

Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance (Review)

Taylor-Robinson DC, Jones AP, Garner P



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ABSTRACT

Background

In areas where intestinal worm infections occur, the World Health Organization recommends treating all school children at regular intervals with deworming drugs to improve growth and school performance. The evidence base for this policy needs to be established for countries to commit resources to implement these programmes.

Objectives

To summarize the effects of deworming drugs used to treat soil-transmitted intestinal worms (nematode geohelminths) on growth and school performance in children.

Search strategy

In May 2007, we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (*The Cochrane Library* 2007, Issue 2), MEDLINE, EMBASE, LILACS, *m*RCT, and reference lists.

Selection criteria

Randomized and quasi-randomized controlled trials (RCTs) comparing deworming drugs for geohelminth worms with placebo or no treatment in children aged 16 years or less, reporting on growth, nutritional status, school performance, or cognition tests.

Data collection and analysis

Two authors independently assessed the trials and evaluated methodological quality; one author extracted data, and another checked a sample. Continuous data were analysed using the weighted mean difference (WMD) with 95% confidence intervals (CI). The random-effects model (RE model) was used in the presence of statistically significant heterogeneity.

Main results

Thirty-four RCTs, including six cluster-RCTs, met the inclusion criteria. Four trials had adequate allocation concealment, and three cluster-RCTs failed to take design effects into account in their analysis. Weight increased after one dose of a deworming drug (WMD 0.34 kg, 95% CI 0.05 to 0.64, RE model; 2448 children, 9 trials); however, there was considerable heterogeneity between trials that was not explained by background intestinal worm infection or intensity. A meta-analysis of multiple dose trials reporting on outcomes within a year of starting treatment showed no significant difference in weight gain (1714 children, 6 trials); however, one cluster-RCT did show effects on weight at one year in a subgroup analysis. In the seven multiple dose trials with follow up beyond 12 months, only one showed a significant increase in weight. Six of seven trials reported clear data on cognitive tests and school performance: five reported no significant effects, and one showed some improvements in three out of 10 cognitive tests.

Authors' conclusions

Deworming drugs used in targeted community programmes may be effective in relation to weight gain in some circumstances but not in others. No effect on cognition or school performance has been demonstrated.

PLAIN LANGUAGE SUMMARY

Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

About a quarter of the world's population is infected with one or more soil-transmitted worms. The main soil-transmitted worms are roundworms, hookworms, and whipworms. Infections are widely distributed in tropical and subtropical areas, with most infected people having more than one type of worm. The burden of disease falls disproportionately on the poor, where there is inadequate sanitation, overcrowding, low levels of education, and lack of access to health care. These infections cause malnutrition and poor growth for children, and some studies have suggested an association with poor performance at school. Improved sanitation and hygiene are likely to be helpful. There are also three basic strategies for using drugs to treat these infections: (1) individual treatment based on a diagnosis of infection (selective treatment); (2) groups at increased risk are treated (targeted treatment); and (3) treating whole communities whether people have the infection or not (universal treatment). The targeted treatment is the one generally used. This review of trials looked at targeted treatment with a range of deworming drugs for children, particularly focusing on growth and school performance. Thirty-four trials were identified. These trials either looked at single or multiple doses, but only some assessed school performance. After just one dose children's weight improved, and more doses did not seem to improve this further. Only one of the seven trials that assessed school performance found any positive effect, so it seems unlikely that there is a benefit here. Two trials looked at adverse events, but the trials were small. Further research is needed.

BACKGROUND

The World Bank rank soil-transmitted worms as number one in terms of global burden of disease in children aged between 5 and 14 years (World Bank 1993). More than a quarter of the world's population is estimated to be infected with one or more of the most common soil-transmitted intestinal worms (nematode geohelminths) (Chan 1997). These include roundworms (*Ascaris lumbricoides*), hookworms (*Necator americanus* and *Ancylostoma duodenale*), and whipworms (*Trichuris trichura*). Infections are widely distributed in tropical and subtropical areas, and most infected people harbour multiple species (Montresor 2002; Cappello 2004). The burden of disease falls disproportionately on the poor, where inadequate sanitation, overcrowding, low levels of education, and lack of access to health care make them particularly susceptible (de Silva 2003b).

The chronic effects of worm infestation are of most concern to policymakers due to their potential effects on the developing child. Hookworm and whipworm disease are associated with iron-deficiency anaemia (Crompton 2000; de Silva 2003a). A fall in blood haemoglobin levels has been associated with increasing intensity of infection (Crompton 2003). Hookworm-induced iron-deficiency anaemia has been associated with decreased physical activity and worker productivity (Crompton 2003).

Worms are associated with malnutrition and growth impairment. Roundworms obtain their nutrition from gastrointestinal contents. The association with malnutrition is possibly mediated through impaired fat digestion, reduced vitamin absorption (particularly vitamin A), and temporary lactose intolerance (WHO 2002). Whipworm infection has also been associated with malnutrition, although the precise mechanism for this is unclear (Cappello 2004). Suggested mechanisms for the effects on growth include appetite suppression, increased nutrient loss, and decreased

nutrient absorption and utilization (Stephenson 2000; de Silva 2003a). Roundworm, hookworm, and whipworm disease have all been associated with impaired physical growth in school children (de Silva 2003a).

Observational studies have reported an association between worm infection and lower scores on tests of school performance (Sakti 1999; Kvalsvig 2003). In a multiple-regression model based on cross-sectional data, Sakti 1999 found that hookworm infection was associated with worse scores in six out of 14 cognitive tests in Indonesian school children. Severe whipworm (*Trichuris* dysentery syndrome) was associated with low IQ, school achievement, and cognitive function after a four-year follow up of a specific group of Jamaican children with severe infection (Callender 1998).

While these associations would suggest potential benefit of deworming, poverty could confound the associations demonstrated. Even with adjustment for known confounding factors, residual confounding could be a problem. Hence randomized controlled trials are important in determining whether these policies are effective.

Policies

Public health interventions to tackle worm infection are either those that improve sanitation and hygiene or are concerned with the administration of drug therapy to the whole population. These have often been coupled with health education. The work of the Rockefeller Sanitary Commission in the early 1900s led to the recognition that sanitary reform was needed alongside chemotherapeutic approaches to have an effect on worm prevalence (Horton 2003). In Japan, worms virtually disappeared over a 20-year period after the Second World War; this has been credited to an integrated programme of sanitary reform combined with screening and treatment of positive cases (Savioli 2002; Horton 2003). A similar experience occurred in Korea (Savioli 2002). The impact

of the chemotherapeutic element is difficult to assess. In countries where an improvement in sanitation and hygiene has occurred as a component of economic growth a parallel decline in the prevalence of geohelminths has occurred: for example, in Italy, between 1965 and 1980, the trichuriasis prevalence dropped from 65% to less than 5% without control activity (Savioli 2002).

The World Health Organization (WHO) policy in 2002 outlined three categories of drug treatment (WHO 2002):

- *Selective*: individual deworming based on a diagnosis of infection.
- *Targeted*: group deworming where a (risk) group is treated without prior diagnosis.
- *Universal*: population deworming in which the whole community is treated irrespective of infection status.

Targeted treatment is promoted in preference to universal approaches. Individual screening is not recommended since the cost is four to 10 times that of the treatment itself. The policy's aim appears to be to control morbidity by reducing the intensity of infection in the most vulnerable populations. The strategy is to target drug treatment at groups: pre-school-age children; school-age children (between six and 15 years); and women of childbearing age. The strategy requires a population survey for prevalence and intensity of infection to determine the appropriate community therapy. This 'community diagnosis' determines the recommended frequency of treatment (Table 01).

The policy promotes the use of schools, maternal and child health clinics, and vaccination campaigns as a means to reach at-risk groups. School-based programmes are advocated due to established delivery channels and utilization of non-medical personnel, with estimated costs varying from US\$ 0.05 to 0.65 per child per year for annual dosing (Savioli 2002; WHO 2002).

In areas with a high prevalence or intensity, the current policy recommends treatment two to three times per year. This is based on modelling and reinfection prevalence studies: following drug treatment worm populations tend to return rapidly to pretreatment levels, in less than a year for roundworm and whipworm (Anderson 1991). Anderson 1991 suggests that to control morbidity in areas of endemic infection, targeted treatment should be repeated every three to four months for roundworm and whipworm, with longer intervals acceptable for longer-lived species such as hookworm.

The WHO recommends monitoring both prevalence and intensity. The control programme is intended to reduce the worm burden in the 10% to 15% of children who are most heavily infected in a particular population and to keep it low through repeated treatments. The aim is to reduce morbidity and improve growth and learning.

Recent policy trends

Current policies being promoted by the WHO (WHO 2002), World Bank (World Bank 2003), and others depend on a belief that mass treatment is effective. Indeed, recently some policymakers advocate treating 'polyparasitism' by treating the parasites that cause ascariasis, trichuriasis, hookworm, lymphatic filariasis, onchocerciasis, schistosomiasis, and trachoma with ivermectin, albendazole, azithromycin, and praziquantel. These four drugs are donated by pharmaceutical companies, and the "overlapping specificity" would mean multiple pathogens would be targeted (Hotez 2006b). There is some conflating of the evidence around these interventions. For example, the WHO states that deworming schistosomes and soil-transmitted helminths helps (1) eradicate extreme poverty and hunger; (2) achieve universal primary education; (3) promote gender equality and empower women; (4) reduce child mortality and improve maternal health; and (5) compact HIV/AIDS, malaria, and other diseases (WHO 2005). It would seem that evaluating the effectiveness of these claims depends on identifying that each ingredient has an effect on the outcomes mentioned in the presence of a particular disease in a community. This review examines the use of deworming drugs for soil-transmitted helminths in relation to growth, nutrition, schooling, and cognition.

Rationale for review

The previous version of this Cochrane Review found limited evidence to support public health policies on deworming, with a small but inconsistent effect on weight gain, and no data to support an effect on cognitive function (Dickson 2000a). The uncertainty raised by this review caused debate, with policy advocates questioning the review findings (Savioli 2000). Because deworming is currently promoted as an effective and cheap way of improving the health of children in poor countries, it is important to establish the evidence base for this potentially powerful intervention. New trials have been recently published, and other unpublished studies have been made available to us. In this review update, we have reapplied the inclusion criteria, repeated data extraction, added new trials, and included additional analyses as recommended by policy specialists. This Cochrane Review does not cover deworming and pregnancy, which is the subject of a separate Cochrane Review (Haider 2005).

OBJECTIVES

To summarize the effects of deworming drugs used to treat soil-transmitted intestinal worms (nematode geohelminths) on growth and school performance in children.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomized and quasi-randomized controlled trials (RCTs) that were randomized by individual or cluster. We excluded cluster-RCTs with only two units of allocation.

Types of participants

Children aged 16 years or less.

Types of intervention

Intervention

Deworming drugs for geohelminth worms, administered at any location (eg health facilities, schools, and communities).

Deworming drugs for geohelminths in the WHO Model List of Essential Medicines (WHO 2006) are albendazole, levamisole, mebendazole, pyrantel, and ivermectin. Others used are nitazoxanide, piperazine, tetrachlorethylene, and thiabendazole.

Control

Placebo or no treatment.

We included trials with concurrent treatment for schistosomiasis only if both intervention and control arms received the same antischistosomal regimen.

Types of outcome measures

Primary

- Growth: changes in weight and height.
- Nutritional status: weight, height, body mass index, mid-upper arm circumference, and skin fold thickness.
- School performance: days absent, number of children dropping out, examination performance.

Secondary

- Any test of cognition (eg tests of memory, concentration, language development, and concept formation).

In trials that report on at least one of our primary or secondary outcomes, we will also extract data, if available, on: (1) measures of fitness or activity; (2) measures of appetite; (3) haemoglobin values.

Adverse events

- Serious adverse events (death, life-threatening events, events leading to hospitalization or significant impairment).
- Adverse events leading to discontinuation of treatment.
- Other adverse events.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Infectious Diseases Group methods used in reviews.

The authors along with the Cochrane Infectious Diseases Group Information Specialist have attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress).

The Information Specialist searched the following databases using the search terms and strategy described in Table 02: Cochrane Infectious Diseases Group Specialized Register (May 2007); Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (2007, Issue 2); MEDLINE (2000 to May 2007); EMBASE (2000 to May 2007); and LILACS (2000 to May 2007). The *metaRegister of Controlled Trials (mRCT)* was also searched using 'helminth* OR anthelminth*' (May 2007).

The authors also drew on existing reviews of the topic and checked the citations of all the trials identified by the above methods. We also re-appraised the studies identified in the previous version of this review (Dickson 2000a).

METHODS OF THE REVIEW

Trial selection

David Taylor-Robinson (DTR) checked the results of the search for potentially relevant trials and retrieved full articles as required. DTR and Paul Garner (PG) independently assessed the trial eligibility using an eligibility form based on the inclusion criteria; where there was uncertainty, all three authors participated in the decision about inclusion. We checked that trials with multiple publications were managed as one study.

Assessment of methodological quality

DTR and PG independently assessed the methodological quality and presented the results in a table. Differences were resolved by discussion. We classified generation of allocation sequence and allocation concealment as adequate, inadequate, or unclear (Juni 2001). Blinding was assessed as open (all parties aware of treatment), participant or care provider/assessor blinded, or participant and care provider blinded. We classified the inclusion of all randomized participants (ie number evaluable/number randomized) as adequate if more than 90% and inadequate if equal or less than 90%. We used sensitivity analyses that excluded trials with inadequate allocation concealment.

Data extraction

DTR extracted data using data extraction forms. PG extracted and cross checked the data from a selection of papers. DTR also requested PG to double-data extract particularly complicated papers. Any differences were resolved by discussion. Where

methods, data, or analyses were unclear or missing, we contacted authors for further details.

If there was discrepancy in the number randomized and the numbers analysed, this was calculated and reported. In the analysis, we used the number of participants reported on. For individually randomized trials, the number of participants with each outcome and the total number in each group were recorded for dichotomous outcomes. For continuous outcome measures, the aim was to record arithmetic means and standard deviations for normally distributed data, and medians and ranges for non-normally distributed data.

For trials randomized using clusters, we recorded the number of clusters in the trial, the average size of clusters, and the unit of randomization (eg household or institution). Where possible, we documented the statistical methods used to analyse the trial along with details describing whether these methods adjusted for clustering or other covariates. When reported, estimates of the intra-cluster correlation (ICC) coefficient for each outcome were recorded. Where results had been adjusted for clustering, we attempted to extract the point estimate and the 95% confidence interval (CI).

Data analysis

We analysed data with Review Manager 4.2. We assessed differences between the intervention and control groups using a 5% significance level. We stratified the analysis by dose (single and multiple). The multiple dose trials are subdivided into those that reported results within a year and after a year from the start of treatment. We examined change from baseline in all outcomes and then examined absolute values at the end of follow up. For trials that did not provide data in this form we extracted medians and ranges, and presented these in a table. For individually randomized trials, we compared dichotomous data using relative risks (RR) and compared continuous data using the weighted mean difference (WMD). Cluster adjusted results were combined in the meta-analysis using the generic inverse variance method. Non-adjusted results were presented in tables.

Heterogeneity

To detect heterogeneity, we inspected forest plots and used the chi-squared test with a 10% level of statistical significance. The degree of heterogeneity was further quantified with reference to the I^2 statistic (Higgins 2003). In the presence of significant heterogeneity, we used the random-effects (RE) model for the analyses and explored the following potential sources in subgroup analyses: population prevalence and intensity of infection (as per Table 01); nature of treatment programme (mass targeted or selective based on screened individuals); age group (< five years versus \geq five years); drug type and manufacturer; treatment setting (community, school, health post, hospital); and whether children were malnourished or not. These were specified before the analysis. In the event, we were able to examine in a subsidiary analysis stratified by the community category in the population

being studied. We categorized the trials into three community categories based on the level of geohelminth infection prevalence or intensity in the study populations that we identified from baseline prevalence and intensity data provided in the papers (WHO 2002; Table 01). This is based on information on both prevalence and intensity of infection. In the trials where information on intensity was not provided, we estimated the community category on the basis of quoted prevalence; it is possible that the community category has been underestimated in these trials.

We also carried out sensitivity analyses excluding trials where children were screened for infection and excluding trials that were inadequately concealed.

DESCRIPTION OF STUDIES

Thirty-four trials reported in 43 articles met the inclusion criteria (see 'Characteristics of included studies'); one was unpublished and kindly supplied by the authors (Hall 2006). Eighteen were excluded (see 'Characteristics of excluded studies'), and three are ongoing (see 'Characteristics of ongoing studies').

Location

The included trials were carried out in 20 different countries: Kenya (4 trials); India (4 trials); Bangladesh (3 trials); Haiti, Ethiopia, Indonesia, South Africa, Jamaica, and Zanzibar (2 trials in each); Guatemala, Zaire, Benin, Cameroon, Sierra Leone, Botswana, Malaysia, Uganda, Vietnam, Indonesia, and Tanzania (1 trial in each).

Population

Children were recruited from school populations in 16 trials, communities in 13 trials, and in health facilities or by health workers in five trials. One of these recruited children on discharge from hospital (Donnen 1998).

Eighteen trials were conducted in populations where worms were of high prevalence or intensity (community category 1), eight in populations with moderate prevalence and low intensity (category 2), and seven in populations with low prevalence and low intensity (category 3). Classification was not possible in one trial (Freij 1979i).

Twenty-seven trials were based on mass targeted treatment of an unscreened population. Seven trials studied children that were screened and selected on the basis of their having high worm loads (Freij 1979i; Freij 1979ii; Kvalsvig 1991i; Nokes 1992; Adams 1994; Simeon 1995; Sarkar 2002), and the purpose of three of these trials was to measure cognitive outcomes (Kvalsvig 1991i; Nokes 1992; Simeon 1995). Stephenson 1993 also studied an infected subgroup of the larger unscreened study population for cognitive outcomes.

Intervention and controls

Twenty-six trials compared deworming drugs with a placebo or no treatment:

- **Albendazole:** 19 trials; seven used a single-dose and 12 used multiple doses (one trial used albendazole plus ivermectin in one arm (Beach 1999)).
- **Mebendazole:** eight trials; three used a single dose and five used multiple doses (two trials used mebendazole plus pyrantel in trial arms (Rousham 1994; Lai 1995)).
- **Pyrantel pamoate:** five trials; two used a single dose and three used multiple doses (one trial used pyrantel in a subgroup; two trials used pyrantel plus mebendazole).
- **Piperazine:** three trials (single dose).
- **Levamisole:** one trial (multiple doses).
- **Tetrachlorethylene:** one trial (single dose).
- **Ivermectin:** one trial (single dose; also used ivermectin plus albendazole in one arm; Beach 1999).

In eight trials, both arms received vitamin or nutritional supplementation, with the control arm receiving vitamins or nutritional supplementation only (Awasthi 1995; Palupi 1997; Kruger 1996; Awasthi 2001; Dossa 2001; Sur 2005; Alderman 2006; Hall 2006).

Design

Six trials were cluster randomized (Table 03), and the other trials used the individual as the unit of analysis.

Three out of the six cluster-RCTs analysed data using an appropriate method to take clustering into account. Stoltzfus 1997 adjusted for within-school correlations using the generalized estimating equations approach; and two trials used the cluster as the unit of analysis and presented summary measures (mean values and associated standard deviations) within a whole cluster (Awasthi 1995; Awasthi 2001; Table 03).

The three remaining cluster-RCTs did not take clustering into account. Rousham 1994 had 13 units of randomization (villages) but analysed the data as if 1476 children were randomized. Alderman 2006 had 50 units of randomization (parishes) but analysed this as if 27,955 people had been individually randomized for the main outcome (table 2 of their paper; Alderman, personal communication). The unpublished trial, Hall 2006, which had 80 units of randomization (schools), analysed the 56,444 as if they were individually randomized, although in this instance the analysis did not demonstrate a significant figure (Hall, personal communication).

Two trials had a factorial design. Kruger 1996 randomized individual participants to albendazole or placebo, and, also, three of the five schools in the trial received soup fortified with vitamins and iron, and two received unfortified soup. Stoltzfus 2001 randomized children to deworming drugs and daily iron; disaggre-

gated data for each treatment allocation group was not provided for each outcome.

Follow-up periods for the trials that used a single dose ranged from one to 11 months, while the follow-up periods for trials that used multiple doses ranged from six months to 2.5 years.

Outcome measures

Growth and nutritional outcomes

These were measured in 33 trials (not measured in Nokes 1992). Some trials reported absolute values or changes in absolute values of weight and height (or other anthropometric measures). Many trials presented anthropometric data in terms of percentage weight-for-age, weight-for-height, and height-for-age, and compared the trial results to an external reference. Sometimes these were converted into Z-scores. The external standard was usually quoted as the National Centre for Health Statistics (NCHS) standard, but a variety of references were quoted (eg anthropometric computer packages or country standards). These data have not been used in the meta-analyses as the results are already incorporated in the values for weight and height.

Outcome data were incomplete in some trials and could not be used in meta-analysis. A number did not report summary outcome data for each trial arm, and the results were reported in terms of regression modelling outcomes or subgroup analyses. The results of these trials are described in Table 04.

Appetite and activity

Five trials assessed appetite by measuring the amount of food consumed for a snack or by a subjective report, and two trials assessed activity levels.

School performance or cognitive outcomes

These were measured in seven trials, of which five used albendazole and two used mebendazole. Five of these trials took place in communities with high prevalence/intensity infections.

Adverse events

Two trials provided information on adverse events (Michaelsen 1985; Fox 2005). These were actively sought in Fox 2005.

METHODOLOGICAL QUALITY

See Table 05 for the methodological quality assessment and the 'Characteristics of included studies' for details of the methods used in each trial.

For the 28 individually randomized trials, generation of allocation sequence was adequate in six (Willett 1979; Simeon 1995; Beach 1999; Garg 2002; Fox 2005; Sur 2005), inadequate in four (Freij 1979i; Freij 1979ii; Lai 1995; Awasthi 2000), and unclear in the other trials. The concealment of allocation was adequate in four trials (Stoltzfus 2001; Garg 2002; Fox 2005; Sur 2005), inadequate in one (Awasthi 2000), and unclear in the other trials. For the six

cluster-RCTs, generation of allocation sequence was adequate in one (Alderman 2006) and unclear in five, and the method used to conceal allocation was unclear in all six.

Two trials provided evidence that the participants, treatment provider, and assessor were blinded (Beach 1999; Sur 2005). Two trials did not use blinding (Awasthi 2001; Alderman 2006). Details of blinding were unclear in seven trials. In the remaining trials one or two of the participants, providers, and assessors were blinded. Thirteen trials described the trial as being 'double blind', with incomplete information on who was blinded.

We calculated the percentage of randomized participants that were evaluable. Overall, this ranged from 34% to 100%, with 12 trials including 90% or more of the randomized participants (adequate) cut-off. No data were available for one trial (Kvalsvig 1991i), and data were unclear for two (Kloetzel 1982; Hall 2006). The percentage was particularly low in two of the trials measuring school performance and cognitive outcomes: 73% in Nokes 1992; and 52% in Stoltzfus 2001.

RESULTS

The results are divided into three sections: (1) nutritional outcomes after a single dose; (2) nutritional outcomes after multiple doses (subdivided into within and after a year of treatment); and (3) school performance and cognitive tests. The nutritional outcome sections have three parts: analyses of change in nutritional outcomes; analyses of end values of nutritional outcomes at completion of follow up; and narrative reports of potentially relevant trials that could not be independently evaluated because they had incomplete data sets (eg number of participants, variance, or values not provided meaning we were unable to analyse the data).

1. Nutritional outcomes after a single dose

Nine trials reported on change (four of these were early values from multiple dose trials), 11 trials reported end values, and seven trials included data that were relevant to this comparison but could not be independently evaluated.

1.1. Change

Weight

Nine trials included data on mean weight change. No consistent pattern was evident: some trials showed high values (over 700 g for three trials), and others did not show a significant difference. The meta-analysis showed an overall gain of 0.34 kg (95% CI 0.05 to 0.64, RE model; 2448 children, 9 trials, Analysis 01.01), with visible and statistical heterogeneity.

The exclusion of the two trials that did screen children for infection (Adams 1994; Sarkar 2002) tipped the meta-analysis into non-significance (2312 children, 7 trials, RE model, subgroup Analysis 08.01.01). In the subgroup analysis by community worm

prevalence and intensity (Table 01), six trials fell into high prevalence/intensity areas, one fell into a moderate prevalence/low intensity area, and two into low prevalence/intensity areas (Analysis 07.01). This did little to explain the heterogeneity, with significant heterogeneity in the five trials in the high prevalence/intensity areas. A sensitivity analysis of trials with adequate or unclear allocation of concealment meant that only one trial was excluded (Awasthi 2000), making little difference to the estimate (Analysis 08.01.02). There was only one trial that concealed allocation, Garg 2002, and this did not reach statistical significance (Analysis 08.01.02).

Height

The single dose showed no statistically significant effect on change in height from the baseline values in the meta-analysis (2449 children, 9 trials, RE model, Analysis 01.02). Heterogeneity was significant and was not explained by community prevalence/intensity (Analysis 07.02). A subgroup analysis of trials that did not screen for infection made no difference to this finding (2313 children, 7 trials, Analysis 08.01.03). A sensitivity analysis of trials with adequate or unclear allocation of concealment did not change this finding (1462 children, 8 trials, Analysis 08.01.04).

Mid-upper arm circumference and skinfold tests

In a similar pattern to the weight gain results, three of the five trials reported a significant effect and significant heterogeneity between the trials. Overall, there was no statistically significant difference in mid-upper arm circumference (5 trials, 823 children, RE model, Analysis 01.03). The same three trials reporting significant effects on weight gain showed concurrent significant effects with changes in triceps skinfold values (WMD 1.27 mm, 95% CI 0.74 to 1.80, RE model; 394 participants, Analysis 01.04) and subscapular skinfold (WMD 1.18 mm, 95% CI 0.90 to 1.46, RE model; 394 participants, Analysis 01.05). Removing the one trial that included screened children, Adams 1994, did not change the conclusions for these three measures (RE model, subgroup Analyses 08.01.05, .06, and .07).

Haemoglobin

The haemoglobin levels did not significantly change from the baseline values after a single dose of mebendazole or albendazole in the two trials that measured this (Garg 2002; Palupi 1997; 538 children, Analysis 01.06).

Appetite

Two trials reported an improvement in measures of appetite after treatment (Adams 1994; Hadju 1996), but the outcome measures were not comparable.

1.2. Values at end of follow up

Weight and height

A single dose had no statistically significant effect on weight (2980 children, 11 trials, Analysis 02.01) or height (2222 children, 8 trials, Analysis 02.02). These conclusions did not change when the trials were grouped by community worm prevalence or intensity

(Analyses 07.05 and .06), or when we removed trials that screened children for infection (Freij 1979i; Adams 1994; Sarkar 2002; Analyses 08.02.01 and .02) or one trial with inadequate allocation concealment (Awasthi 2000; Analyses 08.02.03 and .04).

Mid-upper arm circumference and skinfold values

A single dose had no statistically significant effect on mid-upper arm circumference (864 children, 7 trials, Analysis 02.03), triceps skinfold thickness (407 children, 4 trials, RE model, Analysis 02.04), or body mass index (407 children, 1 trial, Analysis 02.06). The circumference and skinfold results did not alter when we removed trials that screened children for infection (Freij 1979i; Freij 1979ii; Adams 1994; Analyses 08.02.05 and .06). However, there was a statistically significant improvement in subscapular skinfold thickness (WMD 0.73 mm, 95% CI 0.02 to 1.44, RE model; 394 children, 3 trials, Analysis 02.05). This result was no longer significant once we removed Adams 1994, which included children screened for infection (RE model, Analysis 08.02.07).

Haemoglobin

A single dose had no statistically significant effect on haemoglobin levels (646 children, 4 trials, Analysis 02.07). Removing the one trial that screened children for infection, Adams 1994, did not alter this result (Analysis 08.02.08).

Fitness

A single dose significantly improved fitness, as measured by the Harvard Step Test (WMD 6.00, 95% CI 4.31 to 7.69; 86 children, 2 trials, Analysis 02.08).

Adverse events

Only two trials provided this information (Michaelsen 1985; Fox 2005). Fox 2005 found no serious adverse events (albendazole 0/46 versus placebo 0/43). Myalgia and cough were reported significantly more frequently in the placebo group compared to albendazole. Michaelsen 1985, which used tetrachlorethylene, reported that 17% (19/119; results not given for separate trial arms) of the children suffered adverse effects (nausea and ataxia) that began one and a half hours after treatment. All symptoms disappeared within four hours. This drug is not in current use as a deworming drug.

1.3. Potentially relevant trials with incomplete data sets

We provide narrative summaries of the trial authors' conclusions from seven included trials that reported relevant but incomplete data sets (Table 04), which we could not evaluate fully or use in meta-analyses.

Beach 1999 did not detect a nutritional benefit of treatment after four months for the entire study population (no figures provided). Stratification by infection demonstrated small positive effects in the treatment group for some anthropometric outcomes.

Fox 2005 did not provide results for the whole study population. Results for height and weight were presented in the narrative for subgroups infected with hookworm and *Ascaris*, and no significant anthropometric changes were detected (no figures quoted).

In those infected with *Trichuris*, weight gain was greater in the albendazole group.

Greenberg 1981 found no significant difference for all measured anthropometric variables for the total group and for subgroups defined by severity of infection (no figures provided).

Kloetzel 1982 reported the proportion of treatment or control group that improved, deteriorated, or experienced no change. It is unclear which anthropological measures were used in this categorization process. The proportions in each category were not significantly different between trial arms.

Koroma 1996 found significant increases in weight-for-height, weight-for-age, and height-for-age Z-scores recorded in rural and urban treatment groups at six months.

Michaelsen 1985 found no significant difference in change in mean for haemoglobin or weight for height at five months.

Nokes 1992 did not report on growth outcomes.

2. Nutritional outcomes after multiple doses

Eighteen trials investigated the effects of multiple doses of deworming drugs compared with placebo or no treatment, and seven followed the children for more than one year. The dose interval ranged from one to six months. The trials are divided into those that reported outcomes within a year (11 trials) and outcomes at one year or more (8 trials).

2.1. Outcomes within a year of starting treatment

Of the 11 trials that reported outcomes within a year (Willett 1979; Stephenson 1993; Simeon 1995; Kruger 1996; Watkins 1996; Hadju 1997; Stoltzfus 1997; Donnen 1998; Dossa 2001; Stoltzfus 2001; Sur 2005), six trials reported on change, five trials reported end values, and five trials included data that could not be independently evaluated.

2.1.1. Change

Weight and height

Multiple doses of deworming drugs had no statistically significant effect on weight (1714 children, 6 trials, RE model, Analysis 03.01) or height (1715 children, 6 trials, Analysis 03.02). The results did not alter significantly when we conducted a sensitivity analysis and removed Awasthi 2000, the one trial with inadequate allocation concealment (Analyses 08.03.01 and .02), or when we analysed the trials in subgroups based on the estimated community category (Table 01), which takes prevalence and intensity of infection into account (Analyses 07.03 (RE model) and .04).

Mid-upper arm circumference and skinfold values

There was no statistically significant change in mid-upper arm circumference (658 children, 4 trials, RE model, Analysis 03.03). Two trials measured triceps skinfold thickness, with the mean value decreasing with albendazole in one trial and increasing with placebo in the other (254 participants, Analysis 03.04). The one trial that measured subscapular thickness reported an increase in

values (WMD 1.50 mm, 95% CI 1.23 to 1.77; 188 participants, Analysis 03.05); this was the same trial that showed an increase with triceps values.

Haemoglobin

No significant effect was demonstrated for the mean change in haemoglobin (144 children, 2 trials, Analysis 03.06).

2.1.2. Values at end of follow up

No statistically significant effect was demonstrated for weight (5 trials, 2311 children, Analysis 04.01), height (4 trials, 1630 children, Analysis 04.02), or mid-upper arm circumference (3 trials, 581 children, Analysis 04.03). Grouping trials by community category (Table 01) or excluding trials with inadequate allocation concealment did not alter the results for weight (Analyses 07.07 and 08.04.01) or height (Analyses 07.08 and 08.04.02). One trial with 188 children showed significant improvement in mean triceps skinfold (WMD 1.90 mm, 95% CI 1.03 to 2.77; 188 participants, Analyses 04.04) and subscapular thickness (WMD 1.70 mm, 95% CI 1.09 to 2.31; 188 participants, Analyses 04.05). Dossa 2001 measured food intake in a sample from each trial arm, but it did not present results that compared the groups.

2.1.3. Potentially relevant trials with incomplete data

Five trials included data that were relevant to this comparison but provided insufficient data for us to independently evaluate the statistical findings (no variance, no numbers of participants, or values given were from regression analysis) (Table 04). Although these trials meet the inclusion criteria, we could not evaluate the data fully or use them in meta-analyses, and have summarized the trial authors' conclusions below.

Hadju 1997 found no significant differences in change in weight-for-age, height-for-age, weight-for-height, or mid-arm circumference Z-scores detected between treatment groups on basis of multivariate analyses.

Simeon 1995 found no significant differences between treatment groups in height-for-age Z-score or body mass index.

Stoltzfus 1997 was a cluster-RCT in three districts with three arms (placebo, mebendazole twice a year, mebendazole three times a year) with four schools in each arm. Weight and height change were then evaluated at one year, using multiple linear regression to adjust for characteristics that differed at baseline. In a subgroup of under 10 year olds, the twice-yearly treated group experienced significantly greater weight gain (kg) compared to the control group. In the thrice-yearly treatment group the difference was not significant. The thrice-yearly treated group also experienced significantly greater height gain (cm) compared to control, but in the twice-yearly treatment group the difference was not significant. There were no significant differences found in the subgroup of children aged over 10 years. Deworming had no significant effect on haemoglobin change in an adjusted analysis presented for the whole study group.

Stoltzfus 2001 found that treatment significantly reduced the prevalence of mild wasting malnutrition in a subgroup of children aged less than 30 months. Treatment is reported as significantly reducing the prevalence of poor appetite across the whole group.

Willett 1979 found no statistical difference in growth rates in terms of height and weight between the two groups.

2.2. Outcomes one year or more after starting treatment

Of the seven multiple dose trials that reported outcomes at one year or more (Rousham 1994; Awasthi 1995; Lai 1995; Awasthi 2000; Awasthi 2001; Alderman 2006; Hall 2006), three reported on change, two reported on end values, and four included data that were relevant to this comparison but could not be independently evaluated.

2.2.1. Change

Of the three trials, one randomized individuals (Awasthi 2000) and two randomized clusters (Awasthi 1995; Awasthi 2001).

Weight and height

For weight, two trials did not demonstrate a difference or a trend towards a difference, whereas one trial showed a marked increase in weight with albendazole (1219 participants, RE model, Analysis 05.01). The meta-analysis is in the direction of benefit with albendazole, but this is not significant, and the heterogeneity is evident visually and statistically. None of the three trials showed an effect on height (1219 participants, Analysis 05.02). Sensitivity analyses, which excluded the one trial with inadequate allocation concealment (Awasthi 2000), showed again that the point estimate was consistent with benefit for albendazole, but this was not significant (Analysis 08.05).

2.2.2. Values at end of follow up

Weight and height

Two trials reported end values for weight (RE model, Analysis 06.01) and height (Analysis 06.02). One of these trials, Awasthi 2001, showed a difference of borderline significance in favour of albendazole (Analysis 06.01); however, this trial had not shown a difference in weight gain (RE model, Analysis 05.01). Removal of Awasthi 2000 left only one trial in the analysis (Awasthi 2001, Analysis 08.06).

Mid-upper arm circumference and skinfold values

Rousham 1994 reported no significant improvement in Z-scores for mid-upper arm circumference after treatment with mebendazole (Table 06).

Haemoglobin

No significant effect was demonstrated on mean haemoglobin levels (1045 children, 1 trial, Analysis 06.03).

2.2.3. Potentially relevant studies with incomplete data sets

Four trials included data that were relevant to this comparison but were insufficient for us to independently evaluate the statistical findings (no variance, no numbers of participants, no adjustment

for cluster randomization, or values given were from regression analysis). Although these trials met the inclusion criteria, these data are more difficult to evaluate and cannot be used in meta-analyses. Instead we have summarized the trial authors' conclusions (see Table 04).

Lai 1995 found no difference in height or weight between the treatment and control groups at the end of the two-year follow up.

Alderman 2006 reported on weight gain by 27,995 children living in 48 parishes randomized by coin flip to either albendazole or nothing. There was a weight gain of 2.413 kg in the treatment parishes and 2.474 kg in the control parishes at an unspecified follow-up point. Although the 154 g difference was reported as statistically significant in the paper, the trial authors assumed that the children were individually randomized. We contacted the trial authors who confirmed this result was unadjusted; the authors have since submitted a correction to the journal, which shows no significant difference is detected in the difference for weight gain between intervention and control groups (difference 154 g; 95% CI -19.7 to 330 g). Alderman's analysis in the paper also provides regression models looking at weight gain as a function of whether children attended child health days (which ignores randomization). These are corrected for cluster sampling but are not a randomized comparison.

Hall 2006 reported on 80 schools in Vietnam that were randomized to receive albendazole or vitamin A. The authors reported on weight and height gain in children in the intervention and control groups after two years. No significant effect was demonstrated. The analysis assumed individual randomization. A regression analysis controlling for age, sex, socioeconomic status, and days absent from school showed no statistically significant effect on weight, height, or educational tests.

Rousham 1994 randomized 13 villages in which the children received mebendazole, pyrantel, or placebo, and were measured for height and weight. The paper only presents ANOVAs for change in Z-scores for height-for-age, weight-for-age, and weight-for-height, with a follow-up period of about 18 months. No significant improvement in the treatment group was detected.

3. School performance and cognitive tests

The results of the seven trials reporting school performance or learning outcomes are summarized in Table 06. The trials used either albendazole (five trials: one single dose and four multiple dose) or mebendazole (two trials: one single dose and one multiple dose). They examined a variety of outcome measures, including measures of school performance (school attendance and dropout rates) in two trials, development status in two trials, and measured tests of cognition in four trials. Overall, five of the trials demonstrated no treatment effect (Simeon 1995; Watkins 1996; Awasthi 2000; Stoltzfus 2001; Hall 2006), one trial noted an improvement

in three out of 10 cognitive tests used (Nokes 1992), and one trial did not report the results clearly (Kvalsvig 1991i).

DISCUSSION

Trial quality

Only three recent trials provided information to assure good methodological quality in terms of allocation sequence and concealment, blinding, and inclusion of randomized participants in the analysis (Garg 2002; Fox 2005; Sur 2005). Only one other trial used an adequate method to conceal allocation (Stoltzfus 2001). About two-thirds of the trials (22/34) did not include over 90% of the randomized participants in the analysis. This was low in some trials, including trials conducted recently (eg 52% in Stoltzfus 2001).

Of the six cluster-RCTs, only three took adequate account of cluster randomization (Awasthi 1995; Awasthi 2001; Stoltzfus 1997). This has a substantive impact on the interpretation of the trials. For example, the significant difference between intervention and control quoted on the cover of the *BMJ* for Alderman 2006 assumed 27,995 children had been individually randomized. When we clarified this with the authors, they provided the *BMJ* with a correction, which showed that no significant difference was detected in weight gain between intervention and control groups; this correction has not yet been included in the *BMJ* (checked in July 2007).

We excluded one large study, Miguel 2004, an economic analysis of a study where some of the comparisons could potentially have been quasi-randomized cluster comparisons. It included 75 schools with a total of 30,000 pupils enrolled. The intervention was phased over time, and there were two comparisons, one in 1998 and one in 1999 if the analysis is comparative within each individual year. All clusters in the treatment group were assigned albendazole on the basis of a prevalence over 50%. The trial assigned schools to receive praziquantel with schistosomiasis prevalence over 30%. On this basis six of 25 treatment schools met the cut off in 1998, and 16 met the cut-off in 1999. The albendazole/praziquantel treatment was phased over several years, and thus the control group and intervention group changed in size over the course of the trial. In 1998, there were 25 intervention schools (group 1) and 25 control schools (groups 2). In 1999, there were 50 intervention schools (groups 1 and 2) and 25 control schools (group 3). The results for the 1998 comparison were presented. It may be possible to obtain some information in meta-analysis by excluding those schools that were given praziquantel, but this is problematic as it will lead to large, post-randomization exclusions. As it happens, the study did not detect a significant difference at the 95% confidence level in the treatment group for the height-for-age Z-score (0.09, SE 0.05, $P > 0.05$), weight-for-age Z-score (-0.00, SE 0.04), or haemoglobin concentration (1.6 g/L, SE 1.4). Data were given on school participation by subgroup, and some showed benefit

in schools allocated albendazole, but it is not clear whether the significance testing took clustering into account.

Growth and nutritional status outcomes

The included trials reported a range of growth and nutritional status outcomes. We used numerical values for change and for absolute values, but did not use growth data expressed as a percentage of standards. As these data were derived from the absolute values, we used these values for evidence of benefit. We knew the nutritional data would be captured in the absolute values and wanted to reduce selective reporting through collection of multiple variables from papers that are all derived from the same basic outcomes measured in the trial. We noted that in some trials there was a discrepancy between what was measured and what was reported; for example, Nokes 1992 recorded but did not report anthropometric data. This is a concern as it may indicate selective reporting. However, given the relatively poor quality of methods in these papers, we did not systematically analyse this.

The review showed a significant difference in weight change after a single dose of a deworming drug. There was significant heterogeneity and a relatively small number of trials in this analysis, so it is unclear whether this reflects a difference in the size of an effect or that the intervention is effective in some circumstances but not in others. However, the potential size of the effect is quantitatively important, with increases of 0.34 kg during the follow-up period of one to 11 months (range).

The results for multiple dose trials with less than a year's follow up that were evaluable by meta-analysis did not demonstrate an effect. Five other trials provided data that could not be fully evaluated. Three of these showed no significant effect. Two trials, one of which one was cluster randomized, demonstrated improvements in growth outcomes in subgroup analyses (Stoltzfus 1997; Stoltzfus 2001).

For follow up of more than a year, the results for multiple dose trials evaluable in meta-analysis did not demonstrate statistically significant effects on weight or height. For weight change there was heterogeneity in the analysis, with one cluster-RCT showing benefit: interpretation is not easy, but the data tend to suggest that the intervention may be effective in some circumstances and not in others. Four other trials provided data that could not be fully evaluated. Three trials did not show an effect; one was a large, unpublished cluster-RCT from Vietnam. The fourth trial was a cluster-RCT published in the *BMJ* where it reported a significant effect, but this subsequently found to be due to incorrect analysis (Alderman 2006).

Our review included trials reporting on growth, nutritional status, school performance, and cognition measures. It does not comprehensively assess the effects of deworming drugs on haemoglobin values. Gulani and colleagues did this recently and reported a marginal increase in mean values that could translate into small reduc-

tion (they estimate 5% to 10%) in anaemia in a population with a high prevalence of intestinal helminths (Gulani 2007).

The previous version of this review, Dickson 2000a, generated feedback from authors who stated that the impact of treatment must be considered in the context of intensity of infection (Cooper 2000; Savioli 2000). In response, we stratified the trials in terms of estimated community category using WHO methods (Table 01). This reflects the level of the worm infection prevalence or intensity in the study populations. We found that a single dose of a deworming drug has a significant effect on the mean change in weight in the children with an initial high worm prevalence or intensity compared with no effect in the group with low worm prevalence or intensity. This is in line with WHO policy (WHO 2002), which is based on the premise that these groups are likely to benefit most from treatment (Anderson 1991; Montresor 2002; WHO 2005).

Other people responded to the Dickson 2000a version of this Cochrane Review by suggesting that studies of short-term treatment cannot assess the long-term benefits of regular treatment (Bundy 2000). In this update, however, observed short-term improvements in weight gain were generally not reproduced in the multiple dose trials with longer follow up. This is difficult to explain. It has been suggested that resistance to deworming drugs may be a factor that limits the effectiveness of periodic deworming (Hotez 2006b). Some people have also questioned whether albendazole itself can adversely affect growth (Hotez 2006b).

Some policymakers state that our analysis is irrelevant as the purpose of giving deworming drugs to all school children is to benefit a small subgroup with heavy worm infections; they argue that in these circumstances, demonstrating a population effect is irrelevant. Our response to this is that trialists power their studies to detect these differences in these subgroups and then analyse their results by worm burden to evaluate whether their hypothesis is correct. In this systematic review, the stratified analysis by trials in relation to endemicity of worms suggests an effect in high endemicity areas for a single dose, but not for multiple doses.

Schistosomiasis and filariasis are helminth infections that also cause disease. In practice, individuals and communities are often infected with more than one helminth infection, and there are now international policy moves to integrate control of these infections by mass administration of several deworming drugs at once (Molyneux 2005). However, there is a need to demonstrate that a drug is effective on a particular parasite and its effects on humans before conflating all the drugs into a basket treatment for all helminth infections, and assuming they are all effective.

School performance and cognitive outcomes

Only three trials investigated measures of school performance (Simeon 1995; Watkins 1996; Hall 2006). All three of these found that the deworming drugs made no statistical difference compared with the control intervention. All of the trials that reported cog-

nitive outcomes, with the exception of Nokes 1992, also failed to demonstrate any effect. The trials used a range of cognitive tests, which seems to reflect the difficulty inherent in choosing appropriate cognitive performance tests since there is no accepted test battery that can be applied across cultures and settings and, as Miguel 2004 points out, the mechanisms for any putative effects are unknown. Three of the trials studied children selected on the basis of high worm loads (Kvalsvig 1991i; Nokes 1992; Simeon 1995). Simeon 1995 has suggested that treatment may be more beneficial in heavily infected children.

Summary

- A meta-analysis of trials showed that children gained more weight with a single dose of a deworming drug compared to those who did not receive a deworming drug. However, there was variation between trials, with some demonstrating substantial effects and others not detecting a difference. Background helminth infection prevalence and intensity did not explain the differences between trials.
- In trials evaluating multiple doses, 11 trials measured outcomes within a year. In a meta-analysis of six trials examining weight and height change, no significant difference was detected. In one cluster-RCT, significant results were found in subgroups for weight and height, in favour of the intervention.
- In trials evaluating multiple doses, seven trials had outcomes at one year or more. One cluster-RCT showed a statistically significant effect on weight gain, but other trials did not show such effects, including two recent large cluster-RCTs.
- No clear effect has been demonstrated on school performance or cognitive function.

AUTHORS' CONCLUSIONS

Implications for practice

- Deworming drugs used in targeted community programmes may be effective in relation to weight gain in some circumstances but not in others. Also, there is no direct evidence from trials to show that this depends on background helminth prevalence or intensity. Whether it has an effect on school performance or cognition is unknown.
- We suggest that policy advocates make clear the research evidence has sometimes demonstrated benefits and sometimes has not demonstrated benefit. Guideline developers and policy makers at global, national, and local levels should be allowed to

consider carefully the evidence carefully before committing to investing existing resources in delivering these programmes.

Implications for research

- This is a potentially important intervention. The large cluster-RCT in progress in Lucknow, India (Lucknow ongoing) may help in identifying whether this intervention is worthwhile.
- Further research is required to determine the factors that will allow policymakers to predict whether it is worthwhile to implement the intervention in a community.
- Further research is required before policymakers can be clear whether the intervention is of benefit or not on children's long-term growth and school performance.
- Trial authors are encouraged to present trial data in line with CONSORT guidelines (Moher 2001).
- Authors of cluster-RCTs should report their data adjusting for design effects. We recommend trials that use current standards of design and are planned together to allow an individual patient data meta-analysis to correct for clustering and to help explore subgroup effects.

POTENTIAL CONFLICT OF INTEREST

None known.

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REFERENCES

References to studies included in this review

- Adams 1994** {published data only}
Adams EJ, Stephenson LS, Latham MC, Kinoti SN. Physical activity and growth of Kenyan school children with hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* infections are improved after treatment with albendazole. *Journal of Nutrition* 1994;**124**(8):1199–206.
- Alderman 2006** {published data only}
Alderman H, Konde-Lule J, Sebuliba I, Bundy D, Hall A. Effect on weight gain of routinely giving albendazole to preschool children during child health days in Uganda: cluster randomised controlled trial. *BMJ* 2006;**333**(7559):122.
- Awasthi 1995** {published data only}
Awasthi S, Peto R, Fletcher R, Glick H. Controlling parasitic infection in children under five years of age: giving albendazole in conjunction with an Indian government Vitamin A supplement program. *Treating parasitic infestations in children [Monograph No. 3]*. Philadelphia: International Clinical Epidemiology Network (INCLEN), 1995.
- Awasthi 2000** {published and unpublished data}
Awasthi S, Pande VK, Fletcher RS. Effectiveness and cost-effectiveness of albendazole in improving nutritional status of pre-school children in urban slums. *Indian Pediatrics* 2000;**37**(1):19–29.
- Awasthi 2001** {published data only}
Awasthi S, Pande VK. Six-monthly de-worming in infants to study effects on growth. *Indian Journal of Pediatrics* 2001;**68**(9):823–7.
- Beach 1999** {published data only}
Beach MJ, Streit TG, Addiss DG, Prospere R, Roberts JM, Lammie PJ. Assessment of combined ivermectin and albendazole for treatment of intestinal helminth and *Wuchereria bancrofti* infections in Haitian schoolchildren. *American Journal of Tropical Medicine and Hygiene* 1999;**60**(3):479–86.
- Donnen 1998** {published data only}
Donnen P, Brasseur D, Dramaix M, Vertongen F, Zihindula M, Muhamiriza M, et al. Vitamin A Supplementation but not deworming improves growth of malnourished preschool children in eastern Zaire. *Journal of Nutrition* 1998;**128**(8):1320–7.
- Dossa 2001** {published data only}
Dossa RA, Ategbo EA, de Koning FL, van Raaij JM, Hautvast JG. Impact of iron supplementation and deworming on growth performance in preschool Beninese children. *European Journal of Clinical Nutrition* 2001;**55**(4):223–8.
- Fox 2005** {published data only}
Fox LM, Furness BW, Haser JK, Desire D, Brissau JM, Milord MD, et al. Tolerance and efficacy of combined diethylcarbamazine and albendazole for treatment of *Wuchereria bancrofti* and intestinal helminth infections in Haitian children. *American Journal of Tropical Medicine and Hygiene* 2005;**73**(1):115–21.
- Freij 1979i** {published data only}
Freij L, Meeuwisse GW, Berg NO, Wall S, Gebre-Medhin M. Ascariasis and malnutrition. A study in urban Ethiopian children. *American Journal of Clinical Nutrition* 1979;**32**(7):1545–53.
- Freij 1979ii** {published data only}
Freij L, Meeuwisse GW, Berg NO, Wall S, Gebre-Medhin M. Ascariasis and malnutrition. A study in urban Ethiopian children. *American Journal of Clinical Nutrition* 1979;**32**(7):1545–53.
- Garg 2002** {published data only}
Garg R, Lee LA, Beach MJ, Wamae CN, Ramakrishnan U, Deming MS. Evaluation of the Integrated Management of Childhood Illness guidelines for treatment of intestinal helminth infections among sick children aged 2–4 years in western Kenya. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2002;**96**(5):543–8.
- Greenberg 1981** {published data only}
Greenberg BL, Gilman RH, Shapiro H, Gilman JB, Mondal G, Maksud M, et al. Single dose piperazine therapy for *Ascaris lumbricoides*: an unsuccessful method of promoting growth. *American Journal of Clinical Nutrition* 1981;**34**(11):2508–16.
- Hadju 1996** {published data only}
Hadju V, Stephenson LS, Abadi K, Mohammed HO, Bowman DD, Parker RS. Improvements in appetite and growth in helminth-infected schoolboys three and seven weeks after a single dose of pyrantel pamoate. *Parasitology* 1996;**113**(Pt 5):497–504.
- Hadju 1997** {published data only}
Hadju V, Satriono, Abadi K, Stephenson LS. Relationship between soil-transmitted helminthiasis and growth in urban slum school children in Ujung Pandang, Indonesia. *International Journal of Food Sciences and Nutrition* 1997;**48**(2):85–93.
- Hall 2006** {unpublished data only}
Hall A, Nguyen Bao Khanh L, Bundy D, Quan Dung N, Hong Son T, Lansdown R. A randomized trial of six monthly deworming on the growth and educational achievements of Vietnamese school children. Unpublished manuscript.
- Kloetzel 1982** {published data only}
Kloetzel K, Merluzzi Filho TJ, Kloetzel D. Ascariasis and malnutrition in a group of Brazilian children - a follow-up study. *Journal of Tropical Pediatrics* 1982;**28**(1):41–3.
- Koroma 1996** {published data only}
Koroma MM, Williams RA, de la Haye RR, Hodges M. Effects of albendazole on growth of primary school children and the prevalence and intensity of soil-transmitted helminths in Sierra Leone. *Journal of Tropical Pediatrics* 1996;**42**(6):371–2.
- Kruger 1996** {published data only}
Kruger M, Badenhorst CJ, Mansvelt EPG, Laubscher JA, Benade AJS. The effect of iron fortification in a school feeding scheme and anthelmintic therapy on the iron status and growth of 6–8 year old school children. *Food and Nutrition Bulletin* 1996;**17**(1):11–21.
- Kvalsvig 1991i** {published data only}
Kvalsvig JD, Cooppan RM, Connolly KJ. The effects of parasite infections on cognitive processes in children. *Annals of Tropical Medicine and Parasitology* 1991;**85**(5):551–68.
- Lai 1995** {published data only}
Lai KP, Kaur H, Mathias RG, Ow-Yang CK. Ascariasis and *Trichuris* do not contribute to growth retardation in primary school children. *Southeast Asian Journal of Tropical Medicine and Public Health* 1995;**26**(2):322–8.

Michaelsen 1985 {published data only}

Michaelsen KF. Hookworm infection in Kweneng District, Botswana. A prevalence survey and a controlled treatment trial. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1985;**79**(6):848–51.

Nokes 1992 {published data only}

Nokes C, Grantham-McGregor SM, Sawyer AW, Cooper ES, Bundy DA. Parasitic helminth infection and cognitive function in school children. *Proceedings of The Royal Society of London. Series B: Biological sciences* 1992;**247**(1319):77–81.

*Nokes C, Grantham-McGregor SM, Sawyer AW, Cooper ES, Robinson BA, Bundy DA. Moderate to heavy infections of *Trichuris trichiura* affect cognitive function in Jamaican school children. *Parasitology* 1992;**104**(Pt 3):539–47.

Palupi 1997 {published data only}

Palupi L, Schultink W, Achadi E, Gross R. Effective community intervention to improve hemoglobin status in preschoolers receiving once-weekly iron supplementation. *American Journal of Clinical Nutrition* 1997;**65**(4):1057–61.

Rousham 1994 {published data only}

Northrop-Clewes CA, Rousham EK, Mascie-Taylor CN, Lunn PG. Anthelmintic treatment of rural Bangladeshi children: effect on host physiology, growth, and biochemical status. *American Journal of Clinical Nutrition* 2001;**73**(1):53–60.

*Rousham EK, Mascie-Taylor CG. An 18-month study of the effect of periodic anthelmintic treatment on the growth and nutritional status of pre-school children in Bangladesh. *Annals of Human Biology* 1994;**21**(4):315–24.

Sarkar 2002 {published data only}

Sarkar NR, Anwar KS, Biswas KB, Mannan MA. Effect of deworming on nutritional status of ascaris infested slum children of Dhaka, Bangladesh. *Indian Pediatrics* 2002;**39**(11):1021–6.

Simeon 1995 {published data only}

Gardner JM, Grantham-McGregor S, Baddeley A. *Trichuris trichiura* infection and cognitive function in Jamaican school children. *Annals of Tropical Medicine and Parasitology* 1996;**90**(1):55–63.

*Simeon DT, Grantham-McGregor SM, Callender JE, Wong MS. Treatment of *Trichuris trichiura* infections improves growth, spelling scores and school attendance in some children. *Journal of Nutrition* 1995;**125**(7):1875–83.

Simeon DT, Grantham-McGregor SM, Wong MS. *Trichuris trichiura* infection and cognition in children: results of a randomized clinical trial. *Parasitology* 1995;**110**(Pt 4):457–64.

Stephenson 1989 {published data only}

Stephenson LS, Latham MC, Kinoti SN, Kurz KM, Brigham H. Improvements in physical fitness of Kenyan school boys infected with hookworm, *Trichuris trichiura*, and *Ascaris lumbricoides* following a single dose of albendazole. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1990;**84**(2):277–82.

*Stephenson LS, Latham MC, Kurz KM, Kinoti SN, Brigham H. Treatment with a single dose of albendazole improves growth of Kenyan schoolchildren with hookworm, *Trichuris trichiura*, and *Ascaris lumbricoides* infections. *American Journal of Tropical Medicine and Hygiene* 1989;**41**(1):78–87.

Stephenson 1993 {published data only}

Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Pertet A. Physical fitness, growth and appetite of Kenyan school boys with hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* infections are improved four months after a single dose of albendazole. *Journal of Nutrition* 1993;**123**(6):1036–46.

*Stephenson LS, Latham MC, Adams EJ, Kinoti SN, Pertet A. Weight gain of Kenyan school children infected with hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* is improved following once- or twice-yearly treatment with albendazole. *Journal of Nutrition* 1993;**123**(4):656–65.

Stoltzfus 1997 {published and unpublished data}

Stoltzfus RJ, Albonico M, Chwaya HM, Tielsch JM, Schulze KJ, Savioli L. Effects of the Zanzibar school-based deworming program on iron status of children. *American Journal of Clinical Nutrition* 1998;**68**(1):179–86.

*Stoltzfus RJ, Albonico M, Tielsch JM, Chwaya HM, Savioli L. School-based deworming program yields small improvement in growth of Zanzibari school children after one year. *Journal of Nutrition* 1997;**127**(11):2187–93.

Stoltzfus 2001 {published data only}

Stoltzfus RJ, Chwaya HM, Montresor A, Tielsch JM, Jape JK, Albonico M, et al. Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelmintic treatment improves growth, appetite and anemia in Zanzibari preschool children. *Journal of Nutrition* 2004;**134**(2):348–56.

*Stoltzfus RJ, Kvalsvig JD, Chwaya HM, Montresor A, Albonico M, Tielsch JM, et al. Effects of iron supplementation and anthelmintic treatment on motor and language development of preschool children in Zanzibar: double blind, placebo controlled study. *BMJ* 2001;**323**(7326):1389–93.

Sur 2005 {published data only}

Sur D, Saha DR, Manna B, Rajendran K, Bhattacharya SK. Periodic deworming with albendazole and its impact on growth status and diarrhoeal incidence among children in an urban slum of India. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2005;**99**(4):261–7.

Watkins 1996 {published data only}

Watkins WE, Cruz JR, Pollitt E. The effects of deworming on indicators of school performance in Guatemala. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1996;**90**(2):156–61.

*Watkins WE, Pollitt E. Effect of removing *Ascaris* on the growth of Guatemalan schoolchildren. *Pediatrics* 1996;**97**(6 Pt 1):871–6.

Willett 1979 {published data only}

Willett WC, Kilama WL, Kihamia CM. *Ascaris* and growth rates: a randomized trial of treatment. *American Journal of Public Health* 1979;**69**(10):987–91.

References to studies excluded from this review

Bhargava 2003

Bhargava A, Jukes M, Lambo J, Kihamia CM, Lorri W, Nokes C, et al. Anthelmintic treatment improves the hemoglobin and serum ferritin concentrations of Tanzanian schoolchildren. *Food and Nutrition Bulletin* 2003;**24**(4):332–42.

Boivin 1993

Boivin MJ, Giordani B. Improvements in cognitive performance for schoolchildren in Zaire, Africa, following an iron supplement and treatment for intestinal parasites. *Journal of Pediatric Psychology* 1993; **18**(2):249–64.

Cooper 2006

Cooper PJ, Chico ME, Vaca MG, Moncayo AL, Bland JM, Mafra E, et al. Effect of albendazole treatments on the prevalence of atopy in children living in communities endemic for geohelminth parasites: a cluster-randomised trial. *Lancet* 2006; **367**(9522):1598–603.

Cowden 2000

Cowden J, Hotez P. Mebendazole and albendazole treatment of geohelminth infections in children and pregnant women. *Pediatric Infectious Disease Journal* 2000; **19**(7):659–60.

Diouf 2002

Diouf S, Diagne I, Moreira C, Signate SY, Faye O, Ndiaye O, et al. Integrated treatment of iron deficiency, vitamin A deficiency and intestinal parasitic diseases: impact on Senegalese children's growth [Traitement integre de la carence en fer, de l'avitaminose A et des parasitoses intestinales: impact sur la croissance des enfants senegalais]. *Archives de Pédiatrie* 2002; **9**(1):102–3.

Evans 1986

Evans J, Martin J, Mascie-Taylor CGN. *The effect of periodic deworming with pyrantel pamoate on the growth and nutritional status of pre-school children in northern Bangladesh [Monograph No. 3]*. London: Save the Children Fund, 1986.

Fernando 1983

Fernando MA, Balasuriya, Somaratne. Effect of *Ascaris lumbricoides* infestation on growth of children. *Indian Pediatrics* 1983; **20**(10):721–31.

Friis 2003

Friis H, Mwaniki D, Omondi B, Muniu E, Thiong'o F, Ouma J, et al. Effects on haemoglobin of multi-micronutrient supplementation and multi-helminth chemotherapy: a randomized, controlled trial in Kenyan school children. *European Journal of Clinical Nutrition* 2003; **57**(4):573–9.

Gupta 1982

Gupta MC, Urrutia JJ. Effect of periodic antascaris and anti giardia treatment on nutritional status of preschool children. *American Journal of Clinical Nutrition* 1982; **36**(1):79–86.

Hadidjaja 1998

Hadidjaja P, Bonang E, Suyardi MA, Abidin SA, Ismid IS, Margono SS. The effect of intervention methods on nutritional status and cognitive function of primary school children infected with *Ascaris Lumbricoide*. *American Journal of Tropical Medicine and Hygiene* 1998; **59**(5):791–5.

Jinabhai 2001a

Jinabhai CC, Taylor M, Coutsooudis A, Coovadia HM, Tomkins AM, Sullivan KR. Epidemiology of helminth infections: implications for parasite control programmes, a South African perspective. *Public Health Nutrition* 2001; **4**(6):1211–9.

Jinabhai 2001b

Jinabhai CC, Taylor M, Coutsooudis A, Coovadia HM, Tomkins AM, Sullivan KR. A randomized controlled trial of the effect of anti-helminthic treatment and micronutrient fortification on health sta-

tus and school performance of rural primary school children. *Annals of Tropical Paediatrics* 2001; **21**(4):319–33.

Kvalsvig 1991ii

Kvalsvig JD, Cooppan RM, Connolly KJ. The effects of parasite infections on cognitive processes in children. *Annals of Tropical Medicine and Parasitology* 1991; **85**(5):551–68.

Miguel 2004

Miguel E, Kremer M. Worms: Identifying impacts on education and health in the presence of treatment externalities. *Econometrica* 2004; **72**(1):159–217.

Pollitt 1991

Pollitt E, Wayne W, Perez-Escamilla R, Latham M, Stephenson LS. Double blind clinical trial on the effects of helminth infection on cognition. *FASEB Journal* 1991; **5**:A1081.

Taylor 2001

Taylor M, Jinabhai CC, Couper I, Kleinschmidt I, Jogessar VB. The effect of different anthelmintic treatment regimens combined with iron supplementation on the nutritional status of schoolchildren in KwaZulu-Natal, South Africa: a randomized controlled trial. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2001; **95**(2):211–6.

Thein-Hlaing 1991

Thein-Hlaing, Thane-Toe, Than-Saw, Myat-Lay-Kyin, Myint-Lwin. A controlled chemotherapeutic intervention trial on the relationship between *Ascaris lumbricoides* infection and malnutrition in children. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991; **85**(4):523–8.

Yang 2003

Yang WP, Shao JO, Chen YJ. [Effect of chemotherapeutic regimens on soil-transmitted nematode infections in areas with low endemicity]. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 2003; **21**(2):128.

References to ongoing studies**Alam 2006**

Alam MM, Principal Investigator, ICDDR, B: Centre for Health and Population Research. Relative efficacy of two regimens of antehelminthic treatment. ClinicalTrials.gov identifier: NCT00367627.

Lucknow ongoing

Details unavailable. Cluster-randomized controlled trial in Lucknow, India. *Ongoing*.

Stoltzfus 2004

RJ Stoltzfus, Division of Nutritional Sciences, Cornell University. Effects of intestinal helminth infections in early childhood on immune response, inflammation, anaemia and malnutrition. IS-RCTN83988447.

Additional references**Anderson 1991**

Anderson R, May R. *Infectious diseases in humans: dynamics and control*. Oxford: Oxford University Press, 1991.

Bundy 2000

Bundy D, Peto R. Treatment for intestinal helminth infection. Studies of short term treatment cannot assess long term benefits of regular treatment. *BMJ* 2000; **321**(7270):1225.

- Callender 1998**
Callender JE, Walker SP, Grantham-McGregor SM, Cooper ES. Growth and development four years after treatment for the Trichuris dysentery syndrome. *Acta Paediatrica* 1998;**87**(12):1247–9.
- Cappello 2004**
Cappello M. Global health impact of soil-transmitted nematodes. *Pediatric Infectious Disease Journal* 2004;**23**(7):663–4.
- Chan 1997**
Chan, MS. The global burden of intestinal nematode infections -- fifty years on. *Parasitology Today* 1997;**13**(11):438–43.
- Cooper 2000**
Cooper E. Treatment for intestinal helminth infection. Message does not follow from systematic review's findings. *BMJ* 2000;**321**(7270):1225–6.
- Crompton 2000**
Crompton DW. The public health importance of hookworm disease. *Parasitology* 2000;**121** Suppl:39–50.
- Crompton 2003**
Crompton DWT, Torlesse H, Hodges ME. Hookworm infection and iron status. In: CromptonDWT, MontresorA, NesheimMC, SavioliL editor(s). *Controlling disease due to helminth infections*. Geneva: World Health Organization, 2003:23–32.
- de Silva 2003a**
de Silva NR. Impact of mass chemotherapy on the morbidity due to soil-transmitted nematodes. *Acta Tropica* 2003;**86**(2-3):197–214.
- de Silva 2003b**
de Silva NR, Brooker S, Hotez PJ, Montresor A, Engels D, Savioli L. Soil-transmitted helminth infections: updating the global picture. *Trends in Parasitology* 2003;**19**(12):547–51.
- Gulani 2007**
Gulani A, Nagpal J, Osmond C, Sachdev HP. Effect of administration of intestinal anthelmintic drugs on haemoglobin: systematic review of randomised controlled trials. *BMJ* 2007;**334**(7603):1095.
- Haider 2005**
Haider BA, Bhutta ZA. Effects of interventions for helminthic infections in pregnancy. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD005547. DOI:10.1002/14651858.CD005547.
- Higgins 2003**
Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60.
- Higgins 2006**
Higgins JPT, Green S, editors. Highly sensitive search strategies for identifying reports of randomized controlled trials in MEDLINE. *Cochrane Handbook for Systematic Reviews of Interventions* 4.2.6 [updated September 2006]; Appendix 5b. www.cochrane.org/resources/handbook/hbook.htm (accessed 1 May 2007).
- Horton 2003**
Horton J. Global anthelmintic chemotherapy programs: learning from history. *Trends in Parasitology* 2003;**19**(9):405–9.
- Hotez 2006b**
Hotez P, Bundy D, Beegle K, Brooker S, Drake L, de Silva N, et al. Helminth infections: Soil-transmitted helminth infections and schistosomiasis. *Disease control priorities in developing countries*. 2nd Edition. New York: Oxford University Press, 2006:467–82.
- Juni 2001**
Juni P, Altman DG, Egger M. Systematic reviews in health care: Assessing the quality of controlled clinical trials. *BMJ* 2001;**323**(7303):42–6.
- Kvalsvig 2003**
Kvalsvig JD. Parasites, nutrition, child development and public policy. In: CromptonDWT, MontresorA, NesheimMC, SavioliL editor(s). *Controlling disease due to helminth infections*. Geneva: World Health Organization, 2003:55–65.
- Moher 2001**
Moher D, Schulz KF, Altman DG for the CONSORT Group. The CONSORT statement: Revised recommendations for improving the quality of reports of parallel group randomized trials 2001. www.consort-statement.org/Statement/revisestatement.htm (accessed 3 August 2005).
- Molyneux 2005**
Molyneux DH, Hotez PJ, Fenwick A. “Rapid-impact interventions”: How a policy of integrated control for Africa’s neglected tropical diseases could benefit the poor. *PLoS Medicine* 2005;**2**(11):e336.
- Montresor 2002**
Montresor A, Crompton DWT, Gyorkos TW, Savioli L. *Helminth control in school-age children: a guide for managers of control programmes*. Geneva: World Health Organization, 2002.
- Review Manager 4.2**
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 4.2 for Windows. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2003.
- Sakti 1999**
Sakti H, Nokes C, Hertanto WS, Hendratno S, Hall A, Bundy DA, et al. Evidence for an association between hookworm infection and cognitive function in Indonesian school children. *Tropical Medicine & International Health* 1999;**4**(5):322–34.
- Savioli 2000**
Savioli L, Neira M, Albonico M, Beach MJ, Chwaya HM, Crompton DW, et al. Treatment for intestinal helminth infection. Review needed to take account of all relevant evidence, not only effects on growth and cognitive performance. *BMJ* 2000;**321**(7270):1226–7.
- Savioli 2002**
Savioli L, Montresor A, Albonico M. Control strategies. In: HollandCV, KennedyMW editor(s). *The geohelminths: Ascaris, Trichuris and Hookworm*. Netherlands: Kluwer Academic Publishers, 2002: 25–37.
- Stephenson 2000**
Stephenson LS, Latham MC, Ottesen EA. Malnutrition and parasitic helminth infections. *Parasitology* 2000;**121** Suppl:23–38.
- WHO 2002**
WHO Expert Committee on the Control of Schistosomiasis (2001: Geneva, Switzerland). *Prevention and control of schistosomiasis and soil-transmitted helminthiasis: report of a WHO expert committee. WHO technical report series no. 912*. Geneva: World Health Organization, 2002.

WHO 2005

World Health Organization. Strategy Development and Monitoring for Parasitic Diseases and Vector Control Team. *Deworming: The Millennium Development Goals. The evidence is in: deworming helps meet the Millennium Development Goals* [WHO/CDS/CPE/PVC/2005.12]. Geneva: World Health Organization, 2005.

WHO 2006

World Health Organization. WHO Essential Medicines Library. mednet3.who.int/emlib/ 2006 (accessed 13 June 2007).

World Bank 1993

The World Bank. *World Development Report 1993: Investing in health*. Oxford: Oxford University Press, 1993.

World Bank 2003

World Bank. School deworming at a glance. siteresources.worldbank.org/INTPHAAG/Resources/AAGDewormingEng110603.pdf November 2003 (accessed 6 July 2007).

References to other published versions of this review**Dickson 2000a**

Dickson R, Awasthi S, Demellweek C, Williamson P. Anthelmintic drugs for treating worms in children: effects on growth and cognitive performance. *Cochrane Database of Systematic Reviews* 2000, Issue 2.

Dickson 2000b

Dickson R, Awasthi S, Williamson P, Demellweek C, Garner P. Effects of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomised trials. *BMJ* 2000;**320**(7251):1697–701.

*Indicates the major publication for the study

T A B L E S**Characteristics of included studies**

Study	Adams 1994
Methods	Randomized controlled trial Generation of allocation sequence: paired by worm burden Allocation concealment: unclear Blinding: participants only; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 98% (55/56) Length of follow up: 2.25 months (9 weeks)
Participants	Number analysed for primary outcome: 55 Inclusion criteria: children in nursery and standard 1 classes of Mvindeni Primary School in Kwale, Kenya; > 500 eggs/g hookworm or > 1000 eggs/g Trichuris or Ascaris; pre-pubertal; > 5 years old Exclusion criteria: severe anaemia (haemoglobin < 75 g/L)
Interventions	Single dose versus placebo 1. Albendazole: 3 x 400 mg doses on 3 consecutive days 2. Identical placebo Treatment strategy: screened children then randomized and treated infected children

Characteristics of included studies (Continued)

Outcomes	<ol style="list-style-type: none"> 1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment 5. Mean mid-upper arm circumference 6. Mean change in mid-upper arm circumference 7. Mean triceps skinfold thickness 8. Mean change in triceps skinfold thickness 9. Mean subscapular skinfold thickness 10. Mean change in subscapular skinfold thickness 11. Mean haemoglobin post-treatment 12. Activity levels (a measure of gross motor activity of legs) 13. Self rating of appetite <p>Not included in review: helminth prevalence and intensity (arithmetic and geometric mean eggs/g); baseline and post-intervention values for arm muscle area and arm fat area; Z-scores for weight, height, weight-for-height, mid-upper-arm circumference, triceps skinfold, subscapular, arm muscle, and arm fat area</p>
Notes	<p>Location: Kenya</p> <p>Community category: 1</p>
Allocation concealment	B – Unclear

Study **Alderman 2006**

Methods	<p>Cluster-randomized controlled trial</p> <p>Generation of allocation sequence: coin toss</p> <p>Allocation concealment: unclear</p> <p>Blinding: none</p> <p>Inclusion of all randomized participants (number evaluable/number randomized): 75% 27,995/37,165</p> <p>Length of follow up: 3 years</p>
Participants	<p>Number analysed for primary outcome: 27,995 in 48 clusters</p> <p>Age range: 1 to 7 years</p> <p>Inclusion criteria: children aged 1 to 7 in 50 parishes in Uganda selected by the government on the basis that around 60% of children aged 5 to 10 years in these parishes were infected with intestinal nematodes</p> <p>Exclusion criteria: sick children</p>
Interventions	<p>Multiple dose versus no treatment</p> <ol style="list-style-type: none"> 1. Albendazole: 400 mg tablet (Zentel, GSK) every 6 months, although in the event a year elapsed between the first and second treatment round; given in conjunction with a child health package including vaccinations, vitamin A, and health promotion 2. Child health package including vaccinations, vitamin A, and health promotion <p>Treatment strategy: randomized and treated all children</p>
Outcomes	1. Mean change in weight post-treatment
Notes	<p>Location: Uganda</p> <p>Community category: 2</p> <p>Weight gain does not take into account the effects of cluster randomization (correspondence with author)</p>
Allocation concealment	B – Unclear

Study **Awasthi 1995**

Methods	<p>Cluster-randomized controlled trial</p> <p>Generation of allocation sequence: unclear</p> <p>Allocation concealment: unclear</p>
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Characteristics of included studies (Continued)

	<p>Blinding: unclear</p> <p>Inclusion of all randomized participants (number evaluable/number randomized): 87% (3514/3999)</p> <p>Length of follow up: 2.5 years</p>
Participants	<p>Number analysed for primary outcome: 3514</p> <p>Age range: 1 to 4 years</p> <p>Inclusion criteria: children aged 1 to 4 from 50 randomly selected urban slums in Lucknow</p> <p>Exclusion criteria: none stated</p>
Interventions	<p>Multiple doses versus placebo</p> <p>1. Albendazole plus placebo: 400 mg albendazole plus 2 mL vitamin A every 6 months</p> <p>2. Placebo: 2 mL vitamin A every 6 months</p> <p>Treatment strategy: randomized and treated all children</p>
Outcomes	<p>1. Mean change in weight post-treatment</p> <p>2. Mean change in height post-treatment</p> <p>3. Death</p>
Notes	<p>Location: India</p> <p>Community category: 3</p> <p>Means of cluster means used in analysis; details of correspondence from previous review suggest that trial ongoing; data for 3-year follow up are provided from R Dickson's correspondence with the author for the Dickson 2000 Cochrane Review, but the loss to follow up is very high: only 24% analysed</p>
Allocation concealment	B – Unclear

Study

Awasthi 2000

Methods	<p>Quasi-randomized controlled trial</p> <p>Generation of allocation sequence: 32 clusters randomly selected, and then children allocated to a serial number; those with odd or non-zero ending numbers were assigned to placebo</p> <p>Allocation concealment: not concealed</p> <p>Blinding: participants only; provider not blinded; assessor unclear</p> <p>Inclusion of all randomized participants (number evaluable/number randomized): 98% (1045/1061)</p> <p>Follow up: 2 years</p>
Participants	<p>Number analysed for primary outcome: 1045</p> <p>Age range: 1.5 to 3.5 years</p> <p>Inclusion criteria: children living in 32 randomly selected urban slums; registered with an Anganwadi worker (health worker); between 1.5 to 3.5 years of age</p> <p>Exclusion criteria: none stated</p>
Interventions	<p>Multiple doses versus placebo</p> <p>1. Albendazole powder: 600 mg every 6 months for 2 years</p> <p>2. Placebo: calcium powder</p> <p>Treatment strategy: randomized and treated all children</p>
Outcomes	<p>1. Mean weight post-treatment</p> <p>2. Mean change in weight post-treatment</p> <p>3. Mean height post-treatment</p> <p>4. Mean change in height post-treatment</p> <p>5. Developmental status (Denver Questionnaire): reported as proportion with normal development</p> <p>Not included in review: prevalence of underweight and stunting over 2 years as defined by Z-scores, haemoglobin (visual colour estimation), stool examination (non-concentration method), incidence of illness, and death</p>
Notes	<p>Location: India</p> <p>Community category: 3</p>

Characteristics of included studies (Continued)

Allocation concealment C – Inadequate

Study	Awasthi 2001
Methods	Cluster-randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: none Inclusion of all randomized participants (number evaluable/number randomized): 83% (1672/2010) Length of follow up: 1.5 years
Participants	Number analysed for primary outcome: 124 slums randomized containing 1672 children Inclusion criteria: clusters selected if they have functional community workers in slum areas of Lucknow; within each cluster, children recruited if aged between 0.5 and 1 year, on basis of survey register held by each worker of their particular area Exclusion criteria: none stated
Interventions	Multiple doses versus placebo 1. Albendazole plus placebo: albendazole suspension (concentration not stated) (Zentel, SZB) every 6 months and 100,000 units of vitamin A every 6 months 2. Placebo: 100,000 units of vitamin A every 6 months Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment (not used due to question over quoted standard error) Not included in review: stool smear for Ascaris prevalence on a subsample of the group; death rates
Notes	Location: India Community category: 3 Means of cluster means used in analysis. The results (weight gain) in the abstract differ from the text
Allocation concealment	B – Unclear

Study	Beach 1999
Methods	Randomized controlled trial Generation of allocation sequence: random-numbers table Allocation concealment: unclear Blinding: participants, provider, and assessors Inclusion of all randomized participants (number evaluable/number randomized): 88.4% (853/965) Length of follow up: 4 months
Participants	Number analysed for primary outcome: 853 Inclusion criteria: all children attending 5 schools (grades 1 to 4) Exclusion criteria: haematocrit < 22%
Interventions	Single dose versus placebo 1. Albendazole: 400 mg (SmithKlineBeecham, Philadelphia or generic BeltaPharm, Milan) 2. Ivermectin: 200 to 400 µg/kg (mean 282.7 µg/kg) (Merck, West Point, PA) 3. Albendazole plus ivermectin 4. Placebo: 250 mg vitamin C Treatment strategy: randomized and treated all children
Outcomes	1. Height 2. Weight

Characteristics of included studies (Continued)

	3. Stool examination for helminth prevalence and intensity (geometric mean) 4. Haematocrit
Notes	Location: Haiti Community category: 3 Results presented in a stratified analysis as per individual infection: disaggregated results not presented; measures of error not given in tables
Allocation concealment	B – Unclear

Study	Donnen 1998
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): 86% (311/358) Length of follow up: 1 year
Participants	Number analysed for primary outcome: 222 Inclusion criteria: children aged 0 to 72 months eligible on discharge from hospital where primary cause for admission is malnutrition Exclusion criteria: none stated
Interventions	Multiple doses versus placebo and no treatment 1. Mebendazole: 500 mg at start and every 3 months 2. Placebo: 60 mg vitamin A at start and 3 months 3. No treatment Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment 5. Mean mid-upper arm circumference 6. Mean change in mid-upper arm circumference Not included in review: vitamin A levels; Z-scores for height-for-age, weight-for-age, weight-for-height (NCHS reference); egg counts (eggs/g; Kato Katz method)
Notes	Location: Zaire Community category: 1 Unadjusted data not provided in original paper; results of multiple-regression models presented on basis of stratifications into vitamin A status and sex; results in meta-analysis from R Dickson's correspondence with author when preparing the Dickson 2000 Cochrane Review
Allocation concealment	B – Unclear

Study	Dossa 2001
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear for participants, provider, and assessor, but described as "double-blind" Inclusion of all randomized participants (number evaluable/number randomized): 79% (140/177) Length of follow up: 10 months
Participants	Number analysed for primary outcome: 65

Characteristics of included studies (Continued)

	Inclusion criteria: children aged 3 to 5 years; not acutely unwell Exclusion criteria: none stated
Interventions	Multiple doses versus placebo 1. Albendazole plus iron: 200 mg albendazole per day for 3 consecutive days repeated 1 month later plus iron placebo 2. Placebo: iron 3. Albendazole: 200 mg per day for 3 consecutive days repeated 1 month later plus iron placebo 4. Placebo plus placebo Treatment strategy: randomized and treated all children
Outcomes	1. Mean change in weight post-treatment 2. Mean change in height post-treatment 3. Mean change in mid-upper arm circumference 4. Mean change in triceps skinfold thickness 5. Mean haemoglobin post-treatment Not included in review: weight-for-height Z-score and height-for-age Z-score at 3 and 10 months (both after 2 doses) Not included in review Measured but not reported: Z-scores for weight-for-height, height for age using NCHS reference data; egg count (arithmetic and geometric mean); prevalence, intensity; food intake over 3 days in subset at end of trial (not at baseline)
Notes	Location: Benin Community category: 2
Allocation concealment	B – Unclear

Study	Fox 2005
Methods	Randomized controlled trial Generation of allocation sequence: random-number table Allocation concealment: centrally coded allocation system broken after baseline measures taken Blinding: described as double blind; provider unclear Inclusion of all randomized participants (number evaluable/number randomized): 97% (626/646) Length of follow up: 6 months
Participants	Number analysed for primary outcome: 626 Inclusion criteria: children aged 5 to 11 years attending any of 12 primary schools in Haiti where no other deworming activity was taking place Exclusion criteria: none stated
Interventions	Single dose versus placebo: 1. Albendazole 400 mg 2. Placebo (250 mg vitamin C tablet) 3. Albendazole 400 mg plus single dose of 6 mg/kg diethylcarbamazine (DEC) 4. Placebo plus placebo (2 x 250 mg vitamin C tablets) Treatment strategy: randomized and treated all children
Outcomes	1. Weight: final and change in weight 2. Height: final and change in height 3. Adverse effects Not included in review: worm intensity and prevalence; microfilarial density
Notes	Location: Haiti Community category: 2

Characteristics of included studies (Continued)

Weight and height outcomes are only presented for a subgroup of children infected with *Trichuris*

Allocation concealment A – Adequate

Study	Freij 1979i
Methods	<p>Quasi-randomized controlled trial: boys matched into pairs of equal age and nutritional status Generation of allocation sequence: not described Allocation concealment: unclear Blinding: described as double blind Inclusion of all randomized participants (number evaluable/number randomized): 100% (13/13) Length of follow up: 28 days</p>
Participants	<p>Number analysed for primary outcome: 13 Inclusion criteria: boys attending mother and child clinic with <i>Ascaris</i> on stool smear; aged 1.5 to 5 years with no history of diarrhoea for preceding 2 weeks; no fever; no respiratory symptoms; no signs of severe disease Exclusion criteria: children diagnosed with other parasites; excluded girls to eliminate the contamination of samples with urine</p>
Interventions	<p>Single dose versus placebo 1. Piperazine: 3 g single dose 2. Placebo syrup: single dose</p> <p>Treatment strategy: screened children then randomized and treated infected children</p>
Outcomes	<p>1. Weight 2. Mid-upper arm circumference 3. Triceps skinfold thickness</p> <p>Not included in review: <i>Ascaris</i> worm count</p>
Notes	<p>Location: Ethiopia Community category: unclear</p> <p>The authors mention that boys were matched in pairs so that if there were drop outs they could be replaced. They do not indicate if there were any drop outs. Standard deviations calculated from individual data</p> <p>Freij 1979i and Freij 1979ii were reported in the same article</p>
Allocation concealment	B – Unclear

Study	Freij 1979ii
Methods	<p>Quasi-randomized controlled trial: children divided into groups similar for age and nutritional status Generation of allocation sequence: not described Allocation concealment: unclear Blinding: described as double blind Inclusion of all randomized participants (number evaluable/number randomized): 100% (44/44) Length of follow up: 34 days</p>
Participants	<p>Number analysed for primary outcome: 44 Inclusion criteria: 92 children 1 to 5 years from a community morbidity study</p>
Interventions	<p>Single dose versus placebo 1. Piperazine: 3 g/day for 2 days 2. Placebo: for 2 days</p> <p>Treatment strategy: screened children then randomized and treated infected children</p>
Outcomes	<p>1. Mid-upper arm circumference 2. Morbidity</p>

Characteristics of included studies (Continued)

	Not included in review: weight in % of Harvard standard; authors had intended to measure bicep and tricep skinfolds, but staff were unable to take these measurements
Notes	Location: Ethiopia Community category: 3 Freij 1979i and Freij 1979ii were reported in the same article
Allocation concealment	B – Unclear

Study	Garg 2002
Methods	Randomized controlled trial Generation of allocation sequence: computer-generated list of random numbers Allocation concealment: drugs kept in envelope until after baseline assessment Blinding: assessor; participants unclear; provider not blinded Inclusion of all randomized participants (number evaluable/number randomized): 93% (347/370) Length of follow up: 6 months
Participants	Number analysed for primary outcome: 347 Inclusion criteria: sick children 2 to 4 years old presenting to 3 government health centres in Bungamo district, without palmar pallor Exclusion criteria: children with palmar pallor
Interventions	Single dose versus placebo 1. Mebendazole: 500 mg (Vermox, Janssen, Belgium) 2. Placebo: sucrose starch capsule Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment 5. Mean haemoglobin post-treatment 6. Mean change in haemoglobin post-treatment Not included in review: Z-scores for weight-for-age, height-for-age, and weight-for-height; egg count (formol-ethyl acetate concentration method) in categories of intensity
Notes	Location: Kenya Community category: 3
Allocation concealment	A – Adequate

Study	Greenberg 1981
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants; described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 82% (152/185) Length of follow up: 11 months
Participants	Number analysed for primary outcome: 152 aged 1.5 to 8 years Inclusion criteria: children aged 1.5 to 8 years living in Nandipara, Bangladesh; 50% entered into study; only those who provided stool sample and had anthropometric measurements taken at first visit entered Exclusion criteria: none stated
Interventions	Single dose versus placebo 1. Piperazine citrate: 80 mg/kg added to flavoured syrup; 2 doses in 2-week period

Characteristics of included studies (Continued)

	2. Placebo: syrup only
	Treatment strategy: randomized and treated all children
Outcomes	1. Cure rates 2. Reinfection rates 3. Weight-for-height 4. Height-for-age (NCHS reference) 5. Weight-for-age (graphically) 6. Other measured parameters not reported: weight; height; triceps skinfold thickness; mid-upper arm circumference; chest circumference; abdominal girth; egg counts (Dunn's method); prevalence; triceps skinfold for age; mid-upper arm circumference for age (Tanner reference charts)
Notes	Location: Bangladesh Community category: 1 Groups stratified by intensity of <i>Ascaris</i> infection
Allocation concealment	B – Unclear

Study	Hadju 1996
Methods	Randomized controlled trial Generation of allocation sequence: "by descending <i>A. lubricoides</i> egg count" Allocation concealment: unclear Blinding: participants; described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 85% (64/75) Length of follow up: 1.75 months (7 weeks)
Participants	Number analysed for primary outcome: 64 Inclusion criteria: boys aged 6 to 10 years attending second grade at 3 primary schools; completed assessment and provided a stool sample; randomized by descending hookworm count (all treated) Exclusion criteria: none stated
Interventions	Single dose versus placebo 1. Pyrantel palmoate: 10 mg/kg 2. Placebo Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Appetite: consumption test (mL porridge) and self assessment Not included in review: egg counts arithmetic and geometric means (Kato-Katz); weight-for-age (NCHS reference)
Notes	Location: Indonesia Community category: 1 Large drops in geometric mean egg counts in placebo noted
Allocation concealment	B – Unclear

Study	Hadju 1997
Methods	Randomized controlled trial Generation of allocation sequence: "by sex and egg count" Allocation concealment: unclear Blinding: participants and provider; assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 65% (330/507) Length of follow up: 12 months

Characteristics of included studies (Continued)

Participants	Number analysed for primary outcome: 330; mean age 8.3 years Inclusion criteria: all primary school children in grades 1, 2, and 3 in 2 schools in slum areas in Indonesia; randomized according to Ascaris egg count and age Exclusion criteria: children > 11; signs of puberty; signs of severe protein energy malnutrition
Interventions	Multiple doses versus placebo 1. Pyrantel pamoate: 10 mg/kg 2. Pyrantel pamoate: 10 mg/kg repeated at 6 months 3. Albendazole: 400 mg 4. Albendazole: 400 mg repeated at 6 months 5. Placebo Treatment strategy: randomized and treated all children
Outcomes	1. Stool (Kato-Katz) prevalence and intensity 2. Weight 3. Height 4. Mid-upper arm circumference 5. Z-scores: weight-for-age, height for age, weight-for-height, and mid-upper arm circumference Results of multivariate analysis using Z-scores presented and could not be used in meta-analysis; unadjusted results not reported
Notes	Location: Indonesia Community category: 1 Placebo group showed an unexplained drop in egg counts at the 3-month exam
Allocation concealment	B – Unclear

Study	Hall 2006
Methods	Cluster-randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): unclear; 80 schools containing 56,444 pupils randomized, and those from class 3 used in study Length of follow up: 2 years
Participants	Number analysed for primary outcome: 80 schools randomized containing 2659 children in class 3 Mean age: 104.5 months Inclusion criteria: children from class 3 and born in 1990 of 80/81 schools in the Red River delta of north Vietnam
Interventions	Multiple doses versus placebo 1. Albendazole (GlaxoSmithKline): 400 mg every 6 months and 200,000 IU retinol after first 6 months only 2. Retinol: 200,000 IU after first 6 months followed by inert placebo every 6 months Treatment strategy: randomized and treated all children
Outcomes	Measured: 1. Hookworm, Trichuris, and Ascaris prevalence 2. Eggs/g faeces 3. Weight and height
Notes	Location: Vietnam Community category: 1 It is unclear what is meant by “randomization was adjusted so that there were equal numbers of schools in each district of the study group”. It is also appears as if the analysis has not taken into account the effects of cluster randomization

Characteristics of included studies (Continued)

Allocation concealment D – Not used

Study	Kloetzel 1982
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants only; provider and assessor unclear (described as double blind) Inclusion of all randomized participants (number evaluable/number randomized): unclear (337 analysed) Length of follow up: 10 months
Participants	Number analysed for primary outcome: 337; unclear how many randomized; aged 1 to 8 years old Inclusion criteria: enlisted from 9 rural communities in Pariquera-Acu state of S. Paulo Exclusion criteria: none stated
Interventions	Single dose versus placebo 1. Mebendazole: 100 mg twice per day for 3 days 2. Placebo Treatment strategy: randomized and treated all children
Outcomes	1. Weight 2. Height 3. Head, chest, and mid-arm circumference 4. Triceps skinfold 5. Stool egg counts (Kato-Katz)
Notes	Location: Cameroon Community category: 1 Results reported as changes in nutritional status grouped into 3 categories: improved, deteriorated, no change (unclear on basis of which parameter), and proportions compared
Allocation concealment	B – Unclear

Study	Koroma 1996
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): 76% (187/247) Length of follow up: 6 months
Participants	Number analysed for primary outcome: 187 Inclusion criteria: selected (unclear how) urban and rural school primary children aged 6 to 10 years Exclusion criteria: not stated
Interventions	Single dose versus placebo 1. Albendazole: 400 mg 2. Placebo Treatment strategy: randomized and treated all children
Outcomes	1. Prevalence and intensity (arithmetic mean eggs/g) 2. Z-scores (no reference category stated): weight-for-height, weight-for-age, and height-for-age
Notes	Location: Sierra Leone Community category: 2
Allocation concealment	B – Unclear

Characteristics of included studies (Continued)

Study	Kruger 1996
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): 72% (179/247) Length of follow up: 11 months
Participants	Number analysed for primary outcome: 74 aged 6 to 8 years Inclusion criteria: 65 pupils in first year of school randomly selected from each of 5 primary schools; schools included in a feeding scheme Exclusion criteria: age > 9 years; current use of iron supplements; inclusion in an iron fortification trial; infection (raised white cell count)
Interventions	Multiple doses versus placebo 1. Albendazole: 2 x 200 mg repeated at 4 months, daily unfortified soup 2. Placebo: daily unfortified soup Also: whole population 3/5 schools also allocated soup fortified with 20 mg elemental iron per day, and 100 mg vitamin C for 6 months; unclear whether this intervention was cluster randomized. All schools taking part in feeding programme providing bread, soup, and peanut butter to all pupils Treatment strategy: randomized and treated all children
Outcomes	1. Mean change in weight post-treatment 2. Mean change in height post-treatment 3. Mean change in haemoglobin post-treatment Not included in review: other iron indices; stool egg counts (Visser filter method); Z-scores for weight-for-age, height for age, and weight-for-height
Notes	Location: South Africa Community category: 3 In the Dickson 2000 Cochrane Review, the data were combined irrespective of the possible confounding effects of iron allocation; data extracted for albendazole-iron placebo versus placebo-placebo groups only for this review Data stratified by baseline iron stores into 2 groups that were combined for meta-analysis
Allocation concealment	B – Unclear

Study	Kvalsvig 1991i
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): unclear Length of follow up: 1 month
Participants	Number analysed for primary outcome: unclear; age range unclear Inclusion criteria: most severely infected 100 children in a primary school Exclusion criteria: children with schistosomiasis
Interventions	Single dose versus placebo 1. Mebendazole: 500 mg 2. Placebo Treatment strategy: screened children then randomized and treated infected children

Characteristics of included studies (Continued)

Outcomes	1. Cognition tests: card sorting task (coloured cards; cancellation task - striking out of letter 's' in text, number done in a period) Not included in review: height; weight at baseline; standardized using NCHS standards; stool examination (intensity index designed for this trial); no growth outcomes reported that can be used in the review
Notes	Location: South Africa Community category: 1 No data used in meta-analysis since standard deviations not provided
Allocation concealment	B – Unclear

Study **Lai 1995**

Methods	Quasi-randomized controlled trial Generation of allocation sequence: block assignment design by school, then by sex, then by presence of worms as none, light, or moderate/heavy, and then by rank order of body weight in the group; used odd and even numbers; in urban area the odd numbered children were assigned to treatment; in the peri-urban area the even numbered children were assigned to the treatment group Allocation concealment: unclear Blinding: participants only Inclusion of all randomized participants (number evaluable/number randomized): 89% (314/353) Length of follow up: 2 years
Participants	Number analysed for primary outcome: 314 Inclusion criteria: school children aged 8 who provided a stool sample Exclusion criteria: concurrent illness; anthelmintic treatment in previous 3 months
Interventions	Multiple doses versus placebo 1. Mebendazole plus pyrantel: 100 mg mebendazole and 200 mg pyrantel every 3 months for 2 years 2. Placebo: every 3 months for 2 years Treatment strategy: randomized and treated all children
Outcomes	Measured: 1. Hookworm, Trichuris, and Ascaris prevalence 2. Eggs/g faeces 3. Weight and height
Notes	Location: Malaysia Community category: 1 No data used in meta-analysis since standard deviations not provided
Allocation concealment	B – Unclear

Study **Michaelsen 1985**

Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: unclear Inclusion of all randomized participants (number evaluable/number randomized): 53% (121/228) Length of follow up: 5 months
Participants	Number analysed for primary outcome: 121 for growth outcomes; age range 5 to 14 years Inclusion criteria: children from a school identified as having high prevalence of hookworm on the basis of a previous survey Exclusion criteria: children with height above 137 cm girls and 145 cm for boys since these were the upper limits in the reference ranges

Characteristics of included studies (Continued)

Interventions	Single dose versus placebo 1. Tetrachloroethylene: 0.1 mL/kg (max 5 mL dose) 2. Placebo: children's cough medicine Treatment strategy: randomized and treated all children
Outcomes	Measured: 1. Stool: prevalence in subgroup 2. Haemoglobin 3. Weight 4. Height 5. Weight-for-height (WHO reference median 1983) Reported: 1. Stool prevalence (graph) with 95% confidence intervals 2. Haemoglobin mean and difference (no SD) 3. Weight-for-height %, mean and difference (no SD)
Notes	Location: Botswana Community category: 1
Allocation concealment	B – Unclear

Study Nokes 1992

Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants; described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 73% (103/140) Length of follow up: 2.25 months (9 weeks)
Participants	Number analysed for primary outcome: 103; age range 9 to 12 years Inclusion criteria: children from 3 schools in Mandeville; Trichuris egg counts > 1900, but low hookworm counts on 2 occasions before the trial separated by 3 months Exclusion criteria: twins; severe illness; physical handicaps; neurological disorders
Interventions	Single dose versus placebo 1. Albendazole: 400 mg daily for 3 days (SmithKlineBeecham) 2. Placebo: identical Treatment strategy: screened children then randomized and treated infected children
Outcomes	1. School attendance 2. Cognitive tests: digit span forwards/backwards; arithmetic and coding from Wechsler Intelligence Scale for Children; fluency and listening comprehension from the Clinical Evaluation of Language functions; and matching familiar figures test Not included in review: stool egg counts at baseline and 10 days (prevalence and arithmetic mean); height and weight (expressed as % NCHS standard) iron status; school attendance; IQ; socioeconomic status; educational opportunity measures at baseline Outcomes not reported: growth outcomes at 9 weeks cited as too short a follow-up period to demonstrate a change
Notes	Location: Jamaica Community category: 1 There was an infected placebo group and an "uninfected control group"
Allocation concealment	B – Unclear

Characteristics of included studies (Continued)

Study	Palupi 1997
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants; described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 97% (289/299) Length of follow up: 9 weeks (2.25 months)
Participants	Number analysed for primary outcome: 191 Inclusion criteria: children ages 2 to 5 years registered at village health centres Exclusion criteria: none stated
Interventions	Single dose versus placebo 1. Albendazole: 400 mg plus 30 mg elemental iron weekly 2. Elemental iron: 30 mg weekly Treatment strategy: randomized and treated all children
Outcomes	1. Mean change in weight post-treatment 2. Mean change in height post-treatment 3. Mean change in haemoglobin post-treatment 4. Mean haemoglobin post-treatment Not included in review: Z-scores for height-for-age, weight-for-age, and weight-for-height (NCHS reference)
Notes	Location: Java, Indonesia Community category: 2
Allocation concealment	B – Unclear

Study	Rousham 1994
Methods	Cluster-randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 94% (1402/1476) Length of follow up: 18 months
Participants	Number analysed for primary outcome: 1402 Inclusion criteria: children ages 2 to 6 years from 13 villages surrounding a mother and child health centre; subgroup living in 8 villages within waking distance of health centre analysed for additional outcomes Exclusion criteria: none stated
Interventions	Multiple doses versus placebo 1. Mebendazole: 500 mg (Janssen) every 2 months 2. Placebo 3. Pyrantel pamoate and mebendazole: initial dose of 10 mg/kg pyrantel pamoate (Combantrin, Pfizer, UK) then mebendazole 500 mg bimonthly for 8 months (4 doses) Treatment strategy: randomized and treated all children
Outcomes	1. ANOVAs for change in Z-scores for height-for-age, weight-for-age, and weight-for-height (NCHS reference) 2. Change in mid-upper arm circumference at 6, 12, and 18 months (no SD) 3. Other outcomes measured but not reported: height; weight; stool examination for prevalence and intensity in subgroup (eggs/g: modified sedimentation technique); subgroup also analysed for intestinal permeability, albumin, alpha-1-antichymotrypsin, total protein every 2 months
Notes	Location: Bangladesh Community category: 1

Characteristics of included studies (Continued)

No adjustment made for cluster randomization	
Allocation concealment	B – Unclear
Study	Sarkar 2002
Methods	Randomized controlled trial Generation of allocation sequence: unclear Allocation concealment: unclear Blinding: participants described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 94% (81/85) Length of follow up: 4 months (16 weeks)
Participants	Number analysed for primary outcome: 81 Inclusion criteria: children ages 2 to 12 living in Mirpur slum infected with <i>Ascaris</i> Exclusion criteria: none stated
Interventions	Single dose versus placebo 1. Pyrantel pamoate: 11 mg/kg (Combantrin, Pfizer, Bangladesh) 2. Placebo Treatment strategy: screened children then randomized and treated infected children
Outcomes	1. Mean change in weight post-treatment 2. Mean weight post-treatment 3. Mean change in height post-treatment 4. Mean height post-treatment Not included in review: median % weight-for-age, weight-for-height, and height-for-age
Notes	Location: Bangladesh Community category: 1
Allocation concealment	B – Unclear
Study	Simeon 1995
Methods	Randomized controlled trial Generation of allocation sequence: random-numbers table Allocation concealment: unclear Blinding: participants described as double blind; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 96% (392/407) Length of follow up: 6.5 months (26 weeks)
Participants	Number analysed for primary outcome: 392; age range 6 to 12 years Inclusion criteria: children in grades 2 to 5 of 14 schools in Jamaica with intensities of <i>Trichura</i> > 1200 eggs/g Exclusion criteria: children with mental handicaps identified by their teachers
Interventions	Multiple doses versus placebo 1. Albendazole: 800 mg (400 mg in each of 2 days), repeated at 3 months and 6 months 2. Identical placebo Treatment strategy: screened children then randomized and treated infected children
Outcomes	1. Main study (264 children) Wide range achievement test: reading, arithmetic, and spelling subtests; school attendance from children with class registers pre- and post-intervention, height-for-age Z-score, body mass index pre- and post-intervention 2. Subgroup 1 (189 infected children from original population) Digit span; verbal fluency test; visual search; number choice; French vocabulary learning 3. Subgroup 2 (97 children from grade 5) French learning; digit spans (forward and backward); Corsi block span; verbal fluency; picture search; silly sentences

Characteristics of included studies (Continued)

	Other outcomes measured but not reported: stool at baseline and at 8 weeks after second treatment round (Kato): prevalence and intensity, weight, height, Z-scores (NCHS standard)
Notes	Location: Jamaica Community category: 1
Allocation concealment	B – Unclear

Study Stephenson 1989

Methods	Randomized controlled trial Generation of allocation sequence: “at random within sex” Allocation concealment: unclear Blinding: participants and assessor only; provider unclear Inclusion of all randomized participants (number evaluable/number randomized): 88% (150/171) Length of follow up: 6 months
Participants	Number analysed for primary outcome: 150 Inclusion criteria: all available children in lower grades (standards 1 and 2) in Mvindi Primary School, Kwale district (unscreened); subgroup of 36 boys chosen; haemoglobin > 8; willing to co-operate in physical tests; pre-pubertal Exclusion criteria: haemoglobin < 8
Interventions	Single dose versus placebo 1. Albendazole: 2 x 200 mg (SmithKline and French) 2. Placebo: identical Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment 5. Mean mid-upper arm circumference 6. Mean change in mid-upper arm circumference 7. Mean triceps skinfold thickness 8. Mean change in triceps skinfold thickness 9. Mean subscapular skinfold thickness 10. Mean change in subscapular skinfold thickness Not included in review: all above converted to % median for sex and age; prevalence and mean egg counts (arithmetic and geometric means); Harvard Step Test heart rates and score for subgroup
Notes	Location: Kenya Community category: 1
Allocation concealment	B – Unclear

Study Stephenson 1993

Methods	Randomized controlled trial Generation of allocation sequence: “at random within sex by descending hookworm egg count” Allocation concealment: unclear Blinding: participants and assessor only; provider unclear Inclusion of all randomized participants (number evaluable/number randomized): 86% (284/328) Length of follow up: 3.6 months (subgroup) and 8.2 months (main study)
Participants	Number analysed for primary outcome: 284 Inclusion criteria: all school children (unscreened) in grades 1 to 5 in Mvindi Primary School

Characteristics of included studies (Continued)

	<p>Subgroup (53 analysed) of 60 boys chosen because haemoglobin > 80 g/L, willing to cooperate in physical tests and appetite tests, pre-pubertal, infected with at least 1 of helminths (screened), hookworm < 20,000 eggs/g; hookworm or Trichuris count > 1000 eggs/g or Ascaris > 4000 eggs/g Exclusion criteria: Severe anaemia (haemoglobin < 75 g/L)</p>
Interventions	<p>Multiple doses versus placebo</p> <ol style="list-style-type: none">1. Albendazole (single dose) plus placebo: 600 mg (3 x 200 mg) SmithKline Beecham at outset, identical placebo at 3.6 months2. Albendazole (multiple doses): single dose 600 mg repeated at 3.6 months3. Placebo: identical placebo <p>Treatment strategy: randomized and treated all children (but infected children for appetite/activity outcomes)</p>
Outcomes	<ol style="list-style-type: none">1. Mean weight post-treatment2. Mean change in weight post-treatment3. Mean height post-treatment4. Mean change in height post-treatment5. Mean mid-upper arm circumference6. Mean change in mid-upper arm circumference7. Mean triceps skinfold thickness8. Mean change in triceps skinfold thickness9. Mean subscapular skinfold thickness10. Mean change in subscapular skinfold thickness11. Mean haemoglobin post-treatment12. Mean change in haemoglobin post treatment <p>Not included in review: prevalence, eggs/g: geometric and arithmetic mean; converted to percentage of median for age and sex using NCHS references; % weight-for-age, % height for age; % weight-for-height; % arm circumference for age; % triceps for age; % subscapular for age; Harvard Step Test; appetite (self-rating and snack consumed intake in kilojoules); haemoglobin</p>
Notes	<p>Location: Kwale, Kenya Community category: 1</p>
Allocation concealment	B – Unclear
Study	Stoltzfus 1997
Methods	<p>Cluster-randomized controlled trial Generation of allocation sequence: from each of the 4 districts, 3 schools randomly selected and then allocated Allocation concealment: unclear Blinding: participants only; provider and assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 84% (3063/3605) Length of follow up: 12 months</p>
Participants	<p>Number analysed for primary outcome: 3063; mean age 10.5 years Inclusion criteria: children in grades 1 to 5 from 12 randomly selected schools on Pemba island; only grades 1 to 4 included in evaluation of nutritional effect Exclusion criteria: none stated</p>
Interventions	<p>Multiple doses versus placebo</p> <ol style="list-style-type: none">1. Mebendazole: 500 mg twice yearly2. Mebendazole: 500 mg 3 times a year3. Placebo <p>Treatment strategy: randomized and treated all children</p>
Outcomes	<ol style="list-style-type: none">1. Weight gain2. Height gain3. Change in haemoglobin at 12 months

Characteristics of included studies (Continued)

Estimates are provided from multiple regression models taking into account various baseline differences for 2 subgroups above and below 10 years old. Unadjusted outcomes not presented. (These 2 groups were combined in the Dickson 2000 Cochrane Review.)

Other outcomes measured but not reported: micronutrient status (blood) for protoporphyrin and serum ferritin; stool egg count (Kato-Katz); Z-scores for height-for-age and weight-for-height; body mass index

Notes	Location: Zanzibar, Tanzania Community category: 1 Appropriate adjustment made for cluster randomization using general estimating equation
Allocation concealment	B – Unclear

Study	Stoltzfus 2001
Methods	Randomized control trial (factorial design) Generation of allocation sequence: “blocks of 4” Allocation concealment: pills in bottles with unique treatment codes, assigned by 1 investigator, codes kept in sealed envelopes Blinding: participants and provider; assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 52% (359/684 = 52%) Length of follow up: 12 months
Participants	Number analysed for primary outcome: 359 in mebendazole arm aged 6 to 59 months Inclusion criteria: all children in Kengeja village, with age reported as 3 to 56 months by parents; 3 months before planned start of trial (pre-school children) Exclusion criteria: severe anaemia (< 70 g/L)
Interventions	Multiple doses versus placebo 1. Mebendazole: 500 mg given every 3 months at home visits 2. Placebo: identical Treatment strategy: randomized and treated all children Both groups also received: 0.5 mL ferrous sulfate (20 mg/mL); 10 mg iron daily for 1 year or placebo as per factorial design
Outcomes	1. Cognitive outcomes: motor and language development by parents reporting gross motor and language milestones using scoring system developed specifically for the trial 2. Anthropometric measures presented in a stratified manner: (< 30 months, > 30 months), and presented as proportion of children with small arm circumference, mild wasting, and stunting 3. Proportion of children with poor appetite, and proportion with severe anaemia are presented for the whole group 4. Iron indices (not disaggregated, independent of the iron randomization) Not included in review: prevalence and egg counts (no SD/SEM); motor and language scores (results of multiple regression and correlations; raw data not reported) Others measured but not reported: stool (Kato-Katz); weight; height; haemoglobin; malaria film; ferritin; appetite as reported by mothers
Notes	Location: Zanzibar, Tanzania Community category: 2 Factorial design, with households randomized to iron, random allocation of mebendazole by child, stratified by iron allocation and age grouped households. An iron with mebendazole treatment term was tested in all regression models, but it did not reach significance
Allocation concealment	A – Adequate

Characteristics of included studies (Continued)

Study	Sur 2005
Methods	Randomized controlled trial Generation of allocation sequence: computer-generated random numbers sequence Allocation concealment: identical coded bottles Blinding: participants, provider, and assessor Inclusion of all randomized participants (number evaluable/number randomized): 97% (683/702) Length of follow up: 12 months
Participants	Number analysed for primary outcome: 683 Inclusion criteria: all children aged 2 to 5 in slum area of Tiljala identified and enrolled Exclusion criteria: major illnesses; birth defects; and unwillingness to participate
Interventions	Multiple doses versus placebo 1. Albendazole: 400 mg in a vitamin B complex base liquid; repeated at 6 months 2. Placebo: vitamin B complex base Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment (presented graphically) Other outcomes measured but not reported: stool samples from random sample of 30% (formalin concentration technique) for prevalence of <i>Ascaris</i> ; weight-for-age; diarrhoeal episodes
Notes	Location: India Community category: 2
Allocation concealment	A – Adequate

Study	Watkins 1996
Methods	Randomized controlled trial Generation of allocation sequence: “stratified by gender and age” Allocation concealment: unclear Blinding: participants and provider; assessor unclear Inclusion of all randomized participants (number evaluable/number randomized): 90% (226/250) Length of follow up: 6 months
Participants	Number analysed for primary outcome: 226 for growth outcomes, reduced for cognitive outcomes; age 7 to 12 years Inclusion criteria: children attending grades 1 to 4 in primary schools in the Guatemala highlands Exclusion criteria: > 12 years; deworming medicine in last year
Interventions	Multiple doses versus placebo 1. Albendazole: 2 x 200 mg at baseline and 12 weeks 2. Placebo: identical at baseline and 12 weeks Treatment strategy: randomized and treated all children
Outcomes	1. Mean weight post-treatment 2. Mean change in weight post-treatment 3. Mean height post-treatment 4. Mean change in height post-treatment 5. School performance: attendance rates of children actively attending school, dropout rates 6. Mean mid-upper arm circumference 7. Mean change in mid-upper arm circumference 8. Cognitive tests: Interamerican vocabulary test, Interamerican reading test, Peabody picture vocabulary test Not included in review: egg counts (Kato-Katz: arithmetic and geometric mean); Z-scores (NCHS-CDC-WHO reference) for weight-for-age, change in weight-for-age, height, change in height, height-for-age, change in height-for-age, weight-for-height, and change in height-for-age

Notes Location: Guatemala
Community category: 1

Allocation concealment B – Unclear

Study Willett 1979

Methods	Randomized controlled trial Generation of allocation sequence: random-numbers table; “stratified by sex and age” Allocation concealment: unclear Blinding: described as double blind; participants and assessor only; provider unclear Inclusion of all randomized participants (number evaluable/number randomized): 78% (268/341) Length of follow up: 12 months
Participants	Number analysed for primary outcome: 268; age range 6 to 91 months Inclusion criteria: pre-school children from Ubiri village who attended clinic and produced a stool sample Exclusion criteria: none stated
Interventions	Multiple doses 1. Levamisole syrup: 2.5 mg/kg every 3 months 2. Flavoured sucrose syrup: every 3 months Treatment strategy: randomized and treated all children
Outcomes	1. Growth rates in both groups, and subgroup of those infected; these have been corrected for various factors using analysis of covariance (unadjusted data are not reported and the growth rates are not presented with any measure of variance) Measured but not reported: height; length; stool egg count in subgroup (Kato method); growth rates using least square method
Notes	Location: Tanzania Community category: 2
Allocation concealment	B – Unclear
CI: confidence interval; Community category: a measure of the prevalence and intensity of infection (see Table 02); NCHS: National Center for Health Statistics; SD: standard deviation; SEM: standard error of the mean	

Characteristics of excluded studies

Study	Reason for exclusion
Bhargava 2003	Treatment regimen comprised of albendazole for geohelminths and praziquantel against schistosomiasis versus placebo
Boivin 1993	Factorial-designed randomized controlled trial with children allocated to deworming and iron supplementation, and in which the analysis compares the results for the levamisole and iron group against all the other groups combined. (Included in the Dickson 2000 Cochrane Review.)
Cooper 2006	Study of allergy with no nutritional or cognitive outcomes
Cowden 2000	Not a randomized controlled trial
Diouf 2002	Intervention comprised mebendazole, vitamin A, and iron supplementation metronidazole as a combined intervention versus placebo
Evans 1986	Treatments randomized, but some placebo groups accessed treatment. Analysis was by the treatment received, and randomization was ignored. (Included in the Dickson 2000 Cochrane Review.)
Fernando 1983	2 villages allocated to treatment or no treatment on the basis of a coin toss. Essentially a cluster-randomized trial with 2 large clusters. (Included in the Dickson 2000 Cochrane Review, which reported that no conclusions could be drawn from the results due to selective reporting.)

Characteristics of excluded studies (Continued)

Friis 2003	Combined treatment regimen albendazole for geohelminths and praziquantel for <i>Schistosoma mansoni</i> versus placebo
Gupta 1982	Children randomly divided into 4 groups, "taking care that age distribution was similar in each group". The 4 groups were then allocated 1 of 4 different single treatment regimens; no details given. We excluded trials in communities with only 2 units of allocation
Hadidjaja 1998	Cluster-randomized controlled trial with 2 units of allocation to mebendazole and placebo. Authors stated that there were differences in environmental sanitary conditions in the clusters. (Included in the Dickson 2000 Cochrane Review, but it was noted that the groups were not comparable and there was high loss to follow up.)
Jinabhai 2001a	Treatment regimen comprised of albendazole for geohelminths and praziquantel against schistosomiasis versus placebo
Jinabhai 2001b	Treatment regimen comprised of albendazole for geohelminths and praziquantel against schistosomiasis versus placebo
Kvalsvig 1991ii	Incomplete data on the number of children in each arm of the trial. The researchers were unable to re-test children due to major floods in the area
Miguel 2004	Treatment regimen comprised of albendazole for geohelminths and praziquantel against schistosomiasis versus placebo
Pollitt 1991	Not described as randomized; conference proceedings
Taylor 2001	Treatment regimen albendazole for geohelminths and praziquantel for <i>Schistosoma haematobium</i> versus placebo
Thein-Hlaing 1991	3/11 intervention villages were not randomly allocated, and unclear how intervention and control villages were allocated as there is a large imbalance (8 intervention and 13 non-intervention villages)
Yang 2003	Did not consider growth or cognitive outcome measures

Characteristics of ongoing studies

Study	Alam 2006
Trial name or title	"Relative efficacy of two regimens of ante-helminthic treatment"
Participants	Total enrolment: 200 Inclusion criteria: age 2 to 5 years; not suffering from serious chronic illness; stool test positive for soil-transmitted helminths; not taken any anthelmintic drug in previous 6 months; parents/guardian agree their child's participation Exclusion criteria: age < 2 years and > 5 years; stool test negative for any intestinal helminth; suffering from serious chronic illness; parents/guardian not willing to give consent for their child's participation; if he/she receives any anthelmintic drug after survey but before the study interventions
Interventions	1. Conventional treatment of 400 mg of albendazole in a single dose at 6-month interval 2. Intervention group: 400 mg of albendazole in a single-dose treatment at 3-month interval
Outcomes	PRIMARY 1. To determine the relative efficacy of de-worming at every 3 months versus every 6 month single dose of albendazole treatment SECONDARY 2. To compare additional morbidity information such as diarrhoeal diseases, respiratory tract infections, nutritional status and <i>E. histolytica</i> associated morbidity between 2 groups
Starting date	Not yet recruiting
Contact information	Mohammad M Alam MBBS, Principal Investigator, ICDDR,B: Centre for Health and Population Research, masud_icddrb@yahoo.com
Notes	ClinicalTrials.gov identifier: NCT00367627

Characteristics of ongoing studies (Continued)

Sources of support: International Centre for Diarrhoeal Disease Research, Bangladesh (sponsor)

Study	Lucknow ongoing
Trial name or title	Cluster-randomized controlled trial in Lucknow, India
Participants	Details unavailable
Interventions	Details unavailable
Outcomes	Details unavailable
Starting date	Details unavailable
Contact information	Details unavailable
Notes	Details unavailable
Study	Stoltzfus 2004
Trial name or title	“Effects of intestinal helminth infections in early childhood on immune response, inflammation, anaemia and malnutrition”
Participants	Expected enrolment: 2500 Inclusion criteria: 6 to 24 months of age; informed consent; residing in selected communities based on geographic catchment area Exclusion criteria: haemoglobin < 70 g/L; refusal of informed consent
Interventions	1. Mebendazole 2. Identical-looking but inert placebo
Outcomes	PRIMARY 1. Haemoglobin < 70 g/L 2. Mid-upper arm circumference < -2 Z scores of international reference 3. Maternal report of anorexia SECONDARY 4. Weight-for-height < -1 Z scores of international reference 5. Height-for-age < -2 Z scores on international reference 6. Inflammation
Starting date	1 January 2004 End of follow up date: 31 March 2006
Contact information	Ms Rebecca J Stoltzfus, Cornell University Division of Nutritional Sciences, rjs62@cornell.edu
Notes	ISRCTN: 83988447 Sources of support: Burroughs Wellcome Initiative; Wellcome Trust; Cornell University, USA (sponsor)

ADDITIONAL TABLES

Table 01. Community diagnosis categories and recommended treatment strategies (WHO 2002)

Community category	Prevalence [^]	Proportion ^{^^}	School intervention
1. High prevalence or high intensity	> 70%	> 10%	Targeted treatment of school-age children 2 to 3 times per year
2. Moderate prevalence and low intensity	> 50% but < 70%	< 10%	Targeted treatment of school-age children once

Table 01. Community diagnosis categories and recommended treatment strategies (WHO 2002) (Continued)

Community category	Prevalence [^]	Proportion ^{^^}	School intervention per year
3. Low prevalence and low intensity of any worm infection of moderate to heavy infections	< 50%	< 10%	Selective treatment

Table 02. Detailed search strategies

Search set	CIDG SR [^]	CENTRAL	MEDLINE ^{^^}	EMBASE ^{^^}	LILACS ^{^^}
1	helmint*	helmint*	helmint*	helmint\$	helmint*
2	Ancylostoma duodenale	Ancylostoma duodenale	Ancylostoma duodenale	Ancylostoma duodenale	Ancylostoma duodenale
3	Necator americanus	Necator americanus	Necator americanus	Necator americanus	Necator americanus
4	Ascaris	Ascaris	Ascaris	Ascaris	Ascaris
5	Enterobius vermicularis	Enterobius vermicularis	Enterobius vermicularis	Enterobius vermicularis	Enterobius vermicularis
6	trichuris	trichuris	trichuris	trichuris	trichuris
7	Strongyloid*	Strongyloid*	Strongyloid*	Strongyloid*	Strongyloid*
8	albendazole	hookworm*	hookworm*	hookworm\$	1-7/OR
9	mebendazole	roundworm*	roundworm*	roundworm\$	albendazole
10	piperazine	pinworm*	pinworm*	pinworm\$	mebendazole
11	levamisole	whipworm*	whipworm*	whipworm\$	piperazine
12	pyrantel	1-11/OR	1-11/OR	1-11/OR	levamisole
13	tiabendazole	albendazole	albendazole	albendazole	pyrantel
14	-	mebendazole	mebendazole	mebendazole	tiabendazole
15	-	piperazine	piperazine	piperazine	9-14/OR
16	-	levamisole	levamisole	levamisole	8 and 15
17	-	pyrantel	pyrantel	pyrantel	Limit 16 to human
18	-	tiabendazole	tiabendazole	tiabendazole	-
19	-	13 or 14 or 15 or 16 or 17 or 18	13 or 14 or 15 or 16 or 17 or 18	13 or 14 or 15 or 16 or 17 or 18	-
20	-	12 and 19	12 and 19	12 and 19	-
21	-	-	Limit 20 to human	Limit 20 to human	-
	[^] Cochrane Infectious Diseases		^{^^} Search terms used in		

Table 02. Detailed search strategies (Continued)

Search set	CIDG SR [^]	CENTRAL	MEDLINE ^{^^}	EMBASE ^{^^}	LILACS ^{^^}
	Group Specialized Register		combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Higgins 2006); upper case: MeSH or Emtree heading; lower case: free text term		

Table 03. Cluster-randomized controlled trials

Trial	Cluster	No. clusters	Adjustment [^]
Alderman 2006	Parishes	48	Not adjusted (correspondence with author)
Awasthi 1995	Urban slums	50	Means of cluster means
Awasthi 2001	Urban slums	124	Means of cluster means
Hall 2006	Schools	80	Unclear
Rousham 1994	Villages	13	No
Stoltzfus 1997	Schools	12	General estimating equation

[^]for cluster randomization

Table 04. Trials with incomplete statistical data sets

Randomization type	Dose schedule	Trial	Intervention	Results
Individual	Single dose	Beach 1999	Albendazole	A nutritional benefit of treatment was not detectable after 4 months for the entire study population (853 participants, no figures provided). Stratification by infection demonstrated small positive effects in the treatment group for some anthropometric outcomes. In Ascaris-infected children (51), height gain was 0.62 cm greater than placebo in the combination treatment group (P = 0.01) at 4 months. In Trichuris-infected children (158), height gain was 0.56 kg greater than placebo in the combination treatment group (P = 0.01) at 4 months
Individual	Single dose	Fox 2005	Albendazole	No results provided for whole study population. Results for height and weight only presented in the narrative for subgroups infected with hookworm and Ascaris: no significant anthropometric changes detected (no figures quoted). In those infected with Trichuris, weight gain was greater in the albendazole group (difference compared to placebo 0.28 kg, P = 0.038)
Individual	Single dose	Greenberg 1981	Piperazine citrate	Treatment group tended to show worse growth than placebo. Comparison showed no significant difference for all measured anthropometric variables for the total group and for subgroups defined by severity of infection (no figures provided)
Individual	Single dose	Kloetzel 1982	Mebendazole	No significant difference was found between the groups. Results reported as the proportion of treatment or control group that improved, deteriorated, or experienced no change. Unclear which anthropological measures were used in this categorization process. Proportions in each category were not significantly

Table 04. Trials with incomplete statistical data sets (Continued)

Randomization type	Dose schedule	Trial	Intervention	Results
Individual	Single dose	Koroma 1996	Albendazole	<p>different between trial arms (improved: 51% in mebendazole group vs 49% in control; deteriorated: 35% in mebendazole group vs 33% in control; no change: 14% in mebendazole group vs 18% in control; no significance test results quoted)</p> <p>Significant increases in weight-for-height, weight-for-age, and height-for-age Z-scores recorded in rural and urban treatment groups at 6 months</p> <p>Mean increase in rural treatment group compared to placebo: weight-for-height Z-score 0.28 (SE 0.17) $P < 0.05$; weight-for-age Z-score 1.04 (SE 0.03) $P < 0.05$; and height-for-age Z-score 0.83 (SE 0.03) $P < 0.001$</p> <p>Mean increase in urban treatment group compared to placebo: weight-for-height Z-score 1.04 (SE 0.07) $P < 0.05$; weight-for-age Z-score 1.02 (SE 0.09) $P < 0.001$; and height-for-age Z-score 1.01 (SE 0.02) $P < 0.05$</p> <p>Significant increases in weight-for-height, weight-for-age, and height-for-age Z-scores recorded in rural and urban treatment groups at 6 months (mean increase in rural treatment group compared to placebo): weight-for-height Z-score 0.28 (SE 0.17) $P < 0.05$; weight-for-age Z-score 1.04 (SE 0.03) $P < 0.05$; and height-for-age Z-score 0.83 (SE 0.03) $P < 0.001$</p> <p>Mean increase in urban treatment group compared to placebo: weight-for-height Z-score 1.04 (SE 0.07) $P < 0.05$; weight-for-age Z-score 1.02 (SE 0.09) $P < 0.001$; and height-for-age Z-score 1.01 (SE 0.02) $P < 0.05$</p>
Individual	Single dose	Michaelsen 1985	Tetra-chlorethylene	No significant difference in change in mean

Table 04. Trials with incomplete statistical data sets (Continued)

Randomization type	Dose schedule	Trial	Intervention	Results
				for haemoglobin (tetrachloroethylene 0.22 g/100 mL vs placebo 0.09 g/100 mL; quoted as nonsignificant) or weight for height at 5 months (tetrachloroethylene -1.3% of WHO reference mean vs placebo -0.4%; quoted as nonsignificant)
Individual	Single dose	Nokes 1992	Albendazole	Growth measured but not reported: 9 weeks cited as too short a follow-up period to demonstrate a change
Individual	Multiple dose trials > 1 year	Lai 1995	Mebendazole plus pyrantel	No difference in height or weight between treatment and control group at the end of 2-year follow up. Standard deviations not provided. Results stratified for males and females: Females: change in height in treatment arm 12.2 cm vs change in height in placebo arm 12.4 cm; change in weight in treatment arm 5.6 kg vs change in weight in placebo arm 5.6 kg Males: change in height in treatment arm 11.8 cm vs change in height in placebo arm 11.4cm; change in weight in treatment arm 5.7 kg vs change in weight in placebo arm 4.7 kg
Individual	Multiple dose trials < 1 year	Hadju 1997	Pyrantel pamoate Albendazole	No significant differences detected between treatment groups on basis of multivariate analyses controlling for age, sex, and 'times': Change in weight-for-age Z-score: placebo 0.02; pyrantel 1 x treatment 0.03; pyrantel 2 x treatments 0.08; albendazole 1 x treatment - 0.10; albendazole 2 x treatments 0.01 Change in height-for-age Z-score: placebo 0.01; pyrantel 1 x treatment 0.00; pyrantel 2 x treatments 0.04; albendazole 1 x treatment -

Table 04. Trials with incomplete statistical data sets (Continued)

Randomization type	Dose schedule	Trial	Intervention	Results
Individual	Multiple dose trials < 1 year	Simeon 1995	Albendazole	<p>0.07; albendazole 2 x treatments 0.01 Change in weight-for-height Z-score: placebo 0.02; pyrantel 1 x treatment 0.08; pyrantel 2 x treatments 0.05; albendazole 1 x treatment -0.07; albendazole 2 x treatments 0.03 Change mid-arm circumference Z-score: placebo -0.09; pyrantel 1 x treatment -0.11; pyrantel 2 x treatments -0.11; albendazole 1 x treatment -0.07; albendazole 2 x treatments -0.01</p> <p>No significant difference in any reported outcome for whole group: Height-for-age Z-score at baseline in treatment group -0.48 (0.95) and in placebo group -0.39 (0.90). At follow up in treatment group -0.48 (0.97) and in placebo group -0.41 (0.89) Body mass index (kg/m²) at baseline in treatment group 15.3 (1.3) and in placebo group 15.5 (1.3). At follow up in treatment group 15.6 (1.3) and in placebo group 15.8 (1.4)</p>
Individual	Multiple dose trials < 1 year	Stoltzfus 2001	Mebendazole	<p>Mebendazole is reported as significantly reducing the prevalence of mild wasting malnutrition in a subgroup of children aged < 30 months only (adjusted odds ratio for mebendazole 0.38 (95% CI 0.16 to 0.90) for weight-for-height Z-score < -1). Mebendazole is reported as significantly reducing the prevalence of poor appetite across the whole group (adjusted odds ratio for mebendazole 0.52 (95% CI 0.30 to 0.89) for weight-for-height Z-score < -1). Mebendazole had no impact on iron indices. Adjusted effect on motor scores had a tendency to favour mebendazole, but this was not significant</p>

Table 04. Trials with incomplete statistical data sets (Continued)

Randomization type	Dose schedule	Trial	Intervention	Results
Individual	Multiple dose trials < 1 year	Willett 1979	Levamisole	No statistical difference in growth rates in terms of height and weight between the 2 groups. Growth rates presented are adjusted for a number of variables. Weight gain (kg/year) in levamisole group 2.08 vs 1.92 in placebo group (P = 0.06). Height gain (cm/year) in levamisole group 7.58 vs 7.73 in placebo group (no significance quoted)
Cluster-randomized trial (12 schools)	Multiple dose trials < 1 year	Stoltzfus 1997	Mebendazole	Weight gain: in a subgroup of under 10 year olds, the twice-yearly treated group experienced significantly greater weight gain (kg) compared to control (2.38 (SE 0.08) vs 2.11 (SE 0.08), P < 0.05). In the thrice yearly treatment group the difference was not significant (2.31 (SE 0.08) vs 2.11 (SE 0.08), no P value stated) Height gain: in under 10 year olds the thrice-yearly treated group experienced significantly greater height gain (cm) compared to control (4.59 (SE 0.07) vs 4.29 (SE 0.07), P < 0.01). In the twice-yearly treatment group the difference in height gain was not significant (4.42 (SE 0.07) vs 4.29 (SE 0.07), no P value stated). There were no significant differences found in the subgroup of children aged over 10 years Haemoglobin change: deworming had no effect on haemoglobin change in an adjusted analysis presented for the whole study group (g/L): control 11.3 (SE 1.7); twice-yearly treatment group 10.3 (SE 1.7); and thrice-yearly group 12.7 (SE 1.7)
Cluster-randomized trial (50 parishes)	Multiple dose trials > 1 year	Alderman 2006	Albendazole	Trial authors reported average weight gain over a period of up to 3 years for individual children within the 24 treatment parishes

Table 04. Trials with incomplete statistical data sets (Continued)

Randomization type	Dose schedule	Trial	Intervention	Results
Cluster-randomized trial (80 schools)	Multiple dose trials > 1 year	Hall 2006	Albendazole	and the 24 control parishes. In the treatment parishes, the mean (SD) weight gain (g) 2413 (2536) and in the control parishes 2259 (2474) (Alderman 2006; Table 02). Trial authors confirmed that these results were not adjusted to take into account clustering. In table 3 of the same paper, a regression analysis is adjusted for sampling effects Trial authors reported no difference in final and change in weight and height. Mid-upper arm circumference and subscapular skinfold thickness improved significantly in the control group compared to the albendazole group. These results do not appear to have been adjusted for cluster randomization. The results that show no effect, however, will not remain nonsignificant even after appropriate adjustment, though the confidence intervals may change
Cluster-randomized trial (13 villages)	Multiple dose trials > 1 year	Rousham 1994	Mebendazole	ANOVAS of the change in Z-scores revealed no significant improvement with treatment. Change in weight-for-age and weight-for-height Z-scores were significantly worse in the treatment group. Height-for-age Z-score (mebendazole 0.25 v 0.17 in placebo group, P 'nonsignificant'), weight-for-age Z-score (mebendazole 0.03 vs 0.12 in placebo group, P < 0.05), weight-for-height Z-score (mebendazole -0.25 vs -0.05 in placebo group, P < 0.001), and mid-upper arm circumference were presented (mebendazole 0.33 vs 0.23 in placebo group, P 'nonsignificant')

Table 05. Methodological quality assessment

Trial	Design	Sequence[^]	Concealment[^]	Blinding	Inclusion[^]
Adams 1994	Individual	Unclear	Unclear	Participants only; provider and assessor unclear	Adequate
Awasthi 2000	Individual	Inadequate	Inadequate	Participants only; provider not blinded; assessor unclear	Adequate
Beach 1999	Individual	Adequate	Unclear	Participants, provider, and assessors	Inadequate
Donnen 1998	Individual	Unclear	Unclear	Unclear	Inadequate
Dossa 2001	Individual	Unclear	Unclear	Participants, provider, and assessor unclear; described as double blind	Inadequate
Fox 2005	Individual	Adequate	Adequate	Described as double blind; provider unclear	Adequate
Freij 1979i	Individual	Inadequate	Unclear	Described as double blind	Adequate
Freij 1979ii	Individual	Inadequate	Unclear	Described as double blind	Adequate
Garg 2002	Individual	Adequate	Adequate	Assessor; participants unclear; provider not blinded	Adequate
Greenberg 1981	Individual	Unclear	Unclear	Participants; described as double blind; provider and assessor unclear	Inadequate
Hadju 1996	Individual	Unclear	Unclear	Participants; described as double blind; provider and assessor unclear	Inadequate
Hadju 1997	Individual	Unclear	Unclear	Participants and provider; assessor unclear	Inadequate
Kloetzel 1982	Individual	Unclear	Unclear	Participants; provider and assessor unclear; described as double blind	Unclear
Koroma 1996	Individual	Unclear	Unclear	Unclear	Inadequate
Kruger 1996	Individual	Unclear	Unclear	Unclear	Inadequate
Kvalsvig 1991i	Individual	Unclear	Unclear	Unclear	Unclear
Lai 1995	Individual	Inadequate	Unclear	Participants only	Inadequate
Michaelsen 1985	Individual	Unclear	Unclear	Unclear	Inadequate
Nokes 1992	Individual	Unclear	Unclear	Participants described as double blind; provider and assessor unclear	Inadequate
Palupi 1997	Individual	Unclear	Unclear	Described as double blind	Adequate
Sarkar 2002	Individual	Unclear	Unclear	Described as double blind	Adequate
Simeon 1995	Individual	Adequate	Unclear	Participants described as double blind; provider and assessor unclear	Adequate
Stephenson 1989	Individual	Unclear	Unclear	Participants and assessor; provider unclear	Inadequate
Stephenson 1993	Individual	Unclear	Unclear	Participants and assessor; provider unclear	Inadequate

Table 05. Methodological quality assessment (Continued)

Trial	Design	Sequence[^]	Concealment[^]	Blinding	Inclusion[^]
Stoltzfus 2001	Individual	Unclear	Adequate	Participants, provider, and assessor unclear	Inadequate
Sur 2005	Individual	Adequate	Adequate	Participants, provider, and assessor	Adequate
Watkins 1996	Individual	Unclear	Unclear	Participants and provider; assessor unclear	Adequate
Willett 1979	Individual	Adequate	Unclear	Participants and assessor; provider unclear; described as double blind	Inadequate
Alderman 2006	Cluster	Adequate	Unclear	None	Inadequate
Awasthi 1995	Cluster	Unclear	Unclear	Unclear	Inadequate
Awasthi 2001	Cluster	Unclear	Unclear	None	Inadequate
Hall 2006	Cluster	Unclear	Unclear	Unclear	Unclear
Rousham 1994	Cluster	Unclear	Unclear	Participants described as double blind; provider and assessor unclear	Adequate
Stoltzfus 1997	Cluster	Unclear	Unclear	Participants; provider and assessor unclear	Inadequate

[^]Generation of allocation sequence, allocation concealment, and inclusion of all randomized participants

Table 06. Trials evaluating school performance or cognition

Trial	Follow up	Participants	Intervention	Outcome measures	Results
Awasthi 2000	2 years	Indian children aged 1.5 to 3.5 years living in urban slums Number analysed: 1045/1061 Community category: 3	Multiple doses of albendazole versus placebo	Developmental status (Denver Questionnaire)	No difference in development between treatment groups in terms of proportion with “normal” development
Hall 2006	2 years	Children from class 3 and born in 1990 of 80/81 schools in the Red River delta of north Vietnam Community category: 1	Multiple doses of albendazole versus placebo	Mathematics test score, Vietnamese test score	No statistically significant differences in test results at start or end of study. These results do not appear to have been adjusted for cluster randomization. They will remain nonsignificant, however, even after appropriate adjustment, though the confidence intervals may change
Kvalsvig 1991i	1 month	South African children with most severe worm infestations in a school Number analysed: 39/100 Community category: 1	Single dose of mebendazole versus placebo	Card sorting task; cancellation task (number of letter ‘s’ in text deleted in a time period)	Changes in cognitive scores are not clearly reported since “the dose of mebendazole was inadequate to free children from infection”
Nokes 1992	2.25 months	Jamaican children aged 9 to 12 years with Trichuris egg counts > 1900, but low hookworm counts on 2 occasions separated by 3 months before the trial Number analysed: 103/140 Community category: 1	Single dose of albendazole versus placebo	Digit span (forward and backward); arithmetic and coding from Wechsler Intelligence Scale for Children; fluency; listening comprehension from the Clinical Evaluation of Language functions; matching familiar figures test	Mean test scores pre- and post-intervention presented with confidence intervals No comment made on significance of unadjusted data Results of multiple regression suggest a greater improvement in treated children in 3/10 tests (fluency, digit span forwards, digit span backwards)
Simeon 1995	6.5 months	Jamaican children aged 6	Multiple doses of albendazole	1. Main study (264 children)	1. Main study: no difference

Table 06. Trials evaluating school performance or cognition (Continued)

Trial	Follow up	Participants	Intervention	Outcome measures	Results
		to 12 in grades 2 to 5 with intensities of Trichura > 1200 eggs/g Community category: 1	versus placebo	Wide range achievement test: reading, arithmetic, and spelling subtests; school attendance from children with class registers pre- and post-intervention 2. Subgroup 1 (189 children 189 infected children from original population) Digit span; verbal fluency test; visual search; number choice; French vocabulary learning 3. Subgroup 2 (97 children from grade 5) French learning; digit spans (forward and backward); Corsi block span; verbal fluency; picture search; silly sentences	in any reported outcome measure 2. Subgroup 1: no significant effect on any of the outcome measures 3. Subgroup 2: no significant improvement with treatment in any of the tests was found in multiple regression modelling
Stoltzfus 2001	1 year	Zanzibari children reported as 3 to 56 months, 3 months before the trial start Number analysed: 359/684 Community category: 2	Multiple doses of mebendazole versus placebo	Motor and language development by parents reporting gross motor and language milestones using scoring system developed specifically for the trial	Unadjusted data not reported Treatment had no significant effect on motor or language development
Watkins 1996	6 months	Guatemalan children aged 7 to 12 years attending grades 1 to 4 in primary schools Number analysed: 226/250 Community category: 1	Multiple doses of albendazole versus placebo	Interamerican vocabulary test; Interamerican reading test; Peabody picture vocabulary test; attendance rates of children actively attending school; dropout rates	All outcome measures reported as unadjusted scores No difference in any of the tests found between treatment groups

Community category:
a measure of

Table 06. Trials evaluating school performance or cognition (*Continued*)

Trial	Follow up	Participants	Intervention	Outcome measures	Results
prevalence/intensity of infection (see Table 01)					

ANALYSES

Comparison 01. Single dose: change in value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	9	2448	Weighted Mean Difference (Random) 95% CI	0.34 [0.05, 0.64]
02 Height (cm)	9	2449	Weighted Mean Difference (Random) 95% CI	0.04 [-0.16, 0.23]
03 Mid-upper arm circumference (cm)	5	823	Weighted Mean Difference (Random) 95% CI	0.23 [-0.03, 0.48]
04 Triceps skin fold (mm)			Weighted Mean Difference (Random) 95% CI	Subtotals only
05 Subscapular skin fold (mm)			Weighted Mean Difference (Random) 95% CI	Subtotals only
06 Haemoglobin (g/dL)	2	538	Weighted Mean Difference (Fixed) 95% CI	0.09 [-0.12, 0.29]

Comparison 02. Single dose: end value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	11	2980	Weighted Mean Difference (Fixed) 95% CI	0.03 [-0.17, 0.23]
02 Height (cm)	8	2222	Weighted Mean Difference (Fixed) 95% CI	0.16 [-0.56, 0.89]
03 Mid-upper arm circumference (cm)	7	864	Weighted Mean Difference (Fixed) 95% CI	0.08 [-0.11, 0.27]
04 Triceps skin fold (mm)	4	407	Weighted Mean Difference (Random) 95% CI	0.67 [-0.39, 1.72]
05 Subscapular skin fold (mm)			Weighted Mean Difference (Random) 95% CI	Subtotals only
06 Body mass index			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
07 Haemoglobin (g/L)	4	646	Weighted Mean Difference (Fixed) 95% CI	1.49 [-0.39, 3.36]
08 Harvard Step Test			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 03. Multiple dose < 1 year: change in value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	6	1714	Weighted Mean Difference (Random) 95% CI	0.05 [-0.24, 0.33]
02 Height (cm)	6	1715	Weighted Mean Difference (Fixed) 95% CI	-0.02 [-0.15, 0.12]
03 Mid-upper arm circumference (cm)	4	658	Weighted Mean Difference (Random) 95% CI	0.06 [-0.24, 0.36]
04 Triceps skin fold (mm)			Weighted Mean Difference (Random) 95% CI	Subtotals only
05 Subscapular skin fold (mm)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
06 Haemoglobin (g/dL)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 04. Multiple dose < 1 year: end value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	5	2311	Weighted Mean Difference (Fixed) 95% CI	-0.07 [-0.29, 0.14]
02 Height (cm)	4	1630	Weighted Mean Difference (Fixed) 95% CI	-0.32 [-1.16, 0.51]
03 Mid-upper arm circumference (cm)	3	581	Weighted Mean Difference (Fixed) 95% CI	0.04 [-0.21, 0.28]
04 Triceps skin fold (mm)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
05 Subscapular skin fold (mm)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected

Comparison 05. Multiple dose > 1 year: change in value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	3	1219	Weighted Mean Difference (Random) 95% CI	0.46 [-0.47, 1.39]
02 Height (cm)	3	1219	Weighted Mean Difference (Fixed) 95% CI	-0.26 [-0.84, 0.31]

Comparison 06. Multiple dose > 1 year: end value

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Weight (kg)	2	1169	Weighted Mean Difference (Random) 95% CI	0.00 [-0.18, 0.19]
02 Height (cm)	2	1169	Weighted Mean Difference (Fixed) 95% CI	-0.08 [-0.89, 0.72]
03 Haemoglobin (g/dL)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected

Comparison 07. Analysis by worm prevalence or intensity

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Single dose: change in weight (kg)	9	2398	Weighted Mean Difference (Random) 95% CI	0.34 [0.04, 0.64]
02 Single dose: change in height (cm)	9	2449	Weighted Mean Difference (Random) 95% CI	0.04 [-0.16, 0.23]
03 Multiple dose < 1 year: change in weight (kg)	6	1714	Weighted Mean Difference (Random) 95% CI	0.05 [-0.24, 0.33]
04 Multiple dose < 1 year: change in height (cm)	6	1715	Weighted Mean Difference (Fixed) 95% CI	-0.02 [-0.15, 0.12]
05 Single dose: end value for weight (kg)	10	2967	Weighted Mean Difference (Fixed) 95% CI	0.03 [-0.17, 0.23]
06 Single dose: end value for height (cm)	8	2222	Weighted Mean Difference (Fixed) 95% CI	0.16 [-0.56, 0.89]
07 Multiple dose < 1 year: end value for weight (kg)	5	2311	Weighted Mean Difference (Fixed) 95% CI	-0.07 [-0.29, 0.14]
08 Multiple dose < 1 year: end value for height (cm)	4	1630	Weighted Mean Difference (Fixed) 95% CI	-0.32 [-1.16, 0.51]

Comparison 08. Subgroup and sensitivity analyses

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Single dose: change			Weighted Mean Difference (Random) 95% CI	Subtotals only
02 Single dose: end value			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
03 Multiple dose < 1 year: change in value			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
04 Multiple dose < 1 year: end value			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
05 Multiple dose > 1 year: change in value			Weighted Mean Difference (Random) 95% CI	Subtotals only
06 Multiple dose > 1 year: end value			Weighted Mean Difference (Fixed) 95% CI	Totals not selected

INDEX TERMS

Medical Subject Headings (MeSH)

Adolescent; Anthelmintics [pharmacology; *therapeutic use]; Child Development [*drug effects]; Cognition [*drug effects]; Growth [*drug effects]; Helminthiasis [complications; *drug therapy]; Intestinal Diseases, Parasitic [complications; *drug therapy]; Nutritional Status [drug effects]; Randomized Controlled Trials as Topic; Weight Gain [drug effects]

MeSH check words

Child; Child, Preschool; Humans

COVER SHEET

Title	Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance
Authors	Taylor-Robinson DC, Jones AP, Garner P
Contribution of author(s)	David Taylor-Robinson wrote the protocol, applied inclusion criteria, assessed quality, extracted data, conducted data analysis, and wrote the first draft of the review. Ashley Jones helped write the protocol, write the review, and analyse and interpret data. Paul provided advice at all stages of the review production, applied inclusion criteria, assessed quality, quality assured data extraction, helped construct the comparisons, and helped write the review.
Issue protocol first published	1997/3
Review first published	1998/2
Date of most recent amendment	10 November 2007
Date of most recent SUBSTANTIVE amendment	13 August 2007
What's New	2007, Issue 4 (substantive update): author team changed; review title modified from the original title of "Anthelmintic drugs for treating worms in children: effects on growth and cognitive performance"; updated methods, reapplied the inclusion criteria, repeated data extraction, added new trials, and included additional analyses as recommended by policy specialists. 2000, Issue 2 (substantive update): new trials added and review updated 1998, Issue 2: review first published
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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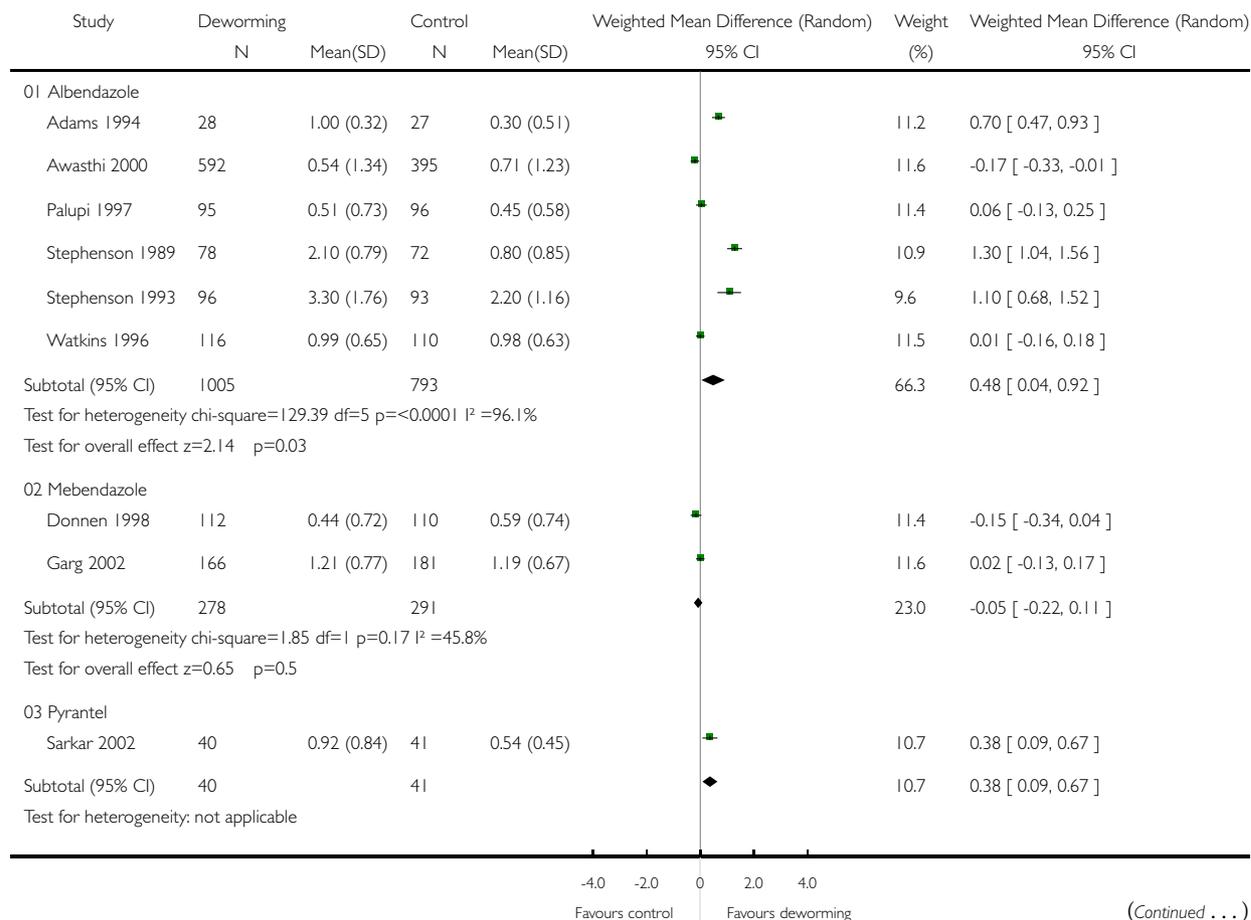
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Single dose: change in value, Outcome 01 Weight (kg)

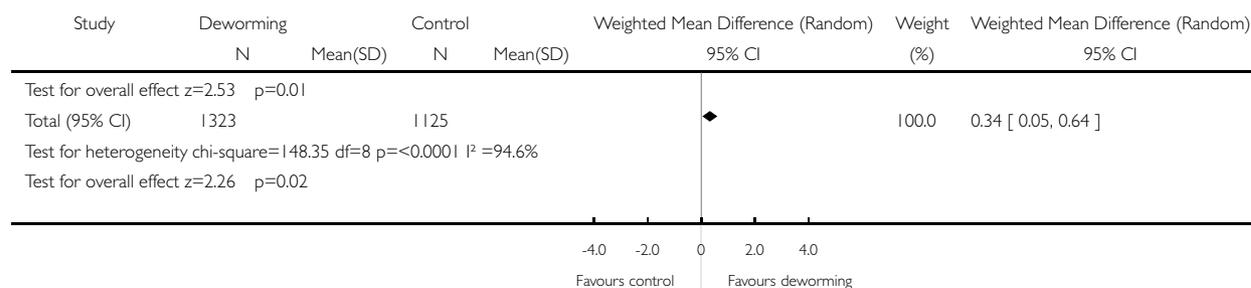
Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 01 Single dose: change in value

Outcome: 01 Weight (kg)



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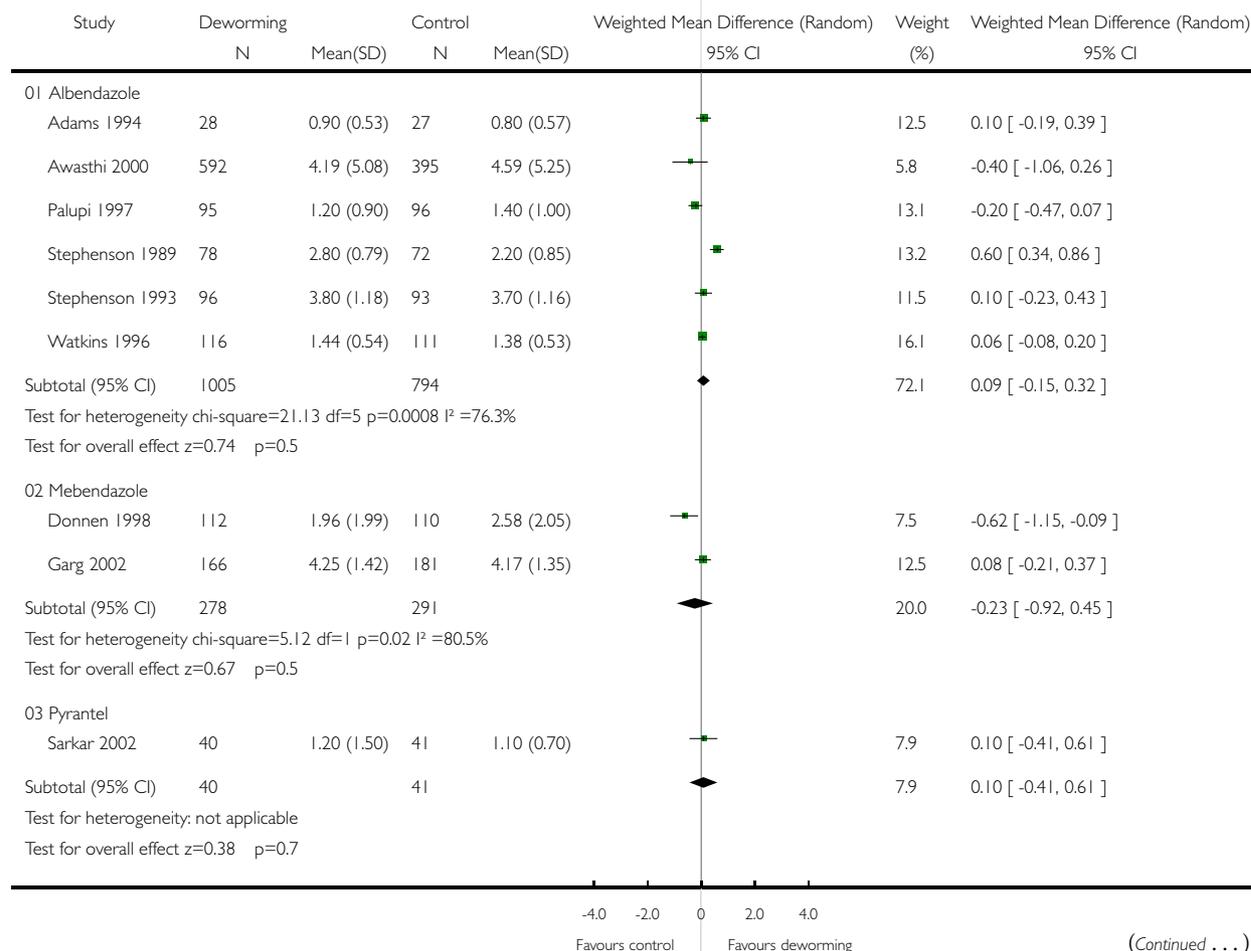


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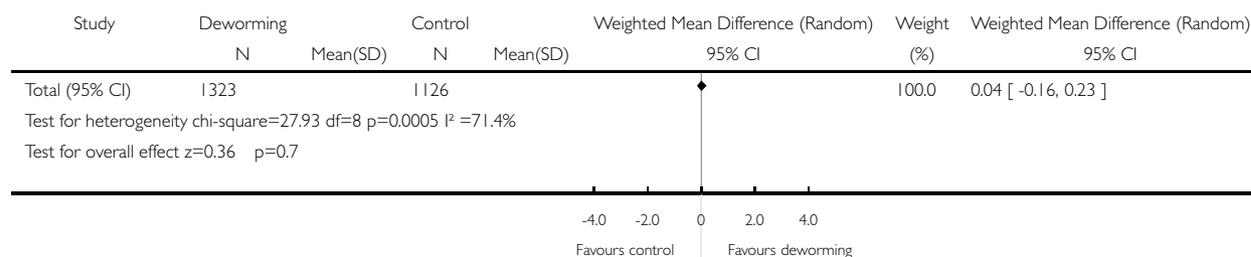
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Outcome: 02 Height (cm)



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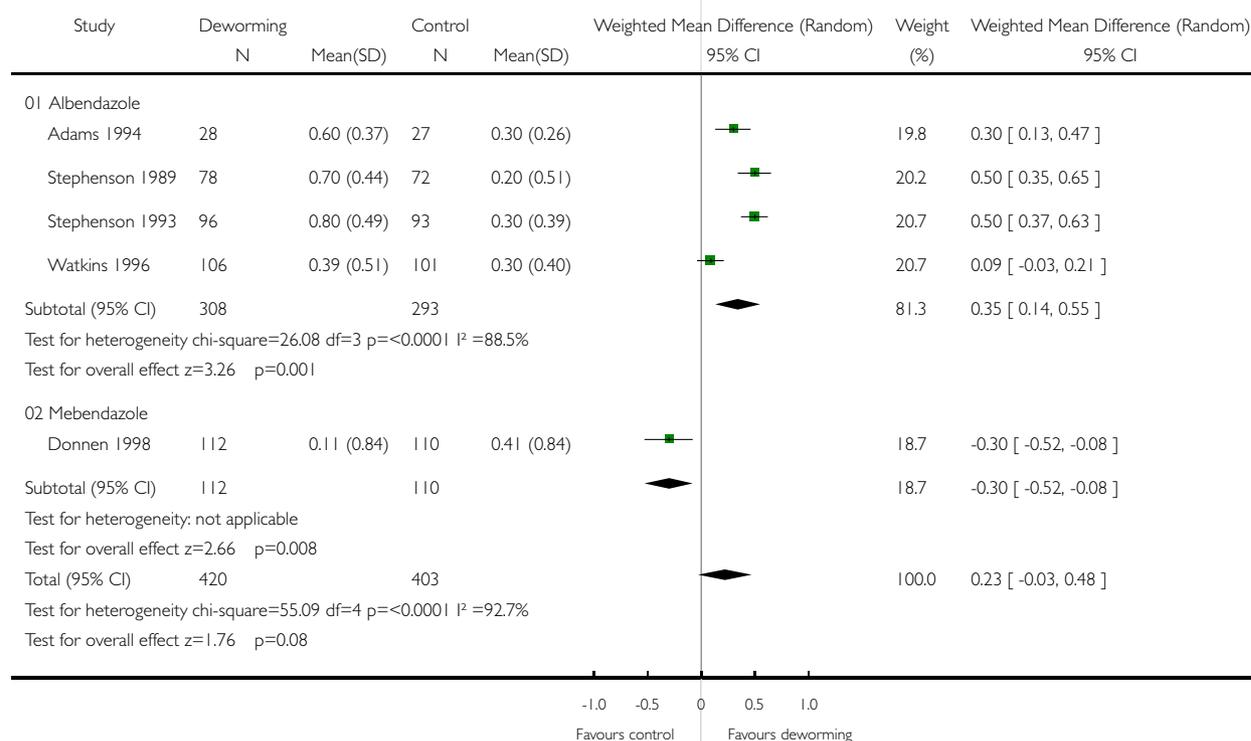


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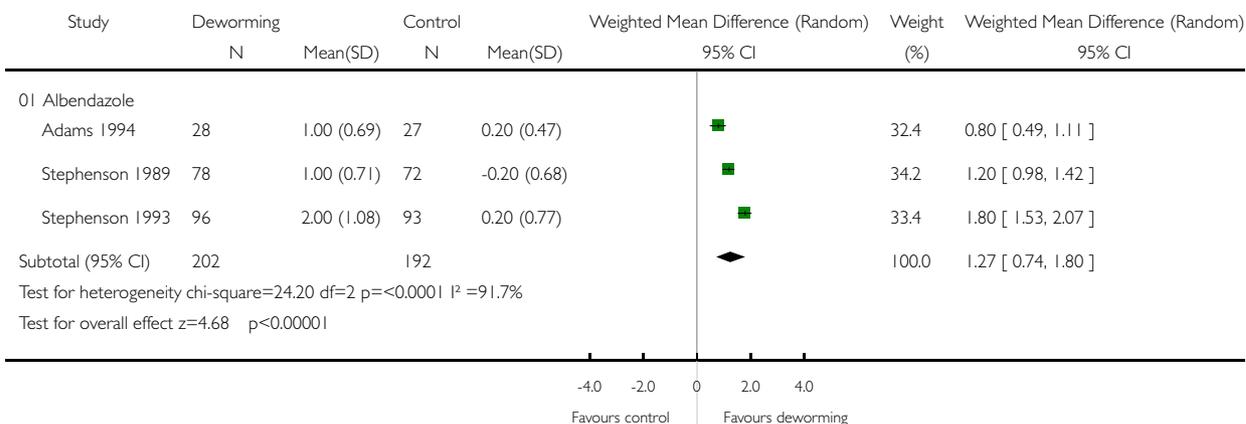


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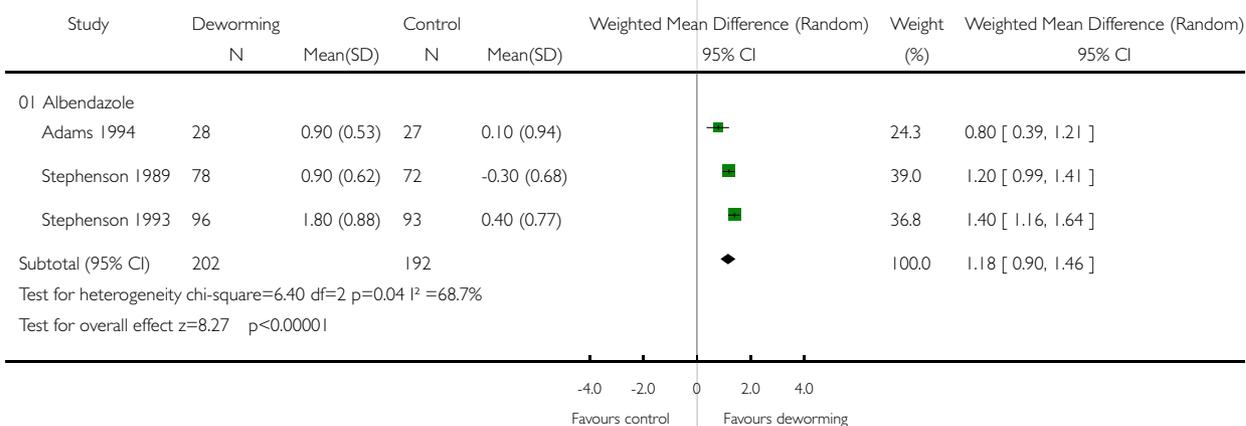


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 01 Single dose: change in value

Outcome: 05 Subscapular skin fold (mm)

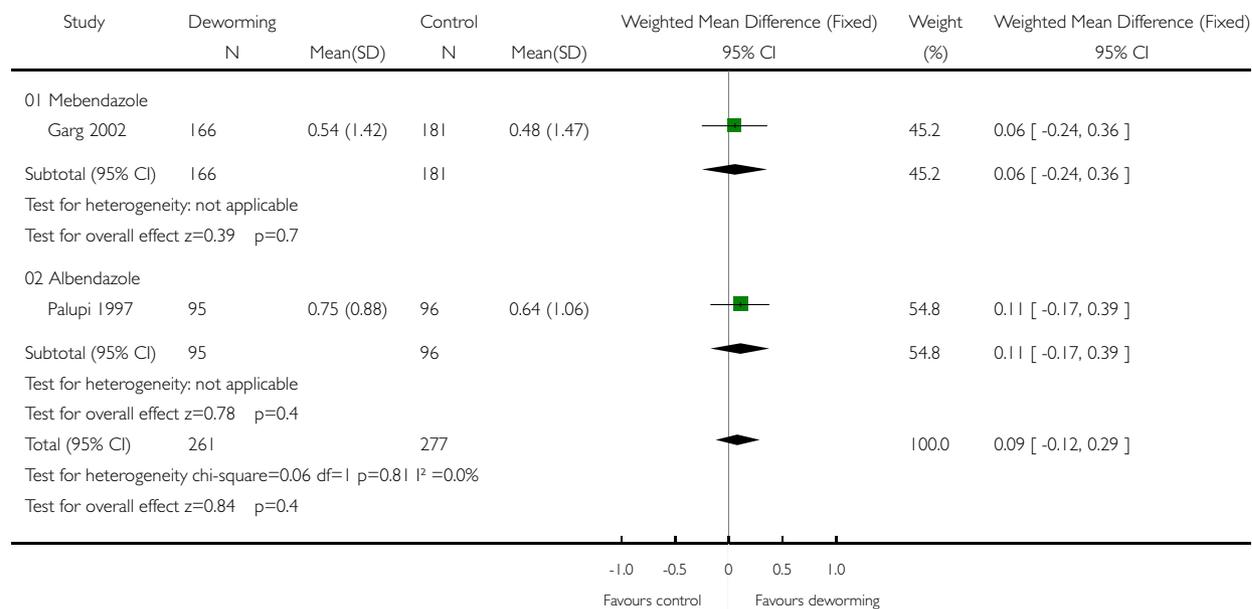


Analysis 01.06. Comparison 01 Single dose: change in value, Outcome 06 Haemoglobin (g/dL)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 01 Single dose: change in value

Outcome: 06 Haemoglobin (g/dL)

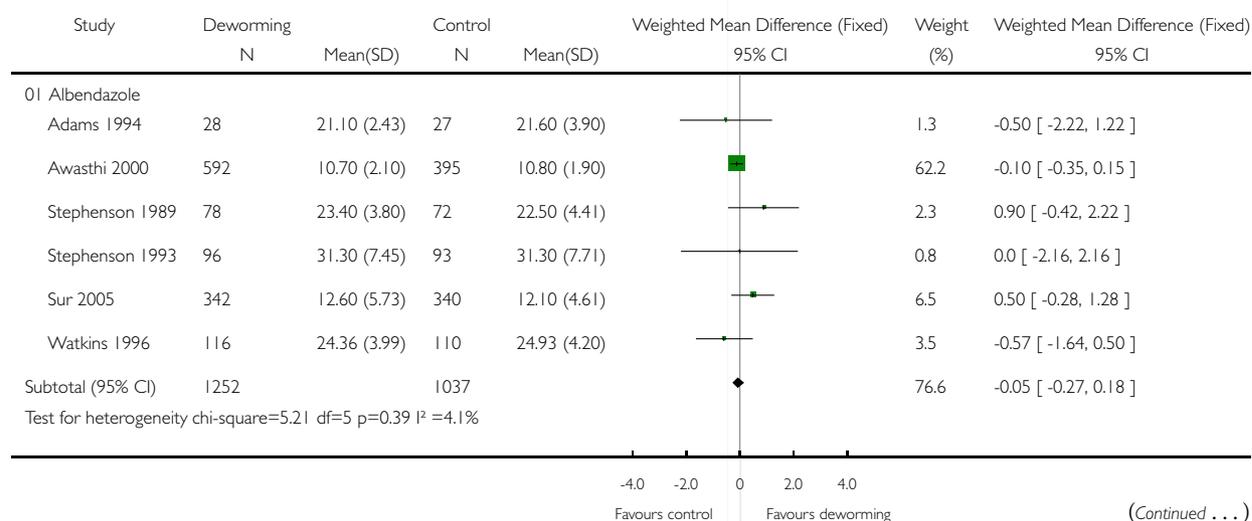


Analysis 02.01. Comparison 02 Single dose: end value, Outcome 01 Weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

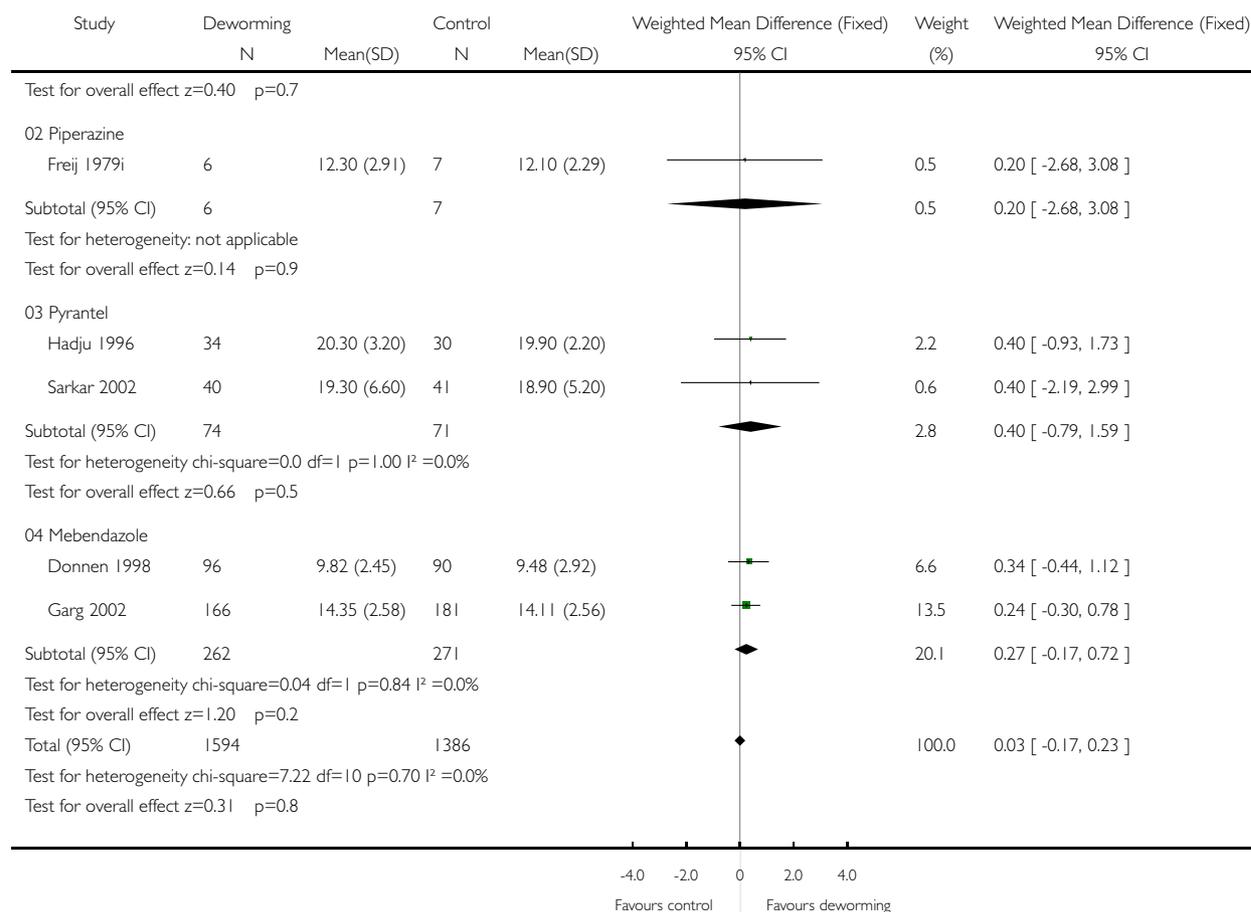
Comparison: 02 Single dose: end value

Outcome: 01 Weight (kg)



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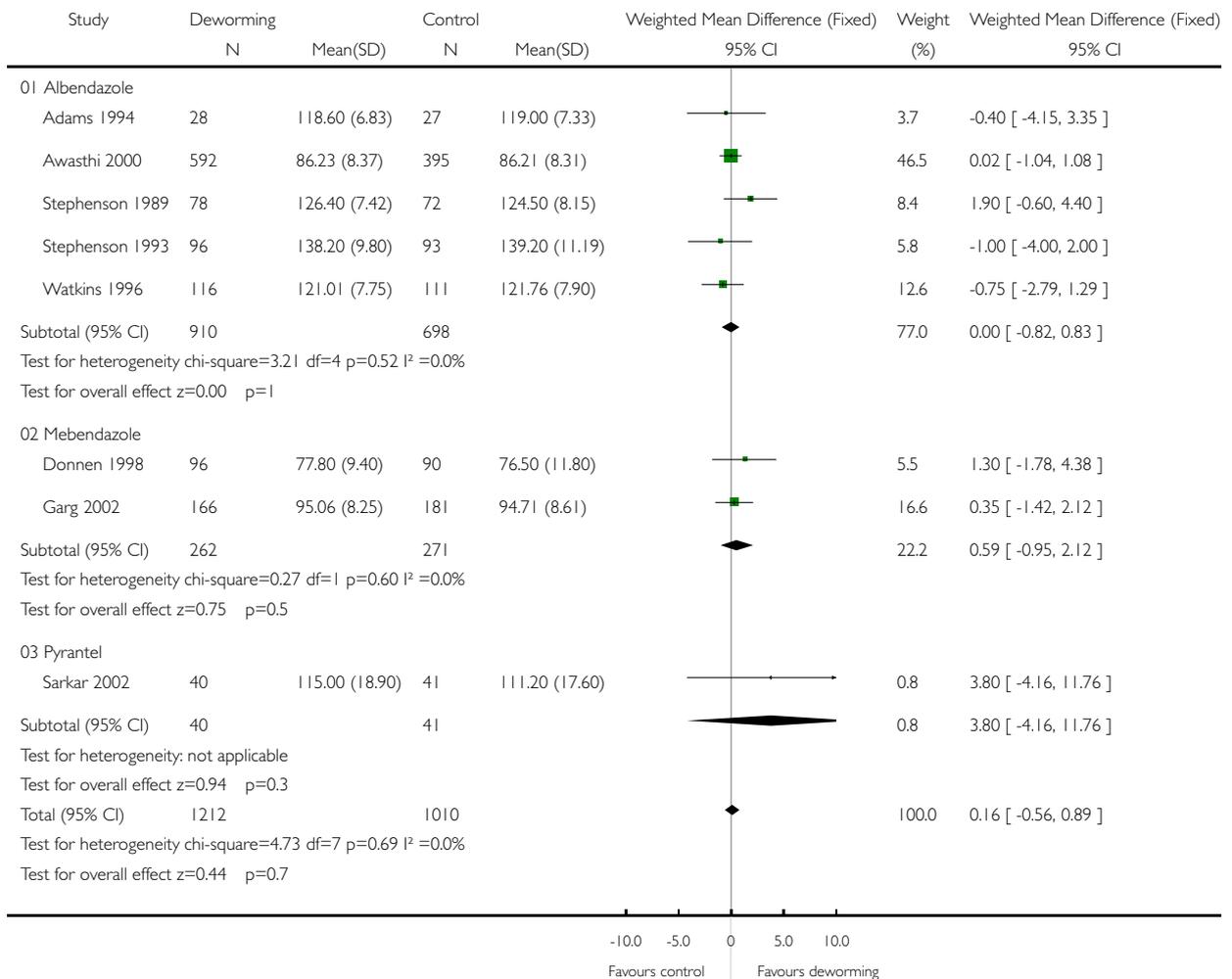


Analysis 02.02. Comparison 02 Single dose: end value, Outcome 02 Height (cm)

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Outcome: 02 Height (cm)

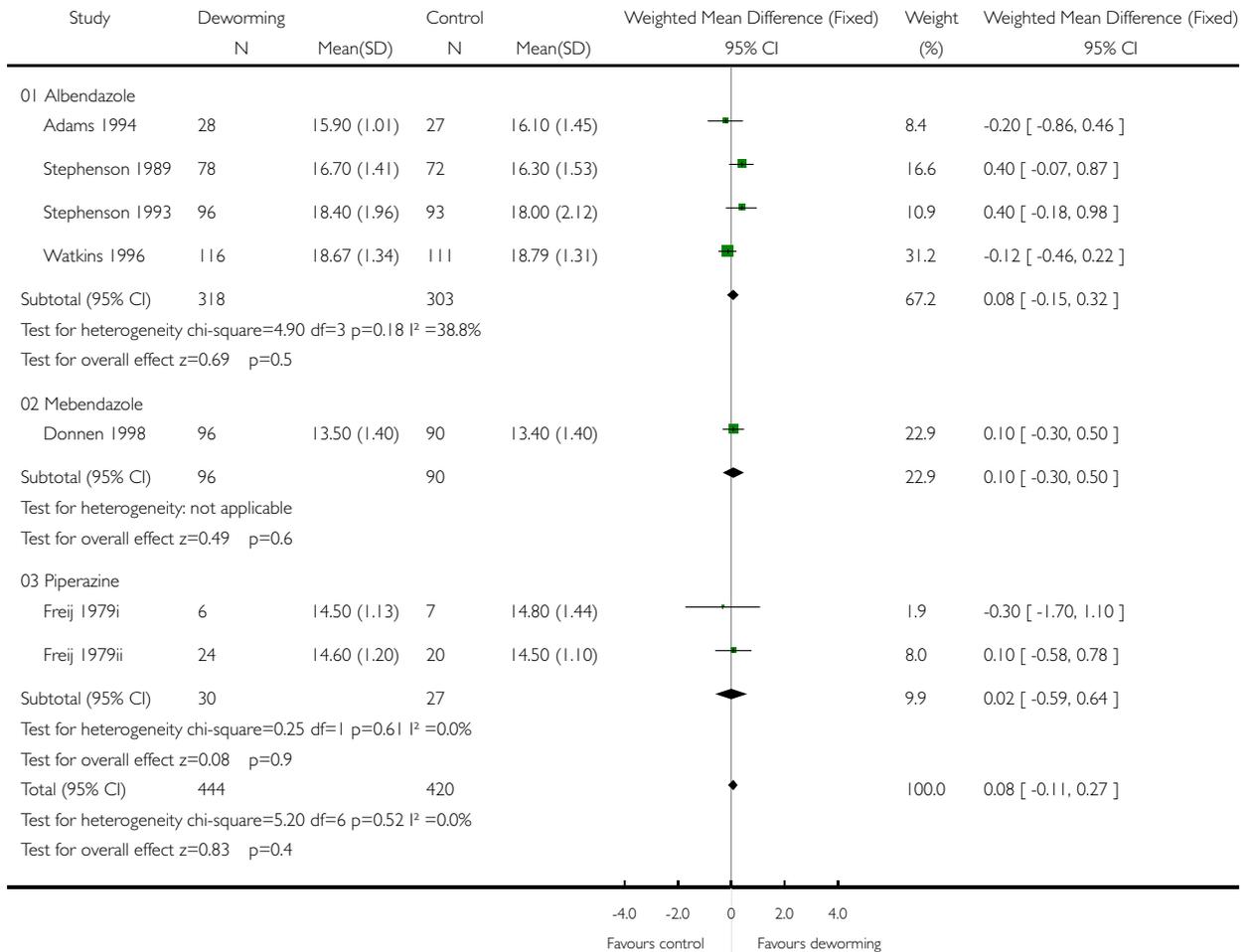


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

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Outcome: 03 Mid-upper arm circumference (cm)

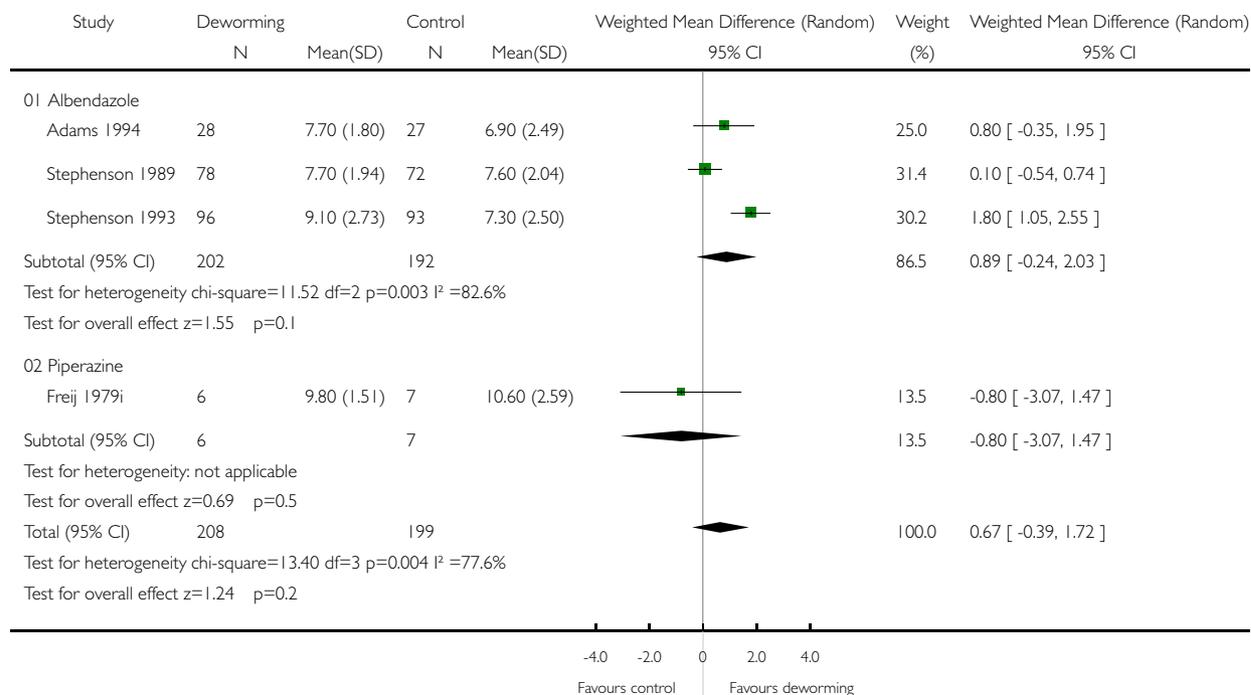


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

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Outcome: 04 Triceps skin fold (mm)

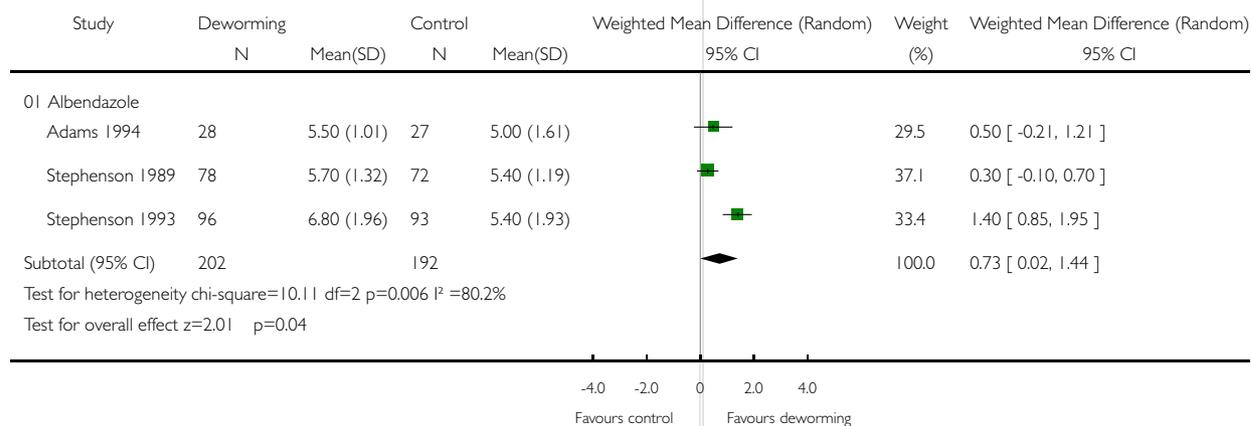


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Outcome: 05 Subscapular skin fold (mm)

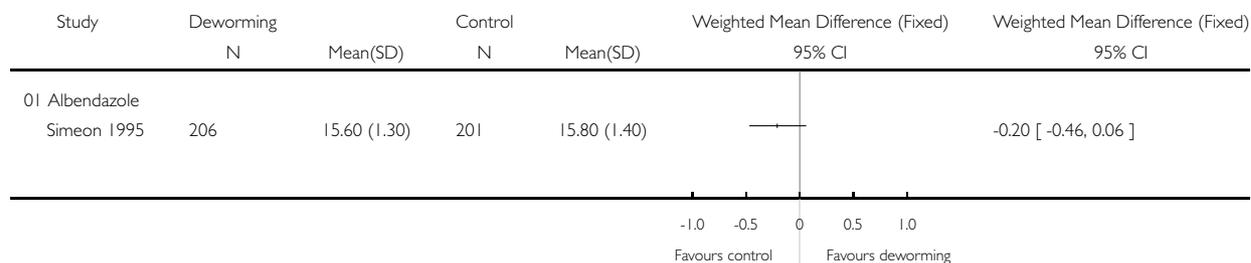


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 02 Single dose: end value

Outcome: 06 Body mass index

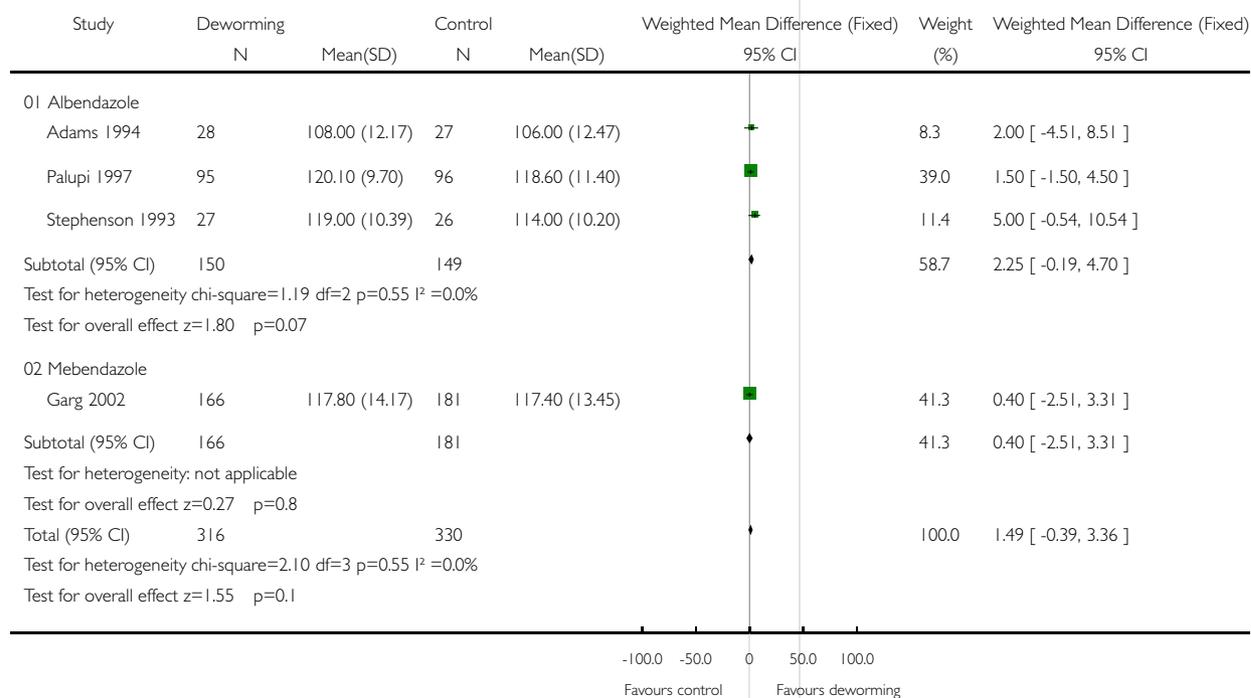


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 02 Single dose: end value

Outcome: 07 Haemoglobin (g/L)

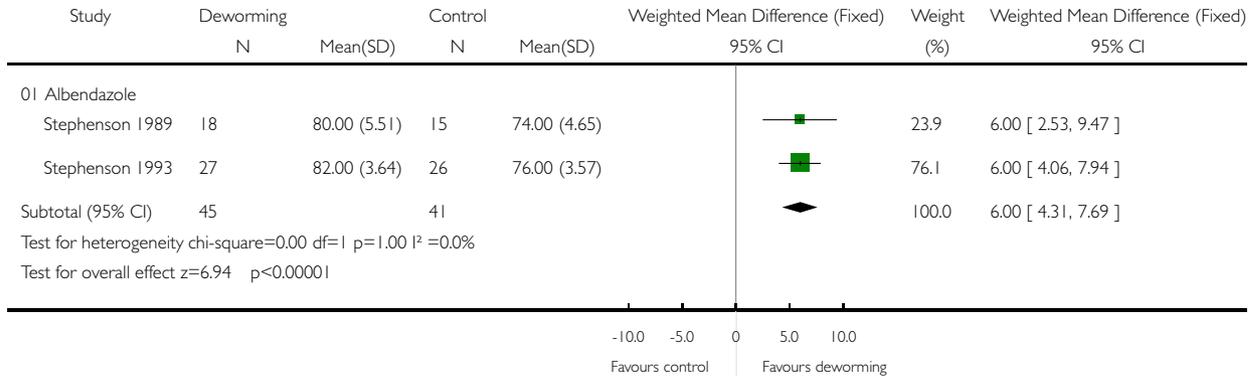


Analysis 02.08. Comparison 02 Single dose: end value, Outcome 08 Harvard Step Test

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 02 Single dose: end value

Outcome: 08 Harvard Step Test

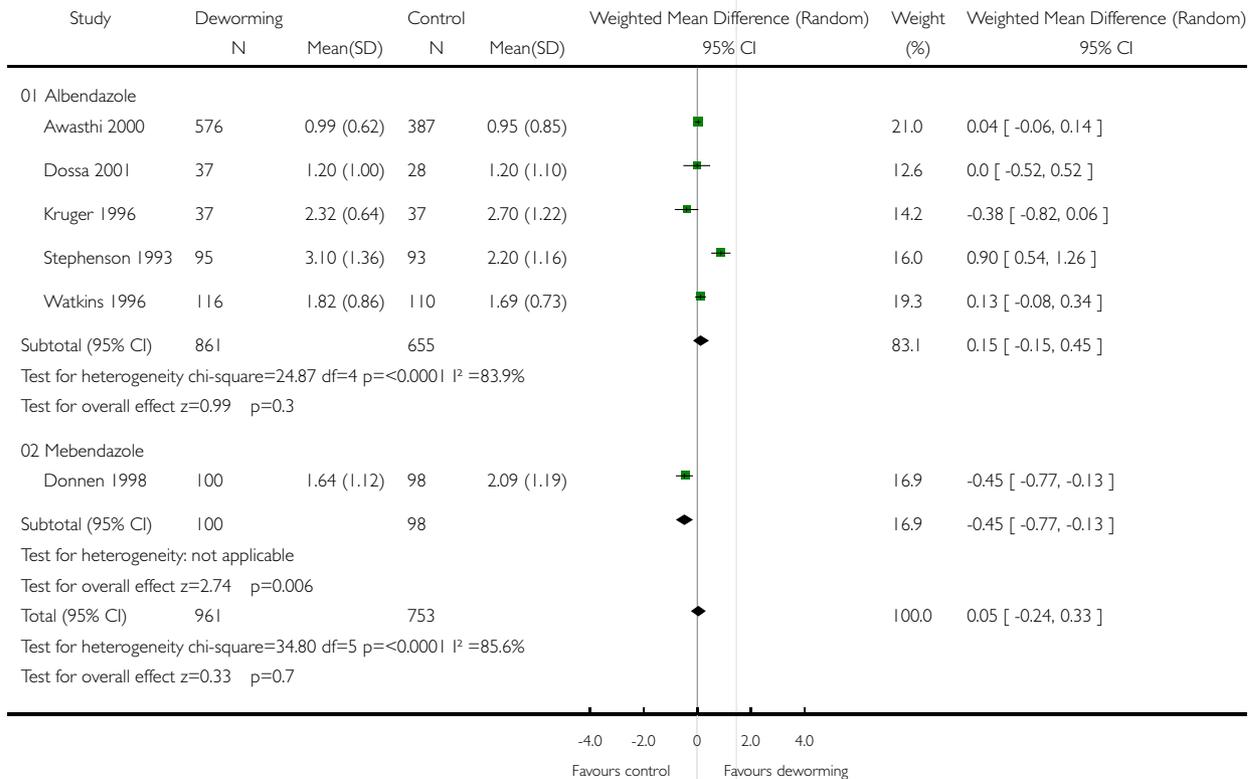


Analysis 03.01. Comparison 03 Multiple dose < 1 year: change in value, Outcome 01 Weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 03 Multiple dose < 1 year: change in value

Outcome: 01 Weight (kg)

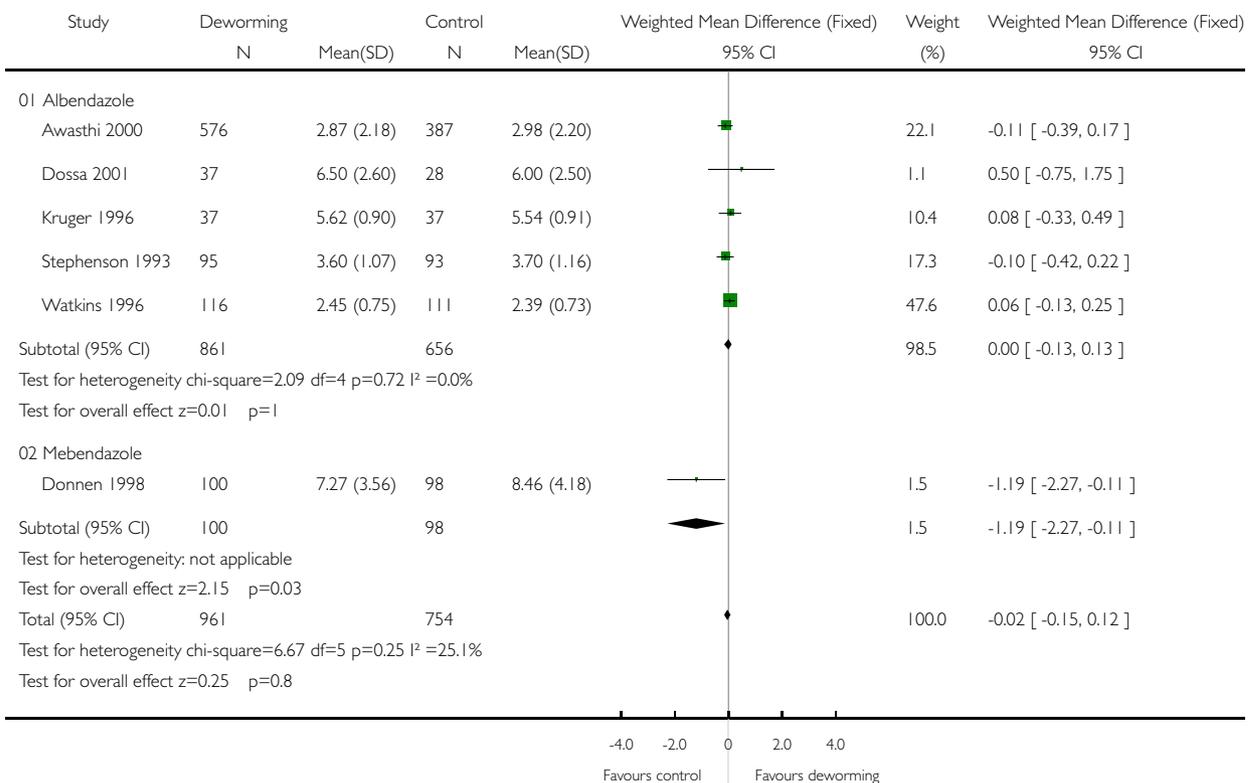


Analysis 03.02. Comparison 03 Multiple dose < 1 year: change in value, Outcome 02 Height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 03 Multiple dose < 1 year: change in value

Outcome: 02 Height (cm)

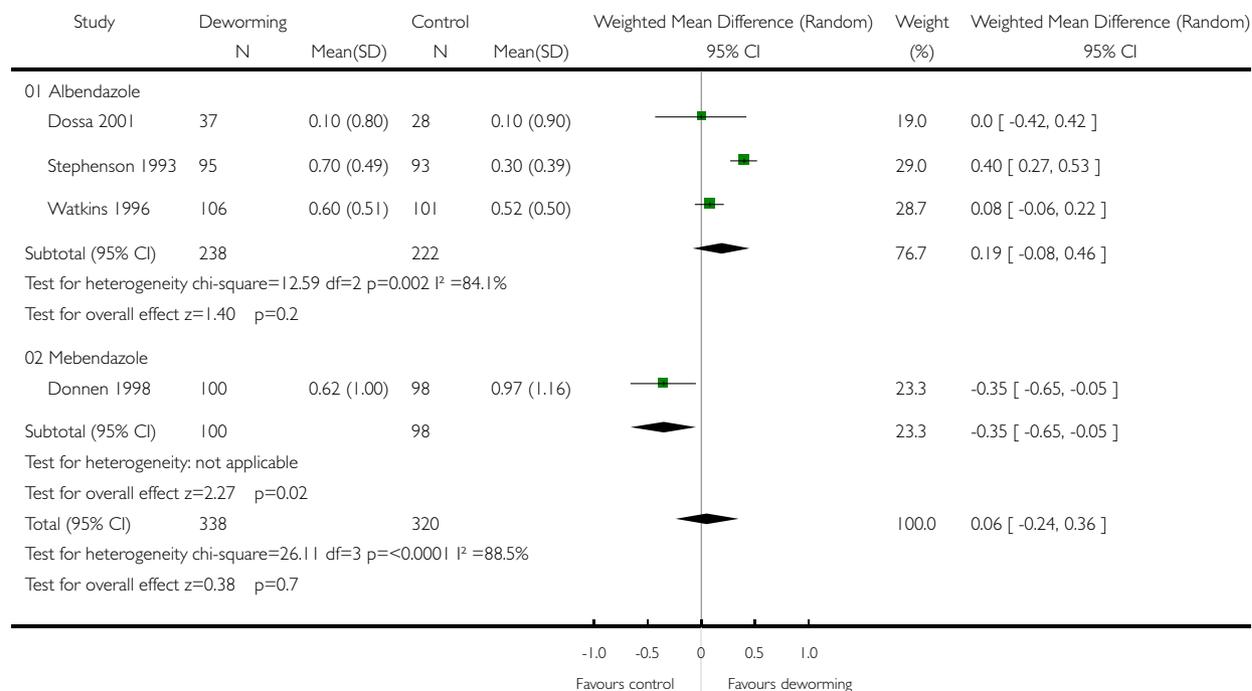


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 03 Multiple dose < 1 year: change in value

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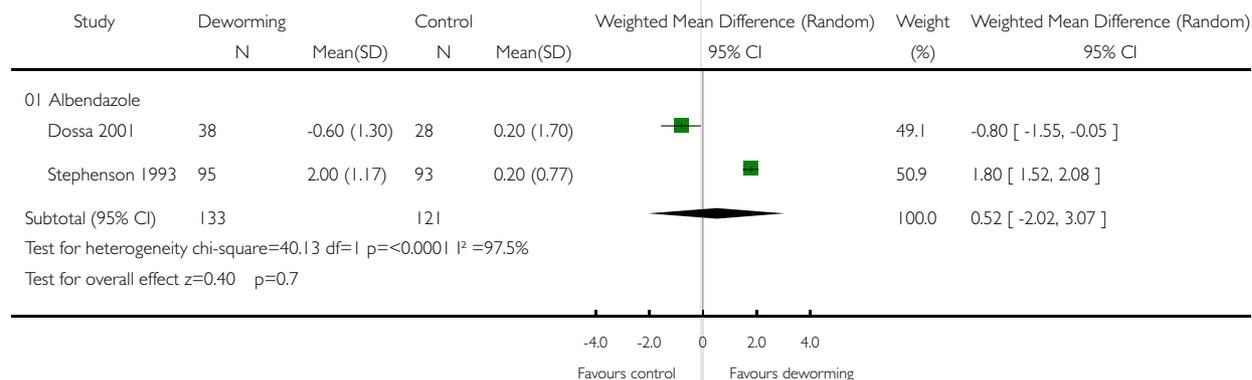


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Comparison: 03 Multiple dose < 1 year: change in value

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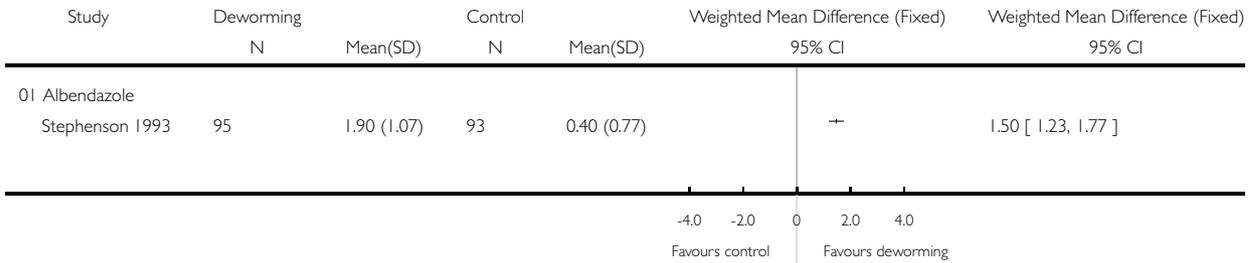


Analysis 03.05. Comparison 03 Multiple dose < 1 year: change in value, Outcome 05 Subscapular skin fold (mm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 03 Multiple dose < 1 year: change in value

Outcome: 05 Subscapular skin fold (mm)

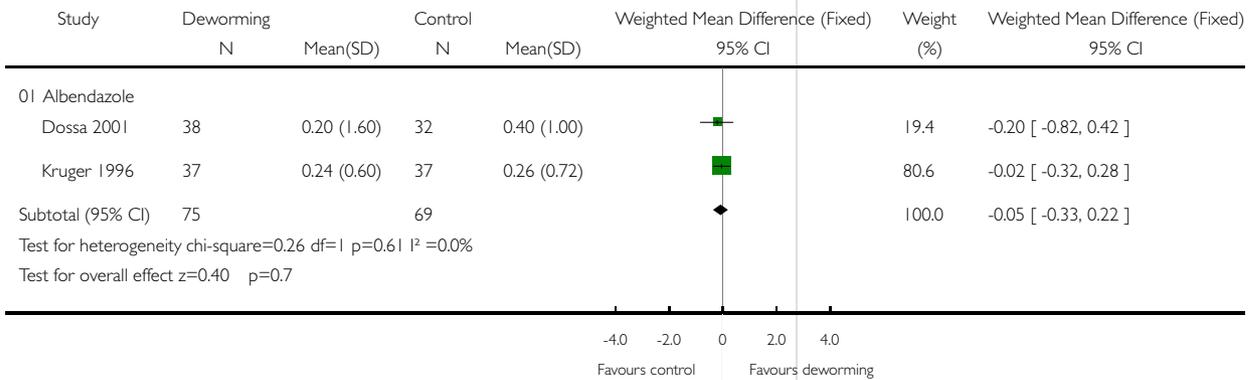


Analysis 03.06. Comparison 03 Multiple dose < 1 year: change in value, Outcome 06 Haemoglobin (g/dL)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 03 Multiple dose < 1 year: change in value

Outcome: 06 Haemoglobin (g/dL)

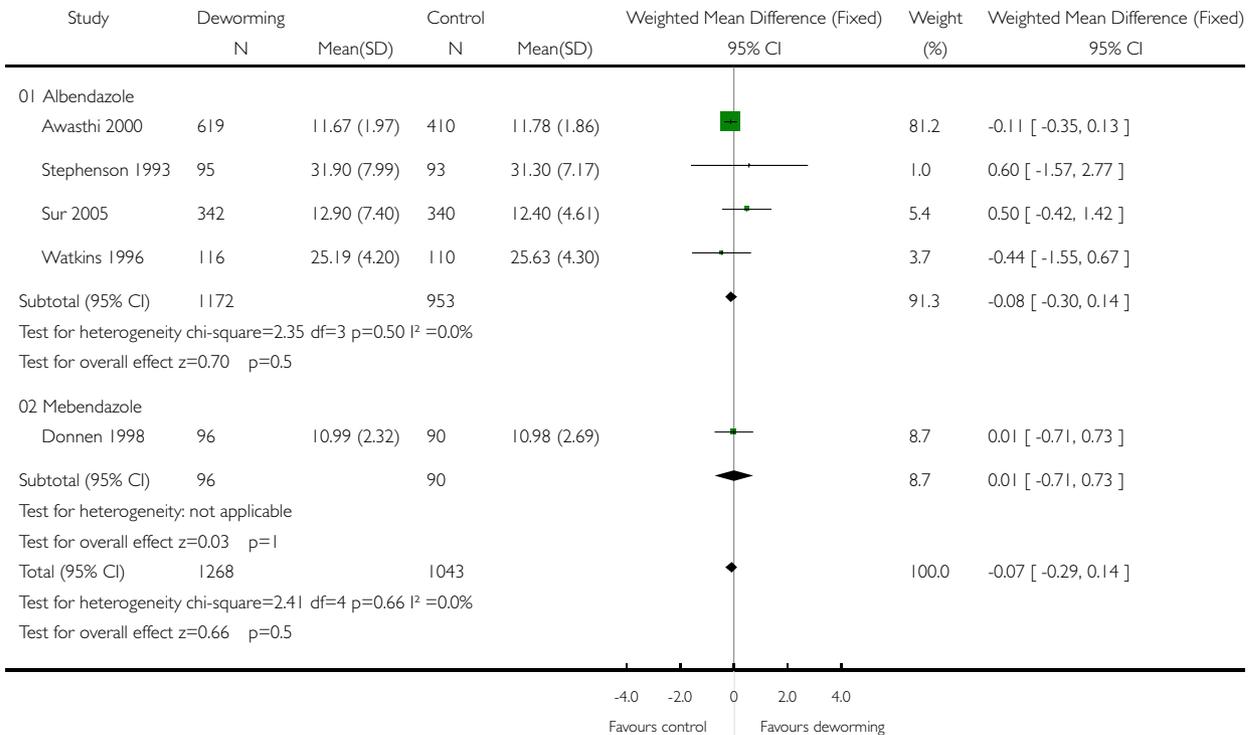


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 04 Multiple dose < 1 year: end value

Outcome: 01 Weight (kg)

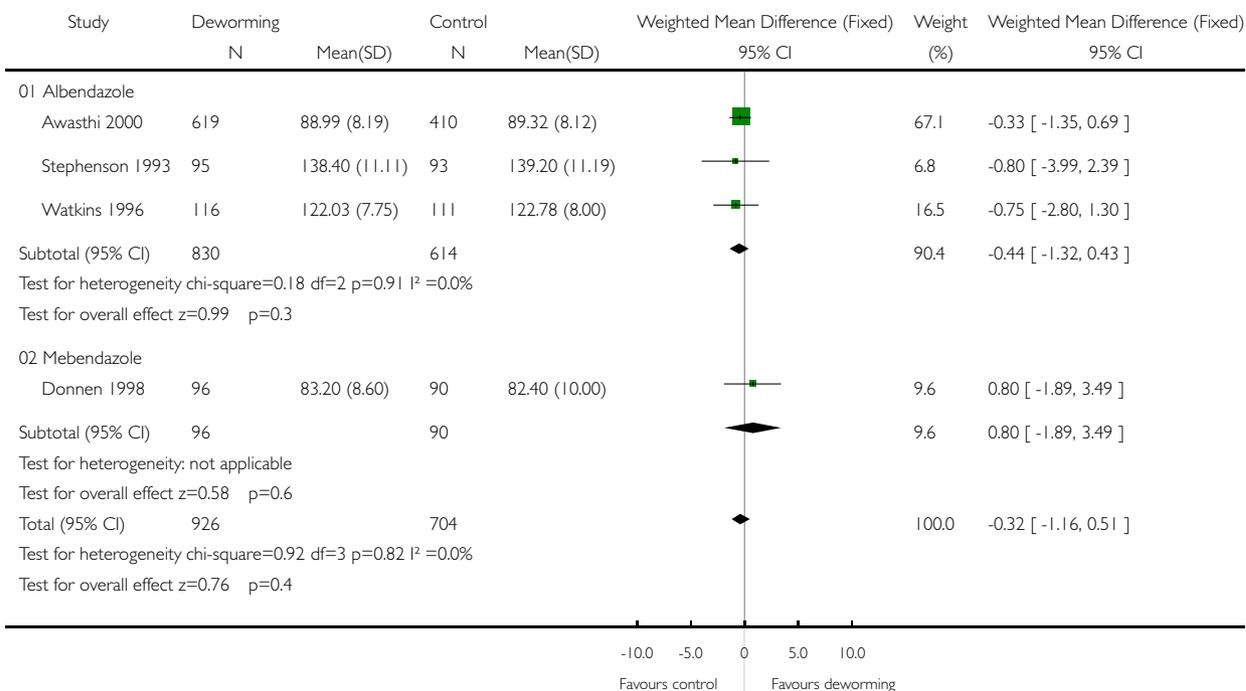


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Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 04 Multiple dose < 1 year: end value

Outcome: 02 Height (cm)

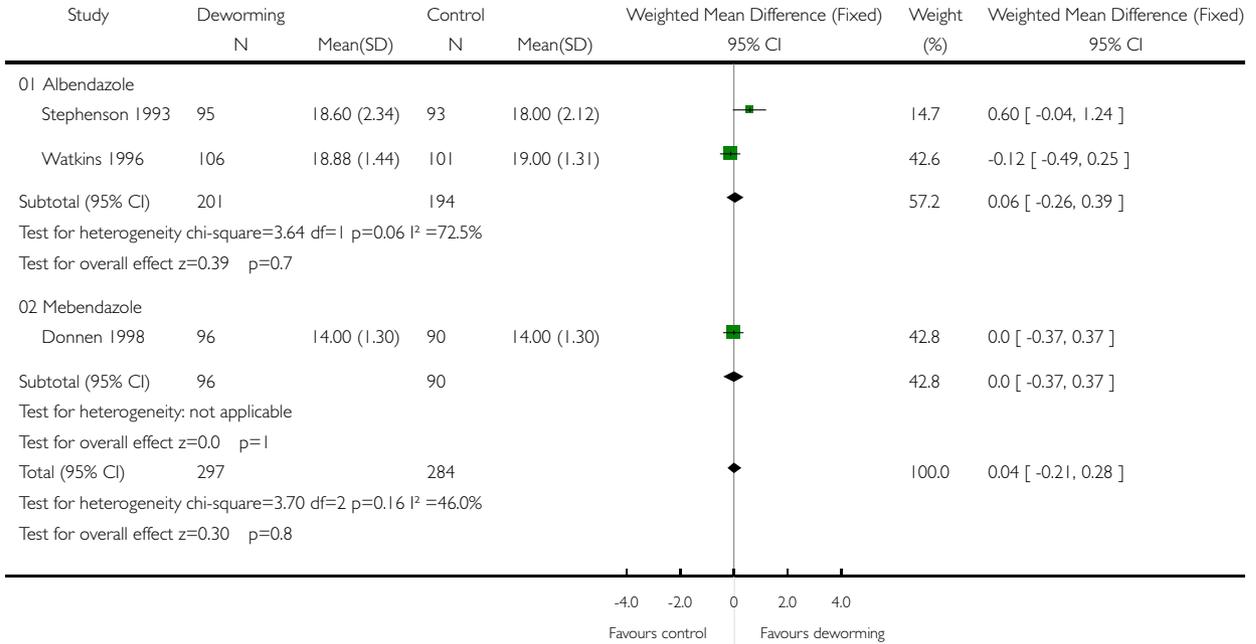


Analysis 04.03. Comparison 04 Multiple dose < 1 year: end value, Outcome 03 Mid-upper arm circumference (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 04 Multiple dose < 1 year: end value

Outcome: 03 Mid-upper arm circumference (cm)

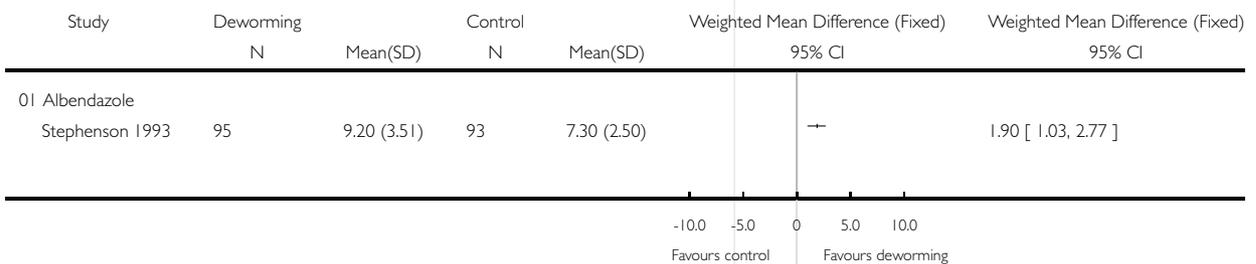


Analysis 04.04. Comparison 04 Multiple dose < 1 year: end value, Outcome 04 Triceps skin fold (mm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 04 Multiple dose < 1 year: end value

Outcome: 04 Triceps skin fold (mm)



Analysis 04.05. Comparison 04 Multiple dose < 1 year: end value, Outcome 05 Subscapular skin fold (mm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 04 Multiple dose < 1 year: end value

Outcome: 05 Subscapular skin fold (mm)

Study	Deworming		Control		Weighted Mean Difference (Fixed)		Weighted Mean Difference (Fixed)	
	N	Mean(SD)	N	Mean(SD)	95% CI		95% CI	
01 Albendazole Stephenson 1993	95	7.10 (2.34)	93	5.40 (1.93)	--		1.70 [1.09, 2.31]	

Analysis 05.01. Comparison 05 Multiple dose > 1 year: change in value, Outcome 01 Weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 05 Multiple dose > 1 year: change in value

Outcome: 01 Weight (kg)

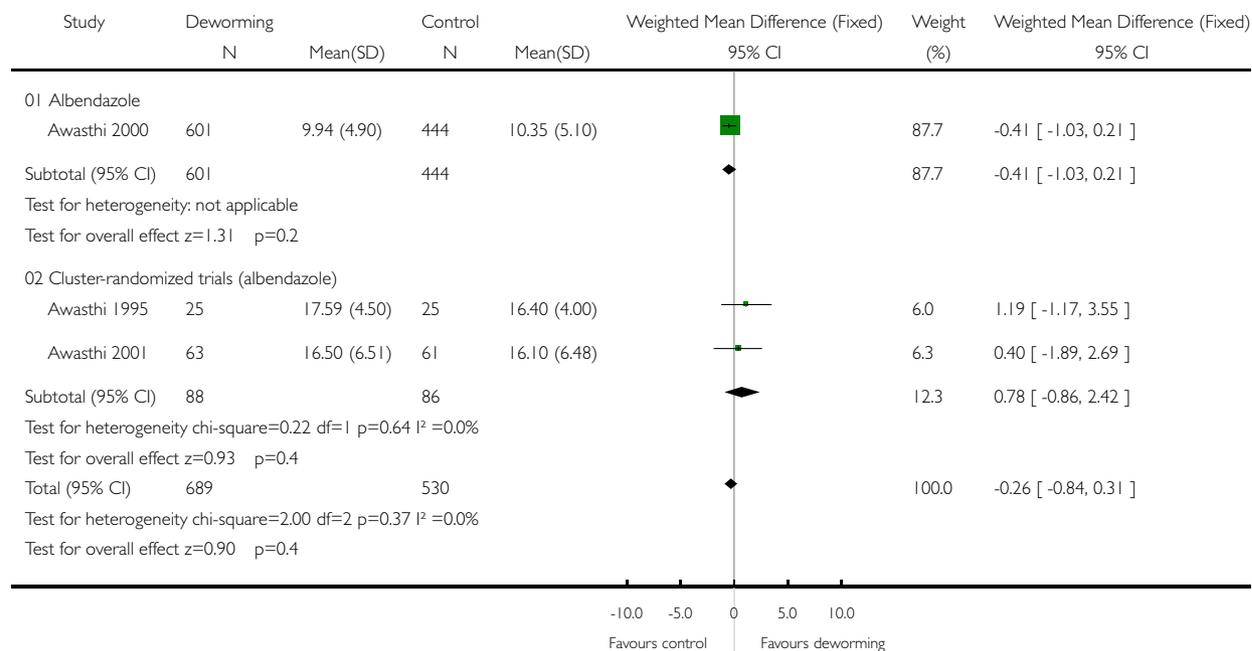
Study	Deworming		Control		Weighted Mean Difference (Random)		Weight (%)	Weighted Mean Difference (Random)	
	N	Mean(SD)	N	Mean(SD)	95% CI			95% CI	
01 Albendazole Awasthi 2000	601	2.63 (1.34)	444	2.68 (1.20)	■		35.2	-0.05 [-0.20, 0.10]	
Subtotal (95% CI)	601		444		◆		35.2	-0.05 [-0.20, 0.10]	
Test for heterogeneity: not applicable									
Test for overall effect z=0.63 p=0.5									
02 Cluster-randomized trials (albendazole) Awasthi 1995	25	4.60 (0.55)	25	3.36 (0.60)	■		34.1	1.24 [0.92, 1.56]	
Awasthi 2001	63	3.22 (2.03)	61	3.05 (1.47)	■		30.7	0.17 [-0.45, 0.79]	
Subtotal (95% CI)	88		86		◆		64.8	0.74 [-0.31, 1.79]	
Test for heterogeneity chi-square=8.99 df=1 p=0.003 I ² =88.9%									
Test for overall effect z=1.39 p=0.2									
Total (95% CI)	689		530		◆		100.0	0.46 [-0.47, 1.39]	
Test for heterogeneity chi-square=50.85 df=2 p<0.0001 I ² =96.1%									
Test for overall effect z=0.96 p=0.3									

Analysis 05.02. Comparison 05 Multiple dose > 1 year: change in value, Outcome 02 Height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 05 Multiple dose > 1 year: change in value

Outcome: 02 Height (cm)

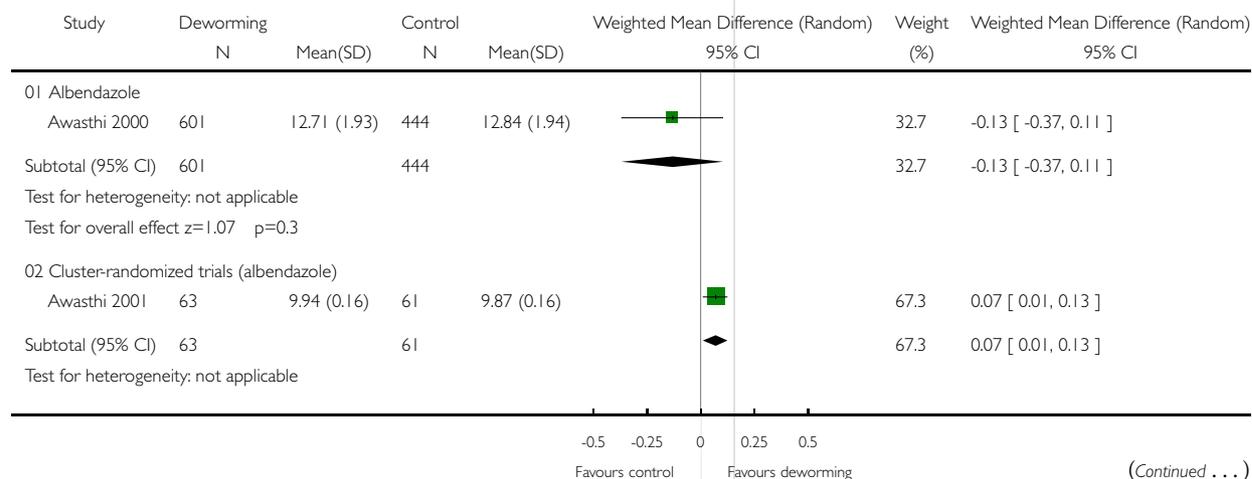


Analysis 06.01. Comparison 06 Multiple dose > 1 year: end value, Outcome 01 Weight (kg)

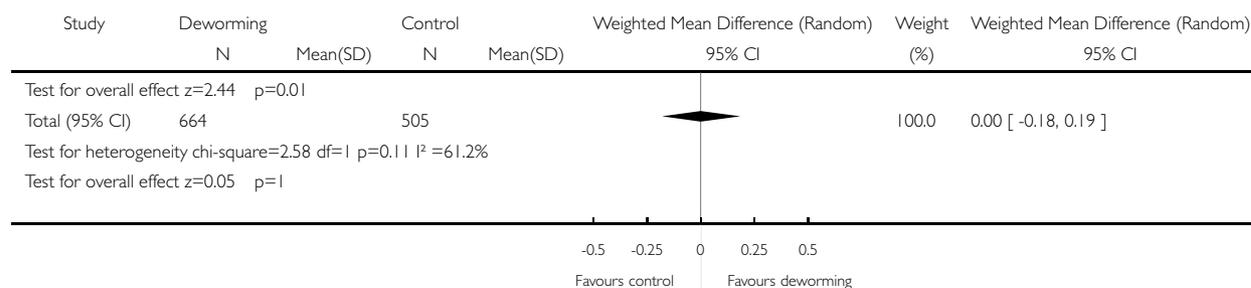
Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 06 Multiple dose > 1 year: end value

Outcome: 01 Weight (kg)



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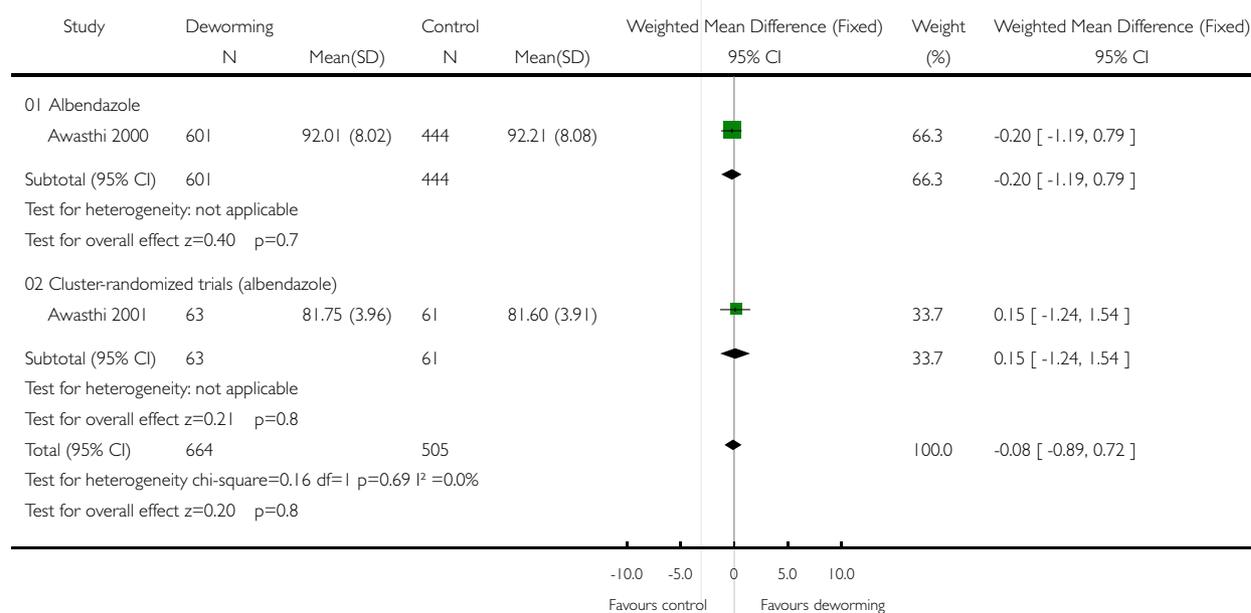


Analysis 06.02. Comparison 06 Multiple dose > 1 year: end value, Outcome 02 Height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 06 Multiple dose > 1 year: end value

Outcome: 02 Height (cm)

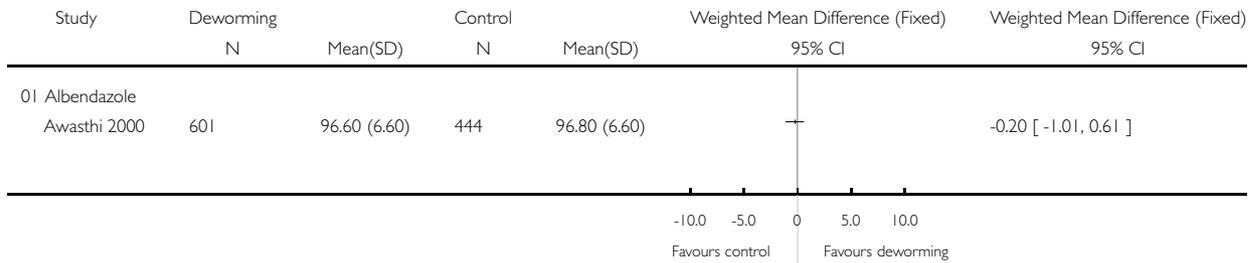


Analysis 06.03. Comparison 06 Multiple dose > 1 year: end value, Outcome 03 Haemoglobin (g/dL)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 06 Multiple dose > 1 year: end value

Outcome: 03 Haemoglobin (g/dL)

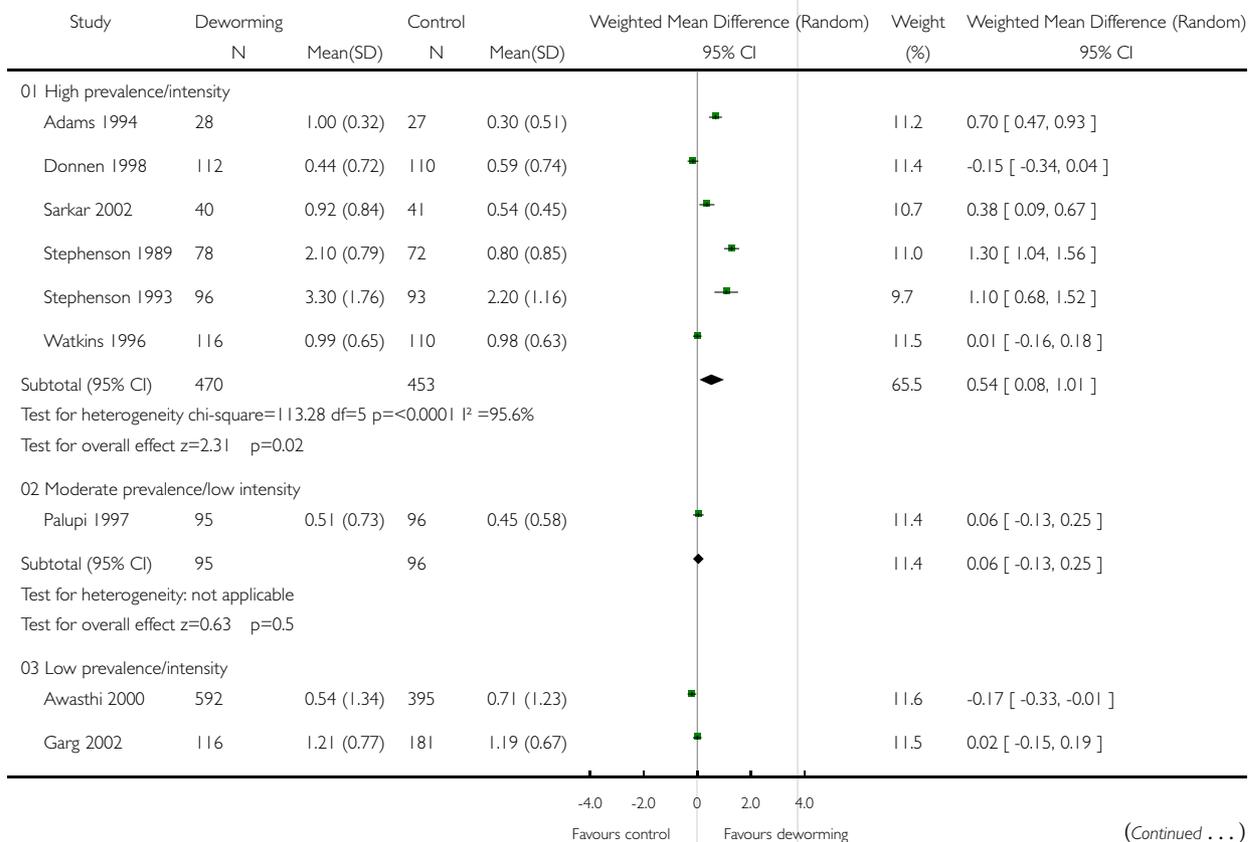


Analysis 07.01. Comparison 07 Analysis by worm prevalence or intensity, Outcome 01 Single dose: change in weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

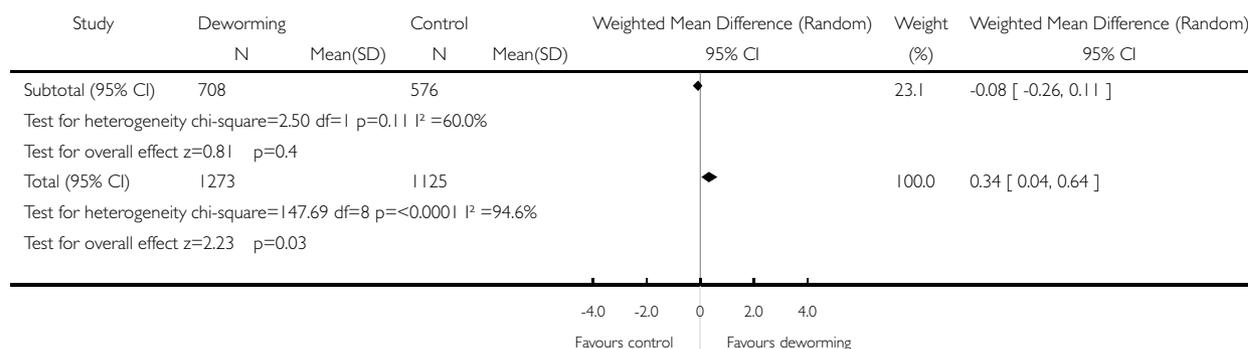
Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 01 Single dose: change in weight (kg)



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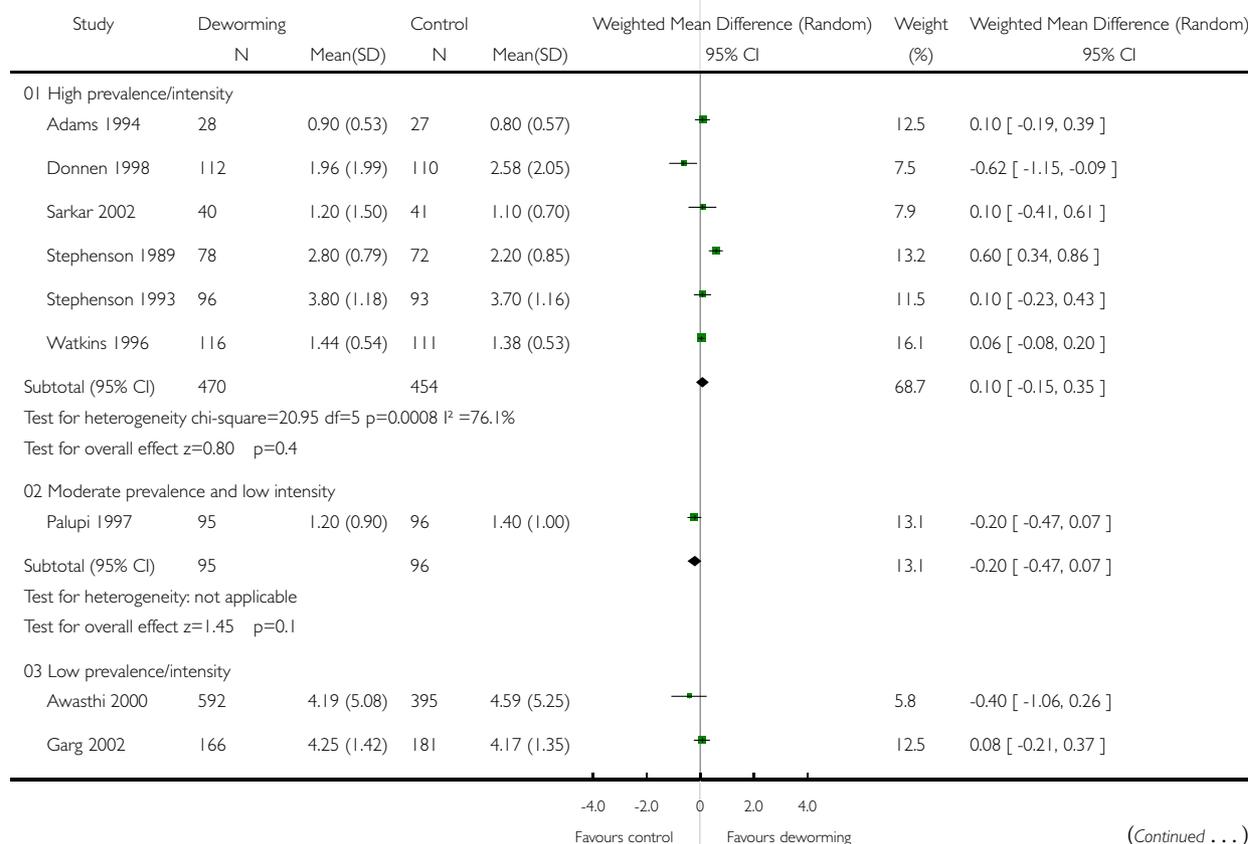


Analysis 07.02. Comparison 07 Analysis by worm prevalence or intensity, Outcome 02 Single dose: change in height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

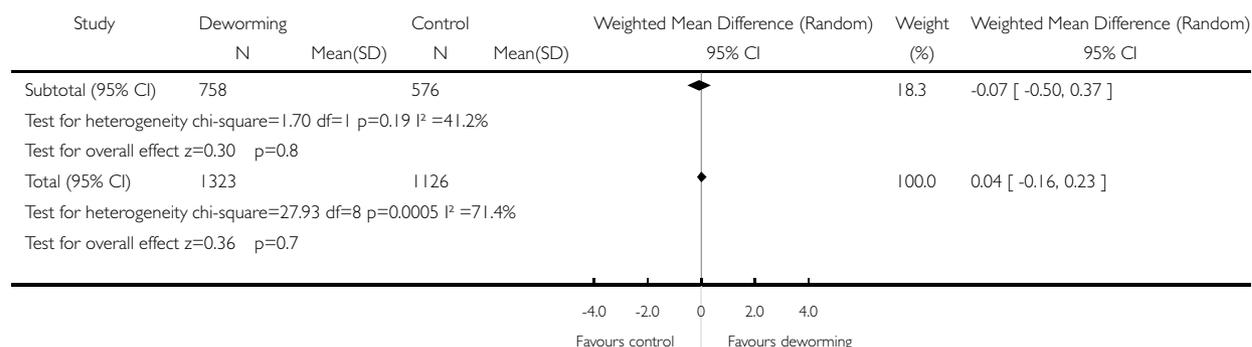
Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 02 Single dose: change in height (cm)



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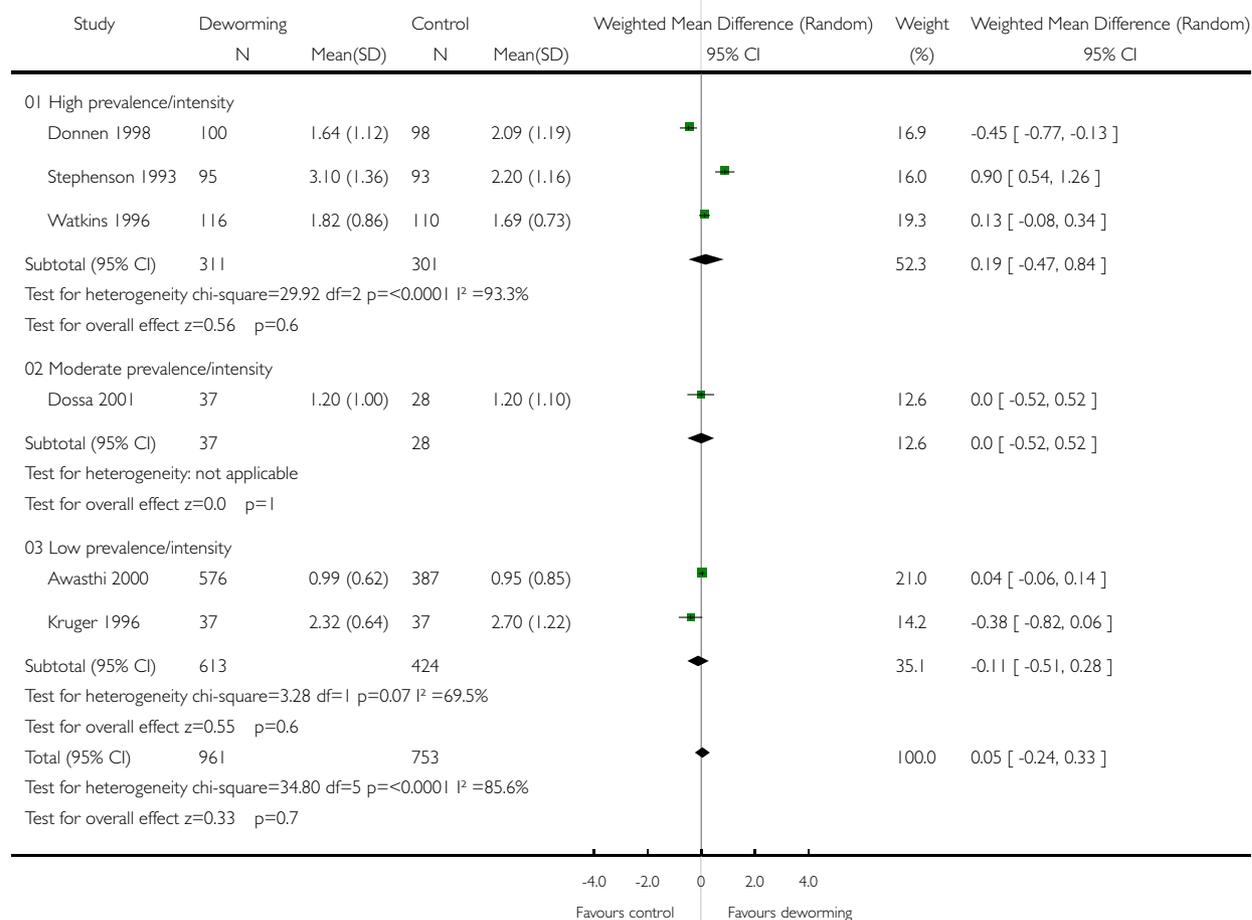


Analysis 07.03. Comparison 07 Analysis by worm prevalence or intensity, Outcome 03 Multiple dose < 1 year: change in weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 03 Multiple dose < 1 year: change in weight (kg)

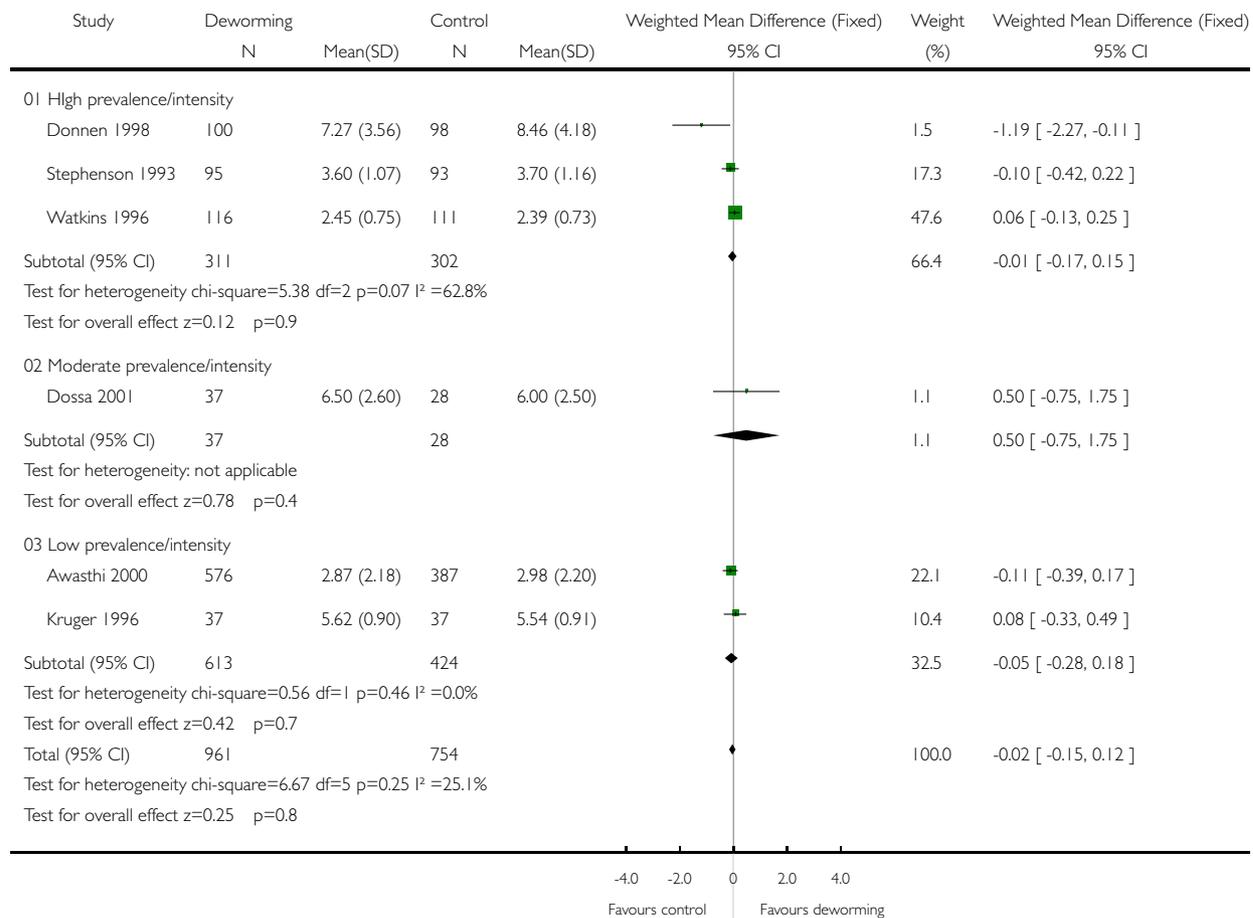


Analysis 07.04. Comparison 07 Analysis by worm prevalence or intensity, Outcome 04 Multiple dose < 1 year: change in height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 04 Multiple dose < 1 year: change in height (cm)

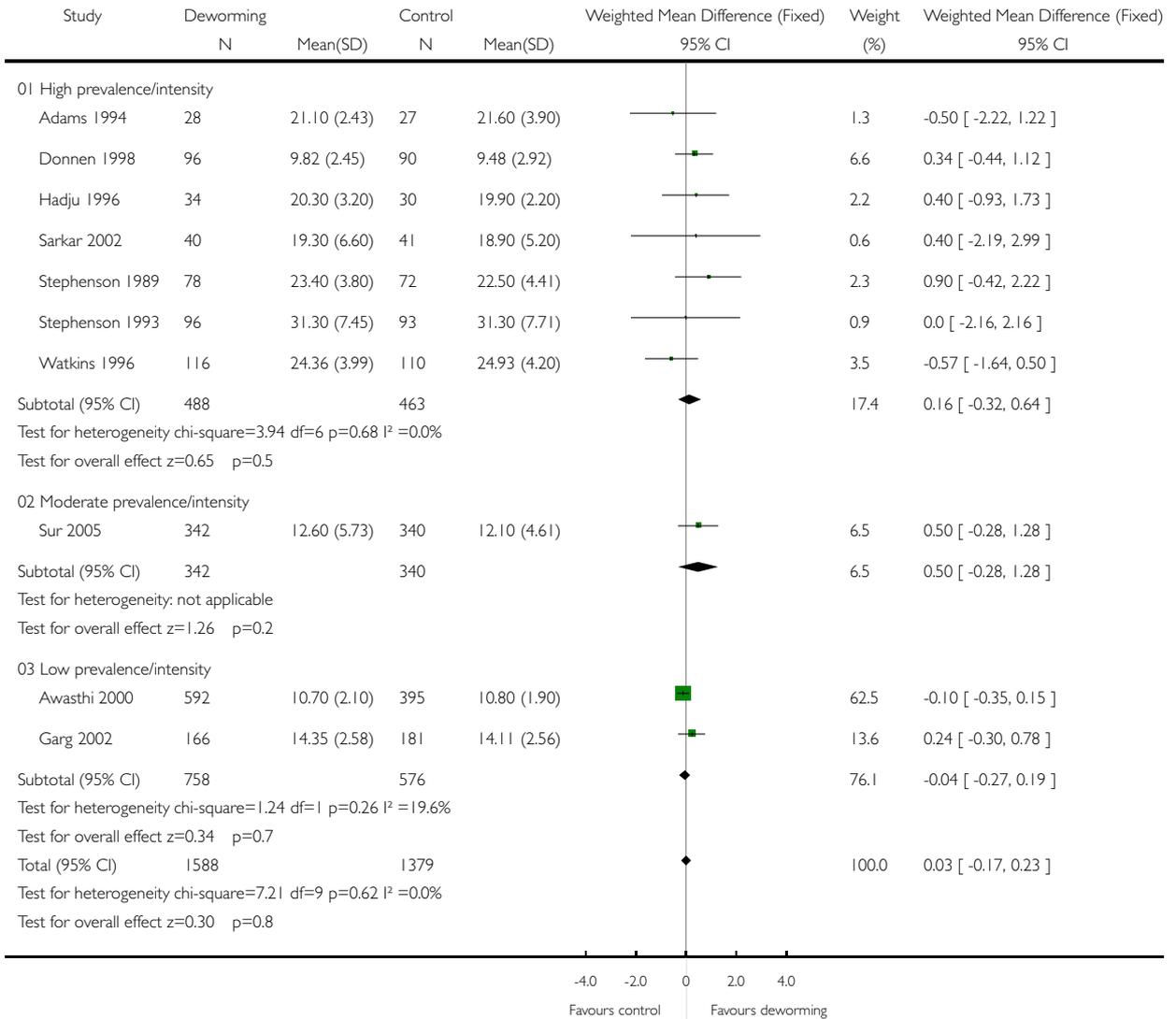


Analysis 07.05. Comparison 07 Analysis by worm prevalence or intensity, Outcome 05 Single dose: end value for weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 05 Single dose: end value for weight (kg)

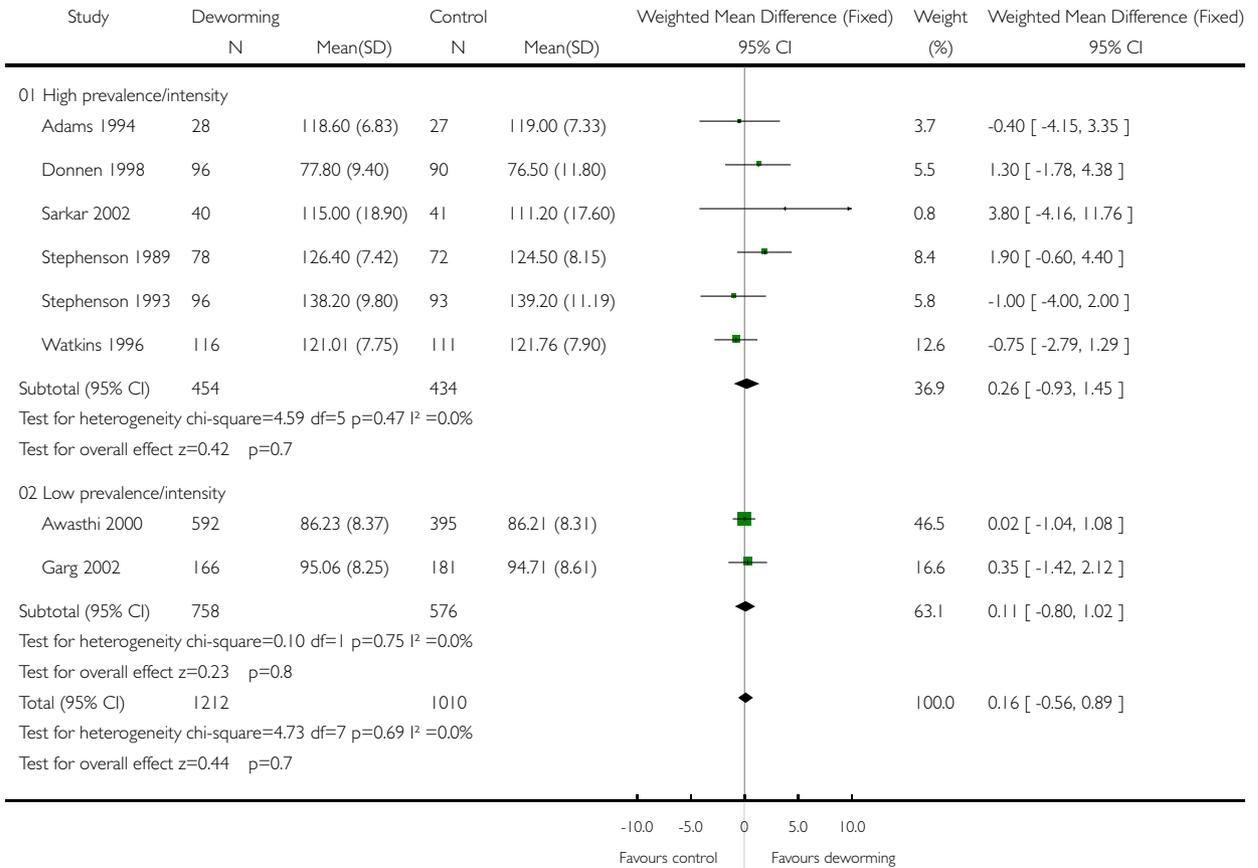


Analysis 07.06. Comparison 07 Analysis by worm prevalence or intensity, Outcome 06 Single dose: end value for height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 06 Single dose: end value for height (cm)

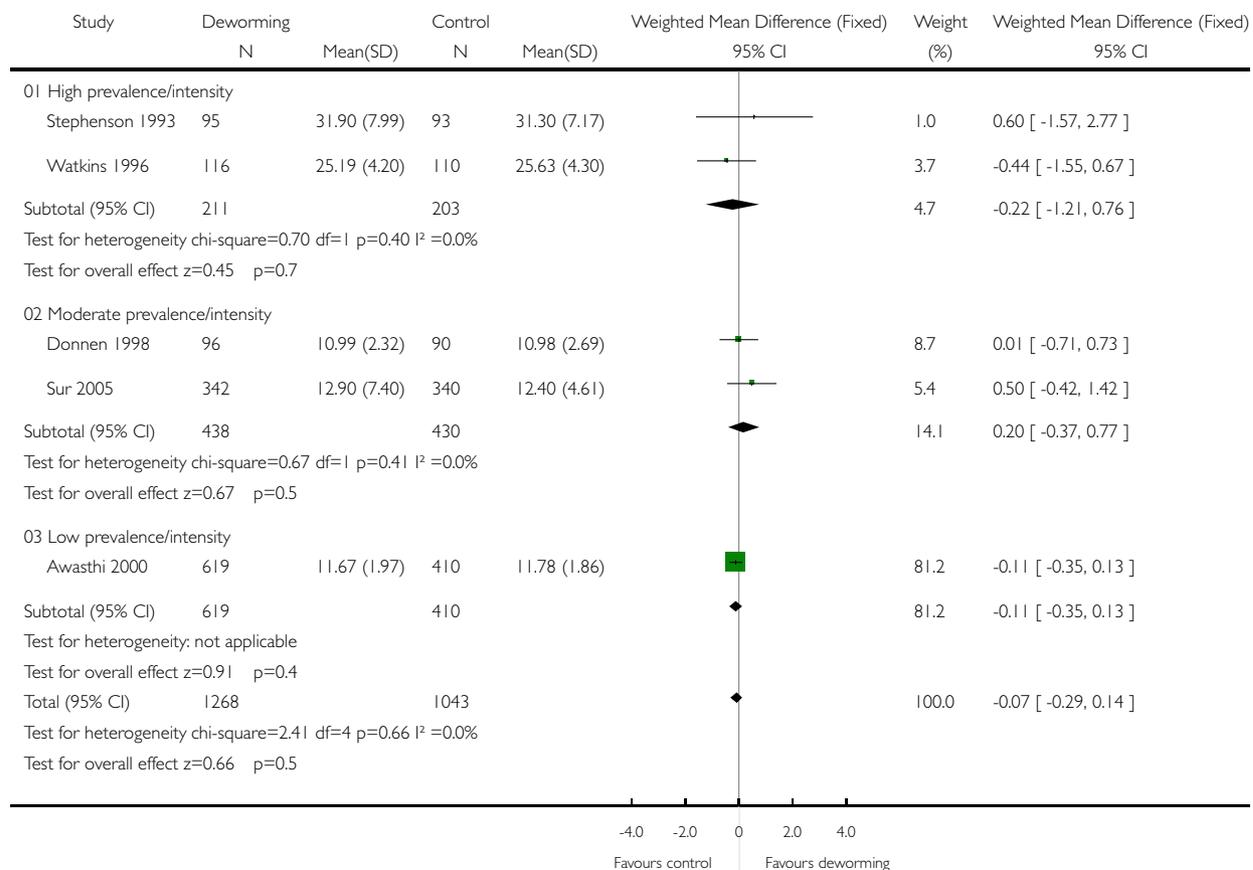


Analysis 07.07. Comparison 07 Analysis by worm prevalence or intensity, Outcome 07 Multiple dose < 1 year: end value for weight (kg)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 07 Multiple dose < 1 year: end value for weight (kg)

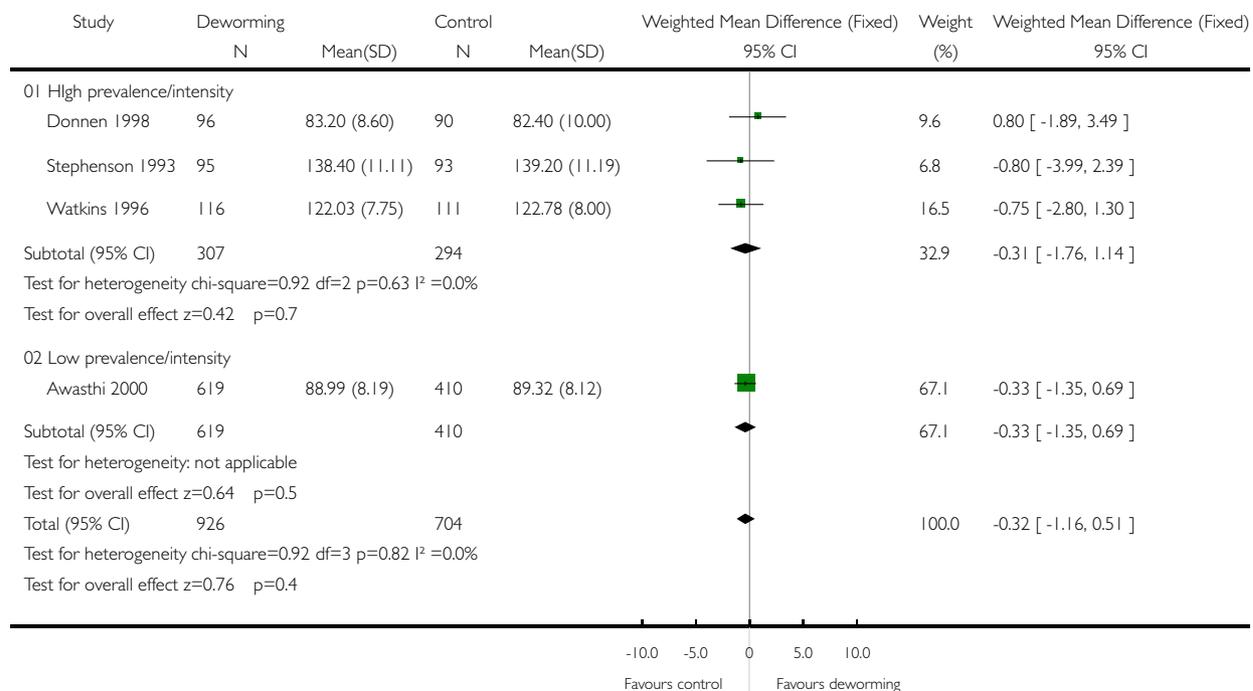


Analysis 07.08. Comparison 07 Analysis by worm prevalence or intensity, Outcome 08 Multiple dose < 1 year: end value for height (cm)

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 07 Analysis by worm prevalence or intensity

Outcome: 08 Multiple dose < 1 year: end value for height (cm)

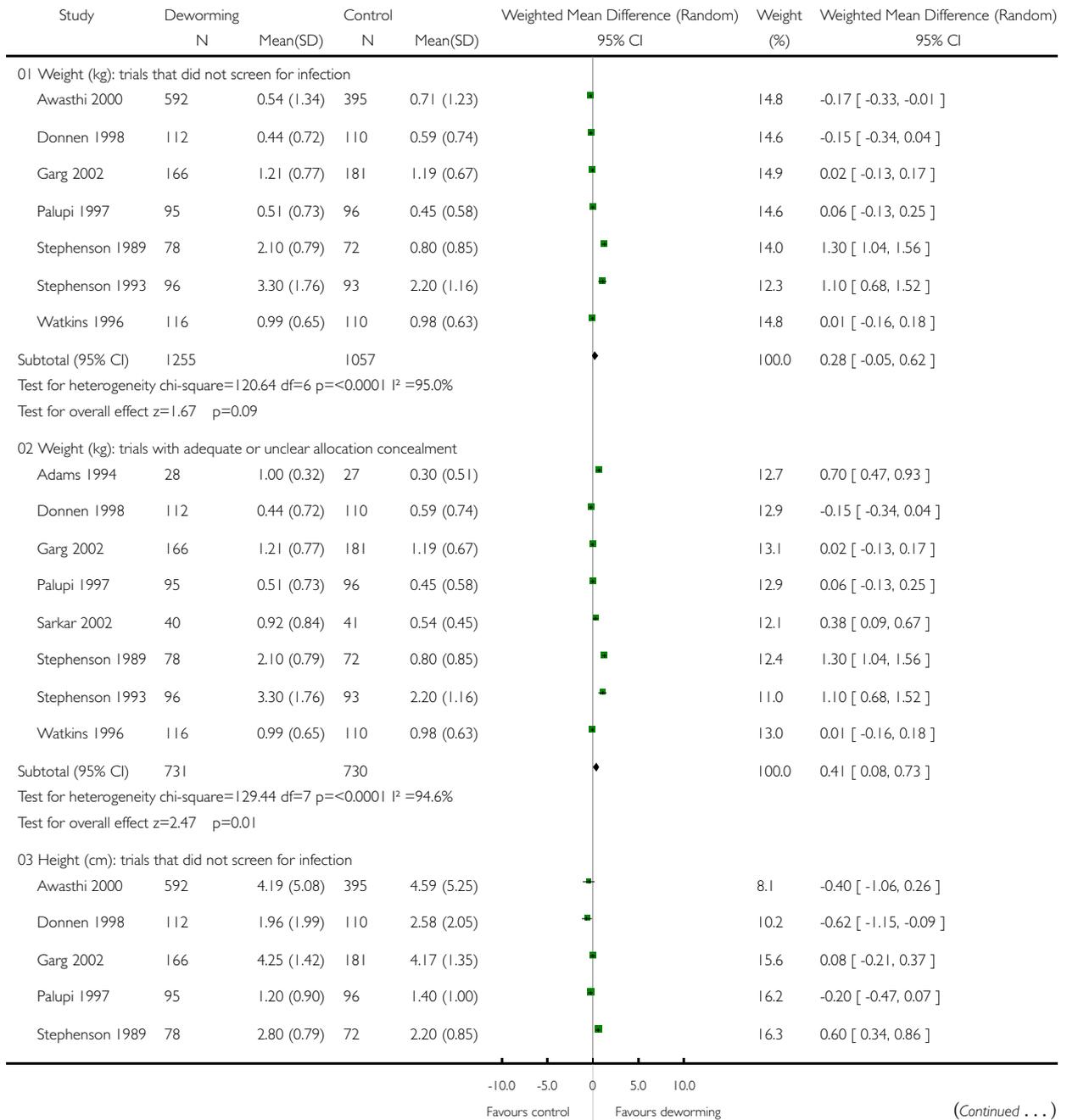


Analysis 08.01. Comparison 08 Subgroup and sensitivity analyses, Outcome 01 Single dose: change

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

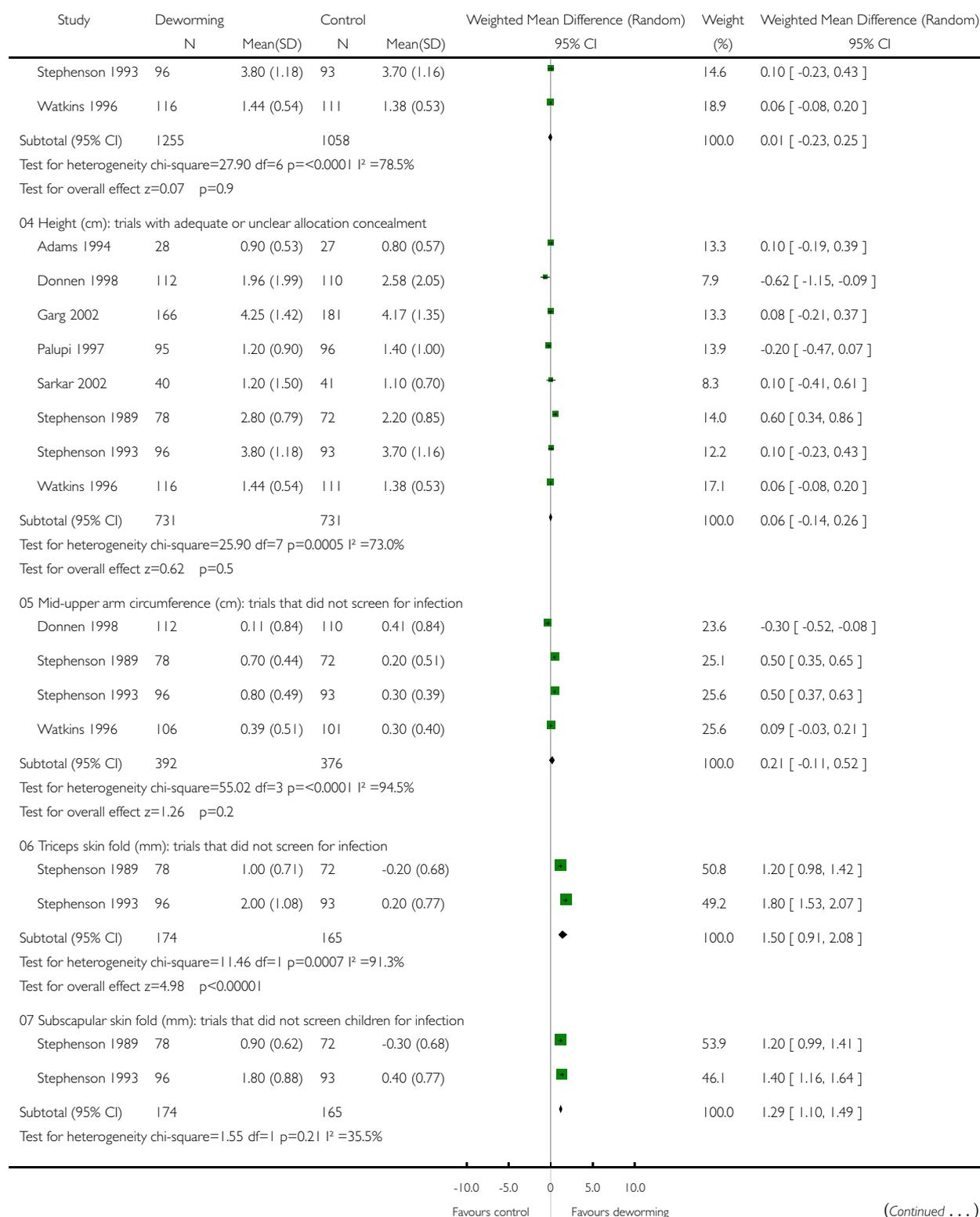
Comparison: 08 Subgroup and sensitivity analyses

Outcome: 01 Single dose: change



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Study	Deworming		Control		Weighted Mean Difference (Random)		Weight (%)	Weighted Mean Difference (Random)	
	N	Mean(SD)	N	Mean(SD)	95% CI			95% CI	

Test for overall effect $z=12.96$ $p<0.00001$

-10.0 -5.0 0 5.0 10.0
Favours control Favours deworming

Analysis 08.02. Comparison 08 Subgroup and sensitivity analyses, Outcome 02 Single dose: end value

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 08 Subgroup and sensitivity analyses

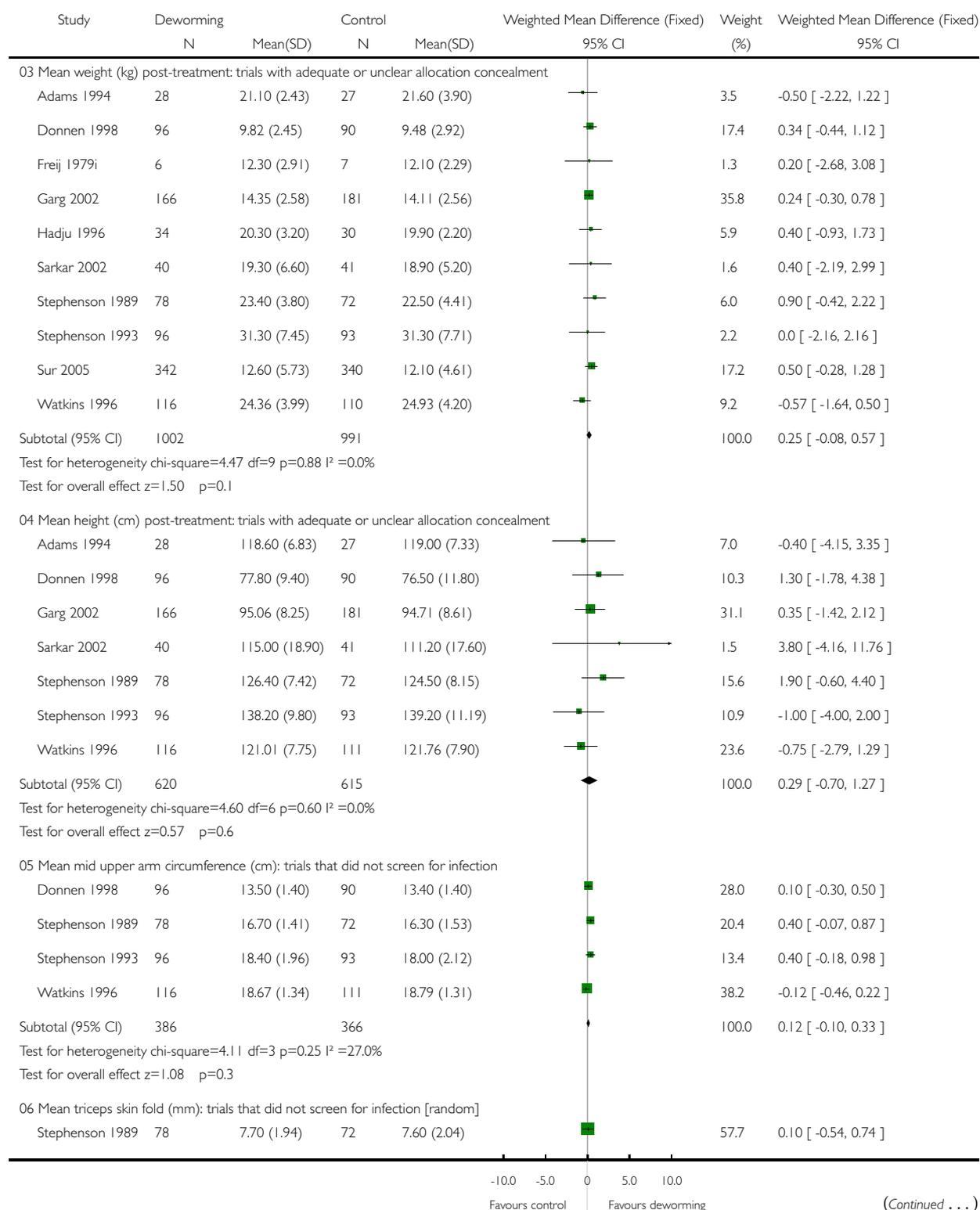
Outcome: 02 Single dose: end value

Study	Deworming		Control		Weighted Mean Difference (Fixed)		Weight (%)	Weighted Mean Difference (Fixed)	
	N	Mean(SD)	N	Mean(SD)	95% CI			95% CI	
01 Mean weight (kg) post-treatment: trials that did not screen for infection									
Awasthi 2000	592	10.70 (2.10)	395	10.80 (1.90)			63.7	-0.10	[-0.35, 0.15]
Donnen 1998	96	9.82 (2.45)	90	9.48 (2.92)			6.7	0.34	[-0.44, 1.12]
Garg 2002	166	14.35 (2.58)	181	14.11 (2.56)			13.9	0.24	[-0.30, 0.78]
Hadju 1996	34	20.30 (3.20)	30	19.90 (2.20)			2.3	0.40	[-0.93, 1.73]
Stephenson 1989	78	23.40 (3.80)	72	22.50 (4.41)			2.3	0.90	[-0.42, 2.22]
Stephenson 1993	96	31.30 (7.45)	93	31.30 (7.71)			0.9	0.0	[-2.16, 2.16]
Sur 2005	342	12.60 (5.73)	340	12.10 (4.61)			6.7	0.50	[-0.28, 1.28]
Watkins 1996	116	24.36 (3.99)	110	24.93 (4.20)			3.6	-0.57	[-1.64, 0.50]
Subtotal (95% CI)	1520		1311				100.0	0.04	[-0.17, 0.24]
Test for heterogeneity $\chi^2=6.77$ $df=7$ $p=0.45$ $I^2=0.0\%$									
Test for overall effect $z=0.35$ $p=0.7$									
02 Mean height (cm) post-treatment: trials that did not screen for infection									
Awasthi 2000	592	86.23 (8.37)	395	86.21 (8.31)			48.7	0.02	[-1.04, 1.08]
Donnen 1998	96	77.80 (9.40)	90	76.50 (11.80)			5.8	1.30	[-1.78, 4.38]
Garg 2002	166	95.06 (8.25)	181	94.71 (8.61)			17.4	0.35	[-1.42, 2.12]
Stephenson 1989	78	126.40 (7.42)	72	124.50 (8.15)			8.8	1.90	[-0.60, 4.40]
Stephenson 1993	96	138.20 (9.80)	93	139.20 (11.19)			6.1	-1.00	[-4.00, 2.00]
Watkins 1996	116	121.01 (7.75)	111	121.76 (7.90)			13.2	-0.75	[-2.79, 1.29]
Subtotal (95% CI)	1144		942				100.0	0.15	[-0.59, 0.89]
Test for heterogeneity $\chi^2=3.84$ $df=5$ $p=0.57$ $I^2=0.0\%$									
Test for overall effect $z=0.40$ $p=0.7$									

-10.0 -5.0 0 5.0 10.0
Favours control Favours deworming

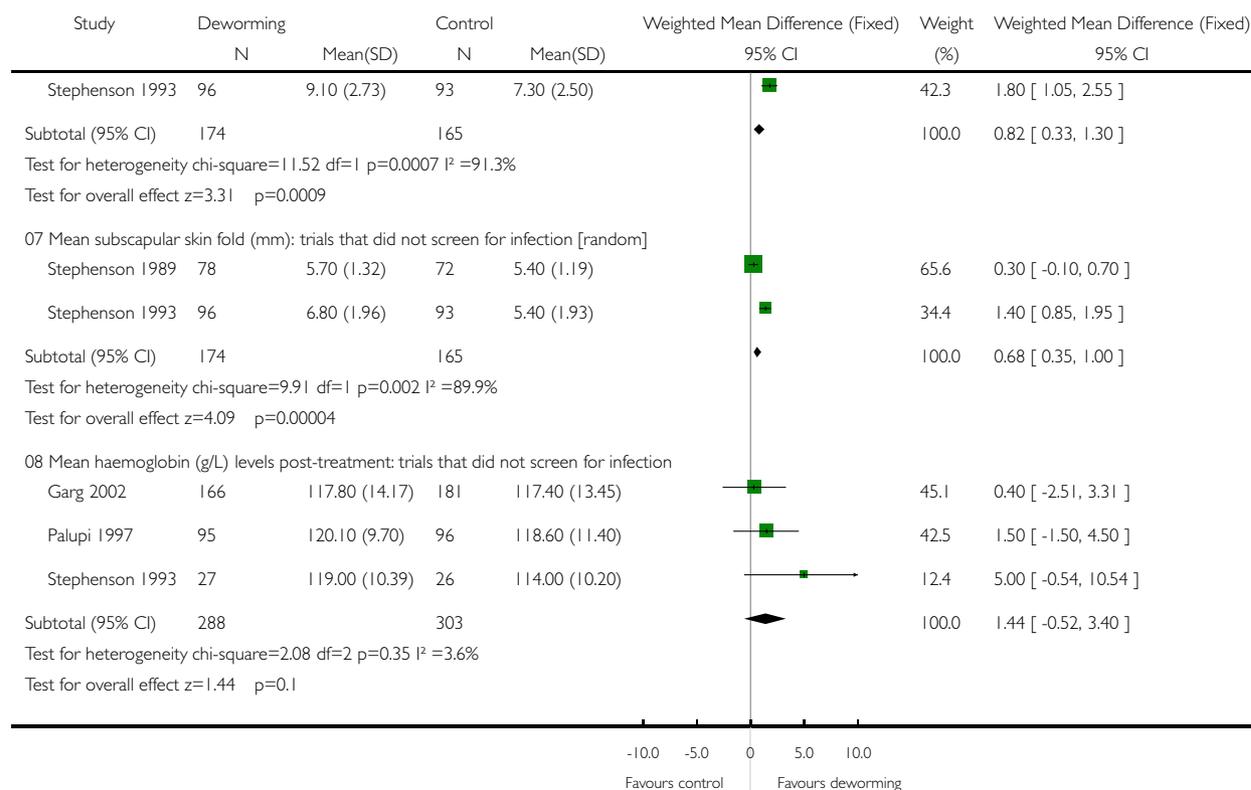
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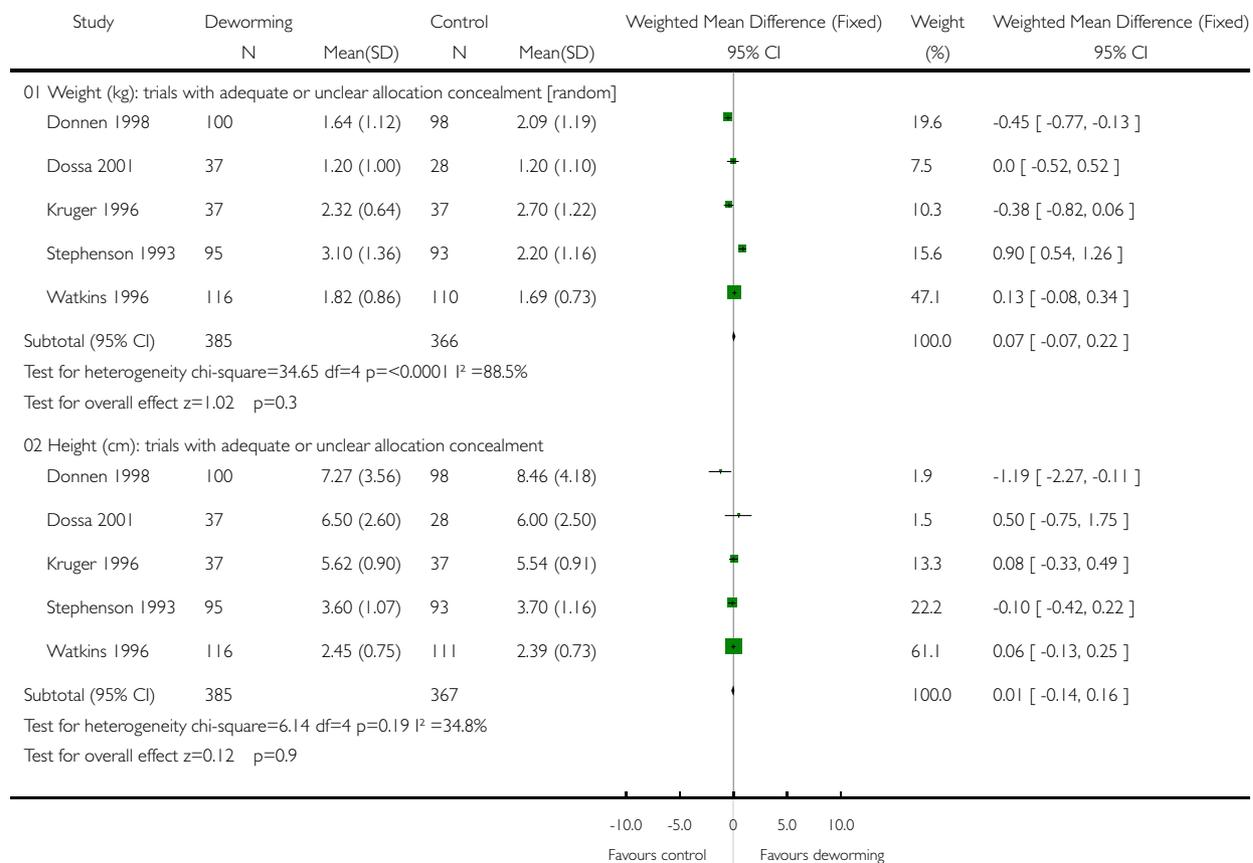


Analysis 08.03. Comparison 08 Subgroup and sensitivity analyses, Outcome 03 Multiple dose < 1 year: change in value

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 08 Subgroup and sensitivity analyses

Outcome: 03 Multiple dose < 1 year: change in value

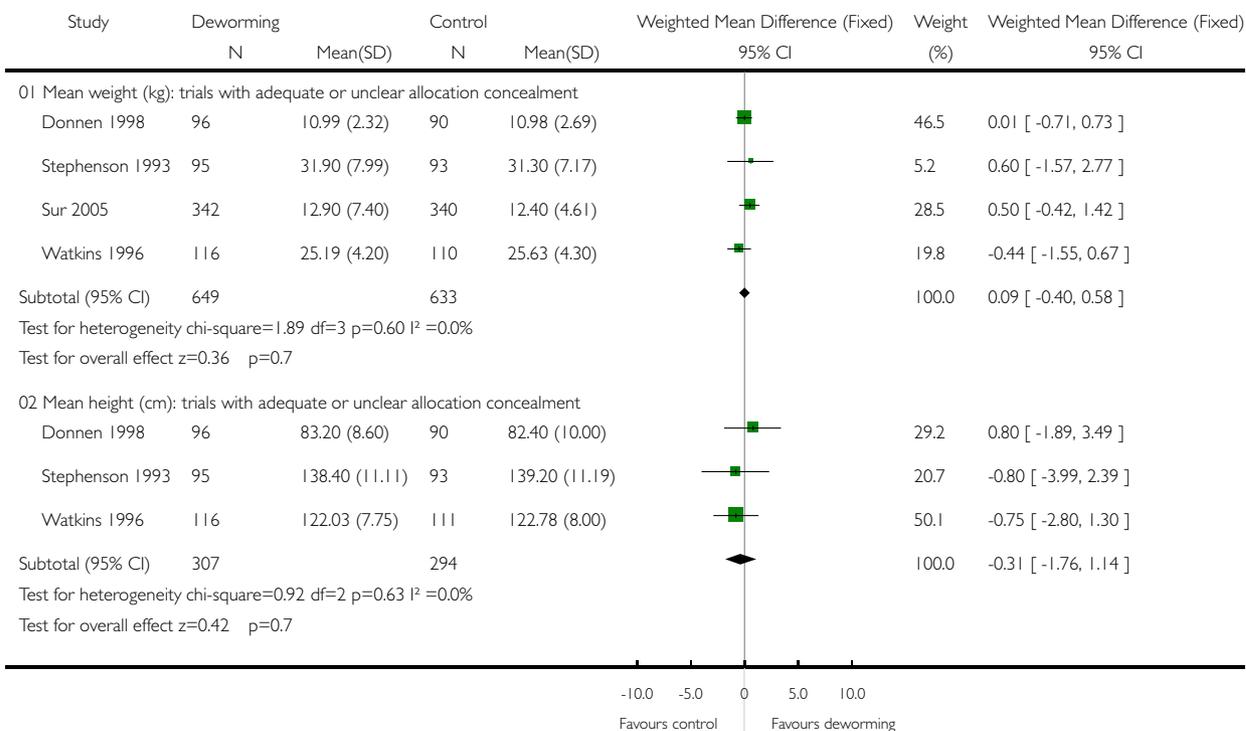


Analysis 08.04. Comparison 08 Subgroup and sensitivity analyses, Outcome 04 Multiple dose < 1 year: end value

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 08 Subgroup and sensitivity analyses

Outcome: 04 Multiple dose < 1 year: end value

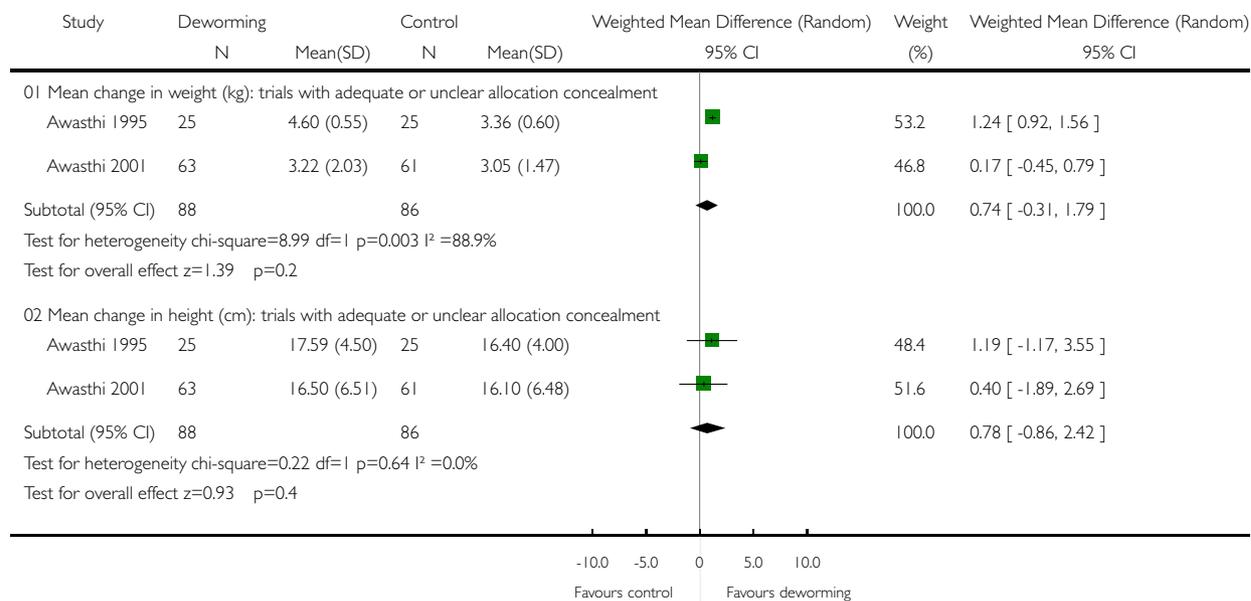


Analysis 08.05. Comparison 08 Subgroup and sensitivity analyses, Outcome 05 Multiple dose > 1 year: change in value

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 08 Subgroup and sensitivity analyses

Outcome: 05 Multiple dose > 1 year: change in value



Analysis 08.06. Comparison 08 Subgroup and sensitivity analyses, Outcome 06 Multiple dose > 1 year: end value

Review: Deworming drugs for treating soil-transmitted intestinal worms in children: effects on growth and school performance

Comparison: 08 Subgroup and sensitivity analyses

Outcome: 06 Multiple dose > 1 year: end value

