

Cluster-randomised trial of the impact of school-based deworming and iron supplementation on the cognitive abilities of schoolchildren in Sri Lanka's plantation sector

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Abstract

OBJECTIVE To assess the impact of deworming and iron supplementation on the cognitive abilities and educational achievement of school-age children in Sri Lanka.

METHODS Prospective, placebo-controlled randomised study. The treatment group received deworming and weekly iron supplementation for 6 months; the control group received placebo for both the anthelmintic and iron. A mixed effects regression model was used to answer the main research question. To increase the precision of this study's estimates, various background variables were controlled for that were not related to treatment but could have some impact on the outcome.

RESULTS The prevalence of soil-transmitted helminth (STH) infection was reduced in the treatment group ($n = 615$), with significant differences between treatment and control groups ($n = 575$) in the levels of *Ascaris* and *Trichuris*. No impact was found on haemoglobin (Hb) levels, nor any significant impact on concentration levels or on educational test scores.

CONCLUSION Decline in STH prevalence alone, in the absence of improved Hb status, produced no evidence of impact on concentration levels or educational test scores.

keywords Sri Lanka, deworming, iron supplementation, school health and nutrition, cognition, educational achievement

Introduction

School health and nutrition (SHN) programmes are increasingly recognised as a key strategy in the global effort to improve educational outcomes. These programmes deliver large gains in education because diseases that affect education are highly prevalent and schoolchildren bear the greatest burden. The diseases are treatable and preventable, and school health programmes are a cost-effective way to treat them (Jukes *et al.* 2008).

Interventions such as school feeding or malaria prevention may increase school attendance (Powell *et al.* 1998; Fernando *et al.* 2006), and school-based deworming can also lead to gains in school attendance (Miguel & Kremer 2004). However, it is less clear whether SHN programmes have a direct impact on a child's cognitive ability, which may be defined as a 'capacity to perform higher mental processes of reasoning, remembering, understanding and problem solving' (Bernstein *et al.*

2008). This includes skills such as concentration, short-term and long-term memory, auditory and visual processing, which affect a child's ability to learn.

About 1 billion school-aged children are estimated to live in areas with stable transmission of at least one STH infection (Pullan & Brooker 2012), while approximately 600 million pre-school and schoolchildren worldwide are estimated to suffer from anaemia. At least half of these cases are due to iron deficiency (WHO/CDC 2008). Thus, deworming and iron supplementation are critical components of many school health programmes.

The results of studies investigating the impact of deworming on cognitive abilities vary: Worm infections are associated with lower cognitive function such as poor working memory (Nokes *et al.* 1992; Sakti *et al.* 1999); lower concentration levels and information processing skills (Jardim-Botelho *et al.* 2008); or delayed reaction times (PCD 2002). However, most of the impact has been found to be in particular subgroups of children such

as those with poor nutritional status (Simeon *et al.* 1995) or children with the heaviest worm loads (PCD 2002). There is also evidence to suggest that treatment may have a greater effect on cognitive function when combined with iron supplementation (Boivin & Giordani 1993). There is more evidence of the impact of anaemia on the cognitive function of school-age children (Freeman *et al.* 1980 as cited in Jukes *et al.* 2008). A study among middle-income school-age children in the United States showed the negative impact of iron deficiency on the educational achievement of school-age children (Haltermann *et al.* 2001). Treatment of iron deficiency also had a positive impact on learning among primary schoolchildren in Indonesia and Thailand (Soemantri *et al.* 1985; Pollitt *et al.* 1989).

Despite the evidence for the efficacy of deworming and iron supplementation, it is not clear that these interventions improve cognitive ability and educational achievement in a programmatic context. A recent Cochrane systematic review of deworming drugs for soil-transmitted intestinal worms in children found very few reliable studies that examined the effect of community-based deworming on school performance or attendance (Taylor-Robinson *et al.* 2012). Most of the studies cited above have been trials of the efficacy of individualised treatment rather than studies of the effectiveness of control programmes (which may be defined 'as gains in intervention coverage and in health effects under real-world conditions, when implementation tends to be less intense and more variable than in efficacy trials', Vicotra *et al.* 2011). As such, these studies assessed the efficacy of individually targeted and tightly regulated treatment, rather than the effectiveness of programmatic treatment provided by school teachers.

The main objective of this study was to assess the impact of two key school-based health interventions, deworming and iron supplementation, on cognitive abilities at individual level. A secondary goal was to evaluate the code transmission test, part of a battery of cognitive tests adapted for group administration from the TEA-Ch (Test of Everyday Attention for Children) battery (Manly *et al.* 1998).

Methods

Study setting

Sri Lanka has a long-standing school health programme dating back to 1918; deworming, iron supplementation and school feeding are major components. Communities in the country's plantation sector are among the most disadvantaged where health and education and

socio-economic indices are below average and infection rates are higher (Gunawardena *et al.* 2011). The majority of inhabitants live and work on the tea and rubber estates situated in five districts in the centre of the country.

Study design

This prospective, placebo-controlled randomised study was conducted from September 2009 to April 2010. Baseline data were collected from September through November 2009. The treatment group then received deworming and 6 months of weekly iron supplementation; whereas the control group received placebo for both anthelmintic and iron. Follow-up testing took place after the 6 months of treatment, between March and May 2010.

Participants

Participants were students (*max* = 20 per class) registered in grade four in 2009, in schools serving the plantation sector in the districts of Badulla, Kandy, Kegalle and Ratnapura. Participant recruitment was restricted to grade four because children in grade five would have moved to other schools at the beginning of the new school year during the follow-up period, thus making follow-up difficult; and the general educational achievement test used was designed to test grade four students in Sri Lanka and would not have been appropriate for a lower grades.

Sampling and randomisation

We used cluster sampling (Magnani 1997), whereby a cluster consisted of one grade 4 class in a school. One hundred schools were chosen: 24 each in Kegalle and Ratnapura and 26 each in Badulla and Kandy. Eligible schools were those with more than 60 students but fewer than 400 students. Cluster randomisation rather than individual randomisation was adopted because it mimics more closely the context of an SHN programme.

The clusters were identified by AP and BK and enrolled under the supervision of RE and KG. Random allocation sequences were generated in blocks of two by AP using Stata version 8.0 before the field work started. The randomisation sequence was concealed in sealed envelopes until required for assignment of clusters to treatment or placebo. After completion of the baseline survey, the schools in each district were ranked and paired according to the prevalence of STH infections to ensure that the prevalence of infection was similar in both groups. Each pair of schools was allocated to treatment or control according to the randomisation sequence under the supervision of NdeS.

Sample size calculation

For educational achievement tests, an overall sample size of 100 schools with 15 children per school (2000 children overall) is enough to detect an effect size of 0.2 standard deviations (SD) assuming an intraclass correlation of 0.2 (varying from 0.1 to 0.2 with mathematics and literacy tests in previous studies) (Hedges & Hedberg 2007; Brooker *et al.* 2010) and a correlation of 0.7 between baseline and final test scores. This sample size was intended to be sufficient to detect an effect size of 0.15 SD for concentration tests, which have a lower intraclass correlation (0.07 in previous studies) (Clarke *et al.* 2008). These figures are based on 80% power to detect differences with 95% confidence.

Ethical issues and ethical clearance

Informed written consent was obtained from parents prior to biomedical testing. The study protocol, including all questionnaires and biomedical testing procedures, received ethical clearance from the Ethics Review Committee of the Faculty of Medicine at the University of Kelaniya, Sri Lanka. The trial was registered with the Sri Lanka Clinical Trials Registry (no. 2009/009). At the end of the follow-up survey, all children were offered treatment with single-dose mebendazole.

School health programme interventions

The class teacher was responsible for administering one 500-mg oral dose of mebendazole or a placebo to all children in the class after baseline testing. Mebendazole and placebo were both from the State Pharmaceutical Manufacturing Corporation of Sri Lanka (lot numbers LTF03 and FD09H03, respectively). Single-dose mebendazole was selected as it is used for all routine deworming activities in the School Health Programme in Sri Lanka. The teacher was also responsible for administering a weekly dose of iron supplementation (tablets containing 200 mg of ferrous sulphate equivalent to 60 mg of elemental iron or placebo) to all children in the class over the study period. The ferrous sulphate tablets were from T.P. Drug Laboratories, Thailand (lot number 151241), while the matching placebo was manufactured by MSJ Industries, Ceylon (lot number 090108). Teachers were educated by the investigators after completion of the baseline survey, on how to administer the tablets, deal with possible adverse events, and record treatment.

Students, teachers and data collectors involved in measuring health and educational outcomes were all blinded regarding allocation of treatment.

Outcome measures

For cognitive assessments, we used the code transmission test to measure children's attention, hypothesised to be a key cognitive domain impacted by poor health and nutrition (Clarke *et al.* 2008). The test was adapted from the TEA-Ch battery (Manly *et al.* 1998). A general education test consisting of two 30-min sections was also administered: a first language (Tamil) test and a math test. All tests were piloted for internal validity and reliability before administration, and the same tests were used in follow-up testing. These tests were adapted from the National Education Research and Evaluation Centre (NEREC), a nationally standardised test developed to assess grade four students in Sri Lanka (NEREC 2012). All tests were administered by trained primary school teachers designated as 'in-service advisors' in the Ministry of Education.

Demographic and health outcomes: All data for the biomedical survey were collected by a team of medical practitioners. Haemoglobin (Hb) levels were estimated using 50 μ l of finger prick blood in a portable photometer (HemoCue Hb201+; Ängelholm, Sweden). Measured Hb levels were then adjusted for altitude using the following formula proposed by the CDC (Centres for Disease Control and Prevention)¹: $\Delta\text{Hb} = -0.032 \times (\text{Alt}) + 0.022 \times (\text{Alt})^2$. Children were diagnosed as anaemic if the adjusted Hb level was <11.0 g/dl for those younger than 12 years. Among older children, anaemia was diagnosed if Hb levels were <12.0 g/dl for boys or <11.5 g/dl for girls (National Health and Nutrition Examination Survey, NHANES II).

Faecal samples were collected and analysed for the presence of *Ascaris lumbricoides*, hookworm and *Trichuris trichiura* eggs using the modified Kato-Katz technique as recommended by the World Health Organization (WHO) (Ash *et al.* 1998). Following WHO guidelines, children were classified into infection categories for each worm type according to the number of worm eggs per gram faeces (Montresor *et al.* 2002). Further details have been published elsewhere (Gunawardena *et al.* 2011).

All relevant information for each pupil was entered on an individual record form. The school-level information collected included data on school attendance for 6 months before and after the study, from school attendance registers; whether the school had a midday meal programme; whether the School Medical Inspection had been carried out within the current school year; and whether or not deworming treatment was part of it.

¹<http://www.biomedcentral.com/1471-2458/9/336>

Data analysis

Data were entered in EpiInfo version 3.5.1 by two independent data entry operators. Data quality was ensured by matching the two sets of entries and verifying records. Statistical analyses were carried out on Stata version 11.

Only those children who were present at both baseline and follow-up testing were included in the final analysis, and the descriptive statistics presented in the article relate to these children only. As it was assumed that there was a degree of correlation between the subjects at school-level, the following mixed effects regression model was used to answer the first research question:

$$Y_{ij} = \beta_0 + \beta_1 \text{Treat}_i + \beta_2 \text{Pretest}_{ij} + \beta_3 \text{Age}_{ij} + \beta_4 \text{Sex}_{ij} + u_j + e_{ij}$$

The variables are defined as:

Y_{ij} = The outcome score on one of the assessments for student i in school j at point B.

Treat_i = A dichotomous variable indicating whether school j is in the treatment or control group.

Pretest_{ij} = The pre-test score for student i in school j on the assessment.

Age_{ij} = Age of the student i in school j at baseline.

$\beta_4 \text{Sex}_{ij}$ = Sex of the student i in school j .

u_j = The classroom-level residual shared by all students in school j .

e_{ij} = The individual residual for student i in school j .

To increase the precision of our estimates, we controlled for various background variables that were not related to treatment but could have affected the outcome: basic indicators such as the child's age, sex and baseline nutritional status; as well as individual socio-economic indicators such as parental education; and school-level indicators, that is, whether or not the school had an ongoing midday meal programme.

To test the hypothesis that children with a low nutritional status at baseline or with a high-intensity worm burden may benefit more from the treatment, a variable was created to control for the interaction between treatment and low nutritional status and high-intensity worm burden.

Results

Figure 1 presents the participatory flow chart. At baseline, 813 children in 49 schools were randomised to treatment, and 808 children in 49 schools were randomised to placebo. Complete data from the biomedical survey and the educational assessments at both baseline and follow-up surveys were available for 615

children in 49 schools in the treatment group, and 575 children in 47 schools in the placebo group. Thus, the losses at follow-up were 24.4% and 28.8%, respectively.

As Table 1 shows, there were significant differences between the treatment and control groups at baseline for mean Hb levels, anaemia and parental education. This baseline imbalance was taken into consideration when analysing the results of the follow-up survey. Table 2 presents the descriptive statistics for cognitive and educational tests for treatment and control groups at baseline. The correlations between the four test scores ranged from 0.428 to 0.793, and each pairwise correlation was significant at the 0.05 alpha level. Although 80% school attendance was about 62% in both groups (Table 3), it is interesting to note that compliance with deworming and 16+ iron tablets was significantly higher in the treatment group than the placebo group. Also, it must be noted that full compliance with the iron treatment was better than the rate of full (over 80%) attendance. This was most probably due to the fact that teachers were instructed to give iron supplements to students whenever they returned to school after being absent.

Minor events associated with treatment were reported to the investigators, but no serious adverse events that could be attributed to the drugs were recorded.

Impact of deworming and iron supplementation on worm infections and anaemia

As Table 4 shows, at follow-up, there was a reduction in prevalence of worm infection in the treatment group, which dropped from 26.2% (as shown in Table 1) to 18.5% with significant differences between treatment and control groups in the levels of *Ascaris* and *Trichuris*. The proportion of anaemic children in the treatment group declined by 3.7% from baseline to follow-up; in the control group, the decline was 5.5%. However, these changes were not significantly different between treatment and control groups.

Effect of deworming and iron supplementation on educational outcomes

Table 5 presents the results of the follow-up educational testing conducted after 6 months of treatment and placebo interventions for both groups. Using the regression model, we were able to assess the impact of treatment on the educational outcomes using the follow-up scores presented in Table 5. Age and sex were controlled for in the basic model to increase the precisions of this study's estimates. The findings are presented

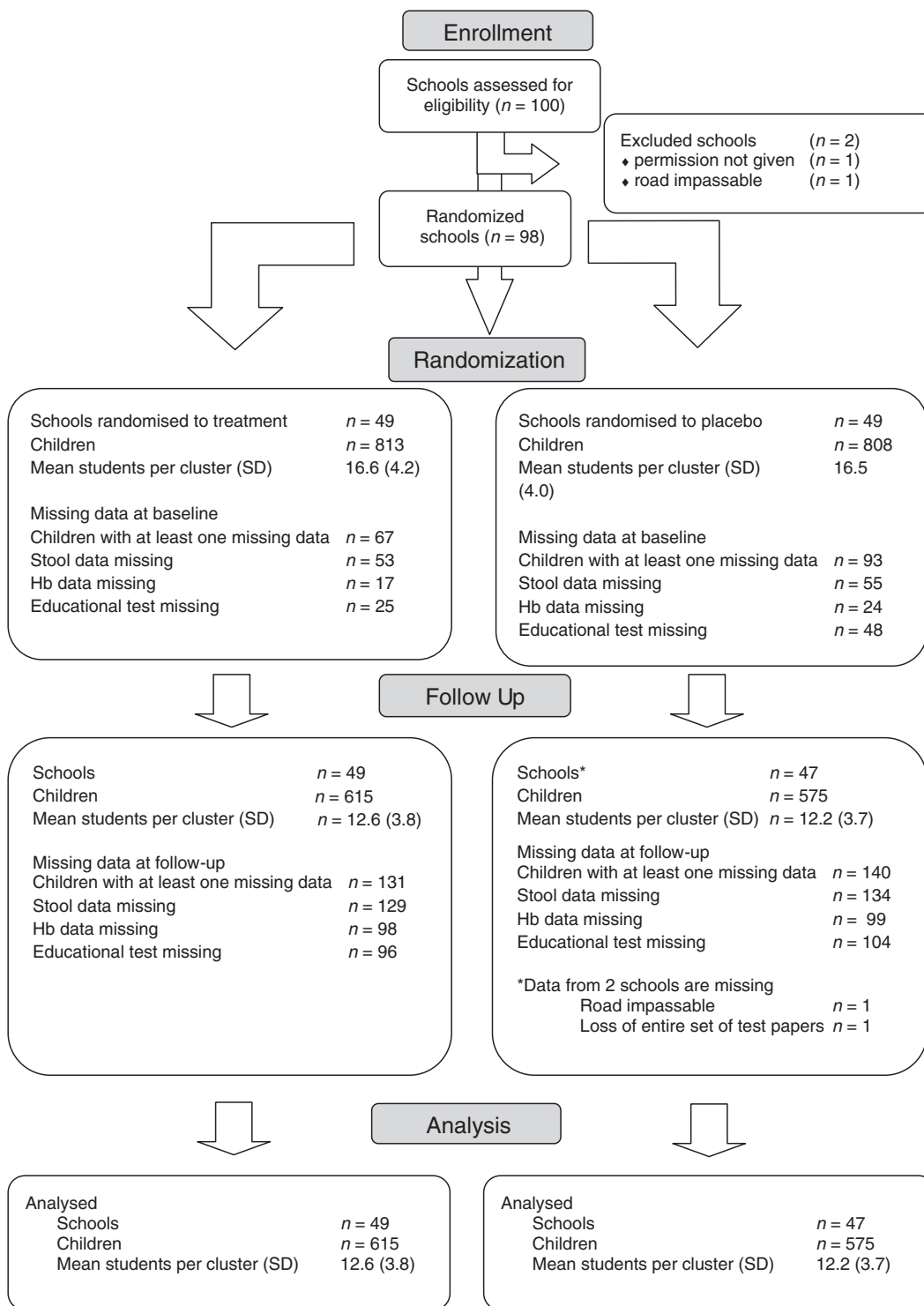


Figure 1 Participatory flow chart.

Table 1 Comparison of basic demographic and health variables at baseline

	Treatment (N = 615)		Control (N = 575)		P
	N	%	N	%	
Anaemia	64	10.4	95	16.5	0.002
Hb					
Mean (g/dl) and (SD)	12.6	(1.13)	12.4	(1.30)	0.010*
Median (g/dl)	12.6		12.5		
Any helminth infection	161	26.2	145	25.2	0.705
Roundworm infection	128	20.8	122	21.2	0.864
Whipworm infection	46	7.5	27	4.7	0.046
Hookworm infection	34	5.5	29	5.0	0.709
<i>Ascaris</i> intensity category					
Light	80	13.0	70	12.2	0.553
Moderate	42	6.8	49	8.5	
Heavy	06	1.0	03	0.5	
<i>Trichuris</i> intensity category					
Light	42	6.8	24	4.2	0.128
Moderate	04	0.7	03	0.5	
Heavy	00	0.0	00	0.0	
Hookworm intensity category					
Light	31	5.0	26	4.5	0.981
Moderate	02	0.3	02	0.4	
Heavy	01	0.2	01	0.2	
Age in months – mean (SD)	114	(8.6)	114	(7.8)	0.193*
Females	310	50.4	269	46.8	0.211
Low Body Mass Index	260	42.3	252	43.8	0.590
Stunting	168	28.1	164	29.4	0.626
Children receiving midday meal	473	76.9	463	80.5	0.129
Mother's education					
No school	81	13.2	48	8.4	0.044
Not completed primary	112	18.2	98	17.0	
Completed primary only	197	32.0	218	37.9	
Completed secondary	80	13.0	80	13.9	
Missing	145	23.6	131	22.8	
Father's education					
No school	58	9.4	54	9.4	0.045
Not completed primary	76	12.4	85	14.8	
Completed primary only	246	40.0	250	43.5	
Completed secondary	90	14.6	91	15.8	
Missing	145	23.6	95	16.5	

Unless indicated, *P* values are based on chi-squared test.**P* value based on *t* test. (SD) Standard Deviation.

in Table 6. Even after controlling for baseline differences in background variables (such as anaemia and parental education), treatment was not found to have a significant impact on cognitive test and educational test scores.

As previous studies have suggested that children with the heaviest worm loads or children with poor nutritional status at baseline may benefit most from the treatment, the interaction between treatment and each of our main explanatory variables were assessed, namely worm infection, baseline anaemia, baseline stunting and low Body Mass Index at baseline. In our second model, this

hypothesis was tested by controlling for each of these interactions, but none were found to be significant.

Discussion

We found no impact of deworming and iron supplementation on Hb levels, anaemia and cognitive test and educational test scores, although the programme was successful in reducing the overall prevalence of worm infections in the treated population over the 6 months of follow-up. Some studies that examined re-infection rates

Table 2 Baseline comparison of cognitive and educational tests

Variable	Treatment (N = 615)	Control (N = 575)	t	P
Code-Transmission single digit (max = 20)	12.4 (6.3)	13.0 (6.3)	1.50	0.134
Code-Transmission double digit (max = 20)	7.4 (5.3)	7.7 (5.5)	0.83	0.407
General education math test (max = 100)	35.7 (25.3)	36.7 (25.6)	0.65	0.516
General education Tamil test (max = 100)	44.9 (25.6)	44.7 (26.7)	0.14	0.887

Table 3 School attendance between baseline and follow-up surveys, and treatment compliance data for treatment and control groups

	Treatment (N = 615)		Control (N = 575)		X ²	P
	N	%	N	%		
Good attendance (80% of school days or more)	378	61.5	351	61.0	0.0221	0.882
Partial attendance	237	38.5	224	39.0		
Treatment compliance						
Mebendazole						
Treated	602	97.9	524	93.6	13.65	<0.001
Not treated	13	2.1	36	6.4		
Iron						
Full dose (16 + tablets)	519	84.4	442	76.9	16.31	<0.001
Partial	92	15.0	115	20.0		
No treatment (4 or less)	4	0.6	18	3.1		

6–12 months after treatment reported rebound to near baseline levels (Albonico *et al.* 1995; Kightlinger *et al.* 1995). However, these studies started with much higher baseline prevalence rates than the present study. As the overall prevalence rate at baseline was over 20%, there is an obvious need for a regular deworming programme in plantations (WHO 2011). The findings demonstrate that school-based deworming can provide an effective alternative to community-based deworming, which is more demanding in terms of logistics and expense.

The results also suggest that the anthelmintic treatment was effective against roundworm and whipworm infections, but not hookworm infection. In contrast to the

Table 4 Comparison of health outcome variables at follow-up

Variable	Treatment (N = 615)		Control (N = 575)		P
	N	%	N	%	
Anaemia	41	6.7	63	11.3	0.007
Change from baseline	23	3.7	32	5.5	0.134
Hb					
Mean (g/dl) and (SD)	12.5	(1.3)	12.2	(1.6)	0.001*
Median (g/dl)	12.6		12.3		
Mean difference in Hb levels from baseline to follow-up (SD)	-0.11	(1.5)	-0.20	(1.7)	0.342
Any helminth infection	114	18.5	163	28.4	<0.001
Roundworm infection	88	14.3	141	24.5	<0.001
Whipworm infection	30	4.9	49	8.5	0.012
Hookworm infection	49	8.0	50	8.7	0.649
<i>Ascaris</i> intensity category					
Nil	527	85.7	434	75.5	<0.001
Light	66	10.7	81	14.1	
Moderate	20	3.3	48	8.4	
Heavy	2	0.3	12	2.1	
<i>Trichuris</i> intensity category					
Nil	585	95.1	526	91.5	0.006
Light	26	4.2	48	8.4	
Moderate	4	0.6	1	0.2	
Heavy	–	–	–	–	
Hookworm intensity category					
Nil	566	92.0	525	91.3	0.751
Light	47	7.6	46	8.0	
Moderate	1	0.2	1	0.2	
Heavy	1	0.2	3	0.5	

Unless indicated, *P* values are based on chi-squared test. **P* value based on *t* test. (SD) Standard Deviation.

prevalence of roundworm which dropped from 20.8% at baseline to 14.3% at follow-up 6 months later, and whipworm, which also dropped from 7.5% to 4.9%, hookworm infection rose from 5.5% to 8.0% in the treatment group. This is consistent with the evidence from other efficacy trials that mebendazole is not as effective in treating hookworm as it is in treating roundworm or whipworm infections (Keiser & Utzinger 2008).

The impact of the programme on Hb status and anaemia is less clear. The overall prevalence of anaemia in this study population is comparable with recent findings in other studies of anaemia among schoolchildren in Sri Lanka (Pathmeswaran *et al.* 2005; Jayatissa & Ranbanda

Table 5 Follow-up comparison of cognitive and educational test scores (summary change from baseline = follow up scores – baseline scores)

Variable Statistics/ parameter	Treatment (N = 615) Mean (SD)	Control (N = 575) Mean (SD)	Difference between arms Mean (SD)	95% CI for the difference
Code-Transmission single digit (max = 20)	15.8 (5.3)	16.0 (5.1)	–0.22 (0.3)	–0.8 – 0.4
Change from baseline	3.4 (6.1)	3.0 (6.3)	0.33 (0.4)	–0.4 – 1.0
Code-Transmission double digit (max = 20)	10.2 (5.4)	10.2 (5.8)	–0.01 (0.3)	–0.6 – 0.6
Change from baseline	2.8 (5.6)	2.6 (5.5)	0.25 (0.3)	–0.4 – 0.9
General education math test (max = 100)	49.6 (27.1)	48.9 (27.5)	0.68 (1.6)	–2.4 – 3.8
Change from baseline	13.9 (17.4)	12.2 (16.1)	1.6 (1.0)	–0.3 – 3.6
General education Tamil test (max = 100)	55.1 (25.9)	56.2 (27.1)	–1.2 (1.5)	–4.2 – 1.9
Change from baseline	10.2 (17.3)	11.5 (16.8)	–1.4 (1.0)	–3.3 – 0.6

Table 6 Regression models for results of the follow-up cognitive and educational testing

	Effect	SE	t	P
Single digit Code-Transmission test				
Baseline	0.34	0.03	12.5	<0.001
Treatment	–0.13	0.37	0.35	0.730
Age	–0.034	0.018	1.86	0.066
Sex	–0.52	0.34	1.52	0.131
Intercept	15.8			
Double digit Code-Transmission test				
Baseline	0.50	0.03	17.2	<0.001
Treatment	0.08	0.39	0.19	0.847
Age	–0.024	0.016	1.52	0.131
Sex	–0.27	0.35	0.77	0.444
Intercept	9.3			
Math test				
Baseline	0.85	0.02	40.8	<0.001
Treatment	1.53	1.42	1.08	0.284
Age	–0.14	0.057	2.45	0.016
Sex	–1.18	0.93	1.27	0.209
Intercept	34.1			
Tamil test				
Baseline	0.77	0.02	37.7	<0.001
Treatment	–1.42	1.24	1.14	0.255
Age	–0.30	0.062	4.80	<0.001
Sex	2.92	0.97	3.03	0.003
Intercept	54.1			

2006). Hb levels dropped from baseline to follow-up assessments in both treatment and control groups, but summary changes in the mean Hb and prevalence of anaemia were not significantly different in the two groups. This overall outcome is puzzling, particularly because a recent systematic review found that intermittent iron supplementation is efficacious in improving haemoglobin concentrations and reduced the risk of anaemia or iron deficiency compared to placebo in children under 12 (De-Regil *et al.* 2011). It is possible

that the study captured a downward drift in Hb levels that results from untreated hookworm infections and dietary deficiency of iron. It is also possible, although unlikely, that the use of microcuvettes from two different manufacturing lots at baseline and at follow-up surveys resulted in a systematic error in Hb measurement. The results suggest that single-dose mebendazole had little impact on hookworm infections and that the weekly iron supplement of 60 mg of elemental iron may be insufficient to counteract the downward drift in Hb levels.

Based on data from three trials, the recent Cochrane review on deworming drugs for soil-transmitted intestinal worms in children suggested that single dose deworming probably had little or no impact on haemoglobin (Taylor-Robinson *et al.* 2012). The same review suggested that single dose deworming has little or no effect on cognition (based on data from two trials). However, another recent review of the effects of deworming on health, on child development and on economic returns questions the validity of using Cochrane processes to assess benefits of deworming (Bundy *et al.* 2013).

We found no difference in school attendance between baseline and follow-up surveys in the treatment and control groups. This in contrast to the observations of Miguel and Kremer (2004), who found that a school-based mass deworming programme in Kenya reduced absenteeism by one-quarter. It is possible that these differences are due to differences in the baseline prevalence and intensity of STH infections. The majority of children in our study had light infections of *A. lumbricoides*, whereas hookworm is much more common in Kenya. It is also possible that the Kenyan children had much heavier intensities of infection than those in our study population.

A few limitations of the study must be noted. First, there were significant differences between treatment and control groups in terms of mean Hb levels and prevalence

of anaemia, as well as in the background variables of parental education. However, we were able to adjust for these differences in the final regression model. Secondly, there was about 25% loss of study participants from allocation to final analysis, with missing data from two entire schools in the control group. However, it is unlikely that this degree of loss due to incomplete data had a significant impact on the final results because it was similar in both arms.

The findings presented here suggest that the use of single-dose mebendazole in a mass deworming programme may result in overall reduction of STH prevalence, but has little impact on hookworm infections. In such a situation, even with intermittent oral iron supplementation, there may be little or no improvement in anaemia and in educational outcomes.

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References

- Albonico M, Smith PG, Ercole E *et al.* (1995) Rate of reinfection with intestinal nematodes after treatment of children with mebendazole or albendazole in a highly endemic area. *Transactions of the Royal Society of Tropical Medicine & Hygiene* **89**, 538–541.
- Ash LR, Orihel TC, Savioli L, Sin MA, Montresor A & Renganathan E (1998) Training Manual on Diagnosis of Intestinal Parasites. World Health Organization, Geneva.
- Bernstein DA, Penner LA, Clarke-Stewart A & Roy EJ (2008) Psychology, 6th edn. Houghton–Mifflin Company, Boston, MA, USA.
- Boivin MJ & Giordani B (1993) Improvements in cognitive performance for schoolchildren in Zaire, Africa, following an iron supplement and treatment for intestinal parasites. *Journal of Pediatric Psychology* **18**, 249–264.
- Brooker S, Okello G, Njagi K *et al.* (2010) Improving educational achievement and anaemia of school children: design of a cluster randomised trial of school-based malaria prevention and enhanced literacy instruction in Kenya. *Trials* **11**, 93.
- Bundy DA, Walson JL & Watkins KL (2013) Worms, wisdom, and wealth: why deworming can make economic sense. *Trends in Parasitology* **29**, 142–8.
- Clarke SE, Jukes MCH, Njagi JK *et al.* (2008) Effect of intermittent preventive treatment of malaria on health and education in schoolchildren: a cluster-randomized, double-blind, placebo-controlled trial. *Lancet* **372**, 127–138.
- De-Regil LM, Jefferds MED, Sylvetsky AC & Dowswell T (2011) Intermittent iron supplementation for improving nutrition and development in children under 12 years of age (Review). *Cochrane Database of Systematic Reviews* Issue 12. Art. No.: CD009085. DOI: 10.1002/14651858.CD009085.pub2.
- Fernando D, de Silva D, Carter R, Mendis KN & Wickremasinghe R (2006) A randomized, double-blind, placebo-controlled, clinical trial of the impact of malaria prevention on the educational attainment of schoolchildren. *American Journal of Tropical Medicine and Hygiene* **74**, 386–393.
- Freeman HE, Klein RE, Townsend JW & Lechtig A (1980) Nutrition and cognitive development among rural Guatemalan children. *American Journal of Public Health* **70**, 1277–1285.
- Gunawardena NK, Kumarendran B, Ebenezer RE, Gunasingha MS, Pathmeswaran A & de Silva NR (2011) Soil transmitted helminth infections among plantation sector school children in Sri Lanka: prevalence after ten years of preventive chemotherapy. *PLoS Neglected Tropical Diseases* **5**, e1341.
- Halterman JS, Kaczorowski JM, Aligne CA, Auinger P & Szilagyi PG (2001) Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States. *Pediatrics* **107**, 1381–1386.
- Hedges LV & Hedberg EC (2007) Intraclass correlation values for planning group-randomized trials in education. *Educational Evaluation And Policy Analysis* **29**, 60–87.
- Jardim-Botelho A, Raff S, Rodrigues Rde A *et al.* (2008) Hookworm, *Ascaris lumbricoides* infection and polyparasitism associated with poor cognitive performance in Brazilian schoolchildren. *Tropical Medicine & International Health* **13**, 994–1004.
- Jayatissa R & Ranbanda RM (2006) Prevalence of challenging nutritional problems among adolescents in Sri Lanka. *Food Nutrition Bulletin* **27**, 153–160.
- Jukes MCH, Drake LJ & Bundy DAP (2008) School Health, Nutrition and Education for All: Levelling the Playing Field. CABI Publishing, Wallingford, UK.

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- Keiser J & Utzinger J (2008) Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. *JAMA* **299**, 1937–1948.
- Kightlinger LK, Seed JR & Kightlinger MB (1995) The epidemiology of *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm in children in the Ranomafana rainforest, Madagascar. *Journal of Parasitology* **81**, 159–169.
- Magnani R (1997) Sampling Guide: Food and Nutrition Technical Assistance Project (FANTA). Academy for Educational Development, Washington, DC, p. 46.
- Manly T, Robertson IH, Anderson V & Nimmo-Smith I (1998) Test of Everyday Attention for Children (TEA-Ch). Thames Valley Test Company, Bury St Edmunds.
- Miguel E & Kremer M (2004) Worms: identifying impacts on education and health in the presence of treatment externalities. *Econometrica* **72**, 159–217.
- Montresor A, Crompton DWT, Gyorkos TW & Savioli L (2002) Helminth Control in School-age Children: A Guide for Managers of Control Programmes. World Health Organization, Geneva.
- NEREC (National Education and Research Evaluation Centre) (2012) National assessment of achievement of students completing Grade 04 in year 2006. NEREC, University of Colombo. Available at: <http://edu.cmb.ac.lk/nerec/?p=124>
- Nokes C, Grantham-McGregor SM, Sawyer AW, Cooper ES & Bundy DAP (1992) Parasitic helminth infection and cognitive function in school children. *Proceedings of the Royal Society of London. Series B: Biological Sciences* **247**, 77–81.
- Pathmeswaran A, Jayatissa R, Samarasinghe S *et al.* (2005) Health status of primary schoolchildren in Sri Lanka. *Ceylon Medical Journal* **50**, 46–50.
- PCD (The Partnership for Child Development) (2002) Heavy schistosomiasis associated with poor short-term memory and slower reaction times in Tanzanian schoolchildren. *Tropical Medicine and International Health* **7**, 104–117.
- Pollitt E, Hathirat P, Kotchabhakdi NJ, Missell L & Valyasevi A (1989) Iron deficiency and educational achievement in Thailand. *American Journal of Clinical Nutrition* **50**, 687–697.
- Powell CA, Walker SP, Chang SM & Grantham-McGregor SM (1998) Nutrition and education: a randomized trial of the effects of breakfast in rural primary school children. *American Journal of Clinical Nutrition* **68**, 873–879.
- Pullan RL & Brooker SJ (2012) The global limits and population at risk of soil-transmitted helminth infections in 2010. *Parasites & Vectors* **5**, 81.
- Sakti H, Nokes C, Hertanto WS *et al.* (1999) Evidence for an association between hookworm infection and cognitive function in Indonesian schoolchildren. *Tropical Medicine and International Health* **4**, 322–334.
- Simeon DT, Grantham-McGregor SM, Callender JE & Wong MS (1995) Treatment of *Trichuris trichiura* infections improves growth, spelling scores, and school attendance in some children. *Journal of Nutrition* **125**, 1875–1883.
- Soemantri AG, Pollitt E & Kim I (1985) Iron deficiency anaemia and educational achievement. *American Journal of Clinical Nutrition* **42**, 1221–1228.
- Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S & Garner P (2012) Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance. *Cochrane Database of Systematic Reviews* Issue 11. Art. No.: CD000371. DOI: 10.1002/14651858.CD000371.pub5.
- Vicotra CG, Black RE, Boerma JT & Bryce J (2011) Measuring impact in the Millennium Development Goal era and beyond: a new approach to large-scale effectiveness evaluations. *Lancet* **377**, 85–95.
- WHO (World Health Organization) (2011) Helminth Control in School Age Children: A Guide for Managers of Control Programmes, 2nd edn. World Health Organization, Geneva, p. 75.
- WHO/CDC (2008) World Health Organization/Centers for Disease Control and Prevention (USA). Worldwide prevalence of anaemia 1993–2005. In: WHO Global Database on Anaemia (eds de Benoist B, McLean E, Egli I & Cogswell M) World Health Organization, Geneva, p. 7.

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