

IMPACT OF NATIONAL HELMINTH CONTROL PROGRAMME ON INFECTION AND MORBIDITY IN RWANDAN POPULATION



YEAR TWO FOLLOW UP REPORT

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Access Project

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ACRONYMS

EI	Earth Institute
GG	Geneva Global
GNNTDC	Global Network for Neglected Tropical Disease Control
Hb	Haemoglobin
IP	Image Pattern
MAL	Mid-Axillary Line
MCL	Mid-Clavicular Line
MDA	Mass Drug Administration
MSL	Mid-Sternal Line
NRL	National Reference Laboratory
NTD(s)	Neglected Tropical Diseases
PDA	Personal Digital Assistant
PPT/F	Periportal Fibrosis
PSL	Para-sternal Line
PVD	Portal Vein Diameter
RNEC	Rwanda National Ethics Committee
SCI	Schistosomiasis Control Initiative
SD	Standard deviation
STH(s)	Soil-Transmitted Helminth(s)
SVI	Sabin Vaccine Institute
WHO	World Health Organization

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ABSTRACT

Background: For the control of schistosomiasis and Soil-Transmitted Helminthiasis (STH), the 54th World Health Assembly passed a resolution urging member states to provide regular drug treatment for high-risk groups. In support of this important milestone in helminthes control, WHO has set the global target of regularly treating at least 75% of all school-aged children by the year 2010. Following the baseline data collection and year one follow-up for schistosomiasis and STHs control in 14 sentinel sites in Rwanda, year two follow-up data were collected to monitor the positive impact of mass drug administration.

Objective: The study aimed to assess the health impact of a national control programme targeting schistosomiasis and STHs in Rwanda, which has provided school- and community-based anthelmintic chemotherapy since 2008.

Methods: Longitudinal surveys on infection status, haemoglobin concentration and clinical morbidity were conducted in 1360 randomly selected school children from 12 schools in five districts, and 96 randomly selected adults from 2 villages, at three time points — before chemotherapy and after one year and two years of annual mass chemotherapy.

Results: Mass treatment with praziquantel and albendazole led to a significant reduction in prevalence, intensity and clinical morbidity indicators. Among school children a significant overall reduction in prevalence of 83.1% (from 8.3% to 1.4%) for *S. mansoni* was observed after two years of treatment. The prevalence decreased by 80.4% (from 27.6% to 5.4%), 7.6% (from 61.4% to 56.7%) and 11.4% (63.2% to 56.0%) for hookworm, *T. trichiura* and *A. lumbricoides*, respectively. Remarkable reduction in mean intensity was observed for *S. mansoni* [84.9% (from 10.6 to 1.6 epg)] and hookworm infections [85.6% (from 44.5 to 6.4 epg)]. Intensity of *T. trichiura* and *A. lumbricoides* infections decreased by 46.8% (from 556.8 to 296.2 epg) and 43.8% (from 5822.4 to 3271.6 epg), respectively. The prevalence of anemia (Hb<12g/dl) decreased by 50.9% (from 16.9% to 8.3%). The signs of early clinical morbidity also decreased. The same improvements were observed among adult individuals.

Conclusion: Anthelmintic treatment delivered as part of a national integrated NTD control programme can decrease infection and morbidity among school children and adult individuals. There is need of maintaining MDA along with Behavior Change Communication (BCC) component and advocacy for availability of safe water and sanitation.

I. INTRODUCTION

For the control of schistosomiasis and STHs, in 2001 the 54th World Health Assembly passed a resolution urging Member States to provide regular drug treatment to high-risk groups. In support of this important milestone in helminth control, WHO set a global target of regularly treating at least 75% of all school-age children [1, 2]. In Africa, schistosomiasis occurs predominantly due to two species — *Schistosoma mansoni* that causes intestinal schistosomiasis and *Schistosoma haematobium* that causes urinary schistosomiasis. Clinical trials have demonstrated that praziquantel is a safe and efficacious treatment against both species, and that repeated chemotherapy decreases infection and related morbidity [3-9]. One of the main control methods is treating school children with praziquantel together with albendazole as part of school health programmes. As this method uses the existing school infrastructure and provides easy accessibility to children, it is a cost-effective public health strategy [10] and many pilot programmes have demonstrated its feasibility, affordability and effectiveness [11-15].

Control of morbidity related to schistosome infection has received new impetus with reduced drug prices [16], new approaches to control [17, 18] and more recently, the establishment of the Schistosomiasis Control Initiative (SCI) [19, 20].

The situation of schistosomiasis and STHs in Rwanda was recently updated by the countrywide mapping conducted by the Rwanda Ministry of Health in partnership with the Columbia University's Access Project. Whilst the main endemic areas for *S. mansoni* infection were found to be much focalized around lakes and swampy areas (Lakes Muhazi, Ruhondo, Bulera, Kivu, Rweru, and Mimuri marshland located in Nyagatare district), STHs were found to be widespread in the whole country [21-24]. This report intends to show the impact of repeated mass preventive chemotherapy for schistosomiasis and STHs in Rwanda, specifically, infection status, haemoglobin concentration and related clinical morbidity.

II. METHODS

Study design

A baseline and two annual longitudinal surveys were conducted in a randomly selected sample of children aged 5–16 years from 12 randomly selected schools distributed in 5 districts, and adults (≥ 17 years) from 2 villages. The nationwide mass treatment was organized every 6 months for STHs while mass treatment for schistosomiasis was provided annually in endemic foci where prevalence was found to be at least 10%. The districts were selected to represent different transmission settings: Burera district along Lake Burera, Musanze district along Lake Ruhondo, Gicumbi district along Lake Muhazi, Rutsiro district along Lake Kivu, and Nyagatare district along Mimuri marshland. Data collection was conducted in two phases (I: Burera and Musanze; II: Gicumbi, Nyagatare and Rutsiro). Within each district, schools were stratified according to their location - distance away from *S. mansoni* infection transmission focus. In phase I, one school located at 1 km away from the lake, one school located between 2 and 3 km away from the lake and one school located between 4 and 5 km away from the lake. In phase II, one school located at 1 km away from the lake/swampy areas and one school located between 2 and 3 km away from the lake/swampy areas. The reduction in the number of schools in phase II was due to logistical reasons and was found to not affect the expected results. This stratification will allow the program to be evaluated in 2 low-, 2 medium- and 2 high- prevalence schools.

For selection of children, the required sample size have been calculated using EpiSchisto tool [25] and based on an expected reduction in mean intensity of 60% (*S. mansoni*) after chemotherapy, to achieve 80% statistical power and a significance level of 5%. The value of 60% was chosen as a conservative estimate of the expected reduction over a 2 year period (2 annual treatments). We have also allowed for an overall drop-out rate of 40% over the course of the monitoring period.

In each school: a *cohort structure* was used, where there were (approximately) equal numbers of boys and girls. The table 1 below shows how this was done (**bold** font for classes indicates new recruits) for the first few years of the survey.

Table 1. Cohort structure

Years	Classes	Total of children (100 in each class)
Baseline	1, 2, 6	300
Follow-up year 1	1, 2, 3, 6	400
Follow-up year 2	1, 2, 3, 4, 6	500

At baseline, a total of 300 children were included from each school. Twelve and 24 months later, we re-visited the school and re-examined the same children when they could be traced. We undertook evaluation surveys every year during February-March in Musanze and Burera districts, August-September in Gicumbi, Nyagatare and Rutsiro districts.

For adult participants, approximately 60 adult individuals were randomly selected from one village (in close proximity with the lake) in each of the 2 districts of Musanze and Burera. These participants were followed after 12 and 24 months when they could be traced.

Ethical considerations

An ethical clearance for the study was obtained from the Rwanda National Ethics Committee (RNEC). The field team held meetings with the teachers and parents to explain the purpose of the study and obtained written informed parental consent before starting the study. We also obtained assent from the children before collecting samples.

Procedures

Faecal samples from each participant were examined by Lab technicians using by the Kato-Katz method [26]. Haemoglobin (Hb) concentration was measured using a portable haemoglobinometer (HemoCue Corporation, Ängelholm, Sweden) [27-29]. Clinical examination consisted of liver and spleen palpation whilst individuals were in a supine position. The liver and spleen changes were assessed by measuring the extensions below the rib cage along the right mid-clavicular line (MCL) and mid-sternal line (MSL) for the liver, and the extension below the rib cage along the left mid-clavicular and mid-axillary lines

(MAL) for the spleen. The firmness of each palpable organ was recorded as normal, soft, firm or hard.



Briefing to school children



Collection of stool specimens



Preparation of KK slides



Hb testing



Abdominal palpation



Interviews

Ultrasonography of the liver was performed using a portable ultrasound apparatus (Aloca® Sonocamera SSD 500) for adult individuals only. Ultrasound image patterns suggestive of periportal fibrosis (PPT/F) were compared with standard images and the corresponding image pattern score was recorded using the WHO-Niamey protocol [30]. The following ultrasound measurements were made: the size of the left liver lobe was measured in the longitudinal parasternal line (PSL); portal vein diameters (PVD) were measured midway between the entrance of the portal hepatic and its bifurcation inside the liver. Following the WHO protocol, measurements of organ size and vein diameter were height-adjusted, using standard reference measurements for healthy members of the same population group. We

assumed that if the PSL height-adjusted value exceeded 2 or 4 standard deviations (SD) in relation to the reference measurement the liver was considered enlarged or much enlarged. If the PVD height-adjusted value exceeded 2 or 4 SD, it indicated portal vein dilatation or marked dilatation.

To minimize inter-observer variation, the same ultrasonographer and we employed the same laboratory technicians (where possible) were in all surveys.

Quality control

The quality control was performed on stool samples by the National Reference Laboratory (NRL) to ensure the quality of parasitological analysis by different microscopists. At least 10% of stool samples were randomly selected and re-examined by a senior laboratory technician from NRL.

Data management and analysis

Data were entered in re-coded questionnaires into an H'Pipaq Personal Digital Assistant (PDA) machine in the field and transferred to the computer in Microsoft Excel. We used STATA MP 10 (StataCorpLP, 4905 Lakeway Drive, College Station, Texas 77845) and SAS (version 9.1; SAS Institute Inc., Cary, NC, USA) for data management and analysis. Data were checked for inconsistencies and measurement error before data analysis. We merged baseline and follow-up data by individual identification (ID) number and checked variables such as age, and sex to see if the same ID represented the same individual.

A case of *S. mansoni* and each of STHs was defined by having at least 1 egg per gram (epg) in a stool specimen. The intensity of infection was estimated by the arithmetic means of epg for all participants. Intensity categories were calculated using WHO definitions [31]:

- *S. mansoni*: (light: 1-99 epg, moderate: 100-399epg, heavy: ≥ 400 epg)
- Hookworm (light: 1-1999 epg, moderate: 2000-3999epg, heavy: ≥ 4000 epg)
- *A. lumbricoides* (light: 1-4999 epg, moderate: 5000-49999epg, heavy: ≥ 50000 epg)
- *T. trichiura* (light: 1-999 epg, moderate: 1000-9999epg, heavy: ≥ 10000 epg)

Anemia case was defined as a person with haemoglobin less than 12g per dl. We have calculated prevalence and arithmetic mean intensities of parasitic infections over the years

for 3 sets of data: one for school children successfully followed for 2 years, the second for successfully followed adults, the last one for newly recruited school children in class 1 and class 6. The latter set of data was used to study trends in transmission of the parasitic infections were calculated. We have provided 95 % Confidence Intervals (CIs) for prevalence and intensity of infection. All the findings included in this report will be studied more in depth, so that multivariate analysis can be performed at a later stage. Morbidity measures such as anemia and self reported symptoms are provided for longitudinal children's data. Ultrasound pathology is provided for adults' data. Scores were calculated based on standardized definition of WHO for Ultrasonography for the Assessment of Schistosomiasis-related Morbidity [30].

III. FINDINGS

A. Successful follow-up

Demographic characteristics

At baseline (2008), 3,422 individuals were recruited from 5 districts, 12 sentinel schools and 2 villages (Tables 2 and 3). The age range was 5-16 for children and 17-85 years for adults. There were 48.24 % males and 51.76% females (sex ratio: 0.93).

At year one follow-up (2009), 2,126 individuals (i.e. 62.16 %=2126/3422) were successfully followed-up compared to baseline, (Table 2).

At year two follow-up (2010), 1392 individuals (i.e. 40.7%=1392/3422) were successfully followed-up (Table 2). There were almost equal successfully followed boys and girls (Table 4). For these 1,496 individuals, parasitological and other morbidity indicators are analyzed separately for children (i.e. age: 5-16 years old) and adults (i.e. age: 17-85 years old). Furthermore, 1,947 and 2,026 completely new children from classes 1 and 6 were recruited at year one and year two, respectively, in order to study parasitological impact during the time points of interest and ultimately make inference about STH's and schistosomiasis' transmission. For the newly recruited children at follow-ups years 1 and 2, we compared their parasitological data in terms of prevalence and intensity for the 3 time points of interest. Such results can be found under the heading 'Cross-sectional results'.

For adults 78.7% who were recruited at baseline (i.e. 96/122) were successfully followed-up in year two survey.

Table 2. Distribution of successfully followed participants for 2 years by district. Longitudinal Monitoring Study on intestinal schistosomiasis and STHs in Rwanda, 2008-2010

Districts	Baseline (2008) n=3422*	Year 1 (2009) n= 2126 (62.1%)*	Year 2 (2010) n=1392 (40.7%)*
Burera	842	489	279
Gicumbi	588	345	243
Musanze	850	499	348
Nyagatare	581	421	267
Rutsiro	561	372	255

* Numbers include school children and adult participants

Table 3. Distribution of successfully followed school children (5-16 years) for 2 years by school. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Districts	Sentinel schools	Frequency	%
Burera	Gafumba	106	7.6
	Mwiko	86	6.2
	Musasa	87	6.3
Musanze	Remera	102	7.3
	Ryandinzi	111	8.0
	Musekera	135	9.7
Rutsiro	Kigeyo	122	8.8
	Maziba	133	9.6
Gicumbi	Nyagatoma	130	9.3
	Rwesero	113	8.1
Nyagatare	Katabagemu	107	7.7
	Nyaruziba	160	11.5
	Total	1392	100

Table 4. Distribution of successfully followed school children (5-16 years) for 2 years by gender. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Gender	Frequency	%	Sex ratio: 0.98
Male	689	49.5	
Female	703	50.5	

Parasitological data

Prevalence and intensity of infections

The health indicators of children surveyed (Tables 5&7) showed that initial prevalence and mean intensity (eggs per gram) of *S. mansoni* infection (in 2008) among those followed-up for two years was 8.3% and 10.6 epg, respectively. In 2010, following two rounds of annual treatment, the prevalence and mean intensity of infection fell to 1.4% (reduction of 83.1%) and 1.6 epg (reduction of 84.9%), respectively. Overall, the prevalence and mean intensity of hookworm infection decreased from 27.6% and 44.5 epg to 5.4% (reduction of 80.4%) and 6.4 epg (reduction of 85.6%), respectively. At baseline, the prevalence of *T. trichiura* and *A. lumbricoides* infections was 61.4% and 63.2%, which decreased to 56.7% (reduction of 7.6%) and 56.0% (reduction of 11.4%), respectively. The mean intensity of *T. trichiura* and *A. lumbricoides* decreased from 556.8 and 5822 epg to 296.2 (reduction of 46.8%) and 3271.6 epg (reduction of 43.8%), respectively. In adults, the prevalence decreased from 33.3%, 27.1%, 78.4% and 71.9% to 4.2% (reduction of 87.4%), 3.1% (reduction of 88.6%), 57.7% (reduction of 26.4%) and 58.3% (reduction of 18.9%) for *S. mansoni*, Hookworm, *T. trichiura* and *A. lumbricoides*, respectively (Table 6). Among school children the mean intensity decreased from 41.4 epg, 15.9 epg, 242.8 epg and 3177.5 epg to 1.6 epg (reduction of 96.1%), 5.4 epg (reduction of 66.0%), 102.9 epg (reduction of 57.6%) and 1481.9 epg (reduction of 53.4%) for *S. mansoni*, Hookworm, *T. trichiura* and *A. lumbricoides*, respectively (Table 9). For all infections the number of cases was reduced for both intensity categories (Tables 8, 10). The reduction in intensity was observed among adult cohort as well

(Tables 11&12). Important decrease in prevalence was observed for *S. mansoni* and hookworm infections in all 5 districts. The prevalence of *S. mansoni* fell to almost 0% in Burera, Nyagatare and Rutsiro. However a light decrease in prevalence was generally observed while light increase prevalence was fund for *A. lumbricoides* in Rutsiro district (Table 7).

Table 5. Prevalence of *S. mansoni* & STHs of successfully followed school children (5-16 years) for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n= 1392)

Parasites	Prevalence			
	Baseline (2008)	Year 1 (2009)	Year 2 (2010)	Overall reduction in %
<i>S. mansoni</i>	8.3[6.8-9.7]	1.9[1.2-2.6]	1.4[0.7-2.0]	83.1
Hookworm	27.6[25.2-29.9]	7.7[6.3-9.1]	5.4[4.2-6.6]	80.4
<i>T. trichiura</i>	61.4[58.8-63.9]	53.5[50.8-56.1]	56.7[54.1-59.3]	7.6
<i>A. lumbricoides</i>	63.2[60.7-65.8]	59.7[57.1-62.3]	56.0[53.4-58.6]	11.4

Table 6. Prevalence of *S. mansoni* & STHs of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n=96)

Parasites	Prevalence			
	Baseline (2008)	Year 1 (2009)	Year 2 (2010)	Overall reduction in %
<i>S. mansoni</i>	33.3[23.9-42.8]	6.3[1.4-11.1]	4.2[0.2-8.2]	87.4
Hookworm	27.1[18.2-36.0]	6.3[1.4-11.1]	3.1[0.0-6.6]	88.6
<i>T. trichiura</i>	78.4[70.2-86.5]	67.7[58.4-77.1]	57.7[47.9-67.6]	26.4
<i>A. lumbricoides</i>	71.9[62.9-80.9]	74.0[65.2-82.7]	58.3[48.5-68.2]	18.9

Table 7. Prevalence by district of *S. mansoni* & STHs of successfully followed school children (5-16 years) for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Districts	Parasites	Prevalence		
		Baseline (2008)	Year 1 (2009)	Year 2 (2010)
Burera (n=279)	<i>S. mansoni</i>	2.9[0.9-4.8]	0.7[0.0-1.7]	0
	Hookworm	5.7[3.0-8.5]	3.6[1.4-5.8]	0.4[0.0-1.1]
	<i>T. trichiura</i>	95.7[93.3-98.1]	86.4[82.3-90.4]	93.2[90.2-96.2]
	<i>A. lumbricoides</i>	91.0[87.7-94.4]	92.8[89.8-95.9]	87.8[84.0-91.7]
Gicumbi (n=243)	<i>S. mansoni</i>	18.9[14.0-23.9]	3.7[1.3-6.1]	2.5[0.5-4.4]
	Hookworm	29.2[23.5-35.0]	4.1[1.6-6.6]	2.1[0.3-3.9]
	<i>T. trichiura</i>	3.7[1.3-6.1]	4.5[1.9-7.2]	2.9[0.8-5.0]
	<i>A. lumbricoides</i>	16.9[12.1-21.6]	8.6[5.1-12.2]	7.8[4.4-11.2]
Musanze (n=348)	<i>S. mansoni</i>	10.9[7.6-14.2]	2.3[0.7-3.9]	2.6[0.9-4.3]
	Hookworm	36.8[31.7-41.9]	1.7[0.3-3.1]	4.9[2.6-7.2]
	<i>T. trichiura</i>	87.6[84.2-91.1]	68.7[63.8-73.6]	76.4[72.0-80.9]
	<i>A. lumbricoides</i>	85.6[81.9-89.3]	83.0[79.1-87.0]	77.9[73.5-82.3]
Nyagatare (n=267)	<i>S. mansoni</i>	2.2[0.5-4.0]	0	0.7[0.0-1.8]
	Hookworm	41.6[35.6-47.5]	17.6[13.0-22.2]	12.0[8.1-15.9]
	<i>T. trichiura</i>	16.5[12.0-21.0]	13.1[9.0-17.2]	12.4[8.4-16.4]
	<i>A. lumbricoides</i>	23.2[18.1-28.3]	13.1[9.0-17.2]	5.2[2.6-7.9]
Rutsiro (n=255)	<i>S. mansoni</i>	6.7[3.6-9.7]	2.7[0.7-4.8]	0.8[0.0-1.9]
	Hookworm	22.7[17.6-27.9]	13.3[9.1-17.5]	7.8[4.5-11.2]
	<i>T. trichiura</i>	89.8[86.1-93.5]	85.8[81.6-90.2]	87.5[83.4-91.5]
	<i>A. lumbricoides</i>	88.2[84.3-92.2]	89.0[85.2-92.9]	90.2[86.5-93.9]

Table 8. Prevalence by district of *S. mansoni* & STHs of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

District	Parasites	Prevalence		
		Baseline (2008)	Year 1 (2009)	Year 2 (2010)
Burera (n=49)	<i>S. mansoni</i>	34.7[21.4-48.0]	0.0	0.0
	Hookworm	8.2[0.2-16.1]	4.1[0.0-9.8]	0.0
	<i>T. trichiura</i>	79.5[68.3-90.9]	73.5[61.1-85.8]	65.3[52.0-78.6]
	<i>A. lumbricoides</i>	71.4[58.8-84.1]	83.7[73.3-94.0]	67.3[54.2-80.5]
Musanze (n=47)	<i>S. mansoni</i>	31.9[18.6-45.2]	12.8[3.2-22.3]	8.5[0.5-16.5]
	Hookworm	46.8[32.0-61.6]	8.5[0.2-16.8]	6.4[0.0-13.6]
	<i>T. trichiura</i>	77.1[65.2-89.0]	61.7[47.8-75.6]	50.0[35.9-64.1]
	<i>A. lumbricoides</i>	72.3[59.6-85.1]	63.8[50.1-77.6]	48.9[34.6-63.2]

Table 9. Mean intensity (epg)* of *S. mansoni* & STHs of successfully followed school children (5-16 years) for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

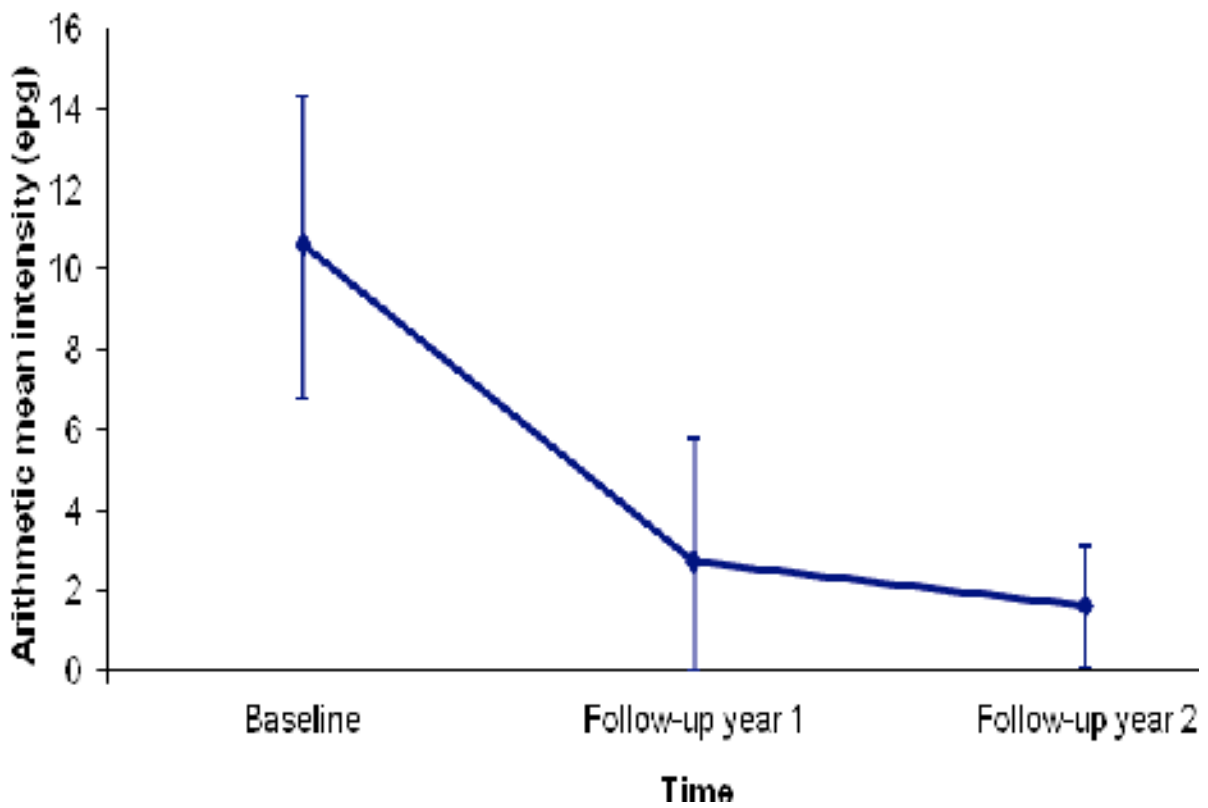
(n=1392)

Parasites	Baseline (2008) Mean (SD)	Year 1 (2009) Mean (SD)	Year 2 (2010) Mean (SD)	Overall reduction in %
<i>S. mansoni</i>	10.6 [6.8-14.3]	2.7 [0.0-5.8]	1.6 [0.1-3.1]	84.9
Hookworm	44.5 [33.8-55.2]	6.3 [4.2-8.3]	6.4 [0.6-12.3]	85.6
<i>T. trichiura</i>	556.8 [460.9-652.7]	217.2 [177.2-257.1]	296.2 [245.4-346.9]	46.8
<i>A. lumbricoides</i>	5822.4[4927.7-6717.0]	3325.4 [2912.8-3737.9]	3271.6 [2863.8-3679.4]	43.8

* Mean intensity equals sum of a parasite eggs divided by number of all individuals tested

Figure 1 Arithmetic mean intensity of *S. mansoni* infection in school children successfully followed up during 2 years

Arithmetic mean intensity of *S. mansoni* infection in school children successfully followed up during 2 years (n=1392)



A tremendous decrease in intensity was observed among the followed school children (fig. 1)

Table 10. Intensity category* of *S. mansoni* & STHs of successfully followed school children (5-16 years) for 2 years. Longitudinal Monitoring Study of Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n=1392)

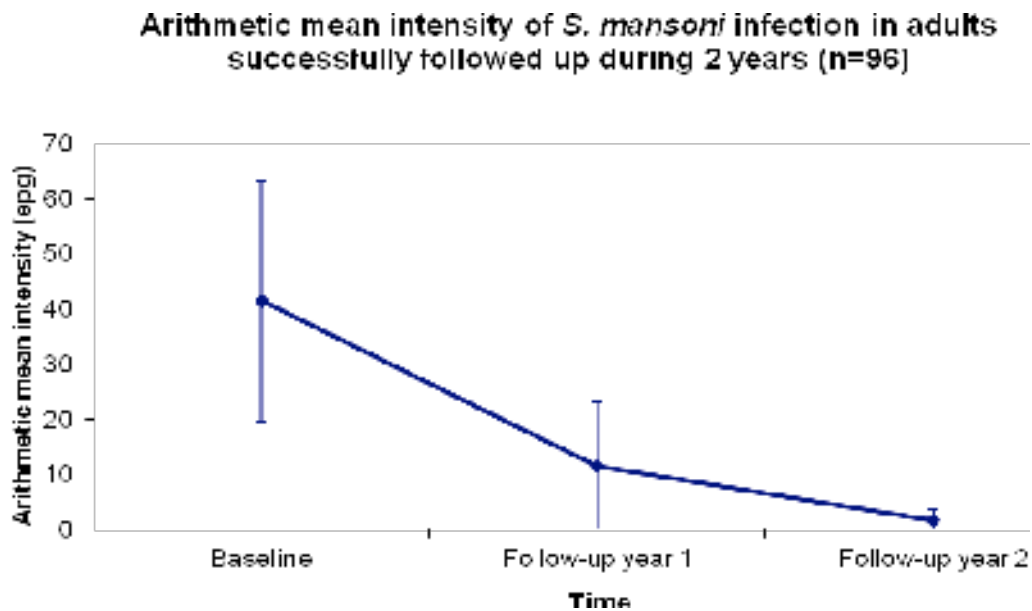
Intensity (epg)	Baseline (2008) (%)	Year 1 (2009) (%)	Year 2 (2010) (%)
<i>S. mansoni</i>			
0 (%)	1277 (91.7)	1366 (98.1)	1373 (98.6)
1-99 (%)	79 (5.7)	21 (1.5)	13 (0.9)
100-399 (%)	31(2.2)	3 (0.2)	5 (0.4)
≥ 400 (%)	5 (0.4)	2 (0.1)	1 (0.1)
Hookworm			
0 (%)	1008 (72.4)	1285 (92.3)	11317 (94.6)
1-1999 (%)	381 (27.4)	107 (7.7)	74 (5.3)
2000-3999 (%)	2 (0.1)	0 (0.0)	0 (0.0)
≥ 4000 (%)	1(0.1)	0 (0.0)	0 (0.0)
<i>T. trichiura</i>			
0 (%)	538 (38.6)	647 (46.5)	581 (46.2)
1-999 (%)	671 (48.2)	673 (48.4)	587 (46.7)
1000-9999 (%)	172 (12.4)	71 (5.1)	88 (7.0)
≥ 10000 (%)	11 (0.8)	1 (0.1)	8 (0.1)
<i>A. lumbricoides</i>			
0 (%)	512 (36.8)	561 (40.3)	613 (44.0)
1-4999 (%)	531 (38.2)	552 (40.3)	531 (38.2)
5000-49999 (%)	320 (23.0)	275 (19.8)	244 (17.5)
≥ 50000 (%)	29 (2.1)	4 (0.3)	4 (0.3)

* Intensity categories according to WHO classification [31]

Table 11. Mean intensity (epg) of *S. mansoni* & STHs of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Parasites	Baseline (2008) Mean (SD)	Year 1 (2009) Mean (SD)	Year 2 (2010) Mean (SD)	Overall reduction in %
<i>S. mansoni</i>	41.4[19.6-63.2]	11.4[0.0-23.0]	1.6[0.0-3.4]	96.1
Hookworm	15.9[7.2-24.5]	5.4[0.0-12.0]	5.4[0.0-12.0]	66.0
<i>T. trichiura</i>	242.8[168.2-317.5]	97.5[62.1-132.9]	102.9[63.8-142.0]	57.6
<i>A. lumbricoides</i>	3177.5[2248.5-4106.6]	3110.4[1661.9-4558.8]	1481.9[843.1-2120.7]	53.4

Figure 2 Arithmetic mean intensity of *S. mansoni* infection in adults successfully followed up during 2 years



A tremendous decrease in intensity was observed among the followed adults (fig. 2)

Table 12. Intensity category of *S. mansoni* & STHs of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n=96)

Intensity (epg)	Baseline (2008) (%)	Year 1 (2009) (%)	Year 2 (2010) (%)
<i>S. mansoni</i>			
0 (%)	64(66.7)	90(93.8)	92(95.8)
1-99 (%)	19(19.8)	2(2.1)	4(4.2)
100-399 (%)	10(10.4)	3(3.1)	0
≥ 400 (%)	3(3.1)	1(1.0)	0
Hookworm			
0 (%)	70(72.9)	90(93.4)	93(96.9)
1-1999 (%)	26(27.1)	6(6.3)	3(3.1)
2000-3999 (%)	0	0	0
≥ 4000 (%)	0	0	0
<i>T. trichiura</i>			
0 (%)	21(21.6)	31(32.0)	41(42.3)
1-999 (%)	73(75.3)	65(67.0)	55(56.7)
1000-9999 (%)	3(3.1)	1(1.0)	1(1.0)
≥ 10000 (%)	0	0	0
<i>A. lumbricoides</i>			
0 (%)	27(28.1)	25(26.0)	40(41.7)
1-4999 (%)	45(46.9)	54(56.3)	47(49.0)
5000-49999 (%)	24(25.0)	16(16.7)	9(9.4)
≥ 50000 (%)	0(0.0)	1(1.0)	0

Clinical morbidity indicators

Among successfully followed schoolchildren a significant decrease in the prevalence of anemia (<12g/dl) was observed from 16.9 to 8.3% (reduction of 50.9%). The prevalence of early clinical signs such as abdominal pain, vomiting, diarrhea and blood in stool decreased from 38.9%, 18.9%, 23.1% and 8.7% to 24.7%, 5.6%, 10.0% and 2.3%, respectively (Table 13).

Table 13. Clinical morbidity indicators of *S. mansoni* & STHs of successfully followed school children (5-16 years) for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Morbidity indicators	Prevalence % (95% CI)			
	Baseline (2008)	Year 1 (2009)	Year 2 (2010)	Overall reduction in %
Anemic (Hb<12 g/dl) (1348)	16.9[14.9-18.9]	15.4[13.5-17.4]	8.3[6.8-9.8]	50.9
Abdominal pain (1377)	38.9[36.3-41.5]	34.1[31.6-36.6]	24.7[22.4-27.0]	36.5
Vomiting (1380)	18.9[16.8-21.0]	6.3[5.0-7.6]	5.6[4.4-6.9]	70.4
Diarrhea (1373)	23.1[20.9-25.3]	16.4[14.4-18.3]	10.0[8.5-11.6]	56.7
Blood in stool (1354)	8.7[7.2-10.2]	3.4[2.4-4.4]	2.3[1.5-3.1]	73.6

Ultrasound measurements

Longitudinal ultrasound examination data for 92 adults. At baseline, 5.4% of adults was completed had liver pattern B (early suggestive changes) that increased to 8.7% after two years of treatment. Individuals who had liver patterns C at baseline were 8.7% that decreased to 3.3% after two rounds of treatment. Individuals with image pattern D increased from 1.1% to 3.3% at baseline and year two, respectively. There were no cases of advanced liver fibrosis with patterns E and F (Table 14). A marked dilated portal vein was recorded in 3.6% of individuals that decreased to 0% in 2010 (Table 15).

Table 14. Liver image patterns (IP) and IP-Score of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n=92)

IP	IP-Score	Baseline		Year 1		Year 2	
		Frequency	%	Frequency	%	Frequency	%
A	0	78	84.9	80	87.0	78	84.8
B	1	5	5.4	7	7.6	8	8.7
C	2	8	8.7	4	4.3	3	3.3
D	4	1	1.1	1	1.1	3	3.3
E	6	0	0.0	0	0.0	0	0.0
F	8	0	0.0	0	0.0	0	0.0

Table 15. Prevalence of dilated portal vein diameter (PVD) of *S. mansoni* & STHs of successfully followed adults for 2 years. Longitudinal Monitoring Study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010 (n=83)

PVD	Baseline (2008)	Year 1 (2009)	Year 2 (2010)
Normal	91.6[85.6-97.5]	89.2[0.0-95.8]	89.2[82.5-95.8]
Dilatation	4.8 [0.2-9.4]	8.4[2.5-14.4]	10.8[4.2-17.5]
Marked dilatation	3.6[0.0-7.6]	2.4[0.0-5.7]	0

B. Cross-sectional results

In this section data of baseline, new recruits of year 1 and year 2 follow-up (classes 1 and 6) are shown (Table 1 6). We combined school children in class 5 and class 6 who almost had the same characteristics.

Table 16. Distribution of school children by district. Cross-sectional study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Districts	Baseline (2008) n=1748 (%)	Year 1 (2009) n=1947(%)	Year 2 (2010) n=2,026 (%)
Burera	403 (23.1)	416 (21.4)	423 (20.9)
Gicumbi	341 (19.5)	358 (18.4)	374 (18.5)
Musanze	496 (28.4)	547 (28.1)	473 (23.3)
Nyagatare	238 (13.6)	296 (15.2)	360 (17.8)
Rutsiro	270 (15.5)	330 (17.0)	396 (19.5)

Prevalence and intensity of helminth infections

Among new recruits, a tremendous decrease in prevalence and intensity of *S. mansoni* and hookworm infections was observed (Table 17&19). While a light decrease in prevalence of *A. lumbricoides* infection was recorded, a light increase in prevalence of *T. trichiura* infection was found (Table 17). Intensity decreased for both *T. trichiura* and *A. lumbricoides* (table 19). Improvements were noted for both classes 1 and 6 (Table 18).

Table 17. Prevalence of *S. mansoni* & STHs among school children. Cross-sectional study on intestinal schistosomiasis and STHs in Rwanda, 2008-2010

Parasites	Prevalence (%)			
	Baseline (2008) (n=1748)	Year 1 (2009) (n= 1947)	Year 2 (2010) (n=2026)	Overall reduction in %
<i>S. mansoni</i>	13.6[12.0-15.2]	2.1[1.4-2.7]	2.1[1.5-2.8]	80.1
Hookworm	27.6[25.5-29.7]	6.0[5.0-7.1]	5.4[4.4-6.4]	80.4
<i>T. trichiura</i>	62.0[59.7-64.3]	48.6[46.4-50.8]	53.5[51.3-55.7]	13.7
<i>A. lumbricoides</i>	63.0[60.7-65.3]	57.4[55.2-59.7]	53.6[51.5-55.8]	14.9

Table 18. Prevalence by class of *S. mansoni* & STHs among school children. Cross-sectional study on Intestinal Schistosomiasis and STHs in Rwanda (2008-2010)

Class	Parasites	Prevalence			
		Baseline (2008)	Year 1 (2009)	Year 2 (2010)	Overall reduction in %
Class1 ^a	<i>S. mansoni</i>	7.4[5.9-9.0]	0.6[0.2-1.1]	2.3[1.4-3.1]	68.9
	Hookworm	25.7[23.2-28.2]	6.5[5.0-7.9]	5.4[4.1-6.8]	79.0
	<i>T. trichiura</i>	62.9[60.1-65.7]	53.1[50.2-56.1]	57.1[54.2-60.1]	9.2
	<i>A. lumbricoides</i>	64.6[61.8-67.4]	61.2[58.4-64.1]	57.8[54.8-60.1]	10.5
Class6 ^b	<i>S. mansoni</i>	25.3[21.9-28.8]	4.0[2.6-5.3]	2.0[1.1-2.9]	92.1
	Hookworm	31.3[27.6-35.0]	5.4[3.9-6.9]	5.4[4.0-6.8]	82.7
	<i>T. trichiura</i>	60.3[56.4-64.2]	42.5[39.1-45.9]	49.5[46.3-52.6]	17.9
	<i>A. lumbricoides</i>	59.9[56.0-63.9]	52.2[48.8-55.6]	49.1[45.9-52.2]	18.0

a: Class1 (n=1144: baseline, n=1114: year1, n=1064:year2)

b: Class6 (n=604: baseline, n=833:year1, n=962:year2)

Table 19. Mean intensity (epg) of *S. mansoni* & STHs among school children. Cross-sectional study on Intestinal Schistosomiasis and STHs in Rwanda, 2008-2010

Parasites	Baseline (2008) (n= 1748) Mean (SD)	Year 1 (2009) (n=1947) Mean (SD)	Year 2 (2010) (n=2026) Mean (SD)	Overall reduction in %
<i>S. mansoni</i>	23.6[18.2-29.0]	1.2 [0.2-2.2]	2.9 [1.0-4.8]	87.7
Hookworm	36.5 [29.6-43.4]	4.7 [3.3-6.2]	6.3 [4.0-8.7]	82.7
<i>T. trichiura</i>	470.5 [398.4- 542.7]	179.4 [152.1-206.6]	325.6 [269.6-381.6]	30.8
<i>A. lumbricoides</i>	5612.3 [4921.1-6303.4]	3224.9 [2902.6-3547.1]	4127.9 [3671.8-4583.9]	26.4

IV. DISCUSSION

The results of the study showed that praziquantel and albendazole can have a significant impact on infection and associated morbidity when delivered as part of a large-scale control programme. Mass treatment led to a tremendous decrease in the prevalence and intensity of *S. mansoni* and hookworm infections. In 3 districts, the prevalence of *S. mansoni* infection fell to almost 0%. A significant decrease in the intensity was also observed for *T. trichiura* and *A. lumbricoides* while the improvement in the prevalence was light. A significant decrease in prevalence of anemia and clinical morbidity was also observed. The reduction in prevalence, intensity of infections and clinical morbidity signs was confirmed by both longitudinal cohort follow-up and cross-sectional survey. This demonstrated that the community was also benefiting from control interventions and probably transmission was reduced. One of the factors likely to have contributed to the great impact was the high nationwide MDA coverage (mean coverage over 80%) in school aged children, achieved by the NTD Control Program [32-35].

The required sample sizes have been calculated using EpiSchisto software [25] and based on an expected reduction in mean intensity of 60% (*S. mansoni*) after chemotherapy, to achieve 80% statistical power and a significance level of 5%. The value of 60% was chosen as a conservative estimate of the expected reduction over a 2 year period (2 annual treatments). The reduction in mean intensity reached 84.9% for *S. mansoni* surpassing expected 60%.

Although an overall drop-out rate of 53% was allowed over the course of the monitoring period, throughout the 2 years, the drop-out rate of cohort children was higher (60%), One of the main reasons was that a proportion of the original cohort (older age groups) had naturally progressed to secondary schools over the study period. Another reason for the loss of cohort children was that children moved from their schools to neighboring schools. Certain drop-outs were due to family migration. High drop-out is indeed a relatively common problem in the monitoring activities of many NTD control programmes in sub-Saharan Africa [36].

Impact on anaemia

The current study provided evidence that the MDA decreased anaemia in school children. Over two years with mass anthelmintic treatment targeting school children, anemia decreased by 50.9%. Among school-aged children living in sub-Saharan Africa, several parasites contribute to anaemia — while predominately due to hookworm infection, it may be caused by schistosome and *Plasmodium falciparum* infection [37– 40]. Hookworm and schistosomes cause iron deficiency anaemia due to intestinal blood loss [37, 38] or chronic infection anemia due to chronic immune activation or inflammatory cytokine disturbances. Though malaria decreases Hb concentration through a number of mechanisms, it occurs principally by the destruction of parasitized and non-parasitized red cells and dyserythropoiesis [40]. Most studies in school-aged children have typically found that hookworm contributes more to anaemia than schistosomiasis or malaria [41,42] and we suggest that the decrease in prevalence of anemia in our study is most likely related to the decrease in the prevalence and intensity of either hookworm or both hookworm and schistosome infections.

Since both praziquantel and albendazole were delivered as part of the same health package we could not separate the relative contribution of either drug to the observed decrease in prevalence of anemia. However, recent experience of a school health programme in Tanzania demonstrated that deworming with albendazole and praziquantel decreased the prevalence of anemia and moderate-severe anemia by 26% and 47%, respectively, 15 months after treatment [14]. In Ugandan school children de-worming decreased anemia by 11.8% and 29.8% after one and two years of treatment, respectively [43].

Clinical morbidity

Among school children, the commonest early clinical signs were abdominal pain, vomiting, diarrhea and blood in stool which decreased significantly following treatment. The prevalence of splenomegaly and hepatomegaly was very low at baseline and follow-ups (results not shown).

After two years of treatment, a light reversibility of schistosomal related PPT/F – image pattern C among the followed adults was observed. Several reports have documented partial or complete resolution of PPT/F after anti-schistosomal chemotherapy, most notably among young subjects [44-50]. Moreover, previous studies showed that the effect on prevalence of PPT/F was largely appreciable after a delay of over two years [51-54]. Furthermore, resolution of PPT/F was reported to be low among subjects from areas with intense transmission and high risk of re-infection [55].

Schistosomal PPT/F may only be reversible early in the disease course [56]. Because resolution of lesions is highest in children and young adults, currently recommended school age-targeted [57] praziquantel-based morbidity control could help avert development of schistosomal PPT/F and its consequences.

V. CONCLUSIONS

Large-scale implementation of anthelmintics delivered through the school system can significantly decrease infection and morbidity among Rwandan schoolchildren. The annual anti-schistosomal treatment delivered to high risk community also can decrease infection and its related morbidity among adults.

The integration of deworming programme into the Mother and Child Health Week interventions plays a key role in increasing treatment coverage among school aged population at low cost. However, a key challenge for national control programmes outside sub-Saharan Africa has been to sustain initial morbidity gains over time [58, 59].

The major challenge for the Rwandan NTD Control Programme would be to ensure regular, continued and sustainable large-scale delivery of anthelmintics to achieve and maintain long lasting health benefits. However, the revision of the national MDA Plan for NTD Program should indicate where mass de-worming can be suspended for a certain period because of the current low risk of disease. The follow-up studies should continue for at least three years in order to measure the progress of control interventions.

Since these NTDs are due to the lack of hygiene, the control package would also continue to include education for adequate hygiene and advocacy for availability of safe water and sanitation in schools, public places and communities.

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