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ORIGINAL COMMUNICATION

Effects on haemoglobin of multi-micronutrient supplementation and multi-helminth chemotherapy: a randomized, controlled trial in Kenyan school children

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Objective: To assess the effects of multi-micronutrient supplementation and multi-helminth chemotherapy on haemoglobin concentration (Hb), using schools as a health delivery system.
Study area and population: Nine hundred seventy-seven children between 9 and 18 y of age from 19 primary schools in Bondo District, western Kenya, were included in the trial. The 746 (76.4%) children on whom baseline Hb was available were included in this study.
Design: The study was a randomized, placebo-controlled, double-blind, two-by-two factorial trial of the effects of multi-micronutrient supplementation and multi-helminth chemotherapy on Hb after 8 months.
Intervention: Single treatment of infected children with albendazole (600 mg) for geohelminths and praziquantel (40 mg/kg) for *Schistosoma mansoni* and daily supplementation with 13 micronutrients.
Results: Multi-micronutrient supplementation (3.5 g/l, 95% CI 1.7, 5.3; $P = 0.0002$) and anthelminthic treatment (2.0 g/l, 95% CI 0.2, 3.9; $P = 0.03$) increased Hb independently (interaction, $P = 0.33$). The effects were also independent of baseline Hb and general nutritional status. The treatment effect was due to reductions in *S. mansoni* and hookworm intensities of infection, in that Hb increased by 0.4 and 0.2 g/l, respectively, per 100 epg reductions in egg output. Interestingly, among *S. mansoni*-infected children, the effect of treatment seemed stronger in those with compared to those without co-existing malaria parasitaemia (interaction, $P = 0.09$).
Conclusion: Multi-micronutrient supplementation and multi-helminth chemotherapy increased Hb among school children, irrespective of initial Hb and nutritional status.
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Introduction

Anaemia is widespread in developing countries, and considered to be a cause of impaired working capacity, cognitive development, and increased infant and maternal morbidity and mortality (Stoltzfus & Dreyfuss, 1998). Both nutritional deficiencies and infectious diseases contribute to anaemia, which is estimated to affect 2 billion people in the world. Deficiencies of iron and other micronutrients impair erythropoiesis, whereas hookworm, *Schistosoma* spp. and other parasitic infections lead to blood loss (Stephenson *et al*,

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2000) and possibly cytokine-induced anaemia. These determinants of anaemia are widespread in developing countries. However, feasible and inexpensive interventions to combat them already exist, and may be particularly cost-effective if administered through schools.

We studied the effects of multi-micronutrient supplementation and multi-helminth chemotherapy among 8–18-y-old school children in 19 primary schools in western Kenya, with an aim of assessing possible benefits of these interventions in future school health programmes. The effects on serum vitamin A have been reported previously (Mwaniki *et al*, 2002), and here we report on the effect on haemoglobin (Hb).

Subjects and methods

The study was conducted on the shores of Lake Victoria in Bondo District, Nyanza Province in western Kenya. The residents of the study area were members of the Luo community and their principal occupations were subsistence crop farming, raising Zebu cattle, commercial fishing and petty trade. Malaria was known to be holoendemic in the study area, and intestinal helminths (hookworm (*Necator americanus*), *Trichuris trichiura* and *Ascaris lumbricoides*) and *Schistosoma mansoni* were prevalent, whereas *S. haematobium* was not endemic. The altitude is 1500 m above sea level.

The study was a randomized, placebo-controlled, double-blind trial of the effects of daily multi-micronutrient supplementation and multi-helminth chemotherapy, using a two-by-two factorial design. From grades 5 and 6 in 19 primary schools in the study area, 1096 children were identified who had their parents' consent to participate. Of these, 38 were ill and therefore received initial treatment and were referred for more definitive management. These and 81 children who were unavailable for baseline examinations were excluded. The remaining 977 children were included in the study. Despite initial consent, some parents or children did not accept blood sampling. Thus, baseline data on Hb was available only on 746 (76.4%) of the 977 children, and the results of the 8-month follow-up of these children are reported here.

Study interventions

After completion of the baseline examinations described below, the children were randomized to daily multi-micronutrient supplementation or identical-looking placebo and independently randomized to multi-helminth chemotherapy or an identical placebo. Multi-micronutrient supplementation comprised a tablet with 13 vitamins and minerals (Almega, Ringsted, Denmark) on all schooldays (five per week) for a full school year. The contents of the micronutrient tablets were: vitamin A, 1000 μg; vitamin C, 50 mg; vitamin B_1, 1.4 mg; vitamin B_2, 1.6 mg; vitamin B_6, 1.7 mg; vitamin B_{12}, 2 μg; folate, 150 μg; niacin, 16 mg; iron, 18 mg; zinc, 20 mg; copper, 2.0 mg; iodine, 150 μg; selenium, 40 μg, corresponding to one RDA (Recommended Dietary Allowances) for 11–14-y-old children (National Research Council, 1989). Multi-helminth chemotherapy was given to children found infected with any of the common geohelminths or *S. mansoni* with albendazole and praziquantel, respectively. Albendazole was given as a single dose of 600 mg (Muchiri *et al*, 2001), and praziquantel as a single dose of 40 mg/kg of body weight (World Health Organization, 1995). The examinations described below were done at baseline and repeated after 8 months.

Haemoglobin concentrations

Blood samples were taken from the antecubital vein between 9 am and 1 pm. Hb and total white blood cell (WBC) counts were determined using an electronic counter (M530, Coulter Electronics, Ltd, UK). The cut-offs used to define anaemia were 115 g/l for children above 5 and below 12 y of age, 120 g/l for non-pregnant girls above 11 and for boys between 12 and 13 y of age, and 130 g/l for boys above 13 y of age (Stoltzfus & Dreyfuss, 1998). Altitude was not adjusted for. Differential WBC counts were determined using conventional manual methods (World Health Organization, 1991).

Clinical examination and anthropometry

The children were examined clinically, questionnaire data were obtained, and blood and stool samples were collected. The clinical examination included assessment of organomegaly and anthropometry. Hepatomegaly was arbitrarily defined as the liver extending 1 cm or more below the costal margin in the mid-clavicular line, as there is no conventional cut-off (World Health Organization, 2000). Splenomegaly was reported according to Hackett's method (Gilles, 1995). Height and weight were measured with the children barefooted and wearing light standard clothing. Heights were measured to the nearest 0.5 cm and weights to the nearest 0.1 kg, using a scale-stadiometer (Seca, Germany), and related to the NCHS-WHO growth references as height-for-age (HAZ) and weight-for-age (WAZ) *Z*-scores (Dean *et al*, 1990). HAZ and WAZ below -2 were considered to reflect stunting and underweight, respectively.

Infections

Two to three stool samples were collected on consecutive days around the time of blood sampling, and examined quantitatively for intestinal helminths and schistosome eggs using the World Health Organization modification of the Kato–Katz method (World Health Organization, 1991). Duplicates of 50 mg cellophane fecal thick smears were prepared from each of the stool samples. The smears were examined for hookworm eggs within one hour, and after at least 24 hours of clearing for eggs of *S. mansoni*, *T. trichiura* and *A. lumbricoides*. The egg output was expressed as mean eggs per gram of faeces (epg). From all children a thick blood slide was examined for malaria parasites. The number of parasites per 200 WBC was counted. If fewer than 10 parasites were seen, then fields containing 500 WBC were examined. If no parasites were found, then 100 microscopic fields were examined before the slide was considered negative. The number of malaria parasites per μl of blood was computed based on the total WBC count. Questionnaire morbidity data, elevated body temperature and neutrophilia were used as indicators of infection. Structured interview data on fever, malaria and diarrhoea within the preceding 2 weeks were used as clinical indicators of infection. Children rarely reported fever, as fever was apparently perceived as malaria or headache. Neutrophilia was arbitrarily defined as an absolute neutrophil count above the 87.5 percentile. Sublingual temperatures were taken using a digital thermometer (Becton Dickinson, New Jersey), and >37.0°C defined elevated body temperature.

Statistical analysis

The distribution of Hb was assessed using normal probability plots. The two-sample *t*-test and the chi-square test were used to test for differences in means and proportions, respectively. Multiple regression analyses were employed to estimate the effects of the two interventions (both coded 0 for placebo and 1 for the active compounds) on Hb, while controlling for potential confounding factors and assessing for interactions. The variables assessed were age, sex, HAZ, WAZ, hepato- and organomegaly, malaria parasitaemia and helminth egg output, sickle cell phenotype, and, as indicators of infection, elevated temperature, neutrophilia and reported morbidity. If interactions were identified, then interaction terms were computed to allow estimation of the effect of one of the variables separately for each level of the other. Data on malaria parasitaemia, *S. mansoni* and intestinal helminth egg output were $\log_{10}(x+1)$ transformed. Standardized residuals were plotted against predicted values and continuous independent variables to assess the model assumptions. *P*-values below 0.05 were considered significant.

Permissions

Permission to conduct the study was obtained from the Kenya Medical Research Institute and National Ethical Review Committee, and the Ministry of Health, Kenya. The children and their parents were given information about the study, and the parents gave their written consent. The Danish Central Medical Ethics Committee also approved the study. All children found infected were treated at the end of the study.

Results

The 746 children included in this study were similar to the 231 children on whom Hb data was not available, with respect to baseline characteristics such as age, sex, nutritional status and prevalence and intensity of infections (data not shown). The children had a mean (range) age of 12.9 (9–18) y, and 387 (51.9%) were girls. The prevalence of malaria parasitaemia was 59%, whereas it was 14% for *A. lumbricoides*, 45% for *T. trichiura*, 55% for hookworm and 71% for *S. mansoni*. The mean WAZ and HAZ were -1.11 (95% confidence interval (95% CI) -1.16, -1.06) and -0.96 (95% CI -1.03, -0.89), respectively. The mean Hb at baseline was 123.7 g/l (95% Cl 122.8, 124.6) with 309 (41.4%) falling below the age- and sex-specific cut-off defining anaemia. Mean Hb was not significantly different for boys and girls (123.3 *vs* 124.1 g/l, $P=0.40$), but the prevalence of anaemia was significantly higher for boys than for girls (50.1 *vs* 33.3%, $P<0.00001$). As seen in Table 1, the simple randomization used resulted in baseline equivalence between the intervention groups. Significance testing was considered redundant since any difference between groups would be due to randomization. However, HAZ appeared to be lower in children allocated to placebo supplementation and anthelminthic treatment.

Haemolobin at follow-up

At 8 months, 575 (77.1%) of the 746 children were followed-up with determination of Hb. The 170 children lost to follow-up were older (13.3 *vs* 12.8, $P=0.0003$), had a higher prevalence (79 *vs* 69%, $P=0.008$) and geometric mean intensities (112 *vs* 56 epg, $P=0.0001$) of *S. mansoni* infection, as well as a higher geometric mean intensity of *T. trichiura* infection (69 *vs* 39 epg, $P=0.02$). In contrast, there were no differences in baseline Hb (123.3 *vs* 123.8, $P=0.68$), and in prevalence or intensity of other infections ($P>0.05$).

The increase in Hb from baseline to the 8 month follow-up examination was 5.5 g/l (95% CI 3.3, 7.6) in children receiving neither of the active compounds (placebo/placebo). However, it was 9.2 g/l (95% CI 7.4, 11.1) in those receiving only micronutrients (micronutrients/placebo), 8.6 g/l (95% CI 6.8, 10.4) in those receiving only anthelminthics (placebo/anthelminthics) and 10.4 g/l (95% CI 8.2, 12.6) in children receiving both active compounds (micronutrients/anthelminthics, $P=0.005$). The 232 (40.3%) children found anaemic at baseline had a higher increase in Hb than the 343 (59.3%) non-anaemic children (13.5 *vs* 5.0 g/l, $P<0.00001$), and this difference between anaemic and non-anaemic children was similar in the four groups: 9.0 g/l in the placebo/placebo, 9.0 g/l in the micronutrient/placebo, 8.5 g/l in the placebo/anthelminthic and 9.5 g/l in the micronutrient/anthelminthic group.

There were no interactions between micronutrient supplementation and anthelminthic treatment as assessed in multiple regression analyses (*P* for interaction $=0.33$). The effect of one intervention could therefore be assessed without taking the other intervention into consideration (Table 2). As seen, the mean increase was 2.7 g/l (95% CI 0.7, 4.7) higher in children assigned to multi-micronutrient supplementation compared with placebo (9.8 *vs* 7.1 g/l, $P=0.008$). Similarly, the mean increase in Hb was 2.1 g/l

Table 1 Baseline characteristics of 746 children independently randomized to daily supplementation with multi-micronutrients or placebo, and treatment with anthelminthics or placebo

	Placebo *Placebo* *(n = 191)*	*Micronutrients* *Placebo* *(n = 188)*	*Placebo* *Anthelminthics* *(n = 187)*	*Micronutrients* *Anthelminthics* *(n = 180)*
Age (y)[a]	12.8 (9.5, 16.5)	13.0 (9.0, 17.0)	13.0 (9.5, 17.0)	13.0 (9.2, 18.0)
Sex (% boys)	47	48	50	47
Nutritional status				
Weight-age *Z*-score[b]	− 1.13 (−1.23, −1.02)	− 1.13 (−1.24, −1.02)	− 1.06 (−1.17, −0.95)	− 1.11 (−1.23, −1.00)
Height-age *Z*-score[b]	− 1.00 (−1.14, −0.86)	− 1.00 (−1.14, −0.86)	− 0.81 (−0.96, −0.67)	− 1.04 (−1.19, −0.90)
Haemoglobin (g/l)[b]	123.3 (121.5, 125.1)	123.4 (121.7, 125.2)	124.1 (122.3, 126.0)	123.8 (122.2, 125.5)
Infections				
Malaria parasitaemia[a]	64% (493)	60% (548)	55% (528)	57% (572)
S. mansoni[d]	72% (82)	69% (61)	73% (60)	70% (65)
Hookworm[d]	52% (57)	61% (37)	52% (61)	55% (54)
T. trichiura[d]	46% (42)	45% (45)	50% (44)	40% (55)
A. lumbricoides[d]	14% (1450)	14% (1461)	14% (2333)	13% (714)

[a] Mean (range).
[b] Mean (95% confidence interval).
[c] Prevalence (geometric mean malaria parasites per μl blood in infected).
[d] Prevalence (geometric mean eggs per gram (epg) faeces in infected).

(95% CI 0.1, 4.1) higher in children treated with anthelminthics compared with placebo (9.5 *vs* 7.4 g/l, $P = 0.04$).

In multiple linear regression analysis, after adjustment for baseline Hb, age, sex and HAZ, the effects of micronutrients and anthelminthics on Hb at the 8 month follow-up were 3.5 g/l (95% CI 1.7, 5.3) and 2.0 g/l (95% CI 0.2, 3.9), respectively (Table 3). The effects of the two interventions were not significantly different between anaemic and non-anaemic children (P for interaction > 0.30). There was no interaction between treatment and sex ($P > 0.80$). However, a marginally significant interaction between micronutrient supplementation and sex ($P = 0.10$) was found, due to a stronger effect of micronutrient supplementation among boys (5.0 g/l, 95% CI 2.4, 7.6, $P = 0.0002$) than among girls (2.1 g/l, 95% CI −0.3, 4.7, $P = 0.09$). Nevertheless, there were no interactions between the interventions and stunting and underweight. Based on previous observations (Friis *et al*, 2000; Friis, unpublished data), we examined the data for an interaction between treatment and malaria parasitaemia among the 394 (68.5%) children with *S. mansoni* at baseline. Interestingly, the effect of treatment on Hb was marginally significantly larger in the 230 (58.4%) children with malaria parasitaemia as compared with the 164 (41.6%) children without baseline malaria parasitaemia (3.5 g/l (95% CI 0.7, 6.3, $P = 0.01$) *vs* −0.2 g/l (95% CI −0.4, 0.3, $P = 0.90$), P for interaction $= 0.09$).

In order to understand how the effects of anthelminthic treatment were mediated, variables expressing the reduction in intensities of the four treated infections were computed and assessed in the regression analyses. As expected, *S. mansoni* and hookworm were the only infections retained in the model as predictors of Hb. When the treatment variable and reductions in egg counts were included in the same model, the regression coefficient of the treatment variable declined and became insignificant, suggesting that the effect of treatment on Hb was explained by the resulting reduction in intensities of *S. mansoni* and hookworm infection. The regression coefficients shown in Table 4, of 0.2 for

Table 2 Effects on haemoglobin concentration (mean (95% confidence interval)) of daily multi-micronutrient supplementation and anthelminthic treatment among 575 children followed up after 8 months

	Supplementation			*Treatment*		
Haemoglobin (g/l)	*Placebo (n = 287)*	*Micronutrients (n = 288)*	P	*Placebo (n = 296)*	*Anthelminthics (n = 279)*	P
Baseline	123.7 (122.2, 125.2)	123.9 (122.5, 125.3)	0.84	123.8 (122.4, 125.2)	123.8 (122.3, 125.2)	0.99
8 months	130.7 (129.3, 132.1)	133.7 (132.3, 135.0)	0.004	131.2 (129.8, 132.6)	133.3 (131.8, 134.7)	0.04
Increase	7.1 (5.7, 8.5)	9.8 (8.4, 11.2)	0.008	7.4 (6.0, 8.9)	9.5 (8.1, 10.9)	0.04
Difference	2.7 (0.7, 4.7)		0.008	2.1 (0.1, 4.1)		0.04

Table 3 Regression model with predictors of haemoglobin concentration (g/l) at follow-up, with regression coefficients (β), 95% confidence intervals (CI) and corresponding *P*-values; $n = 524$, adjusted $r^2 = 0.27$[a]

Variables	β	*95% CI*	P
Micronutrients[a]	3.5	1.7, 5.3	0.0002
Anthelminthics	2.0	0.2, 3.9	0.03

[a]Adjusted for baseline haemoglobin concentration, age, sex, height-for-age *Z*-scores.

hookworm and 0.4 for *S. mansoni*, correspond to a 0.2–0.4 g/l increase in Hb per 100 epg reduction in intensity of infection. Based on this model, male sex (−2.4 g/l, 95% CI −4.2, −0.6), splenomegaly (−6.3 g/l, 95% CI −9.5, −3.1) and low serum retinol at follow-up were also predictors of Hb at follow-up (not shown). Since the effect of *S. mansoni* on Hb was partly mediated by a reduction in splenomegaly, the regression coefficient of *S. mansoni* decreased slightly with splenomegaly in the model. Using serum retinol above 1.05 μmol/l as the reference category, levels below 0.70 and between 0.70 and 1.05 μmol/l were associated with 5.2 (95% CI 1.8, 8.7, $P = 0.003$) and 1.8 (95% CI −0.2, 3.9, $P = 0.08$) lower Hb, respectively.

Discussion

In populations where anaemia is common, the whole distribution curve of Hb is shifted to the left, as the majority of individuals have sub-optimal Hb. Therefore, studies aimed at identifying appropriate interventions should use Hb as effect parameter, and programmes using such interventions should target populations rather than anaemic individuals.

Both multi-micronutrient supplementation and multi-helminth chemotherapy were associated with increased Hb after 8 months among school children in western Kenya. These effects were independent, ie the effect of supplementation was similar in children allocated to anthelminthics and placebo, and vice versa. Interestingly, there was a notable increase in Hb during the study period, which was explained neither by micronutrients nor anthelminthics. In fact, children allocated to the two placebo interventions had a 5.5 g/l increase in Hb over the 8 months from February to October. This may partially have been due to occasional mixing of micronutrient and placebo tablets, in which case the effect of micronutrient supplementation is underestimated. Furthermore, the increase may reflect seasonal changes (February to October) in malaria transmission or diet, as similar changes were found for vitamin A (Mwaniki *et al*, 2002), and for Hb and serum ferritin in a study in the neighbouring district (A Olsen, Personal Communication).

Table 4 Regression model with predictors of haemoglobin concentration (g/l) at follow-up, with regression coefficients (β), 95% confidence intervals (CI) and corresponding *P*-values; $n = 498$, adjusted $r^2 = 0.30$[a]

Variables	β	*95% CI*	P
Micronutrients	3.9	2.1, 5.8	0.00004
Reduction in infection intensity (0–8 months)			
S. mansoni (100 epg)	0.4	0.01, 0.7	0.006
Hookworm (100 epg)	0.2	0.04, 0.4	0.02

[a]Adjusted for baseline haemoglobin concentration, age, sex, height-for-age *Z*-scores.

Multi-helminth chemotherapy

Both infections with *Schistosoma* spp and several geohelminths may contribute to anaemia, although through somewhat different mechanisms. During the tissue-phase of primary infections with any of these helminths, and probably during established infection with *Schistosoma* spp., anaemia may develop due to cytokine-mediated suppression of erythropoiesis and haemolysis. In addition, established infection with *Schistosoma* spp., hookworm and, in young children, *T. trichiura*, may all cause chronic loss of blood (Stephenson, *et al*, 2000), which eventually leads to iron-deficiency anaemia if the dietary iron intake is inadequate.

Although our study was not designed to clarify the relationships between specific infections and Hb, our analysis suggests that the effect of anthelminthic treatment on Hb was mediated by reductions in intensities of *S. mansoni* and hookworm infection, but not of *A. lumbricoides* and *T. trichiura*. It was estimated that Hb increased by 0.4 and 0.2 g/l per 100 epg reduction in intensities of *S. mansoni* and hookworm infection, respectively. Data from Tanzanian schoolchildren suggested that hookworm was responsible for 6% and *S. haematobium* for 15% of anaemia cases, and that the cost of multi-helminth chemotherapy per averted case of anaemia was 6–8 US$ (Guyatt *et al*, 2001).

However, the effects of these infections on Hb may be more complex. For example, we have recently reported results from a study among schoolchildren from an area in Sudan where neither *S. mansoni* nor geohelminths were endemic (Friis *et al*, 2000). *S. haematobium*, in addition to reducing Hb, was found to interact with malaria, apparently by protecting against malaria-induced splenomegaly (Friis *et al*, 2000) and anaemia (Friis, unpublished data). This was found plausible, since *S. haematobium* has been shown to upregulate the anti-inflammatory cytokine interleukin-(IL)-10 (van den Biggelaar *et al*, 2000), known to counterregulate the proinflammatory cytokines responsible for malaria-anaemia (Ho *et al*, 1998; Kurtzhals *et al*, 1998; Othoro *et al*, 1999). Furthermore, the finding was consistent with the fact that few studies to our knowledge has been able to show that treatment of *S. haematobium* alone leads to increases in Hb. In view of this effect modification, and on the assumption that *S. mansoni* and *S. haematobium* have similar effects on the immune system, we specifically examined our data for an interaction between anthelminthic treatment and malaria parasitaemia among children with *S. mansoni* infection at baseline. Interestingly, a marginally significant interaction was revealed, due to a significant increase in Hb following treatment, but only among those with malaria parasitaemia. Thus, our data confirm that schistosome infection and malaria parasitaemia interact, but *S. mansoni* and *S. haematobium* infection may differ with respect to how they interact with malaria. Nonetheless, this aspect may have important public health implications and should be further studied.

Multi-micronutrient supplementation

We have previously reported that the micronutrient intervention led to an increase in serum retinol among the study participants (Mwaniki *et al*, 2002). The effect of micronutrient supplementation on Hb could be due not only to increased iron status, but also to vitamin A, riboflavin, folate, vitamin B_{12}, zinc and other micronutrients essential to normal erythropoiesis (Hercberg & Galan, 1992; van den Broek & Letsky, 2000). Furthermore, in addition to these independent effects of various micronutrients, the existence of interactions between micronutrients is another argument for supplementing with multiple instead of single micronutrients. For example, vitamin C increases the absorption of iron, copper deficiency may lead to iron deficiency anaemia (Allen, 1998; Lönnerdal, 1998), and zinc is involved in the conversion of β-carotene to vitamin A (Dijkhuizen & Wieringa, 2001). Micronutrients may also affect Hb indirectly, by reducing the susceptibility to infections that would reduce Hb. For example, zinc and vitamin A supplementation may reduce malaria morbidity (Shankar *et al*, 1997, 1999), and zinc and iron supplementation may result in a lower helminth reinfection rate or intensity (Friis *et al*, 1997; Olsen *et al*, 2000).

School-based health programmes

Since schools offer a pre-existing and comprehensive system for health care delivery (Bundy & Guyatt, 1996), school-based interventions are among the most cost-effective public health interventions (World Bank, 1993). School children have high nutritional requirements due to continuous growth and the pubertal growth spurt, and should be an important target group for nutritional interventions that may have effects on school attendance and performance. Similarly, it may be particularly cost-effective to include periodic multi-helminth chemotherapy with albendazole (effective against *A. lumbricoides*, *T. trichiura* and hookworm) and praziquantel (effective against *S. haematobium* and *S. mansoni*) in school health programmes, because the prevalence and intensity of helminth infections often peak at school age, and because schools and surroundings may be important transmission sites.

Conclusion

Multi-micronutrient supplementation and multi-helminth treatment independently increased Hb among school children, irrespective of baseline Hb or general nutritional status. The cost-effectiveness of the interventions may be further improved when schoolchildren in populations with lower micronutrient status, and higher intensities of *S. mansoni* and hookworm infection are targeted. The interaction between schistosomiasis and malaria warrants further studies.

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