

UNIVERSITY OF WESTMINSTER



WestminsterResearch

<http://www.wmin.ac.uk/westminsterresearch>

Evaluation of efficacy of school-based anthelmintic treatments against anaemia in children in the United Republic of Tanzania.

Helen L. Guyatt¹

Simon Brooker¹

Charles M. Kihamia²

Andrew Hall*^{1,3}

Donald A. P. Bundy^{1,3}

* Andrew Hall now works in the School of Integrated Health, University of Westminster

¹ Wellcome Trust Centre for the Epidemiology of Infectious Disease, Department of Zoology, University of Oxford, England

² Tanzania Partnership for Child Development, Ocean Road Hospital, Dar es Salaam, United Republic of Tanzania.

³ Scientific Coordinating Centre of the Partnership for Child Development, University of Oxford, England.

This is an electronic version of an article published in Bulletin of the World Health Organization, 79 (8). pp. 695-703, August 2001. Bulletin of the World Health Organization is available online at:

[http://www.who.int/entity/bulletin/archives/79\(8\)695.pdf](http://www.who.int/entity/bulletin/archives/79(8)695.pdf)

The WestminsterResearch online digital archive at the University of Westminster aims to make the research output of the University available to a wider audience. Copyright and Moral Rights remain with the authors and/or copyright owners. Users are permitted to download and/or print one copy for non-commercial private study or research. Further distribution and any use of material from within this archive for profit-making enterprises or for commercial gain is strictly forbidden.

Whilst further distribution of specific materials from within this archive is forbidden, you may freely distribute the URL of WestminsterResearch. (<http://www.wmin.ac.uk/westminsterresearch>).

In case of abuse or copyright appearing without permission e-mail wattsn@wmin.ac.uk.

Evaluation of efficacy of school-based anthelmintic treatments against anaemia in children in the United Republic of Tanzania

Helen L. Guyatt,¹ Simon Brooker,¹ Charles M. Kihamia,² Andrew Hall,^{1, 3} & Donald A.P. Bundy^{1, 3}

Objective To determine the impact of deworming on anaemia as part of a large-scale school-based anthelmintic treatment programme in the Tanga Region of the United Republic of Tanzania.

Methods Both the reduction in the prevalence of anaemia and the cost per case prevented were taken into consideration. Cross-sectional studies involved parasitological examination and anaemia evaluation before and at 10 months and 15 months after schoolchildren were dewormed.

Findings Baseline studies indicated that the prevalence of anaemia (haemoglobin < 110 g/l) was high (54%) among schoolchildren, particularly those with high intensities of hookworm and schistosomiasis. Attributable fraction analysis suggested that hookworm and schistosomiasis were responsible for 6% and 15% of anaemia cases, respectively. Fifteen months after deworming with albendazole and praziquantel the prevalence of anaemia was reduced by a quarter and that of moderate-to-severe anaemia (haemoglobin <90 g/l) was reduced by nearly a half. The delivery of these anthelmintics through the school system was achieved at the relatively low cost of US\$ 1 per treated child. The cost per anaemia case prevented by deworming schoolchildren was in the range US\$ 6–8, depending on the haemoglobin threshold used.

Conclusions The results suggested that deworming programmes should be included in public health strategies for the control of anaemia in schoolchildren where there are high prevalences of hookworm and schistosomiasis.

Keywords Anthelmintics/therapeutic use; Albendazole/therapeutic use/administration and dosage; Praziquantel/therapeutic use/administration and dosage; Anemia/parasitology; Hookworm infections/drug therapy/complications; Schistosomiasis/drug therapy/complications; Child; School health services; Cross-sectional studies; Logistic models; Regression analysis; United Republic of Tanzania (*source: MeSH*).

Mots clés Antihelminthiques/usage thérapeutique; Albendazole/usage thérapeutique/administration et posologie; Praziquantel/usage thérapeutique/administration et posologie; Anémie/parasitologie; Ankylostomiase/chimiothérapie/complication; Schistosomiase/chimiothérapie/complication; Enfant; Service hygiène scolaire; Etude section efficace; Modèle logistique; Analyse régression; République-Unie de Tanzanie (*source: INSERM*).

Palabras clave Antihelmínticos/uso terapéutico; Albendazol/uso terapéutico/administración y dosificación; Praziquantel/uso terapéutico/administración y dosificación; Anemia/parasitología; Infecciones por uncinaria/quimioterapia/complicaciones; Esquistosomiasis/quimioterapia/complicaciones; Niño; Servicios de salud escolar; Estudios transversales; Modelos logísticos; Análisis de regresión; República Unida de Tanzania (*fuentes: BIREME*).

Bulletin of the World Health Organization, 2001, **79**: 695–703.

Voir page 701 le résumé en français. En la página 702 figura un resumen en español.

Introduction

Iron-deficiency anaemia can affect the mental and motor development of children (1, 2) with potential long-term consequences for productivity and wage-earning potential in adulthood (3). Parasitic worms contribute to iron-deficiency anaemia among children in sub-Saharan Africa, the predominant species being the hookworms *Ancylostoma duodenale* and *Necator americanus* (which inhabit the gut) and *Schistosoma* spp. (which inhabit the blood vessels surrounding the gut and bladder). The amount of

¹ Wellcome Trust Centre for the Epidemiology of Infectious Disease, Department of Zoology, University of Oxford, South Parks Road, Oxford, OX1 3FY, England. Correspondence should be addressed to Dr Guyatt (HGuyatt@wtnairobi.mimcom.net).

² Tanzania Partnership for Child Development, Ocean Road Hospital, PO Box 9383, Dar es Salaam, United Republic of Tanzania.

³ Scientific Coordinating Centre of the Partnership for Child Development, University of Oxford, South Parks Road, Oxford OX1 3FY, England.

blood loss resulting from iron-deficiency anaemia depends on the intensity of infection (4, 5), the dietary intake of iron (6, 7), and the presence of other parasitic diseases that can cause blood loss or haemolysis, such as malaria and *Trichuris trichiura* infection (8–10). School-age children are particularly vulnerable to iron-deficiency anaemia exacerbated by parasitic infection because they typically harbour the heaviest worm loads in communities (11). A recent analysis of the association between hookworm and anaemia in school-age children in Zanzibar suggested that 25% of all anaemia cases, 35% of iron-deficiency anaemia cases, and 73% of severe anaemia cases could be attributed to hookworm infection (9). Hookworm has been shown to contribute more than schistosomiasis or malaria to iron-deficiency anaemia in school-age children (5, 12).

Infections with intestinal worms and *Schistosoma* spp. are widespread and common among school-age children in United Republic of Tanzania. The Tanzania Partnership for Child Development (*Ushirikiano wa Kummwendeleza Mtoto Tanzania*) was established to undertake operations research on the delivery of mass treatment with anthelmintics to children through the school system. WHO recommends the mass treatment of all children with anthelmintic drugs when the prevalence of infection with intestinal worms or schistosomiasis is greater than 50% (13). A school health package, comprising albendazole treatment against intestinal worms, praziquantel treatment against *Schistosoma haematobium*, and health education aimed at preventing reinfection, was issued for children in primary schools in three districts of Tanga Region. Treatment with the anthelmintics, delivered through the education system at a cost of about US\$ 1 per child (14) to schools where both were needed, led to significantly improved growth and haemoglobin concentrations. We report the associations between hookworm, *S. haematobium*, and anaemia in this school population and attempt to evaluate the impact and cost-effectiveness of the first round of anthelmintic treatments against anaemia.

Methods

Study population and survey design

The programme of the Tanzania Partnership for Child Development is being implemented in all 352 government primary schools in Tanga, Muheza, and Korogwe Districts of Tanga Region on the country's north-east coast. The process of interpreting and evaluating the programme is described below (see also Fig. 1).

1. A survey of intestinal parasitic infection and blood in urine was undertaken in a small sample of schools throughout the region in May 1995 using the Kato–Katz method of stool examination (15). The prevalence of infection with intestinal worms was high enough to warrant mass treatment with

albendazole in all schools, and there were foci of urinary schistosomiasis.

2. A questionnaire survey of self-reported urinary schistosomiasis, called *kichocho* in Kiswahili, was undertaken in August 1995 in all districts of Tanga Region to identify schools in which the prevalence of infection was estimated to be greater than 50% and thus warranted mass treatment (16). *Schistosoma haematobium* was the predominant species of schistosome in Tanga Region. *S. mansoni* has only been found in small foci and at a low prevalence (17).
3. A baseline survey was undertaken in March and April 1996 in 20 randomly selected schools. Schools were eligible for selection if the prevalence of self-reported infection with *S. haematobium* was estimated to be more than 50%, if there were more than 150 enrolled pupils, and if there were likely to be enough children to be studied in two age groups. Samples of equal numbers of male and female children in the age groups 8–9 years and 12–14 years were randomly selected for study in each school. A fresh urine specimen was collected from each child between 10:00 and 14:00. *S. haematobium* eggs were collected by filtering 10 ml of each urine sample through a polycarbonate membrane, and their concentration was expressed as eggs per 10 ml urine. A fresh faecal sample was examined by the Kato–Katz technique and the concentration of eggs per g faeces for each nematode species was determined. Since the eggs of the two hookworm species cannot be distinguished apart, the term hookworm is used for both. A venous blood sample was collected in a 50% subsample of children and the haemoglobin concentration was estimated using a portable haemoglobinometer (HemoCue, Sheffield, England). Height was measured with a stadiometer to an accuracy of 0.1 cm and weight was measured to an accuracy of 0.1 kg by means of electronic scales. A total of 466 children were examined for both parasites and their haemoglobin level.
4. In April 1996 all children in all schools in the three intervention districts received a single dose of 400 mg albendazole against intestinal helminths. Furthermore, all the children in the schools where the questionnaire survey had indicated the prevalence of *S. haematobium* to be above 50% received a single dose of praziquantel at a target dose of 40 mg/kg, determined on the basis of height. With a view to helping teachers to inform children about parasitic worms and nutrition, all schools were provided with flip-charts designed by the Tanzania Partnership for Child Development.
5. About six weeks after treatment, stool and urine specimens were collected from 413 children in 10 schools originally surveyed to check that the prevalence of infection with intestinal worms and *S. haematobium* was significantly lower than during the baseline survey. The children surveyed were not necessarily the same as those in the baseline survey.

6. Ten months after treatment, stool and urine specimens and blood samples were obtained in 10 schools from 429 children who were originally included in the baseline survey.
7. In July 1997, some 15 months after the treatments had been given, a follow-up survey was undertaken in 20 randomly selected schools and in randomly selected children. Care was taken to verify that all children examined in the intervention schools had been treated with both albendazole and praziquantel. For each child, a urine specimen was examined quantitatively for *S. haematobium* eggs, a stool sample was examined by the Kato-Katz method, and a fingerprick blood sample was obtained for the determination of the haemoglobin concentration. A total of 1121 children were examined for both parasites and haemoglobin level. Whereas the use of capillary blood can lead to the misclassification of anaemia status in individuals, only very small biases result in respect of the prevalence of anaemia in a population or sample of individuals (18).

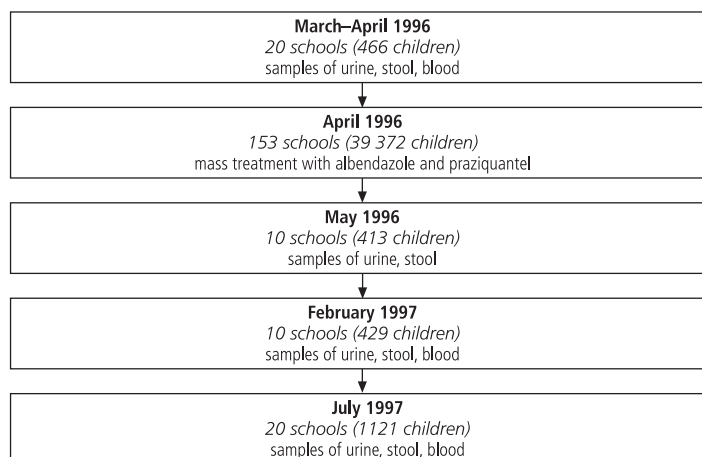
Data analysis

Anaemia is defined as a haemoglobin level in blood of <110 g/l; the thresholds for moderate-to-severe anaemia and severe anaemia are 90 g/l and 70 g/l, respectively (19). In the present study the recently published age-specific definitions of anaemia (20) were also applied: a haemoglobin concentration of <15 g/l for children aged 5–11 years and of <120 g/l for children aged 12–14 years. Height-for-age z-scores were calculated using the NCHS reference values. Children with z-scores >2 standard deviations below the NCHS median height-for-age were classified as stunted. Differences in the prevalence of infection or anaemia between groups subdivided by age or sex were assessed using χ^2 tests.

Logistic regression models were developed to assess the effect on being anaemic or not of the following explanatory variables: age; sex; being stunted or not; the presence or absence of infection with hookworm, *Ascaris lumbricoides*, *T. trichiura* or *S. haematobium*; and different classes of intensity of infection with hookworm and *S. haematobium*. The presence of interactions between the main effects and confounding effects was determined, and variables were removed in a stepwise manner. Adjusted odds ratios were calculated (21). The statistical analyses were performed using SPSS (Release 7.0, SPSS, Chicago, IL, 1989–1995).

Attributable fraction analysis provides an estimate of the proportion of cases of anaemia that can be attributed to a given parasitic infection for subjects who are infected (the infected attributable fraction) and for all subjects whether infected or not (the population attributable fraction), both of which were calculated using previously described methods (22). The analysis was performed by comparing uninfected and infected individuals, for hookworm and *S. haematobium* separately, and for uninfected or lightly infected children against heavily infected

Fig. 1. Summary of cross-sectional surveys used to evaluate anthelmintic treatment of primary-school children in Tanga, Muheza and Korogwe Districts, Tanga Region, United Republic of Tanzania



WHO 01.143

individuals, using different thresholds: > 750 eggs/g faeces, > 1250 eggs/g, and > 2500 eggs/g for hookworm; and > 250 eggs/10ml of urine and more than 500 eggs/10 ml for *S. haematobium*. Variance and 95% confidence intervals (CI) for the infected attributable fraction and the population attributable fraction were calculated using a previously described method (23).

Since the logistic regression showed that age was an important predictor of anaemia, estimates weighted by age group were also calculated. A weighted sum technique (24) was used to obtain estimates of the prevalence ratio, the infected attributable fraction, and the population attributable fraction. This approach provided age-specific estimates weighted in proportion to the number of anaemia cases in each stratum, in accordance with the formula:

$$AFI_w = \frac{\sum_j N_{cj} AFI_j}{\sum_j N_{cj}}$$

where AFI is the infected attributable fraction and N_{cj} is the frequency of anaemia cases in each stratum.

The weighted population attributable fraction was provided by:

$$AFP_w = \frac{\sum_j N_{cj} AFP_j}{\sum_j N_{cj}}$$

A previously described method was used to calculate the 95% CI (25).

Cost-effectiveness analysis

The cost per child treated was US\$ 0.23 for albendazole and US\$ 0.79 for praziquantel, i.e. US\$ 1.02 per child treated with both drugs (14). This represents the price of the drug and all delivery costs including those of distribution, training, and prior screening for *S. haematobium*. A detailed break-

down of the cost calculations has been given previously (14). The total cost per child of US\$ 1.02 comprises US\$ 0.58 for praziquantel (Cost, Insurance and Freight, CIF), US\$ 0.20 for albendazole (CIF), US\$ 0.10 for training, US\$ 0.06 for drug distribution, US\$ 0.05 for the schistosomiasis questionnaire and US\$ 0.03 for drug clearance, movement, and repackaging. Albendazole was given to children in all 352 schools in the three districts, whereas praziquantel was only given to children in 153 schools where the prevalence of infection was estimated to be greater than 50%. A total of 39 372 children were treated with both praziquantel and albendazole at a cost of US \$ 40 159.44.

The effectiveness of treatment with both drugs was assessed as the number of anaemia cases prevented over 15 months, the approximate period between treatment and the second post-treatment survey. This was calculated as the difference between the proportions of children with anaemia at the baseline survey and the second survey multiplied by the number of children treated. The cost per anaemia case prevented was calculated for a range of thresholds (haemoglobin <70 g/l to <120 g/l).

Comparison districts

In the cost-effectiveness analysis it was assumed that the reduction in anaemia was caused solely by the intervention. This was supported by data from the three neighbouring districts of Handeni, Pangani and Lushoto, where anthelmintics were not given. In this comparison area the arithmetic mean haemoglobin level and the prevalence of anaemia (haemoglobin <110 g/l) remained unchanged over the evaluation period: 107.8 g/l and 55% anaemic at baseline ($n = 443$) compared with 108.5 g/l and 51% anaemic ($n = 1024$) at follow-up 15 months later. Since the evaluations in the comparison and intervention districts were made within a few weeks of each other, external factors such as seasonal changes in food availability were unlikely to have had a confounding effect. The data from these areas were also comparable in terms of malaria transmission: the inclusion criterion of schistosomiasis prevalence exceeding 50% meant that all highland schools were excluded.

Results

Baseline parasitology and anaemia

The baseline survey of 466 children in Muheza, Tanga, and Korogwe districts suggested that 87% of children aged 8–14 years were infected with at least one of the helminth species examined (intestinal nematodes and *S. haematobium*). The most common parasites were hookworms (61%) and *S. haematobium* (59%) and many children (37%) were infected with both of these; in only 17% of children were both of these parasites absent. In approximately 20% of the children there were more than 750 hookworm eggs/g faeces and more than 250 *S. haematobium* eggs/10ml

of urine. *A. lumbricoides* and *T. trichiura* were present at low levels in 21% and 14% of children, respectively.

Both the prevalence of *S. haematobium* infection and heavy infection (egg counts >250/10 ml) were significantly higher in children aged 11–14 years than in those aged 8–10 years (63% vs. 50% ($P < 0.005$) and 21 % vs. 9% ($P < 0.01$), respectively). In contrast, the prevalence of hookworm infection or heavy infection did not differ significantly between the age groups.

A total of 54% of the children had haemoglobin values < 110 g/l, and 10% had moderate-to-severe anaemia (< 90 g/l). Severe anaemia (<70 g/l) was identified in fewer than 2% of the children. Over two-thirds of the children were stunted and the prevalence of anaemia was slightly higher in this group (56% vs. 50%, $P = 0.20$). Anaemia was strongly associated with the intensity of infection with hookworm and *S. haematobium* (Table 1). Logistic regression analysis revealed that age group, stunting and the intensity of infection with hookworm and *S. haematobium* were the important predictive variables for anaemia (haemoglobin < 110 g/l) (Table 2). Infection with *A. lumbricoides* or *T. trichiura* was not related to anaemia.

Table 3 summarizes the attributable fraction analysis for the association between helminth infection and anaemia. The unweighted analysis suggests that 6% of anaemia cases (<110 g/l haemoglobin) could be attributed to hookworm. The attributable fraction was 0.16 for children aged 8–10 years and 0.05 for those aged 11–14 years. The unweighted population-attributable fraction for *S. haematobium* was more than twice that for hookworm at 15%. The estimated risk of anaemia associated with *S. haematobium* was 0.9 among children aged 8–10 years and 0.12 among those aged 11–14 years. The differences in the attributable fractions of the two infections by age was caused by the differences in the prevalence of infection and anaemia between the age groups. In the case of *S. haematobium*, the prevalence was higher among older children, whereas for hookworm infection there was no difference between the age groups. The prevalence of anaemia, in contrast, was higher among younger children. As a result, the weighted attributable fraction estimates (both at 10%) were higher than the crude estimates for hookworm infection and lower for *S. haematobium* (Table 3). The proportions of moderate-to-severe anaemia cases (haemoglobin < 90 g/l) attributable to hookworm and schistosomiasis were higher at 14% and 25%, respectively.

Impact of treatment

Fig. 2 illustrates the changes in hookworm and *S. haematobium* infection at intervals of 6 weeks, 10 months, and 15 months after the baseline survey — treatment having been administered just after this survey. At 6 weeks the prevalences of hookworm and *S. haematobium* had been reduced by 82% and 94%, respectively (Fig. 2). The prevalence of heavy

infection was reduced by more than 97%, and the mean intensities of infection of hookworm and *S. haematobium* fell from 738 eggs/g to 18 eggs/g and from 194 eggs/10 ml to 2 eggs/10 ml, respectively. The surveys at 10 months and 15 months after treatment suggested a steady increase in the prevalence of infection, particularly that of hookworm. At 15 months the prevalence of hookworm (49%) had increased to almost the pretreatment value, whereas that of *S. haematobium* (24%) was less than half the pretreatment value. The prevalence of heavy infection for both species remained below 50% of the pretreatment level (Fig. 2).

The changes in anaemia after treatment are summarized in Table 4. An improvement in anaemic status, as defined by mean haemoglobin and a haemoglobin level <110 g/l, only became evident 15 months after treatment, when the administration of albendazole and praziquantel appeared to have reduced the prevalence of anaemia by a quarter and the prevalence of moderate-to-severe anaemia by almost 50%. The difference in the prevalence of anaemia between the baseline survey and follow-up 15 months later was used to estimate the proportion of anaemia cases prevented. Among the 39 372 children treated with both albendazole and praziquantel, 281 cases of severe anaemia (haemoglobin < 70 g/l) were prevented; for moderate-to-severe anaemia (< 90 g/l) and anaemia (<110 g/l) the numbers of cases prevented were 1445 and 5661, respectively. The cost for preventing these cases was US\$ 40 150.44, the total cost of mass treatment with albendazole and praziquantel. The costs per anaemia case prevented are illustrated in Fig. 3 for a range of haemoglobin cut-offs (70–120 g/l at intervals of 5 g/l). The relationship was markedly non-linear: the cost per anaemia case prevented was high and variable at low haemoglobin thresholds but relatively stable (<US\$ 10) at thresholds above 100 g/l. Using a haemoglobin threshold of <110 g/l for anaemia corresponds to a cost per case prevented of US\$ 7.23, increasing to US\$ 145.71 for a case of severe anaemia prevented (< 70g/l).

Discussion

The present study indicates that infection with hookworm and schistosomiasis could be responsible for 6% and 15%, respectively, of anaemia cases in school-age children (10% for both if weighted by age) in an area where the prevalence of both infections was estimated to be greater than 50%. If anthelmintic drugs were to reduce infection by 100%, concurrent relative reductions in the prevalence of anaemia would be predicted. In fact, treatment with albendazole and praziquantel reduced the prevalence of anaemia by 26% up to 15 months after deworming. This was achieved without iron supplementation. Combining these data with those on the costs of delivery and treatment suggests that the cost per anaemia case prevented over 15 months could be US\$ 7.43 if the school system is used to deliver

Table 1. Association between anaemia and intensity of helminth infection, Tanga Region, United Republic of Tanzania, March–April 1996

Helminth infection	n	% Prevalence of anaemia (<110g/l)	% Prevalence of moderate-to-severe anaemia (<110g/l)	Mean haemoglobin level (mg/l)
Hookworm (eggs/g)				
Uninfected	172	50.6	6.4	108.8 (13.4) ^a
>0 eggs/g	294	56.1	11.6	106.5 (15.1)
>750 eggs/g	108	63.0	13.9	103.9 (14.9)
>1250 eggs/g	62	59.7	16.1	103.0 (16.0)
>2500 eggs/g	33	75.8	27.3	97.9 (17.0)
<i>S. haematobium</i> (eggs/10 ml)				
Uninfected	199	46.2	7.5	110.0 (14.5)
>0 eggs/10ml	267	59.9	11.2	105.3 (14.3)
>250 eggs/10ml	82	73.2	15.9	101.5 (14.3)
>500 eggs/10ml	52	75.0	15.4	100.8 (14.3)

^a Figures in parentheses are 95% confidence intervals.

Table 2. Logistic regression analysis of factors affecting the risk of being anaemic (haemoglobin <110 g/l), with calculated odds ratios

Main effects	Coefficient (B)	Standard Error of B	P-value	Odds ratio
Constant	-2.52	0.16		
Age group (1 = 8–10 years, 2 = 11–14 years)	-0.54	0.15	<0.001	0.59 (0.44–0.79)
<i>S. haematobium</i> ^a	0.33	0.08	<0.001	1.39 (1.19–1.62)
Hookworm ^b	0.16	0.06	<0.006	1.17 (1.05–1.32)
Stunted (1 = yes, 2 = no)	0.45	0.16	<0.005	1.57 (1.14–2.15)

^a 0 = uninfected, 1 = 1–249 eggs/10 ml, 2 = 250–499 eggs/10 ml, 3 = =500 eggs/10 ml.

^b 0 = uninfected, 1 = 1–749 eggs/g, 2 = 750–1249 eggs/g, 3 = 1250–2499 eggs/g, 4 = =2500 eggs/g.

anthelmintics. Furthermore, these effects are likely to last longer than 15 months, since the intensities of hookworm and schistosomiasis infection, important factors in the causation of anaemia, had still not recovered to pretreatment values.

In order to place these results in context it is necessary to make similar calculations on the cost per anaemia case prevented for other interventions that improve anaemia status. The cost per moderate-to-severe anaemia case (haemoglobin < 90 g/l) prevented during one year of mebendazole treatment (three times a year) of 30 000 schoolchildren on Zanzibar was US\$ 3.57; for severe anaemia (haemoglobin <70 g/l) the corresponding cost was US\$ 16.30 (19). This is approximately an eighth of the cost estimated in the present analysis for a single treatment with praziquantel and albendazole. The difference arises because of the very low cost of

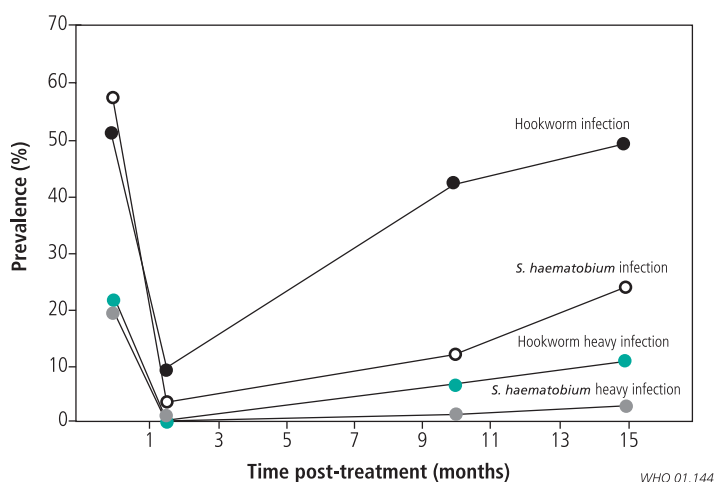
Table 3. **Attributable fraction analysis for anaemia and helminth infection**

Anaemia level/Intensity of infection ^a	Prevalence ratio (PR _w)	Crude population attributable fraction	Age-weighted population attributable fraction
Hb < 110 g/l			
Hookworm (eggs/g)			
>0	1.19	0.06	0.10 (0–0.27)
>750	1.29	0.05	0.06 (0–0.13)
>1250	1.28	0.02	0.04 (0–0.09)
>2500	1.44	0.03	0.03 (0–0.07)
Schistosoma haematobium (eggs/10ml)			
>0	1.19	0.15	0.10 (0–0.26)
>250	1.13	0.08	0.03 (0–0.10)
>500	1.14	0.05	0.02 (0–0.08)
Hb <90 g/l			
Hookworm (>0)	1.30	0.14	0.14 (0.06–0.23)
<i>S. haematobium</i> (>0)	1.82	0.25	0.25 (0.19–0.30)
Hb <70 g/l			
Hookworm (>0)	1.48	0.34	0.22 (0–0.79)
<i>S. haematobium</i> (>0)	0.53	0.15	– ^b

^a Hb = haemoglobin.

^b Negative value.

Fig. 2. **Prevalence of infection and heavy infection with hookworm and *Schistosoma haematobium* at baseline and 6 weeks, 10 months and 15 months after treatment** (heavy hookworm infection: >750 eggs/faeces; heavy *S. haematobium* infection: >250 eggs/10ml urine)



mebendazole, estimated to be US\$ 0.08 per child per year plus US\$ 0.07 for delivery. The combined treatment with albendazole and praziquantel is more

expensive but is of comparable effectiveness. Assuming an equivalent population of 30 000, a single treatment with albendazole and praziquantel would reduce by 1080 the number of moderate-to-severe anaemia cases in the present study in the United Republic of Tanzania over 15 months, compared with 1208 cases prevented in Zanzibar as a result of using mebendazole three times in 12 months. These analyses are not directly comparable since there are variations in the time frame for effectiveness (longer in the present study), the levels of infection and anaemia at baseline, and the methodologies employed to estimate cases prevented (in the Zanzibar study, extrapolation was performed from incidences in control and treatment groups over 6 months). However, the analysis provides some indication of the potential effectiveness of employing anthelmintics in reducing anaemia in schoolchildren.

Improvements in haemoglobin levels were not detected until at least 10 months after anthelmintic treatment. It had previously been concluded that, whereas iron supplementation can lead to rapid improvements in haemoglobin levels, the effects of deworming may appear up to 15–20 months after treatment (6). A more detailed follow-up survey including other indicators of anaemia, such as ferritin, may shed more light on this apparent delay in haemoglobin recovery.

The most traditional approach to improving iron balance is to use iron supplementation. However, we found no studies in the literature that presented the cost per anaemia case prevented. A recent economic analysis assessed the cost-effectiveness, expressed as cost per averted disability-adjusted life year, of oral iron supplementation in preventing severe anaemia (packed cell volume <25%) among infants in the United Republic of Tanzania (26). This outcome measure permits comparison across disease conditions, but requires many assumptions in translating cases into years of disability and death. Unfortunately, the costs in terms of cases prevented were not indicated, but it is possible to get some indication of them by referring back to the control trial on which the analysis was based (27). If, for example, 40% of infants have severe anaemia, and iron supplementation prevents 30% of severe cases in the first year of life, the cost per severe case prevented would be US\$ 14.77 at 1996 prices, assuming an intervention cost of US\$ 4121 for 2322 infants (26). In an operational setting, however, effectiveness may be markedly diminished because of the failure of patients to adhere to a therapy that involves multiple treatments. Furthermore, although the cost of iron supplements may be low, i.e. < US\$ 0.10 per year for a school-age child, the cost of delivery may be high unless existing channels such as those of the health and school systems are utilized. The cost–benefits of iron supplementation in adults were assessed in terms of increased productivity for improvement in negative iron balances (28). For Indonesia the resulting cost–benefit ratio was around

6; in Mexico it was almost 10 because of substantially higher wage rates. This suggests that iron supplementation would represent an efficient use of resources. Although increasing the iron status of schoolchildren would not directly translate into increased worker productivity, the improvement of the anaemia status of this age group is likely to have a positive effect on schooling. For example, cognitive skills might be increased (1), which would lead to better employment prospects and wage-earning capacity in adulthood (3). Stunting affects school performance adversely (29–31); adults of relatively short stature are less productive than taller adults (32, 33). Growth places demands on iron levels, and thus these two health outcomes are intrinsically related. With regard to the deworming of schoolchildren, the subsequent improvements in relation to both anaemia and stunting are particularly important (19, 34, 35). In addition there are direct associations between intestinal nematode infection and cognitive achievement. Expressing effectiveness as anaemia cases prevented clearly underestimates the full potential benefits of deworming on the mental and physical development of schoolchildren.

For ethical reasons, different children were sampled in each survey of the present study. Consequently, the reported changes in anaemia are only trends. A cohort design would have been more precise. Furthermore, the costs did not include that of health education materials. Two flip-charts were provided for each school at a cost of US\$ 17 per chart, increasing the cost per anaemia case prevented to US\$ 8.01. As anecdotal evidence suggests that the teachers did not use the charts, however, it is unlikely that they helped to reduce the prevalence of anaemia.

We have shown that school-based deworming programmes can favourably influence the anaemia status of children at a cost of US\$ 6–8 per anaemia case prevented over 15 months. The regular deworming of schoolchildren should therefore be given serious consideration as an approach to anaemia control and should be assessed in relation to iron supplementation and other traditional ways of improving iron status. ■

Acknowledgments

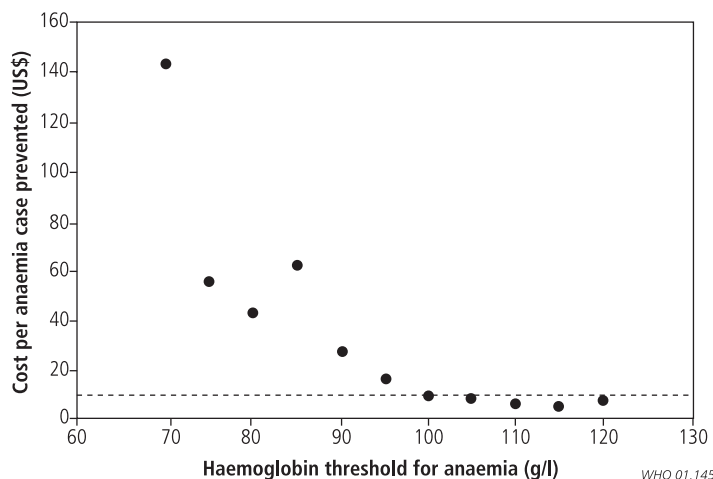
We gratefully acknowledge the support of the United Nations Development Programme, the Rockefeller Foundation, WHO, the Department for International Development of the United King-

Table 4. Effect of mass treatment with albendazole and praziquantel on anaemia in school-age children

Anaemia	Baseline pretreatment (n = 466)	10 months post-treatment (n = 429)	15 months post-treatment (n = 1121)
Mean haemoglobin level (g/l)	107.3 (14.5) ^a	108.0 (13.2)	112.8 (15.1)
Prevalence of anaemia			
Hb <110 g/l	54.1%	52.7%	40.0%
Hb <90 g/l	9.7%	5.8%	6.1%
Hb <70 g/l	1.5%	0.7%	0.8%

^a Figures in parentheses are standard deviations.

Fig. 3. Relationship between cost per anaemia case prevented and haemoglobin threshold for anaemia (the broken line represents a cost of US\$10 per anaemia case prevented)



dom, the United Nations Children's Fund, the World Bank, the Edna McConnell Clark Foundation, the James S. McDonnell Foundation, and the Wellcome Trust. The programme of the Tanzania Partnership for Child Development is supported by the Edna McConnell Clark Foundation. *H.L.G.* is in receipt of a Wellcome Trust Research Career Development Fellowship (055100), and *S.B.* a Wellcome Trust Prize Studentship. We thank Tom Smith for advice.

Conflicts of interest: none declared.

Résumé

République-Unie de Tanzanie : évaluation de l'efficacité des traitements anthelminthiques en milieu scolaire pour lutter contre l'anémie chez l'enfant

Objectif Déterminer l'effet du traitement vermifuge sur l'anémie dans le cadre d'un programme à grande échelle de traitement par les anthelminthiques dans les écoles de la région de Tanga, en République-Unie de Tanzanie.

Méthodes On a tenu compte à la fois de la réduction de la prévalence de l'anémie et du coût par cas évité. Dans

les études transversales, on a effectué un examen parasitologique et une évaluation de l'anémie chez les écoliers avant le traitement vermifuge, puis 10 et 15 mois après.

Résultats Au départ, les études indiquaient que la prévalence de l'anémie (hémoglobine <110 g/l) était

élevée (54 %) chez les écoliers, en particulier chez ceux qui présentaient de fortes charges parasitaires (ankylostomes et schistosomes). L'analyse du risque attribuable laisse à penser que l'ankylostomiase et la schistosomiase sont responsables de 6 et 15 % des cas d'anémie, respectivement. Quinze mois après le traitement vermifuge par l'albendazole et le praziquantel, la prévalence de l'anémie avait été réduite d'un quart et celle de l'anémie modérée à grave (hémoglobine <90 g/l) de près de la moitié. L'administration de ces anthelminthiques par le biais du système scolaire a été réalisée pour

un coût relativement faible de US \$1 par enfant traité. Le coût par cas d'anémie évité en appliquant un traitement vermifuge aux enfants est de l'ordre de US \$6 à 8, selon le seuil employé pour le taux d'hémoglobine.

Conclusion Ces résultats laissent à penser que des programmes de traitement vermifuge doivent figurer dans les stratégies de santé publique pour lutter contre l'anémie chez l'enfant d'âge scolaire, lorsque la prévalence de l'ankylostomiase et de la schistosomiase sont élevées.

Resumen

Evaluación de la eficacia de los tratamientos antihelmínticos escolares contra la anemia en niños de la República Unida de Tanzania

Objetivo Determinar el impacto del tratamiento vermifugo en la anemia como parte de un programa de tratamiento antihelmíntico escolar en gran escala emprendido en la Región de Tanga, República Unida de Tanzania.

Métodos Se consideraron tanto la reducción de la prevalencia de la anemia como el costo por caso evitado. Los estudios transversales realizados comprendían el análisis parasitológico y la evaluación de la anemia antes del tratamiento vermifugo de los escolares y a los 10 y 15 meses del tratamiento.

Resultados Los estudios basales mostraron que la prevalencia de anemia (hemoglobina < 110 g/l) era elevada (54%) entre los escolares, en particular en aquellos que presentaban una alta carga de anquilostoma y esquistosoma. El análisis de la fracción atribuible permitió relacionar la anquilostomiasis y la esquistoso-

miasis con el 6% y el 15% de los casos de anemia, respectivamente. Quince meses después del tratamiento vermifugo con albendazol y praziquantel, la prevalencia de anemia se había reducido en una cuarta parte, y la de anemia moderada-grave (hemoglobina < 90 g/l) lo había hecho casi en un 50%. El suministro de esos antihelmínticos a través de las escuelas pudo hacerse a un costo relativamente bajo, US\$ 1 por niño tratado. El costo por caso de anemia evitado mediante el tratamiento vermifugo de los escolares se situaba en el intervalo US\$ 6–8, dependiendo del umbral de hemoglobina empleado.

Conclusión Los resultados indican que las estrategias de salud pública deben incluir programas de tratamiento vermifugo para combatir la anemia entre los escolares en los casos en que concurre una alta prevalencia de anquilostomiasis y esquistosomiasis.

References

1. **Nokes C, van den Bosch C, Bundy DAP.** *The effects of iron deficiency and anaemia on mental and motor performance, educational achievement, and behaviour in children. An annotated bibliography.* Washington, DC, International Nutritional Anaemia Consultative Group, 1998.
2. **Pollitt E.** Effects of a diet deficient in iron on the growth and development of preschool and school-age children. *Food and Nutrition Bulletin*, 1991, **13**: 110–118.
3. **Guyatt HL.** Do intestinal worms affect productivity in adulthood? *Parasitology Today*, 2000, **16**: 153–158.
4. **Stoltzfus RJ et al.** Hemoquant determination of hookworm-related blood loss and its role in iron deficiency in African children. *American Journal of Tropical Medicine and Hygiene*, 1996, **55**: 399–404.
5. **Stephenson LS et al.** Relationships of *Schistosoma haematobium*, hookworm and malaria infections and metrifonate treatment to haemoglobin levels in Kenyan school children. *American Journal of Tropical Medicine and Hygiene*, 1985, **34**: 519–528.
6. **Roche M, Layrissé M.** The nature and causes of hookworm anaemia. *American Journal of Tropical Medicine and Hygiene*, 1966, **15**: 1031–1110.
7. **Tatala S, Svanberg U, Mduma B.** Low dietary iron availability is a major cause of anaemia: a nutritional survey in Lindi District of Tanzania. *American Journal of Clinical Nutrition*, 1998, **68**: 171–178.
8. **Robertson LJ et al.** Haemoglobin concentrations and concomitant infections of hookworm and *Trichuris trichiura* in Panamanian primary school children. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1992, **86**: 654–656.
9. **Stoltzfus RJ et al.** Epidemiology of iron deficiency in Zanzibari school children: the importance of hookworms. *American Journal of Clinical Nutrition*, 1997, **65**: 153–159.
10. **Olsen A et al.** The contribution of hookworm and other parasitic infection to haemoglobin and iron status among children and adults in western Kenya. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1998, **92**: 643–649.
11. **Bundy DAP.** Population ecology of intestinal helminth infections in human communities. *Philosophical Transactions of the Royal Society of London: B*, 1988, **321**: 405–420.
12. **Stephenson LS.** *Impact of helminth infection in human nutrition.* New York, Taylor & Francis, 1987.
13. *Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at the community level.* Geneva, World Health Organization, 1998 (unpublished document WHO/CTD/SIP/98.1).
14. **Partnership for Child Development.** Cost of school-based drug treatment in Tanzania. *Health Policy and Planning*, 1998, **13**: 384–396.
15. *Basic laboratory methods in medical parasitology.* Geneva, World Health Organization, 1991.
16. *Health and education of the school-age child in Tanga Region.* Dar es Salaam, UKUMTA, 1997 (Report Series No. 8).
17. **Partnership for Child Development.** The health of school-age children: experience from school health programmes in Ghana and Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1998, **92**: 254–261.

18. **Morris SS et al.** Precision, accuracy, and reliability of haemoglobin assessment with use of capillary blood. *American Journal of Clinical Nutrition*, 1999, **69**: 1243–1248.
19. **Stoltzfus R et al.** Effects of the Zanzibar school-based deworming program on iron status of children. *American Journal of Clinical Nutrition*, 1998, **68**: 179–186.
20. **Stoltzfus RJ, Dreyfuss ML.** *Guidelines for the use of iron supplements to prevent and treat iron deficiency anaemia*. Washington, DC, ILSI Press, 1998.
21. **Altman DG.** *Practical statistics for medical research*. London, Chapman & Hall, 1992: 351–355.
22. **Booth M.** The application of attributable risk analysis in helminth epidemiology. *Parasitology Today*, 1998, **14**: 497–450.
23. **Greenland S.** Bias in methods for deriving standardised morbidity ratios and attributable fraction estimates. *Statistics in Medicine*, 1984, **3**: 131–141.
24. **Walter SD.** The estimation and interpretation of attributable risk in health research. *Biometrics*, 1976, **32**: 829–849.
25. **Walter SD.** Calculation of attributable risks from epidemiologic data. *International Journal of Epidemiology*, 1978, **7**: 175–182.
26. **Alonso Gonzalez M et al.** Cost-effectiveness of iron supplementation and malaria chemoprophylaxis in the prevention of anaemia and malaria among Tanzanian infants. *Bulletin of the World Health Organization*, 2000, **78**: 97–107.
27. **Menendez C et al.** Randomised placebo-controlled trial of iron supplementation and malaria chemoprophylaxis for prevention of severe anaemia and malaria in Tanzanian infants. *Lancet*, 1997, **350**: 844–850.
28. **Levin HM.** A benefit-cost analysis of nutritional programs for anaemia reduction. *Research Observer*, 1986, **1**: 219–245.
29. **Partnership for Child Development.** Short stature and delayed enrollment in primary school: studies from two African countries. *Social Science and Medicine*, 1999, **48**: 675–682.
30. **Jamison D.** Child malnutrition and school performance in China. *Journal of Development Economics*, 1986, **20**: 299–309.
31. **Moock P, Leslie J.** Childhood malnutrition and schooling in the Terai Region of Nepal. *Journal of Development Economics*, 1986, **20**: 33–52.
32. **Bundy DAP.** Health and early child development. In: Young ME, ed. *Early child development*. Washington, DC, World Bank, 1997.
33. **Spurr GB.** Marginal malnutrition in childhood: implications for adult work capacity and productivity. In: Collins KJ, Roberts DF, eds. *Capacity for work in the tropics*. Cambridge, Cambridge University Press, 1988 (Symposium 26 of the Society for the Study of Human Biology).
34. **Stephenson LS et al.** Treatment with a single dose albendazole improves growth of Kenyan schoolchildren with hookworm, *Trichuris trichiura*, and *Ascaris lumbricoides* infections. *American Journal of Tropical Medicine and Hygiene*, 1989, **41**: 78–87.
35. **Stoltzfus RJ et al.** School-based deworming program yields small improvement in growth of Zanzibari school children after one year. *Journal of Nutrition*, 1997, **127**: 2187–2193.