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Changing Patterns of Soil-Transmitted Helminthiases in Zanzibar in the Context of National Helminth Control Programs

Stefanie Knopp, Khalfan A. Mohammed, David Rollinson, J. Russell Stothard, I. Simba Khamis, Jürg Utzinger, and Hanspeter Marti*

Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland; Helminth Control Laboratory Unguja, Ministry of Health and Social Welfare, Zanzibar, Tanzania; Wolfson Wellcome Biomedical Laboratories, Department of Zoology, Natural History Museum, London, United Kingdom; Department of Medical and Diagnostic Services, Swiss Tropical Institute, Basel, Switzerland

Abstract. Helminth control programs have been implemented in Zanzibar for over a decade. In June/July 2007, ~6 months after the last school-based anthelmintic treatment, a cross-sectional survey was carried out in two schools, and results were compared with data obtained in the same schools in 1994. Multiple stool samples collected from 368 school children were subjected to the Kato-Katz, Koga agar plate, and Baermann methods. The prevalence of *Trichuris trichiura*, hookworm, *Ascaris lumbricoides,* and *Strongyloides stercoralis* was 46.6%, 21.6%, 16.9%, and 10.2%, respectively. Infection intensities were generally low. Compared with 1994, the prevalence of *S. stercoralis*, hookworm, *A. lumbricoides,* and *T. trichiura* decreased by 81.0%, 80.5%, 70.6%, and 48.6%, respectively. Infection intensities decreased by > 95% for all helminth species studied. Our study confirms that preventive chemotherapy successfully reduces the level and intensity of helminth infections. To consolidate achievements made, additional control measures such as health education and environmental sanitation are needed.

INTRODUCTION

Infections with soil-transmitted helminths (STHs) are common across sub-Saharan Africa and elsewhere in developing nations.[1,2] STH infections typically afflict the poorest population segments and impact on human health, nutrition, and worker productivity and hence exacerbate poverty.[3] Efforts are under way to control diseases caused by chronic infections with STHs. The most widely used strategy is morbidity control by means of preventive chemotherapy, which is the large-scale application of anthelmintic drugs (e.g., albendazole and mebendazole), usually to school-aged children without prior diagnosis.[1,2,4] Emphasis on school-aged children is justified because high levels of STH infections are observed in this age group and because schools offer a convenient platform to reach those in need for treatment.[5,6]

In Unguja and Pemba, the two main islands forming Zanzibar, STH infections were recognized as a major public health problem in the early 1990s. Indeed, school-aged children were virtually all infected with at least one of the three common STHs, namely *Ascaris lumbricoides*, *Trichuris trichiura,* and hookworm (*Ancylostoma duodenale* and *Necator americanus*).[7,8] Additionally, infections with *Strongyloides stercoralis*, the most neglected STH species,[9] were found in one third of the children examined in the schools of Chaani and Kinyasini in Unguja.[8] In 1994, the Ministry of Health and Social Welfare (MoHSW) of Zanzibar, in collaboration with the World Health Organization (WHO), established an action plan for the control of STHs and urinary schistosomiasis.[10] Over the past decade, albendazole, mebendazole, and praziquantel have been administered to children in primary schools on a fairly regular basis (Figure 1).[11,12] For example, in Chaani and Kinyasini, children received annual treatment with mebendazole and praziquantel from 1995 to 2000 through the national helminth control program and, after a shortage of drug donations, albendazole and praziquantel were again distributed from 2003 onward to school children as part of the "Kick out Kichocho Program."[13–15] Starting in 2001, the Global Program to Eliminate Lymphatic Filariasis (GPELF) targeted eligible individuals in Zanzibar (including children ≥ 5 years of age) annually with ivermectin plus albendazole.[13,16,17] Of note, ivermectin (single oral dose of 200 µg/kg) is not only efficacious against filarial worms but also against *S. stercoralis* and *A. lumbricoides*.[8,18] By 2006, Zanzibar and Burkina Faso were the first territories in the WHO African Region achieving the target of regular anthelmintic drug administration to at least 75% of all school-aged children at risk of morbidity.[19]

The aim of this study was to determine the prevalence and intensity of STH infections, including *S. stercoralis*, among a random sample of school children in Chaani and Kinyasini, using a rigorous diagnostic approach. The findings were compared with data from 1994 obtained in the same schools to study the dynamics of STH infections in the face of preventive chemotherapy. The findings from Zanzibar might be of interest to public health specialists in defining and refining end-point targets of present de-worming initiatives.

MATERIALS AND METHODS

Study area and population. The study was carried out in June/July 2007 in the schools of Chaani and Kinyasini in Unguja, the main island of Zanzibar, in collaboration with the Helminth Control Laboratory Unguja (HCLU) of the MoHSW. These two schools were selected because a similar survey had been conducted there in 1994, before the launch of national helminth control programs.[8] Chaani (geographic coordinates: 5°55′48″ S latitude, 39°17′58″ E longitude) and Kinyasini (5°58′13″ S, 39°18′30″ E) are located 40 and 35 km northeast from Zanzibar Town, respectively. Pupils from both schools were subjected to large-scale administration of anthelmintic drugs, most recently in December 2006. The sample size was calculated using an equation given by Fleiss.[20] We assumed that the smallest change would have occurred in the prevalence of *S. stercoralis* infections because the benzimidazoles (albendazole and mebendazole) only show a low

*Address correspondence to Hanspeter Marti, Department of Medical and Diagnostic Services, Swiss Tropical Institute, PO Box, CH–4002 Basel, Switzerland. E-mail: hanspeter.marti@unibas.ch

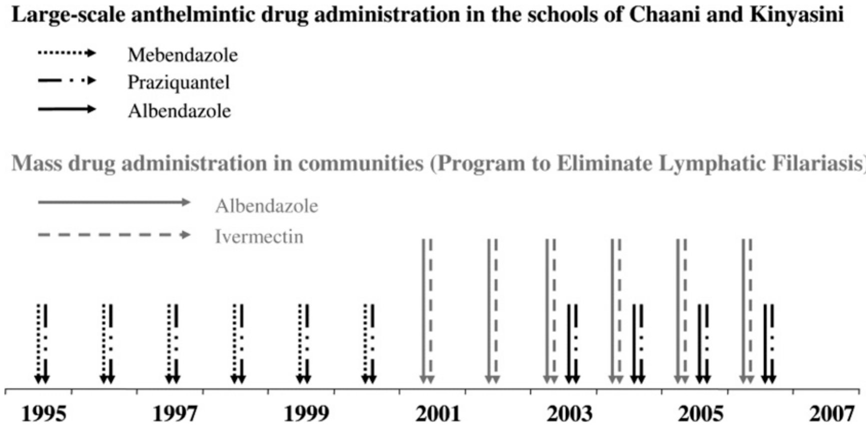

FIGURE 1. Diagram detailing the treatment with mebendazole (dotted arrowed line), albendazole (arrowed line), ivermectin (dashed arrowed line), and praziquantel (dotted and dashed arrowed line) since the onset of large-scale anthelmintic drug administration in 1995 until the cross-sectional survey reported here in June/July 2007. The school-based national helminth control program started with mebendazole (500 mg, single oral dose) and praziquantel (40 mg/kg, single oral dose) in 1995 and, after a break because of drug shortage, changed to albendazole (400 mg, single oral dose) and praziquantel (40 mg/kg) in 2003 as part of the "Kick out Kichocho Program." The program to eliminate lymphatic filariasis started in 2001 distributing ivermectin (200 μg/kg, single oral dose) plus albendazole (400 mg, single oral dose) to the whole eligible population.

efficacy in clearing this parasite.[8,18] With a given prevalence of 30% for *S. stercoralis* infections in 1994 and an estimated prevalence of 20% in 2007, and using an α error of 5% to detect a significant difference in prevalences and a power of 80%, the required number of individuals was calculated to be 312. We assumed a return rate (compliance) for providing stool samples of 90% per collection day. In view of the required number of participants and allocating for participants lost because of collection of multiple stool samples, ~400 subjects had to be included in the study.

Field and laboratory procedures. The purpose and procedures of the study were explained in detail to the headmasters and teachers of the schools. Subsequently, a teacher and a member of the HCLU team explained the study to the pupils in lay terms in their local language (Swahili). Based on our sample size calculation, we randomly selected 401 school children from all seven grades and invited them to provide three stool samples over consecutive days. Stool samples were collected in the morning (between 8:00 AM and 9:00 AM), transferred to HCLU, and within 3 hours, processed with the Kato-Katz technique,[21] the Koga agar plate method,[22] and the Baermann technique.[23] Detailed descriptions of the methods used have been presented elsewhere.[24] In brief, Kato-Katz thick smears (using 41.7-mg templates) were quantitatively examined for *A. lumbricoides*, hookworm, and *T. trichiura* eggs. The number of *S. stercoralis* larvae was quantified with the Baermann technique. Additionally, the presence of *S. stercoralis* and/or hookworm larvae was assessed qualitatively with the Koga agar plate method. A random sample of 5% of the Kato-Katz thick smears was re-examined by a senior technician for quality control.

Marti and others,[8] in 1994, collected a single stool sample from 1,204 school children (median age = 14 years) from the schools in Chaani and Kinyasini. Stool samples were subjected to a single Kato-Katz thick smear (41.7-mg template) for quantitative diagnosis of *A. lumbricoides*, hookworm, and *T. trichiura* and a single Baermann test for detection of *S. stercoralis* larvae.

Statistical analysis. Data were double entered in Excel version 10.0 (edition 2002; Microsoft, Redmond, WA) and cross-checked in EpiData version 3.1 (EpiData Association, Odense, Denmark).

For analyses, the statistical packages JMP version 5.0.1 (SAS Institute, Cary, NC) and STATA version 9.2 (StataCorp, College Station, TX) were used. Only individuals who submitted two stool samples of sufficient quantity were eligible for subsequent analyses. The helminth species-specific "true" prevalences and the sensitivity (i.e., proportion of true positives identified as positive) of the individual diagnostic methods were calculated using a mathematical model.[25] This model calculates the "true" prevalence by relating the number of stool samples found to be positive for a given helminth species to the number of false-negative results obtained for the same participant on multiple sampling. To predict the sensitivity of the diagnostic test, the model uses the frequency of positive test results among stool samples submitted by the same individual. The procedure follows an approach developed by Mullen and Prost[26] and has been previously used for estimating the "true" prevalence of STHs, including *S. stercoralis*.[24,27,28]

Helminth species-specific egg counts from the Kato-Katz thick smear readings were multiplied by a factor of 24 to derive infection intensities, expressed as eggs per gram of stool (EPG). For each individual, the arithmetic mean EPG for each helminth was calculated from the Kato-Katz thick smears. Infection intensities were stratified into light, moderate, and heavy, according to thresholds issued by WHO.[29,30] For the study cohort, the geometric mean EPG for *A. lumbricoides*, hookworm and *T. trichiura* helminth species, and for *S. stercoralis* the geometric mean larval count, was calculated using the formula provided by Montresor and others.[29]

A linear regression analysis was used to study the association between EPG and school grade. The Pearson χ^2 test was used to explore for associations between infection and age, sex, and school. In univariate and multivariate analyses, odds ratios (ORs) including 95% confidence intervals (CIs) were calculated for age, sex, and school. Cases were defined as presence of infection (at least one helminth egg detected in a Kato-Katz thick smear or at least one larvae detected in the Koga agar plate or Baermann) in at least one stool sample. Differences were considered significant at a level of 5%.

Ethical considerations and treatment. Clearance for the study was given by the institutional research commission of the Swiss Tropical Institute (Basel, Switzerland) and the institutional review board of the National Health Service Local Research Ethics Committee (application 03.36) of St. Mary's Hospital (London, UK) on behalf of the Natural History Museum/Imperial College London. The study protocol was approved by WHO, MoHSW, and the Ministry of Education of Zanzibar (Zanzibar, Tanzania).

The study was embedded in one of the parasitologic surveys carried out by HCLU in the schools of Unguja. The headmasters and teachers of Chaani and Kinyasini schools were informed about the purpose and procedures of the study. Detailed explanations were given to the school children by trained staff of the HCLU and the teachers. Participation was voluntary, and each child could withdraw from the study any time without further obligation. Parents or legal guardians signed a written informed consent sheet for all anticipated medical interventions, including parasitologic surveys at schools when they registered their children for school attendance. Oral consent to participate in this study was obtained from all children in the presence of local health and education authorities.

Both schools were subjected to anthelmintic drug administration conducted by HCLU in the following months, where all school children were treated with a single oral dose of albendazole (400 mg) and praziquantel (40 mg/kg) regardless of their infection status. Additionally, all participants diagnosed with a *S. stercoralis* infection were treated with a single oral dose of ivermectin (200 µg/kg).

RESULTS

Study profile and compliance. Figure 2 shows the study profile and compliance to submit multiple stool samples. From the 401 randomly selected school children (202 in Kinyasini and 199 in Chaani), 25 did not participate further and 8 submitted only a single stool sample. At least two stool samples were obtained from the remaining 368 children (96.3%). Because of insufficient quantities of feces and the priority for the sequence of tests used, two Kato-Katz thick smear results were available from 367 children, two Koga agar plate readings were done for 366 children, and 364 children had two Baermann results. Complete data records were available for 362 children, resulting in an overall compliance of 90.3%. This final cohort included 209 girls and 153 boys, with a median age of 12 years (range, 7–20 years).

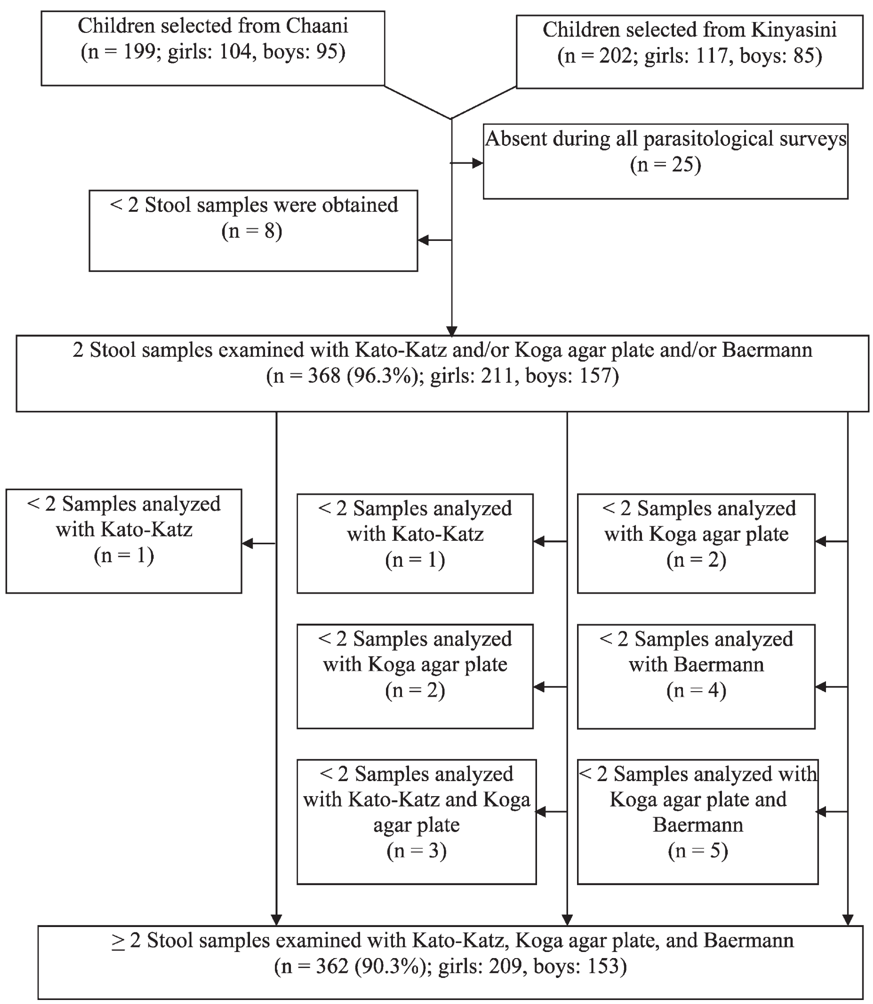

FIGURE 2. Diagram detailing the study participation and compliance of randomly selected school children from Kinyasini and Chaani, Unguja, Zanzibar. All children providing at least two stool samples were included in the final analysis. The final cohort comprised children with complete datasets (i.e., at least two stool samples examined with three methods each).

TABLE 1

Observed and estimated "true" prevalence of helminth infections among school children in Chaani and Kinyasini in Unguja, Zanzibar in June/July 2007 and sensitivity of diagnostic methods/method combinations in relation to sampling effort

Characteristics	*A. lumbricoides* (Kato-Katz method)		*T. trichiura* (Kato-Katz method)		Hookworm (Kato-Katz plus Koga agar plate method)		*S. stercoralis* (Koga agar plate plus Baermann method)	
	No. of children	Positive (%)	No. of children	Positive (%)	No. of children	Positive (%)	No. of children	Positive (%)
Two stool samples analyzed	367		367		365		363	
Cumulative positive result after analysis of								
First stool sample	52	14.2	94	25.6	43	11.8	20	5.5
Second stool sample	60	16.3	143	39.0	69	18.9	30	8.3
Second and/or third stool sample	62	16.9	171	46.6	79	21.6	37	10.2
Estimated "true" prevalence (SD)	17.1% (4.0%)		48.4% (5.5%)		23.1% (4.7%)		14.4% (6.0%)	
Sensitivity of method (two samples)	98.9%		96.3%		93.6%		70.7%	
Sensitivity of method (one sample) (SD)	89.3% (6.2%)		80.8% (5.1%)		74.6% (8.7%)		45.8% (17.9%)	

Prevalence and intensity of helminth infections. Table 1 summarizes the prevalence of helminth infections in relation to the diagnostic method used and the sampling effort. The prevalence of *T. trichiura* and *A. lumbricoides*, based on two Kato-Katz thick smear readings per individual, was 46.6% and 16.9%, respectively. An overall hookworm prevalence of 21.6% was found, as assessed by the combined results from the Kato-Katz and Koga agar plate method. The prevalence of *S. stercoralis* based on two stool samples subjected to the Baermann and Koga agar plate method was 10.2%. Using a mathematical model,[25] the "true" prevalence of *T. trichiura*, hookworm, *A. lumbricoides,* and *S. stercoralis* was 48.4%, 23.1%, 17.1%, and 14.4%, respectively.

The sensitivity for detecting a *S. stercoralis* infection increased by 54.4% when two samples rather than a single stool sample were subjected to the Koga agar plate plus Baermann methods. For hookworm diagnosis, duplicate Kato-Katz thick smears plus duplicate Koga agar plate tests improved the sensitivity by 25.5% compared with a single stool sample subjected to these methods. The sensitivity of *T. trichiura* and *A. lumbricoides* diagnosis improved by 19.2% and 10.8%, respectively, when two Kato-Katz thick smears, rather than one, were examined.

Table 2 summarizes the EPGs and *S. stercoralis* larval counts of our final study cohort and indicates that, according to WHO thresholds, all children had light infection intensities of hookworm (100%) and most had light infection intensities of *T. trichiura* (99.4%) and *A. lumbricoides* (91.9%). The remaining children had medium infection intensities; none of the children exhibited a heavy infection.

Multiple helminth infections. In the final study cohort, 59.7% (216/362) of the children were infected with one or more helminth species. There were 126 children (34.8%) infected with a single, 56 children (15.5%) with two, 29 children (8.0%) with three, and 5 children (1.4%) with four different helminth species. Three quarters of the children with a dual helminth infection harbored *A. lumbricoides* and *T. trichiura* concurrently.

Comparison with data obtained in 1994. Key results of the study from Marti and colleagues[8] carried out in 1994 are summarized in Table 2.

Comparing the overall prevalence of STH infections observed in 1994 with 2007, there was a drop of 39.6% (from 98.9% [95% CI: 98.3–99.5%] in 1994 to 59.7% [95% CI: 54.6–64.7%] in 2007). When the same diagnostic approach for species-specific helminths were considered, we found a reduction in the prevalence of *S. stercoralis* by 81.0% (prevalence in 1994 dropped from 34.8% to 6.6% in 2007). The respective relative prevalence drop for hookworm was 80.5% (from 93.9% to 18.3%), that for *A. lumbricoides* was 70.6% (from 57.5% to 16.9%), whereas *T. trichiura* prevalence decreased by 48.6% (from 90.6% to 46.6%). The infection intensities of all helminth species were significantly lower in 2007 than in 1994. The geometric mean infection intensity decreased from 554.7 to 1.1 EPG for hookworm (−99.8%), from 250.1 to 5.2 EPG for *T. trichiura* (−97.9%), and from 99.8 to 2.1 EPG for *A. lumbricoides* (−97.9%), and the count of *S. stercoralis* larvae dropped from 3.7 to 0.05 larvae (−98.7%).

Results from univariate and multivariate analyses. The results from the univariate and multivariate analyses focusing

TABLE 2

Characteristics of helminth infections in children from Chaani and Kinyasini in Unguja, Zanzibar, as determined with the Kato-Katz method (*A. lumbricoides*, hookworm, and *T. trichiura*) and the Baermann technique (*S. stercoralis*) in 1994 and 2007

Year	Parasite species	Method	No. of children infected/examined	Prevalence (95% CI)	Geometric mean of EPG* or larvae† (95% CI)	Maximal EPG* or larvae†	No. (%) of infected children, stratified by infection intensity‡		
							Light	Moderate	Heavy
1994	*A. lumbricoides*	Kato-Katz	685/1,192	57.5 (54.7, 60.3)	99.8 (78.7, 126.5)	84,720	406 (59.3)	271 (39.6)	8 (1.2)
	T. trichiura	Kato-Katz	1,080/1,192	90.6 (88.9, 92.3)	250.1 (221.4, 283.4)	43,248	793 (73.4)	280 (26.0)	7 (0.7)
	Hookworm	Kato-Katz	1,119/1,192	93.9 (92.5, 95.2)	554.7 (492.1, 625.3)	32,064	809 (72.3)	172 (15.4)	138 (12.3)
	S. stercoralis	Baermann	419/1,204	34.8 (32.1, 37.5)	3.7 (3.3, 4.1)	660	ND	ND	ND
2007	*A. lumbricoides*	Kato-Katz	62/367	16.9 (13.1, 20.7)	2.1 (1.4, 3.1)	17,520	57 (91.9)	5 (8.1)	0
	T. trichiura	Kato-Katz	171/367	46.6 (41.5, 51.7)	5.2 (4.0, 6.7)	2,880	170 (99.4)	1 (0.6)	0
	Hookworm	Kato-Katz	67/367	18.3 (14.3, 22.2)	1.1 (0.8, 1.5)	2,400	67 (100)	0	0
	S. stercoralis	Baermann	24/364	6.6 (4.0, 9.2)	0.05 (0.02, 0.07)	24	ND	ND	ND

* EPG, eggs per gram of stool, as determined by Kato-Katz method.
† Number of *S. stercoralis* larvae, as determined by Baermann examination.
‡ WHO classification, the thresholds for moderate and heavy infections are 5,000 and 50,000 EPG for *A. lumbricoides*, 1,000 and 10,000 EPG for *T. trichiura*, and 2,000 and 4,000 EPG for hookworm, respectively.
ND = not determined.

on the final cohort of 362 school children and studying the effect of age, sex, and school location on helminth infection are shown in Table 3. Children in Chaani were at a significantly lower risk for *T. trichiura* infection than pupils attending the Kinyasini school, using univariate analysis (OR = 0.39, 95% CI: 0.25–0.59; $P < 0.001$). Adjustment for age and sex in multivariate analysis did not change this result (OR = 0.37, 95% CI: 0.24–0.57; $P < 0.001$). Children in Chaani were at a significantly lower risk of a hookworm infection than their counterparts in Kinyasini, both in univariate (OR = 0.52, 95% CI: 0.31–0.88; $P = 0.013$) and multivariate analyses (OR = 0.50, 95% CI: 0.29–0.86; $P = 0.011$). Boys were at a 2.6-fold higher risk of a hookworm infection than girls, both in univariate (OR = 2.55, 95% CI: = 1.52–4.25; $P < 0.001$) and multivariate analyses (OR = 2.63, 95% CI: 1.56–4.43; $P < 0.001$).

No significant association of *A. lumbricoides* and *S. stercoralis* infections with sex, school location, or age was observed, and there was no linear relationship between the EPG of either helminth species and the different school grades (data not shown).

DISCUSSION

In Zanzibar, preventive chemotherapy targeting helminth infections has been implemented for over a decade now. The large-scale administration of anthelmintic drugs to school-aged children and other high-risk groups successfully reduced the morbidity caused by helmintic diseases.[13] This study confirmed that the prevalence and intensity of STH infections, including *S. stercoralis*, decreased sharply among school children in Unguja, in two settings where anthelmintic drugs have been administered on a fairly regular schedule. Indeed, although we found 40.3% of the 362 school children with complete data records to be free of any STH infection, in 1994, only 1.1% of > 1,200 school children were considered non-infected. Moreover, most of the infected children from our study harbored only one helminth species (58.3%), and infections were primarily of light intensity, which is different from the situation in 1994.[8]

It is important to note that the prevalence of *T. trichiura* (46.6%), hookworm (21.6%), *A. lumbricoides* (16.9%), and *S. stercoralis* (10.2%) in 2007 was determined on the basis of at least two stool samples examined from each child using different methods, whereas in 1994, only one stool sample per individual was subjected to the Kato-Katz method for the diagnosis of common STHs and the Baermann method for *S. stercoralis*. Hence, the diagnostic approach adopted in this study was more sensitive than the one in 1994. It is therefore conceivable that the reported helminth prevalence in 1994 was an underestimation of the true situation at the time, and hence, the calculated reduction in prevalence of helminth infections might be higher than reported here. The significant reduction in the prevalence and the decline in infection intensity by > 95% of each STH infection are encouraging. Indeed, these findings are likely the result of regular administration of anthelmintic drugs. Additionally, improvements in water supply and sanitation and targeted health education since 1994 might have contributed to lowering STH infections. However, no related data were collected in 1994 and 2007 and, as discussed below, the sanitary infrastructure was deemed to still be inadequate in 2007. It should be noted, however, that the overall prevalence of STH infections in 2007, ~6 months after the most recent treatment round, remains > 50% in children attending the schools of Kinyasini and Chaani. Hence, according to WHO guidelines,[29] annual treatment with anthelmintic drugs is still warranted. Of note, the real helminth prevalence among school-aged children might be higher, because some children do not attend school in Zanzibar (primary school

Table 3
Association of exposure and infection with soil-transmitted helminths in 362 school children from Chaani and Kinyasini, Unguja, Zanzibar

	Univariate model (association with infection)				Multivariate model (association with infection)			
Variable	OR	(95% CI)	χ^2 (1 df)	*P* value	OR	(95% CI)	χ^2 (3 df)	*P* value
N = 362								
A. lumbricoides							1.29	0.732
Sex (baseline = female)								
Male (42.3%)	1.35	(0.78, 2.34)	1.14	0.286	1.34	(0.77, 2.32)		
School (baseline = Kinyasini)								
Chaani (47.0%)	1.07	(0.62, 1.85)	0.06	0.805	1.08	(0.62, 1.87)		
Age (continuous)	1.02	(0.90, 1.16)	0.11	0.738	1.02	(0.90, 1.16)		
T. trichiura							23.24	< 0.001*
Sex (baseline = female)								
Male (42.3%)	1.38	(0.91, 2.09)	2.23	0.135	1.45	(0.94, 2.24)		
School (baseline = Kinyasini)								
Chaani (47.0%)	0.39	(0.25, 0.59)	19.68	< 0.001*	0.37	(0.24, 0.57)		
Age (continuous)	0.99	(0.90, 1.08)	0.09	0.760	0.95	(0.86, 1.05)		
Hookworm							19.98	< 0.001*
Sex (baseline = female)								
Male (42.3%)	2.55	(1.52, 4.25)	13.06	< 0.001*	2.63	(1.56, 4.43)		
School (baseline = Kinyasini)								
Chaani (47.0%)	0.52	(0.31, 0.88)	6.18	0.013*	0.50	(0.29, 0.86)		
Age (continuous)	1.04	(0.93, 1.17)	0.44	0.509	1.01	(0.90, 1.14)		
S. stercoralis							4.83	0.185
Sex (baseline = female)								
Male (42.3%)	1.70	(0.86, 3.36)	2.32	0.128	1.73	(0.87, 3.45)		
School (baseline = Kinyasini)								
Chaani (47.0%)	0.58	(0.29, 1.18)	2.35	0.125	0.57	(0.28, 1.16)		
Age (continuous)	1.01	(0.86, 1.18)	0.01	0.921	0.99	(0.84, 1.16)		

* Significant *P* values ($P < 0.05$).

enrollment in Zanzibar was 97.8% in 2006[31]). It is conceivable that these non-attendees are at a higher risk of STH infection.

The observed prevalence of helminth infections in our study—with the exception of *A. lumbricoides*—increased by > 80% when multiple stool samples per individual were examined and a combination of diagnostic methods was considered. Underlying reasons, among others, include (1) low egg output caused by light infection intensities, which was observed in most of the infected children; (2) day-to-day variation in egg output; and (3) lack of sensitivity of the diagnostic assays.[24,32,33] Areas subjected to large-scale anthelmintic drug administrations are characterized by low helminth infection intensities, which call for diagnostic tests with a high sensitivity.[27,34–36] Examination of repeated stool samples increases diagnostic sensitivity,[24,37–39] but this approach raises concerns about compliance. In our study, however, > 90% of the children supplied at least two stool samples of sufficient quantity to perform a suite of diagnostic tests.

School children in Kinyasini had a higher risk of *T. trichiura* and hookworm infections than those from Chaani. Local risk factors sustaining helminth transmission can include specific environmental differences, such as soil composition and moisture, as well as socioeconomic discrepancies and differences in sanitation, hygiene, and health-seeking behavior.[12,40–44] The lack of detailed appraisal of some of these risk factors is a limitation of this study and is the focus of our ongoing work. The observed higher risk for boys to be infected with hookworm coincides with findings from Pemba and elsewhere in Africa and might result from behavioral, immunological, or genetic idiosyncracies.[41,45–47] Age showed no significant association with infection prevalence of any helminth species and the school grade showed no association with infection intensity. This implies that older children in higher grades were not better off because of multiple rounds of school-based treatments than their younger counterparts who were only treated once or twice before our survey. These findings are in contrast to a previous study conducted in Pemba, where lower mean infection intensities with *A. lumbricoides*, hookworm, and *T. trichiura* in children in grade 5 compared with children in grade 1 were explained as a beneficial effect of regular treatment.[48] However, in the Pemba study, children in grade 1 had not been treated before, whereas in our study, the youngest children were 7 years old and thus had most likely experienced at least one round of mass drug administration in the frame of the GPELF, which distributed albendazole plus ivermectin to the whole eligible population older than 5 years of age.[17] Additionally, all children who participated in our study in June/July 2007 were supposed to have been treated in their schools in December 2006. However, because of an interruption in drug distributions in the two schools in 2001–2003, children in higher grades were unlikely to have experienced more than four rounds of school-based treatment (2003–2006).

In this study, 59.7% of the children were infected with STHs, primarily at low intensity, although they had been subjected, most likely, to one or even more rounds of anthelmintic drug administration in the frame of school-based treatment campaigns and the GPELF. The following reasons are offered for consideration why the de-worming interventions were not more effective in terms of prevalence reduction. First, infections with *T. trichiura* count for the largest part of this high overall helminth prevalence. Indeed, the prevalence of *T. trichiura* in mid-2007 was still 46.6%, and the relatively smaller decrease in prevalence (reduction of 48.6%) compared with *A. lumbricoides*, hookworm, and *S. stercoralis* (reductions of > 70%) confirms the reported low efficacy of the benzimidazoles albendazole and mebendazole against *T. trichiura*.[4,8,49] Conflicting results have been reported regarding the efficacy of an albendazole-ivermectin combination against *T. trichiura* infections in the frame of the GPELF.[50,51] Hence, new research is needed to determine the efficacy and safety of new drugs and combination of existing drugs targeting *T. trichiura*. Second, children not attending school or those missing the day of treatment, together with preschool children, might contribute substantially to the overall transmission of STHs, which leads to rapid re-infection of children who have been de-wormed successfully. Third, insufficient knowledge on STH transmission might result in risky behavior (e.g., eating unpeeled fruits or walking barefoot) and (un) intentional pollution of the environment abetted by a lack of sanitary infrastructures and access to clean water. Hence, to render preventive chemotherapy campaigns more effective, regular informal meetings of health professionals, community leaders, and headmasters must be organized to keep awareness high. Regular teaching and training lessons for locally involved health staff (e.g., health teachers and village health workers) must be held to guarantee knowledge transfer to villagers and school children and hence to change behavior of high-risk groups. Periodic de-worming campaigns in schools and whole communities could be used not only for drug administration, but could go hand-in-hand with focused health education on how to prevent worm infection and transmission. Preventive chemotherapy coupled with "preventive behavior" might, however, only reduce STH transmission successfully if they are complemented by improvements in water and sanitation. At present, children attending Chaani and Kinyasini schools have reasonable access to wells or tap water at home,[52] but only a small proportion of households has latrines, and there is no communal system for solid waste management. These contextual factors might explain why the prevalence of STH infections in Unguja is still high, coupled with the risk of rapid "re-worming" after successful de-worming.

We conclude that the national helminth control programs in Zanzibar have been successful in reducing both prevalence and intensity of STH infections, and hence, morbidity and transmission have likely decreased. However, similar to other large-scale and long-term helminth control programs, for example the one in China,[53] efforts to control intestinal nematode infections with conventional chemotherapeutic agents may not be sufficient to yield a lasting reduction in prevalence and intensity. Therefore, it will be important to find out about the needs of educational, behavioral, and environmental changes in Zanzibar to specifically target future health interventions. From a more global perspective, the observations on Zanzibar represent particularly pertinent information for public health strategists developing disease forecasting predictions in the face of ongoing de-worming initiatives in various endemic countries. Through a combination of pragmatic field research and application of epidemiologic models, it should be possible to predict the true impact of chemotherapy on several STH infections simultaneously. By setting clear endpoint targets in terms of prevalence and intensity of infection, better monitoring and evaluation of programs seem in reach.

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Authors' addresses: Stefanie Knopp and Jürg Utzinger, Department of Public Health and Epidemiology, Swiss Tropical Institute, PO Box, CH-4002 Basel, Switzerland, Tel: 41-61-284-8226 and 41-61-284-8129). Khalfan A. Mohammed and I. Simba Khamis, Helminth Control Laboratory Unguja, Ministry of Health and Social Welfare, PO Box 236, Mianzini, Zanzibar, Tanzania, Tel: 255-24-23-4512 and 255-24-23-4512. J. Russell Stothard and David Rollinson, Wolfson Wellcome Biomedical Laboratories, Biomedical Parasitology Division, Department of Zoology, Natural History Museum, Cromwell Road, London SW7 5BD, UK, Tel: 44-207-942-5490 and 44-207-942-5181. Hanspeter Marti, Department of Medical and Diagnostic Services, Swiss Tropical Institute, PO Box, CH-4002 Basel, Switzerland, Tel: 41-61-284-8256.

Reprint requests: Hanspeter Marti, Department of Medical and Diagnostic Services, Swiss Tropical Institute, PO Box, CH-4002 Basel, Switzerland, E-mail: hanspeter.marti@unibas.ch.

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