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Evidence Summaries

Does regular deworming of school children in areas endemic for intestinal worms improve their physical health and school performance? Summary of the evidence and implications for public health programmes

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ABSTRACT

An update of a Cochrane Review summarized the effects on nutritional indicators, haemoglobin, cognition, school attendance; and the impacts on school performance and mortality of deworming programmes for soil-transmitted intestinal worms in children from randomised, quasi-randomised, and cluster randomised trials. It included data from 41 trials that randomised 65,168 children (<17 years) in high, medium, and low helminth-endemic areas from 23 countries in Africa, China, South Asia, and South East Asia, to selective or targeted deworming (with mostly albendazole or mebendazole), or to placebo or no treatment.

The review found that selective deworming programmes, where schoolchildren screened and detected to be infected with intestinal helminths are treated, will probably increase weight and haemoglobin but the evidence base is small. The effects of multiple doses of deworming drugs given to children without screening for infection and followed up for more than one year were uncertain for all outcomes sought due to the very low quality of the evidence.

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1. The evidence

An update of a Cochrane Review of 41 community-based clinical trials that randomised 65,168 children below 17 years from 23 countries in Africa, China, South Asia, and South East Asia found that:

- In children identified as infected after screening, a single dose of deworming drugs probably increased weight and

may have increased haemoglobin, compared to no deworming, but its effects on school performance were uncertain.

- Single or multiple doses of deworming drugs given to all school children in endemic areas without screening had inconsistent or uncertain benefit, or little evidence of benefit, on their physical health or school attendance.

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Review on which this evidence summary is based

Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P. Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance. *Cochrane Database of Systematic Reviews* 2012, Issue 7. Art. No.: CD000371. <http://dx.doi.org/10.1002/14651858.CD000371.pub4>.

This evidence summary is based on the substantial update of the referenced Cochrane systematic review that was first published in 1998, and updated in 2000, 2007 and most recently in 2012. This summary presents an overview of the findings and the implications for low and middle income countries. For further details, please read the full review that can be downloaded, free of charge (through various funded provisions) in most parts of the world, from *The Cochrane Library* (www.thecochranelibrary.com). The results of this updated review were debated extensively in: *The PLOS Medicine Community Blog* of July 18, 2012: Should deworming policies in the developing world be reconsidered? (<http://blogs.plos.org/speakingofmedicine/>); *The Berkeley Blog: Cochrane's incomplete and misleading summary of the evidence on deworming* (<http://blogs.berkeley.edu/2012/07/20/cochrane-incomplete-and-misleading-summary-of-the-evidence-on-deworming/>); and *The GiveWell Blog* (<http://blog.givewell.org/2012/07/13/new-cochrane-review-of-the-effectiveness-of-deworming/>).

- Deworming involves single or multiple doses of anti-helminthic drugs (commonly albendazole or mebendazole) given once, twice, or thrice a year to children in endemic areas, depending on the prevalence of infection, and the likelihood of re-infection.
- While deworming can be selectively given to children identified by screening to be infected, screening increases costs; and WHO promotes community and school programmes that give deworming drugs regularly to all children in low-income countries (targeted deworming) in order to improve their nutrition, haemoglobin, cognition, school attendance, school performance and to promote economic productivity.
- Many countries have adopted routine periodic targeted deworming of school children and this policy has many advocates, including the World Bank and many other organisations that consider it one of the most cost-effective interventions for global health. Consequently, a considerable amount of public money is invested in achieving the postulated benefits.
- Others question these estimates and argue that the apparent benefits may apply to some helminthic infections such as schistosomiasis, but not necessarily to all helminthic infections.
- The 2007 version of this Cochrane review reported uncertainty about the assumed benefits and concluded that deworming may be effective in relation to weight gain in the short-term in some areas, but not in others. The potential long-term impact on weight was unclear, and no convincing effect on school performance was evident from the very limited data available.
- The current update included more studies, added schooling as an outcome, and incorporated advances in the methods of research synthesis developed by The Cochrane Collaboration since the previous review.

2. Why is this question important?

- The World Health Organization (WHO) reports that around 270 million pre-school children and over 600 million school children live in areas where they are likely to be infected with one or more of the soil-transmitted intestinal worms.¹
- These worm infections have been shown to lead to anaemia and to limit physical and cognitive development through impaired absorption of nutrients and loss of appetite.

What did the systematic review seek and what did they find?

Review objectives: To summarise the effects on nutritional indicators, haemoglobin, cognition, school attendance; and the impacts on school performance and mortality of deworming programmes for soil-transmitted intestinal worms (nematode geohelminths) in children.

	What did the review authors search for?	What did the review find?
Types of studies	Randomised controlled trials, quasi-randomised trials (where allocation may be predicted) and cluster randomised trials with more than two clusters allocated to each arm.	Forty-two trials reported in 53 articles (including one unpublished trial with no available results) met the inclusion criteria. The included trials were conducted in 23 countries: Bangladesh (four trials); Ethiopia (two trials); Haiti (two trials); India (five trials); Indonesia (two trials); Jamaica (two trials); Kenya (five trials); South Africa (two trials); Vietnam (three trials); Zanzibar (two trials); Benin, Botswana, Cameroon, Guatemala, Java, Malaysia, Nigeria, Philippines, Sierra Leone, Tanzania, Uganda, Zaire (one trial in each); China, Philippines and Kenya (one multicentre trial).

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	What did the review authors search for?	What did the review find?
Setting	Communities (drugs could be administered in health facilities, schools, and communities).	Nine of the trials randomised clusters (schools, development blocks, urban slums, households, etc.). Four trials used factorial designs aimed at assessing the potential interaction of nutritional supplements combined with deworming. Children were recruited from schools or the community in 36 trials, and from health facilities in six.
Participants	Children less than 17 years randomised in the community. Trials of sick children or children being treated for malnutrition were excluded.	One trial recruited adolescents aged 17–19 years, but the trials predominantly included children less than 17 years.
Interventions	Single or multiple doses of deworming drugs (WHO recommended) for geohelminth worms versus placebo or no treatment. Studies that provided other additional interventions (e.g. growth monitoring, micronutrient supplementation, malaria chemoprevention, or other drugs) to both intervention and control arms were also included.	Twenty-nine trials used albendazole, of which five additionally used other anti-helminthic drugs in both arms. Mebendazole was used in ten trials, two of which combined it with pyrantel. Pyrantel palmoate was used in three trials, piperazine in two, piperazine citrate, tetracholoethylene, and levimasole in one trial each. Most trials used placebo or no treatment in the control group, while four used vitamins or calcium powder. In 13 trials, both arms were also given nutritional supplements. Thirty-five trials used mass targeted treatment of an unscreened population. Fourteen of these trials were conducted in populations where worms were of high prevalence or intensity, 10 in populations with moderate prevalence and low intensity, and 11 in populations with low prevalence and low intensity. Seven trials studied children that were screened and selected on the basis of their having high worm loads.
Outcomes	The primary outcomes of the review were weight, haemoglobin, and psychometric tests of cognition. The secondary outcomes sought were other nutritional indicators such as height, measures of well-being, school attendance, and school performance (measured by examination results), death due to any cause, serious adverse events of drugs such as death, life threatening events, or events leading to hospitalisation, and other adverse events.	Nutritional indicators were measured in 42 trials; not all trials reported data in a form that could be used in meta-analyses. Seventeen trials measured haemoglobin, and data from five of these trials could not be used in meta-analysis. Nine trials measured intellectual development using formal tests. Two trials measured physical well-being using the 100-point Harvard Step Test. Three trials measured school attendance, and one trial evaluated performance in examinations. Two trials provided data on adverse events. One study of one million children conducted in India studied mortality as the primary outcome and the results are awaited.
Date of the last search: 31 May 2012		
Funding sources: Liverpool School of Tropical Medicine, UK; Department for International Development, UK. The funding sources had no role in the production of this review.		
Limitations: None detected. This review followed standard methods of the Cochrane Collaboration and the Cochrane Infectious Diseases Group. The review authors assessed the overall quality of the evidence for the pre-selected outcomes considered important to decision-making using the GRADE approach, and used additional criteria in assessing risk of bias in cluster randomised trials. This update addressed comments on the previous version of the review and demonstrated no differential effects when trials were stratified by the intensity of the infection or by the duration of follow up. The review failed to find consistent effects for deworming in large studies done in the past 10 years compared to the benefits in three trials done more than 15 years ago, and this suggested that secular trends in decreasing worm burden may underpin this lack of benefit in the later studies.		
What were the effects of deworming on the main outcomes sought in the review?	The review presented five sets of comparisons. This evidence update presents the summary of findings (adapted from the Cochrane review) for two of these comparisons (Tables 1 and 2). Selective deworming: A single dose of deworming drugs in infected children probable increased weight and may have increased haemoglobin levels, but the effects on cognition were uncertain due to insufficient data (Table 1). Single dose deworming in infected children also resulted in	

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gains in terms of mid-upper arm circumference, triceps and subscapular skinfold values; though no difference in height or body mass index were detected. Data on formal tests for cognition were inadequate. No data for school attendance, school performance, mortality or adverse events were reported.

Targeted deworming: The effects of multiple doses of deworming drugs given to children without screening for infection and followed up for more than one year were uncertain for all outcomes sought due to the very low quality of the evidence (Table 2).

Multiple dose deworming drugs for treating soil-transmitted intestinal worms in unscreened children, did not significantly increase the mean weight measured within one year in seven trials of 2460 children done in high (2), medium (2) and low prevalence (3) areas. Very low quality evidence for haemoglobin levels, cognition and school attendance also demonstrated no significant differences with deworming compared to no deworming.

A single dose of deworming drugs given to children as part of targeted deworming (not screened for infection) in communities endemic for soil-transmitted worm infection had uncertain effects on weight gain, as beneficial effects were only seen in two early trials done in the same location in Kenya and not in seven subsequent trials done elsewhere. Its effects on haemoglobin were not significant and on cognitive performance were uncertain due to lack of useable data. It may have a benefit on physical well-being with a 6% difference (4%–8%) seen in in two trials done in the same high prevalence area in Kenya.

Stratified analysis to seek subgroup effects in trials from low, medium and high endemic areas did not demonstrate any differences in effects. No significant effects for any primary outcomes were detected in a sensitivity analysis only including trials with adequate allocation concealment.

Data on mortality are awaited from one completed trial of one million children in India that is yet to be published. In another trial from the same area in India, deaths did not differ with deworming (10 deaths) and without deworming (13 deaths).

What were the effects of deworming drugs on other outcomes?

Data were not available for adverse events and school attendance (children dropping out). Narratively reported data on height and weight in three trials did not show significant effects with deworming.

What were the conclusions of the review?

The review authors concluded that “it is *probably misleading to justify contemporary deworming programmes based on evidence of consistent benefit on nutrition, haemoglobin, school attendance or school performance as there is simply insufficient reliable information to know whether this is so*”.

What were the assessments of the overall quality of the evidence?

The overall evidence quality was graded low or very low using the GRADE approach for important outcomes in the review. This indicates uncertainty in the effect estimates.

It might appear that some of these judgements were unduly severe. However, higher grades of evidence quality would only increase our confidence in the estimates showing little or no benefit with deworming drugs.

Did the results and conclusions of the review differ from other reviews on this topic?

The results of this review differed from those of an earlier World Bank funded review and meta-analysis² that presented evidence in favour of an effect of deworming on weight gain (mean difference 0.21 kg 95% CI 0.17 to 0.26, 11 studies); and a narrative review⁷ that explored the evidence for the impact of deworming on pre-school age children, and concluded that deworming has been shown to improve growth.

The systematic approach and robust methods of the Cochrane review and the differences in the studies included explain the differing conclusions.

What are the implications of the review for public health?

1. Selective deworming programmes, where school children screened and detected to be infected with intestinal helminths are treated, will probably increase weight and haemoglobin but the evidence base is small. The frequency of the screening, the resource costs, and the effectiveness of subsequent doses are not known.

2. There is insufficient evidence from randomised trials to recommend deworming drugs in community programmes targeting school children who are not detected to have worm infestations.

3. Countries that are implementing such mass deworming programmes should consider the evidence in this review before continuing to fund such programmes. Although harms were not demonstrated for deworming, the assumed benefits do not appear sufficient to justify commitment of resources to deliver such programmes at the expense of other potentially beneficial approaches such as improving sanitation, water quality, and nutrition.

4. If current deworming programmes are continued in spite of the lack of supporting evidence from this systematic review of RCTs, then outcomes such as changes in nutritional indicators and school performance as a result of these programmes should be evaluated to justify their continuation.

Table 1 – Selective deworming: single dose deworming drugs for treating soil-transmitted intestinal worms in children living in areas endemic for intestinal helminths screened and detected as infected. Summary of findings on the effects on nutrition and school performance: follow up 4–16 weeks.

Outcomes	Comparative absolute effects (95% CI)		Number of participants (trials)	Overall evidence quality
	No deworming ^a	Deworming: single dose		
Weight (kg)		The mean weight (kg) with the intervention was 0.58 higher (0.4–0.76 higher)	149 (3)	Moderate (downgraded for serious study limitations)
Haemoglobin (g/dL)		The mean haemoglobin (g/dL) with the intervention was 0.37 higher (0.1–0.64 higher)	108 (2)	Low (downgraded for serious study limitations and serious imprecision)
Formal tests of cognition		Data from two trials could not be pooled	(2)	Very low (data not reported adequately)

a The trials used endpoint values or changes from baseline values that were pooled in meta-analyses; CI = confidence intervals.

Table 2 – Targeted deworming: multiple doses of deworming drugs for treating soil-transmitted intestinal worms given to children who were not screened for infection and were living in areas endemic for intestinal helminths: summary of findings on the effects on nutrition and school performance measured after one year.

Outcomes	Comparative absolute effects (95% CI)		Number of randomised units (trials)	Overall evidence quality
	No deworming ^a	Deworming: multiple doses		
Weight (kg) Follow up: 1.5–3 years		One cluster trial in India (2008) showed an average difference of 0.98 kg but in 6 trials non-significant differences of less than 0.2 kg weight gain were seen	2460 (302 clusters, 1045 individually randomised children) (7)	Very low (downgraded for study limitations, inconsistency, and imprecision)
Height (cm) Follow up: 1.5–2 years		The mean height (cm) with the intervention was 0.26 lower (0.84 lower to 0.31 higher)	1219 (174 clusters, 1045 individually randomised children) (3)	Very low (downgraded for study limitations and imprecision)
Haemoglobin (g/dL) Follow up: 14 months–2 years	The mean haemoglobin in the control groups ranged from 9 to 10 g/dL	The mean haemoglobin (g/dL) with the intervention was 0.02 lower (0.03 lower to 0.27 higher)	1365 (2)	Very low (downgraded for study limitations)
Formal tests of cognition Follow up: 2 years		No significant difference was seen with the intervention in two trials (data could not be pooled)	(2)	Very low (downgraded for study limitations)
School attendance Follow up: 2 years	The mean school attendance in the control group was 66.3%	The mean attendance with the intervention was 5% higher (0.5% lower to 10% higher)	50 clusters (1)	Very low (downgraded for study limitations)
Death		Data from one completed study in India are not published as yet	One million children (1)	

a Some trials reported endpoint values and others presented changes from baseline values that were pooled in meta-analyses; CI = Confidence intervals.

Conflicts of interest

Thambu David Sudarsanam and Prathap Tharyan are contributors to The Cochrane Collaboration. TDS is an editor with the Cochrane Infectious Diseases Group. PT is a programme partner of the Effective Health Care Research Consortium.

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