Interventions for treating schistosomiasis mansoni (Review)

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[Intervention Review]

Interventions for treating schistosomiasis mansoni

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ABSTRACT

Background

Schistosoma mansoni is a parasite carried by freshwater snails. *S. mansoni* infects the intestine, liver and spleen and can be fatal.

Objectives

To assess the effects of oxamniquine and praziquantel for treating *S. mansoni* infection.

Search strategy

We searched the Cochrane Infectious Diseases Group specialized trials register (September 2005), CENTRAL (*The Cochrane Library* Issue 3, 2005), MEDLINE (1966 to September 2005), EMBASE (1980 to September 2005), LILACS (September 2005), and reference lists of articles. The Revista da Sociedade Brasileira de Medicina Tropical and Brazilian Tropical Medicine Congress abstracts were hand searched

Selection criteria

Randomised and quasi-randomised trials comparing oxamniquine and/or praziquantel with placebo for the treatment of *S. mansoni*.

Data collection and analysis

Two reviewers independently assessed trial quality and extracted data.

Main results

Thirteen trials met the inclusion criteria. Oxamniquine and praziquantel are effective in curing *S. mansoni* infection when compared to placebo. In Africa, 15 mg/kg oxamniquine is less effective than 40 mg/kg praziquantel in people older than 14 years (OR 0.23, 95% CI 0.09 to 0.60), but no difference was shown using 30 mg/kg oxamniquine (OR 2.88, 95% CI 0.69 to 11.96). In Brazil, 15 to 19 mg/kg oxamniquine is as effective as 50 to 70 mg/kg praziquantel in people older than 14 years (OR 0.61, 95% CI 0.26 to 1.46). Both drugs appear safe. No difference in reinfection rate between zinc supplementation and placebo has been shown.

Authors' conclusions

Oxamniquine and praziquantel both appear to be effective for treatment of *S. mansoni*, although lower doses of oxamniquine (less than 30 mg/kg) may not be as effective in some areas.

PLAIN LANGUAGE SUMMARY

Interventions for treating schistosomiasis mansoni

Schistosoma mansoni is a parasite that infects the intestine, liver and spleen and can be fatal. People become infected when they come in contact with contaminated water. The review found that the drugs oxamniquine and praziquantel are both effective for curing the infection. Evidence from one trial shows that zinc supplements do not help to prevent re-infection. A small number of patients given oxamniquine have suffered seizures which could mean that this drug is less safe.

BACKGROUND

People become infected with *Schistosoma mansoni* when they come in contact with water contaminated with the parasite that is carried by freshwater snails. The disease occurs in the tropics, including countries in South America, the Caribbean, Africa, and the eastern Mediterranean (WHO 1993). Infection usually occurs in recognised geographical areas, and sometimes 80% of inhabitants in a village may be infected (Elliott 1996).

The life cycle of *S. mansoni* is complicated. It has two hosts. A particular species of snail (Biomphalaria genus) release larvae (called cercariae) into surrounding fresh water. The larvae swim seeking a host, attracted by body heat in the water. Larvae can survive up to 48 hours in water, but their infectiousness drops after four hours of leaving the snail.

The oral sucker of the larvae attaches to human skin. Enzymes assist the parasite to migrate through the epidermis into the blood stream. From here, the worms migrate along the pulmonary capillaries to enter the left side of the heart. Schistosomula - the parasite with a protective shell - are carried with the arterial blood flow through the aorta to the mesenteric arteries, splanchnic capillaries and portal veins. As schistosomula mature in the blood vessels of the liver, they pair with the opposite sex. The female is carried by the male worm, migrating against the blood flow to the mesenteric veins where the female worms lay hundreds to thousands of eggs per day (Elliott 1996).

Schistosomiasis infects the intestine, liver, and spleen. It can cause bloody diarrhoea, bloody stools, and abdominal pain (Gryseels 1992; WHO 1993). Infection of the liver and spleen causes liver fibrosis and portal hypertension that are generally irreversible in the late stages and kill patients, sometimes as a result of haemorrhage from varices (WHO 1993). Liver failure may also occur, especially when *S. mansoni* infection is associated with viral hepatitis (Pereira 1994).

Diagnosis of infection is by direct microscopy for parasite eggs in the stool or rectal mucosa (Rabello 1992a; Rabello 1992b). Quantitative methods are recommended for epidemiological purposes because it is possible to estimate the worm burden and to evaluate the impact of control programmes (WHO 1985). Among the quantitative methods of stool examination, the Kato/Katz technique is preferable because it has the greatest capacity to concentrate eggs (Costa 1984), and the estimate of intensity of infection remains constant for periods of days and months (Rabello 1992a; Rabello 1992b).

Currently, doctors use either oxamniquine or praziquantel for treatment, both given by mouth, although food appears to retard absorption of oxamniquine and limits the concentration achieved in plasma (Tracy 1996). Lower doses of oxamniquine are given in South America, the Caribbean islands, and West Africa from where the New World parasites were introduced; a single dose of 15 mg/kg for adult patients and 20 mg/kg for children. In other countries of Africa and the Arabian Peninsula, higher doses are given, the total dose varying from 30 mg/kg to 60 mg/kg (Foster 1987). Differences in the susceptibility of parasites to the drug seem to account for the variation in dosage (Tracy 1996).

Development of drug-resistant parasites, poor drug absorption or malabsorption, and immunosuppressed host status all contribute

toward the reduced efficacy of schistosomicidal drugs. Moreover, susceptibility to schistosomicides is related to the sex and age of the parasites. Adult male *S. mansoni* are more sensitive than are the female worms, and immature worms are more resistant to oxamniquine and praziquantel than adult worms (Brindley 1994).

As the morbidity of *S. mansoni* infection is associated with worm burden, chemotherapy plays an important role in the strategy of control and in the reduction and prevention of morbidity. Periodic treatment has been established as a central component of schistosomiasis control. Several useful approaches for community-based chemotherapy have been developed (WHO 1993). These include:

1. Mass treatment: treatment of the entire population without regard to individual infection status.

2. Selective population treatment: treatment of infected persons identified by a diagnostic survey of the entire population.

3. Selective group treatment: treatment of all, or infected members, of a high-risk age or occupational group.

4. Phased treatment: use of the above strategies in a sequence of progressively greater selectivity.

High prevalence areas may justify treatment of entire populations without further individual diagnosis. If there is some impact on infection, programmes can move to a selective approach (WHO 1993). However, programmes have not always had the impact that was expected. Environmental change is required to reduce exposure, and chemotherapeutic programmes are hampered by reinfection (WHO 1993).

As there was no systematic review evaluating the effectiveness of oxamniquine and praziquantel in the treatment of *S. mansoni* infection, we decided to review the effectiveness of these two drugs, and seek information on comparative effectiveness. We also analysed the role of zinc supplementation in the prevention of *S. mansoni* reinfection.

OBJECTIVES

1. To evaluate whether oxamniquine and praziquantel are effective for treating *Schistosoma mansoni* infection.

2. To compare the effectiveness of oxamniquine and praziquantel for treating *S. mansoni* infection.

3. To evaluate whether zinc supplementation is effective in preventing reinfection with *S. mansoni*.

Effectiveness was evaluated in terms of parasitic cure and clinical improvement, and tolerability by adverse effects.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised or pseudo-randomised (individual or group) controlled clinical trials of oxamniquine and/or praziquantel. Randomised or pseudo-randomised controlled trials comparing zinc supplementation with placebo.

Types of participants

Any adults or children with *Schistosoma mansoni* diagnosed by positive stool examination for viable eggs.

Types of interventions

- Oxamniquine or praziquantel versus placebo
- Oxamniquine versus praziquantel
- Zinc supplementation versus placebo

Types of outcome measures

Parasitic outcomes

- Cure (primary outcome): absence of viable eggs of *S. mansoni* in the stool or biopsy of the rectal mucosa.
- Reinfection: presence of viable eggs of *S. mansoni* in successfully treated individuals.

Clinical outcomes

- Diarrhoea
- Bloody diarrhoea
- Abdominal pain
- Spleen and liver size reductions measured by ultrasound or physical examination

Tolerability outcomes

Adverse clinical events

- Neurological: headache, seizures, sleepiness, dizziness
- Gastrointestinal: nausea, vomiting, diarrhoea, abdominal pain
- Systemic side effects: skin rash, fever, myalgia (muscle pain), asthenia (weakness).

Adverse biochemical changes

The time interval from the start of drug use to the development of biochemical abnormalities was estimated in the assessment of drug toxicity. The laboratory tests analysed include:

- Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase to evaluate hepatotoxicity. Only elevation twice the upper limit of normal was considered in the evaluation of possible drug-induced liver disease in the analysis.
- Serum creatinine to evaluate nephrotoxicity.

Search methods for identification of studies

The trials register of the Cochrane Infectious Diseases Group was searched for trials (published or in progress) up to April 2003. The topic search terms used were: *Schistosoma mansoni*, schistosomiasis, bilharziasis, esquistossomose, schistosomicides, praziquantel, oxamniquine, and zinc supplementation.

The reviewers searched the Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (Issue 3, 2005). This contains mainly reference information to randomized controlled trials and controlled clinical trials in health care.

The following databases were also searched: MEDLINE (1966 to September 2005); EMBASE (1980 to September 2005); and LILACS (September 2005), using the search terms in combination with the search strategy developed by the Cochrane Collaboration and detailed in the Cochrane Reviewers' Handbook (Clarke 2003). Specific search terms used: *Schistosoma mansoni*, schistosomiasis, bilharziasis, esquistossomose, schistosomicides, praziquantel, oxamniquine and zinc supplementation.

The bibliographic references of books and review articles relating to schistosomiasis and tropical diseases were searched in order to find randomised controlled trials not already identified by electronic searching.

In addition, the Revista da Sociedade Brasileira de Medicina Tropical and Brazilian Tropical Medicine Congress' abstracts were handsearched.

Data collection and analysis

The main reviewer applied inclusion criteria to all potential studies. Independently, a second reviewer applied the same inclusion criteria. If there was disagreement a third person was asked for an opinion in order to reach consensus. Methodological quality was assessed by both reviewers using the standard approach of the Infectious Diseases Group (see module editorial information for details). Pre-specified trial characteristics were extracted from each included study by the first reviewer and checked by the second.

Studies were excluded if they reported more than 20% drop-out or were duplicate publications of a study already included.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Thirteen randomised controlled trials met the inclusion criteria. Six studies were carried out in Brazil and seven in Africa. The follow-up period varied between one and 12 months. In six studies follow-up was longer than one month. These studies were analysed separately because, in this instance, the probability of underestimated results is greater since the rate of reinfection may be high.

Six studies examined only children younger than 15 years old. Two other studies included only individuals older than 14 years. Five studies evaluated both children and adults. Different dose schedules of oxamniquine and praziquantel were compared according to age. The schedules also varied according to geographic area, and the African studies used higher doses than the studies carried out in Brazil.

Stool examination, according to Kato or Kato/Katz methods, was the assessment method used in 10 studies. The number of stool samples varied between one and three, but the results of each sample were not always reported. In Cunha 1986, stool examination was performed according to the Hoffman, Pons & Janer, and Kato/Katz methods, and a rectal mucosa biopsy was also done.

Two trials compared oxamniquine with placebo (Ayele 1986; de Jonge 1991). Comparison between praziquantel and placebo was performed in three trials (de Jonge 1991; Jaoko 1996; Sukwa 1993); however, the Jaoko trial only evaluated side effects.

The trial by de Jonge 1991 was carried out in individuals with mixed *Schistosoma mansoni* and *S. haematobium* infections. This study evaluated the effects of oxamniquine and praziquantel (and metrifonate) by measuring the serum level of circulating anodic antigens and comparing cure rate based on stool examination.

Clinical improvement through physical examination was evaluated in only one trial (Sukwa 1993) in which school children were allocated to receive praziquantel or placebo. Physical examination was performed at the time of enrolment, then at six months and 12 months after the treatment. The cure rate, however, was not provided.

Friis 1997 evaluated the rate of reinfection with *S. mansoni* after zinc supplementation in children.

Risk of bias in included studies

The included studies did not provide clear descriptions of allocation concealment or randomisation methods.

Six studies used double-blind methods. In two trials the outcome measurement was blinded, but there was no indication if the patients were blinded. Double-blind method was not described in five trials.

The drop-out rate was variable. In most of the included studies, the loss to follow-up was more than 10%. Three trials were excluded from the efficacy analysis because the loss was more than 20% after three months of follow-up. These studies were included in the analysis of tolerance outcomes because these were recorded one to seven days after treatment when drop-out was minimal.

Effects of interventions

Any drug versus placebo

Two trials compared oxamniquine (60 mg/kg) with placebo (Ayele 1986; de Jonge 1991), showing the drug to be more effective for parasitological cure (61/93 versus 0/61; OR 17.68, 95% CI 9.02 to 34.64). The de Jonge trial included patients with mixed *Schistosoma mansoni* and *S. haematobium* infections.

One trial comparing praziquantel (40 mg/kg) with placebo reported on parasitic outcome (de Jonge 1991). As mentioned above, infections in this trial were mixed *S. mansoni* and *S. haematobium*. Cure of *S. mansoni* was higher with praziquantel than in the placebo group (31/48 v 0/21; OR 13.10, 95% CI 4.71 to 36.44).

Only Sukwa 1993 was included in the analysis of clinical improvement. It was not possible to conclude whether praziquantel was more effective than placebo in the reduction of morbidity when the control cure was achieved after six months or 12 months.

Oxamniquine versus praziquantel

Parasitological cure after one month

Comparison between oxamniquine at a dose of 15 mg/kg and praziquantel at a dose of 40 mg/kg was reported in Taddese 1988. Praziquantel was given to one treatment group as a single dose and to another group as two doses of 20 mg/kg. Praziquantel showed a higher cure rate than oxamniquine, in single dose (OR 0.23, 95% CI 0.08 to 0.66) or split dose (OR 0.34, 95% CI 0.12 to 0.94) and overall (OR 0.23, 95% CI 0.09 to 0.60). When the dose of oxamniquine was increased to 30 mg/kg no difference was shown between oxamniquine and praziquantel in single dose (OR 2.80, 95% CI 0.38 to 20.52) or split dose (OR 4.07, 95% CI 0.79 to 21.04) or overall (OR 2.88, 95% CI 0.69 to 11.96).

One trial compared oxamniquine 20 mg/kg with praziquantel 40 mg/kg in an area where the cure rate with praziquantel is low (Stelma 1997). Parasitological cure was higher in the group using oxamniquine than in the praziquantel group and the difference was statistically significant (OR 4.22, 95% CI 2.16 to 8.23).

Only one trial compared oxamniquine 60 mg/kg with praziquantel 40 mg/kg in mixed *S. mansoni* and *S. haematobium* infections (de Jonge 1991). No statistically significant difference was shown (OR 0.54, 95% CI 0.24 to 1.17).

Parasitological cure, follow-up greater than two months

In adults (Taddese 1988), oxamniquine 15 mg/kg was less effective than praziquantel 40 mg/kg (overall OR 0.46, 95% CI 0.26 to 0.81; praziquantel single dose OR 0.58, 95% CI 0.31 to 1.07; praziquantel split dose OR 0.40, 95% CI 0.21 to 0.76). After three months or more, no difference was shown between oxamniquine 30 mg/kg and praziquantel 40 mg/kg single dose (OR 2.02, 95% CI 0.97 to 4.23) or split dose (OR 1.39, 95% CI 0.63 to 3.09) or overall (OR 1.65, 95%CI 0.87 to 3.14).

Higher dose praziquantel (50-70 mg/kg) did not result in a higher cure rate, at greater than two months follow-up in two studies, than oxamniquine 15-19 mg/kg, in individuals older than 14 years. Single dose praziquantel OR 0.61, 95% CI 0.26 to 1.46 (Cunha 1986; Fernandes 1986); split dose praziquantel OR 0.54, 95% CI 0.15 to 1.90 (Fernandes 1986).

No trials were found to allow us to explore differences between praziquantel and oxamniquine in children.

Tolerability

Adverse clinical events

There were several adverse clinical effects reported, but no deaths, after administration of oxamniquine or praziquantel. The most serious side effect reported was seizure, and this was observed in two patients using oxamniquine out of a total of 372 patients evaluated (Taddese 1988; Rezende 1985). Other neurological side effects were commonly reported with both drugs. No statistical difference was shown in incidence of headache, dizziness or sleepiness in individuals taking oxamniquine or praziquantel.

Diarrhoea and abdominal pain were less frequently reported as side effects in oxamniquine-treated patients: diarrhoea 38/544 (7%) patients compared to 74/536 (14%) praziquantel-treated patients (OR 0.48, 95% CI 0.32 to 0.71); abdominal pain 15/571 (20%) compared to 240/563 (42%) praziquantel-treated patients (OR 0.34, 95% CI 0.26 to 0.44). No difference in vomiting or nausea was shown.

Other systemic side effects, such as asthenia and skin rash, were less frequent and similar with the two treatments. Myalgia did occur with oxamniquine (7/352) but was not reported with praziquantel (0/327). Fever was reported with praziquantel treatment (4/267) but not with oxamniquine (0/272).

Only one trial (Jaoko 1996) compared side effects between praziquantel and placebo. Headache, dizziness, nausea, abdominal pain, and fever were reported more frequently in the group using praziquantel. Bloody diarrhoea was reported in one praziquantel patient, as was urticaria.

Adverse biochemical changes

No abnormality suggesting nephrotoxicity or hepatotoxicity was observed after administration of oxamniquine or praziquantel in terms of development of biochemical abnormalities reported in one study (Silva 1986). Both drugs appeared to be safe.

Zinc supplementation

Only one included trial (Friis 1997) compared zinc supplementation with placebo to prevent reinfection with *S. mansoni*. No statistical difference in the incidence of reinfection was shown in 261 patients (OR 0.82, 95% CI 0.47 to 1.41).

DISCUSSION

The methodological quality of the included studies was poor. None clearly described concealment of allocation or randomisation procedures. Few studies were double blind and loss to follow-up was as high as 20%. Follow-up time of more than six weeks does not appear appropriate (Stelma 1997) because the probability of underestimation of treatment effect may occur as the reinfection rate could be high after this period.

An important question is the ideal dose for a patient's age, and whether different doses are required in different geographic areas. Lack of data precluded exploring these questions.

Compared with placebo, oxamniquine (60 mg/kg) has been shown in one study to be effective in curing *Schistosoma mansoni* infection (88% of evaluated patients cured versus 2% given placebo). The same dose of oxamniquine in one other study, and 40 mg/kg praziquantel, was also more effective than placebo in curing *S. mansoni* infection in patients with mixed *S. mansoni* and *S. haematobium* infections (49% cure rate with oxamniquine, 64% with praziquantel, versus 0% with placebo).

Comparing the two drugs, praziquantel at a dose of 40 mg/kg was more effective than oxamniquine at a dose of 15 mg/kg in individuals older than 14 years, but when the dose of oxamniquine was increased to 30 mg/kg or more no statistical difference has been shown between the two drugs.

Both praziquantel and oxamniquine appear to be similarly safe, except that two oxamniquine-treated patients had seizures which could suggest that oxamniquine might be less safe.

The available evidence from one trial (261 patients) suggests that zinc supplementation is not more effective than placebo in preventing reinfection with *S. mansoni*.

AUTHORS' CONCLUSIONS

Implications for practice

1. Oxamniquine and praziquantel are effective treatments for *Schistosoma mansoni* infection. No compelling evidence shows a difference between the two drugs. However, oxamniquine at a dose of 15 mg/kg is less effective than 40 mg/kg praziquantel.

2. In mixed *Schistosoma mansoni* and *S. haematobium* infections no difference has been shown between 60 mg/kg oxamniquine and 40 mg/kg praziquantel.

3. It is not possible to conclude whether oxamniquine or praziquantel has an effect on morbidity caused by infection.

4. Oxamniquine might be less safe than praziquantel based on two patients who had seizures.

5. There is no evidence from randomised trials that zinc supplementation is effective to prevent reinfection with *S. mansoni*.

Implications for research

1. A systematic review of observational studies, including case reports, is required to document potential toxicity and tolerability of the two drugs.

2. A good randomised trial is needed to examine clinical effectiveness in terms of morbidity outcomes.

3. Further work to explore varying effectiveness with geographic area may be useful.

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REFERENCES

References to studies included in this review

Ayele 1986 *{published data only}*
Ayele T. Preliminary clinical trial of oral oxamniquine in the treatment of Schistosoma mansoni in children in Ethiopia. *East Afr Med J* 1986;**63**:291–294.

Branchini 1982 *{published data only}*
Branchini M, Pedro R de J, Dias LC, Deberaldini ER. Double-blind clinical trial comparing praziquantel with oxamniquine in the treatment of patients with schistosomiasis mansoni. *Rev Inst Med Trop São Paulo* 1982;**24**:315–321.

Cunha 1986 *{published data only}*
Cunha AS, Pedrosa RC. Double-blind therapeutical evaluation based on the quantitative oogram technique comparing praziquantel and oxamniquine in human schistosomiasis mansoni. *Rev Inst Med Trop São Paulo* 1986;**28**:337–351.

de Jonge 1991 *{published data only}*
de Jonge N, Schommer G, Feldmeier H, Krijer FW, Dafalla AA, Bienzle U, Deelder AM. Mixed Schistosoma haematobium and S. mansoni infection: Effect of different treatments on the serum level of circulating anodic antigen (CAA). *Acta Trop* 1991;**48**:25–35.

Fernandes 1986 *{published data only}*
Fernandes P, Oliveira CC. Comparative study of the efficacy of praziquantel in 2 dose schedules and oxamniquine in the treatment of schistosomiasis mansoni [Estudo comparativo da eficácia do praziquantel, em dois esquemas posológicos, e da oxamniquina no tratamento da esquistossomose mansônica]. *F Méd* 1986;**93**: 389–393.

Friis 1997 *{published data only}*
Friis H, Ndhlovu P, Mduluza T, Kaondera K, Sandström B, Michaelson KF, Vennervald BJ, Christensen NO. The impact of zinc supplementation on Schistosoma mansoni reinfection rate and intensities: A randomized, controlled trial among rural Zimbabwean schoolchildren. *Eur J Clin Nutr* 1997;**51**:33–37.

Jaoko 1996 *{published data only}*
Jaoko WG, Muchemi G, Oguya FO. Praziquantel side effects during treatment of Schistosoma mansoni infected pupils in Kibwezi, Kenya. *East Afr Med J* 1996;**73**:499–501.

Katz 1982 *{published data only}*
Katz N, Rocha RS. Double-blind clinical trial comparing praziquantel with oxamniquine in schistosomiasis mansoni. *Rev Inst Med Trop São Paulo* 1982;**24**:310–314.

Rezende 1985 *{published data only}*
Rezende GL. Survey on the clinical trial results achieved in Brazil comparing praziquantel and oxamniquine in the treatment of mansoni schistosomiasis. *Rev Inst Med Trop São Paulo* 1985;**27**: 328–336.

Silva 1986 *{published data only}*
da Silva LC, Zeitune JMR, Rosa-Eid LMF, Lima DMC, Antoneli RH, Christo CH, Saez-Alquezar A, Carboni AC. Treatment of patients with schistosomiasis mansoni: a double-blind clinical trial comparing praziquantel with oxamniquine. *Rev Inst Med Trop São Paulo* 1986;**28**:174–180.

Stelma 1997 *{published data only}*
Stelma FF, Sall S, Daff B, Sow S, Niang M, Gryseels B. Oxamniquine cures Schistosoma mansoni infection in a focus in which cure rates with praziquantel are unusually low. *J Infect Dis* 1997;**176**:304–307.

Sukwa 1993 *{published data only}*
Sukwa TY. A community-based randomized trial of praziquantel to control schistosomiasis morbidity in schoolchildren in Zambia. *Ann Trop Med Parasitol* 1993;**87**:185–194.

Taddese 1988 *{published data only}*
Taddese K, Zein Z. Comparison between the efficacy of oxamniquine and praziquantel in the treatment of Schistosoma mansoni infection on a sugar estate in Ethiopia. *Ann Trop Med Parasitol* 1988;**82**:175–180.

References to studies excluded from this review

Abu-Ely-Azeed 1993 *{published data only}*
Abu-Ely-Azeed R, Podgore JK, Mansour NS, Kilpatrick ME. Field trial of 1% niclosamide as a topical antipenetrant to Schistosoma mansoni cercariae. *Am J Trop Med Hyg* 1993;**49**:403–409.

Barakat 1995 *{published data only}*
Barakat R, El Masry AG, Farghaly A, El Morshidy HN, El Sayed MK, Husein MH, Miller FD. Impact of population-based selective chemotherapy on prevalence and intensity of Schistosoma mansoni infections in the Nile Delta: Kafr El Sheikh. *Trop Geogr Med* 1995; **47**:266–270.

Bella 1982 *{published data only}*
Bella H, Rahim AGA, Mustafa MD, Ahmed MAM, Wasfi S, Bennett JL. Oltipraz - Antischistosomal efficacy in sudanese infected with Schistosoma mansoni. *Am J Trop Med Hyg* 1982;**31**: 775–778.

Coutinho 1983 *{published data only}*
Coutinho A, Domingues ALC, Neves J, Almeida ST. Treatment of hepatosplenic schistosomiasis mansoni with praziquantel (preliminary report on tolerance and efficacy). *Arzneim Forsch* 1983;**33**(I):787–791.

Coutinho 1984 *{published data only}*
Coutinho AD, Domingues AL, Florencio JN, Almeida ST. Treatment of hepatosplenic schistosomiasis mansoni with praziquantel [Tratamento da esquistossomose mansonica com praziquantel]. *Rev Inst Med Trop São Paulo* 1984;**26**:38–50.

Creasey 1986 *{published data only}*
Creasey AM, Taylor P, Thomas JEP. Dosage trial of a combination of oxamniquine and praziquantel in the treatment of schistosomiasis in Zimbabwean schoolchildren. *Cent Afr J Med* 1986;**32**:165–167.

Cunha 1982 *{published data only}*
Cunha AS. The assessment of therapeutic Oxamniquine in human schistosomiasis by the method of oograma by biopsy of rectal mucosa [A avaliação terapêutica da oxamniquine na esquistossomose mansoni humana pelo método do oograma por biopsia de mucosa retal]. *Rev Inst Med Trop São Paulo* 1982;**24**: 88–94.

Cunha 1987 *{published data only}*
Cunha AS, Cançado JR, Rezende GL. Therapeutical evaluation of different dose regimens of praziquantel in schistosomiasis mansoni, based on the quantitative oogram technique. *Rev Inst Med Trop São Paulo* 1987;**29**:295–304.

Cury 1986 *{published data only}*
Cury AA, Nogueira JER. [Avaliação do índice de cura da esquistossomose mansoni (E.M.) com utilização da oxamniquine em zona endêmica]. *Rev Bras Clin Terap* 1986;**15**:63–64.

De Clerq 1997 *{published data only}*
De Clerq D, Sacko M, Vercruysse J, Bussche V, Landouré A, Diarra A, Gryseels B, Deelder A. Assessement of cure by detection of circulating antigens in serum and urine, following schistosomiasis mass treatment in two villages of Office du Niger, Mali. *Acta Tropica* 1997;**68**:339–346.

El Tayeb 1988 *{published data only}*
El Tayeb TM, Dafalla A, Kardman M, See R, Fenwick A. Praziquantel and oltipraz: the treatment of schoolchildren infected with schistosomiasis mansoni and/or schistosomiasis haematobium in Gezira, Sudan. *Ann Trop Med Parasitol* 1988;**82**:53–57.

Emanuel 1983a *{published data only}*
Emanuel A, Prata A. Praziquantel in the treatment of schistosomiasis mansoni in children [Praziquantel no tratamento da esquistossomose mansoni em crianças]. *Rev Inst Med Trop São Paulo* 1983;**25**:178–181.

Emanuel 1983b *{published data only}*
Emanuel A, Prata A. Comparison between praziquantel and oxamniquine in the treatment of schistosomiasis mansoni [Comparação entre praziquantel e oxamniquine no tratamento da esquistossomose mansoni]. *Rev Soc Bras Med Trop* 1983;**16**:90–93.

Gryseels 1989 *{published data only}*
Gryseels B, Nkulikyinka L. Two year follow up of Schistosoma mansoni infection and morbidity after treatment with different regimens of oxamniquine and praziquantel. *Trans R Soc Trop Med Hyg* 1989;**83**:219–228.

Guiniady 1994 *{published data only}*
Guiniady MAE, Touny MAE, Abdel-Bary MA, Abdel-Fatah SA, Metwally A. Clinical and pharmacokinetic study of praziquantel in egyptian schistosomiasis patients with and without liver cell failure. *Am J Trop Med Hyg* 1994;**51**:809–818.

Guisse 1997 *{published data only}*
Guisse F, Polman K, Stelma FF, Mbaye A, Talla I, Niang M, Deelder AM, Ndir O, Gryseels B. Therapeutic evaluation of two different dose regimens of praziquantel in a recent Schistosoma mansoni focus in Nothern Senegal. *Am J Trop Med Hyg* 1997;**56**:511–514.

Guyatt 1998 *{published data only}*
Guyatt HL, Chan M-S. An investigation into the interaction between drug efficacy and drug price of praziquantel in determining the cost-effectiveness of school-target treatment for Schistosoma mansoni using a population dynamic model. *Trop Med Internt Health* 1998;**3**:425–435.

Igail 1985 *{published data only}*
Igail ABE, El Tayeb M, Kardman MW, Daffalla AA, Dixon HG, Fenwick A. Dose-finding trial using Oltipraz to treat schoolchildren infected with Schistosoma mansoni in Gezira, Sudan. *J Trop Med Hyg* 1985;**88**:101–104.

Kardman 1983 *{published data only}*
Kardman MW, Amin MA, Fenwick A, Cheesmond AK, Dixon HG. A field trial using praziquantel (Biltricide) to treat Schistosoma mansoni and Schistosoma haematobium infection in Gezira, Sudan. *Ann Trop Med Parasitol* 1983;**77**:297–304.

Kardman 1985 *{published data only}*
Kardman MW, Fenwick A, El IA, El TM, Dafalla A, Dixon H. Treatment with praziquantel of schoolchildren with concurrent Schistosoma mansoni and S. haematobium infections in Gezira, Sudan. *J Trop Med Hyg* 1985;**88**:105–109.

Katz 1979 *{published data only}*
Katz N, Rocha RS, Chaves A. Clinical trials with praziquantel in human infections due to Schistosoma mansoni. *Bull World Health Organ* 1979;**57**(5):781–785.

Katz 1983 *{published data only}*
Katz N, Rocha AS, Lambertucci JB, Greco DB, Pedroso ERP, Rocha MOC, Flan S. Clinical trial with oxamniquine and praziquantel in the acute and chronic phases of schistosomiasis mansoni. *Rev Inst Med Trop São Paulo* 1983;**25**:173–177.

Katz 1991 *{published data only}*
Katz N, Rocha RS, Souza CP, Coura Filho P, Bruce JI, Coles GC, Kinoti GK. Efficacy of alternating therapy with oxamniquine and praziquantel to treat Schistosoma mansoni in children following failure of first treatment. *Am J Trop Med Hyg* 1991;**44**:509–512.

Kilpatrick 1982 *{published data only}*
Kilpatrick ME, Masry NAE, Bassily S, Farid Z. Oxamniquine versus niridazole for treatment of uncomplicated Schistosoma mansoni infection. *Am J Trop Med Hyg* 1982;**31**:1164–1167.

Lapierre 1983 *{published data only}*
Lapierre J, Keita A, Faurant C, Heyer F, Tourte-Schaefer C, Angelle T, Dupouy-Camet J. Treatment of 700 cases of bilharziasis with the new drugs oxamniquine, oltipraz, praziquantel [A propos du traitement de 700 cas de bilharziose par les medicaments récents: oxamniquine, oltipraz, praziquantel]. *Bull Soc Pathol Ex* 1983;**76**: 526–533.

Lieshout 1994 *{published data only}*
Lieshout L, Jonge N, El-Masry N, Mansour MM, Bassily S, Krijger FW, Deelder AM. Monitoring the efficacy of different doses of praziquantel by quantification of circulating antigens in serum and urine of schistosomiasis patients. *Parasitology* 1994;**108**:519–526.

McMahon 1981 *{published data only}*
McMahon JE. Praziquantel: a new schistosomicide against Schistosoma mansoni. *Arzneim Forsch* 1981;**31**(I):592–596.

Mohamed-Ali 1991 *{published data only}*
Mohamed-Ali Q, Doehring-Scwerdtfeger E, Abdel-Rahim IM, Schlake J, Kardorff R, Franke D, Kaiser C, Elsheikh M, Abdalla M, Schafer P, Ehrich HH. Ultrasonographical investigation of periportal in children with Schistosoma mansoni infection: Reversibility of morbidity seven months after treatment with praziquantel. *Am J Trop Med Hyg* 1991;**44**:444–451.

Nozais 1979 *{published data only}*
Nozais JP, Geunier M. Efficacy of UK 4271 (oxamniquine, Pfizer) in Schistosoma mansoni bilharziasis in western Africa

(parasitological and serological study of 252 children) [Étude de l'efficacité de L'UK 4271 (Oxamniquine, Pfizer) dans la bilharziose a Schistosoma mansoni en afrique de L'Ouest]. *Bull Soc Pathol Exot Filiales* 1979;**72**:153–164.

Nozais 1980 *{published data only}*
Nozais JP. A fifteen-month study on the efficacy of a single 15 mg/kg dose of oxamniquine (Vansil) in Schistosoma mansoni in an endemic area. *Rev Inst Med Trop São Paulo* 1980;**22**(suppl 4): 52–57.

Odongo-Aginya 1996 *{published data only}*
Odongo-Aginya EI, Doehring M, Lakwo TL, Etyono S, Luyinda LB, Roth J, Doehring E. Integrated control trial of schistosomiasis at Nakiwogo fishing village near Entebbe, Uganda. *East Afr Med J* 1996;**73**:495–498.

Omer 1981 *{published data only}*
Omer AHS. Praziquantel in the treatment of mixed S. haematobium and S. mansoni infections. *Arzneim Forsch* 1981;**31** (I):605–608.

Pedroso 1987 *{published data only}*
Pedroso ERP, Lambertucci JR, Greco DB, Rocha MOC, Ferreira S, Raso P. Pulmonary schistosomiasis mansoni: post-treatment pulmonary clinico-radiological alterations in patients in the chronic phase: double-blind study. *Trans R Soc Trop Med Hyg* 1987;**81**: 778–781.

Picquet 1998 *{published data only}*
Picquet M, Vercruysse J, Shaw DJ, Diop M, Ly A. Efficacy of praziquantel against Schistosoma mansoni in northern Senegal. *Trans R Soc Trop Med Hyg* 1998;**92**:90–93.

Polderman 1988 *{published data only}*
Polderman A, Gryseels B, De Calwe P. Cure rates and egg reduction in treatment of intestinal schistosomiasis with oxamniquine and praziquantel in Maniema, Zaire. *Trans R Soc Trop Med Hyg* 1988; **82**:115–116.

Prata 1982 *{published data only}*
Prata A, Castro CN, Silva AE, Paiva M, Macedo V, Junqueira Jr LF. Praziquantel in the treatment of schistosomiasis mansoni [Praziquantel no tratamento da esquistossomose mansoni]. *Rev Inst Med Trop São Paulo* 1982;**24**:95–103.

Rahim 1988 *{published data only}*
Rahim IMA, Haridi AAM, Abdel-Hameed AA. Field study of different oxamniquine dose for Schistosoma mansoni in Gezira, Sudan. *J Trop Med Hyg* 1988;**91**:131–137.

Rees 1975 *{published data only}*
Rees P, Bowry H, Roberts J, Thuku J. The treatment of schistosomiasis mansoni in Murang'a District, Kenya: a double-blind controlled trial of three hycanthone regimens and oxamniquine. *Am J Trop Med Hyg* 1975;**24**:823–826.

Rouquayrol 1976 *{published data only}*
Rouquayrol MZ, Almeida YM, Oliveira EG, Silva ZF, Pinto VAM, Alencar JE. [Hycanthone e oxamniquine no tratamento de crianças portadoras de S. mansoni]. *Rev Soc Bras Med Trop* 1976;**10**:91–101.

Rugemalila 1984 *{published data only}*
Rugemalila JB, Asila J, Chimbe A. Randomised comparative trials of the newer antischistosomal drugs at Mwanza, Tanzania. I. Praziquantel and oxamniquine for the treatment of schistosomiasis mansoni. *J Trop Med Hyg* 1984;**87**:231–235.

Saladin 1983 *{published data only}*
Saladin B, Saladin K, Holzer B, Dennis E, Hanson A, Degremont A. A pilot control trial of schistosomiasis in central Liberia by mass chemotherapy of target populations, combined with focal application of moluscicide. *Acta Trop* 1983;**40**:271–295.

Santos 1986 *{published data only}*
Santos ML, Coura JR. Morbidity of schistosomiasis in Brazil. IV - Evolution in treated patients and among controls [Morbidade da esquistossomose no Brasil. IV – Evolução em pacientes tratados e seus controles]. *Mem Inst Oswaldo Cruz* 1986;**81**:53–60.

Schwerdtfeger 1992 *{published data only}*
Doehring-Schwerdtfeger E, Abdel-Rahim IM, Kardorff R, Kaiser C, Franke D, Schlake J, Richter J, Elsheikh M, Mohamed-Ali Q, Ehrich JHH. Ultrasonographical investigation of periportal fibrosis in children with Schistosoma mansoni infection: Reversibility of morbidity twenty-three months after treatment with praziquantel. *Am J Trop Med Hyg* 1992;**46**:409–415.

Shafei 1979 *{published data only}*
Shafei A. A preliminary report on the treatment of intestinal schistosomiasis with oxamniquine. *J Trop Med Hyg* 1979;**82**:18–20.

Strickland 1982 *{published data only}*
Strickland GT, Merritt W, El-Sahly A, Abdel-Wahab F. Clinical characteristics and response to therapy in Egyptian children heavily infected with Schistosoma mansoni. *J Infect Dis* 1982;**146**:20–29.

Taylor 1988 *{published data only}*
Taylor P, Murare H, Manomano K. Efficacy of low doses of praziquantel for Schistosoma mansoni and S Haematobium. *J Trop Med Hyg* 1988;**91**:13–17.

Teesdale 1984 *{published data only}*
Teesdale CH, Chitsulo L, Pugh RNH. Oxamniquine dosage in Malawi. *East Afr Med J* 1984;**61**:40–44.

Zwingenberger 1987 *{published data only}*
Zwingenberger K, Queiroz JA, Poggensee U, Alencar JE, Valdegunas J, Esmeralda F, Feldmeier H. Efficacy of oxamniquine, praziquantel and a combination of both drugs in schistosomiasis mansoni in Brazil. *Inst Med Trop São Paulo* 1987;**29**:305–311.

References to studies awaiting assessment

Butterworth 1991 *{published data only}*
Butterworth AE, Sturrock RF, Ouma JH, Mbugua GG, Fulford AJC, Kariuki HC, Koech D. Comparison of different chemotherapy strategies against Schistosoma mansoni in Machakos District, Kenya: Effects on human infection and morbidity. *Parasitology* 1991;**103**:339–355.

Lambertucci 1982 *{published data only}*
Lambertucci JR, Grecco DB, Pedroso ER, Costa da Rocha MO, Salazar HM, Lima DP. A double-blind trial with oxamniquine in chronic schistosomiasis mansoni. *Trans R Soc Trop Med Hyg* 1982; **76**:751–755.

Additional references

Brindley 1994
Brindley PJ. Relationship between chemotherapy and immunity in schistosomiasis. *Adv Parasitol* 1994;**34**:133–161.

Clarke 2003
Clarke M, Oxman AD, editors. Optimal search strategy. Cochrane Reviewers' Handbook 4.1.5 [updated January 2003]; Appendix 5c. In: The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration. Oxford: Update Software; 2003, issue 1.

Costa 1984
Costa MFFL, Rocha RS, Katz N. Evaluation of the stability in Schistosoma mansoni egg count by Kato-Katz method in an endemic area of schistosomiasis [Avaliação da estabilidade na contagem de ovos de Schistosoma mansoni pelo método de Kato–Katz em uma zona endêmica]. *Rev Soc Bras Med Trop* 1984; **17**:7–12.

Elliott 1996
Elliott DE. Schistosomiasis. Pathophysiology, diagnosis, and treatment. Gastroenterol. *Clin North America* 1996;**25**:599–526.

Foster 1987
Foster R. A review of clinical experience with oxamniquine. *Trans R Soc Trop Med Hyg* 1987;**81**:55–59.

Gryseels 1992
Gryseels B. Morbidity due to infection with Schistosoma mansoni: an update. *Trop Geogr Med* 1992;**44**:189–200.

Pereira 1994
Pereira LMMB, Melo MCV, Lacerda C, Spinelli V, Domingues ALC, Massarolo P, Mies S, Saleh MG, McFarlane IG, Williams R. Hepatitis B virus infection in schistosomiasis mansoni. *J Med Virol* 1994;**42**:203–206.

Rabello 1992a
Rabello ALT. Parasitological diagnosis of schistosomiasis mansoni: fecal examination and rectal biopsy. *Mem Inst Oswaldo Cruz* 1992; **87**(suppl II):325–331.

Rabello 1992b
Rabello ALT, Rocha RS, Mendes de Oliveira JP, Katz N, Lambertucci JR. Stool examination and rectal biopsy in the diagnosis and evaluation of therapy of schistosomiasis mansoni. *Rev Inst Med Trop São Paulo* 1992;**34**:601–608.

Tracy 1996
Tracy JW, Webster Jr LT. Drugs used in the chemotherapy of helminthiasis. In: Hardman JG, Limbrid LE, Molinoff PB, Puddon RW, Gilman AG editor(s). *The pharmacological basis of therapeutics*. 9th Edition. New York: McGraw-Hill Co. Inc, 1996:1009–1026.

WHO 1985
World Health Organization. *The control of schistosomiasis (Technical Report Series, No. 728)*. Geneva: World Health Organization, 1985.

WHO 1993
World Health Organization. *The control of schistosomiasis (Technical Report Series, No. 830)*. Geneva: World Health Organization, 1993.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ayele 1986

Methods	Random allocation, but the method of randomisation not clearly described Blinded outcome measurement (stool examination), but blinding patients is not described
Participants	n=162 patients children below 15 years of age
Interventions	1. Oxamniquine 15 mg/kg twice daily for two days (total 60 mg/kg) 2. Oxamniquine 20 mg/kg twice daily for one day (total 40 mg/kg) 3. Oxamniquine 15 mg/kg twice daily for one day (total 30 mg/kg) 4. Placebo
Outcomes	Stool examinations according Kato to evaluate parasitic cure or improvement after 4 months of the treatment
Notes	Setting: Ethiopia

Branchini 1982

Methods	Random allocation, but method of randomisation unspecified Double blind
Participants	n=101 patients, age varied from 10 to 65 years, mean age 29.7 years
Interventions	1. Oxamniquine an average dose of 13.8 mg/kg 2. Praziquantel an average dose of 45.4 mg/kg
Outcomes	Stool examinations according Kato/Katz to evaluate parasitic cure or improvement after 4 months of the treatment Clinical and biochemical tolerance
Notes	Setting: Brazil Follow-up: 6 months Drop-out in the end of the study higher than 20% Not included in the efficacy analysis

Cunha 1986

Methods	Random allocation, but method of randomisation unspecified Double blind
Participants	n=54 patients between 15 and 55 years of age. Intestinal and hepatointestinal forms were present in 54% and 46 % of the individuals, respectively
Interventions	1. Oxamniquine an average dose of 18 mg/kg 2. Praziquantel an average dose of 65 mg/kg

Cunha 1986 (*Continued*)

Outcomes	Stool examinations according Kato/Katz and spontaneous sedimentation methods; Rectal mucosa biopsy Tolerance: clinical
Notes	Setting: Brazil Parasitological control at the end of 1, 2, 4 and 6 months, but they present analysis of the 6th month Drop-out 14.81%

de Jonge 1991

Methods	Random allocation, but the method of randomisation not clearly described Double blind method not described
Participants	n=160 children with mixed *Schistosoma haematobium* and *Schistosoma mansoni* infections
Interventions	The patients were divided in four groups: 1. Metrifonate 20 mg/kg: 38 patients 2. Oxamniquine 60 mg/kg single dose: 53 patients 3. Praziquantel 40 mg/kg single dose: 48 patients 4. Placebo: 21 patients
Outcomes	Stool examinations using Kato method Urine examination Blood samples to determine circulating anodic antigen
Notes	Setting: Sudan Follow-up: 1 and 5 months after treatment Drop-out: 14.4% after 1 month, and 18.8% after 5 months

Fernandes 1986

Methods	Random allocation, but the method of randomisation not clearly described Double blind method not described
Participants	n=120 patients with egg counts in the range 112-1296 eggs/g of *S. mansoni* in the stool
Interventions	1. Oxamniquine: 15 mg/kg single dose 2. Praziquantel: 70 mg/kg in a single dose 3. Praziquantel: 35 mg/kg twice daily
Outcomes	Stool examinations according Kato/Katz Clinical improvement
Notes	Setting: Brazil Parasitological control after 2, 4 and 6 months

Friis 1997

Methods	Random allocation by "simple randomization" Details of the allocation concealment is not described Double blind
Participants	n=313 children with *Schistosoma mansoni* and/or *Schistoma haematobium* infections
Interventions	Supplementation with zinc sulphate (30 or 50 mg according to weight of children) Placebo with identical-looking of zinc sulphate tablets
Outcomes	*Schistoma mansoni* and *Schistosoma haematobium* reinfections
Notes	Setting: Zimbabwe Parasitological examination was done 6 weeks and 3, 6, and 12 months after treatment Compliance rate was 47% among children in whom reinfections could be assessed Drop-out rate: 17%

Jaoko 1996

Methods	Random allocation but allocation concealment is not described. Double blind is not mentioned
Participants	n=320 children with *Schistosoma mansoni* infection
Interventions	1. Praziquantel: 40 mg/kg 2. Placebo
Outcomes	Prevalence of side effects
Notes	Setting: Kenya

Katz 1982

Methods	Random allocation, but method of randomisation unspecified Double blind
Participants	n=120 children with active *Schistosoma mansoni* living in two endemic areas
Interventions	Oxamniquine 20 mg/kg single dose Praziquantel 65 mg/kg single dose
Outcomes	Three consecutive daily stool examinations according Kato/Katz method Clinial and laboratorial tolerance
Notes	Setting: Brazil Follow-up: 6 months Drop-out rate higher than 20% Not included in the efficacy analysis

Rezende 1985

Methods	Random allocation, but randomisation method is not described. Double blind
Participants	n=539 adults and children, no previous anti-schistosomiasis treatment
Interventions	1. Oxamniquine an average dose of 16 mg/kg 2. Praziquantel an average dose of 55 mg/kg
Outcomes	Three consecutive daily stool examinations according to Kato/Katz method Clinical and biochemical side effects
Notes	Setting: Brazil Follow-up of six months

Silva 1986

Methods	Random allocation, but the method of randomisation not clearly described Double blind method
Participants	n= 120 patients selected by three pre-treatment egg counts according to Kato/Katz method. Only intestinal and hepatointestinal forms were included
Interventions	1. Oxamniquine 15 mg/kg single dose 2. Praziquantel 55 mg/kg single dose
Outcomes	Stool examinations according Kato/Katz method Rectal mucosa biopsy with negative stool examination in the 6th month Side effects
Notes	Setting: Brazil Follow-up: 10 months Drop-out: 21.7% Not included in the efficacy analysis

Stelma 1997

Methods	Random allocation, but allocation concealment is not descibed Double blind method is not described
Participants	n=138 patients The participants were prestratified by age, intensity of infection, and history of previous praziquantel treatment
Interventions	1. Praziquantel 40 mg/kg 2. Oxamniquine 20 mg/kg
Outcomes	Parasitological cure after 6 weeks according stool examinations by Kato method

Stelma 1997 (*Continued*)

Notes	Setting: Senegal The study were performed in a area where cure rate with praziquantel is low Follow-up: 6 weeks Drop-out: no mention

Sukwa 1993

Methods	Random allocation, but the method of randomisation not clearly described Blinded outcome measurement (physical examination), but blinding patients is not described
Participants	n=377 children All eligible children received a initial dose of 40 mg/kg of praziquantel. After initial treatment, 190 children were retreated with praziquantel at six month follow-up, irrespective of *Schistosoma mansoni* infection status; and 187 children received placebo at the same time
Interventions	1. Praziquantel 40 mg/kg 2. Placebo
Outcomes	Physical examination to evaluate clinical improvement
Notes	Setting: Zambia Follow-up: 12 months Drop-out less than 10%

Taddese 1988

Methods	Random allocation, but the method of randomisation not clearly described Double blind method not described
Participants	n=200 individuals with a geometric mean egg excretion rate of at least 50 eggs/g of faeces aged from 17-52 years
Interventions	1. Oxamniquine 15 mg/kg single dose 2. Oxamniquine 30 mg/kg twice 3. Praziquantel 40 mg/kg single dose 4. Praziquantel 40 mg/kg twice
Outcomes	Stool examinations according Kato/Katz were performed 1, 3 and 6 months after treatment Spleen and liver size
Notes	Setting: Ethiopia Drop-out: 9%

Characteristics of excluded studies *[ordered by study ID]*

Abu-Ely-Azeed 1993	The study is a randomised double-blind controlled trial evaluating the effectiveness and safety of 1% niclosamide skin lotion in the prevention of the penetration of *Schistosoma mansoni* cercariae.
Barakat 1995	This is not a randomised controlled trial. The study design is a cross-sectional.
Bella 1982	The study compares different dosages of oltipraz. There was no description of randomisation method.
Coutinho 1983	Randomised study comparing two different dosages of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Coutinho 1984	Randomised study comparing two different dosages of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Creasey 1986	This is a randomised controlled trial, but the comparison was between a combination of oxamniquine plus praziquantel with placebo.
Cunha 1982	Compares different doses of oxamniquine, however, there was no comparison between oxamniquine and praziquantel or placebo, and the authors did not describe the allocation method, and there was no description whether random method had been used.
Cunha 1987	Randomised study comparing two different dosages of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Cury 1986	The study is not a randomised controlled trial comparing oxamniquine with placebo, and the drop-out rate was 61.6%.
De Clerq 1997	This is not randomised controlled trial.
El Tayeb 1988	This is a randomised controlled trial, but the comparison was between praziquantel and oltipraz, and there was no comparison between praziquantel and oxamniquine or placebo.
Emanuel 1983a	Randomised study comparing different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Emanuel 1983b	The study is not a randomised controlled trial.
Gryseels 1989	Three villages were evaluated. Residents of two villages received different regimens of oxamniquine and residents of the other received two different regimens of praziquantel, and the study compared the prevalence and morbidity in each village. They did not compare praziquantel with oxamniquine in each village.
Guiniady 1994	Does not meet inclusion criteria. This study evaluated the pharmacokinetics of praziquantel and did not compare praziquantel with placebo or oxamniquine. There was no description of random allocation method.
Guisse 1997	Randomised study comparing two different dosages of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.

(*Continued*)

Guyatt 1998	This is a decision analysis. The study analyses the interaction between drug efficacy and drug price of different brands of praziquantel in determining the cost-effectiveness of treatment of schistosomiasis mansoni. This is not a randomised controlled trial.
Igail 1985	The study is a randomised controlled trial comparing different doses of oltipraz in the treatment of *Schistosoma mansoni* infection. Praziquantel or oxamniquine were not evaluated.
Kardman 1983	Randomised study comparing two different regimens of praziquantel, a single dose of 40 mg/kg body-weight, and a divided dose 2 x 20 mg/kg body-weight. However, there was no comparison between praziquantel and oxamniquine or placebo.
Kardman 1985	Randomised study comparing two different regimens of praziquantel, a single dose of 40 mg/kg body-weight, and a divided dose 2 x 20 mg/kg body-weight. However, there was no comparison between praziquantel and oxamniquine or placebo.
Katz 1979	The study compares different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo. Furthermore, the authors did not describe the allocation method, and there was no description whether a random method had been used.
Katz 1983	The study compares praziquantel with oxamniquine, but the authors did not describe the allocation method, and there was no description whether a random method had been used.
Katz 1991	The study compare praziquantel with oxamniquine, but the authors did not describe the allocation method, and there was no description whether a random method had been used.
Kilpatrick 1982	This is a randomised controlled trial, but the comparison was between oxamniquine and niridazole; there was no comparison between oxamniquine and praziquantel or placebo.
Lapierre 1983	This study do not appear to be a randomised controlled trial, and there was no description of how the treatment was allocated.
Lieshout 1994	The study compares praziquantel 60 mg/kg of body weight (Group 1) with praziquantel 40mg/kg of body weight (Group 2), but the authors did not describe if the patients were randomly allocated.
McMahon 1981	Randomised study comparing different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Mohamed-Ali 1991	Randomised study comparing different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Nozais 1979	Randomised study comparing two different doses of oxamniquine, however, there was no comparison between praziquantel and praziquantel or placebo.
Nozais 1980	The study evaluated oxamniquine in dose of 15-20 mg/kg, however, there was no comparison between praziquantel or placebo. It is a descriptive study. There was no description of randomisation method.
Odongo-Aginya 1996	This is not randomised controlled trial. All of the people infected with *Schistosoma mansoni* were treated with praziquantel 40 mg/kg of body weight.

(*Continued*)

Omer 1981	Randomised study comparing different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Pedroso 1987	The study compared oxamniquine with placebo in pulmonary *Schistosoma mansoni*. However, the authors did not describe the allocation method, and there was no description whether random method had been used.
Picquet 1998	This is not a randomised controlled trial.
Polderman 1988	This study did not appear to be a randomised controlled trial, and there was no description of how the treatment was allocated.
Prata 1982	Randomised study comparing three different doses of praziquantel. However, there was no comparison between praziquantel and oxamniquine or placebo.
Rahim 1988	Randomised study comparing three different doses of oxamniquine, however, there was no comparison between oxamniquine and praziquantel or placebo.
Rees 1975	This is a randomised controlled trial, but the comparison was between oxamniquine and hycanthone; there was no comparison between oxamniquine and praziquantel or placebo.
Rouquayrol 1976	This is a randomised controlled trial, but the comparison was between oxamniquine and hycanthone; there was no comparison between oxamniquine and praziquantel or placebo.
Rugemalila 1984	Drop-out rate higher than 20%, and the study did not evaluated cure rate.
Saladin 1983	This study is not a randomised controlled trial.
Santos 1986	Randomised controlled trial comparing oxamniquine with placebo, but the drop-out rate was higher than 20%.
Schwerdtfeger 1992	Randomised study comparing two different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo.
Shafei 1979	This study is not randomised controlled trial.
Strickland 1982	The authors wrote that two subjects were randomly chosen in each group of six to receive placebo or oxamniquine, but they did not clearly state the allocation method, nor was it possible to determine whether the study was randomised.
Taylor 1988	Randomised study comparing four different doses of praziquantel, however, there was no comparison between praziquantel and oxamniquine or placebo. One group did not receive praziquantel, but the author did not say if this group received placebo or not.
Teesdale 1984	Drop-out rate higher than 20 per cent.

(*Continued*)

Zwingenberger 1987	This study is a randomised controlled trial, but the comparison was between a low-dose combination of oxamniquine plus praziquantel against oxamniquine or praziquantel alone, and the drop-out rate was more than 20%.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Butterworth 1991

Methods	-
Participants	-
Interventions	-
Outcomes	-
Notes	-

Lambertucci 1982

Methods	-
Participants	-
Interventions	-
Outcomes	-
Notes	-

DATA AND ANALYSES

Comparison 1. Oxamniquine versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure	2		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
1.1 Oxamniquine 60mg/kg	2	154	Peto Odds Ratio (Peto, Fixed, 95% CI)	17.68 [9.02, 34.64]

Comparison 2. Praziquantel versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
1.1 Praziquantel 40mg/kg versus placebo	1	69	Peto Odds Ratio (Peto, Fixed, 95% CI)	13.10 [4.71, 36.44]
2 Clinical improvement after 6 months	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
2.1 Diarrhoea	1	101	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.15 [0.52, 2.52]
2.2 Bloody diarrhoea	1	50	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.80 [0.26, 2.52]
2.3 Abdominal pain	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	Not estimable
2.4 Hepatomegaly	1	168	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.12 [0.61, 2.04]
2.5 Splenomegaly	1	59	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.85 [0.30, 2.43]
3 Clinical improvement after 12 months	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
3.1 Diarrhoea	1	101	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.70 [0.25, 1.99]
3.2 Bloody diarrhoea	1	50	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.92 [0.06, 15.20]
3.3 Hepatomegaly	1	168	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.07 [0.57, 2.04]
3.4 Splenomegaly	1	59	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.27 [0.80, 6.41]
4 Clinical side effects	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
4.1 Headache	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	4.43 [2.77, 7.10]
4.2 Dizziness	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.03 [0.94, 4.39]
4.3 Nausea	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.11 [1.55, 6.26]
4.4 Bloody diarrhoea	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.91 [0.05, 329.60]
4.5 Abdominal pain	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.68 [1.68, 4.26]
4.6 Fever	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.38 [1.00, 5.66]
4.7 Urticaria	1	436	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.91 [0.05, 329.60]

Comparison 3. Oxamniquine versus Praziquantel

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parasitological cure after 1 month	3		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
1.1 Oxamniquine 15mg/kg versus Praziquantel 40mg/kg	1	100	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.23 [0.08, 0.66]
1.2 Oxamniquine 15mg/kg vs Praziquantel 2 x 20mg/kg	1	100	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.34 [0.12, 0.94]
1.3 Oxamniquine 20mg/kg vs Praziquantel 40mg/kg	1	138	Peto Odds Ratio (Peto, Fixed, 95% CI)	4.22 [2.16, 8.23]
1.4 Oxamniquine 30mg/kg vs Praziquantel 40mg/kg	1	100	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.80 [0.38, 20.52]
1.5 Oxamniquine 30mg/kg vs Praziquantel 2 x 20mg/kg	1	100	Peto Odds Ratio (Peto, Fixed, 95% CI)	4.07 [0.79, 21.04]
1.6 Oxamniquine 60mg/kg vs Praziquantel 40mg/kg	1	101	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.54 [0.24, 1.17]
2 Parasitological cure, follow-up >2 months	3		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
2.1 Oxamniquine 15mg/kg versus Praziquantel 40mg/kg	1	200	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.58 [0.31, 1.07]
2.2 Oxamniquine 15mg/kg vs Praziquantel 2 x 20mg/kg	1	200	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.40 [0.21, 0.76]
2.3 Oxamniquine 15-19 mg/kg vs Praziquantel 50-70mg/kg	2	134	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.61 [0.26, 1.46]
2.4 Oxamniquine 15-19mg/kg vs Praziquantel 50-70mg/kg (two doses)	1	80	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.54 [0.15, 1.90]
3 Parasitological cure, follow-up 3 months or more	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
3.1 Oxamniquine 30mg/kg vs Praziquantel 40mg/kg	1	200	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.02 [0.97, 4.23]
3.2 Oxamniquine 30mg/kg vs Praziquantel 2 x 20mg/kg	1	200	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.39 [0.63, 3.09]
4 Clinical side effects	7		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
4.1 Any side effect	4	829	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.92 [0.67, 1.26]
4.2 Neurological: Seizures	2	739	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.32 [0.46, 117.06]
4.3 Neurological: Headache	7	1254	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.26 [0.88, 1.82]
4.4 Neurological: Dizziness	7	1254	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.23 [0.97, 1.56]
4.5 Neurological: Sleepiness	5	953	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.96 [0.67, 1.40]
4.6 Gastro-intestinal: Nausea	5	953	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.94 [0.63, 1.41]
4.7 Gastro-intestinal: Vomiting	5	1080	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.08 [0.67, 1.76]
4.8 Gastro-intestinal: Diarrhoea	5	1080	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.48 [0.32, 0.71]
4.9 Gastro-intestinal: Abdominal pain	6	1134	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.34 [0.26, 0.44]
4.10 Other systemic: Myalgia	2	659	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.47 [1.68, 33.11]

4.11 Other systemic: Asthenia	3	779	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.47, 1.67]
4.12 Other systemic: Fever	1	539	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.13 [0.02, 0.94]
4.13 Other systemic: Skin rash	3	713	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.36 [0.05, 2.59]
5 Biochemical side effects	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Hepatotoxicity: ALT	1	120	Mean Difference (IV, Fixed, 95% CI)	-3.83 [-8.21, 0.55]
5.2 Hepatotoxicity: AST	1	120	Mean Difference (IV, Fixed, 95% CI)	-0.48 [-2.29, 1.33]
5.3 Hepatotoxicity: Gamma-glutamyl transpeptidase	1	120	Mean Difference (IV, Fixed, 95% CI)	-3.02 [-13.22, 7.18]

Comparison 4. Zinc supplementation versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Reinfection rate	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 Oxamniquine versus placebo, Outcome 1 Parasitological cure.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 1 Oxamniquine versus placebo

Outcome: 1 Parasitological cure

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Oxamniquine 60mg/kg					
Ayele 1986	35/40	1/40		59.1 %	29.71 [12.38, 71.30]
de Jonge 1991	26/53	0/21		40.9 %	8.36 [2.92, 23.92]

Analysis 2.1. Comparison 2 Praziquantel versus placebo, Outcome 1 Parasitological cure.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 2 Praziquantel versus placebo

Outcome: 1 Parasitological cure

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Praziquantel 40mg/kg versus placebo					
de Jonge 1991	31/48	0/21		100.0 %	13.10 [4.71, 36.44]

Analysis 2.2. Comparison 2 Praziquantel versus placebo, Outcome 2 Clinical improvement after 6 months.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 2 Praziquantel versus placebo

Outcome: 2 Clinical improvement after 6 months

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Diarrhoea					
Sukwa 1993	23/52	20/49		100.0 %	1.15 [0.52, 2.52]
Subtotal (95% CI)	**52**	**49**		**100.0 %**	**1.15 [0.52, 2.52]**
Total events: 23 (Treatment), 20 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.35 (P = 0.73)					
2 Bloody diarrhoea					
Sukwa 1993	16/26	16/24		100.0 %	0.80 [0.26, 2.52]
Subtotal (95% CI)	**26**	**24**		**100.0 %**	**0.80 [0.26, 2.52]**
Total events: 16 (Treatment), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.37 (P = 0.71)					
3 Abdominal pain					
Subtotal (95% CI)	**0**	**0**		**0.0 %**	**0.0 [0.0, 0.0]**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: not applicable					

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Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Test for overall effect: not applicable					
4 Hepatomegaly					
Sukwa 1993	43/89	36/79		100.0 %	1.12 [0.61, 2.04]
Subtotal (95% CI)	**89**	**79**		**100.0 %**	**1.12 [0.61, 2.04]**
Total events: 43 (Treatment), 36 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.35 (P = 0.72)					
5 Splenomegaly					
Sukwa 1993	17/28	20/31		100.0 %	0.85 [0.30, 2.43]
Subtotal (95% CI)	**28**	**31**		**100.0 %**	**0.85 [0.30, 2.43]**
Total events: 17 (Treatment), 20 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.30 (P = 0.76)					
Test for subgroup differences: Chi^2 = 0.45, df = 3 (P = 0.93), I^2 =0.0%					

Analysis 2.3. Comparison 2 Praziquantel versus placebo, Outcome 3 Clinical improvement after 12 months.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 2 Praziquantel versus placebo

Outcome: 3 Clinical improvement after 12 months

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Diarrhoea					
Sukwa 1993	42/52	42/49		100.0 %	0.70 [0.25, 1.99]
Subtotal (95% CI)	**52**	**49**		**100.0 %**	**0.70 [0.25, 1.99]**
Total events: 42 (Treatment), 42 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.66 (P = 0.51)					
2 Bloody diarrhoea					
Sukwa 1993	1/26	1/24		100.0 %	0.92 [0.06, 15.20]
Subtotal (95% CI)	**26**	**24**		**100.0 %**	**0.92 [0.06, 15.20]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: not applicable					

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Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Test for overall effect: Z = 0.06 (P = 0.95)					
3 Hepatomegaly					
Sukwa 1993	60/89	52/79		100.0 %	1.07 [0.57, 2.04]
Subtotal (95% CI)	**89**	**79**		**100.0 %**	**1.07 [0.57, 2.04]**
Total events: 60 (Treatment), 52 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.22 (P = 0.83)					
4 Splenomegaly					
Sukwa 1993	20/28	16/31		100.0 %	2.27 [0.80, 6.41]
Subtotal (95% CI)	**28**	**31**		**100.0 %**	**2.27 [0.80, 6.41]**
Total events: 20 (Treatment), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.55 (P = 0.12)					
Test for subgroup differences: Chi^2 = 2.56, df = 3 (P = 0.46), I^2 =0.0%					

Analysis 2.4. Comparison 2 Praziquantel versus placebo, Outcome 4 Clinical side effects.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 2 Praziquantel versus placebo

Outcome: 4 Clinical side effects

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Headache					
Jaoko 1996	116/320	7/116		100.0 %	4.43 [2.77, 7.10]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**4.43 [2.77, 7.10]**
Total events: 116 (Treatment), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 6.19 (P < 0.00001)					
2 Dizziness					
Jaoko 1996	31/320	5/116		100.0 %	2.03 [0.94, 4.39]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**2.03 [0.94, 4.39]**
Total events: 31 (Treatment), 5 (Control)					
Heterogeneity: not applicable					

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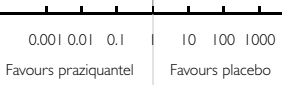
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Test for overall effect: Z = 1.80 (P = 0.072)					
3 Nausea					
Jaoko 1996	42/320	3/116		100.0 %	3.11 [1.55, 6.26]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**3.11 [1.55, 6.26]**
Total events: 42 (Treatment), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.19 (P = 0.0014)					
4 Bloody diarrhoea					
Jaoko 1996	1/320	0/116		100.0 %	3.91 [0.05, 329.60]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**3.91 [0.05, 329.60]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.60 (P = 0.55)					
5 Abdominal pain					
Jaoko 1996	113/320	17/116		100.0 %	2.68 [1.68, 4.26]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**2.68 [1.68, 4.26]**
Total events: 113 (Treatment), 17 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.16 (P = 0.000032)					
6 Fever					
Jaoko 1996	25/320	3/116		100.0 %	2.38 [1.00, 5.66]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**2.38 [1.00, 5.66]**
Total events: 25 (Treatment), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.96 (P = 0.049)					
7 Urticaria					
Jaoko 1996	1/320	0/116		100.0 %	3.91 [0.05, 329.60]
Subtotal (95% CI)	**320**	**116**		**100.0 %**	**3.91 [0.05, 329.60]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.60 (P = 0.55)					
Test for subgroup differences: Chi^2 = 4.12, df = 6 (P = 0.66), I^2 =0.0%					

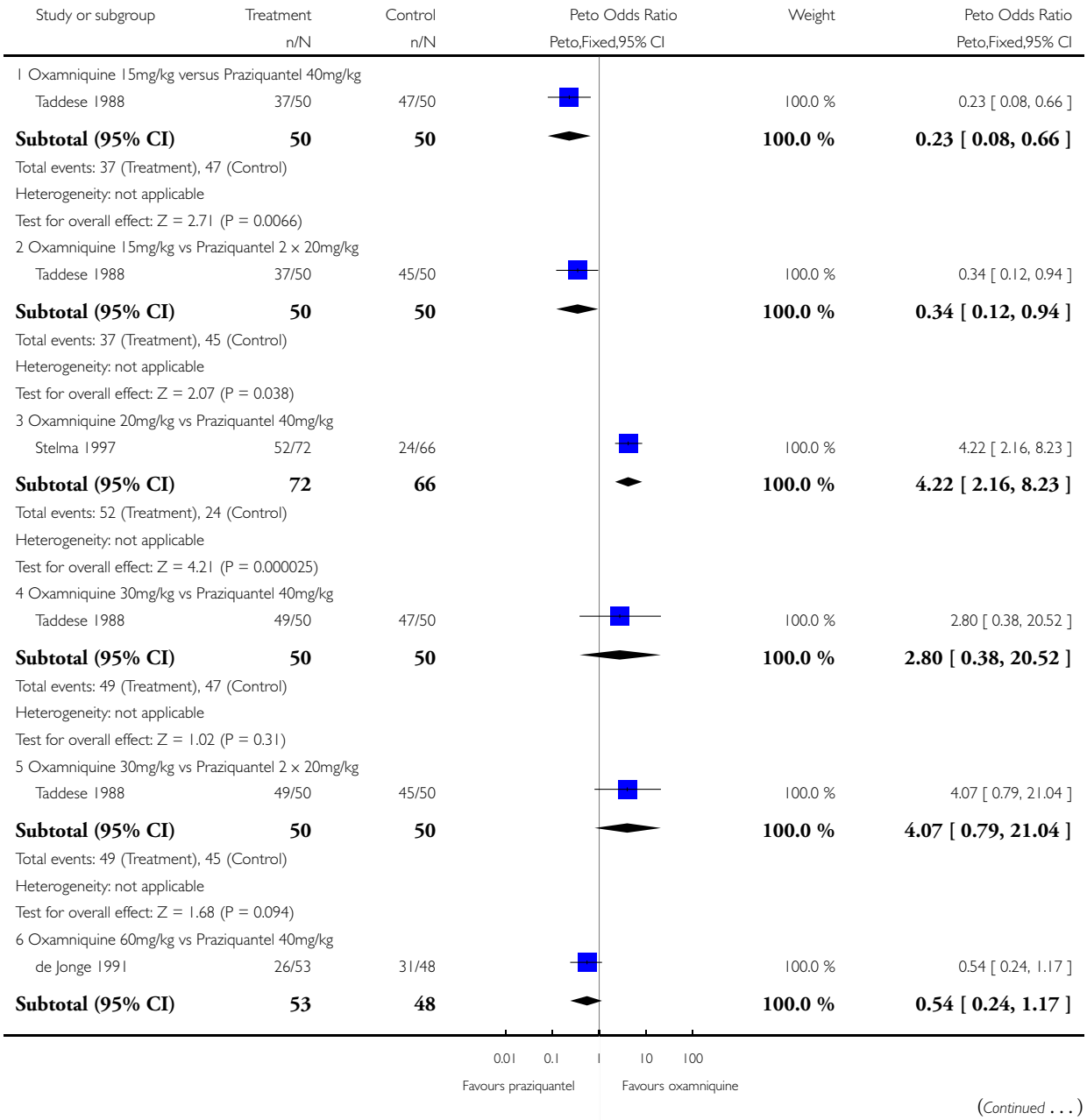


Analysis 3.1. Comparison 3 Oxamniquine versus Praziquantel, Outcome 1 Parasitological cure after 1 month.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 3 Oxamniquine versus Praziquantel

Outcome: 1 Parasitological cure after 1 month



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Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Total events: 26 (Treatment), 31 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.56 (P = 0.12)					
Test for subgroup differences: Chi² = 35.47, df = 5 (P = 0.00), I² =86%					

Analysis 3.2. Comparison 3 Oxamniquine versus Praziquantel, Outcome 2 Parasitological cure, follow-up >2 months.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 3 Oxamniquine versus Praziquantel

Outcome: 2 Parasitological cure, follow-up >2 months

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Oxamniquine 15mg/kg versus Praziquantel 40mg/kg					
Taddese 1988	67/100	78/100		100.0 %	0.58 [0.31, 1.07]
Subtotal (95% CI)	**100**	**100**		**100.0 %**	**0.58 [0.31, 1.07]**
Total events: 67 (Treatment), 78 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.74 (P = 0.082)					
2 Oxamniquine 15mg/kg vs Praziquantel 2 x 20mg/kg					
Taddese 1988	67/100	84/100		100.0 %	0.40 [0.21, 0.76]
Subtotal (95% CI)	**100**	**100**		**100.0 %**	**0.40 [0.21, 0.76]**
Total events: 67 (Treatment), 84 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.79 (P = 0.0053)					
3 Oxamniquine 15-19 mg/kg vs Praziquantel 50-70mg/kg					
Cunha 1986	19/27	22/27		49.3 %	0.55 [0.16, 1.90]
Fernandes 1986	33/40	35/40		50.7 %	0.68 [0.20, 2.30]
Subtotal (95% CI)	**67**	**67**		**100.0 %**	**0.61 [0.26, 1.46]**
Total events: 52 (Treatment), 57 (Control)					
Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² =0.0%					
Test for overall effect: Z = 1.11 (P = 0.27)					
4 Oxamniquine 15-19mg/kg vs Praziquantel 50-70mg/kg (two doses)					

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Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Fernandes 1986	33/40	36/40		100.0 %	0.54 [0.15, 1.90]
Subtotal (95% CI)	**40**	**40**		**100.0 %**	**0.54 [0.15, 1.90]**
Total events: 33 (Treatment), 36 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.97 (P = 0.33)					
Test for subgroup differences: Chi^2 = 0.87, df = 3 (P = 0.83), I^2 =0.0%					

Analysis 3.3. Comparison 3 Oxamniquine versus Praziquantel, Outcome 3 Parasitological cure, follow-up 3 months or more.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 3 Oxamniquine versus Praziquantel

Outcome: 3 Parasitological cure, follow-up 3 months or more

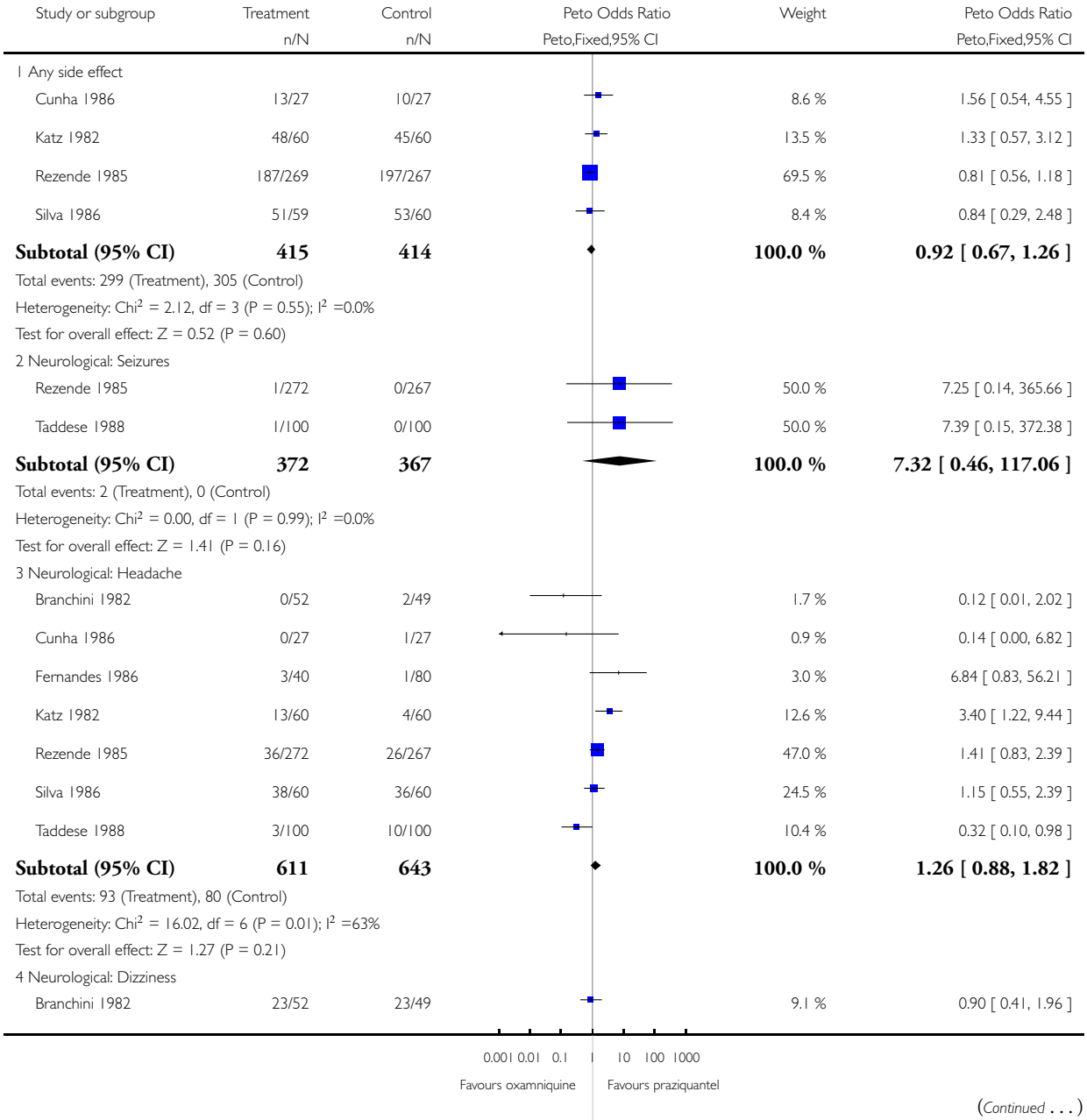
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 Oxamniquine 30mg/kg vs Praziquantel 40mg/kg					
Taddese 1988	88/100	78/100		100.0 %	2.02 [0.97, 4.23]
Subtotal (95% CI)	**100**	**100**		**100.0 %**	**2.02 [0.97, 4.23]**
Total events: 88 (Treatment), 78 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.88 (P = 0.060)					
2 Oxamniquine 30mg/kg vs Praziquantel 2 x 20mg/kg					
Taddese 1988	88/100	84/100		100.0 %	1.39 [0.63, 3.09]
Subtotal (95% CI)	**100**	**100**		**100.0 %**	**1.39 [0.63, 3.09]**
Total events: 88 (Treatment), 84 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.81 (P = 0.42)					
Test for subgroup differences: Chi^2 = 0.46, df = 1 (P = 0.50), I^2 =0.0%					

Analysis 3.4. Comparison 3 Oxamniquine versus Praziquantel, Outcome 4 Clinical side effects.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 3 Oxamniquine versus Praziquantel

Outcome: 4 Clinical side effects



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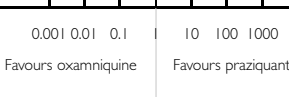
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Cunha 1986	8/27	5/27		3.6 %	1.82 [0.53, 6.25]
Fernandes 1986	6/40	15/80		5.6 %	0.77 [0.29, 2.09]
Katz 1982	18/60	9/60		7.6 %	2.35 [1.00, 5.51]
Rezende 1985	116/272	90/267		46.1 %	1.46 [1.03, 2.06]
Silva 1986	38/60	36/60		10.3 %	1.15 [0.55, 2.39]
Taddese 1988	38/100	44/100		17.6 %	0.78 [0.45, 1.37]
Subtotal (95% CI)	**611**	**643**		**100.0 %**	**1.23 [0.97, 1.56]**
Total events: 247 (Treatment), 222 (Control)					
Heterogeneity: Chi^2 = 7.52, df = 6 (P = 0.28); I^2 =20%					
Test for overall effect: Z = 1.73 (P = 0.084)					
5 Neurological: Sleepiness					
Cunha 1986	6/27	2/27		6.2 %	3.17 [0.72, 14.01]
Fernandes 1986	0/40	2/80		1.6 %	0.22 [0.01, 4.22]
Katz 1982	7/60	5/60		9.8 %	1.44 [0.44, 4.74]
Rezende 1985	38/272	39/267		59.3 %	0.95 [0.59, 1.54]
Silva 1986	16/60	21/60		23.1 %	0.68 [0.31, 1.47]
Subtotal (95% CI)	**459**	**494**		**100.0 %**	**0.96 [0.67, 1.40]**
Total events: 67 (Treatment), 69 (Control)					
Heterogeneity: Chi^2 = 4.66, df = 4 (P = 0.32); I^2 =14%					
Test for overall effect: Z = 0.19 (P = 0.85)					
6 Gastro-intestinal: Nausea					
Cunha 1986	2/27	4/27		5.8 %	0.48 [0.09, 2.57]
Fernandes 1986	7/40	4/80		9.6 %	4.43 [1.20, 16.42]
Katz 1982	3/60	3/60		6.1 %	1.00 [0.19, 5.13]
Rezende 1985	28/272	32/267		57.1 %	0.84 [0.49, 1.44]
Silva 1986	11/60	14/60		21.3 %	0.74 [0.31, 1.78]
Subtotal (95% CI)	**459**	**494**		**100.0 %**	**0.94 [0.63, 1.41]**
Total events: 51 (Treatment), 57 (Control)					
Heterogeneity: Chi^2 = 6.45, df = 4 (P = 0.17); I^2 =38%					
Test for overall effect: Z = 0.30 (P = 0.77)					
7 Gastro-intestinal: Vomiting					
Branchini 1982	1/52	2/49		4.5 %	0.48 [0.05, 4.69]
Katz 1982	7/60	4/60		15.3 %	1.81 [0.53, 6.24]
Rezende 1985	19/272	15/267		48.6 %	1.26 [0.63, 2.52]
Silva 1986	9/60	7/60		21.3 %	1.33 [0.47, 3.80]
Taddese 1988	1/100	6/100		10.3 %	0.23 [0.05, 1.03]



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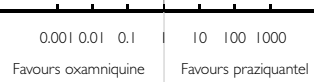
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Subtotal (95% CI)	**544**	**536**		**100.0 %**	**1.08 [0.67, 1.76]**
Total events: 37 (Treatment), 34 (Control)					
Heterogeneity: Chi² = 5.59, df = 4 (P = 0.23); I² =28%					
Test for overall effect: Z = 0.32 (P = 0.75)					
8 Gastro-intestinal: Diarrhoea					
Branchini 1982	2/52	6/49		7.4 %	0.32 [0.08, 1.35]
Katz 1982	4/60	8/60		10.9 %	0.48 [0.15, 1.57]
Rezende 1985	14/272	32/267		42.1 %	0.42 [0.23, 0.76]
Silva 1986	4/60	12/60		14.0 %	0.32 [0.11, 0.91]
Taddese 1988	14/100	16/100		25.6 %	0.86 [0.39, 1.86]
Subtotal (95% CI)	**544**	**536**		**100.0 %**	**0.48 [0.32, 0.71]**
Total events: 38 (Treatment), 74 (Control)					
Heterogeneity: Chi² = 3.24, df = 4 (P = 0.52); I² =0.0%					
Test for overall effect: Z = 3.66 (P = 0.00025)					
9 Gastro-intestinal: Abdominal pain					
Branchini 1982	6/52	12/49		6.3 %	0.42 [0.15, 1.15]
Cunha 1986	2/27	0/27		0.8 %	7.68 [0.47, 126.06]
Katz 1982	12/60	30/60		11.7 %	0.27 [0.13, 0.57]
Rezende 1985	46/272	122/267		49.1 %	0.26 [0.18, 0.38]
Silva 1986	10/60	29/60		11.2 %	0.24 [0.11, 0.51]
Taddese 1988	39/100	47/100		20.9 %	0.72 [0.41, 1.26]
Subtotal (95% CI)	**571**	**563**		**100.0 %**	**0.34 [0.26, 0.44]**
Total events: 115 (Treatment), 240 (Control)					
Heterogeneity: Chi² = 15.07, df = 5 (P = 0.01); I² =67%					
Test for overall effect: Z = 8.27 (P < 0.00001)					
10 Other systemic: Myalgia					
Rezende 1985	4/272	0/267		57.4 %	7.34 [1.03, 52.37]
Silva 1986	3/60	0/60		42.6 %	7.65 [0.78, 74.93]
Subtotal (95% CI)	**332**	**327**		**100.0 %**	**7.47 [1.68, 33.11]**
Total events: 7 (Treatment), 0 (Control)					
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² =0.0%					
Test for overall effect: Z = 2.65 (P = 0.0082)					
11 Other systemic: Asthenia					
Fernandes 1986	3/40	0/80		6.8 %	21.14 [1.88, 237.98]
Katz 1982	1/60	2/60		7.7 %	0.51 [0.05, 4.97]
Rezende 1985	15/272	20/267		85.5 %	0.72 [0.36, 1.43]
Subtotal (95% CI)	**372**	**407**		**100.0 %**	**0.89 [0.47, 1.67]**



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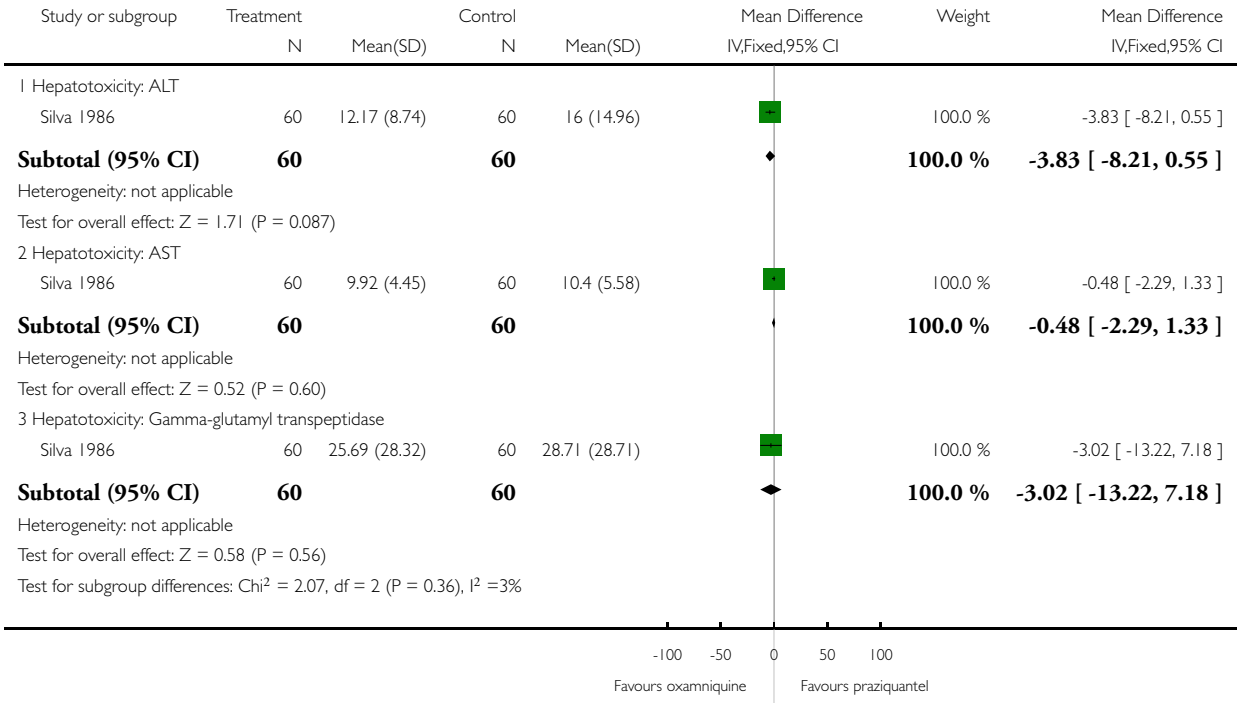
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Total events: 19 (Treatment), 22 (Control)					
Heterogeneity: Chi² = 7.17, df = 2 (P = 0.03); I² =72%					
Test for overall effect: Z = 0.38 (P = 0.71)					
12 Other systemic: Fever					
Rezende 1985	0/272	4/267		100.0 %	0.13 [0.02, 0.94]
Subtotal (95% CI)	**272**	**267**		**100.0 %**	**0.13 [0.02, 0.94]**
Total events: 0 (Treatment), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.02 (P = 0.043)					
13 Other systemic: Skin rash					
Cunha 1986	1/27	0/27		25.0 %	7.39 [0.15, 372.38]
Katz 1982	0/60	1/60		25.0 %	0.14 [0.00, 6.82]
Rezende 1985	0/272	2/267		50.0 %	0.13 [0.01, 2.12]
Subtotal (95% CI)	**359**	**354**		**100.0 %**	**0.36 [0.05, 2.59]**
Total events: 1 (Treatment), 3 (Control)					
Heterogeneity: Chi² = 3.02, df = 2 (P = 0.22); I² =34%					
Test for overall effect: Z = 1.01 (P = 0.31)					
Test for subgroup differences: Chi² = 87.32, df = 12 (P = 0.00), I² =86%					

Analysis 3.5. Comparison 3 Oxamniquine versus Praziquantel, Outcome 5 Biochemical side effects.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 3 Oxamniquine versus Praziquantel

Outcome: 5 Biochemical side effects

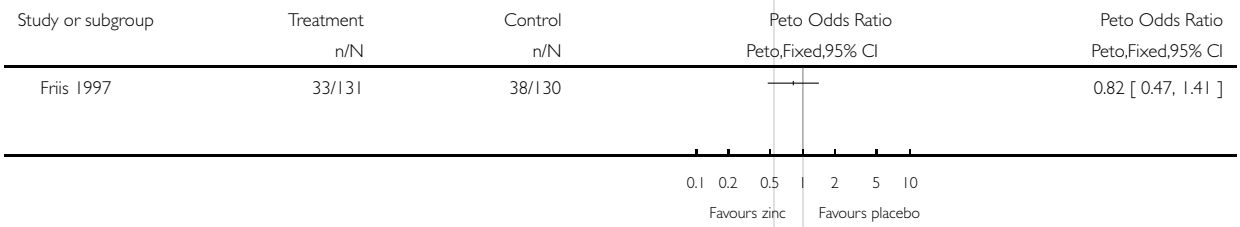


Analysis 4.1. Comparison 4 Zinc supplementation versus placebo, Outcome 1 Reinfection rate.

Review: Interventions for treating schistosomiasis mansoni

Comparison: 4 Zinc supplementation versus placebo

Outcome: 1 Reinfection rate



WHAT'S NEW

Last assessed as up-to-date: 6 September 2005.

24 September 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 4, 1997

Review first published: Issue 1, 1998

5 September 2005	New search has been performed	New studies sought but none found.
11 May 2000	Amended	Edited text, including abstract, and added a 'Plain language summary' (previously called 'Synopsis').
26 May 1999	Amended	Modified title, added two trials (Jaoko 1996; Friis 1997), and excluded some studies.

DECLARATIONS OF INTEREST

We certify that we have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of the review (e.g. employment, consultancy, stock ownership, honoraria, expert testimony).

SOURCES OF SUPPORT

Internal sources

- Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior, Brazil.
- Federal University of Rio Grande do Norte, Brazil.

External sources

- Department for International Development, UK.
- European Commission (Directorate General XII), Belgium.
- International Clinical Epidemiology Network, USA.
- Liverpool School of Tropical Medicine, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Oxamniquine [*therapeutic use]; Praziquantel [*therapeutic use]; Schistosomiasis mansoni [*drug therapy]; Schistosomicides [*therapeutic use]

MeSH check words

Humans