**A four-year follow-up of school children after mass-treatment for Schistosomiasis and Soil Transmitted Helminths in Mwea, Central Kenya**

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**SUMMARY**

**Poly-parasitism infections are common in school children in tropical regions, especially in Africa. In a school based schistosomiasis and soil-transmitted helminths de-worming model project in Mwea, Kenya, approximately 40,000 school age children from 86 schools were treated annually with a standard dose of praziquantel (40mg/kg body weight) and albendazole (400mg). A cohort of approximately 2,300 children from 5 sentinel schools were followed up at multiple time points each year for four years and examined for intestinal helminths (*Schistosoma mansoni*, *Trichuris trichiura*, Hookworm (*Necator americanus*) and *Ascaris lumbricoides*). The overall prevalence of infection in the five schools before treatment was 47.4% for *S. mansoni*, 16.7% for *N. americanus*, 0.8% for *T. trichiura* and 1.7% for *A. lumbricoides.* The mean intensity of infection, as measured by eggs per gram of faeces (*epg*) was 146.2 for *S. mansoni*, 36.3 for *N. americanus* 1.0 for *T. trichiura* and 35.8 for *A. lumbricoides*. After 4 rounds of treatment, prevalence of *S. mansoni* reduced significantly by 88.7% to 5.4% (95%CI=3.6% - 7.1%), a 97.1% reduction. The prevalence and intensity of *S. mansoni* infection varied by school according to its proximity to irrigated area, with those schools closest to the irrigated areas presenting higher infection prevalence and intensity. Re-infection with schistosomiasis following treatment was observed and is likely to reflect continued environmental transmission due to non-treatment of the adult population. Soil-transmitted helminths are less prevalent in the cohort, with corresponding lower intensity. This may allow albendazole treatment to be reduced to every 2 or 3 years. This study has shown that periodic administration of anthelminthic drugs reduces the prevalence and intensity (which is likely to be a close proxy of morbidity) of intestinal parasitic infections in school-age children. Adults in the community could also be targeted where resources allow in order to further increasing the effectiveness of de-worming programmes.**

**Key words:** Soil transmitted helminths, Schistosomiasis, school age, prevalence, Intensity, mass de-worming, school children

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## Introduction

Schistosomiasis and Soil Transmitted Helminthiasis (STH) are important public health problems responsible for extensive morbidity and mortality in Sub-Saharan Africa. It is estimated that worldwide more than 200 million people are infected with schistosomes, with 85% of the cases occurring in Africa, and more than 1.5 billion are infected with STHs (Chitsulo et al., 2000; Chan et al., 1994). Hosts infected with *Schistosoma mansoni* (which causes intestinal schistosomiasis), are often co-infected with soil-transmitted helminths (hookworm, *Ascaris lumbricoides* and *Trichiuris trichiura*) (Lwambo et al., 1999; Raso et al., 2004).

Schistosomes and STH infections may impair growth and have an impact on the physical fitness and cognitive performance of children (Stolzfus et al., 1997; Partnership for Child Development, 2002).

More recent research adds to our understanding of the negative effects of schistosomes and various soil-transmitted helminth infections on the course and outcome of pregnancy, children's growth and physical and intellectual development, and worker productivity (Savioli et al., 2002; Utzinger and Keiser., 2004). It has been hypothesized that treatment with praziquantel not only decreases the worm burden, and thus reducing morbidity, but also that immunological changes induced by chemotherapy can improve resistance to re-infection and better protect against morbidity upon re-infection (Mutapi et al., 1998; Colley and Secor., 2004).

Both schistosomes and STHs infections tend to be highly aggregated in a host population; that is a small percentage of infected persons have very high worm burdens whilst the majority have low or zero worm burdens (Anderson and May, 1991). School-age children typically harbour the heaviest burden of infection due to their behavioral practices and/or their lack of acquired immunity (Anderson and May, 1991, Hatz et al., 1998) and are thought to contribute most to transmission (Hatz et al., 1998). For these reasons, and the logistical advantages of treating in schools, school-age children tend to be the target of control programmes. Targeting children is likely to yield benefit to the individuals, community, and nation, including improvement of social and economic development, increased productivity and enhancement of quality of life (Li-ping et al., 2005).

In 2004, the Japanese International Co-operation Agency (JICA), Kenya Medical Research Institute, and Kenyan Ministries of Health and Education initiated a model parasite control programme targeting schistosomiasis and STHs in school age children in Mwea Division, Kenya. School-based health programmes appear to constitute a cost effective approach as they can take advantage of an existing infrastructure serving an accessible population (Olsen et al., 2003). This study followed school-age children before and after treatment with a single dose of praziquantel (40mg/kg body weight) and melbendazole (400mg) in a cohort of five schools in Mwea, over a period of 4 years. Results presented in this paper indicate moderate re-infection patterns of *Schistosoma mansoni*. It is empirical that treatment of school age children will reduce worm load significantly, however, without instituting other interventions including treatment of adult population re-infections will quickly peak up again especially *Schistosoma mansoni*.

## Material and methods

### *Study area*

The study was conducted 100Km North-East of Nairobi in Mwea Division, Kirinyaga District, Central Province. Mwea is situated in the lower altitude zone of the district in an expansive flat land mainly characterized by black and red soils. The division has 3270 households living in 36 villages with a total population of 125,962 distributed on 513 $Km^2$. Kirinyaga district has a total of 168,176 school age children (5 – 19years) (Kenya population census, 1999). The main economic activity in this area is rice farming, which is done by gravity flow irrigation using water from the river Thiba, and also the river Nyamidi. The mean annual rainfall is 1036.6 mm and the relative humidity varies between 79.6% and 95.2%. The mean temperature varies between $15.6^0$C and $27.8^0$C (data obtained from Kenya agricultural Research Institute Mwea field station 2003). The area is endowed with plenty of flowing ground water used in the rice irrigation scheme where perennial transmission of schistosomiasis takes place (Kihara et al., 2007). After sensitizing and educating the community, health officers and education officers in the District/Division about the parasite control programme, school children attending primary schools were de-wormed in 86 schools. Prior to the de-worming, baseline prevalence and intensity of parasitic infections were determined through examination of stool samples of class three children (age range 9 – 14 years). Thereafter, periodic (every three months) stool sample examination was carried out in all children in 5 sentinel schools for four years. Treatment of all school age children (> 40,000), with praziquantel and albendazole, was conducted yearly by trained school teachers under close supervision from local health personnel.

**Parasitological examination**

Screening of infection for both soil transmitted helminths and schistosomes was based on a single Kato-Katz smear of 41.7 mg prepared from fresh stool samples (WHO, 1998). The sample was sieved through a wire mesh, and then deposited onto a template placed on a glass slide. Cellophane soaked in glycerine/malachite green was then placed on the deposit, pressed on a soft surface and left to clear for a minimum of 45 minutes and examined under the microscope. Hookworm eggs were counted within one hour of preparation since eggs would be cleared thereafter. The total number of eggs was expressed as eggs per gram of faeces (epg).

***Treatment***

Approximately 40,000 school-children from 86 schools in Mwea Central province were treated annually (every March) with a combination of praziquantel (Prazitel® Cosmos, 40mg/Kg body weight) against schistosomiasis, and albendazole (Unibazole® UP K Ltd, 400mg single dose) against STHs (*Ascaris lumbricoides, Trichuris trichiura,* and the hookworm *Necator americanus*). Dose poles were used to determine the correct number of praziquantel tablets per child (Montresor et al., 2001). Trained schoolteachers in all the schools distributed the drugs accordingly, under close supervision of health personnel from the nearby health facility. Drugs and registration materials were supplied to the various schools a day before the actual treatment in the school. Children were asked to bring with them some food that they would take just before swallowing the tablets to reduce the chances of developing adverse side effects from the drugs. A cohort of approximately 2,300 children from 5 sentinel schools (*Nyangati, Mathiga, Mbui njeru, Mianya*, and *Mukou*) were followed up at multiple time points each year (January, May, September), to monitor the effectiveness of the control programme.

***Statistical methodology***

ata were collected as paper records and subsequently coded and entered into Microsoft Excel 2003® and analysed using R version 2.3.1 (http://www.r-project.org/). Infection prevalence and intensity are reported with 95% confidence intervals (95% CI) (Kirkwood and Sterne., 2003); comparison of means was calculated via z-tests of the normal distribution for large sample sizes on the intensity values (Kirkwood and Sterne., 2003). Prevalence values prior to the introduction of the control programme and three years later were compared by z-test on the difference between two proportions. Schistosomiasis infections were categorised in heavy, medium, and light infections according to WHO guidelines, which define light infection with intestinal schistosomiasis as that in which the individual presents with <100 epg; medium infection as 100-400 epg, and heavy infection as >400 epg (Montresor et al., 2002), The lower burden of STH infections made this categorisation unfeasible for STH species.

## Results

There were significant and substantial reductions in prevalence and intensity of *S. mansoni* infections following treatment. After 4 rounds of treatment, prevalence reduced by 88.8% ($p<0.001$) from 47.9% (95% Confidence Interval: 45.4-49.4%) to 5.4% (3.6-7.1%). Correspondingly, there was a 97.1% ($p<0.001$) reduction in intensity of infection from 146.2 eggs per gram of faeces (epg; 130.5 162.0epg) to 4.2 (1.7-6.7epg), Table 1.

**Figure 1**: The changes in prevalence and intensity of intestinal schistosomiasis infection in a cohort of Kenyan school children following 4 rounds of targeted praziquantel treatment each March (black arrows). Left axis (solid black line with diamond data points) indicates the prevalence of infection (as measured by eggs in faeces). The right axis (dashed grey line with square data points) indicates the arithmetic mean of the intensity of infection.

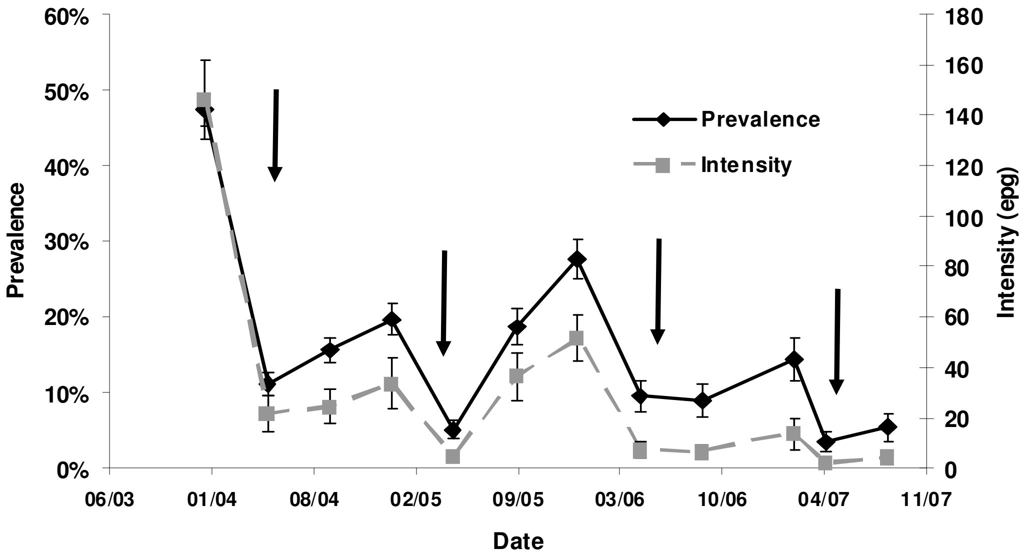
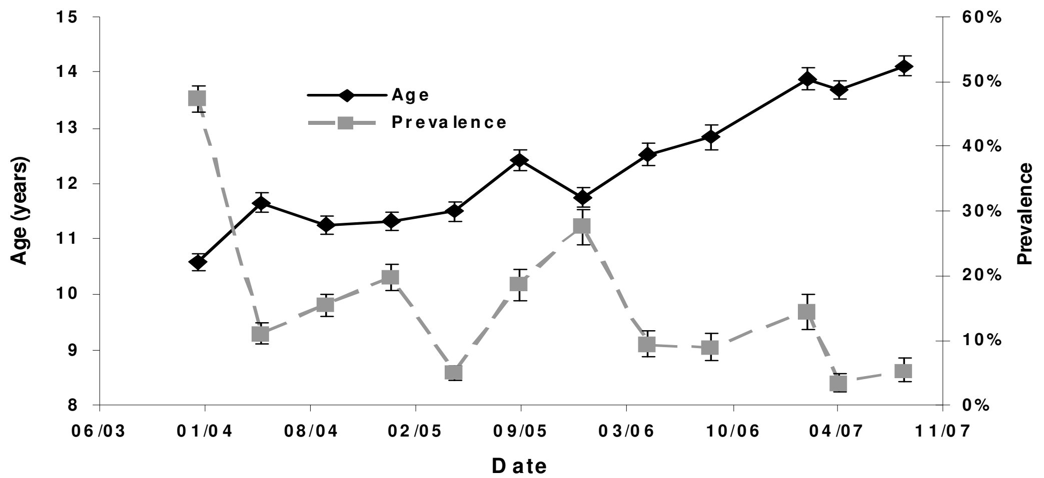



**Table 1**:Reduction in prevalence and intensity of schistosomiasis and STH infection in the Mwea parasite control programme (2004 – 2007).

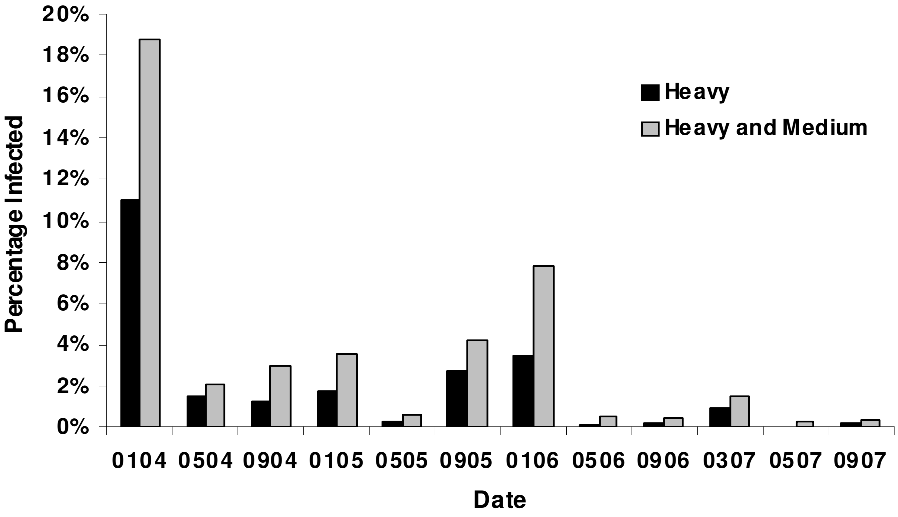
| | | Pre-treatment (Jan 2004) | 95% CI | Post 4 rounds of treatment (Sept 2007) | 95% CI | Percentage reduction | p-value |
|---|---|---|---|---|---|---|---|
| ***Schistosoma mansoni*** | Prevalence | 47.9% | 45.4% - 49.4% | 5.4% | 3.6% - 7.1% | 88.8% | **<0.001** |
| | Intensity (epg) | 146.2 | 130.5 - 162.0 | 4.2 | 1.7 - 7.7 | 97.1% | **<0.001** |
| **Any STH infection** | Prevalence | 18.7% | 17.1% - 20.3% | 0.2% | 0% -0.5% | 99.1% | **<0.001** |
| **Hookworm** | Prevalence | 16.7% | 15.2% - 18.2% | 0.0% | - | 100.0% | **<0.001** |
| | Intensity (epg) | 36.3 | 25.4 - 47.1 | 0.0 | - | 100.0% | **<0.001** |
| ***Ascaris lumbricoides*** | Prevalence | 1.7% | 1.1% - 2.2% | 0.0% | - | 100.0% | **<0.01** |
| | Intensity (epg) | 35.8 | 0.2 - 71.3 | 0.0 | - | 100.0% | **0.048** |
| ***Trichuris trichiura*** | Prevalence | 0.8% | 0.5% - 1.2% | 0.2% | 0% - 0.5% | 80.3% | 0.077 |
| | Intensity (epg) | 1.0 | 0.1 - 1.8 | 0.0 | 0 - 0.1 | 95.9% | **0.031** |

**Figure 2:** Average age of the cohort (left-hand scale, solid black line) compared to the trend in *S. mansoni* infection prevalence (right-hand scale, broken grey line) for the school children in Mwea participating in the control programme between 2004 and 2007.




Over the course of the control programme, there have been dramatic reductions in both heavy and moderate infections (Figure 3). Heavy infections have fallen by 98.5% (from 11.0% to 0.2%, $p<0.001$), and combined medium and heavy infections by 98.3% (from 18.8% to 0.3%, $p<0.001$). This indicates that morbidity is likely to have been reduced substantially in those children treated.

**Figure 3:** Proportion of all children (positives and negatives) suffering from 'heavy' and 'medium and heavy' infections, as classified by WHO.




**Intestinal schistosomiasis by gender**

Boys were more likely to be infected with schistosomiasis (49.9%) than girls (44.7%) at pre-treatment baseline ($p<0.05$) and after 4 rounds of treatment (post-treatment) ($p<0.05$), which is likely to relate to differences in behaviour that increase water contact, and thus the chances of acquiring infection. However, there were no differences between the intensity of infection at either time point ($p>0.05$) (Table 2). Boys had higher relative risk of infection than girls before (1.1) and after treatment (2.07).

**Table 2**: Sex related differences in intestinal schistosomiasis prevalence and intensity of infection before and after treatment.

| ***Schistosoma mansoni*** | | | | **Relative Risk** | **p** |
|---|---|---|---|---|---|
| Pre-treatment | Prevalence | Boys<br>Girls | 49.9%<br>44.7% | 1.11 | **0.014** |
| | Intensity (epg) | Boys<br>Girls | 143.2<br>149.6 | 0.96 | 0.695 |
| Post-treatment | Prevalence | Boys<br>Girls | 7.3%<br>3.5% | 2.07 | **0.038** |
| | Intensity (epg) | Boys<br>Girls | 4.7<br>3.7 | 1.27 | 0.693 |

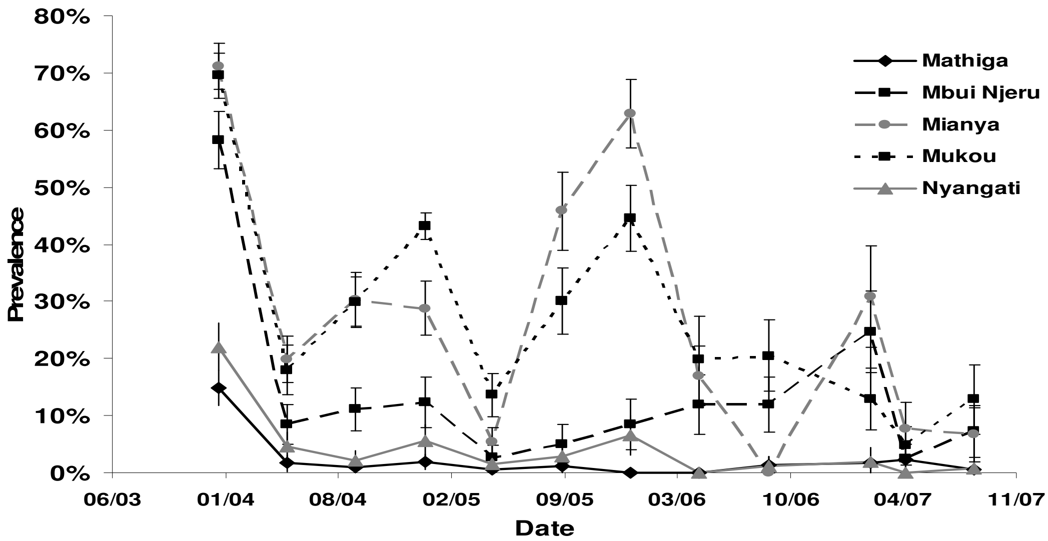
Relative Risk (also known as Risk Ratio) is estimated as the ratio of the dependent variable in one exposure group (boys) to the dependent variable in the other exposure group (girls). P-values are then calculated with paired z-tests for large sample sizes on the difference between two proportions for prevalence, and the difference between two means for the intensity.

## Comparison of intestinal schistosomiasis by schools

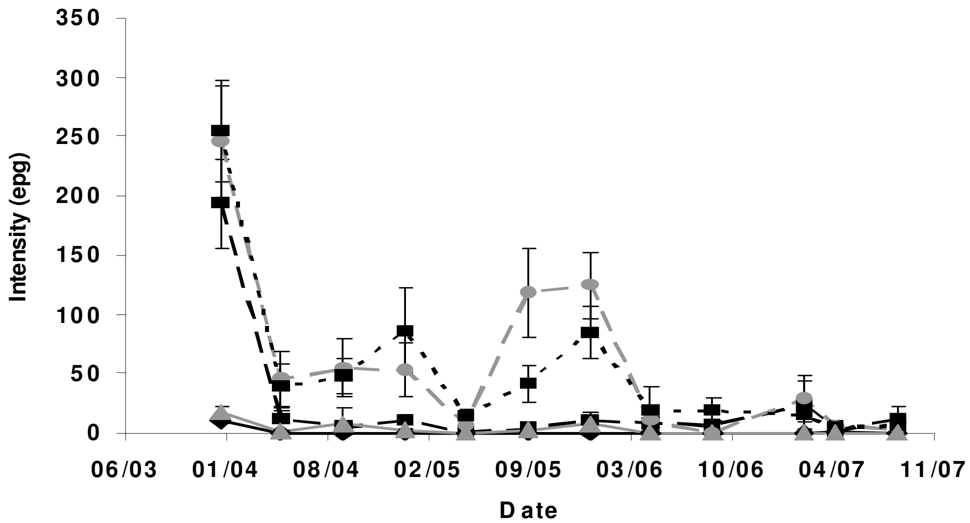
The pattern of intensity and prevalence showed similar patterns between schools before and after intervention.

**Figure 4**: School-level **A)** prevalence and **B)** intensity of *S. mansoni* infection by sentinel school over the four years of the control programme.

A.

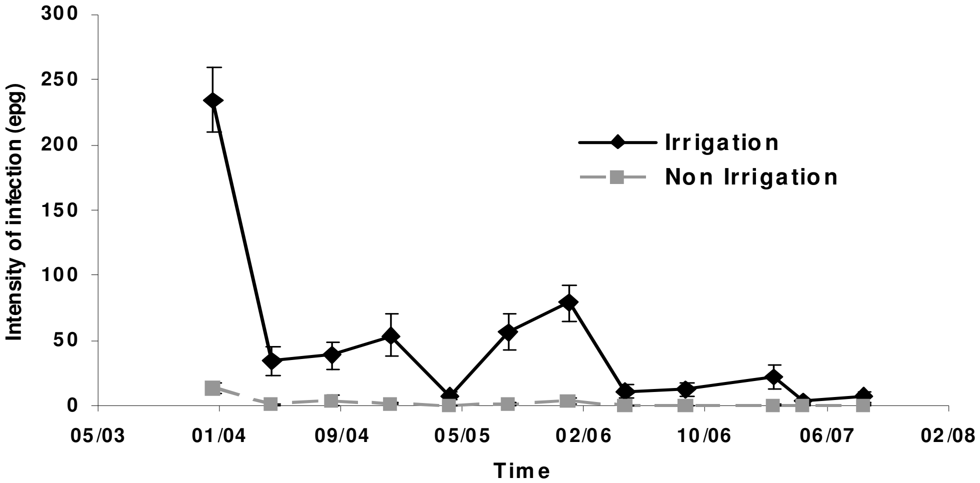



B



Schools were categorised based on whether they are close to irrigation systems or not (Figure 5). As with changes in prevalence and intensity of *S. mansoni* infection in school children over the years, as observed earlier (Figure 1), the trend is reflected among schools situated around the Mwea irrigation system.

**Figure 5:** Intensity of *S. mansoni* infection at school-level depending on whether the school is situated within an irrigation system (black solid lines) or not (grey broken lines).




**Discussion**

School health programmes have been identified as among the most cost-effective of public health interventions (World Bank., 1993) and school-based delivery of drugs is currently promoted by several international organizations (WHO, 1995). Control of intestinal helminths and schistosomiasis in schoolchildren is feasible through chemotherapy in an integrated control effort including health education, together with the long term provision of safe water and sanitation (Esrey et al., 1991; Evans and Stephenson, 1995). The control programme initiated in Mwea, as a model for school-based parasite control in the country, has yielded results comparable to a study carried out by Pascal and colleagues (1997) in Matuga Division in Kwale District where prevalence and intensity of parasitic infections reduced tremendously after subsequent treatments. As in Kwale, teachers in this programme participated fully in the health promotion activities in the schools and treatment of the children after training by health personnel from the District/Divisional team. The procedures of the control programme were simple and easy to perform in the school environment, with 40,000 school-age children de-wormed on the same day.

This treatment follow-up study of school children has demonstrated that intestinal schistosomiasis and STHs have been reduced to manageable levels in this area of Kenya. The moderate bouncing back of infection, especially schistosomiasis, is important to note and is attributed to compounding factors such as the non-treatment of community members (adults) who are potentially infected, and lack of control of the intermediate hosts (snails) leading to re-infection. The pattern of infections among the three occupational groups studied in Edo state Nigeria indicated that the school children were more infected than others Nmorsi, 2005, Another recent study, by Stothard and Albis-Francesco, 2007, reported that infections in other sections of the community are mostly overlooked because it is assumed that their water contact levels are insufficient for substantial risk of infection and/or that light intensity infections predominate. Contrary to this assumption, we observed that in the rice growing area, the majority of members of the community (adults) are involved in rice cultivation and, therefore, are equally exposed to schistosomiasis infection while spending many hours in snail infested water that is 'cercariae positive'.

As expected, chemotherapy provides an immediate and significant reduction in prevalence and intensity of infection. This is followed by a gradual rebound over the course of the year, most likely due to re-infection, although to below pre-treatment levels (Figure 1). A greater degree of re-infection is seen in 2005 compared to other years. Possible reasons for this are the seasonality of transmission and/or the schedule of rice cultivation in Mwea. In the irrigation area, farmers are restricted from planting rice for several months each year which could have had an impact on schistosomiasis transmission. Another contributing factor is likely to be the ageing of the cohort: given that there is no further enrolment into the study once it is underway, and that it is known that children aged 12-15 years experience the greatest burden of infection and disease, then there will be a general propensity for prevalence and intensity to increase throughout the study as the study population ages (Figure 2). Given this, the overall reductions seen over the 4 years of the study are even more impressive.

It is hypothesised that the degree of schistosomiasis-related morbidity in *S. mansoni* infections, (hepatomegaly and splenomegaly in the shorter-term, and Symmers' fibrosis in the longer-term) is closely correlated with the intensity of infection. However, the measure of intensity, faecal egg counts, is subject to methodological variations, immunogenetic predisposition, and other confounding factors (Gryseels., 1992). In order to gain an understanding on the proportion of children likely to suffer from morbidity, we calculated the numbers of children suffering from 'heavy' and 'medium' infections. These are classified by the World Health Organization as over 400 epg of faeces and between 100 and 399 epg of faeces respectively (Montresor., 2002). Averages were calculated based on all the positives and negative individuals. In an earlier study, approximately half of *S. mansoni* infections (48.4%) in Mwea school children were classified as heavy infection and 29.3% as moderate infection (Kihara et al., 2007).

One of the major strengths of this study is the length of time and regularity with which the 5 sentinel schools were monitored over the control programme. It can be seen that there is considerable inter-school variability of infection prevalence and intensity (Figure 4). This reflects the fact that, unlike STHs, schistosomiasis tends to be a highly focal disease. Understanding the distribution of an infection within and between schools helps to determine the correct treatment regime in that school, and enables treatment to be targeted where it is really needed (Olsen 2003). In the case of Mwea Division where de-worming was initiated in a large number of schools, the results of this study will allow subsequent treatment protocols in the area to be determined, which may include moving to targeted treatment in some areas.

The three monthly follow up of stool examination over the four years provides detailed information on the rate of parasite re-infection following chemotherapy which will be very useful when devising future treatment protocols and fitting mathematical models. In our study, we achieved a reduction of 88% and 100% for schistosomiasis and hookworm respectively (Table 1). It has been suggested that the reduction of prevalence of STH is more likely to be as a result of health education and improved sanitary conditions or behavioral changes without which the prevalence is likely to return to pre-treatment levels if treatment is stopped (Engels et al 1994;). The drastic reduction in prevalence of hookworm to less than 2% over the four years may be in part a result of our intervention and the general awareness of the control programme, though the slow rate of reinfection could also be attributed to the relatively low endemic intensity of this infection in this area. Following WHO guidelines for STH control, yearly treatment for STHs is not warranted in our control programme since the prevalence and intensities are so low (Table 1, Figure 6). It would be more appropriate to institute other control strategies such as health education, provision of safe water and proper sanitation to maintain the low prevalence of STH infections.

The irrigation system provides a putative location for the snail intermediate host that is necessary for the parasite to complete its life-cycle. Thus, the observed infection markers are likely to be related to the school's proximity to suitable habitats infected with positive snails and therefore transmission areas. As expected in rice growing irrigation scheme, children are more infected with schistosomiasis due to the frequent water contact while planting and/or weeding rice. Children are more desirable for this activity due to their agility in planting/weeding of rice and/or because they represent cheap labour especially over the weekends when they are not in school (personal observation).

It is generally reported that prevalence and intensity of infection with schistosomiasis decreases after children reach a certain age (Anderson and May, 1991). This could be due to a possible build up of immunity, but is also likely to be affected by changes in water contact behavior, as older children may have other responsibilities in their homes and are not likely to frequently wade in snail infested water in the rice irrigation area. The difference in behavior that increases water contact shows that boys are more likely to be infected with schistosomiasis than girls in Mwea. This agrees with a study by Rudge and colleagues (2008) who observed that boys were significantly more likely to report water contact activities and showed higher mean exposure indices than girls. These results support the hypothesis that prevalence of schistosomiasis in children is typically male biased as a result of higher cercarial exposure, as opposed to any kind of sex-difference in biological mechanisms of resistance or egg output.

*Schistosoma mansoni* infection showed almost the same pattern of prevalence and intensity of re-infection in all five sentinel schools throughout the period, confirming the focality of transmission in this area (Figure 4 a & b). At baseline, levels of infection with hookworms, *A. lumbricoides* and *T. trichiura* were at very low levels and as expected they were kept suppressed by four consecutive rounds of chemotherapy (Table 1).

After the mass de-worming in 86 schools in Mwea, the follow-up survey data in 5 sentinel schools over the four years has yielded very important indices that could be incorporated into a school based schistosomiasis and STHs parasite control programme. However, before policy makers decide the optimum treatment policy for an area, they should consider the strong stabilizing effects of community webs on transmission, as if one individual uses multiple water sites then a single untreated person can maintain local transmission for an indefinite period (Woolhouse et al, 1997; 1998).

Low income countries, especially those in sub-Saharan Africa, have had greater difficulties in implementing and sustaining chemotherapy based control strategies than other countries. Early pilot projects in Mali, Congo, Madagascar and Malawi, showed promising results in the short term but floundered when foreign assistance ended (WHO, 2002; Gryseels and Polderman, 1991; Chitsulo et al, 2000). The control of schistosomiasis and soil transmitted helminths in the Mwea model site has benefited from the partnership of the various organizations and the two Ministries of Health and Education in Kenya. Strengthening management and capacity in the implementation at national and district level is vital for sustainability of the control programme. Teachers have been trained in both treatment and health education in the schools, and therefore the provision of drugs and logistical capability to the District will go a long way to sustaining the programme even after the team leaves.

The study raises the issue of involving the adult population in treatment strategies for effective school-based parasite control and the need to include other control measures to reduce transmission in endemic areas. De-worming in the community (including the schools) as a development process should therefore be emphasized. The Constituency Development Fund (CDF) which is funded by the government in Kenya can play a useful part in sustaining such a worthy programme in endemic areas. The results of our study indicate that more frequent follow-up of cohort schoolchildren after mass chemotherapy is beneficial in the long term in determining treatment strategies for effective schistosomiasis and STHs parasite control programmes.

**Conflict of interest statement**

The authors have no conflict of interest concerning the work reported in this paper.

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