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# Exploring factors associated with *Trichuris trichiura* infection in school children in a high-transmission setting in Kenya

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A R T I C L E I N F O

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Soil-transmitted helminths
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A B S T R A C T

*Objectives:* Kenya has implemented a national school-based deworming program, which has led to substantial decline in the prevalence of soil-transmitted helminths (STHs), although some pockets of infections remain. To effectively design an STH control program that leads to significant reductions of *Trichuris trichiura,* there is a need to understand the drivers of persistent infection despite ongoing treatment programs.
*Methods:* This study was conducted between July and September 2019 at the south coast of Kenya, using a two-stage sampling design. First, a school-based cross-sectional survey was conducted in 2265 randomly selected school children from selected schools in areas known to be endemic for *T. trichiura*. After this, we conducted a nested case-control study wherein all children positive for *T. trichiura* (142) were matched to 148 negative controls based on age and village. A household survey was then conducted with all household members of cases and controls. In addition, a subsample of 116 children found to be infected with *T. trichiura* were followed up to assess the efficacy of albendazole at day 21 post-treatment. The predictors of presence of *T. trichiura* were investigated through multilevel logistic regression, considering clustering of infection.
*Results:* Overall, 34.4% of the children were infected with at least one STH species; *T. trichiura* was the most common (28.3%), 89.1% of those with *T. trichiura* had light-intensity infections. The prevalence of *T. trichiura* was significantly higher in male children and was positively associated with younger age and number of people infected with *T. trichiura* in a household. The parasitological cure rate and egg reduction rate of *T. trichiura* were 35% and 51%, respectively. Other STHs identified were hookworm (9.6%) and *Ascaris lumbricoides* (5.7%).
*Conclusions:* *T. trichiura* remains a significant public health challenge in the study area with albendazole treatment efficacy against the parasite, remaining lower than the World Health Organization–recommended thresholds. Because of the observed focal transmission of *T. trichiura* in the current area, control efforts tailored to local conditions and targeting lower implementation units should be used to achieve optimal results on transmission.

## Introduction

Soil-transmitted helminths (STHs), comprising *Ascaris lumbricoides, Trichuris trichiura,* and hookworms (*Necator americanus, Ancylostoma duodenale*), are a group of often co-endemic, intestinal helminths with similar risk profiles. The current World Health Organization (WHO) strategy for controlling STH is based on mass drug administration (MDA) of benzimidazoles, albendazole, or mebendazole to specific at-risk groups, including preschool-aged children (PSAC), school-aged children (SAC), and women of reproductive age [1,2] using different delivery platforms.

Kenya was among the first countries in Africa to implement a national school-based deworming program (NSBDP), launched jointly by the Ministries of Health and Education in 2009 and subsequently rolled out in 2012 [3]. An impact evaluation conducted after 5 years of NSBDP highlighted that although there was a high (91.6%) relative reduction (prevalence) in hookworm infection over the 5-year period, the relative reduction was only 28% for *T. trichiura* infection [3]. A simi-

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lar pattern has been observed, to a certain extent, in countries where community-wide treatment, including albendazole alongside either diethylcarbamazine or ivermectin, has been delivered as part of lymphatic filariasis (LF) or onchocerciasis control program [4,5].

Several possible reasons have been proposed underlying the persistence of *T. trichiura* despite STH MDA, such as the low therapeutic efficacy of albendazole and mebendazole against *T. trichiura* [6], treatment frequency [7], access to and use of water and hygiene sanitation (WASH) [7], and socioeconomic factors. Although it has been suggested that socioeconomic factors may contribute to persistence of *T. trichiura*, to the best of our knowledge, no community-based study has been conducted to understand further drivers of persistent infection in the context of multiple years of treatment through a successful deworming program. To further explore the sociodemographic and micro-geographical risk factors at the school and household level that drive *T. trichiura* transmission, a case-control study was conducted.

To effectively design an STH control program that leads to significant reductions or even elimination of *T. trichiura,* there is a need to understand the drivers of persistent infection in the community, despite ongoing treatment. We conducted two-stage parasitology surveys in schools and then in selected households to assess the risk factors associated with *T. trichiura* in a region of coastal Kenya where pockets of high *T. trichiura* transmission remain, despite albendazole treatment delivered via school and community platforms over the last 8 years. Furthermore, we assessed the efficacy of albendazole in school children.

## Methods

### *Study setting*

The study was conducted in Kwale County, an ecologically heterogeneous region, situated on the south coast of Kenya. The region is inhabited primarily by Digo and Duruma communities and Kamba in certain parts. Subsistence farming and livestock keeping of animals, such as cattle, sheep, goats, and chicken, are common economic activities. Estimates from the national school surveys in 2017 indicated the STH prevalence in this region to be in the range of 4% to 11% in school children [3]. During the TUMIKIA trial, conducted in 2015-2017 across Kwale, where hookworm was the predominant STH, a significant decline in prevalence was observed but no significant decline was observed in *T trichiura* infection, which is only common around the shores of the Indian Ocean (3.6% in 2015 and 2.7% in 2017) [8]. The current study focused on *T. trichiura* and targeted the Pongwe/Kidimu and Kikoneni wards, which where purposively selected based on the results of TUMIKIA trial, which showed that *T. trichiura* transmission was disproportionately high [8].

### *Study design and sample size calculation*

The study involved a two-stage design, with an initial school-based cross-sectional survey, where the inclusion criteria for children were ages 5-14 years with parental/guardian consent, assent from children (those aged above 13 years provided written assent) to participate in the study, resident in the study area/village for the last 6 months, and no reported receipt of deworming medication in the last 6 months [9]. The school survey was designed to assess the prevalence of *T. trichiura* in school children. The sample size was calculated assuming a *T. trichiura* prevalence of 5% in school children based on previous studies [3]. To estimate prevalence with a precision of 5%, a sample size of 1825 children was estimated to be sufficient. To achieve this sample size, 15 of 20 schools in the Pongwe-Kidimu ward were purposively selected based on the catchment area of *T. trichiura* prevalence extrapolated from the cluster-level prevalence observed during the TUMIKIA surveys in 2017 [8]. For the nested case-control analysis, a sample size of 200 (100 cases and 100 controls) was estimated based on the following assumptions: matched cases (*T. trichiura* eggs detected) and controls (No *T. trichiura* eggs detected) (by village [residence of children] and age [categorized as 6-8, 9-10, and 11-13 years] based on observed age distribution).

The sample size of the treatment efficacy sub-study was based on the requirement for 50 participants per STH species based on all positive cases as per WHO recommendations for the assessment anthelmintics drug efficacy evaluations [10].

### *School surveys: recruitment and sample collection and processing*

Between 100 and 200 children (30-50% of school population) were randomly selected from each school, proportional to the school population. On the day of the survey, children were lined up and a random number generated list was used to recruit children into the survey. Sampled children were provided with instructions and materials to enable the collection and return of their stool sample within 15-30 minutes. After stool collection, structured questionnaires were administered to the children who provided samples to collect information on sociodemographic variables, such as age, sex, recent deworming, and indicators of water and sanitation access.

School-level data on WASH were collected using a questionnaire administered to the head teacher or deputy head teacher and through visual inspection of facilities. Conditions of school latrines were assessed based on observed “cleanliness” status of the latrine. The ratio of children (disaggregated by sex) per latrine was determined as an indicator of sanitation access. Head teachers were also asked about the source of drinking water, availability of water and soap, and hand washing facilities near latrines. Schools were geolocated using the smartphones’ Global Positioning System.

All stool samples were transferred to the laboratory within 4 hours of collection for processing on the same day. Stool samples were examined based on duplicate slides using the Kato-Katz thick smear (41.7-mg template) for presence and quantity of STH eggs by two independent technicians. For quality assurance, 20% of all the positive and negative thick smears were re-examined by a third laboratory technician blinded to the results of the other two technicians.

### *Household surveys*

After the school survey, the six schools with the highest *T. trichiura* infection (28-63%) were retained as a sampling frame for the case-control study where all the children who tested positive were included. A case was defined as a child ≥5 years of age who is infected with *T. trichiura* based on at least one egg, regardless of whether any other STHs was detected in Kato-Katz thick smear. While controls were defined as children ≥5 years of age, with no STH detected in the Kato-Katz thick smear. The selected children were subsequently matched as cases and controls. Household parasitology surveys were then conducted with all household members of the cases and controls (Figure 1).

The households of all case and control children were visited by the research team. All eligible members of these households fulfilling the inclusion/exclusion criteria (>5 years old, resident of the village for at least 6 months, and provision of informed consent/assent) were invited to participate and provide a stool sample for STH examination by Kato-Katz thick smears, as described previously. At each participating household, a household questionnaire was administered to the head of the household or another adult if the head was absent or unable to respond for any reason. Data were collected on household assets and type of construction, among other variables. Access to WASH was assessed by direct observation and included source of drinking water and presence of a pit latrine.

### *Treatment efficacy assessment*

To assess the treatment efficacy of albendazole*,* 265 children found infected with *T. trichiura* were selected from the school survey (one or more slides with *T. trichiura* egg analyzed by Kato-Katz thick smear

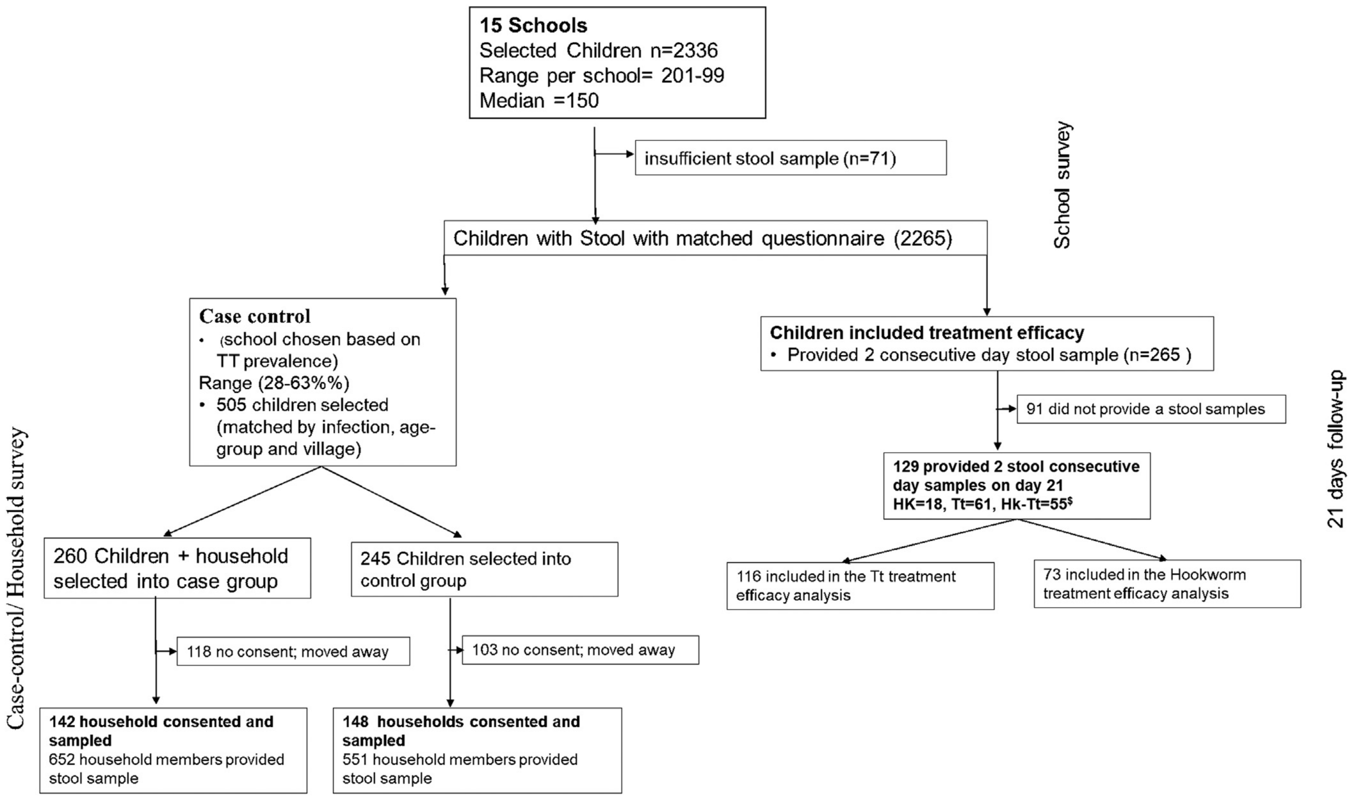


**Figure 1.** Study flow diagram showing adherence in the screening survey conducted in school children in the 15 selected schools in Kwale county, Coastal Kenya.

method) and asked to provide a second stool sample on the consecutive day to serve as a baseline. Children were then treated with 400 mg albendazole in directly observed therapy, delivered by a member of the study team. To reduce the confounding effect of vomiting after drug administration, children were observed for 2 hours after treatment. A follow-up was conducted at day 21 post-treatment where the participants were asked to provide another set of 2-day consecutive stool samples analyzed using the Kato-Katz thick smear method [10] to assess the egg reduction rate (ERR) and cure rate (CR) of albendazole in this population.

*Ethical approval*

The study was approved by the Kenya Medical Research Institute Scientific and Ethical Review Committee (SERU 3873). Permission to conduct the survey was obtained from the county health management team and the county school management. Chiefs and village elders invited community members to a meeting where the study procedures were explained by a study team member, along with an explanation of the risks and benefits of participation, and information sheets were provided for review. Before enrollment in the school surveys, the school head teachers were called for a meeting and study procedures explained. Before enrollment, written informed consent was obtained from the household head, all participating individuals and parents/guardians of children, and all individual adults in the households and assent from children aged 12 years and older. All the individuals found positive for STHs were treated with single dose albendazole (400 mg) by community health workers.

*Data management and analysis*

Data were collected using Kobo Collect software (https://www.kobotoolbox.org/) and downloaded into Excel sheets. Subsequent data management and analyses were performed using STATA version 15.0 (StataCorp LLC, College Station, TX, USA). The prevalence of each STH species, together with the 95% confidence interval (CI), were calculated using binomial regression analysis considering clustering by school. To allow the overdispersed distribution of egg counts, arithmetic mean eggs per gram (EPG) with their 95% CIs were estimated using negative binomial regression model, considering school clustering.

The intensity of infection was expressed as EPG of feces. Infection intensities were also classified into light, moderate, and heavy infections according to WHO guidelines [11]. Asset ownership variables were used to generate a wealth index based on principal component analysis [11], which was then divided into two groups (poor and less poor) based on the median score. Latrine cleanliness indicators collected included presence of visible feces, excessive smell, and excessive flies, which were combined by principal component analysis.

Summary statistics were calculated for all individual-, household-, and school-level characteristics of children. Individual- and school-level risk factors associated with *T. trichiura* were investigated in participants in the school survey using mixed-effects regression models with a random school intercept. Univariable analyses were performed, including one covariate at a time, and significant variables ($P \leq 0.10$ based on likelihood ratio test) were included in the multivariable analysis. Parsimonious regression models were developed using a backward variable selection approach, eliminating one variable at a time based on the highest *P*-value, and retaining only variables with $P \leq 0.05$.

CRs were calculated as the percentage of participants who were positive for eggs at baseline who became egg-negative after treatment (day 21) for the species of STH identified at baseline. For ERR calculation, the mean egg count of the two Kato-Katz thick smears was multiplied by a factor of 24 to calculate the EPG. The ERR was defined as the percentage of mean reduction at follow-up compared with baseline. All children were retained in the analysis and none were excluded on account of vomiting shortly after drug administration.

**Table 1**
Description of *T. trichiura* infection and demographic and sanitation characteristics in school children in Kwale county.

| Characteristic | Overall N = 2265 | *T. trichiura* positive N = 640 | Crude odds ratio (95% CI) | *P*-value | Adjusted odds ratio (95% CI) | *P*-value |
|---|---|---|---|---|---|---|
| Sex | | | | | | |
| Male | 1157 51.1) | 301 (47.0) | 1 | | 1 | |
| Female | 1108 (48.9) | 339 (53.0) | 1.33 (1.10-1.62) | 0.004 | 1.29 (1.05-1.58) | 0.015 |
| Age-group (years) | | | | | | |
| 5-8 | 352 (15.5) | 112 (17.5) | 1 | | 1 | |
| 9-10 | 624 (27.6) | 203 (31.7) | 1.01 (0.75-1.36) | 0.015 | 0.97 (0.71-1.33) | 0.007 |
| 11-12 | 673 (29.7) | 178 (27.8) | 0.76 (0.57-1.03) | | 0.77 (0.57-1.06) | |
| >13 | 616 (27.2) | 147 (22.9) | 0.69 (0.50-0.95) | | 0.69 (0.50-0.96) | |
| *Ascaris lumbricoides* infection | | | | | | |
| No | 2136 (94.3) | 549 (85.8) | 1 | | 1 | |
| Yes | 129 (5.7) | 91 (14.2) | 7.88 (5.12-12.12) | <0.001 | 6.61 (4.27-10.26) | <0.001 |
| Hookworm infection | | | | | | |
| No | 2045 (90.3) | 531 (83.0) | 1 | | 1 | |
| Yes | 219 (9.7) | 109 (17.0) | 3.54 (2.58-4.85) | <0.001 | 2.80 (2.02-3.88) | <0.001 |
| Source of water for drinking at home | | | | | | |
| Unimproved | 1124 (49.6) | 322 (50.3) | 1 | | | |
| Improved | 1141 (50.4) | 318 (49.7) | 0.99 (0.78-1.26) | 0.949 | | |
| Defecation at home | | | | | | |
| Open | 952 (42.0) | 233 (36.4) | 1 | | | |
| Pit latrine | 1313 (58.0) | 407 (63.6) | 0.99 (0.80-1.23) | 0.958 | | |
| Defecation at school | | | | | | |
| Open | 372 (16.4) | 98 (15.3) | 1 | | | |
| Pit latrine | 1893 (83.6) | 542 (84.7) | 0.94 (0.71-1.26) | 0.714 | | |
| Pit latrine at school | | | | | | |
| Dirty | 960 (42.4) | 315 (32.8) | 1 | | | |
| Clean | 1305 (57.6) | 325 (24.9) | 0.69 (0.30-1.60) | 0.387 | | |
| Visible faces around the edge | | | | | | |
| No | 1121 (49.5) | 265 (41.1) | 1 | | | |
| Yes | 1144 (50.5) | 375 (58.6) | 1.58 (0.68-3.63) | 0.284 | | |
| Source of drinking water at school | | | | | | |
| Piped | 396 (17.5) | 75 (11.7) | 1 | | | |
| Borehole | 1293 (57.1) | 397 (62.0) | 1.61 (0,46-5.71) | 0.706 | | |
| Rain | 576 (25.4) | 168 (26.3) | 1.21 (0.30-4.95) | | | |
| Level of school infection | | | | | | |
| Hookworm | | | | | | |
| <10% | 1460 (64.5) | 461 (72.0) | 1 | | | |
| >=10% | 805 (35.4) | 179 (28.0) | 0.77 (0.31-1.90) | 0.568 | | |
| *A. lumbricoides* | | | | | | |
| <10% | 1995 (88.1) | | 1 | | | |
| >=10% | 270 (11.9) | 587 (88.6) | 0.99 (0.28-3.53) | 0.989 | | |
| *T. trichiura* | | 73 (11.4) | | | | |
| <20% | 772 (34.1) | 92 (14.4) | 1 | | 1 | |
| >=20% | 1493 (65.9) | 548 (85.6) | 4.31 (2.57-7.22) | <0.001 | 4.28 (2.46-7.45) | <0.001 |

CI, confidence interval.

## Results

### *Study population*

The school survey included 15 schools, with an average 155 children randomly selected for inclusion into the study from each school (range 89-199). Of the 2336 children initially selected, 71 (3.1%) children provided insufficient stool (Figure 1). In total, 2265 children were included in the school survey analysis. Of the children surveyed at school, 505 were included into the case-control: 260 as cases were randomly selected and 245 matched as controls based on STH infection status, age, and village of residence. In the case group (children with at least one *T. trichiura* egg in the school survey), 142 households provided consent, whereas 148 provided consent for the control (children who had a zero egg count in the school survey) group. In total, 290 households and 1203 household members were included.

### *Description of school survey*

Overall, 34.4% of the 2265 sampled school children were infected with STHs. The most common species was *T. trichiura* (28.3%), followed by hookworm (9.7%) and then *A. lumbricoides* (5.7%) (Table 1). Infections with multiple helminth species were uncommon (8.1%); *T. trichiura* -hookworm co-infection was the most prevalent (4.8%). Most of the infected individuals (441 of 495) exhibited light *T. trichiura* infections (<1000 EPG). The arithmetic mean *T. trichiura* intensity was 110 EPG (SD 16) and the geometric mean was 392 EPG (SD 56) in infected individuals.

The geographical distribution of STH varied by species: *T. trichiura* prevalence showed marked heterogeneity in occurrence albeit on a small scale (Figure 2); the highest prevalence was observed closest to the Indian Ocean shore (range by school 5.7-63.0%) (Figure 2b). Hookworm infection was clustered in a few schools (range by school 1-30%), whereas *A. lumbricoides* was the least common, with a heterogeneous distribution (range by school 3.9-21%).

Of 640 children who were infected with *T. trichiura*, 36.4% reported practicing open defecation when at home, whereas 84.7% said they used pit latrines at school. Of those who were infected with *T. trichiura,* 58.6% attended schools with pit latrines with visible feces at the edges of the holes. All 15 schools had pit latrines; however, only half (8 of 15) were functional at the time of observation. Half (8 of 15) the schools had hand washing facilities near the latrine, and only six facilities contained water and were in use.

### *Factors associated with T. trichiura at school level*

In the univariable and multivariable analyses at the school level, being male and having an infection with either hookworm or *A. lumbricoides* was found to be associated with increased odds of *T. trichiura*

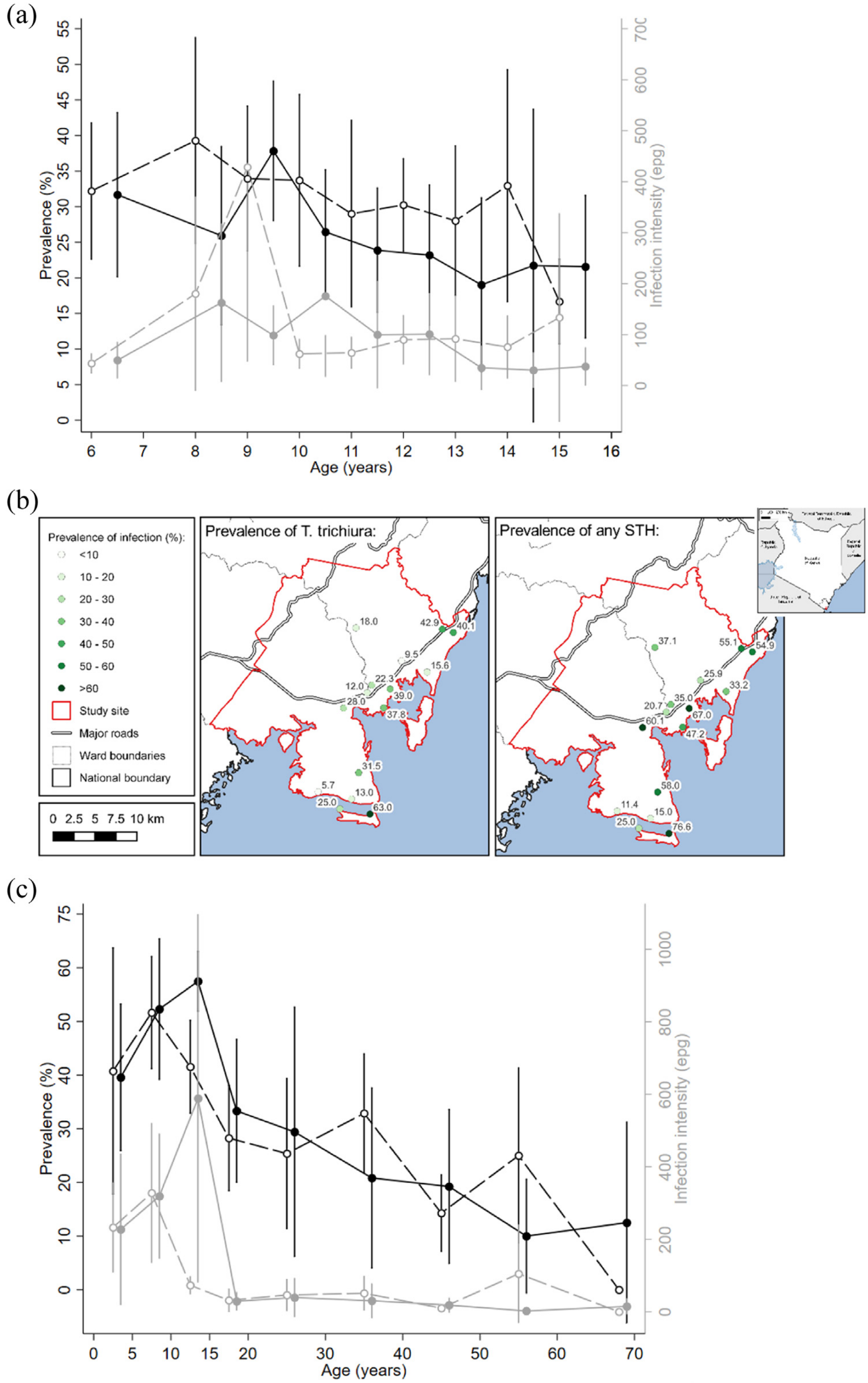


**Figure 2.** (a) Age infection profiles for *T. trichiura* in 2265 school children in 15 schools in Kwale county, south coast. Prevalence (dark lines) and intensity (grey lines) males solid line and circles: females dashed lined and empty circles; 95% confidence intervals calculated considering school clusters. (b) School-specific prevalence of soil-transmitted helminth across fifteen school in Kwale county. (c) Age infection profiles for *T. trichiura* individuals in 4 villages in Kwale county, south coast. Prevalence (dark lines) and intensity (grey lines) males solid line and circles: females dashed lined and empty circles; 95% confidence intervals calculated considering village clusters.
STHs, soil-transmitted helminths.

infection. In addition, older children were shown to have reduced odds of having *T. trichiura* infection (Table 1).

*Case-control*

Of the 640 children who had *T. trichiura* fecal egg counts ≥24 EPG, 148 were randomly selected as cases. On the other hand, 142 children who did not have *T. trichiura* eggs in their stools were selected as controls. The mean (SD) ages of cases and controls were 9.8 (0.2) and 9.7 (0.2) years, respectively. There were more females than males in the cases and control (55.5% vs 64.1%); however, this difference was not significant. In the univariable analysis, coming from a larger household and having more than one person with *T. trichiura* infection was positively associated with *T. trichiura* infection (Table 2). Only households having more than one infected person retained significance in the multivariable analysis.

**Table 2**
Unmatched univariable analysis for risk factor of *Trichuris trichiura* infection at the household level.

| Characteristic | Cases n (%) N = 142 | Control n (%) N = 148 | Odds ratio | P-value |
|---|---|---|---|---|
| Household head education | | | | |
| No education | 26 (17.5) | 28 (19.7) | 1 | |
| Incomplete Primary | 39 (26.4) | 37 (26.1) | 1.14 (0.56-2.28) | |
| Complete Primary | 71 (48) | 62 (43.7) | 1.23 (0.65-2.32) | 0.630 |
| Complete secondary | 12 (8.1) | 15 (1-.6) | 0.86 (0.34-2.17) | |
| Socio economic status | | | | |
| Poor | 69 (60.5) | 72 (55.4) | 1 | |
| Less poor | 45 (39.5) | 58 (44.6) | 0.97 (0.91-1.03) | 0.361 |
| Family size | | | | |
| Less than 7 people | 77 (54.2) | 62 (41.9) | 1 | |
| 7 or more people | 65 (45.8) | 86 (58.1) | 1.76 (1.04-2.97) | 0.034 |
| Presence of children under 5 years | | | | |
| No | 47 (31.8) | 62 (40.9) | 1 | |
| Yes | 101 (68.2) | 86 (59.1) | 1.48 (0.92-2.40) | 0.108 |
| Presence of school aged children 6-15 | | | | |
| 1 | 67 (45.3) | 68 (47.9) | 1 | |
| 2 | 81 (54.7) | 74 (52.1) | 1.11 (0.70-1.76) | 0.655 |
| Presence of toilet | | | | |
| No | 61 (41.2) | 83 (58/5) | 1 | |
| Yes | 87 (58.8) | 59 (41.5) | 0.97 (0.62-1.57) | 0.954 |
| Handwashing facilities | | | | |
| Present | 86 (58.1) | 74 (52.1) | 1 | |
| Absent | 62 (41.9) | 68 (47.9) | 0.78 (0.49-1.24) | 0.305 |
| Source if drinking water | | | | |
| Unprotected | 93 (62.8) | 80 (56.3) | 1 | |
| Protected | 55 (31.6) | 66 (43.7) | 0.76 (0.48-1.22) | 0.260 |
| Number of people infected | | | | |
| 0 | 31 (21.0) | 25 (38.0) | 1 | |
| 1 | 40 (27.0) | 42 (29.6) | 1.65 (0.89-3.08) | 0.01 |
| >1 | 77 (52.0) | 46 (32.4) | 2.91 (1.64-5.17) | |

*Factors associated with T. trichiura infection at the household level*

Overall, the proportion of *T. trichiura* infection was 40.4% (95% CI 32.9-49.6%) in the community survey, 41.6% in those aged 2-4 years, 49.7% in those aged 5-15 years, and 24.0% in adults (Figure 2c). Most of the infected individuals (441 of 495) exhibited light infections (<1000 EPG). The arithmetic mean *T. trichiura* intensity was 237 EPG (SD 36) and the geometric mean was 587 EPG (SD 87) in those infected.

After adjusting for individual- and household-level predictors, several factors remained significant in the multivariable analysis (Table 3). Younger age groups were associated with higher odds of infection, irrespective of sex. Attending primary school and having an infection with either *A. lumbricoides* or hookworm infection were associated with increased odds of *T. trichiura* infection. Households having a hand washing facility were associated with reduced odds of *T. trichiura* infection (adjusted odds ratio 0.76, 95% CI 0.59-0.99).

*Treatment efficacy*

The CR for *T. trichiura* infection was 35.3% (41 of 116), whereas fecal ERR was 50.8% (Table 4). Figure 3 shows the change in EPG before and after treatment. There was a significant reduction in the EPG after treatment. A visual representation of paired data EPG before and at day 21 after treatment showed that the reduction of the EPG was independent of the initial EPG.

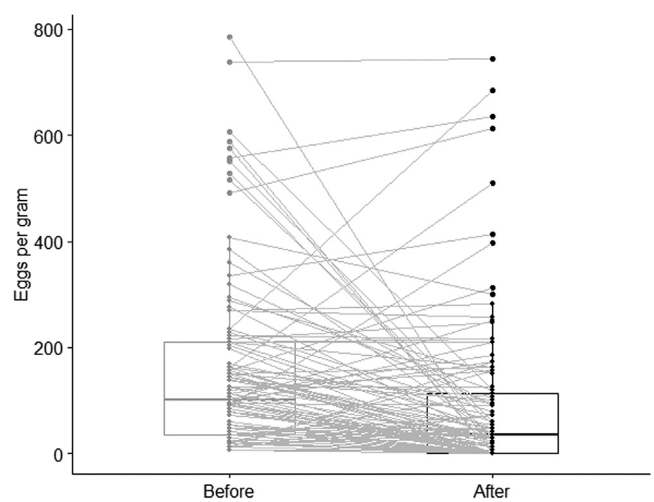


**Figure 3.** Infection intensities of individuals *T. trichiura* before and 21 days after treatment with albendazole. Three outliers >eggs per gram 1500 excluded.

**Discussion**

Our findings provide a snapshot of the epidemiology of *T. trichiura* infection at the school and community levels in a *T. trichiura* hotspot within an ongoing STH deworming program. Our study showed a protective association between household presence of a handwashing facility and *T. trichiura* infection. On the other hand, sex, age, household size, village level infection, and school infection were positively associated with *T. trichiura* infection. Our results are consistent with those of the NSBDP that showed a considerable overall decline in STH prevalence with enduring focal pockets of high *T. trichiura* transmission [3]. This study provides findings that are useful for control programs in many STH endemic countries that are currently experiencing a generally low STH transmission with *T. trichiura* hotspots owing to the uptake of school-based control programs [3].

The prevalence of *T. trichiura* in the school survey in this study was much higher than that observed during the NSBDP monitoring and evaluation surveys conducted a year previously (1.7%) after six rounds of MDA [3]. In the community survey, the proportion of individuals with *T. trichiura* was similar to studies conducted in the same area between 2009 and 2015 [3,9]. We observed lower prevalence of *A. lumbricoides* and hookworm in the school and community survey, which is corrob-

**Table 3**
Univariable and multivariable association of *T. trichiura* infection with individual and household factors.

| Characteristics | Infected with *T. trichiura*/N (%) | Odds ratio | *P*-value | Adjusted odds ratio | |
|---|---|---|---|---|---|
| Individual characteristics | | | | | |
| Sex | | | | | |
| Male | 230/522 (44.1) | 1 | | | |
| Female | 265/703 (37.7) | 0.75 (0.59-0.95) | 0.017 | | |
| Age group | | | | | |
| Pre-SAC (2-4) | 83/205 (40.5) | 2.16 (1.49-3.13) | | 2.03 (1.38-2.99) | 0.018 |
| SAC (5-15) | 317/625 (50.7) | 3.30 (2.48-4.39) | <0.001 | 2.33 (1.50-3.61) | |
| Adults (>15) | 95/395 (24.0) | 1 | | 1 | |
| Male | | | | | |
| Pre-SAC (2-4) | 96/301 (18.3) | 2.30 (1.20-4.41) | | | |
| SAC (5-15) | 301/522 (57.7) | 3.91 (2.42-6.32) | <0.001 | | |
| Adults (>15) | 125/522 (24.0) | 1 | | | |
| Female | | | | | |
| Pre-SAC (2-4) | 109/703 (15.5) | 2.27 (1.31-3.93) | | | |
| SAC (5-15) | 324/703 (46.1) | 2.74 (1.92-3.93)) | <0.001 | | |
| Adults (>15) | 270/703 (38.4) | 1 | | | |
| *A. lumbricoides* | | | | | |
| No | 5/725 (0.7) | 1 | | 1 | |
| Yes | 55/495 (11.1) | 18.4 (7.18-47.02) | <0.001 | 15.01 (5.75-39.15) | <0.001 |
| Hookworm | | | | | |
| No | 33/730 (4.5) | 1 | | 1 | |
| Yes | 50/495 (10.1) | 2.88 (1.80-6.62) | <0.001 | 2.20 (1.31-3.72) | 0.003 |
| Attends primary school | | | | | |
| No | 190/624 (30.4) | 1 | | 1 | |
| Yes | 305/601 (50.8) | 2.24 (1.77-2.84) | <0.001 | 1.51 (1.01-2.26) | 0.045 |
| Village | | | | | |
| Proportion of village infection <40% | 178/575 (31.1) | 1 | | 1 | |
| Proportion of village infection>40% | 317/650 (48.8) | 2.27 (1.48-3.48) | <0.001 | 2.01 (1.32-3.07) | 0.001 |
| Socio economic status | | | | | |
| Poor | 227/539 (42.1) | 1 | | | |
| Less poor | 163/482 (33.8) | 0.75 (0.57-0.98) | 0.038 | | |
| Presence of toilet | | | | | |
| No | 250/7573 (45.6) | 1 | | | |
| Yes | 245/652 (37.5) | 0.78 (0.62-1.04) | 0.091 | | |
| Handwashing facilities | | | | | |
| Absent | 301/703 (41.2) | 1 | | 1 | |
| Present | 161/462 (32.5) | 0.76 (0.59-0.98) | 0.037 | 0.76 (0.59-0.99) | 0.045 |

SAC, school-age children.

**Table 4**
Treatment efficacy of albendazole on *Trichuris trichiura* (N = 116) based on two stool samples.

| Variable | Pre treatment | EPG | Post treatment | EPG | Cure rate | Egg reduction rate |
|---|---|---|---|---|---|---|
| Proportion infected | 116 (100) | 179 | 75 (64.7) | 99 | 35.3% | 50.8% |
| Infection intensity | | | | | | |
| No infection | 0 | | 41 (35.3) | | | |
| < EPG 240 | 93 (80.2) | 90 | 60 (51.7) | 68 | 35.5% | 24.1% |
| > EPG 240 | 23 (19.8) | 630 | 15 (12.9) | 220 | 34.8% | 65.1% |

EPG, eggs per gram.

orated by data from the same region [9]. Taken together, the current data suggest that despite the high treatment coverage of NSBDP and additional community-based interventions, such as the National Program for Elimination of Lymphatic Filariasis and TUMIKIA study in this area, there has been little change in the prevalence of *T. trichiura* along the Indian Ocean coast, whereas the prevalence of hookworm and *A. lumbricoides* has significantly declined [3,8,12].

An association was observed between *A. lumbricoides* infection and *T. trichiura* in SAC, which can be attributed to a common fecal-oral route of transmission, similar risk factors, and overlap in distribution [13,14]. In such conditions, co-infection of *T. trichiura* and *A. lumbricoides* has been commonly observed. Although mostly asymptomatic, these coinfections could contribute to negative effects on nutrition and growth.

As expected, the prevalence and intensity of *T. trichiura* infection varied by age and sex, with highest prevalence observed in males in PSAC and SAC. In *T. trichiura* endemic areas, an age-dependent decline in prevalence is often observed in adults (aged >15 years), probably owing to reduced exposure and age-acquired immunity [15]. Male children have been shown to have a higher prevalence and intensity of *T. trichiura* than females in several studies [9,16]. This can be contributed to sociocultural differences physical activity, behaviors, and greater soil exposure [16]. In the adult population, most *T. trichiura* infections were observed in women, as reported in studies from high *T. trichiura* transmission areas [16]. It is likely that adult women have higher rates of infection because they care for and live in closer proximity to infected children who contaminate the nearby environment. The PSAC account for a substantial proportion of *T. trichiura* infection and, although included in the NSBDP, their treatment coverage is often low because they are not directly targeted by the program. PSAC who are already attending early childhood development schools are expected to travel to the nearest primary school for treatment, which presents challenges because of distance and other logistics. As result, this age group could be a potential reservoir of *T. trichiura* infection contributing to ongoing transmission in endemic communities.

Children attending schools closer to the Indian shore had the higher *T. trichiura* prevalence than those in schools further inland, an observation that has been made in other *T. trichiura* endemic areas [16]. This could be because of the focal transmission in areas close to large water bodies most possibly because of low altitude, moderated temperatures, and high soil moisture near water [17,18]. In contrast to previous reports of positive association between toilet use and *T. trichiura* infection [19,20], reported toilet use at household level and school was not associated with *T. trichiura* infection in the present study. Nevertheless, this somewhat counter-intuitive finding corroborates the observation from a previous study that community sanitation is protective to *T. trichiura* infection rather than toilet use at the household level [21], perhaps explained by the possibility of *T. trichiura* eggs surviving longer in the community than other STHs. However, the reported presence of a handwashing facility was observed to be protective to *T. trichiura* infection. At the household level, the number of people living in households and number of people infected were the risk factors in the case-control rather than household sanitation, adding weight to *T. trichiura* exposure being driven by environmental factors [22]. In countries where there was improvement in economic conditions and sanitation in addition to access to periodic preventive chemotherapy in SAC, these have led to a decrease in STHs [23].

We observed a low *T. trichiura* CR of 35%, consistent with previous studies, which also observed similar CR for albendazole (400 mg). A WHO analysis on treatment efficacy showed the ERRs for mebendazole (~70%); however, the efficacy of albendazole varied (50-64%) [10]. Similarly, a rigorous meta-analysis by Moser *et al.* showed *T. trichiura* CRs of 31% for albendazole (400 mg) and 42% for mebendazole [6]. More recently, a study that looked at higher dose of albendazole (800 mg) also showed low efficacy regarding *T. trichiura* treatment [24]. Recent trials have shown a variable but uniformly poor efficacy of albendazole across diverse geographic regions [25,26]. The ERR for *T. trichiura* was consistent with the expected ERR reference efficacy for albendazole (≥50%). Although it is acknowledged that the ERR in cases of infection with *T. trichiura* is expected to be significantly lower than that for the other STHs, it is also appreciated that when the drug is used at regular intervals, as is the case in school health programs, it is sufficient to eliminate high-intensity infections and progressively reduce prevalence [10].

The low efficacy of benzimidazoles underscores the need for new efficacious drug regimens against *T. trichiura* because the poor efficacy of the currently used drugs regimens against *T. trichiura* could slow down the success of STH elimination programs. Indeed, the development of more effective medicines and medicine to improve patient outcomes and mitigate the risk of emergence of drug resistance has been highlighted as a critical action for STHs in the current WHO Neglected Tropical Diseases Roadmap 2021-2030 [27]. Although STHs have similar but not identical epidemiology and a shared control strategy, there exists a possibility of residual *T. trichiura* infection after the transmission of *A. lumbricoides* and hookworm is interrupted [28]. Several approaches might be useful in addressing the persistence of foci with high *T. trichiura* prevalence. Mebendazole performs better than albendazole in cases of infections of higher intensities, and the growing evidence provided by several experimental studies that have shown that *T. trichiura* is susceptible to co-administration of benzimidazoles with ivermectin, with a reported ERR range of 63-97% [29,30]. Therefore, co-administration of ivermectin with albendazole could increase efficacy against *T. trichiura*. There is an ongoing study in the same setting where our study was conducted, exploring the safety of a fixed-dose ivermectin and albendazole for treatment of *Strongyloides stercoralis*, hookworms, and *T. trichiura*, which has the potential to improve the STH control program's effectiveness by providing a higher ERR for *T. trichiura* while simplifying drug procurement because of the drug co-formulation (ClinicalTrials.gov Identifier: NCT05124691). Moreover, in 2017, WHO endorsed the use of triple drug therapy with ivermectin, albendazole, and diethylcarbamazine as an alternative MDA regimen for LF elimination programs [2]. This new treatment regimen could potentially have additional benefits in the control of *T. trichiura* in LF-*T. trichiura* co-endemic areas. Kenya meets the requirement to conduct triple drug therapy with ivermectin, albendazole, and diethylcarbamazine and rolled out the pilot treatment in one county (Lamu) in 2018, with plans to scaleup to the whole of the LF-endemic areas in Kenya.

### *Limitation*

The current study had some limitations worth highlighting. First, diagnosis was based on routine parasitological procedures and we acknowledge that Kato-Katz microscopy may miss light infections and a single stool sample may underestimate the prevalence of helminth infection. To improve the sensitivity of Kato-Katz, we used the 2-day consecutive stool samples approach for the drug efficacy evaluation. Second, household-level information was collected only for those households of children who were invited to the case-control study.

## Conclusion

Data at micro-epidemiological level suggest that there is substantial heterogeneity in the prevalence of individual STHs between villages and a need to rethink how to implement and evaluate STH MDA. Generally, STHs are considered together because of their theoretical susceptibility to the same anthelmintic, although studies have repeatedly shown that some benzimidazoles, such as albendazole, are less efficacious against *T. trichiura*. Therefore, in areas that have a high *T. trichiura* transmission, there is a need to develop *T. trichiura*-targeted control strategies, bearing in mind the focal transmission nature, age groups at risk, and provision of effective drug regimens.

## Declarations of competing interest

Stella Kepha reports financial support was provided by African Research Network for Neglected Tropical Diseases. The remaining authors have no competing interest to declare.

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## Author contributions

SK, KEH, and CSM designed the study; SK and WEO performed the analysis; and RP and HDM contributed to the statistical aspects of the study. All other authors played an important role in finalizing the study protocol and data interpretation. SK and KEH drafted the manuscript, and all authors have read and approved the final manuscript.

## References


[1] World Health Organization. WHO Expert Committe: prevention and control of schistosomiasis and soil-transmitted helminthiasis. *World Health Organ Tech Rep S* 2002;**912**:1–57.

[2] World Health Organization *Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups*. Geneva: World Health Organization; 2017.

[3] Mwandawiro C, Okoyo C, Kihara J, Simiyu E, Kepha S, Campbell SJ, et al. Results of a national school-based deworming programme on soil-transmitted helminths infections and schistosomiasis in Kenya: 2012–2017. *Parasit Vectors* 2019;**12**:76. doi:10.1186/s13071-019-3322-1.

[4] Tun A, Myat SM, Gabrielli AF, Montresor A. Control of soil-transmitted helminthiasis in Myanmar: results of 7 years of deworming. *Trop Med Int Health* 2013;**18**:1017–20. https://www.ncbi.nlm.nih.gov/pubmed/23701018. doi:10.1111/tmi.12130.

[5] World Health Organization, World Health Organization. Soil-transmitted helminthiases: number of children treated in 2012. *Wkly Epidemiol Rec* 2018;**93**:681–92.

[6] Moser W, Schindler C, Keiser J. Efficacy of recommended drugs against soil transmitted helminths: systematic review and network meta-analysis. *BMJ* 2017;**358**:j4307. https://www.ncbi.nlm.nih.gov/pubmed/28947636. doi:10.1136/bmj.j4307.

[7] Anderson R, Truscott J, Hollingsworth TD. The coverage and frequency of mass drug administration required to eliminate persistent transmission of soil-transmitted helminths. *Philos Trans R Soc Lond B Biol Sci* 2014;**369**:20130435. doi:10.1098/rstb.2013.0435.

[8] Pullan RL, Halliday KE, Oswald WE, McHaro C, Beaumont E, Kepha S, et al. Effects, equity, and cost of school-based and community-wide treatment strategies for soil-transmitted helminths in Kenya: a cluster-randomised controlled trial. *Lancet* 2019;**393**:2039–50. doi:10.1016/S0140-6736(18)32591-1.

[9] Halliday KE, Oswald WE, McHaro C, Beaumont E, Gichuki PM, Kepha S, et al. Community-level epidemiology of soil-transmitted helminths in the context of school-based deworming: baseline results of a cluster randomised trial on the coast of Kenya. *PLoS Negl Trop Dis* 2019;**13**:e0007427. doi:10.1371/journal.pntd.0007427.

[10] World Health Organization *Assessing the efficacy of anthelminthic drugs against schistosomiasis and soil-transmitted helminthiases(WHO/HTM/NTD/PCT/2013.4)*. Geneva: World Health Organization; 2013.

[11] Filmer D, Pritchett LH. Estimating wealth effects without expenditure data–or tears: an application to educational enrollments in states of India. *Demography* 2001;**38**:115–32. doi:10.1353/dem.2001.0003.

[12] Njenga SM, Kanyi HM, Mutungi FM, Okoyo C, Matendechero HS, Pullan RL, et al. Assessment of lymphatic filariasis prior to re-starting mass drug administration campaigns in coastal Kenya. *Parasit Vectors* 2017;**10**:99. doi:10.1186/s13071-017-2044-5.

[13] Brooker S, Clements AC, Bundy DA. Global epidemiology, ecology and control of soil-transmitted helminth infections. *Adv Parasitol* 2006;**62**:221–61. doi:10.1016/S0065-308X(05)62007-6.

[14] Owada K, Lau CL, Leonardo L, Clements ACA, Yakob L, Nielsen M, et al. Spatial distribution and populations at risk of *A. lumbricoides and T. Trichiura* co-infections and infection intensity classes: an ecological study. *Parasit Vectors* 2018;**11**:535. doi:10.1186/s13071-018-3107-y.

[15] Bundy D, Peto R. Anthelmintic treatment for infestation with Trichuris trichiura. *Lancet* 1998;**352**:1935. doi:10.1016/S0140-6736(05)60428-X.

[16] Muñoz-Antoli C, Pérez P, Pavón A, Toledo R, Esteban JG. Soil-transmitted helminth infections and anemia in schoolchildren from corn island archipelago (RAAS, Nicaragua). *Am J Trop Med Hyg* 2018;**99**:1591–7. doi:10.4269/ajtmh.18-0195.

[17] Manz KM, Clowes P, Kroidl I, Kowuor DO, Geldmacher C, Ntinginya NE, et al. *Trichuris trichiura* infection and its relation to environmental factors in Mbeya region, Tanzania: a cross-sectional, population-based study. *PLoS One* 2017;**12**:e0175137. doi:10.1371/journal.pone.0175137.

[18] Pullan RL, Gething PW, Smith JL, Mwandawiro CS, Sturrock HJW, Gitonga CW, et al. Spatial modelling of soil-transmitted helminth infections in Kenya: a disease control planning tool. *PLOS Negl Trop Dis* 2011;**5**:e958. doi:10.1371/journal.pntd.0000958.

[19] Strunz EC, Addiss DG, Stocks ME, Ogden S, Utzinger J, Freeman MC. Water, sanitation, hygiene, and soil-transmitted helminth infection: a systematic review and meta-analysis. *PLoS Med* 2014;**11**:e1001620. doi:10.1371/journal.pmed.1001620.

[20] Ziegelbauer K, Speich B, Mäusezahl D, Bos R, Keiser J, Utzinger J. Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Med* 2012;**9**:e1001162. doi:10.1371/journal.pmed.1001162.

[21] Oswald WE, Kepha S, Halliday KE, McHaro C, Safari T, Witek-McManus S, et al. Patterns of individual non-treatment during multiple rounds of mass drug administration for control of soil-transmitted helminths in the TUMIKIA trial, Kenya: a secondary longitudinal analysis. *Lancet Glob Health* 2020;**8**:e1418–26. doi:10.1016/S2214-109X(20)30344-2.

[22] Else KJ, Keiser J, Holland CV, Grencis RK, Sattelle DB, Fujiwara RT, et al. Whipworm and roundworm infections. *Nat Rev Dis Primers* 2020;**6**:44. doi:10.1038/s41572-020-0171-3.

[23] Pullan RL, Freeman MC, Gething PW, Brooker SJ. Geographical inequalities in use of improved drinking water supply and sanitation across sub-Saharan Africa: mapping and spatial analysis of cross-sectional survey data. *PLoS Med* 2014;**11**:e1001626. doi:10.1371/journal.pmed.1001626.

[24] Patel C, Coulibaly JT, Schulz JD, N'Gbesso Y, Hattendorf J, Keiser J. Efficacy and safety of ascending dosages of albendazole against *Trichuris trichiura* in preschool-aged children, school-aged children and adults: a multi-cohort randomized controlled trial. *EClinicalMedicine* 2020;**22**:100335. doi:10.1016/j.eclinm.2020.100335.

[25] Hürlimann E, Keller L, Patel C, Welsche S, Hattendorf J, Ali SM, et al. Efficacy and safety of co-administered ivermectin and albendazole in school-aged children and adults infected with *Trichuris trichiura* in Cote d'Ivoire, Laos, and Pemba Island, Tanzania: a double-blind, parallel-group, phase 3, randomised controlled trial. *Lancet Infect Dis* 2022;**22**:123–35. doi:10.1016/S1473-3099(21)00421-7.

[26] Matamoros G, Sánchez A, Gabrie JA, Juárez M, Ceballos L, Escalada A, et al. Efficacy and safety of albendazole and high-dose ivermectin coadministration in school-aged children infected with *Trichuris trichiura* in Honduras: a randomized controlled trial. *Clin Infect Dis* 2021;**73**:1203–10. doi:10.1093/cid/ciab365.

[27] World Health Organization *Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030*. Geneva: World Health Organization; 2020.

[28] Truscott JE, Hollingsworth TD, Brooker SJ, Anderson RM. Can chemotherapy alone eliminate the transmission of soil transmitted helminths? *Parasit Vectors* 2014;**7**:266. doi:10.1186/1756-3305-7-266.

[29] Knopp S, Mohammed KA, Speich B, Hattendorf J, Khamis IS, Khamis AN, et al. Albendazole and mebendazole administered alone or in combination with ivermectin against *Trichuris trichiura*: a randomized controlled trial. *Clin Infect Dis* 2010;**51**:1420–8. doi:10.1086/657310.

[30] Speich B, Moser W, Ali SM, Ame SM, Albonico M, Hattendorf J, et al. Efficacy and reinfection with soil-transmitted helminths 18-weeks post-treatment with albendazole-ivermectin, albendazole-mebendazole, albendazole-oxantel pamoate and mebendazole. *Parasit Vectors* 2016;**9**:123. doi:10.1186/s13071-016-1406-8.