Research

Impact of a national helminth control programme on infection and morbidity in Ugandan schoolchildren

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Objective We aimed to assess the health impact of a national control programme targeting schistosomiasis and intestinal nematodes in Uganda, which has provided population-based anthelmintic chemotherapy since 2003.
Methods We conducted longitudinal surveys on infection status, haemoglobin concentration and clinical morbidity in 1871 randomly selected schoolchildren from 37 schools in eight districts across Uganda at three time points — before chemotherapy and after one year and two years of annual mass chemotherapy.
Findings Mass treatment with praziquantel and albendazole led to a significant decrease in the intensity of *Schistosoma mansoni* — 70% (95% confidence interval (CI): 66–73%) after one year and 82% (95% CI: 80–85%) after two years of treatment. Intensity of hookworm infection also decreased (75% and 93%; unadjusted). There was a significant increase in haemoglobin concentration after one (0.135 g/dL (95% CI: 0.126–0.144)) and two years (0.303 g/dL (95% CI: 0.293–0.312)) of treatment, and a significant decrease in signs of early clinical morbidity. The impact of intervention on *S. mansoni* prevalence and intensity was similar to that predicted by mathematical models of the impact of chemotherapy on human schistosomiasis. Improvements in haemoglobin concentration were greatest among children who were anaemic or harbouring heavy *S. mansoni* infection at baseline.
Conclusion Anthelmintic treatment delivered as part of a national helminth control programme can decrease infection and morbidity among schoolchildren and improve haemoglobin concentration.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

In Africa, schistosomiasis occurs predominantly due to two species — *Schistosoma haematobium* that causes urinary schistosomiasis and *S. mansoni* that causes intestinal 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.[1–7] One of the main control methods is treating schoolchildren 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,[8] and many pilot programmes have demonstrated its feasibility, affordability and effectiveness.[9–13] It is unclear, however, whether the observed health benefits of such a control method can be replicated under nationwide programmatic conditions. Earlier large-scale helminth control efforts typically evaluated infection indicators, often prevalence, rather than morbidity indicators,[14,15] but rarely continued due to financial problems and decreased effectiveness. 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] We report the impact of repeated chemotherapy for schistosomiasis in Uganda — the first country to implement a control programme on a national scale — specifically, infection status, haemoglobin concentration and related clinical morbidity.

Methods

The national control programme

S. mansoni occurs throughout much of Uganda, with highest prevalence on the shores of the Albert Nile, Lake Albert and Lake Victoria.[21] *S. haematobium* occurs only in a small focus and is of minor public health significance. Hookworm (predominantly *Necator americanus*) is prevalent throughout the country, whereas *Ascaris lumbricoides* and *Trichuris trichiura* are restricted to southwest Uganda.[22] Uganda implemented the SCI-supported control programme in April 2003 with a pilot phase

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covering > 400 000 schoolchildren and community members (i.e. adults and school-aged children).[23] Initially working in one sub-county in each of the 18 most affected districts, the programme expanded to cover 0.53 million schoolchildren and 0.7 million community members in 23 districts in 2004, and 1.56 million schoolchildren and 1.43 million community members in 2005. In schools, the programme provides mass treatment with praziquantel and albendazole to all children by schoolteachers. Community drug distributors provide treatment to all individuals above 94 cm in height within targeted communities. The annual mass treatment campaign is carried out between April and July every year.

Study design

We conducted three annual longitudinal surveys in a randomly selected sample of children aged 6–14 years from 37 schools in eight districts following annual mass treatment. The districts were selected to represent different transmission settings: Arua, Moyo and Nebbi, along the Albert Nile; Hoima and Masindi along Lake Albert; and Bugiri, Busia and Mayuge along Lake Victoria. Within each district, schools were stratified according to *S. mansoni* infection prevalence: two with high prevalence (⩾ 50%), two with medium prevalence (10–49%) and one with low prevalence (< 10%). In each school, 30 children (15 males and 15 females) were randomly selected from four age groups: six, seven, eight and eleven years, yielding 120 children. Twelve and 24 months later, we re-visited the schools and re-examined the same children if they could be traced. We undertook evaluation surveys every year during February–March in the Lake Victoria area, March–April in Lake Albert area, and October–November in the Albert Nile.

We obtained ethical clearance for our study from the Uganda National Council of Science and Technology and the Ethics Committee of Imperial College, London. We held meetings with the teachers and parents to explain the purpose of the study and obtained informed parental consent before commencing the study. We also obtained assent from the children before samples were collected.

Procedures

We examined faecal samples from each child by the Kato-Katz method. Haemoglobin (Hb) concentration was estimated to an accuracy of 1 g/dL using a portable haemoglobinometer (Hemocue Ltd, Sheffield, England). Clinical examination consisted of liver and spleen palpation whilst children were in a supine position. We assessed liver and spleen changes 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. Experienced technicians conducted ultrasound measurements using a portable ultrasound machine (Aloca® Sonocamera SSD 500) on children in Hoima and Mayuge districts only. We involved the same technicians in each survey to minimize inter-observer variation. We classified liver patterns on the basis of parenchymal fibrosis or other parenchymal pattern according to the World Heath Organization's (WHO) protocol (Niamey-Belo Horizonte).[24] 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.

Data analysis

We analysed the differences between dropouts and children successfully followed up using the Kruskall-Wallis test for means and a χ^2 test for proportions using SAS V8 (SAS Institute Inc., Cary, NC, USA).

We investigated the impact of treatment on health outcomes using multivariate analysis. The analyses sought to overcome the presence of correlated data structures, whereby individual observations are nested within units and superunits that make it likely that individual observations are not independent.[25] In our study this involved children within schools and repeated measurements as data refer to baseline and two years of follow-up. To overcome this problem we performed a multi-level analysis that accounted for the interdependence of observations and partitioned the total variance into different components of variation due to cluster levels in the data,[26] using Mlwin (Multilevel Models Project, Institute of Education, London).

We used linear multi-level models to analyse changes in Hb levels among children in relation to their *S. mansoni* and/or hookworm infection intensity category (at follow-up there were very few children heavily infected with hookworm and therefore the convergence of the fitting algorithm in some of the models required pooling heavy and moderate hookworm intensities into one category), by adjusting for age, sex and anaemia status. Haemoglobin at baseline and every year following treatment was modelled through 3-level models, where level-1 represented the three time points, level-2 the children and level-3 the schools. To take into account the longitudinal data structure, we included two dummy variables corresponding to the second and third years of the study as covariates in the model with the baseline as the reference category. Changes in Hb in relation to their baseline *S. mansoni* and/or hookworm infection intensity category and anaemia status from baseline to second year follow up were modelled through 2-level (children and schools) hierarchical models. Anaemia status was also included in the explanatory part of the model to examine increases in Hb in anaemic and non-anaemic subjects.[27] Models were fitted using maximum likelihood methods using "iterative generalized least squares". Since the negative binomial distribution is a good empirical approximation of egg counts,[28] we attempted initially to fit a 3-level negative binomial model to evaluate factors that affected *S. mansoni* egg counts and to quantify changes over time. However, we encountered numerical problems during estimation and therefore fitted a 3-level "normal model" on the logarithmically transformed *S. mansoni* egg counts ($ln(\chi+1)$), using, due to its stochastic nature, a Markov chain Monte Carlo (MCMC) procedure.[26]

We performed Wald tests to ascertain the statistical significance of the

Table 2. **Health characteristics of Ugandan schoolchildren successfully followed up for two years (2003–05) and monitored as part of an evaluation of a national schistosomiasis control programme**

		2003	2004	2005
Parasitology (n = 1704)				
% infected with *Schistosoma mansoni*		42.4 (40.0–44.7)[a]	26.8 (24.7–28.9)	17.9 (16.1–19.7)
% infected with hookworm		50.9 (48.6–53.3)	24.1 (22.1–26.2)	10.7 (9.3–12.2)
% infected with *Ascaris lumbricoides*		2.8 (2.0–3.6)	1.6 (1.0–2.3)	0.6 (0.3–1.0)
% infected with *Trichuris trichiura*		2.2 (1.5–2.9)	2.5 (1.7–3.2)	1.6 (1.0–2.2)
Mean *S. mansoni* intensity (epg)		219.6 (191.8–247.4)	73.3 (58.6–88.0)	37.4 (27.4–47.5)
Mean hookworm intensity (epg)		309.4 (232.4–386.3)	76.8 (62.9–90.7)	21.9 (13.7–30.1)
Haematology (n = 1852)				
Mean haemoglobin (g/dL)		11.4 (11.3–11.5)	11.7 (11.6–11.7)	12.0 (11.9–12.1)
% anaemic		51.6 (49.3–53.8)	45.5 (43.3–47.8)	36.2 (34.0–38.4)
Ultrasound examination (n = 180)				
% with liver grading B		39.4 (32.3–46.6)	9.4 (5.2–13.7)	1.7 (0.0–3.5)
% with PVD score 0: 'normal'		82.2 (76.6–87.8)	98.0 (95.6–99.9)	96.7 (94.0–99.3)
% with PVD score 4: 'dilatation'		17.8 (12.2–23.4)	2.2 (0.1–4.4)	3.3 (0.7–6.0)
% with PSL score 0: not enlarged		45.6 (38.3–52.8)	40.0 (32.8–47.2)	47.2 (39.9–54.5)
% with PSL score 1: enlarged		41.7 (34.5–48.9)	48.3 (41.0–55.6)	40.0 (32.8–47.2)
% with PSL score 2: much enlarged		12.8 (7.9–17.7)	11.7 (7.0–16.4)	12.8 (7.9–17.7)
Clinical examination (n = 368)				
Liver				
Median (range) in cm	MSL	0.0 (0–12)	0.0 (0–14)	0.0 (0–14)
	MCL	2.0 (0–5)	2.0 (0–5)	0.0 (0–6)
Consistency	% normal	16.1 (12.4–19.9)	70.5 (65.8–75.2)	73.7 (69.3–78.3)
	% soft	20.5 (16.4–24.6)	26.2 (21.7–30.7)	25.4 (20.9–29.9)
	% firm	62.5 (57.6–67.5)	3.2 (1.5–5.1)	0.8 (0.0–1.7)
	% hard	0.8 (0.0–1.7)	0.0	0.0
Tender %		2.0 (0.5–3.4)	1.1 (0.0–2.2)	0.0
Spleen				
Median (range) in cm	MCL (n = 368)	3.0 (0–10)	0.0 (0–11)	0.0 (0–10)
	MAL (n = 367)	0.0 (0–5)	0.0 (0–6)	0.0 (0–5)
Consistency	% normal	26.1 (21.6–30.6)	63.3 (58.4–68.2)	–
	% soft	12.2 (8.9–15.6)	22.6 (18.3–26.8)	–
	% firm	58.4 (53.4–63.5)	14.1 (10.6–17.7)	–
	% hard	3.2 (1.5–5.1)	0.0	

epg, eggs per gram faeces; MAL, mid-axillary lines; MCL, mid-clavicular line; MSL, mid-sternal line; PVD, portal vein diameters; PSL, parasternal line.
[a] 95% confidence intervals in parentheses.

fixed effects (i.e. those coefficients in the model which are treated as fixed values, such as age, sex). For the random effects, we performed likelihood ratio tests for the Hb models and the MCMC Deviance Information Criterion for the egg counts models. All models presented are random intercept models with multiple independent variables.

Mathematical models of expected impact

Within programme districts, we could not implement the programme on a school-by-school basis. This was because, following discussions with national and district stakeholders, it was felt that having non-intervention schools would not bear relevance to the operational reality of a national control programme. Consequently, it was not possible to have a control population that did not receive treatment. We therefore compared observed epidemiological changes in infection and disease and quantitative predictions arising from mathematical models,[29,30] which predicted the impact of chemotherapy. The models, which were implemented using the EPISCHISTO software tool,[31] were successfully validated against data for *S. mansoni* in Kenya[29] and can reliably predict the impact of intervention using data aggregated by district.[32] Pre-intervention survey data on initial mean egg count, M, and estimated negative binomial aggregation parameter, k, were used as input data in the model predictions. We assumed that all children aged 5–15 years were treated and drug efficacy was 95%.[2] The model predicts the mean egg count and prevalence of infection for children aged 5–16 years.

Findings

We enrolled 4351 children from 37 schools, of which 2815 (64.7%) were traced and treated at one year follow-up and 1871 (43.0%) at two year follow-up. The baseline characteristics did not differ significantly among those included in the evaluation one-year post treatment and those lost to follow-up (see Table 1, available at http://www.who.int). However, we found the prevalence and mean intensity of *S. mansoni* to be sig-

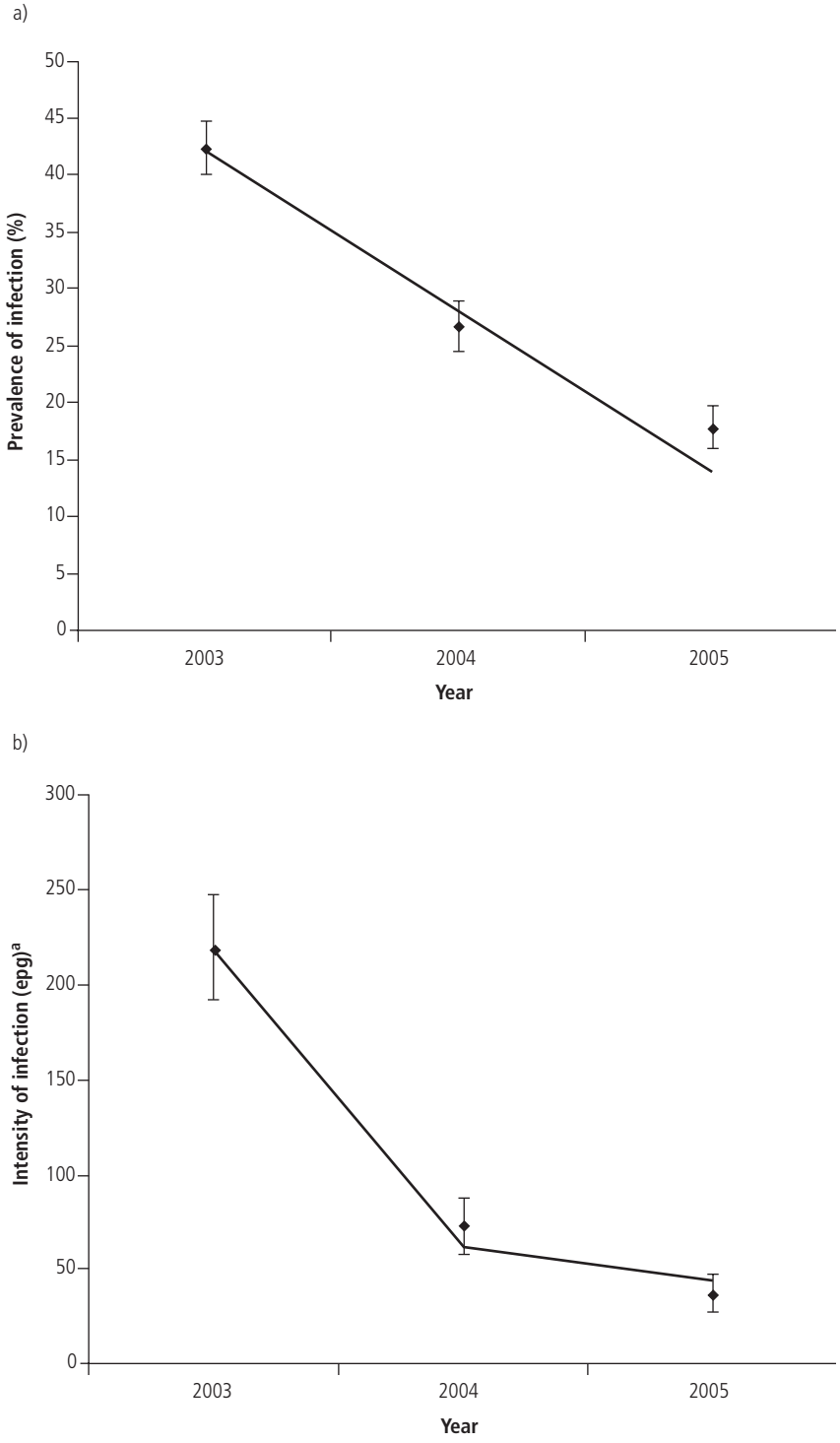
nificantly higher among those children who were lost to follow-up compared to those successfully followed up two years post treatment.

Prevalence and intensity of infection

The health indicators of children surveyed (Table 2) showed that initial prevalence and intensity of *S. mansoni* infection (in 2003) among those followed up for two years was 42.4% and 219.6 eggs per gram faeces (epg), respectively. In 2005, following two rounds of annual treatment, the prevalence and intensity of infection was 17.9% and 37.4 epg, respectively. The function of negative binomial aggregation parameter to mean worm burden was estimated as $k = 0.0278 + 0.0003$. Overall, the mathematical model predicted the changes in the prevalence of infection and mean egg count within the confidence intervals of the observed data, indicating a close correspondence between the observed changes and the expected impact of intervention (Fig. 1) Overall, the prevalence and intensity of hookworm infections decreased from 50.9% and 309.4 epg to 10.7% and 37.4 epg (Table 2). At baseline, the prevalence of *A. lumbricoides* and *T. trichiura* was 2.8% and 2.2%, which decreased to 0.6% and 1.6%, respectively after two years.

The results of the multi-level "normal model" of the change in *S. mansoni* egg counts two years post treatment as well as differences in *S. mansoni* egg counts between different groups of children at baseline (Table 3) showed an overall significant decrease in the *S. mansoni* egg counts by 70% and 82%, one and two years post treatment, respectively ($P < 0.001$). At baseline, children aged six, seven and eight years had significantly lower *S. mansoni* egg counts compared to those that were ⩾ 11 years old after adjusting for sex and anaemia status. Our analysis also showed that anaemic children at baseline had significantly 15% more *S. mansoni* egg counts than non-anaemic children; the between-school variation in *S. mansoni* egg counts was wider than that of between children within schools.

Fig. 1. **Comparisons of observed changes in (a) prevalence of *Schistosoma mansoni* infection and (b) intensity of *S. mansoni* infection as part of a national schistosomiasis control programme in Uganda, 2003–05**



[a] epg, eggs per gram faeces

Figures show expected changes based on predictions arising from a deterministic mathematical model of the expected impact of school-based chemotherapy.

Diamonds show the observed values and solid lines show the model prediction. Errors bars indicate 95% confidence intervals.

Haemoglobin concentration

A significant increase in haemoglobin (Hb) (11.4 to 12.0 g/dL) and a significant decrease in the prevalence of anaemia (51.6 to 36.2%) were observed from 2003 to 2005 (Table 2). The 3-level linear multi-level model of changes in Hb concentration suggests that there was an overall significant increase of 0.135 g/dL in Hb concentration after one treatment and of 0.303 g/dL after two treatments (Table 4). Our analysis also showed that children moderately infected with *S. mansoni* had significantly lower Hb (–0.169 g/dL) compared to uninfected

children at baseline, while heavily infected children had significantly further lower Hb (–0.328 g/dL). Children with moderate or heavy hookworm infection at baseline had significantly lower Hb (–0.493 g/dL) than those uninfected after adjusting for *S. mansoni* intensity, age, sex and anaemia status. We found that while the random effects variance components indicated much of the variance being between children within a school, there was also statistically significant variance between schools. Of the total variability in Hb, 31.6% occurred between children within a school and 5.6% occurred across schools.

The 2-level linear multilevel model of changes in Hb during 2003–05 indicated that this change varied significantly only as a function of baseline heavy *S. mansoni* infection and baseline anaemia status (Table 5). For children heavily infected with *S. mansoni* at baseline, Hb increased by 0.25 g/dL compared to those uninfected with *S. mansoni* at baseline. Additionally, for anaemic children compared to the non-anaemic Hb increased by 1.20 g/dL.

Clinical and ultrasound measurements

We had complete longitudinal clinical examination data for 368 children, aged 6–13 years and complete longitudinal ultrasound data for 180 children, aged 8–13 years. The percentage of children with a firm liver significantly decreased from 62.5% in 2003 to 3.2% in 2004 and 0.8% in 2005 (Table 2). While three (0.8%) children had a hard liver in 2003, by 2004 none had a hard liver. The prevalence of hardened spleens decreased from 3.2% in 2003 to none in 2004; the prevalence of firm spleens also significantly decreased over time. At baseline, 39.4% of children had liver pattern B (early suggestive changes) that significantly decreased to 9.4% in 2004 and 1.7% in 2005 (Table 2). No schoolchild had patterns C to F (indicative of fibrosis). We recorded a dilated portal vein in 17.8% children in 2003, 2.2% in 2004 and 3.3% in 2005. No schoolchild had marked dilation in any of the surveys.

Table 3. **Estimates from 3-level normal hierarchical model for log transformed *Schistosoma mansoni* egg counts before and after treatment among 1682 Ugandan schoolchildren, 2003–05**

	Parameter	Coefficient (95% CIs)	*P* values
Sex[a]			
Female	γ_{01}	-11% (-21% to 0%)	0.049
Age at baseline[b]			
9 years old	γ_{02}	-6.5% (-20% to 9%)	0.387
8 years old	γ_{03}	-21% (-31% to -9%)	< 0.001
7 years old	γ_{04}	-31% (-42% to -18%)	< 0.001
6 years old	γ_{05}	-62% (-70% to -50%)	< 0.001
Effect of follow-up (relative to baseline)			
Follow-up year 1	γ_{06}	-70% (-73% to -66%)	< 0.001
Follow-up year 2	γ_{07}	-82% (-85% to -80%)	< 0.001
Anaemia status at baseline[c]			
Anaemic	γ_{08}	15% (4% to 28%)	0.008
Random effects[d]		**Variance components (SE)**	
Level-3 (between schools) variance $\sigma_v^2 = Var(v_{0k})$		0.468 (0.123)	
Level-2 (between children within a school) variance $\sigma_u^2 = Var(u_{0jk})$		0.100 (0.011)	
Level-1 (measurement occasions within a child) variance $\sigma_\varepsilon^2 = Var(\varepsilon_{0ijk})$		0.516 (0.013)	
Deviance		10980.13	

CI, confidence interval; SE, standard error.
[a] Reference category: male.
[b] Reference category: ⩾ 11 years old.
[c] Reference category non-anaemic children.
[d] Random effects variance components refer to log *Schistosoma mansoni* egg counts.

Discussion

Our results 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 decrease in the prevalence and intensity of *S. mansoni* and hookworm infections, a significant increase in Hb and a decrease in clinical morbidity. Children who were anaemic or harbouring heavy *S. mansoni* infection at baseline recorded the maximum increase in Hb concentration.

Limitations and plausibility

Cluster-randomized trials are the accepted gold standard for the evaluation of health interventions delivered at the community level.[33,34] However, we could not study control cohorts of children because a randomized controlled design, i.e. a probability design,[35] probably would not bear relevance to the operational reality of the national programme and would be politically difficult to implement and ethically inappropriate.[14] Therefore, chance and bias could perhaps contribute to the differences observed compared to randomized controlled trials. Potential biases included the influence of unobserved potential confounders, many which are difficult to measure such as duration of residence.[36] An important unmeasured confounder could be secular changes in the exposure to, as well as potential treatment of, malaria infections, which influence both Hb and splenomegaly.[5] However, our study presented plausible evidence of the impact of the intervention since we observed significant changes in infection and morbidity in randomly sampled children in 37 schools across different transmission settings in the country, after adjusting estimates for age and sex differences and potentially confounding variables. Additionally, there was a close agreement between the observed impact and mathematical model predictions of programme effectiveness. Thus, our analyses provided further validation of the models and showed that the observed impact is similar to that expected on the basis of the known population dynamics of infection and disease as well

as the well-established therapeutic efficacy and health benefits of praziquantel and albendazole.[29,37] That our observed changes were indeed actual and significant is further strengthened by two key observations — first, both the intensity of infection and the rates of anaemia and clinical morbidity decreased after drug treatment; and second, our multi-level analysis indicated that the increase in Hb was highest among children who harboured heavy *S. mansoni* infection at baseline. We believe that as countrywide delivery of interventions with known health benefits are progressively being implemented, it may be increasingly difficult to include control groups in programme evaluation. Such a situation inevitably however, lessens the plausibility of any statement attributing a health impact of the intervention. Clearly there is a trade-off between what is scientifically desirable and what is politically realistic.

Impact on anaemia

Our evaluation provided evidence that the programme increased Hb in schoolchildren. 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.[38–41] Hookworm and schistosomes cause iron deficiency anaemia due to intestinal blood loss[38,39] 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.[41] Most studies in school-aged children have typically found that hookworm contributes more to anaemia than schistosomiasis or malaria[42,43] and we suggest that the increase in Hb 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 increase in Hb. However, recent experience of a school health programme in Tanzania demonstrated that deworming with albendazole and praziquantel decreased the prevalence of anaemia and moderate-severe anaemia by 26% and 47%, respectively, 15 months after treatment.[12]

Table 4. **Estimates from 3-level hierarchical model for haemoglobin concentration before and after treatment among 1789 Ugandan schoolchildren, 2003–05**

	Parameter	Coefficient (SE)	*P* values
Intercept	γ_{00}	11.814 (0.084)	< 0.001
Intensity of *Schistosoma mansoni* infection at baseline[a]			
Light	γ_{01}	−0.081 (0.051)	0.113
Moderate	γ_{02}	−0.169 (0.068)	0.013
Heavy	γ_{03}	−0.328 (0.075)	< 0.001
Intensity of hookworm infection at baseline[a]			
Light	γ_{04}	0.014 (0.040)	0.117
Moderate/Heavy	γ_{05}	−0.493 (0.157)	0.002
Sex[b]			
Female	γ_{06}	0.066 (0.045)	0.144
Age at baseline[d]			
9 years old	γ_{07}	−0.209 (0.051)	< 0.001
8 years old	γ_{08}	−0.316 (0.048)	< 0.001
7 years old	γ_{09}	−0.563 (0.062)	< 0.001
6 years old	γ_{10}	−0.608 (0.082)	< 0.001
Effect of follow-up (relative to baseline)			
Follow-up year 1	γ_{11}	0.135 (0.044)	0.002
Follow-up year 2	γ_{12}	0.303 (0.051)	< 0.001
Random effects		**Variance components[e] (SE)**	
Level-3 (between schools) variance $\sigma_v^2 = Var(v_{0k})$		0.097 (0.028)	
Level-2 (between children within a school) variance $\sigma_u^2 = Var(u_{0jk})$		0.539 (0.031)	
Level-1 (measurement occasions within a child) variance $\sigma_\varepsilon^2 = Var(\varepsilon_{0ijk})$		1.069 (0.025)	
Deviance		17314.6	

SE, standard error.
[a] Reference category: uninfected.
[b] Reference category: male.
[c] Reference category: ⩾ 11 years old.
[d] The total variance is 1.705, the sum of the three variance components [Var(v_{0k}), Var(u_{0jk}) and Var(ε_{0ijk})]. Of the total variance, 0.097/1.705=5.6 percent is situated at the school level while 0.539/1.705=31.61% is situated at the children level.

Clinical morbidity

We did not observe periportal fibrosis among schoolchildren, which was not surprising since studies indicated a time lag of 5–10 years between peak intensity of infection and the occurrence of fibrosis, with greatest prevalence among adults.[7,36] However, 39.4% of children had liver pattern B, indicative of early signs of morbidity. Following treatment, the prevalence of liver pattern B decreased significantly. These findings are in accordance with previous studies among schoolchildren which showed marked reversal in periportal fibrosis,[6,44] and marked and prolonged decrease in the prevalence of splenomegaly and hepatomegaly.[45,46] These reports together with our findings suggests that limiting the effects of infection at an early age can decrease early disease and possibly prevent permanent liver damage. Given our study design, however, other confounding factors, such as malaria and chronic hepatitis B, cannot be completely excluded.

Conclusions

We found that large-scale implementation of anthelmintics delivered through the school system can significantly decrease infection and morbidity among Ugandan schoolchildren. The experience of the Uganda national control programmes confirms that the potential of helminth control, previously demonstrated through pilot programmes,[8,12,13] can be realized at realistic geographical scale in sub-Saharan Africa. However, a key challenge for national control programmes outside sub-Saharan Africa has been to sustain initial morbidity gains over time.[47, 48] We conclude that the major challenge for the Ugandan programme would be to ensure regular, continued and sustainable large-scale delivery of anthelmintics to achieve and maintain long lasting health benefits. ■

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Table 5. **Estimates from 2-level hierarchical model for the change in haemoglobin concentration among 1789 Ugandan schoolchildren, 2003-05**

	Parameter	Coefficient (SE)	*P* values
Intercept	γ_{00}	0.027 (0.107)	0.800
Intensity of *Schistosoma mansoni* infection at baseline[a]			
Light	γ_{01}	−0.072 (0.092)	0.436
Moderate	γ_{02}	−0.032 (0.111)	0.774
Heavy	γ_{03}	0.250 (0.108)	0.020
Intensity of hookworm infection at baseline[a]			
Light	γ_{04}	−0.009 (0.066)	0.896
Moderate/Heavy	γ_{05}	0.245 (0.201)	0.223
Sex[b]			
Female	γ_{06}	−0.021 (0.062)	0.734
Age at baseline[c]			
9 years old	γ_{07}	0.014 (0.087)	0.875
8 years old	γ_{08}	−0.012 (0.088)	0.891
7 years old	γ_{09}	−0.106 (0.090)	0.240
6 years old	γ_{10}	0.027 (0.107)	0.800
Anaemia status at baseline[d]			
Anaemic	γ_{11}	1.204 (0.064)	<0.001
Random effects		**Variance components (SE)**	
Level-2 (between schools) variance $\sigma_u^2 = Var(u_{0jk})$		0.105 (0.034)	
Level-1 (between children within a school) variance $\sigma_\varepsilon^2 = Var(\varepsilon_{0ijk})$		1.675 (0.057)	
Deviance		6051.5	

SE, standard error.
[a] Reference category: uninfected.
[b] Reference category: male.
[c] Reference category: ⩾ 11 years old.
[d] Reference category: non-anaemic children.

Résumé

Impact d'un programme national de lutte contre les helminthes sur les taux d'infestation et de morbidité dues à ces parasites chez des écoliers ougandais

Objectif Nous nous sommes efforcés d'évaluer l'impact sur la santé d'un programme national de lutte contre la schistosomiase et contre les nématodes intestinaux en Ouganda, qui dispense une chimiothérapie antihelminthique en population depuis 2003.

Méthodes Nous avons réalisé une enquête longitudinale sur le statut infectieux, le taux d'hémoglobine et la morbidité clinique chez 1871 écoliers, choisis au hasard parmi 37 écoles relevant de 8 districts, répartis à travers l'Ouganda, en mesurant ces paramètres à trois moments différents : avant chimiothérapie, un an après une chimiothérapie massive annuelle et deux ans après ce traitement.

Résultats Le traitement massif par le praziquantel et l'albendazole a entraîné une diminution importante de l'intensité de l'infestation par *Schistosoma Mansoni* : 70 % [intervalle de confiance à 95 % (IC) = 66 – 73 %] après un an et 82 % [intervalle de confiance à 95 % (IC) = 80 – 85 %] après deux ans de traitement. L'intensité de l'infestation par les ankylostomes a aussi baissé [de 75 % et de 93 % respectivement (valeurs non ajustées)]. On a relevé une hausse importante du taux d'hémoglobine après un an [0,135 g/dl (IC à 95 % = 0,126 – 0,144)] et deux ans [0,303 g/dl (IC à 95 % = 0,293 – 0,312)] de traitement et une diminution notable des signes précoces de morbidité clinique. L'impact de l'intervention sur les concentrations de *S. mansoni* a été similaire à celui prévu par des modèles de l'impact de la chimiothérapie sur la schistosomiase humaine. C'est chez les enfants anémiques ou fortement infestés par *S. mansoni* au départ que l'on a relevé les plus fortes améliorations du taux d'hémoglobine.

Conclusion Le traitement antihelminthique délivré dans le cadre d'un programme national de lutte contre les helminthes est en mesure de faire baisser les taux d'infestation et de morbidité chez les écoliers et d'améliorer leur taux d'hémoglobine.

Resumen

Impacto de un programa nacional de lucha antihelmíntica en la intensidad de la infección y la morbilidad entre escolares de Uganda

Objetivo Decidimos evaluar el impacto sanitario de un programa nacional de control centrado en la esquistosomiasis y las infecciones intestinales por nematodos en Uganda, país que viene proporcionando tratamiento antihelmíntico a nivel poblacional desde 2003.

Métodos Realizamos estudios longitudinales sobre la intensidad de la infección, la concentración de hemoglobina y la morbilidad clínica en 1871 escolares seleccionados al azar en 37 escuelas de ocho distritos de Uganda en tres momentos: antes del tratamiento, y al cabo de uno y dos años de la antibioticoterapia masiva anual.

Resultados El tratamiento masivo con prazicuantel y albendazol se tradujo en una importante disminución de la intensidad de la infección por *Schistosoma mansoni*: 70% (intervalo de confianza (IC) del 95%: 66%–73%) al cabo de un año, y 82% (IC95%: 80%–85%) a los dos años de tratamiento. La intensidad de la anquilostomiasis también disminuyó (75% y 93%; cifras no ajustadas). Se produjo un aumento considerable de la concentración de hemoglobina al cabo de un año (0,135 g/dl (IC95%: 0,126–0,144)) y a los dos años (0,303 g/dl (IC95%: 0,293–0,312)) de tratamiento, así como una disminución significativa de los signos de morbilidad clínica precoz. El impacto de la intervención en la prevalencia y la intensidad de la infección por *S. mansoni* fue similar al proyectado por los modelos matemáticos del impacto de la antibioticoterapia en la esquistosomiasis humana. La concentración de hemoglobina mejoró sobre todo entre los niños que estaban anémicos o que presentaban signos serios de infección por *S. mansoni* al comienzo del estudio.

Conclusión El tratamiento antihelmíntico suministrado en el marco de un programa nacional de control de helmintos permite reducir la intensidad de la infección y la morbilidad entre los escolares y mejorar la concentración de hemoglobina.

ملخص

تأثير برنامج وطني لمكافحة الديدان الطفيلية على العدوى والمراضة لدى تلاميذ المدارس في أوغندا

الهدف: استهدفت هذه الدراسة تقييم الأثر الصحي لبرنامج وطني لمكافحة داء البلهارسيات والديدان الممسودة المعوية في أوغندا، حيث قدِّم هذا البرنامج معالجة كيميائية طاردة للديدان للسكان منذ عام 2003.

الطريقة: أجرينا في إطار هذه الدراسة مسوحات طولية لمعرفة وضع العدوى، وتركيز الهيموغلوبين، والمراضة السريرية لدى 1871 من تلاميذ المدارس الذين تم انتقاؤهم عشوائياً من 37 مدرسة في ثماني مناطق في أوغندا وفي ثلاثة أوقات مختلفة: قبل المعالجة الكيميائية، وبعد سنة من المعالجة الكيميائية الجموعية السنوية، وبعد سنتين من هذه المعالجة.

الموجودات: أدت المعالجة الجموعية بالبرازيكوانتيل والبيندازول إلى خفض كبير في كثافة البلهارسية المنسونية، إذ حققت انخفاضاً مقداره 70% (عند فاصلة الثقة 95% حيث تراوح الانخفاض من 66 إلى 73%) بعد سنة من المعالجة، وانخفاضاً مقداره 82% (عند فاصلة الثقة 95%، حيث تراوح الانخفاض من 80 إلى 85%) بعد سنتين من المعالجة. وانخفضت أيضاً شدة العدوى بالدودة الشِّصِّية (الأنكلستوما) بنسبة 75% بعد سنة وبنسبة 93% بعد سنتين (غير مصحَّحة). ولوحظت زيادة مهمة إحصائياً في تركيز الهيموغلوبين بعد سنة من المعالجة (مقدارها 0.135 غ/ديسي لتر) (عند فاصلة الثقة 95%: حيث تراوحت من 0.126 إلى 0.144)، وبعد سنتين من المعالجة (مقدارها 0.303 غ/ديسي لتر) (عند فاصلة الثقة 95%: حيث تراوحت من 0.293 إلى 0.312)، كما لوحظ انخفاض مهم إحصائياً في العلامات الدالة على المراضة السريرية المبكرة. وبيَّنت الدراسة أن أثر التدخل العلاجي على انتشار البلهارسية المنسونية وشدته مماثل لتأثير المعالجة الكيميائية على البلهارسية البشرية، وفقاً لتوقعات النماذج الرياضية. وكان التحسن في تركيز الهيموغلوبين أعلى ما يكون لدى الأطفال المصابين بفقر الدم أو المصابين بعدوى شديدة بالبلهارسية المنسونية في الأساس.

الاستنتاج: إن المعالجة الطاردة للديدان، المقدمة في إطار برنامج وطني لمكافحة الديدان الطفيلية تحد من العدوى والمراضة بين تلاميذ المدارس، وتحسِّن تركيز هيموغلوبين الدم.

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Table 1. **Baseline characteristics of Uganda schoolchildren followed up for one year and not followed up, and of children followed up for two years (2003–05) and not followed up**

	Followed for one year	Not followed up	*P* value	Followed for two years	Not followed up	*P* value
Mean (range) age	8.1 (*n* = 2815)	8.1 (*n* = 1536)	0.615	8.0 (*n* = 1871)	8.1 (*n* = 2480)	0.216
% male	51.0 (*n* = 2004)	50.2 (*n* = 705)	0.726	55.1 (*n* = 1867)	50.5 (*n* = 844)	0.804
% infected with *S. mansoni*	44.3 (*n* = 2719)	46.7 (*n* = 1470)	0.135	42.0 (*n* = 1806)	47.5 (*n* = 2383)	< 0.001
% infected with hookworm	51.8 (*n* = 2718)	51.4 (*n* = 1470)	0.771	51.0 (*n* = 1806)	52.2 (*n* = 2382)	0.454
Mean (SD) *Schistosoma mansoni* intensity (epg)	245.1 (619.6)	322.8 (809.7)	0.056	217.3 (579.3)	314.1 (765.7)	< 0.001
Mean (SD) hookworm intensity (epg)	277.5 (917.9)	299.9 (1367.9)	0.944	302.9 (1577.18)	283.8 (877.3)	0.169
% anaemic[a]	49.9 (*n* = 2785)	49.2 (*n* = 1486)	0.630	51.5 (*n* = 1857)	48.3 (*n* = 2414)	0.140
Mean (SD) haemoglobin (g/dL)	11.4 (1.4)	11.4 (1.4)	0.872	11.4 (1. 4)	11.4 (1.4)	0.184
% with liver grading 'B'	38.6 (*n* = 298)	29.7 (*n* = 263)	0.083	39.4 (*n* = 180)	32.02 (*n* = 381)	0.022
% with abnormal PVD score	15.8 (*n* = 298)	16.73 (*n* = 263)	0.759	17.8 (*n* = 180)	15.5 (*n* = 381)	0.492
% with abnormal PSL score	57.1 (*n* = 298)	59.7 (*n* = 263)	0.526	54.5 (*n* = 180)	60.1 (*n* = 381)	0.204
% with abnormal liver consistency	83.4 (*n* = 375)	80.09 (*n* = 523)	0.194	83.9 (*n* = 368)	79.85 (*n* = 660)	0.113
% with abnormal spleen consistency	73.8 (*n* = 367)	74.6 (*n* = 650)	0.824	NA	NA	NA

epg, eggs per gram faeces; SD,standard deviation; NA, Data not collected; PSL, parasternal line; PVD, portal vein diameters.

[a] Anaemia was defined for all tables displayed (according to WHO guidelines), as Hb less than 11.5 g/dL for children from 5 to 11 years old and for children between 12 and 14 years old as Hb less than 12.0 g/dL.