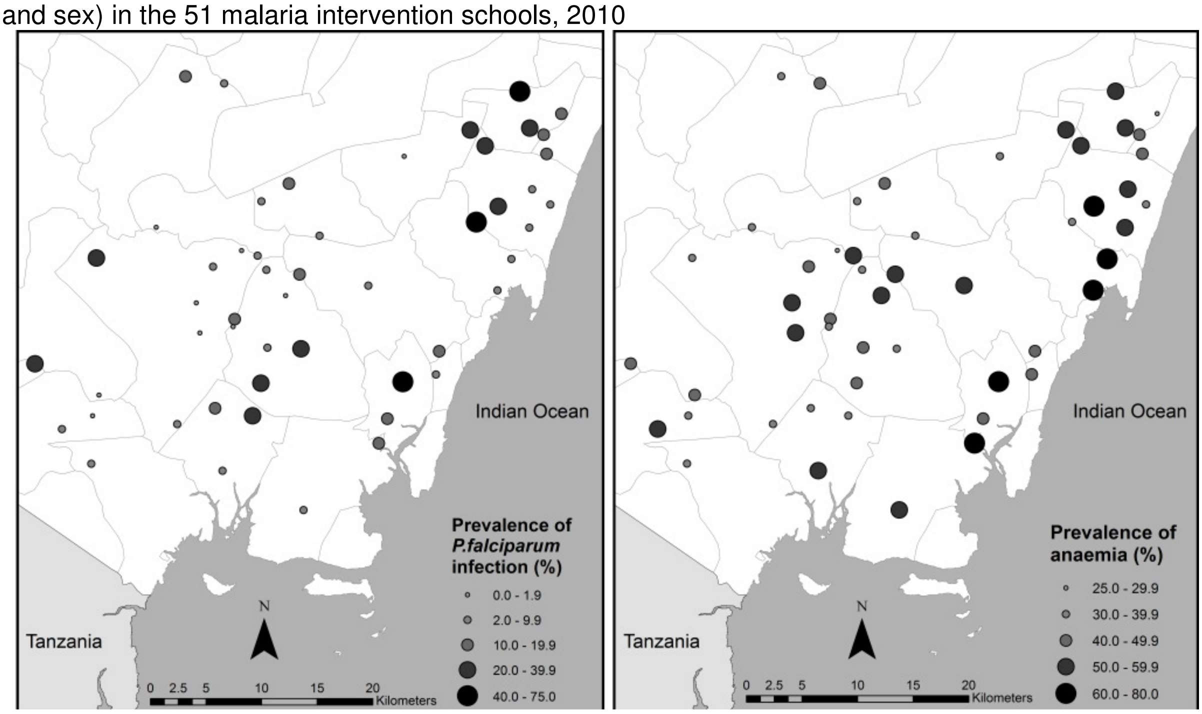
FGDs and IDIs were conducted in either Kiswahili, the language predominantly spoken along the Kenyan Coast, or in English. Interviews were recorded, transcribed and translated (where necessary). All transcripts were reviewed by the lead investigator (GO). Interview transcripts were managed using Nvivo 8 (QSR International, Doncaster, Australia). The conceptual framework (figure 1) was used to inform a framework for data coding and further analysis. The focus of the current analysis is on local perceptions and the acceptability of IST for malaria in school children. A separate paper will discuss the implementability of school-based malaria control in schools through IST.

Baseline findings/Descriptive statistics

Of the 7,337 children randomly selected to be included in the study, 78.6% (n=5772) consented and 70.5% (n=5177) were included in the baseline survey. Tables A3.1-5 in Appendix 3 provides individual, household and school characteristics of the recruited children by the four randomised groups. At the school-level, examination scores and coverage of deworming are reasonably similar (Table A3.1). There were differences among schools in the availability of school feeding and reported malaria control activities. Schools tended to be smaller in the Literacy Intervention-Malaria Control group and have more young children than the other three groups (Table A3.2). The numbers of children recruited per class is broadly similar between the four groups. Distributions of household characteristics were broadly comparable between the four groups with some apparent differences in socio-economic status (Table A3.3): children in the two malaria intervention groups tended to have some better household assets. In terms of baseline educational measures for both Class 1 and Class 5, groups are broadly comparable (Table A3.5).Separate analysis investigates baseline characteristics by malaria group (see tables 3 and 4).

The overall prevalence of anaemia was 42.3% (2188/5177) and was broadly similar across all groups (Table A3.4). In the malaria intervention groups for whom blood slides were taken, the overall prevalence of *P. falciparum* infection was 11.6%. Infection prevalence varied markedly by school, ranging from 0 to 75.0% (Figure 7a): with no children found infected in seven schools and a prevalence exceeding 40% in three schools. Marked heterogeneity was also observed in the school-level prevalence of anaemia (range: 26.3-80.0%) (Figure 7b). Overall, 61.6% of children reported sleeping under a mosquito net the previous night, with similar levels among the four study groups.

Figure 7. The geographical distribution of (a) *Plasmodium falciparum* infection and (b) anaemia (adjusted for age and sex) in the 51 malaria intervention schools, 2010



In multivariable analysis, the odds of anaemia were significantly associated with *P. falciparum* infection, with the odds increasing with increasing parasite density, and for children who were stunted, whereas significantly lower odds of anaemia were associated with children who were female, aged 10-12 years old versus 5-9 years old (Table 2) [61]. School feeding was associated with lower odds of anaemia in schools closest to the coast with no evidence of an association for schools positioned further from the coast.

Table 2: Multivariable risk factor analysis for anaemia among children in the 51 malaria intervention schools, 2010.

Variable (N=2364)	**Adjusted[a] Odds Ratio**	**95% confidence interval**	**P-value[b]**
Sex			
Male	1		
Female	0.80	0.67-0.95	0.009
Age (years)			
5-9	1		
10-12	0.71	0.58-0.87	
13-18	0.97	0.78-1.20	0.002
P. falciparum density (p/µl)			
No infection	1		
Low (1-999)	1.41	1.05-1.89	
Medium/high (>=1000	3.68	2.12-6.38	<0.001
HAZ (z-scores)			
Not stunted	1		
Stunted	1.26	1.03-1.54	0.022
Education level of household head			
No schooling	1		
Primary	0.78	0.64-0.94	
Secondary	1.12	0.83-1.50	0.014
College/degree	0.89	0.53-1.48	
Elevation (m)			
0-50	1		
51-100	0.58	0.40-0.83	
101-200	0.58	0.34-1.00	0.012
Effect of school feeding programme by elevation group[6]			
0-50m No school feeding	1		
School feeding	0.46	0.28-0.76	0.002
51-100m No school feeding	1		
School feeding	1.05	0.72-1.51	0.810
101-200m No school feeding	1		
School feeding	0.82	0.48-1.39	0.453

[a] Adjusted for variables included in final multivariable regression model as shown.
[b] p-value derived from Likelihood Ratio Test in multivariable multilevel, logistic regression model, adjusted for school-level clustering
[c] There was statistical evidence of an interaction between elevation of schools and schools having feeding programmes on anaemia in schoolchildren, therefore the stratum specific results are reported for school feeding (Liklihood ratio test for interaction between elevation and school feeding in multivariate model is p=0.042)

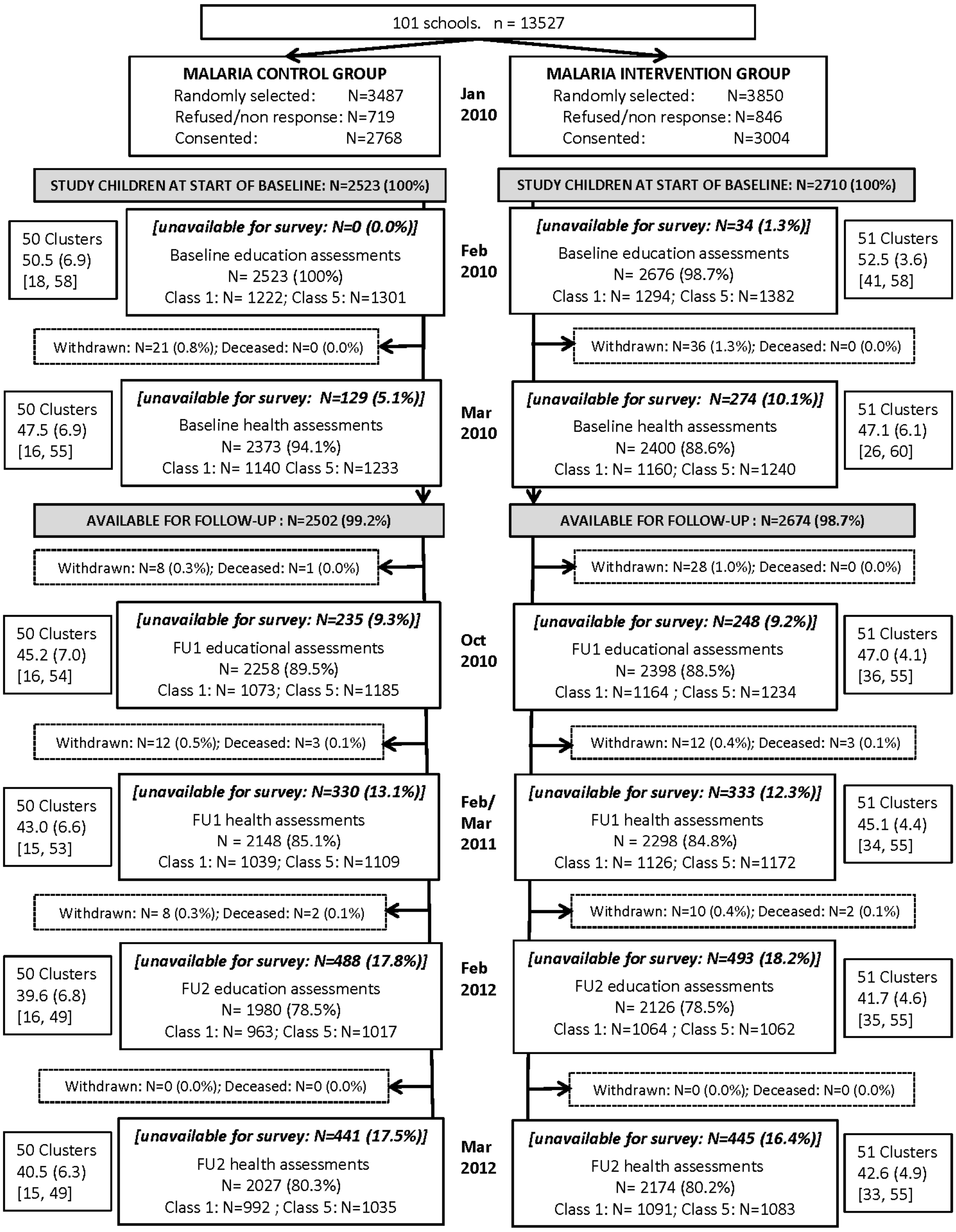
Mixed-method analysis of the malaria intervention

Quantitative Impact evaluation of the malaria intervention

Study profile and comparability of baseline data

One hundred and one schools were randomized to one of the two malaria intervention groups (Figure 8). In total, 7,337 children were randomly selected in January 2010, with 5,772 (79%) consented, 5233 study children at the start of the baseline surveys and 5,176 (70.5%) eligible for follow-up after the baseline assessments. The numbers of children assessed per school ranged from 18 to 58 but overall were well balanced between groups (control: median, 52 inter-quartile range [IQR], 50-54 and intervention: median, 53 IQR, 50-55).

Figure 8. Study profile of children included in the evaluation of the malaria intervention



Characteristics of the children included in each of the malaria intervention groups are shown in Tables 3 and 4.

Table 3. Baseline school, child and household characteristics by malaria study group.

Characteristic; n (%) [a]		**Control**	**Intervention**
School characteristics [b]		**50 schools**	**51 schools**
Exam score	Mean (sd)	223.4 (27.7)	225.8 (29.0)
School size	Median (IQR) [min, max]	505 (308, 961) [85,4891]	568 (389, 692) [225,1344]
School programmes	Feeding	22 (44.0)	27 (52.9)
	De-worming	50 (100.0)	49 (96.1)
	Malaria control	9 (18.4)	12 (23.5)
Child characteristics [b]		**2523 children**	**2710 children**
Age	Mean (sd)	10.1 (2.8)	10.3 (2.8)
	5-9	1041 (41.2)	1069 (39.5)
	10-12	877 (34.8)	925 (34.1)
	13-20	605 (24.0)	716 (26.4)
Sex	Male	1257 (49.8)	1319 (48.7)
Child sleeps under net	Usually	1668 (67.3)	1682 (63.1)
	Last night	1606 (96.3)	1609 (95.7)
Nutritional Status	Underweight	266 (27.0)	231 (23.9)
	Stunted	600 (25.2)	612 (24.9)
	Thin	482 (20.2)	450 (18.3)
Household characteristics [b]			
Parental Education	No schooling	726 (29.4)	925 (34.7)
	Primary schooling	1292 (52.2)	1381 (51.8)
	Secondary schooling	353 (14.3)	278 (10.4)
	Higher education	102 (4.1)	83 (3.1)
Socioeconomic status	Poorest	440 (17.7)	655 (24.4)
	Poor	483 (19.5)	564 (21.0)
	Median	465 (18.7)	495 (18.5)
	Less poor	524 (21.1)	509 (19.0)
	Least poor	572 (23.0)	458 (17.1)
Household size	1-5	697 (28.1)	703 (26.4)
	6-9	1444 (58.3)	1580 (59.3)
	10-31	338 (13.6)	382 (14.3)

[a] % of non-missing children in each study group presented for categorised data. For continuous data mean(sd) [min,max] is presented;
[b] All characteristics have less than 2% missing data with the exception of following indicators (reported as control/intervention): stunted and thin both (138/248 [5.5/9.2%] missing), underweight (1538/1744 [61.0/64.4%] missing), net use last night (661/840 [26.2/31.0%] missing).

Children in the malaria intervention groups were broadly similar in regard to age, sex, anthropometric indices, bednet use, and household characteristics, with some slight apparent differences in school size and socioeconomic status (Table 3). The primary outcomes, anaemia and educational measures, were also similar between groups, with prevalence of anaemia 45.2% in the control group and 45.5% in the intervention group at baseline. The prevalence of *P. falciparum,* assessed only in the intervention group at baseline, was 12.9% (Table 4).

Table 4. Baseline study endpoints of children in the control and IST intervention schools.

Characteristic; n (%) [a]		Control	Intervention
Study endpoints-baseline [c]		**2523 children**	**2710 children**
Anaemia prevalence [e] (k=0.21)	Age-sex specific	1073 (45.2)	1114 (45.5)
	Severe (<70g/L)	14 (0.6)	14 (0.6)
	Moderate (70-89 g/L)	43 (1.8)	55 (2.2)
	Mild (90-109 g/L)	530 (22.3)	518 (21.1)
	None (≥110 g/L)	1786 (75.3)	1864 (76.1)
Haemoglobin (g/L)	Mean (sd)	117.3 (13.0)	117.5 (13.7)
***P.falciparum* prevalence** [d e] (k=1.03)		- -	311 (12.9)
CLASS 1 [e f]		**1222 children**	**1317 children**
Score: 0-20 (ICC=0.07)	Sustained attention [g]	11.9 (6.7) [0, 20]	12.1 (6.6) [0, 20]
Score: 0-20 (ICC=0.29)	Spelling	8.6 (4.5) [0, 19]	7.7 (4.4) [0, 20]
Score: 0-30 (ICC=0.11)	Arithmetic	2.6 (2.4) [0, 17]	2.6 (2.5) [0, 15]
CLASS 5 [e f]		**1301 children**	**1393 children**
Score: 0-20 (ICC=0.23)	Sustained attention [g]	9.9 (6.0) [0, 20]	10.4 (5.7) [0, 20]
Score: 0-78 (ICC=0.09)	Spelling	27.9 (11.8) [0, 63]	25.8 (11.2) [1, 59]
Score: 0-38 (ICC=0.22)	Arithmetic	29.4 (5.6) [0, 38]	28.5 (5.8) [0, 38]

[a] % of non-missing children in each study group presented for categorised data. For continuous data mean(sd) [min,max] is presented;
[c] Study endpoints have less than 5% missing data at baseline with the exception of the following (reported as control/intervention): Hb (147/255 [5.8/9.4%] missing), *P.falciparum* infection (274 [10.1%] missing in intervention group), class 5 attention (79/72 [6.1/5.2%] missing).
[d] Not measured at baseline in the control group;
[e] Coefficient of variation (k) estimated for binary outcomes using available baseline (i.e. only using data from IST schools for *P.falciparum*) and Interclass correlation coefficient (ICC) estimated for continuous outcomes using baseline measures.
[f] Presented as mean(sd) [min,max]
[g] In class 1 sustained attention was measured by the "pencil tap test" and in class 5 sustained attention was measured by the "two digit code transmission test".

Performance of screening and compliance with treatment

RDT performance, examined against a gold standard of expert microscopy, revealed consistently high specificity, greater than 90% at all rounds, whereas sensitivity was more variable ranging from 68.7% to 94.6% across surveys, with higher sensitivity observed during the wet season compared to the dry season (Table 5).

During the 24 months of intervention, an average of 2,340 children (88.4% of eligible study children) in the 51 intervention schools were screened at each visit, of whom, on average 17.5% were RDT-positive (Table 5). Of the study children, 84% were screened at four or more IST rounds and 66.8% were screened at all five rounds. By the fifth screening round, 3.3% children were lost due to withdrawal or death and a further 17.7% of children were lost due to out-migration. The percentage of children RDT-positive at each screening ranged from 14.9% to 19.2%, with no distinct trend over time. Overall, 99.1% of RDT-positive results led to treatment across the five screening rounds and 92.6% of these were recorded as receiving the fully supervised six-dose treatment regime, (Table 2). There was an apparent decline in full supervision (a proxy for compliance) with time, falling from 96.9% at the first round to 81.7% at the fifth round.

Table 5: Summary for 2710 study children in the IST intervention group by screening round: number screened, proportion RDT positive, proportion started on treatment and proportion completing a supervised treatment regime. Additionally sensitivity and specificity of RDTs compared to expert microscopy is displayed.

IST Round	Season	Study children [a]	N (%) Screened	N (%) RDT Positive	N (%) Treated	N (%) Supervised treatment [b]	RDT sensitivity /specificity [c]
Feb-Mar 2010	Dry	2674 (98.7)	2454 (91.8)	453 (18.5)	449 (99.1)	435 (96.9)	78.5 / 90.6
Jun-Jul 2010	Wet	2654 (97.9)	2430 (91.6)	466 (19.2)	465 (99.8)	440 (94.6)	89.2 / 90.4
Sept 2010	Wet	2651 (97.8)	2368 (89.3)	444 (18.8)	443 (99.8)	422 (95.3)	94.6 / 90.3
Feb-Mar 2011	Dry	2630 (97.0)	2290 (87.1)	340 (14.9)	335 (98.5)	306 (91.3)	68.7 / 91.9
Oct 2011	Wet	2621 (96.7)	2157 (82.3)	345 (16.0)	338 (98.0)	276 (81.7)	NA
TOTALS		**13230**	**11699 (88.4)**	**2048 (17.5)**	**2030 (99.1)**	**1879 (92.6)**	**82.7 / 90.8**

[a] Study children are shown as a percentage of the 2710 initially eligible for the intervention and loss at each stage represents withdrawals and/or deaths. Child transfer events are not included.
[b] Children treated who were directly observed taking doses 1,3 and 5 in school at the correct time and who reported taking the evening doses.
[c] Microscopy results not available for visit 5

Follow-up

Of the 5,233 children enrolled initially, 4,446 (85.0%) were included in the 12 months follow-up health survey and 4201 (80.3%) were included in the 24 month health survey (Figure 7). At 12 and 24 months, children lost to follow-up across both study arms were largely similar to children followed up (Tables A4a and A4b in Appendix 4) with slightly lower spelling scores in those children lost to follow-up across both groups and a higher proportion of children whose parents had no schooling in those lost to follow-up in the intervention schools. The prevalence of *P. falciparum*, in the intervention group, was lower in children lost to follow-up (8.6%) compared to those followed-up (13.6%) at both 12 and 24 months.

Overall, 4,656 (89.0%) of children were included in the 9 month follow-up education survey and 4,106 (78.5%) in the 24 month follow-up survey. Children unavailable for the follow-up educational surveys at 9 and 24 months were similar across the two study groups (Tables A4c and A4d in Appendix 4), with a slight imbalance in SES and parental education categories seen between children available and unavailable for the survey in the intervention group. Additionally baseline prevalence of *P. falciparum* was lower in children lost to follow-up (9.1%) compared to those followed-up (13.3%) in the intervention arm.

As intention-to-treat analysis was performed, no adjustment was made for children transferring between schools and study groups at the follow-ups. Overall, 308 children were recorded as transferred by the end of the study. Of those, 46 (0.9%), 71 (1.8%) and 308 (5.9%) children were assessed in a different school from their initial enrolment school, at 9-month, 12-month and 24-month follow-ups, respectively. Sensitivity analysis excluding these transfers resulted in no change in direction or magnitude of results

Effect of IST on anaemia and P. falciparum

At 12 months follow-up, 2,148 children in the control schools and 2,298 in the intervention schools provided a finger-prick blood sample for Hb assessment, and at 24 months 2027 and 2174 children provided finger prick samples in the control and intervention groups respectively. There was no significant difference in either the prevalence of anaemia or mean Hb between children in the two groups at 12 or 12 month follow-ups (p=0.52 and p=0.85) (Table 6). There was also no significant difference in the prevalence of *P. falciparum* between study groups at 12 or 24 months.

Table 6. Effect of the IST intervention at 12 and 24 months follow-up on health outcomes anaemia and *Plasmodium falciparum* prevalence for study children. Results presented (i) for all children with outcome data (unadjusted) and (ii) for those with baseline measurements of each outcome and accounting for age, sex and stratification effects as the primary pre-specified analysis.

Outcome	**Control (50 schools)**		**Intervention (51 schools)**		**Risk ratio[b] (95% CI)**	**p-value**	**Cluster-size; range (average)**
		n (%)[a]		**n (%)[a]**			
12 month follow-up	N=2478		N=2631				
Prevalence of anaemia[c]							
Unadjusted	2146	837 (39.0%)	2297	920 (40.1%)	1.03 (0.92,1.16)	0.60	15-55 (44.0)
Adjusted	2048	788 (38.5%)	2142	858 (40.1%)	1.03 (0.93,1.15)	0.62	15-55 (41.5)
Prevalence of *P.falciparum*							
Unadjusted	2106	302 (14.3%)	2276	243 (10.7%)	0.76 (0.49,1.18)	0.22	11-55 (43.4)
Adjusted[d]	2106	302 (14.3%)	2276	243 (10.7%)	0.71 (0.46,1.11)	0.13	11-55 (43.4)
24 months follow-up	N=2468		N=2619				
Prevalence of anaemia[c]							
Unadjusted	2027	809 (39.9%)	2173	910 (41.9%)	1.05 (0.91,1.21)	0.51	15-55 (41.6)
Adjusted	1935	765 (39.5%)	2027	842 (41.5%)	1.00 (0.90,1.11)	0.95	14-55 (39.5)
Prevalence of *P.falciparum*							
Unadjusted	2001	169 (8.5%)	2139	253 (11.8%)	1.42 (0.84,2.42)	0.19	15-55 (41.0)
Adjusted[d]	2001	169 (8.5%)	2139	253 (11.8%)	1.53 (0.89,2.62)	0.12	15-55 (41.0)

N=number of children eligible for follow up (not withdrawn or deceased)
[a] Number and percentage with outcome
[b] Risk ratios presented for binary outcomes (anaemia & *P. falciparum* prevalence) and are obtained from GEE analysis accounting for school-level clustering.
[c] Age-sex specific anaemia was defined using age and sex corrected WHO thresholds of haemoglobin concentration: <110g/l in children under 5 years; <115g/l in children 5 to 11 years; <120g/l in females 12 years and over and males 12 to 14.99 years old; and <130g/l in males ≥ 15 years. All female adolescents are assumed to not be pregnant.
[d] Not including baseline *P.falciparum* infection
Unadjusted: All children with outcome measures, not adjusted for any baseline or study design characteristics.
Adjusted: for baseline age, sex, school mean exam score and literacy group (to account for stratification) and baseline measure of the outcome, where available.

Subgroup analysis of the impact of IST intervention on anaemia according to *Plasmodium* prevalence at baseline (using 12 month estimates for the control group as a proxy for baseline), demonstrated no differential impact by prevalence category (<5%, 5-19% and 20%+) at either follow-up (Table 7). Similarly, no difference was seen when analysis was stratified, within the intervention group only, by numbers of treatments received across the study period (Table 8).

Table 7: Effect of the IST malaria intervention at 12 and 24 months follow-up on the prevalence of anaemia, by baseline prevalence category of *P.falciparum* (control school prevalence estimated using 12 month follow-up data) with basic adjustment (i.e. for age, sex, school-exam score and literacy group).

Prevalence of anaemia	Control (50 schools)		Intervention (51 schools)		Mean difference [a] (95% CI)	p-value
Follow-up 12 months	N=2478		N=2631			
Baseline % *P.falciparum* [a]						
<5%	787	265 (33.7%)	751	270 (36.0%)	1.01 (0.84,1.23)	
5-19.9%	606	220 (36.3%)	858	358 (41.7%)	1.09 (0.95,1.26)	0.56
≥20%	655	303 (46.3%)	533	230 (43.2%)	0.99 (0.87,1.13)	
Follow-up 24 months	N=2468		N=2619			
Baseline % *P.falciparum* [a]						
<5%	740	264 (35.7%)	710	243 (34.2%)	0.95 (0.78,1.16)	
5-19.9%	572	226 (39.5%)	803	364 (45.3%)	0.99 (0.86,1.14)	0.84
≥20%	623	275 (44.1%)	514	235 (45.7%)	1.03 (0.86,1.24)	

[a] Control school *P.falciparum* prevalence was estimated using 12 month follow-up data.
Basic adjustment: for age, sex, school-exam score and literacy group and baseline anaemia.
N=numbers not withdrawn or died by the time of follow-up.

Table 8: Effect of the IST intervention at 12 and 24 months follow-up within the intervention group by number of positive results and subsequent treatments received at the individual level.

Prevalence of anaemia	Intervention (51 schools)		Risk ratio		p-value[b]	p-value[c]
Follow-up 12 months	N=2631					
No. treatments received [a]						
0	1418	545 (38.5%)	0			
1	594	242 (40.7%)	0.99	(0.90, 1.09)	0.86	0.75
2-3	286	133 (46.5%)	1.05	(0.92, 1.20)	0.46	
Follow-up 24 months	N=2173					
No. treatments received [a]						
0	1336	546 (40.9%)	0			
1-2	569	237 (41.7%)	0.96	(0.88, 1.04)	0.32	0.39
3-5	268	127 (47.4%)	1.04	(0.89, 1.22)	0.60	

[a] Baseline anaemia was controlled for in all analyses.
[b] P value obtained through the Wald test
[c] P value obtained through the Multivariate Wald test
N=numbers not withdrawn or died by the time of follow-up.

Effect of IST on sustained attention and educational achievement

At both 9 and 24 months follow-up, there was no statistical difference in mean scores for sustained attention between study groups in either class (Table 9). Similarly there was no significant difference between groups on scores for spelling in the older class at 9 and 24 month follow-ups (p=0.52 and p=0.18) nor for arithmetic at either follow-up (Table 10). However, at 9 months follow-up, children in the younger class in the intervention group had lower mean adjusted scores for the spelling task and the same trend was observed at 24 months (Adjusted mean difference (MD): -0.65, 95%CI: -1.11, -0.18 p=0.01). Similarly at 24 months, in the younger class, children in the intervention group scored on average 0.60 points lower in the arithmetic assessments than children in the control group (Adj.MD: -0.60, 95%CI: -1.02, -0.19 p<0.01).

Table 9. Effect of the IST intervention at 9 and 24 months follow-up on sustained attention outcomes for younger (class 1) and older (class 5) children. Results presented (i) for all children with FU1 measurements of an outcome (unadjusted) and (ii) for those with baseline measurements of each outcome and accounting for age, sex and stratification effects as the primary pre-specified analysis.

Outcome		**Control (50 schools)**		**Intervention (51 schools)**	**Mean difference[b] (95% CI)**	**p-value**	**Cluster-size; range (mean)**
9 months follow-up		**Mean (sd)[a]**		**Mean (sd)[a]**			
CLASS 1	N=1210		N=1281				
Sustained Attention[c] (score:0-20)							
Unadjusted	1070	8.48 (3.63)	1162	8.43 (3.76)	-0.04 (-0.58,0.51)	0.90	8-27 (22.1)
Adjusted	1030	8.52 (3.65)	1144	8.43 (3.77)	-0.13 (-0.66,0.39)	0.62	5-27 (21.7)
CLASS 5	N=1283		N=1365				
Sustained Attention[d] (score:0-20)							
Unadjusted	1180	13.38 (5.45)	1231	13.35 (5.13)	-0.09 (-0.77,0.56)	0.80	8-30 (23.9)
Adjusted	1178	13.38 (5.45)	1221	13.40 (5.10)	-0.21 (-0.81,0.39)	0.49	8-30 (23.8)
24 months follow-up							
CLASS 1	N=1201		N=1269				
Sustained Attention[c] (score:0-20)							
Unadjusted	960	13.45 (5.15)	1059	13.20 (4.96)	-0.26 (-0.95,0.43)	0.46	8-26 (20.0)
Adjusted	923	13.49 (5.15)	1041	13.18 (4.96)	-0.44 (-1.09,0.21)	0.18	4-25 (19.6)
CLASS 5	N=1267		N=1350				
Sustained Attention[d] (score:0-20)							
Unadjusted	1007	14.22 (4.90)	1052	14.66 (5.13)	0.40 (-0.14,0.94)	0.14	6-31 (20.4)
Adjusted	1006	14.21 (4.90)	1044	14.70 (5.10)	0.28 (-0.23,0.79)	0.28	6-29 (20.3)

N=number of children eligible for follow up (not withdrawn or deceased)
[a] Mean score and sd at follow-up
[b] Mean difference (intervention-control) are obtained from GEE analysis accounting for school-level clustering.
[c] Pencil tap test was conducted at baseline and single digit code transmission task was conducted at 9 and 24 months follow-ups.
[d] Double digit code transmission was conducted at baseline and both follow-ups.
Unadjusted: All children with outcome measures, not adjusted for any baseline or study design characteristics.
Adjusted: for baseline age, sex, school mean exam score and literacy group (to account for stratification) and baseline measure of the outcome, where available.

Table 10. Effect of the IST intervention at 9 and 24 months follow-up on educational achievement (spelling and arithmetic) outcomes for younger (class 1) and older (class 5). Results presented (i) for all children with FU1 measurements of an outcome (unadjusted) and (ii) for those with baseline measurements of each outcome and accounting for age, sex and stratification effects as the primary pre-specified analysis.

Outcome; N (%)	**Control (50 schools)**		**Intervention (51 schools)**		**Mean difference [b] (95% CI)**	**p-value**	**Cluster-size; range (mean)**
9 months follow-up		**Mean (SD) [a]**		**Mean (SD) [a]**			
CLASS 1	N=1210		N=1281				
Spelling (score:0-20) [c]							
Unadjusted	1068	11.70 (4.59)	1162	10.47 (4.57)	-1.23 (-2.21,-0.24)	0.02	8-27 (22.1)
Adjusted	1060	11.69 (4.59)	1133	10.49 (4.58)	-0.67 (-1.26,-0.08)	0.03	8-27 (21.7)
Arithmetic(score:0-20) [e]							
Unadjusted	1071	4.21 (3.13)	1162	4.04 (3.27)	-0.17 (-0.60, 0.26)	0.43	8-27 (22.1)
Adjusted	1069	4.21 (3.12)	1143	4.07 (3.28)	-0.21 (-0.54, 0.12)	0.21	8-27 (21.9)
CLASS 5	N=1283		N=1365				
Spelling (score: 0-75) [d]							
Unadjusted	1169	31.34 (12.61)	1223	28.73 (12.36)	-2.73 (-5.26,-0.19)	0.04	8-30 (23.7)
Adjusted	1154	31.37 (12.60)	1214	28.76 (12.34)	-0.31 (-1.26,0.63)	0.52	8-30 (23.4)
Arithmetic(score:0-30) [g]							
Unadjusted	1180	31.15 (5.49)	1229	30.72 (5.17)	-0.49 (-1.40, 0.42)	0.29	8-30 (23.9)
Adjusted	1173	31.14 (5.50)	1210	30.73 (5.17)	0.13 (-0.41, 0.68)	0.63	8-30 (23.6)
24 months follow-up							
CLASS 1	N=1201		N=1269				
Spelling (score:0-20) [c]							
Unadjusted	961	12.03 (3.05)	1062	11.04 (3.49)	-0.97 (-1.54,-0.40)	<0.01	8-26 (20.0)
Adjusted	954	12.02 (3.05)	1036	11.04 (3.50)	-0.65 (-1.11,-0.20)	<0.01	8-25 (19.7)
Arithmetic(score:0-30) [f]							
Unadjusted	962	5.97 (3.05)	1061	5.38 (2.97)	-0.59 (-1.08, -0.10)	0.02	8-26 (20.0)
Adjusted	960	5.97 (3.04)	1042	5.40 (2.97)	-0.60 (-1.02, -0.19)	<0.01	8-25 (19.9)
CLASS 5	N=1267		N=1350				
Spelling (score: 0-78) [d]							
Unadjusted	1010	35.28 (12.91)	1060	33.97 (12.79)	-1.58 (-4.01,0.85)	0.20	6-31 (20.5)
Adjusted	996	35.33 (12.85)	1052	34.04 (12.75)	0.71 (-0.34,1.76)	0.18	6-29 (20.3)
Arithmetic(score:0-30) [g]							
Unadjusted	1016	21.20 (5.47)	1062	20.15 (5.68)	-1.07 (-2.15, -0.00)	0.05	6-31 (20.6)
Adjusted	1009	21.20 (5.48)	1045	20.18 (5.69)	-0.49 (-1.32, 0.34)	0.24	6-29 (20.3)

N=number of children eligible for follow up (not withdrawn or deceased)
[a] Mean score and sd at follow
[b] Mean difference (intervention-control) for scores on spelling and arithmetic are obtained from GEE analysis accounting for school-level clustering
[c] The same class 1 spelling task was given at baseline, 9 and 24 months follow-ups, with different words used for the 24 month follow-up.
[d] The same class 5 spelling task was given at baseline, 9 and 24 months follow-ups, with different words used for the 24 month follow-up.
[e] Same addition task conducted at 9 months follow-up and at baseline, hence baseline adjustment is for the same task.
[f] Addition task conducted at baseline and arithmetic task containing addition, subtraction, multiplication and division conducted at 24 months follow-up, hence baseline adjustment for different task.
[g] Same arithmetic task conducted at at baseline, 9 and 24 months follow-ups, with different sums used for the 24 month follow-up.
Unadjusted: All children with outcome measures, not adjusted for any baseline or study design characteristics.
Adjusted: for baseline age, sex, school mean exam score and literacy group (to account for stratification) and baseline measure of the outcome, where available.

Surveillance of adverse events

Active surveillance found that 4.5% (92/2030) children reported one or more adverse effects within 2 days of receiving treatment, including headache (68; 3.3%), stomach ache (38; 1.9%), dizziness (17; 0.8%), vomiting (7; 0.3%) and pruritis (10; 0.5%). During the 24 months of follow-up, 11 children died: 5 in the intervention group and 6 in the control group. Cause of death was investigated and included yellow fever, heart defect, leukaemia, drowning, trauma, pneumonia and paediatric HIV. In the intervention group, none of these deaths occurred within 30 days of the screening and treatment and therefore were not attributed to the intervention.

Interpretation of findings

We conducted the first cluster-randomised trial of the impact of school-based intermittent screening and treatment (IST) of malaria. We failed to detect any overall benefit of IST using AL on the health, attention or educational achievement of school children in this low-moderate malaria transmission setting. A likely explanation for the lack of overall impact of IST on anaemia at the group or individual level was high, localised, rates of re-infection and acquisition of new infections between screening rounds, indicated by the remarkably similar percentage of children RDT positive at each screening round. The marked, but stable heterogeneity of *Plasmodium* infection observed over the two years (school-level prevalence range: 0-75%) resulted in several schools experiencing no infection throughout all screening rounds, and a small sample of schools exhibiting repeatedly high proportions of RDT positive study children at each round, reflecting focal regions of high transmission. This heterogeneity, compounded by the large proportion of untested and treated asymptomatic carriers remaining in the communities likely led to study children in localised hotspots being exposed to high risk of infection immediately after treatment

The use of AL for IST may have contributed to rapid re-infection rates following treatment. Studies have demonstrated an average post-treatment protection period of between 14 and 28 days for AL [62-63]. Such a protection period would have provided extensive time at risk of acquiring new infections before the next treatment, on average 4 months later in our study. The beneficial impact observed with the use of the longer acting drug SP+AQ, given at 4 month intervals in the trial of IPT, suggests the primary method of action in this high transmission setting was a prophylactic rather than a treatment effect. A potential alternative would be dihydroartemisinin-piperaquine [64], which would afford longer post-treatment prophylaxis period than AL between screening rounds, as recently evaluated as part of IPT in Uganda [65].

The evaluation identified two further limitations of the IST approach. First, there was variability in RDT performance between screening rounds, with lowest RDT sensitivity during the dry season. The use of PCR would constitute a more sensitive tool, additionally detecting subpatent infections which contribute to transmission [66-68], but would be operationally challenging. Second, there was a decline in supervised treatment over time, as it became logistically challenging for children who were absent on screening day and subsequently treated on a repeat visit, to be followed up on treatment day two and three by the nurse. They were given the full regimen with instructions on how to take the doses at home over the three days. Although evidence indicates that unsupervised treatment is as effective at clearing parasitaemia as fully supervised treatment in clinical cases [69], unsupervised compliance may be lower when treating asymptomatic infection.

Our finding of no significant differences between groups for attention in either the younger or older classes at either follow-up is consistent with expectations, based on the lack of effect of IST on the assumed mediator, health. This is also true of the adjusted literacy and numeracy scores in the older class at both follow-ups, where no significant differences between groups were found. However, in the younger class, at both 9 and 24 months there was an apparent negative effect of the IST intervention on literacy scores and on arithmetic scores at 24 months. This seemingly negative impact of IST was found only in the younger class, where the literacy intervention was implemented, although as no statistical interaction between the two interventions was detected, the differences between study groups cannot be attributed to an effect of the literacy intervention. Alternatively these findings could demonstrate a negative effect of the termly screening, involving an uncomfortable finger prick [32], with the intervention group experiencing increased apprehension of the finger prick during the education assessments as they associated the presence of our research team with the IST process, or reduced classroom attendance throughout the year in this group to avoid the IST intervention, or a combination. However, attendance measured at spot checks, and at all health and education assessment visits indicated no significant differences in attendance between the groups. Findings of negative educational or cognitive effects of health interventions are rare but not unprecedented [70] and speak to the need for experimental evaluations to test assumptions about the educational benefits of health programs.

However, the evaluation results do highlight a role for schools as screening platforms. School screenings using RDTs could provide an operationally efficient method to initially identify transmission hotspots for targeted community control. National school surveys have proved a useful platform for defining heterogeneities in *Plasmodium* transmission over large geographical areas in a rapid and low cost manner [71-72]. The results from the screening rounds in this study present a case for the use of schools in also depicting local transmission heterogeneities, which can be extrapolated to the local community [73] and aid in developing targeted community-wide comprehensive interventions, such as localised indoor residual screening and larviciding, with biennial school screenings used to monitor the success of these interventions.

Costs and cost-effectiveness of the malaria intervention

Costs were assessed from a government perspective using an ingredient costing approach, assuming a five year programme. The total financial cost of providing a five-year programme of malaria screening and treatment to 3,685 children was estimated to be US$ 365,104 or US$ 6.61 per child screened. The economic costs of the programme are US$ 69,062 per year, US$ 6.24 per child screened or US$ 18.72 per child per year. Table 11 provides a breakdown of financial and economic costs. The largest single contributors to cost are salaries (36%) and RDTs (22%). Almost half (47%) of the intervention cost comprises redeployment of existing resources including health worker time and use of hospital vehicles. The new funds required are largely due to RDTs and other consumables, their distribution to local facilities and staff per diems.

Table 11. Financial and economic costs of malaria intermittent screening and treatment in schools in coastal Kenya by resource category (US$ 2010)

Resource	Financial Cost[1]			Annual Economic Cost	Economic cost per child screened	Cost Profile(%)[6]
	New funds	Existing resources	Total			
Personnel:						
Salaries	-	132,516	132,516	25,077	2.27	36
Per Diems	22,852	-	22,852	4,357	0.39	6
	22,852	**132,516**	**155,368**	**29,434**	**2.66**	**43**
Transport:						
Vehicle	-	17,387	17,387	3,292	0.30	5
Fuel	11,771	-	11,771	2,229	0.20	3
Servicing	-	16,884	16,884	3,197	0.29	5
Distribution[2]	33,104	-	33,104	6,246	0.57	9
	44,875	**34,271**	**79,146**	**14,965**	**1.35**	**22**
Facility:						
Rent[3]	-	5,016	5,016	957	0.09	1
Other[4]	2,761	-	2,761	534	0.05	1
	2,761	**5,016**	**7,777**	**1,490**	**0.13**	**2**
Field Equipment:						
RDTs	80,650	-	80,650	15,217	1.38	22
Anti-malarials	9,919	-	9,919	1,872	0.17	3
Other[5]	32,243	-	32,243	6,084	0.55	9
	122,813	**-**	**122,813**	**23,173**	**2.10**	**34**
TOTAL	**193,301**	**171,803**	**365,104**	**69,062**	**6.24**	**100**
%	**53**	**47**				

[1] Financial costs are the undiscounted direct monetary costs for the programme over five years.
[2] Cost of transporting extra RDTs and anti-malarials to the district hospital
[3] Includes utilities and furniture.
[4] Includes office consumables and computer equipment.
[5] Includes blood lancets, cotton wool, gauze roll, gloves, paper towels, disinfectant dispenser, thermometer, biscuit packs, milk cartons, bottled water, paracetamol, pencils, erasers, sharpeners, masking tape, garbage bag, marker pens, scissors, dust bin, triple timers, weighing scales and mobile phone credit.
[6] Applies to both financial and economic costs.

Table 12 presents the resource costs cross-tabulated against the intervention activities and shows that the majority of the costs are spent on screening (52%), followed by treatment follow-up (21%) and intervention administration (20%). Data from the health worker time surveys indicates that daily travel to and from the schools during screening took on average 3 hours 20 minutes or 47% of total time. Undertaking the screening and providing treatment took 3 hours 16 minutes (45%), with preparation in the schools taking 36 minutes (8%).

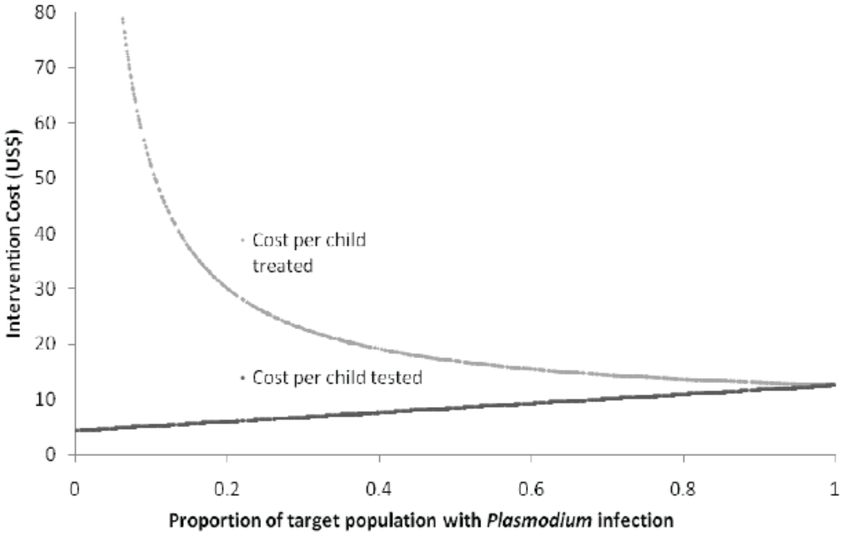
Table 12. The costs of malaria intermittent screening and treatment in schools in coastal Kenya by resource category and intervention activity (US$ 2010)

	Resource					
Activity	Personnel	Transport	Facility	Field Equipment	**TOTAL**	%
Sensitisation	872	231	166	-	**1,270**	2
Training	943	-	44	17	**1,003**	1
Screening	12,642	2994	-	20,399	**36,035**	52
Treatment Follow-Up	6,317	5,494	-	2,757	**14,568**	21
Monitoring	2,126	-	132	-	**2,258**	3
Administration	6,535	6,246	1,148	-	**13,929**	20
TOTAL	**29,434**	**14,965**	**1,490**	**23,173**	**69,062**	100
%	43	22	2	34	100	

Sensitivity analysis showed that the choice of RDT had a large impact on overall costs (12% reduction or 33% increase), whereas drug choice had negligible impact. The biggest cost saving was removing the treatment follow-up (21%), whilst not including technicians in the screening teams reduced costs by 7%. Other variations altered costs by less than 10%.

Figure 9 shows the relationship between the prevalence of *P. falciparum* infection (as based on RDT results) and the cost per child screened and cost per RDT-positive child treated. As RDT-positivity increases, the cost per child screened increases in a linear fashion as more anti-malarials are required. As prevalence of infection decreases the cost per child treated rises exponentially.

Figure 9. The relationship between the cost of school-based intermittent screening and the prevalence of *Plasmodium falciparum* in school children



In light of the lack of impact of malaria intervention, no cost-effectiveness analysis was performed.

Local perceptions of the malaria intervention

A qualitative evaluation sought to identify key assumptions and conditions underlying potential implementation of the IST intervention, focusing on issues of (i) acceptability to the local community and key stakeholder; (ii) feasibility; and potential implementation. The detailed findings arising from the focus group discussions and in-depth interviews on the local perceptions of IST for malaria are presented in Okello et al. [74]. The summary findings of this work were as follows:

- It was clear across the different transmission settings in the study area that knowledge of malaria and its consequences was high and all stakeholders recognized the importance of tackling clinical malaria among school children.

- The perceptions of health managers, health workers, CHWs, educational officials and teachers and parents of the burden of malaria in school children and the benefits of school based malaria control through IST played a significant role in the positive attitudes towards IST that were found in this study.

- However, there was a strong demand from parents for mosquito net distribution to be undertaken as a complementary intervention to IST to prevent clinical disease.

- While IST was clearly perceived to contribute to a reduction in clinical disease, few participants appear to have been aware that the principal aim of IST is the reduction of asymptomatic parasitemia, rather than the treatment of clinical disease. Although this lack of awareness did not appear to impact on the acceptability of the intermittent screening component of the intervention, the findings do suggest that it may affect willingness to adhere to the full treatment regime. That is, some parents were concerned that their children were put on malaria treatment when they were perceived to be healthy.

- In a few cases these parents encouraged their child not to take their medication and instead used the drugs to treat other sick siblings and in other instances children were reported to have thrown away the tablets as they didn't perceive themselves to be ill. These findings suggest that, while the concept of screening and treatment for malaria is generally acceptable, adherence to treatment given to children with asymptomatic parasitemia may be problematic.

- In addition, the complex six-dose regimen of AL which requires that all doses be correctly spaced and be given with food may present a major challenge in a school setting especially if drugs are issued to children or teachers to pass to their parents without proper information on dosage and a simpler antimalarial regimen would enhance compliance.

- The use of health workers to implement the IST interventions in schools is likely to be acceptable because this is a health intervention which forms part of health worker roles.

- Regardless of who implements the intervention, the support of health workers is critical to the successful implementation of the IST intervention in schools. Their involvement is particularly necessary in terms of training and supervising the delivery agents implementing the strategy in schools, in facilitating safe waste disposal, and in handling referral cases arising from schools.

- While the use of teachers to deliver antihelmintic treatment in schools has been found to be acceptable elsewhere, their use in the delivery of IST in schools appeared to be generally unacceptable to most participants in this study. The main reason for their lack of acceptability is that IST involves taking blood samples from school children, something that is perceived to be beyond teachers' scope of practice and can therefore create role conflicts, overburden the already overworked teachers and undermine their ability to discharge their normal duties.

- While the testing caused concerns, the use of teachers to administer treatment to school children after testing was, however, acceptable to most participants as it reflected their previous experiences with other school health programmes that involved providing treatment to school children without parasitologically confirmed diagnosis.

- Most of the concerns raised about the IST intervention were related to rumours about blood sample taking and covert HIV testing. Rumours, particularly those about blood, are often directly related to medical research and health interventions and are very common across sub-Saharan Africa.

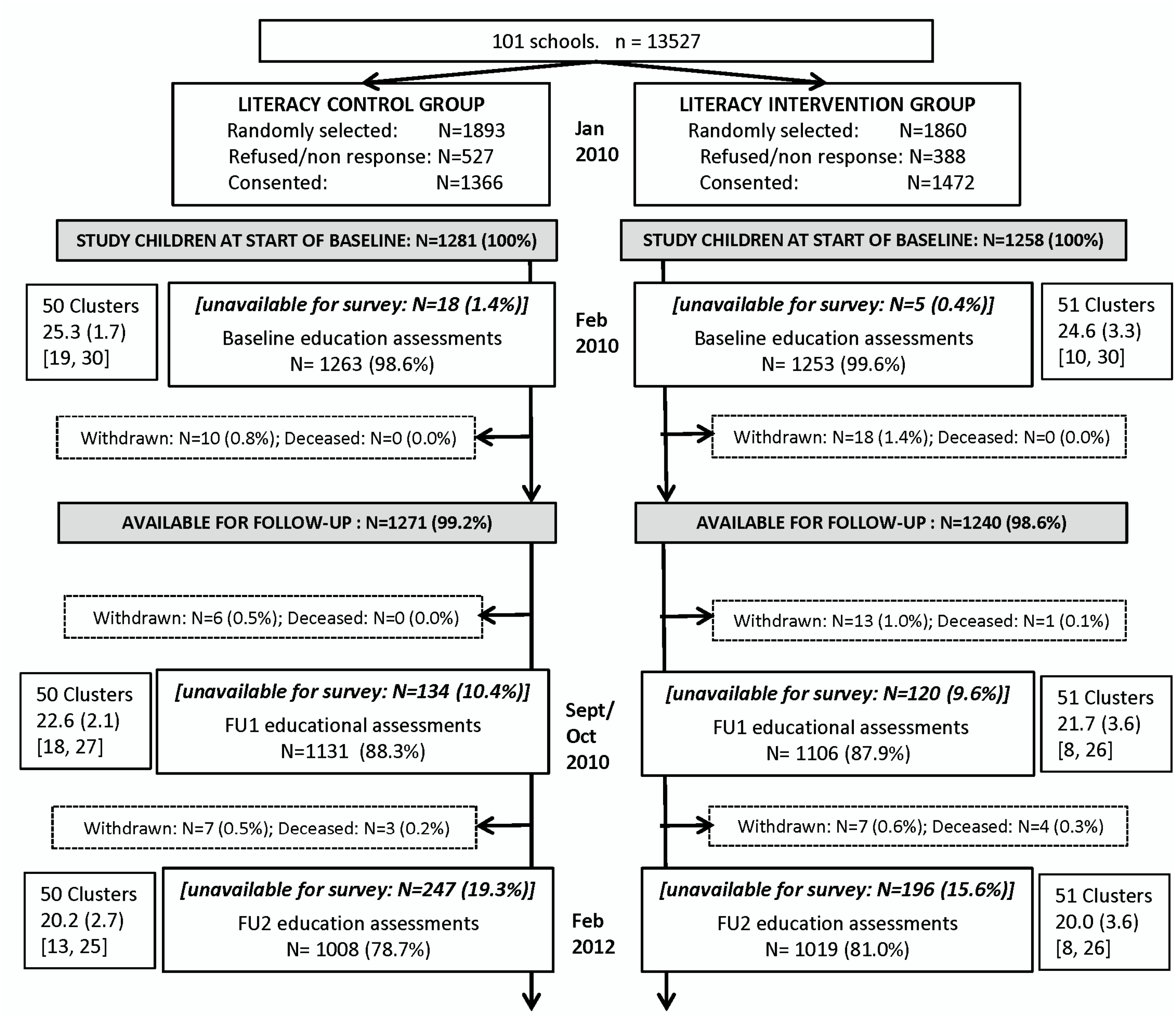
Mixed-method analysis of the literacy intervention

Quantitative impact evaluation of the literacy intervention

Study profile and comparability of baseline data

The one hundred and one schools were randomized to one of the two literacy intervention groups (Figure 10). The literacy intervention was only implemented in early primary (class 1 who progressed to class 2 in the second year). Hence class 5 children are not included in the following analyses. In total, 3,753 children were randomly selected in January 2010, with 2,838 (75.6%) consented, 2539 study children at the start of the baseline surveys and of those 2511 (98.9%) were eligible for follow-up after the baseline assessments.

Figure 10. Study profile of children included in the evaluation of the literacy intervention.



Characteristics of the class 1 children included in each of the literacy intervention groups are shown in Tables 13 and 14. School level factors were broadly similar across study groups in terms of exam scores and despite the differences in variability of school sizes by study group, the median school size was similar. However, a higher proportion of schools in the control group had school feeding programmes when surveyed in January 2010.

Table 13. Baseline school, child and household characteristics by malaria study group.

Characteristic; n (%) [a]		**Control**		**Intervention**	
School characteristics [b]		**50 schools**		**51 schools**	
Exam score	Mean (sd)	227.3 (27.3)		221.1 (28.4)	
School size	Median (IQR) [min, max]	599 (371, 900) [199,1439]		513 (352, 686) [85,4891]	
School programmes	Feeding	29	(58.0)	20	(39.2)
	De-worming	49	(98.0)	50	(98.0)
Child characteristics [b]		**1281 children**		**1258 children**	
Age	Mean (sd)	7.9	(1.7)	7.7	(1.7)
	5-6	287	(22.4)	305	(24.2)
	7-8	525	(41.0)	573	(45.6)
	9-10	397	(31.0)	322	(25.6)
	11-15	72	(5.6)	58	(4.6)
Sex	Male	637	(49.7)	656	(52.2)
Nutritional Status	Underweight	261	(27.7)	235	(24.3)
	Stunted	314	(27.0)	270	(23.0)
	Thin	238	(20.5)	225	(19.2)
School experience	Attended school before class1	1158	(95.5)	1149	(95.4)
	Failed a grade	386	(32.4)	374	(31.6)
	Reads aloud in class	1068	(87.3)	1062	(86.6)
Household characteristics [b]					
Parental Education	No schooling	435	(34.4)	363	(29.1)
	Primary schooling	667	(52.7)	692	(55.5)
	Secondary schooling	133	(10.5)	145	(11.6)
	Higher education	30	(2.4)	47	(3.8)
Socioeconomic status	Poorest	338	(26.5)	240	(19.2)
	Poor	268	(21.0)	249	(19.8)
	Median	222	(17.4)	266	(21.2)
	Less poor	235	(18.4)	250	(19.9)
	Least poor	213	(16.7)	250	(19.9)
Household size	1-5	370	(29.0)	365	(29.5)
	6-9	735	(57.6)	730	(59.0)
	10-31	170	(13.3)	142	(11.5)
Language spoken at home	Digo	520	(41.0)	644	(51.6)
	Duruma	376	(29.7)	170	(13.6)
	Kamba	158	(12.5)	177	(14.2)
	Kiswahili	169	(13.3)	194	(15.5)
	Other	44	(3.5)	63	(5.1)
No. times parent read last week	0	281	(35.7)	280	(33.0)
	1-3	338	(43.0)	400	(47.1)
	4-6	97	(12.3)	79	(9.3)
	7 and above	71	(9.0)	90	(10.6)

[a] % of non-missing children in each study group presented for categorised data. For continuous data mean(sd) [min,max] is presented;
[b] All characteristics have less than 2% missing data with the exception of following indicators: stunted, thin and underweight.

Children in the literacy intervention groups were broadly similar in regard to age and sex, with a slightly higher proportion of stunted and underweight children in the control schools. The school experiences of the children were highly comparable across study groups. However, there were some apparent differences in language spoken at home and socioeconomic status. An SES imbalance was observed in the control group, with a higher proportion of children in the lowest SES quintile and a lower proportion in the highest (Table 13).

The health indicators were similar between groups, with prevalence of anaemia 49.0% in the control group and 47.3% in the intervention group at baseline. The prevalence of *P. falciparum,* was 16.6% and 15.8% in the control and intervention groups respectively, but this was assessed in only half of the schools (malaria intervention group) at baseline (Table 14).

Table 14. Baseline study endpoints of children in the control and IST intervention schools.

Characteristic; n (%) [a]		**Control**	**Intervention**
Study endpoints-baseline [c]		**1281 children**	**1258 children**
Anaemia prevalence [e]	Age-sex specific	571 (49.0)	550 (47.3)
	Severe (<70g/L)	8 (0.7)	9 (0.8)
	Moderate (70-89 g/L)	30 (2.6)	33 (2.8)
	Mild (90-109 g/L)	340 (29.2)	325 (28.0)
	None (≥110 g/L)	778 (67.6)	795 (68.4)
Haemoglobin (g/L)	Mean (sd)	114.1 (12.6)	114.2 (12.7)
***P.falciparum* prevalence** [d e]		93 (16.6)	95 (15.8)
Literacy assessments		**1251 children**	**1245 children**
Score: 0-100	English letter knowledge	16.6 (15.11) [0, 87]	16.3 (15.0) [0, 78]
Score: 0-100	Swahili sounds	5.2 (9.0) [0, 55]	7.5 (11.6) [0, 66]
Score: 0-20	Spelling	7.8 (4.3) [0, 19]	8.4 (4.6) [0, 20]

[a] % of non-missing children in each study group presented for categorised data. For continuous data mean(sd) [min,max] is presented;
[c] Study endpoints have less than 5% missing data at baseline with the exception of *Plasmodium falciparum* infection
[d] Not measured at baseline in the malaria control group;
[e] Presented as mean(sd) [min,max]

Teacher compliance with literacy intervention

A total of 62 class 1 teachers were initially trained in February 2010 as some schools had multiple streams. Teachers transferred in during the first term were given a one-day intensive training in their school. At the start of the second year (February 2011), 59 teachers were trained, 38 of whom taught class 1 the previous year and moved to class 2 with their class, so received refresher training; and 21 of whom were new class 2 teachers who had not taught class 1 the previous year and so were provided with the initial and refresher training.

Table 15. The attendance of the teachers to be trained for the literacy intervention at the three training workshops held over the 24 month study period.

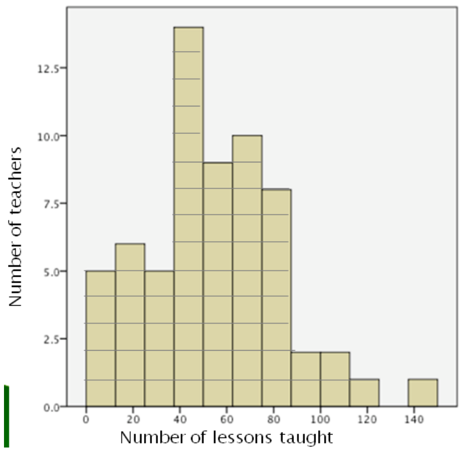
Date	Teacher training session	Attendance rate (%)
Feb-Mar 2010	Initial training	95.2*
July 2010	Follow up training 1	98.4
Feb-Mar 2011	Follow up training 2	96.3

*Additional training sessions were conducted on site in 3 schools to accommodate teachers who were not available for the initial group HALI-training.

During the year, teacher compliance in the intervention group was monitored through self reported weekly summary sheets and their weekly text message responses. These two monitoring methods gave a quantitative estimation of the number of intervention lessons being taught throughout the study period as well as a qualitative evaluation of the teachers' thoughts and experiences of the intervention as a whole.

Teachers were requested to record the lessons they used each week, what worked well, and their suggestions for improvement on standardised summary sheets. Even though teachers reacted positively to the intervention components, their use of the provided lessons varied. During the first 26 weeks of the intervention, the mean number of lessons taught by the 62 teachers was 54.6 lessons, on average two per week. The standard deviation of 28.89 showed the variability of use (Figure 11). For example, one teacher reported teaching 144 lessons, which would be approximately one per school day. Conversely, two teachers reported teaching nine lessons during the 26 weeks. Some teachers documented barriers to use of the lessons on the summary sheets. On teacher wrote, "*I think my school seems to be having more problems than expected so it has been taking a lot of time to teach not only the HALI lessons but even the other lessons because… since in most cases we have the headmaster out and the deputy is on attachment, so I play more roles than just a classroom teacher".*

Figure 11. Graph of self reported lessons taught during first 26 weeks of intervention.



Weekly communication was sent to teachers via text messages to offer information and motivation to implement the lesson plans. The average response rate averaged 87% for the 37 weeks that we asked a question in year 1 and 84% in year 2. Lack of response to the weekly text message could be viewed as an indication of lack of compliance with the daily intervention in the classroom.

Classroom inventories conducted during the first year of the intervention documented the use of materials provided to the teachers during the training. We observed that over 90% of the intervention teachers displayed materials (e.g., pocket chart) to increase the amount of visible text in the classroom.

Follow up

Of the 2539 children enrolled initially, 2237 (88.0%) were included in the 9 month follow-up education survey and 2027 (79.8%) were included in the 24 month education survey (Figure 9), and the proportions available were similar across the study groups. By the end of the 24 month follow-up 69 (2.7%) children had exited the study as they were deceased or withdrawn. As intention-to-treat analysis was performed, no adjustment was made for children transferring between schools and study groups at the follow-ups.

Effect of literacy intervention on literacy outcomes

At the 9 month follow-up, children in the literacy intervention group had significantly higher mean adjusted scores for the spelling task (Adjusted mean difference (MD): 1.43, 95%CI: 0.86, 2.00 $p<0.001$), with a large effect size, than children from control schools (Table 16). This gain was sustained into the 24 month follow-up, although with a smaller effect size observed (Adj.MD: 0.53, 95% CI: 0.10, 0.97 $p=0.02$).

At the 9 month follow-up, children in the literacy intervention group scored significantly higher on assessment of Swahili sound knowledge, with a greater than five point mean difference between the intervention and control group (Adj.MD: 5.28, 95%CI: 3.18, 7.39 $p<0.001$). Similarly at 24 months, the same trend was observed with the children in the intervention group scoring on average nearly five points higher in Swahili sound knowledge than children in the control group (Adj.MD: 4.87, 95%CI: 2.25, 7.48 $p<0.001$). These large effect sizes, maintained across the 24 months of the intervention indicate a substantial impact of the intervention on the foundation of Swahili literacy acquisition. Furthermore, this impact was translated into an improved performance in Swahili word reading after 24 months, whereby children in the intervention group scored on average 2.3 points higher in this assessment than children in the control group (Adj.MD: 2.30, 95%CI: 0.03, 4.58 $p=0.047$). However, at both 9 and 24 month follow-ups no statistical difference in mean score was observed for English letter knowledge.

Interaction between the malaria and literacy intervention

There was no evidence of a synergistic effect between the two interventions, with p-values of 0.45, 0.26 and 0.6 for spelling, Swahili letter sounds and English letter knowledge respectively in Class 1 children.

Table 16. Effect of the literacy intervention on education outcomes for 2491 and 2470 class 1 children who had not withdrawn and were not dead at 9 and 24- months follow-up. Cluster sizes range from 8 - 27 children for all outcomes.

Outcome; N (%)		**Control (50 schools)**		**Intervention (51 schools)**	**Mean difference [b] (95% CI)**	**p-value**	**Cluster-size; range (mean)**
		Mean (SD) [a]		**Mean (SD) [a]**			
9 months follow-up	N=1265		N=1226				
Spelling (score: 0-20) [cs]							
Unadjusted	1127	10.18 (4.28)	1103	11.94 (4.78)	1.76 (0.81, 2.71)	<0.001	8-27 (22.1)
Adjusted	1104	10.19 (4.29)	1089	11.97 (4.77)	1.43 (0.86, 2.00)	<0.001	8-27 (21.7)
Swahili letter sounds (lpm)							
Unadjusted	1129	4.78 (8.99)	1104	10.38 (13.10)	5.65 (3.12, 8.17)	<0.001	8-27 (22.1)
Adjusted	1112	4.83 (8.84)	1097	10.39 (13.11)	5.28 (3.18, 7.39)	<0.001	8-27 (21.9)
English letter sounds (lpm)							
Unadjusted	1129	22.52 (16.59)	1105	22.59 (16.60)	0.15 (-2.77, 3.06)	0.92	8-27 (22.1)
Adjusted	1112	22.60 (16.64)	1098	22.60 (16.59)	0.27 (-1.68, 2.21)	0.79	8-27 (21.9)
24 months follow-up	N=1255		N=1215				
Spelling (score: 0-20) [c]							
Unadjusted	1005	11.12 (3.46)	1018	11.90 (3.14)	0.78 (0.20,1.37)	0.008	8-26 (20.0)
Adjusted	984	11.13 (3.46)	1006	11.89 (3.15)	0.53 (0.10, 0.97)	0.02	8-25 (19.7)
Swahili letter sounds (lpm)							
Unadjusted	992	6.48 (13.04)	1014	11.37 (15.87)	5.28 (2.39, 8.17)	<0.001	8-26 (19.9)
Adjusted	976	6.58 (13.12)	1005	11.38 (15.89)	4.87 (2.25, 7.48)	<0.001	8-25 (19.6)
English letter sounds (lpm)							
Unadjusted	1003	33.57 (19.20)	1014	33.29 (18.90)	-0.38 (-3.70, 2.95)	0.83	8-26 (20.0)
Adjusted	987	33.57 (19,19)	1005	33.26 (18.91)	-0.04 (-2.60, 2.53)	0.98	8-26 (19.7)
Swahili words (wpm)							
Unadjusted	981	17.63 (17.54)	1004	20.32 (17.38)	2.78 (-0.08, 5.64)	0.06	8-26 (19.7)
Adjusted	966	17.67 (17.53)	995	20.27 (17.37)	2.30 (0.03, 4.58)	0.047	8-25 (19.4)

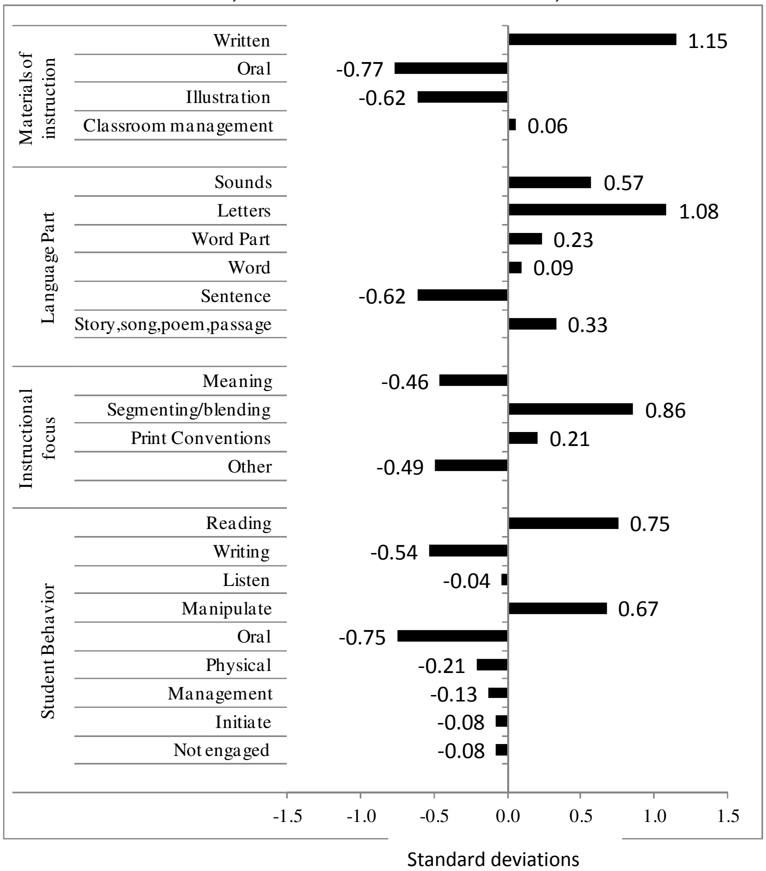
N=number of children eligible for follow up (not withdrawn or deceased)
[a] Mean score and sd at follow
[b] Mean difference (intervention-control) for scores are obtained from GEE analysis accounting for school-level clustering
[c] The same class 1 spelling task was given at baseline, 9 and 24 months follow-ups, with different words used for the 24 month follow-up.
[e] Same addition task conducted at 9 months follow-up and at baseline, hence baseline adjustment is for the same task.
[f] Addition task conducted at baseline and arithmetic task containing addition, subtraction, multiplication and division conducted at 24 months follow-up, hence baseline adjustment for different task.
Unadjusted: All children with outcome measures, not adjusted for any baseline or study design characteristics.
Adjusted: for baseline age, sex, school mean exam score and malaria group (to account for stratification) and baseline measure of the outcome, where availab

Impact on teaching and class behaviors : classroom observations

In order to better understand the mechanisms through which the literacy intervention influenced teaching and student learning, classroom observations, conducted during the first year of the intervention, recorded the instructional focus of the teachers and the amount of time class 1 students were engaged in literacy activities in the classroom. The observations were made at the individual level for the teachers, but the class level for the children and the findings are based on the average across observations of both an English and a Swahili lesson made during a single visit to each school. Classroom inventories conducted also documented the instructional materials used during lessons and quantity of text displayed in the classroom.

Figure 12 shows model-based effect sizes reported in terms of standardized coefficients (standard deviations). These estimates were modeled controlling for teacher characteristics – teacher language, years of experience teaching and education level and were modelled at the school level, (classroom observations were not possible in 2 schools) rather than the individual child level.

Figure 12. Effect sizes ((intervention mean-control mean)/pooled standard deviation) of the impacts of the literacy intervention on modes of instruction by teacher, emphasis given by teacher on language (sounds, letter, ward parts etc.), teacher instructional focus, and overall class behavior, based on classroom observations.



Increases in processes that promote literacy development, such as children engaging more with text, were observed across all aspects of teacher instructional focus and student engagement in the intervention schools. Intervention teachers were found to use significantly more written (textual) material when teaching (+1.15 sd) and less oral (-0.77sd) and visual materials (-0.62 sd), which contain no visual text. Additionally intervention teachers spent significantly more time on appropriate behaviours for early literacy development such as manipulating the building blocks, letters (+1.08 sd) and sounds, and blending and segmenting (+0.86sd) these parts. This was complemented by a reduction in inappropriate behaviours such as a focus on sentences and meaning observed in the intervention classrooms when compared to the control classrooms. An overall reduction in oral learning (e.g. choral repetition) and writing was seen by the students in the intervention classrooms, and an increase in reading and manipulating of text was observed, ultimately allowing the students to develop the processes necessary for literacy acquisition.

Analysis of potential mediators of the literacy intervention on spelling outcomes at 9 months

Based on the review of previous literature, five possible predictors of spelling outcomes at follow up 1 were identified for assessment through a mediation analysis. These were: (1) focus on letters and sounds; (2) focus on written mode of instruction; (3) print displayed in classroom; (4) focus on teaching blending and segmenting; and (5) student time spent reading in class. Initially five single mediation analyses were conducted using generalized estimating equation models, whereby each potential mediator was looked at individually. In contrast to Figure 12 above, which reports standardized coefficients (effect sizes) at the teacher level, Table 17 reports unstandardised coefficients and is modeled at the child level, controlling for child age, sex and baseline spelling scores and so uses 2491 observations. Figure 13 depicts a conceptual model of the single mediation pathways displayed in table 17.

Figure 13. Conceptual model of single mediation analysis

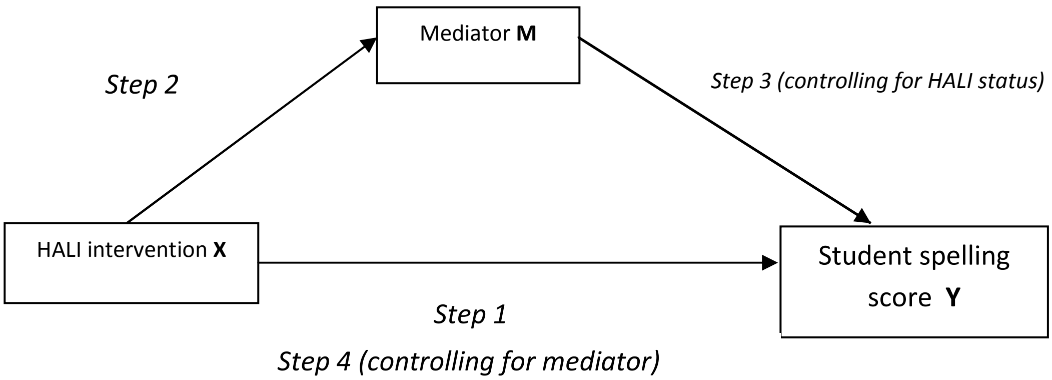


Table 17. Teacher behaviours and their role in the mediation of the literacy intervention impacts on spelling outcomes at 9 months for 2492 class 1 children.

Step 1: X predicts Y (path c)
Step 2: X predicts M (path a)
Step 3: M predicts Y controlling for X
Step 4: X on Y controlling for M is zero

Primary teaching behaviors we hope to change	Step 1 (X-->Y)	Step 2 (X-->M)	Step 3 (M-->Y | X)	Step 4 (X-->Y | M is 0)	**Mediation**
Focus on letters and sounds (combined)	1.77***	0.048***	4.15	1.38***	Partial, step 3 not significant
Focus on written mode of instruction	1.77***	0.164***	1.68	1.24***	Partial, step 3 not significant
Print displayed (from inventory)	1.77***	5.96***	0.031*	1.39***	partial
Blending or segmenting	1.77***	0.141***	0.838	1.40***	Partial, step 3 not significant
Student time spent reading	1.77***	0.099***	2.15*	1.29***	partial

*p<0.05 **p<.01 ***p<0.001
All analyses control for child covariates – age, sex and baseline spelling score
Each row represents a separate analysis.

These results show evidence of partial mediation for print displayed in the classroom, and student time spent reading in class. The other three mediators - time spent on letters and sounds, focus on written material, and time spent teaching blending and segmenting of words - all reduced the size of the overall literacy intervention treatment impact when included in the model, indicating that they could be responsible for a small part of the literacy intervention impact. However, as step 3 in the pathway for these mediators was not statistically significant, they cannot be described as mediators.

Table 18 present results of the multiple mediation analysis, which included all five possible mediators in the same analysis, with each pathway controlling for all others (hence the coefficients are smaller) and adjusting for clustering within schools as well as child baseline spelling scores, child sex and child age. Here standardised coefficients (effect sizes) are reported, as is in figure 12. It was observed that in the context of all five mediators, the direct pathway of treatment status on spelling was no longer significant (p=0.273). The analysis also shows significant indirect effects for print displayed and student time reading in class indicating that these are the largest and statistically significant pathways through which the treatment impact on spelling is occurring.

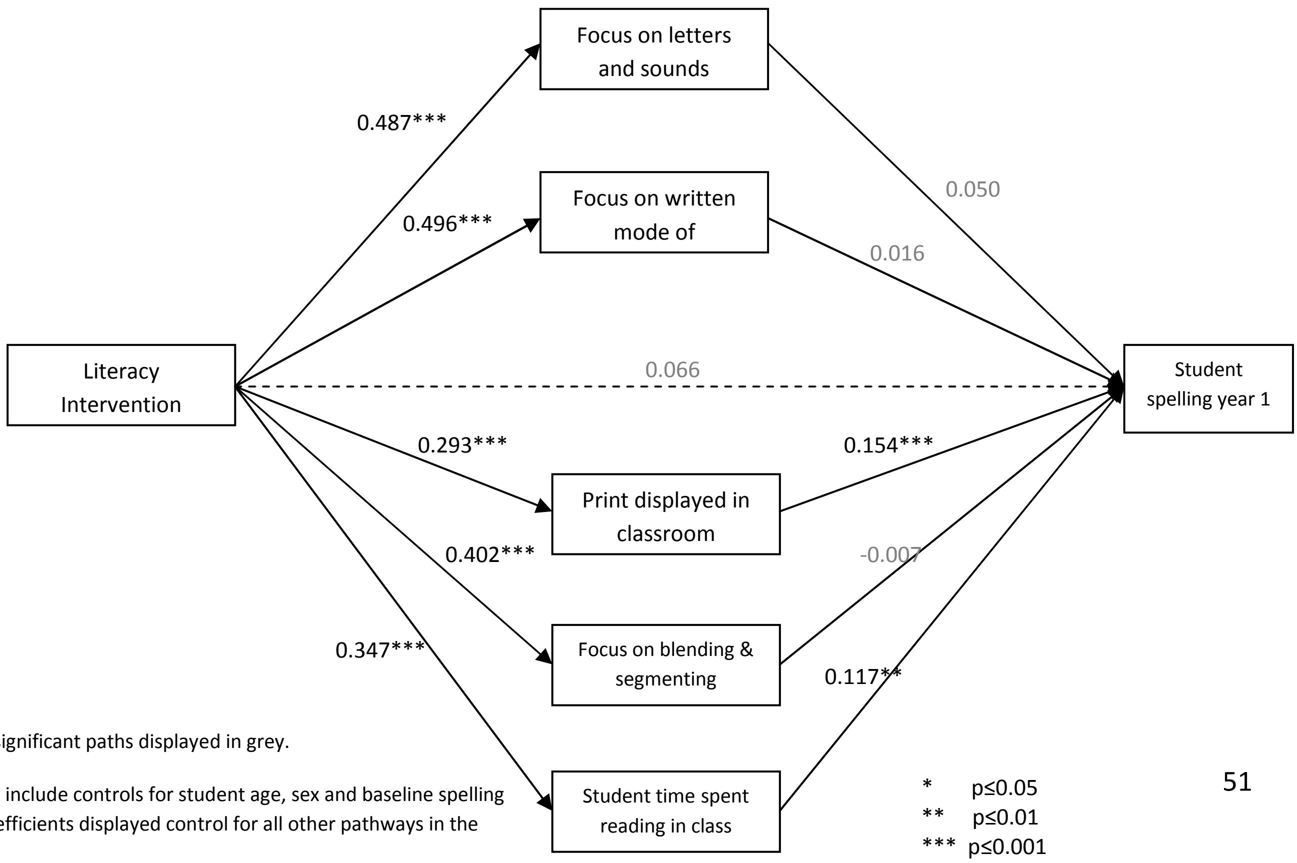
Table 18. Multiple mediation analysis of impacts on teacher literacy practices and child spelling outcomes at year 9 months for 2492 class 1 children.

	Standardized coefficient (*b*) for path					
	Intervention to mediator		**Mediator to spelling**		**Standardized Indirect Effects**	
Focus on letters and sounds (combined)	0.487	***	0.050		0.024	
	(0.067)		(0.066)		(0.033)	
Focus on written mode of instruction	0.496	***	0.016		0.008	
	(0.067)		(0.058)		(0.029)	
Print displayed (from inventory)	0.293	***	0.154	***	0.045	*
	(0.086)		(0.044)		(0.019)	
Focus on belnding and segmenting	0.402	***	-0.007		-0.003	
	(0.085)		(0.057)		(0.023)	
Student time spent reading in class	0.347	***	0.117	**	0.041	
	(0.101)		(0.044)		(0.018)	*

*p<0.05 **p<.01 ***p<0.001
Model controls for child covariates – age, sex and baseline spelling score and is adjusted for school level clustering.

The results from Table 18 are shown schematically in Figure 14, whereby the direct pathway of intervention status B=0.066 p=0.273 is shown in addition to the mediation pathways, adjusted for the others. The indirect pathways of print displayed and time spent reading are significant.

Figure 14. A schematic of the mediation pathways from the intervention to the spelling outcomes at follow-up 1 for the multiple mediation model. Standardised coefficients reported.



NOTE: Non-significant paths displayed in grey.

All pathways include controls for student age, sex and baseline spelling score. All coefficients displayed control for all other pathways in the model.

Costs and cost-effectiveness of the literacy intervention

We estimated the cost of the literacy intervention for a typical Kenya district with 62 teachers and reaching 3844 children, based on empirical costs collected in the study. The total cost of the modelled district level programme was US$ 32,940 (Table 20) or US$ 531 per teacher and US$ 8.57 per child. Direct financial costs comprised 76% of the total cost.

Table 19: Summary of Total, Direct and Indirect Cost (US$ 2010)

	Total Cost	Direct Cost[1]	Indirect Cost[2]
District Level Programme	32940	25049	7907
Per Teacher	531	404	128
Per Child	8.57	6.52	2.06
%		76	24

[1]Direct costs includes all financial expenditure
[2]Indirect costs include the opportunity cost of teacher and ministry officials during training and programme support.

Table 20 presents the cost breakdown by intervention component and resource type. It is most easily accessed by the percentage of total costs where we can see that three main intervention component contributors to cost were a) the initial training (32.4%) b) the teacher materials (28.6%) and c) the SMS support (20.4%). Consumables were the greatest driver of costs (53.7%).

Table 20: Programme costs by resource type and intervention component (US$ 2010)

	Intervention Component							
Resource Type	Manual	Teaching Materials	SMS Support	Initial Training	Follow-Up Training	District Admin	TOTAL	%
Consumables	1454	8911	5596	1735	-	-	17695	53.7
Personnel	35	195	1005	3785	1954	1078	8052	24.4
Transport	-	330	-	942	942	-	2215	6.7
Facility	16	-	107	4206	349	300	4979	15.1
TOTAL	1504	9437	6707	10668	3246	1378	32940	
%	4.6	28.6	20.4	32.4	9.9	4.2		

A fuller cost-effectiveness analysis of the literacy intervention is underway.

Acceptability of the literacy intervention from the teachers perspective

During the follow-up trainings, facilitators led a combination of small focus group discussions of 6 to 12 people and individual interviews. These, together with the weekly summary sheets and the text message communications provided means by which to gauge the success of the intervention and which aspects could be improved on for future when considering scale up.

Training workshops

The workshops were well received by the teachers who suggested more workshops would be useful. Comments such as, "*Because in this forum you meet different people and share your ideas",* were representative of their desire to learn new methods, develop camaraderie with other teachers from the region, and change in routine. Furthermore we learned that teachers preferred the practical aspects of the training to the theory. One comment was representative of what many teachers said, "*What I can say is there was a lot of theory".* Therefore, the subsequent workshops included more practice to explore the provided lessons because they, "*Want to go through the file (the manual) because there (at the schools) we don't have the time to go through the file so up to now there are some things we don't know"*.

Teacher manual

Many teachers commented on the overall approach introduced in the manual: "*I really like the methodology. The new methods of teaching compared to the ones we had they have really assisted in making a change in classes like the phonetics, letter making, sounds".*

Some teachers expressed a desire to share the methods with others: "*I try to call my colleagues from Standard two and three and introduce them to the lessons. They are trying it and they are very much curious to learn it. They find it very much enjoyable and it helps the children."* We also have comments on the children responses to the intervention lessons: "*Because before changing to the HALI lessons the pupils were having a very hard time reading. But since I started teaching them how to read and get letter sounds they can even read the words without my help".*

Teachers shared their opinions about the lessons provided in the manual. It was discovered that the Swahili lessons often took more than the specified time. However, even though many teachers had a similar sentiment, they felt the time was useful, "*I normally go beyond the period schedule only that my pupils enjoy it so much and I find it is helping even in the other lessons. HALI lesson helps even to teach in understanding the English, Kiswahili and the rest of the subjects although it normally consumes quite a lot I normally use two periods".* As a result teachers were encouraged to use those lessons over two separate 35-minute classes instead of just one. Similarly, based on the progress that teachers made in the first few months, it was realized that the daily lessons intended for just one school year would be sufficient for two.

Classroom materials

The materials were well received yet were not without problems. Most frequently teachers identified how the materials enhanced their instruction with comments such as, "*The string and those small paper cards - they normally work very well when I am teaching blending and I have a string so I can put the letters there then I merge them. They (*the children*) form a word and I form a word on the other side".* Yet, the teachers whose classrooms did not have doors or cabinets had added responsibilities to avoid theft: "*Sometimes you fix charts and find that they have been plucked".* Examples were cited whereby the cards with words and letters created by the teachers were also lost to theft: "*During the weekend they cut the strings through the window then they pull it away they take the pegs and throw the cards away"*.

Weekly text messages

The text messages (SMS) were effective for several reasons. For one, they helped to maintain regular interactive communication. Secondly, the SMS exchanges helped to keep teachers motivated to use the HALI lessons. One teacher said "*SMS's are good because they motivate me to teach the HALI lessons.* And the text messages were considered informative. *I find them to be educative. I get new ideas sometimes from the SMS".* They also enabled close monitoring of the teachers' involvement in the intervention, such as when a teacher transferred out and so left the intervention, or when there were exams and so the lessons were suspended. The text messages also helped gauge which methods were the most engaging to the children or those that the teachers preferred (and ultimately used) which were subsequently promoted in the follow-up trainings. Finally, we learned when the original intent of the method was not translating well into practice so we shared tips on how to use the method.

Interpretation of findings

The main goal of the literacy intervention was to develop teachers' capacity to influence their students' reading achievement. The intervention had a significant impact on both Swahili sound knowledge at the end of the first year, sustained into the second year of the intervention, which was translated into significantly improved Swahili word reading by the end of the second year. However, the lack of impact observed in English letter knowledge was somewhat surprising given that a strong positive impact of the intervention was observed in English spelling abilities at both 9 and 24 months. This could potentially be due to the fact that prior to implementing the intervention, Swahili sounds were given less attention in the classroom, indicated by the much lower baseline scores in Swahili sounds compared with English letter assessments. Thus there was more to gain from the intervention in terms of this aspect of language development and this also contributed to increased abilities in spelling, despite the fact that the words were being spelled in English rather than Swahili.
At 12 months follow-up, intervention teachers' knowledge related to beginning literacy instruction was significantly higher than those just entering the intervention and classroom observations demonstrated an impact of the intervention on many aspects of teachers' instructional focus, student engagement and use of classroom materials. However, the mediation of the intervention impact seen on spelling appears to be primarily driven by two specific mediators: students engaging with text displayed visually and increased time spent reading are relatively simple innovations to be made in the classroom, and seem to promote significant impacts on literacy development.

The intent of this intervention was not to implement a full curriculum but rather to explore the amount of support needed to facilitate teacher's use of the intervention methods shown to be effective in other contexts. To that end, we explored two sets of considerations when designing an effective literacy intervention. The primary consideration examined how to bridge the gap between current practice and recommendations based on the scientific literature on effective instruction. We found that teachers will implement new instructional methods that build from their prior experiences and we made these connections obvious in all interactions. The secondary consideration involved designing an intervention that could be replicated, scaled up and adopted by the government. This was achieved through sustainable methods such as sourcing the intervention materials locally, allowing for a common understanding of materials but with a novel way of using them.

A crucial component of a scalable intervention is cost and, the cost per child of US$ 8.57 appears relatively inexpensive compared with a range of educational interventions [75]. Although it is difficult to draw direct comparisons with other contexts, interventions such as "School in a bag" implemented in Malawi at $8.91 per child had no impact on educational performance (0.09 SD on maths assessments) compared with this intervention having a 0.4 SD impact on literacy assessments.

The teachers' perceptions of the intervention were generally very positive. Their high response rate to the weekly text message and their feedback through the self report methods such as summary sheets and focus group discussions provided good insight into successful aspects of the intervention as wells as aspects to improve on for the future. A key concern was the increased time taken to (sometimes prepare and) conduct the intervention lessons compared with the standard curriculum, but it was broadly recognised that the lessons were popular with the students in terms of increasing engagement and improving their literacy acquisition.

The teachers were not compensated for participating in the intervention, although they were sent a weekly credit top-up of Ksh 50 ($0.57) to enable them to respond to the weekly message. Compliance to the intervention was generally high, but variable and based on self report and hence caution must be applied when considering the roll out of such an intervention. Even if teachers are supportive of changing their instructional methods to meet the instructional needs of more children in this setting, actually changing their practices at a national scale, in the face of limited resources and time, requires a high level of commitment that is challenging to sustain.

Policy implications and recommendations

Malaria intervention

The intermittent screening and treatment (IST) of children in schools was identified as a possible intervention strategy in the Kenya National Malaria Strategy, 2009-2017, under a newly launched *Malaria-free schools initiative*. Our quantitative and qualitative evaluation resulted in the following key findings:

- The randomised impact evaluation showed that three rounds of IST did not reduce the prevalence of anaemia or the prevalence of *P. falciparum* infection after 12 or 24 months. No impact of IST on measures of sustained attention was observed.

- The cost analysis shows that in the current setting IST was a relatively expensive intervention, primarily due to the RDT costs and the follow-up visits to observe treatment on day 2 and 3.

- The qualitative evaluation showed that although IST was acceptable to most parents and other stakeholders, lack of understanding of the consequences of asymptomatic parasitemia and the complexity of the treatment regimens may undermine full adherence to treatment among children who are seemingly healthy.

- In terms of who delivers IST, the general consensus of stakeholders was that health workers were best placed to undertake the screening and provide treatment, and most participants were opposed to teachers taking finger prick blood samples from children, but all recognized that the involvement of teachers will be critical to the success of the programme.

POLICY IMPLICATIONS: Malaria intervention

(1) **Intermittent screening and treatment should not implemented in low to moderate malaria transmission settings in Kenya.** While infected children received treatment, they quickly become re-infected and there was no lasting impact of treatment on their health or education.

(2) **Schools could serve as screening platforms for targeted community control.** Screening of schoolchildren using rapid diagnostic tests provides a clear picture of the malaria situation in an area. School screenings conducted every 2-4 years can help target community-wide interventions, including localized larval control and community mass treatment, and help reduce overall transmission.

Literacy intervention

Our qualitative and quantitative evaluation resulted in the following key findings:

- Teachers in the study region focused on oral language development at the expense of explicit and systematic teaching of letter sounds.

- The literacy intervention increased the focus on letters and sounds in the classroom.

- The randomised impact evaluation showed that the intervention improved children’s spelling (an outcome capturing a wide range of early literacy skills) and knowledge of Swahili letter sounds. It did not improve children’s knowledge of English letters.

- Analysis of the classroom observations indicated that children's literacy improved most when teachers focused instruction on letters and sounds. Teachers in the literacy intervention group spent more time teaching letters and sounds and how to combine and take apart letters and sounds to read words. Students in intervention classrooms spent more time interacting with text and less time writing/copying from the blackboard.

- The cost of the literacy intervention was US$ 8.29 per child, with compares favourably with similar education interventions.

- Text messaging is one relatively low-cost intervention that could support teachers in implementing new pedagogical approaches. Further investigation of the usefulness of this approach is encouraged.

POLICY IMPLICATIONS: Literacy intervention

(3) Literacy instruction should include systematic teaching of letter-sound correspondence and text interaction. Focusing on the specific skills of putting letters, sounds or syllables together and breaking them apart can increase children's literacy abilities. Displaying more text in the classroom with which children can interact, such as posters, can also contribute to better literacy.

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Appendices

Appendix 1: Statistical analysis plan

Health and Literacy Intervention (HALI) Trial Interim Analyses and Analyses of One-Year Follow-Up Data

Statistical Analysis Plan

January 2012

1. Introduction

The HALI trial aims to evaluate the impact of school-based malaria prevention and enhanced literacy instruction on the health and educational achievement of school children in Kenya. HALI is a 2x2 factorial cluster randomised control trial conducted over two years starting in February 2010 with a random sample of approximately 6000 children attending selected Classes 1 or 5 of 101 primary schools in the Kwale and Msambweni districts of coastal Kenya. The primary outcomes are educational achievement and anaemia [1].

The malaria (Mal) intervention involves once-a-term screening of study children in both Classes 1 and 5 using a malaria rapid diagnostic test (RDT). Children (with or without malaria symptoms) found to be RDT-positive are treated with artemether-lumefantrine, AL (Coartem, Novartis), an artemisinin-based combination therapy. Testing and treatment is administered by district health workers and supported by the Division of Malaria Control (DoMC), Ministry of Public Health and Sanitation (MoPHS). The literacy (Lit) intervention comprises training of Class 1 teachers to improve literacy instruction within the classroom. The main components of the literacy intervention include: (i) a teacher manual, which includes 140 lessons for Class 1 teachers to develop literacy skills in English and Swahili; (ii) an initial three-day training workshop in year 1 and a follow-up one day workshop in years 1 and 2; and (iii) ongoing support which includes weekly interactive text messaging, and monthly written communiqués providing information and motivation.

The 101 schools were randomised to one of four groups: (i) the malaria intervention alone (Mal INT + Lit control); (ii) the literacy intervention alone (Mal control + Lit INT), (iii) the malaria and literacy interventions combined (Mal INT + Lit INT); or (iv) the control group (Mal control + Lit control) where neither intervention is implemented so that the school operates as usual.

The current document describes the HALI trial and provides details of the first planned analyses to evaluate the effectiveness of the two interventions based on their effect on health and educational outcomes measured in the first year of the trial. Analyses of final outcomes will be described in a separate document.

2. Sample Size

The intervention will be considered to have public health value if the intervention has a reduction of at least 25% in anaemia.

Such a reduction can be achieved with a sample size of 27 schools in each malaria intervention arm with 50 children sampled per school for an assumed baseline prevalence of 20%, coefficient of variation of 0.2, power of 80% and significance level of 5%.

As described in the trial protocol [1], educational achievement and cognitive tests sample size calculations were calculated separately for Classes 1 and 5 based on mean differences in test score between the 50 intervention schools and 50 control schools for the malaria and literacy intervention separately. A sample size of 100 schools with 25 children per class per school was assumed for each calculation. For achievement tests, this is sufficient to detect an effect size of 0.192 standard deviation (SD) with 80% power at the 5% significance level assuming an ICC of 0.2 (ICC varied from 0.1 to 0.2 with mathematics and literacy tests in class 2 in 210 schools in Western Kenya with ICC expected to be lower in class 1) and a correlation between baseline and final outcome of 0.7. Under the same conditions, except for a change in ICC this sample size is sufficient to detect an effect size of 0.15 SD for tests of sustained attention, which have a lower ICC of 0.1.

3. Randomisation

Randomisation of schools to the two interventions proceeded in two stages in public randomisation ceremonies.

In the first stage, 51 and 50 schools were randomised to the literacy intervention and control. Since Kenyan schools are arranged into so-called *school-clusters* as created by the District Education Office that regularly meet and share information, randomisation of these school-clusters was performed to avoid contamination. School-cluster size ranged from 3-6 schools. Additionally, stratification was used in the first stage, using the mean of the school-cluster's previous year's exam score. Such stratification was used to account for imbalance in educational achievement at baseline.

In the second stage, within the 51 literacy intervention and 50 literacy control schools, 26 and 25 schools were randomly selected to receive the malaria intervention. In this second stage, individual schools and not school-clusters were randomised. As for the first stage, stratification was used whereby quintiles of the previous year's exam scores were created within each of the allocated literacy intervention arms to create 5 strata of 10 schools each (with an additional school in the literacy intervention). The malaria intervention and control were then randomly allocated within each of the 10 resultant strata each comprising 10 schools (with an additional school in the literacy intervention) so that 5 schools within each stratum were allocated to the malaria intervention and 5 schools to the malaria control.

Therefore, overall, the units of randomisation where different in the two stages as were the strata (although they were derived based on the same principle). Such features will be accounted for the in the analysis phase

4. Study Population

Overall, the study population comprises all children in classes 1 and 5 enrolled in January 2010 in one of the 101 study schools which themselves comprise all schools in Msambweni District (except for the most inaccessible regions for logistical reasons) and all schools in the half of Kwale District which were not already involved in a literacy programme administered by a different organisation (namely, schools west of Shimba Hills). The cohort of children enrolled at baseline will be followed for the duration of the study i.e. all analyses will be based on the cohort rather than on cross-sectional surveys of the classes over time.

Two specific cohorts are identified to assess effectiveness of the two interventions:

- Effectiveness of the malaria intervention will be assessed in all children in the study population i.e. in both classes 1 and 5 together. However, the effect of the malaria intervention on educational outcomes must be assessed separately in the two classes as the educational outcome measures are different.

- Effectiveness of the literacy intervention, will only be assessed in children in class 1 as the intervention was only designed and administered for such children.

As a consequence, any analyses of synergy of the two interventions will only be assessed in the class 1 cohort of children.

5. Trial flow chart

Data on the number of clusters randomised (with exclusions and reasons for exclusion), the flow of children through enrolment, allocation to intervention, follow-up (including withdrawals and the stage of the trial at which they occur) and analysis will be presented in a flow chart [2].

If parents choose to withdraw consent for participation of their child, all data for that child will be removed from further analyses from the point at which consent was withdrawn with reasons for withdrawal noted.

Table A1.1. Predefined primary and secondary outcomes for each intervention and their interaction

		Intervention		
Type of outcome	Outcome	Malaria	Literacy	Malaria x literacy
<u>Primary outcomes</u>				
Health outcome (Classes 1 & 5)	Age- sex specific anaemia	x	-	-
	Plasmodium falciparum infection	-*	-	x
Class 1 educ. outcome – Attention	Single digit code transmission[Δ] (score 0-20)	x	-	-
Literacy	Spelling (score 0-20)	-*	x	x
	Swahili letter sounds (lpm) †	-*	x	x
	English letter knowledge (lpm)	-*	x	x
Class 5 educ. outcome - Attention	Double digit code transmission (score 0-20)	x	-	-
<u>Secondary outcomes</u>				
Health outcomes (Classes 1 & 5)	Haemoglobin concentration (Hb)	x	-	
	Moderate-Severe anaemia	x	-	
Class 1 educational outcomes				
Cognition	Ravens (score	-	X	-
Literacy	Beginning sounds (score 0-10)	x	x	x
	Receptive language (score 0-25)	x	x	x
	Swahili word identification (wpm)	x		
			x	x
Numeracy	Number Identification (score 0-4) ††	x	-	-
	Quantity Discrimination (score 0-4) ††	x	-	-
Arithmetic	Addition (score 0-30)	x	-	-
Class 5 educational outcomes				
Literacy	Spelling (score 0-53)	x	-	-
	Comprehension - silly sentences (score 0-40)	x	-	-
Numeracy	Arithmetic (score 0-38)	x	-	-

Note: The literacy intervention and its interaction with the malaria intervention will be assessed in Class 1 children only.
Note: wpm – words per minute, lpm – letters per minute; Note: All educational outcomes were measured at baseline except those indicated
[Δ] Not measured at baseline as test was not anticipated to be appropriate for such young children. Thus, no adjustment for baseline measurements can be made.
* Considered a secondary outcome for the malaria intervention.
† Baseline distributions indicated floor effects with a large spike at 0 words. It is anticipated that a dichotomised version of this variable will be used as the primary measure. However, the planned analysis of covariance may demonstrate that dichotomisation is not necessary.
†† The sum of these two variables will be analysed to provide an overall measure of numeracy.

6. Outcome Definitions

Anaemia will be defined according to WHO age-specific cut-offs for haemoglobin (g/l) (<110 for <5 yrs; <115 for 5yrs- <12yrs; <120 for girls 12+yrs; <120 for boys 12-<15yrs and <130 for boys 15+). Since this primary health outcome is age-specific, all efforts will be made to identify correct and complete age data. A definitive age variable will be derived by cross-validating child and parent-reported ages of the child. Sensitivity analyses will be performed where all main analyses are conducted using both parent and child-reported ages.

7. Timing of outcome measures

The measurement schedule is as follows:

- Follow-up 1 (FU1)
  - FU1 analyses of educational outcomes (Edu FU1) using measurements at 9 months
  - FU1 analyses of health outcomes (Health FU1) using measurements at 12 months
- Follow-up 2 (FU2)
  - FU2 analyses of educational outcomes (Edu FU2) using measurements at 24 months
  - FU2 analyses of health outcomes (Health FU2) using measurements at 24 months

8. Data Sets

9.1 Analysis levels and general principles of analysis

Statistical analysis will be carried out at the child level with clustering accounted for using generalised estimating equations (GEE) [3]. Given the design of the trial, whereby the literacy intervention was implemented in Class 1 children only whereas the malaria intervention was implemented in both Classes 1 and 5, separate analyses of the two interventions will form the basis of the primary analyses.

Literacy intervention In the first stage of randomisation in which the literacy intervention was allocated, school-clusters were the unit of randomisation and therefore clustering will be at that level in all these analyses. Furthermore, since stratification based on tertiles of mean school-cluster exam score for each group of school-cluster size used in the randomisation procedure, this will be accounted for by inclusion of that mean exam score as a covariate in the GEE model.

Malaria intervention In the second stage of randomisation in which the malaria intervention was allocated, schools (i.e. not school-clusters) were the unit of randomisation and therefore clustering will be at that level in these analyses. Furthermore, since stratification was used based on quintiles of mean school exam score (i.e. not mean school-cluster exam score) within the allocated treatment for the literacy intervention, a similar pragmatic approach to account for stratification will be used, but this time the mean school exam score will be used (i.e. rather than the mean school-cluster exam score). Since age is a strong predictor of anaemia and *P. falciparum* infection, age will be adjusted for in all analyses of the malaria intervention including the primary analysis.

Interaction between malaria and literacy interventions Secondary research questions will explore potential synergy between the interventions. Such analyses can be conducted in Class 1 children only. To accommodate the different units of randomisation for the two interventions, the smallest unit of randomisation (i.e. the school) will be accounted for. Similarly, stratification will be accounted for by adjustment for mean school exam score. In the case that there is evidence of an interaction (not hypothesised) at the 5% level, results in Class 1 will be presented as a four-arm trial.

For analysis of each outcome, baseline measures of that outcome will be included (i.e. analysis of covariance) except for those of *P.falciparum*, as such data is not available in malaria control schools.

9.2 Intention-to-treat and Per-protocol datasets

Primary analyses will be conducted using intention-to-treat data sets.

The intention-to-treat datasets

These will include data pertaining to all outcomes, including data on children and schools. Children will be assigned to one of the four arms of the trial according to their class and school at enrolment irrespective of whether they participated in either intervention

The per-protocol data sets
We do not expect that such data sets will be identified in the context of this trial. More specifically, any such identified data sets will form the basis of sensitivity analyses based on compliance.

9. Demographic and Other Characteristics
Tabulation of demographic and other characteristics will be generated using the intention-to-treat datasets. No significance tests will be performed to test for differences at baseline. Descriptive statistics for continuous variables will include the mean, standard deviation, median, range and the number of observations. Categorical variables will be presented as numbers and percentages.

School-level characteristics will be tabulated by treatment arm (Dummy tables 1.1a-1.1c) both by the four treatment arms (Dummy Table 1.1a) and separately for the treatment assignment of the 101 schools by education intervention arm (Dummy Table 1.1b) and malaria intervention arm (Dummy Table 1.1c), respectively. Such tables will help to differentiate between features of the two-stage randomisation process.

School-group level characteristics will be tabulated by the two arms of the literacy intervention arm.

Enrolment level baseline characteristics of children will be tabulated by the four treatment arms (Dummy tables 2.1-2.3).

10. Measurements of Compliance with the interventions
Simple measures of compliance will be reported for both the educational and malaria interventions separately. Educational measures of compliance will include a measure of teacher attendance at training, the number of HALI lessons taught and measures of classroom environment (e.g. presence of project-related materials in the classroom). These will be ascertained through scheduled and unannounced classroom visits and similar measures will be available in the control schools. Compliance to the malaria intervention will be measured by a summary of adherence to treatment in children with a positive RDT. The following will be reported at each round: (i) % of children tested each round (ii) compliance of person reading the test with test result (iii) adherence of child to first dose & full course of treatment.

11. Assessment of Effectiveness
12.1 Analysis of effectiveness of each of the malaria and literacy intervention

12.1.1 Primary analyses of the outcome(s) will follow the intention to treat principle and will be performed separately for the literacy and malaria intervention (see Section 9.1 above). All analyses will be performed at the child-level and will account for clustering (by school-cluster for the literacy intervention and by school for the malaria intervention) and for stratification (by mean school-cluster exam score and mean school exam score, respectively). Data from all children (both classes 1 and 5) enrolled in the 101 schools will be used to evaluate effectiveness of the malaria intervention whereas only data from class 1 children in the 101 schools can be used to evaluate effectiveness of the literacy intervention.

All analyses will account for the nature of the distribution of the outcome and report appropriate measures of effect and 95% CIs. Continuous outcomes will also be reported on SD scales for comparability of effect estimates. (Dummy table 3.1).

Approximately 15 outcomes (including the primary outcome and excluding secondary outcomes for which floor effects are anticipated whereby the distribution of the outcome shows a heavy-left tail i.e. clumping at 0) will be considered for formal statistical testing at the 5% level for each of the two interventions (see table of Section 6) in each class.

An important secondary analysis will be conducted in class 1 children only whereby the malaria and literacy interventions are analysed at the same time to assess sensitivity of the estimated effectiveness of the literacy intervention accounting for the malaria intervention. Clustering will be accounted for at the school level.

12.1.2 Secondary analyses

Additional educational measures in Class 1 for which floor effects are anticipated will be examined without formal testing. The following measures of literacy will be considered for both the literacy and malaria intervention: English word identification (wpm); English oral reading fluency (wpm); English comprehension (score 0-5); Swahili oral reading fluency (wpm); Swahili comprehension (score 0-5). The shape recognition test with an anticipated ceiling effect whereby the distribution shows a heavy-right tail (i.e. clumping at upper end of distribution) (score 0-4) will be considered for both interventions, with the missing number test (score 0-10) also considered for the malaria intervention. The subtraction test will be examined in Class 1 for the effect of the malaria intervention.

12.1.3. Examination of Subgroups

All sub-group analyses will be performed by including a variable (or variables, as appropriate) for the sub-group and its interaction with the treatment effect in the GEE model. Then differences between sub-groups will be identified by significance of the interaction. Although no formal adjustment to account for multiple testing will be performed, the conclusions drawn from the series of analyses will be interpreted with caution in light of the problems of a Type 1 error with a large number of tests.

The following sub-groups will be considered for analysis of one of the interventions or both: high, medium or low baseline prevalence of *P. falciparum* infection schools with one or more malaria case at baseline (based on strata created by propensity scoring to account for missing baseline information in malaria control schools), low, medium and high ITN coverage at baseline, high, medium and low baseline educational achievement, compliance to the intervention, preschool attendance, mother's education, language spoken at home, anaemia, stunting. In addition analysis of additional tests will be considered for children where the proposed tests failed to discriminate adequately.

12.2 Statistical/analytical issues

12.2.1 Adjustments for Covariates

Unadjusted and adjusted results will be presented for all analyses. Adjustment for age and gender is pre-specified as the main adjusted analysis for each outcome. A second, 'fully' adjusted analysis will be conducted for each outcome with additional adjustment for baseline nutritional status (measured by height-for-age), school-feeding, number of other children in the household, mother's education, wealth (measured by type of walls at home and whether the household owns a radio), time of baseline and time since baseline (to account for seasonality). Note that, as stated in Section 12.1.1, unadjusted results obtained using analysis of covariance will account for the baseline measurement of the outcome (except for baseline *P.falciparum* as data are missing for the malaria control arm).

12.2.2 Sensitivity analyses

Sensitivity analyses will be conducted for primary and secondary outcomes where floor effects are anticipated. Pre-specified alternative baseline measures are indicated in the table in the Appendix.

12.2.3 Dropouts and Missing Data

The data coordinating centre in Nairobi will be responsible for logging all data as they arrive and informing the trial manager about any missing data. Missing data will be chased until it is received or confirmed as not available when the analysis stage is reached. Data quality, follow up and trial monitoring will be facilitated through the development of a trial specific database, including validation, verification, monitoring and compliance assessment. Therefore we do not anticipate needing to undertake any formal imputations. However, if there appeared to be differential attrition by treatment arm, inverse probability weighting would be considered to support the conclusions arrived at from the complete case analysis [4].

12.2.4 Interim Analysis and Data Monitoring

The trial is planned to last for 2 years. An independent Data Monitoring Committee (DMC) will be established to review, in strict confidence, data from the FU1 analyses of the trial described in the present document. The DMC will meet approximately four months after collection of the FU1 data to allow for seeking out missing data and for data cleaning and analysis i.e. in the latter half of 2011. The Chair of the DMC may also request additional meeting/analyses. No recommendations for stopping for effectiveness are specified. If a problem were to be detected, this could lead to a recommendation to amend aspects of the protocol. The committee will agree terms of reference. Meetings will be organised by the trial statistician at a date convenient to the DMC. A brief report from the DMC will be supplied to the trial steering committee following the meeting, with feedback sent to the funder on approval of the steering committee.

12.2.5 Multiple Comparisons/Multiplicity
The number of secondary outcomes that will be tested for significant differences between arms is small and thus no formal adjustment for multiple comparisons will be made. However a large number of subgroup analyses have been pre-specified and the results of these will be treated with appropriate caution.

13. Safety Evaluation

13.1 Adverse Events (AEs) and Serious Adverse Events (SAEs)
The malaria treatment, artemether-lumefantrine, is a well-tolerated and widely used drug, with very low incidence of reported SAEs [5]. Because of these low risks, AEs and SAEs were actively monitored by the study team for three days after each treatment, and a further 28 days thereafter using a passive surveillance system in schools and local health centres. The results of this monitoring will be given to the DMC at the time of the interim analysis

13.2 Deaths
Information of all SAEs and deaths will be collected and reported in both arms of the trial. Deaths are monitored during routine school visits. The DMC will be notified whenever a death occurs within 30 days of treatment in the malaria intervention arm. Other deaths and possible causes are recorded.

References

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Appendix 2: Members of the Data Monitoring Committee (DMC)

DMC members included experts with extensive experience in cluster randomized trials and impact evaluations from both a malaria and an education perspective:

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Appendix 3: Baseline characteristics by the four study groups

Table A3.1. Baseline school-level characteristics by study groups

Characteristic; n (%)	Double control	Literacy only	IST only	Both IST + Literacy
Number of schools	25	25	25	26
School characteristics – 2009				
Exam score -Mean (sd)	228.3 (29.0)	218.5 (25.5)	226.4 (26.0)	225.2 (31.6)
School size -Median (IQR)	681 (345,961)	371(298, 555)	544 (389, 727)	579 (413,686)
Min, max	199, 1439	85, 4891	225, 1344	257, 1031
School programmes†				
Feeding	13 (52.0)	9 (36.0)	16(64.0)	11 (42.3)
De-worming	25 (100)	25 (100)	24 (96.0)	25 (96.2)
Malaria control	7 (28.0)	2 (8.3)*	8 (32.0)	4 (15.4)
Division†				
Diani	4 (16.0)	10 (40.0)	7 (28.0)	6 (23.1)
Lunga Lunga	9 (36.0)	5 (20.0)	9 (36.0)	12 (46.2)
Msambweni	7 (28.0)	5 (20.0)	3 (12.0)	4 (15.4)
Kubo	5 (20.0)	5 (20.0)	6 (24.0)	4 (15.4)
Children enrolled in HALI ††				
Class 1				
10-14	0	2 (8.0)	0	0
15-19	0	2 (8.0)	0	0
20-24	5 (20.0)	5 (20.0)	4 (16.0)	6 (23.1)
25-29	20 (80.0)	16 (64.0)	21 (84.0)	20 (76.9)
Mean (SD)	25.1 (1.4)	23.4 (4.3)	25.7 (1.9)	25.2 (1.4)
Min, max	22,29	9,29	21,29	21,28
Class 5				
10-14	1 (4.0)	2 (8.0)	0	0
15-19	1 (4.0)	1 (4.0)	1(4.0)	1 (3.9)
20-24	4 (16.0)	1 (4.0)	2 (8.0)	3 (11.5)
25-29	13 (52.0)	14 (56.0)	14 (56.0)	18 (69.2)
30-34	6 (24.0)	7 (28.0)	8 (32.0)	4 (15.4)
Mean (SD)	25.7 (4.0)	25.8 (5.3)	27.6 (3.7)	26.4 (2.8)
Min, max	14,30	8,30	16,32	19,32

† % of schools in each arm; †† % of those in recruited in each study group within each class;
* information missing for one school (Mkanda), % of non-missing

Table A3.2. Baseline demographic characteristics of 5177 HALI study children by study group.

Characteristic; n (%)	Double control	Literacy only	IST only	Both IST + Literacy
Total children	1270	1232	1334	1341
Sex†				
Male	614 (48.4)	634 (51.5)	630 (47.2)	669 (49.9)
Age†				
5-6	140 (11.0)	178 (14.5)	143 (10.7)	121 (9.0)
7-9	363 (28.6)	352 (28.6)	392 (29.4)	395 (29.5)
10-12	455 (35.8)	416 (33.8)	433 (32.5)	484 (35.1)
13-14	248 (19.5)	236 (19.2)	292 (21.9)	272 (20.3)
15-19	64 (5.0)	50 (4.1)	74 (5.6)	69 (5.2)
Mean (SD)	10.2 (2.8)	10.0 (2.9)	10.4 (2.9)	10.3 (2.8)
Min, max	5,18	5,19	5, 18	5,18
Class 1††	628 (49.5)	586 (47.6)	643 (48.1)	654 (48.8)
Sex				
Male	315 (50.2)	308 (52.6)	315 (49.0)	340 (52.0)
Age				
5-6	140 (22.3)	178 (30.4)	143 (22.2)	121 (18.5)
7-9	355 (56.5)	332 (56.7)	386 (60.0)	389 (59.5)
10-12	129 (20.5)	74 (12.6)	112 (17.4)	141 (21.6)
13-14	4 (0.6)	1 (0.2)	2 (0.3)	2 (0.3)
15-19	0	1 (0.2)	0	1 (0.2)
Mean (SD)	8.0 (1.8)	7.4 (1.6)	7.9 (1.7)	8.0 (1.7)
Min, max	5,14	5,15	5,13	5,15
Class 5††	642 (50.5)	646 (52.4)	691 (51.8)	687 (51.2)
Sex				
Male	299 (46.6)	326 (50.5)	315 (45.6)	329 (47.9)
Age				
5-6	0	0	0	0
7-9	8 (1.2)	20 (3.1)	6 (0.9)	6 (0.9)
10-12	326 (50.8)	342 (52.9)	321 (46.5)	343 (49.9)
13-14	244 (38.0)	235 (36.4)	290 (42.0)	270 (39.3)
15-19	64 (10.0)	49 (7.8)	74 (10.7)	68 (9.9)
Mean (SD)	12.5 (1.5)	12.3 (1.6)	12.6 (1.5)	12.5 (1.6)
Min, max	9,18	8,19	9,18	9,18

† % of total children in each study group; †† % of children in each study group for each class

Table A3.3. Baseline socio-economic status and home environment of 5177 children at baseline by study group.

Characteristic; n (%)†	Double control	Literacy only	IST only	Both IST + Literacy
Total children	1270	1232	1334	1341
Education level of HH*				
No schooling	421 (33.9)	302 (24.8)	482 (36.7)	427 (32.3)
Primary	622 (50.1)	661 (54.4)	673 (51.2)	696 (52.7)
Secondary	161 (13.0)	188 (15.5)	127 (9.7)	150 (11.4)
College/degree	37 (3.0)	65 (5.4)	33 (2.5)	48 (3.6)
Missing	29 (2.3)	16 (1.3)	19 (1.4)	20 (1.5)
Home environment				
Water source				
Covered	1030 (82.8)	1097 (89.6)	1061 (80.2)	1225 (92.4)
Uncovered	214 (17.2)	127 (10.4)	262 (19.8)	101 (7.6)
Missing	26 (2.1)	8 (0.7)	11 (0.8)	15 (1.1)
Roof type				
Makuti/grass/thatch	855 (68.7)	760 (62.1)	967 (73.1)	999 (75.3)
Iron sheets/tiles	389 (31.3)	464 (37.9)	356 (26.9)	328 (24.7)
Missing	26 (2.1)	8 (0.7)	11 (0.8)	14 (1.0)
Wall material				
Mud/clay/wood	945 (76.0)	848 (69.3)	1028 (77.7)	1052 (79.3)
Bricks/Cement	299 (24.0)	376 (30.7)	295 (22.3)	275 (20.7)
Missing	26 (2.1)	8 (0.7)	11 (0.8)	14 (1.0)
Electricity	38 (3.1)	91 (7.4)	38 (2.9)	22 (1.7)
Missing	26 (2.1)	8 (0.7)	11 (0.8)	14 (1.0)
Pit latrine	733 (58.9)	832 (68.0)	702 (53.1)	718 (54.1)
Missing	26 (2.1)	8 (0.7)	11 (0.8)	14 (1.0)
Household assets				
Bicycle	666 (53.5)	661 (54.0)	673 (50.8)	713 (53.7)
Motorcycle	51 (4.0)	81 (6.6)	57 (4.3)	62 (4.7)
Radio	778 (62.5)	821 (67.1)	745 (56.3)	848 (63.9)
Television	113 (9.1)	166 (13.6)	114 (8.6)	94 (7.1)
Mobile phone	752 (60.5)	793 (64.8)	724 (54.7)	762 (57.4)
Missing††	26 (2.1)	8 (0.7)	11 (0.8)	14 (1.0)
Household size				
1-5	318 (25.6)	372 (30.5)	358 (27.1)	341 (26.0)
6-7	460 (37.0)	444 (36.4)	500 (37.9)	480 (36.6)
8-9	274 (22.0)	259 (21.2)	292 (22.1)	291 (22.2)
10-31	191 (15.4)	145 (11.9)	172 (13.0)	200 (15.2)
Missing	27 (2.1)	12 (1.0)	12 (0.9)	29 (2.2)
Child sleeps under net				
Usually	824 (66.3)	830 (68.0)	822 (62.2)	844 (64.4)
Missing	27 (2.1)	12 (1.0)	12 (0.9)	30 (2.2)
Last night	800 (63.0)	794 (64.4)	785 (58.8)	808 (60.361.)
Missing	447 (35.2)	402 (32.6)	512 (38.4)	497 (37.1)
Number of nets in household				
0	193 (16.9)	150 (13.4)	205 (17.6)	196 (16.5)
1-2	343 (30.0)	340 (30.3)	392 (33.6)	342 (28.7)
3-4	457 (40.0)	432 (38.5)	441 (37.8)	449 (37.7)
5+ (max 13)	149 (13.1)	199 (17.8)	129 (11.1)	203 (17.1)
Missing	128 (10.1)	111 (9.0)	167 (12.5)	151 (11.3)

† All percentages of children with non-missing data in each study group. Missing numbers indicated with percentage of total in study group.
†† Same number missing for each category of household assets in each study group.
* HH: Household head.

Table A3.4. Baseline measures of falciparum, anaemia and health for 5177 HALI children by study group.

Health measure; n (%)†	Double control	Literacy only	IST only	Both IST + Literacy
Total children	1270	1232	1334	1341
Anaemia				
Age-sex specific*	553 (46.0)	520 (44.4)	563 (46.3)	552 (44.6)
Severe (<70 g/l)	7 (0.6)	7 (0.6)	6 (0.5)	8 (0.7)
Moderate (70-89 g/l)	17 (1.4)	26 (2.2)	24 (2.0)	31 (2.5)
Mild (90-109 g/l)	283 (23.5)	247 (21.1)	270 (22.2)	248 (20.1)
None (≥110 g/l)	895 (74.4)	891 (76.1)	915 (75.3)	950 (76.8)
Haemoglobin				
Mean (SD) (g/l)	117.1 (12.6)	117.6 (13.4)	117.4 (13.3)	117.6 (14.0)
Missing	68 (5.4)	61 (5.0)	119 (8.9)	104 (7.8)
P. falciparum* infection*	$	$	158 (13.3)	153 (12.6)
Missing			148 (11.1)	123 (9.2)
Anthropometric measures***				
Wasted	149 (31.4)	114 (22.5)	113 (23.4)	118 (24.7)
Missing	28 (5.6)	24 (4.5)	52 (9.7)	38 (7.4)
Stunted	330 (27.4)	269 (22.9)	300 (24.7)	310 (25.0)
Missing	67 (5.3)	56 (4.6)	121 (9.1)	103 (7.7)
Underweight	254 (21.1)	225 (19.1)	225 (18.6)	225 (18.2)
Missing	67 (5.3)	56 (4.6)	121 (9.1)	104 (7.8)

† All percentages of children with non-missing data in each study group. Missing numbers indicated with percentage of total in study group.
* Age-sex specific anaemia was defined using age and sex corrected WHO thresholds of haemoglobin concentration:
<110g/l in children under 5 years;
<115g/l in children 5 to 11 years;
<120g/l in females 12 years and over and males 12 to 15 years old; and
<130g/l in males over 15 years.
** By blood slide reading.
$ Not measured in 50 malaria control schools at baseline.
*** By WHO Anthroplus software according to z-scores of weight, height and BMI for age. Wasting defined for <10 years only so that missing % presented only for those < 10 years.

Table A3.5. Baseline educational measures for 5177 HALI study children by study group.

Educational measure; median (IQR) min, max / missing	Double control	Literacy only	IST only	Both IST + Literacy
Total number of children	1270	1232	1334	1341
Class 1				
Number of children	628	586	643	654
Attention				
Single digit code transmission (score: 0-20) $				
Literacy				
Spelling (score: 0-20)	7 (5,11)	8 (6, 13)	7 (4, 10)	7 (5, 10.5)
	0, 19 / 3	0, 19 /5	0, 18 / 22	0, 20 /10
Swahili letter sounds (lpm)	0 (0,9)	1 (0,16)	0 (0, 6)	0 (0,9)
	0 , 50 / 6	0, 66 / 3	0, 55 /23	0, 53 / 10
Swahili word identification (wpm)	0 (0,1)	0 (0,2)	0 (0,1)	0 (0,1)
	0, 39 / 6	0, 31 /3	0, 32 /23	0, 33 / 10
English letter knowledge (lpm)	16 (4,29)	15 (1,29)	10.5 (0,25)	12 (2,27)
	0, 75 / 6	0, 78 / 3	0, 87 / 23	0, 68 / 9
Beginning sounds (score: 0-10)	5 (3,7)	5 (4,7)	5 (3,7)	5 (3,7)
	0, 10 / 0	1, 10 / 3	0, 10 / 23	0, 10 / 7
Receptive language (score: 0-25)	19 (16,21)	19 (17,21)	18 (15,21)	19 (16,21)
	1, 25 / 5	3, 25 / 4	2, 25 / 28	0, 25 / 11
Ravens (score: 0-22)	8(6,9)	7 (6,9)	7 (6,9)	7 (6,8)
	0, 18 / 0	0, 17 /3	0, 18 / 22	0, 17 / 9
Numeracy				
Total score* (score: 0-30)	2 (2,4)	2 (2,5)	2 (2,3)	2 (2,4)
Arithmetic	0,13 / 7	0,18 / 5	0,20 / 24	0,16 / 10
Addition (score: 0-30)	2 (1,3)	2 (1,3)	2 (0,3)	2 (1,3)
	0,14 / 1	0,17 / 3	0,13 / 24	0,15 / 10
Class 5				
Number of children	642	646	691	687
Attention				
Double digit code transmission (score: 0-20)	10 (4,14)	11 (5,15)	11 (6,15)	11 (6,15)
	0,20 / 0	0,20 / 2	0,20 / 9	0,20 / 4
Literacy				
Spelling (score: 0-53)	22 (17.5,28)	24 (18,30)	22 (16,27)	23 (17,28)
	0,45 / 2	0,44 / 1	1,43 / 7	1,42 / 5
Comprehension - English (score: 0-40)	30 (25,35)	31 (26,36)	29 (24,33)	29 (25,35)
	0,40 / 0	0,40 / 1	4,40 / 10	0,40 / 7
Numeracy				
Arithmetic (score: 0-38)	30 (26, 33)	30 (26, 33)	30 (25, 33)	29 (26, 33)
	0 ,38 / 5	4,38 / 3	1,38 / 14	0,38 / 10

lpm: letters per minute; wpm: words per minute
$ Not measured at baseline. ***** Total score: number identification + quantity discrimination

Appendix 4: Methods and results for the missing data models

We performed a missing data analysis using a likelihood based repeated measures analysis. In order to gain power and account for missing data, we used a likelihood-based approach and fitted random effects models to the one-year and two-year follow-up data simultaneously. In this case, the logit link was used for binary outcomes to obtain odds ratios of the intervention effect. As a consequence, the intervention effects from these models are not directly comparable to the population-averaged risk ratios obtained from the GEE model. Time was modeled as a categorical variable so that we did not assume a specific linear effect of time. Specifically, we allowed the IST effect to differ at the two time-points by including an interaction between IST and time. We additionally adjusted for variables expected to predict missingness. We expected that older children and those with lower wealth index would be more likely to have missing follow-up data. By accounting for age and wealth index in the models, we can obtain valid estimates of the intervention effect in the presence of missing follow-up data. The results of this analysis are detailed in the following tables.

Table A4a: Baseline measures for study children with missing FU1 health data vs. those not missing FU1 health data across both the control and intervention groups.

Characteristic; n (%)		CONTROL GROUP		INTERVENTION GROUP	
		Missing outcome data	Outcome data available	Missing outcome data	Outcome data available
Child characteristics [d]		N=375	N=2148	N=412	N=2298
Age [a]	Mean (sd)	10.4 (3.1)	10.1 (2.8)	10.6 (3.1)	10.3 (2.8)
	5-9	155 (41.3)	886 (41.2)	155 (37.6)	914 (39.8)
	10-12	107 (28.5)	770 (35.9)	120 (29.1)	805 (35.0)
	13-20	113 (30.1)	492 (22.9)	137 (33.3)	579 (25.2)
Sex [b]	Male	193 (51.5)	1064 (49.5)	208 (50.5)	1111 (48.3)
Child sleeps under net [b]	Usually	229 (63.6)	1439 (67.9)	238 (60.1)	1444 (63.7)
	Last night	223 (97.4)	1383 (96.1)	225 (94.5)	1384 (95.8)
Nutritional Status [b]	Underweight	42 (30.7)	224 (26.4)	26 (22.6)	205 (24.1)
	Stunted	80 (24.1)	520 (25.3)	72 (22.4)	540 (25.2)
	Thin	64 (19.3)	418 (20.4)	47 (14.6)	403 (18.8)
Household characteristics [d]					
Parental Education [b]	No schooling	101 (28.2)	625 (29.6)	158 (39.6)	767 (33.8)
	Primary schooling	180 (50.3)	1112 (52.6)	196 (49.1)	1185 (52.2)
	Secondary schooling	59 (16.5)	294 (13.9)	30 (7.5)	248 (10.9)
	Higher education	18 (5.0)	84 (4.0)	15 (3.8)	68 (3.0)
Socioeconomic status [b]	Poorest	67 (18.6)	373 (17.6)	98 (24.5)	557 (24.4)
	Poor	84 (23.3)	399 (18.8)	88 (22.0)	476 (20.9)
	Median	63 (17.5)	402 (18.9)	84 (21.0)	411 (18.0)
	Less poor	60 (16.7)	464 (21.8)	72 (18.0)	437 (19.2)
	Least poor	86 (23.9)	486 (22.9)	58 (14.5)	400 (17.5)
Household size [b]	1-5	122 (33.9)	575 (27.1)	117 (29.5)	586 (25.8)
	6-9	193 (53.6)	1251 (59.0)	211 (53.3)	1369 (60.3)
	10-31	45 (12.5)	293 (13.8)	68 (17.2)	314 (13.8)
Study endpoints-baseline [d]		Class 1 N=183 Class 5 N=192	Class 1 N=1039 Class 5 N=1109	Class 1 N=191 Class 5 N=221	Class 1 N=1126 Class 5 N=1172
Anaemia prevalence [b]	Age-sex specific	144 (44.4)	929 (45.3)	128 (41.6)	986 (46.0)
	Severe (<70g/L)	2 (0.6)	12 (0.6)	0 (0.0)	14 (0.7)
	Moderate (70-89 g/L)	10 (3.1)	33 (1.6)	7 (2.3)	48 (2.2)
	Mild (90-109 g/L)	66 (20.4)	464 (22.6)	55 (17.9)	463 (21.6)
	None (≥110 g/L)	246 (75.9)	1540 (75.2)	246 (79.9)	1618 (75.5)
Haemoglobin (g/L)	Mean (sd)	117.7 (13.6)	117.3 (12.9)	118.9 (13.3)	117.3 (13.7)
***P.falciparum* prevalence** [b c]		- -	- -	26 (8.6)	285 (13.6)
Sustained attention [a]					
<u>Class 1</u> Score: 0-20	Pencil-tap test [min, max]	11.9 (6.7) [0, 20]	11.9 (6.7) [0, 20]	11.8 (6.6) [0, 20]	12.2 (6.6) [0, 20]
<u>Class 5</u> Score: 0-20	Code transmission [min, max]	9.9 (6.1) [0, 20]	9.9 (6.0) [0, 20]	9.6 (5.7) [0, 20]	10.6 (5.7) [0, 20]
Educational achievement [a]					
<u>Class 1</u> Score: 0-20	Spelling [min, max]	8.0 (4.2) [0, 19]	8.7 (4.5) [0, 19]	7.4 (4.5) [0, 19]	7.7 (4.4) [0, 20]
Score: 0-30	Arithmetic [min, max]	2.4 (2.3) [0, 12]	2.6 (2.4) [0, 17]	2.3 (2.6) [0, 13]	2.6 (2.5) [0, 15]
<u>Class 5</u> Score: 0-78	Spelling [min, max]	24.0 (11.6) [0, 51]	28.6 (11.7) [0, 63]	24.2 (11.1) [0, 56]	26.1 (11.2) [0, 59]
Score: 0-38	Arithmetic [min, max]	28.6 (6.1) [5, 38]	29.5 (5.5) [0, 38]	27.2 (7.0) [1, 38]	28.8 (5.5) [0, 38]

[a] mean/sd, min/max;
[b] % of non-missing children in each arm;
[c] Not measured at baseline in the control group;
[d] All characteristics have less than 2% missing data with the exception of nutritional status indicators (between 52-225(4.9-8.6%) obs missing), netuse last night (848/1009(33.9/37.7%)obs missing) and *P.falciparum* prevalence (272(10.2%) obs missing).

Table A4b: Baseline measures for study children with missing FU2 health data vs. those not missing FU2 health data across both the control and intervention groups.

Characteristic; n (%)		CONTROL GROUP		INTERVENTION GROUP	
		Missing outcome data	Outcome data available	Missing outcome data	Outcome data available
Child characteristics [d]		N=496	N=2027	N=536	N=2174
Age [a]	Mean (sd)	10.5 (3.1)	10.0 (2.8)	10.9 (3.1)	10.2 (2.7)
	5-9	196 (39.5)	845 (41.7)	184 (34.3)	885 (40.7)
	10-12	140 (28.2)	737 (36.4)	149 (27.8)	776 (35.7)
	13-20	160 (32.3)	445 (22.0)	203 (37.9)	513 (23.6)
Sex [b]	Male	240 (48.4)	1017 (50.2)	248 (46.3)	1071 (49.3)
Child sleeps under net [b]	Usually	308 (64.4)	1360 (68.0)	324 (62.4)	1358 (63.3)
	Last night	298 (96.8)	1308 (96.2)	310 (95.7)	1299 (95.7)
Nutritional Status [b]	Underweight	50 (28.6)	216 (26.7)	27 (18.7)	204 (24.8)
	Stunted	102 (23.0)	498 (25.7)	106 (24.3)	506 (25.0)
	Thin	76 (17.1)	406 (20.9)	66 (15.1)	384 (19.0)
Household characteristics [d]					
Parental Education [b]	No schooling	147 (30.8)	579 (29.0)	203 (39.0)	722 (33.6)
	Primary schooling	237 (49.7)	1055 (52.9)	257 (49.4)	1124 (52.4)
	Secondary schooling	75 (15.7)	278 (13.9)	42 (8.1)	236 (11.0)
	Higher education	18 (3.8)	84 (4.2)	18 (3.5)	65 (3.0)
Socioeconomic status [b]	Poorest	95 (19.8)	345 (17.2)	124 (23.8)	531 (24.6)
	Poor	105 (21.9)	378 (18.9)	115 (22.0)	449 (20.8)
	Median	87 (18.2)	378 (18.9)	99 (19.0)	396 (18.3)
	Less poor	73 (15.2)	451 (22.5)	105 (20.1)	404 (18.7)
	Least poor	119 (24.8)	453 (22.6)	79 (15.1)	379 (17.6)
Household size [b]	1-5	158 (33.1)	539 (26.9)	144 (27.7)	559 (26.0)
	6-9	262 (54.8)	1182 (59.1)	298 (57.4)	1282 (59.7)
	10-31	58 (12.1)	280 (14.0)	77 (14.8)	305 (14.2)
Study endpoints-baseline [d]		Class 1 N=230 Class 5 N=266	Class 1 N=992 Class 5 N=1035	Class 1 N=226 Class 5 N=310	Class 1 N=1091 Class 5 N=1083
Anaemia prevalence [b]	Age-sex specific	206 (47.0)	867 (44.8)	194 (45.9)	920 (45.4)
	Severe (<70g/L)	2 (0.5)	12 (0.6)	1 (0.2)	13 (0.6)
	Moderate (70-89 g/L)	8 (1.8)	35 (1.8)	9 (2.1)	46 (2.3)
	Mild (90-109 g/L)	98 (22.4)	432 (22.3)	83 (19.6)	435 (21.4)
	None (≥110 g/L)	330 (75.3)	1456 (75.2)	330 (78.0)	1534 (75.6)
Haemoglobin (g/L)	Mean (sd)	117.3 (13.3)	117.3 (12.9)	118.5 (13.6)	117.3 (13.7)
***P.falciparum* prevalence** [b c]		- -	-	37 (8.9)	274 (13.8)
Sustained attention [a]					
Class 1 Score: 0-20	Pencil-tap test [min, max]	11.6 (6.7) [0, 20]	11.9 (6.7) [0, 20]	11.6 (6.8) [0, 20]	12.3 (6.5) [0, 20]
Class 5 Score: 0-20	Code transmission [min, max]	9.8 (6.1) [0, 20]	9.9 (6.0) [0, 20]	9.4 (5.5) [0, 20]	10.7 (5.7) [0, 20]
Educational achievement [a]					
Class 1 Score: 0-20	Spelling [min, max]	8.5 (4.1) [0, 19]	8.6 (4.6) [0, 19]	7.7 (4.7) [0, 19]	7.6 (4.4) [0, 20]
Score: 0-30	Arithmetic [min, max]	2.6 (2.3) [0, 12]	2.6 (2.4) [0, 17]	2.6 (2.8) [0, 15]	2.6 (2.4) [0, 12]
Class 5 Score: 0-78	Spelling [min, max]	24.2 (11.4) [0, 52]	28.9 (11.7) [0, 63]	22.5 (10.7) [1, 51]	26.7 (11.1) [1, 59]
Score: 0-38	Arithmetic [min, max]	28.6 (6.2) [4, 38]	29.6 (5.4) [0, 38]	27.3 (6.4) [3, 38]	28.8 (5.6) [0, 38]

[a] mean/sd, min/max;
[b] % of non-missing children in each arm;
[c] Not measured at baseline in the control group;
[d] All characteristics have less than 2% missing data with the exception of nutritional status indicators (between 52-225(4.9-8.6%) obs missing), netuse last night (848/1009(33.9/37.7%)obs missing) and *P.falciparum* prevalence (272(10.2%) obs missing).

Table A4c: Baseline measures for study children with missing FU1 education data vs. those not missing FU1 education data across both the control and intervention groups.

Characteristic; n (%)		CONTROL GROUP		INTERVENTION GROUP	
		Missing outcome data	Outcome data available	Missing outcome data	Outcome data available
Child characteristics [d]		N=265	N=2258	N=312	N=2398
Age [a]	Mean (sd)	10.0 (3.2)	10.1 (2.8)	10.5 (3.1)	10.3 (2.8)
	5-9	125 (47.2)	916 (40.6)	121 (38.8)	948 (39.5)
	10-12	71 (26.8)	806 (35.7)	91 (29.2)	834 (34.8)
	13-20	68 (26.0)	536 (23.7)	100 (32.1)	616 (25.7)
Sex [b]	Male	134 (50.6)	1123 (49.7)	157 (50.3)	1162 (48.5)
Child sleeps under net [b]	Usually	167 (66.8)	1501 (67.3)	174 (58.6)	1508 (63.7)
	Last night	164 (98.2)	1442 (96.1)	169 (97.1)	1440 (95.5)
Nutritional Status [b]	Underweight	38 (34.9)	228 (26.0)	17 (19.5)	214 (24.3)
	Stunted	55 (24.6)	545 (25.2)	44 (19.2)	568 (25.4)
	Thin	48 (21.4)	434 (20.1)	39 (17.0)	411 (18.4)
Household characteristics [d]					
Parental Education [b]	No schooling	81 (32.5)	645 (29.0)	127 (42.8)	798 (33.7)
	Primary schooling	128 (51.4)	1164 (52.3)	141 (47.5)	1240 (52.3)
	Secondary schooling	30 (12.0)	323 (14.5)	17 (5.7)	261 (11.0)
	Higher education	10 (4.0)	92 (4.1)	12 (4.0)	71 (3.0)
Socioeconomic status [b]	Poorest	55 (22.0)	385 (17.2)	84 (28.1)	571 (24.0)
	Poor	54 (21.6)	429 (19.2)	66 (22.1)	498 (20.9)
	Median	42 (16.8)	423 (18.9)	53 (17.7)	442 (18.6)
	Less poor	46 (18.4)	478 (21.4)	62 (20.7)	447 (18.8)
	Least poor	53 (21.2)	519 (23.2)	34 (11.4)	424 (17.8)
Household size [b]	1-5	90 (36.0)	607 (27.2)	88 (29.6)	615 (26.0)
	6-9	118 (47.2)	1326 (59.5)	171 (57.6)	1409 (59.5)
	10-31	42 (16.8)	296 (13.3)	38 (12.8)	344 (14.5)
Study endpoints-baseline [d]		Class 1 N=149 Class 5 N=116	Class 1 N=1073 Class 5 N=1185	Class 1 N=153 Class 5 N=159	Class 1 N=1164 Class 5 N=1234
Anaemia prevalence [b]	Age-sex specific	93 (42.9)	980 (45.5)	98 (45.2)	1016 (45.5)
	Severe (<70g/L)	1 (0.5)	13 (0.6)	1 (0.5)	13 (0.6)
	Moderate (70-89 g/L)	8 (3.7)	35 (1.6)	9 (4.1)	46 (2.1)
	Mild (90-109 g/L)	43 (19.8)	487 (22.6)	44 (20.3)	474 (21.2)
	None (≥110 g/L)	165 (76.0)	1621 (75.2)	163 (75.1)	1701 (76.1)
Haemoglobin (g/L)	Mean (sd)	116.6 (14.1)	117.4 (12.9)	117.5 (15.0)	117.5 (13.6)
***P.falciparum* prevalence** [b c]		- -	- -	19 (9.1)	292 (13.3)
Sustained attention [a]					
Class 1 Score: 0-20	Pencil-tap test [min, max]	11.0 (6.8) [0, 20]	12.0 (6.6) [0, 20]	12.3 (6.7) [0, 20]	12.1 (6.6) [0, 20]
Class 5 Score: 0-20	Code transmission [min, max]	9.8 (5.8) [0, 20]	9.9 (6.0) [0, 20]	9.5 (5.8) [0, 20]	10.6 (5.6) [0, 20]
Educational achievement [a]					
Class 1 Score: 0-20	Spelling [min, max]	8.2 (4.3) [0, 19]	8.6 (4.5) [0, 20]	7.1 (4.2) [0, 18]	7.7 (4.4) [0, 20]
Score: 0-30	Arithmetic [min, max]	2.8 (2.8) [0, 13]	2.5 (2.3) [0, 17]	2.8 (2.9) [0, 13]	2.5 (2.4) [0, 15]
Class 5 Score: 0-78	Spelling [min, max]	24.6 (11.1) [2, 52]	28.2 (11.8) [0, 63]	25.1 (11.2) [1, 51]	25.9 (11.2) [1, 59]
Score: 0-38	Arithmetic [min, max]	28.3 (6.6) [5, 38]	29.5 (5.5) [0, 38]	27.8 (7.2) [3, 38]	28.6 (5.6) [0, 38]

[a] mean/sd, min/max;
[b] % of non-missing children in each arm;
[c] Not measured at baseline in the control group;
[d] All characteristics have less than 2% missing data with the exception of nutritional status indicators (between 52-225(4.9-8.6%) obs missing), netuse last night (848/1009(33.9/37.7%)obs missing) and *P.falciparum* prevalence (272(10.2%) obs missing).

Table A4d: Baseline measures for study children with missing FU2 education data vs. those not missing FU2 education data across both the control and intervention groups.

Characteristic; n (%)		CONTROL GROUP		INTERVENTION GROUP	
		Missing outcome data	Outcome data available	Missing outcome data	Outcome data available
Child characteristics [d]		N=543	N=1980	N=584	N=2126
Age [a]	Mean (sd)	10.5 (3.1)	10.0 (2.8)	10.9 (3.1)	10.2 (2.7)
	5-9	213 (39.2)	828 (41.8)	202 (34.6)	867 (40.8)
	10-12	161 (29.7)	716 (36.2)	167 (28.6)	758 (35.7)
	13-20	169 (31.1)	436 (22.0)	215 (36.8)	501 (23.6)
Sex [b]	Male	271 (49.9)	986 (49.8)	270 (46.2)	1049 (49.3)
Child sleeps under net [b]	Usually	343 (65.2)	1325 (67.8)	345 (61.0)	1337 (63.7)
	Last night	334 (97.4)	1272 (96.0)	328 (95.1)	1281 (95.8)
Nutritional Status [b]	Underweight	49 (26.1)	217 (27.2)	37 (22.8)	194 (24.1)
	Stunted	114 (23.7)	486 (25.5)	121 (25.0)	491 (24.8)
	Thin	90 (18.7)	392 (20.6)	74 (15.3)	376 (19.0)
Household characteristics [d]					
Parental Education [b]	No schooling	167 (31.8)	559 (28.7)	229 (40.4)	696 (33.1)
	Primary schooling	258 (49.1)	1034 (53.1)	271 (47.8)	1110 (52.9)
	Secondary schooling	82 (15.6)	271 (13.9)	46 (8.1)	232 (11.0)
	Higher education	18 (3.4)	84 (4.3)	21 (3.7)	62 (3.0)
Socioeconomic status [b]	Poorest	102 (19.4)	338 (17.3)	138 (24.3)	517 (24.5)
	Poor	119 (22.6)	364 (18.6)	125 (22.0)	439 (20.8)
	Median	92 (17.5)	373 (19.1)	110 (19.3)	385 (18.2)
	Less poor	86 (16.3)	438 (22.4)	109 (19.2)	400 (18.9)
	Least poor	128 (24.3)	444 (22.7)	87 (15.3)	371 (17.6)
Household size [b]	1-5	163 (31.0)	534 (27.3)	152 (26.9)	551 (26.3)
	6-9	293 (55.7)	1151 (58.9)	335 (59.2)	1245 (59.3)
	10-31	70 (13.3)	268 (13.7)	79 (14.0)	303 (14.4)
Study endpoints-baseline [d]		Class 1 N=259 Class 5 N=284	Class 1 N=963 Class 5 N=1017	Class 1 N=253 Class 5 N=331	Class 1 N=1064 Class 5 N=1062
Anaemia prevalence [b]	Age-sex specific	213 (44.9)	860 (45.3)	211 (44.8)	903 (45.6)
	Severe (<70g/L)	2 (0.4)	12 (0.6)	1 (0.2)	13 (0.7)
	Moderate (70-89 g/L)	10 (2.1)	33 (1.7)	9 (1.9)	46 (2.3)
	Mild (90-109 g/L)	104 (21.9)	426 (22.4)	91 (19.3)	427 (21.6)
	None (≥110 g/L)	358 (75.5)	1428 (75.2)	370 (78.6)	1494 (75.5)
Haemoglobin (g/L)	Mean (sd)	117.4 (13.4)	117.3 (12.9)	118.7 (13.6)	117.2 (13.7)
***P.falciparum* prevalence** [b c]		- -	-	47 (10.2)	264 (13.6)
Sustained attention [a]					
Class 1 Score: 0-20	Pencil-tap test [min, max]	11.8 (6.6) [0, 20]	11.9 (6.7) [0, 20]	11.9 (6.6) [0, 20]	12.2 (6.6) [0, 20]
Class 5 Score: 0-20	Code transmission [min, max]	9.9 (6.1) [0, 20]	9.9 (6.0) [0, 20]	9.6 (5.6) [0, 20]	10.7 (5.7) [0, 20]
Educational achievement [a]					
Class 1 Score: 0-20	Spelling [min, max]	8.5 (4.2) [0, 19]	8.6 (4.6) [0, 19]	7.6 (4.6) [0, 19]	7.7 (4.4) [0, 20]
Score: 0-30	Arithmetic [min, max]	2.5 (2.3) [0, 12]	2.6 (2.4) [0, 17]	2.6 (2.7) [0, 13]	2.6 (2.4) [0, 15]
Class 5 Score: 0-78	Spelling [min, max]	25.4 (11.6) [0, 53]	28.6 (11.7) [0, 63]	23.1 (11.1) [1, 59]	26.6 (11.1) [1, 59]
Score: 0-38	Arithmetic [min, max]	28.7 (6.3) [4, 38]	29.5 (5.3) [0, 38]	27.7 (6.3) [3, 38]	28.8 (5.6) [0, 38]

[a] mean/sd, min/max;
[b] % of non-missing children in each arm;
[c] Not measured at baseline in the control group;
[d] All characteristics have less than 2% missing data with the exception of nutritional status indicators (between 52-225(4.9-8.6%) obs missing), netuse last night (848/1009(33.9/37.7%)obs missing) and *P.falciparum* prevalence (272(10.2%) obs missing).

Appendix 5: List of HALI publications and presentations

Peer-reviewed publications

Brooker S, Okello G, Njagi K, Dubeck M, Halliday KE, Inyega H & Jukes MC (2010) Improving educational achievement and anaemia among school children: design of a cluster randomised trial of school-based malaria prevention and enhanced literacy instruction in Kenya. *Trials* 11, 93.

Drake T, Okello G, Njagi K, Halliday KE, Jukes MCH, Mangham L & Brooker S (2011). Cost analysis of school-based intermittent screening and treatment of malaria in Kenya. *Malaria Journal* 10, 273.

Dubeck M, Jukes MCH & Okello G (2012). Early primary literacy instruction in Kenya. *Comparative and International Education* 56, 48-68.

Halliday KE, Karanja P, Turner EL, Okello G, Njagi K, Allen E, Dubeck M, Jukes MCH & Brooker S (2012). *Plasmodium falciparum*, anaemia, classroom attention and educational performance in schoolchildren in coastal Kenya: Baseline results of a cluster randomized controlled trial. *Tropical Medicine and International Health* 17, 532-549.

Okello G, Ndegwa S, Halliday KE, Hanson K, Brooker S & Jones C (2012). Local perceptions of intermittent screening and treatment for malaria in schoolchildren on the south coast of Kenya. *Malaria Journal* 11, 185.

Okello G, Jones C, Bonareri M, Ndegwa S, Mcharo C, Kengo J, Kinyua K, Dubeck MM, Halliday KE, Jukes MCH, Molyneux S & Brooker SJ (2013). Consent and community engagement for school-based health research in Africa: experiences from a cluster randomized impact evaluation on the Kenyan south coast. *Trials* 14, 142.

Manuscripts under review

Dubeck M, Jukes MCH, Brooker S, Drake T & Inyega H. Designing a program of teacher professional development to improve children's achievement in coastal Kenya. *Comparative and International Education* (submitted).

Halliday KE, Okello G, Turner EL, Njagi K, Mcharo C, Kengo J, Allen E, Dubeck MM, Jukes MCH & Brooker SJ. Impact of intermittent screening and treatment for malaria among school children in Kenya: a cluster randomised trial. *PLoS Medicine* (submitted)

Presentations at national and international meetings

Brooker S. *Malaria control in schools and Education for All*. World Bank, Washington D.C., USA. 13th January 2011

Brooker S. *Influencing policy and practice: experience of school-based parasite control in Africa*. The Wellcome Trust, London, UK. 21st January 2011

Brooker S. *Intermittent screening and treatment of school children on the Kenyan coast*. Division of Malaria Control, Ministry of Public Health, Nairobi, Kenya. 17th February 2011

Dubeck, M. M. *HALI project: Literacy intervention in coastal Kenya.* Comparative International Education Society annual meeting, Montreal, Canada, 5th May 2011.

Jukes, M.C. *Assessing effective pedagogy in the HALI project.* Comparative International Education Society annual meeting, Montreal, Canada, 5th May 2011

Okello G. *Qualitative evaluation of community acceptability of intermittent screening and treatment of malaria in school children in Kwale and Msambweni districts, Kenya*. The Kenya National Malaria Forum, Nairobi, 10-12th October 2011.

Brooker, S. *The impact of malaria on the health and education of African school children.* Invited talk at International Child Health Group of the Royal College of Paediatrics and Child Health, Bristol University, 3rd November 2011.

Brooker, S. *School-based screening and treatment for malaria in Kenya.* Making Malaria Treatment Available: Modes of Access. The World Bank, Washington DC, 9th December 2011.

Okello G. *The acceptability and feasibility of school based malaria control through intermittent screening and treatment of malaria in school children in the Kenyan south coast.* KEMRI Annual Scientific Conference, Nairobi, 8th-10th February 2012.

Halliday, K.E. *The HALI (Health and Literacy Intervention) Project: school-based screening and treatment for malaria*. Msambweni District Health Stakeholders' Meeting, Kwale, Kenya. 28th March 2012.

Jukes MCH. *The Health and Literacy Intervention Project in Kenya: Evaluating strategies to achieve Reading for All.* Invited Presentation at Stanford University, March 2012

Jukes MCH. *The Health and Literacy Intervention Project in Kenya: Evaluating strategies to achieve Reading for All.* International Development Conference, Harvard Kennedy School. April 2012.

Jukes MCH. *Experimental evaluations of two strategies to improve reading achievement in Kenya: enhanced literacy instruction and treatment of malaria.* Society for Research in Educational Effectiveness, Washington, D. C. April 2012.

Dubeck, M.M. *HALI project literacy intervention in coastal Kenya: Using text messages and a manual to support teachers.* Comparative International Education Society annual meeting, San Juan Puerto Rico, 26th April, 2012.

Jukes MCH. *Evaluating the Health and Literacy Intervention (HALI) in Kenya.* Comparative International Education Society annual meeting, Puerto Rico, 26th April 2012.

Jukes MCH. *Interactions between health and education interventions.* The HALI project in Coastal Kenya. Comparative International Education Society annual meeting, Puerto Rico, 26th April 2012.

Halliday K. *The spatial and temporal heterogeneity of asymptomatic Plasmodium falciparum parasitaemia among Kenyan school children.* American Society of Tropical Medicine and Hygiene annual meeting, Atlanta, 13th November 2012.

Brooker S. *Malaria in African school children: consequences and options for control.* Imperial College London, UK, 29th January 2013.

Brooker S. *Malaria control in schools: rationale and evidence.* Save the Children Malawi and Malawi Ministry of Health, Liwonde, Malawi, 22nd April 2013.

Halliday K. *Malaria control in schools.* Save the Children, London, UK, 21st May 2013.

Appendix 6: Capacity building

The HALI project has been strongly committed to developing local expertise in impact evaluation and public health research. To this end, the following people and activities have been supported:

- Mr George Okello, project coordinator, 2010-2012, and investigator of the qualitative evaluation. Awarded a Wellcome Trust MSc training fellowship *Cost-effectiveness and acceptability of school-based malaria control in Kenya.* Obtained a MSc, Public Health in Developing Countries, London School of Hygiene and Tropical Medicine.

- Ms Peris Karanja, health survey coordinator. MSc Public Health, Institute of Tropical Medicine and Infectious Diseases, Jomo Kenyatta University, Nairobi, Kenya, 2010-2011. Funded by the Wellcome Trust.

- Mr George Okello and Dr Kiambo Njagi. Impact Evaluation Methods training, World Bank inter-country workshop, Cape Town, South Africa, December 2009. Funded by the World Bank. Mr George Okello and Dr Kiambo Njagi attended.

- Mr George Okello and Dr Andrew Nyandigisi. 3ie policy influencing clinic, Rome, Italy, April 17-18, 2012. Funded by 3ie.