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[Intervention Review]

Antibiotic treatment for travellers' diarrhoea

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ABSTRACT

Background

Using a pilot system we have categorised this review as: Current question - update pending (See "Published notes" section for an explanation).

Traveller's diarrhoea is a syndrome frequently encountered in persons crossing an international boundary. Diarrhoea can lead to significant discomfort and interference with travel plans. Bacterial pathogens are a frequent cause of this syndrome. Several antibiotics have been tested for efficacy in reducing the duration and severity of the illness.

Objectives

The aims of this review were to assess the effects of antibiotics on traveller's diarrhoea in relation to duration of illness, severity of illness, and adverse effects of medications.

Search methods

The Cochrane Collaboration Trials Register, MEDLINE, and EMBASE were searched. Additional trials were identified by hand searching. Content experts were contacted.

Selection criteria

All trials in any language in which travellers older than 5 years were randomly allocated to treatment for acute non-bloody diarrhoea with antibiotics and where the causative organism is not known at allocation.

Data collection and analysis

Two reviewers assessed trial quality and extracted data.

Main results

Twenty published studies met inclusion and quality criteria for inclusion. Twelve studies were placebo-controlled.

A meta-analysis for the primary outcome was not feasible. All of the 10 trials reported a significant reduction in duration of diarrhoea in participants treated with antibiotics compared with placebo.

Data from two trials demonstrated a small reduction for antibiotic treated patients in the number of unformed stools passed per each 24 hour period from randomisation up to 72 hours.

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Data from six trials demonstrated a greater number of participants being cured of diarrhoea by 72 hours (odds ratio 5.90, 95% confidence interval 4.06 to 8.57).

Data regarding side effects were available from five trials. There was wide variation in the prevalence of side effects reported in different trials. Persons taking antibiotics experienced more side effects than those taking placebo (odds ratio 2.37, 95% confidence interval 1.50 to 3.75).

Authors' conclusions

Antibiotic treatment is associated with shorter duration of diarrhoea but higher incidence of side-effects. Trials generally do not report duration of post-treatment diarrhoea using time-to-event analyses, and should do.

8 May 2019

No update planned

Other

Many trials of antibiotics in travellers' diarrhoea have been conducted and demonstrate shorter illness following antibiotic treatment. Travellers' diarrhoea is a self-limiting illness. Therefore an update is not a current priority for the CIDG.

PLAIN LANGUAGE SUMMARY

Antibiotic treatment reduces duration and severity of travellers' diarrhoea.

Using a pilot system we have categorised this review as: Current question - update pending. (See "Published notes" section for an explanation).

Diarrhoea is a common problem for travellers, particularly travellers going from developed to less developed nations. The illness is frequently caused by a bacterial infection. Although the illness is unlikely to result in death, diarrhoea can disrupt travel plans and lead to severe or incapacitating symptoms. The review showed that antibiotic treatment shortens the duration and severity of diarrhoea. Persons taking antibiotics reported more side effects, but most side effects were minor, or resolved on stopping the antibiotic.

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BACKGROUND

Travellers' diarrhoea is an acute syndrome occurring in people who have crossed a national boundary and who experience watery or unformed bowel motions which are passed more frequently than usual, sometimes accompanied by nausea, vomiting, abdominal pain or cramping. Recovery within five days is normal, although in about 10% of cases symptoms will persist beyond seven days (DuPont 1993, Farthing 1992). The syndrome is most commonly caused by intestinal bacteria known as enterotoxigenic Escherichia coli (ETEC), although other bacteria including Campylobacter, Shigella, and Salmonella species have all been frequently incriminated (Black 1986, Gorbach 1975, Taylor 1991). Travellers' diarrhoea lasting for 14 days or more is sometimes termed "persistent diarrhoea" and is considered separately as the causes and management differ from the usual travellers' illness. Some 10% of travellers with diarrhoea develop dysentery, defined as diarrhoea mixed with visible blood, indicating a potentially serious condition which differs from travellers' diarrhoea and warrants separate investigation and management. Mortality is rare in simple travellers' diarrhoea although the condition is potentially serious in the very young and the elderly, who may not tolerate fluid loss, as well as in children and younger adults. Those with an impaired immune response, reduced gastric acidity, and some forms of heart disease may also be considered at risk of more severe effects from travellers' diarrhoea (BSSI 1996).

The magnitude of the problem is considerable. With the advent of modern air travel, between 1950 and 1990 there was an increase from approximately 25 million to 425 million persons travelling worldwide (Hundt 1996). Travellers' diarrhoea has been commonly reported to occur in 30-60% of travellers to developing countries, in contrast to reported incidence rates of 5% or less in travellers to Europe and North America (Cartwright 1997).

The incidence of the syndrome appears to vary according to the itinerary, to the season in which travel occurs, and to factors surrounding eating behaviour and style of travel, with the younger adult more at risk than the middle-aged (Steffen 1983, Mattila 1993). Nevertheless, diarrhoea still occurs in the well-informed and prepared traveller (McIntosh 1997), including those who stay exclusively in "five star" accommodation.

As the international traveller is often on a restricted schedule because of pre-planned tour itineraries or business demands, even a day lost to illness can be unexpectedly disruptive, creating a demand for prompt relief. Medical treatment may not always be easily accessible to the traveller because of factors such as an unfamiliar health system, language barriers, remoteness, and time constraints, so it is an attractive option for the traveller to carry self-treatment for some common conditions.

The mainstay of treatment for diarrhoea of all degrees of severity is adequate replacement of fluids and electrolytes. Moreover, the use of antibiotics to treat diarrhoea has been tested in a number of clinical trials (Katelaris 1995, NIH-CDCS 1985).

This review was designed to examine the effectiveness of antibiotic treatment for acute diarrhoea. We also considered adverse effects reported in trials, as the aim of treatment is termination of diarrhoea and relief of symptoms, rather than reduction in a more serious clinical endpoint. We did not examine several other important issues, such as cost of treatment, which may be better evaluated in other ways.

Several related reviews are planned, including assessment of the effectiveness of non-antibiotic treatments, and of combination treatments for diarrhoea.

OBJECTIVES

To assess the effects of antibiotics on diarrhoea in relation to: (a) duration of illness; (b) severity of illness; and (c) adverse effects.

METHODS

Criteria for considering studies for this review

Types of studies

All trials in any language in which travellers are randomly allocated to a treatment for non-bloody diarrhoea lasting not more than 14 days and where the causative organism is not known at allocation; to include placebo controlled trials and comparison trials.

Types of participants

Adults and children 5 years or older who develop acute non-bloody diarrhoea lasting not more than 14 days (i.e. to exclude dysentery and persistent diarrhoea at randomisation).

Travellers are defined as people who are travelling outside their usual country of residence, and are resident in the country of study for less than six months.

Types of interventions

1. Any antibiotic therapy versus placebo.
2. Any antibiotic versus another antibiotic.

Treatments were self-administered or issued by a physician according to a study protocol with no prior knowledge of bacterial culture results.

Other treatments were acceptable within intervention and control groups, so long as both groups remain comparable in this respect; examples include fluid replacement, dietary advice, and malaria prophylaxis.

Types of outcome measures

Duration

Duration of diarrhoea, as assessed by time to last unformed stool.

Severity

Number of loose stools passed per 24 hour period: 0-24 hours; 25-48 hours; 49-72 hours; > 72 hours.

Tolerability

Number of subjects who report any side effect of treatment.

Search methods for identification of studies

We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press or in progress).

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The topic search terms used for searching trial registers and databases were: "travel$" for traveler, traveller, "diarr$" for "diarrhea", "diarrhoea", "diarrea", "reisediarrhoe", and "turista".

The Cochrane Infectious Diseases Group (CIDG) Specialized Register was searched for relevant trials up to September 2003. Details of the CIDG methods and the journals hand-searched are published in The Cochrane Library in the section on Collaborative Review Groups.

The Cochrane Central Register of Controlled Trials (CENTRAL) published in *The Cochrane Library* (Issue 3, 2004) was searched.

The following databases were searched using the topic search terms using the topic search terms in combination with the Cochrane highly sensitive search strategy for identifying trials as outlined in Appendix 5c of the Cochrane Handbook: MEDLINE (1966 to September 2003); and EMBASE (1988 to September 2003).

Additional trials were identified through hand searching of abstracts from the biennial International Society for Travel Medicine Conferences and other selected meetings including the annual meetings of the American Gastroenterological Society.

We contacted content experts in the field who have conducted and published randomised controlled trials on travellers' diarrhoea, aiming to identify any remaining published or unpublished trials. We also attempted to get original data from North American trialists, but these data could not be retrieved.

Finally, the reference lists in all identified studies were scanned in an effort to identify missing trials.

Data collection and analysis

A full text version of each article identified through the various search strategies was independently assessed by two reviewers in terms of its quality in the following categories (for details see the Policy Statement of the Cochrane Infectious Diseases Group): allocation concealment; generation of allocation sequence; inclusion of all randomised participants.

Data extraction was performed for outcome variables.

Calculation of treatment effects was performed using Cochrane statistical software, RevMan version 4.04. Results of dichotomous variables are expressed as Mantel Haenszel odds ratio (OR) and 95% confidence interval (95% CI). Continuous outcomes are expressed as mean difference (MD) and 95% CI.

RESULTS

Description of studies

Thirty-three potentially eligible trials of antibiotic treatment for diarrhoea were identified. Twenty five studies were identified by searching MEDLINE, 11 by searching EMBASE (two unique), and four by hand searching of abstracts. An additional two unpublished articles were found through consultation with a content expert.

Six studies are awaiting further evaluation (See 'Characteristics of studies awaiting classification'). This includes three trials published in German language journals. Two studies are unpublished trials about which the principal investigator provided methodological details, but requested that the data not be included. One trial was available only in abstract form, and further data are awaited. Two studies were excluded for not meeting inclusion criteria and three trials did not meet predefined quality assessments (see 'Characteristics of excluded studies'). Of the remaining studies, two were duplicate publications of prior reports, and were considered together with the original study. This left a total of 20 studies which were included in the present analysis (see 'Characteristics of included studies').

Seven trials (Christensen 1988, DuPont 1992, Ericsson 1983, Mattila 1993, Salam 1994, Wistrom 1989, Wistrom 1992) were studies of a single antibiotic agent against a placebo agent. Five trials (DuPont 1982, DuPont 1992b, Ericsson 1987, Ericsson 1990, Steffen 1993) were comparisons of multiple agents, or multiple regimens of a single agent, and included a placebo group. Five studies (DuPont 1984, Ericsson 1992, Ericsson 1997, Kuschner 1995, Thornton 1992) were direct comparisons of one antibiotic against another antibiotic, or multiple regimens of different durations using the same antibiotic, without use of a placebo group. Three studies (Ericsson 1986, Petrucelli 1992, Taylor 1991) compared an antibiotic against an antibiotic-antimotility agent combination.

Eleven studies were conducted in Mexico, of which 10 were among US adult students attending summer classes in Guadalajara, Mexico. Two studies were based in Thailand, and one each in Belize, Egypt, The Gambia, India, and Morocco. Two studies included people travelling to various destinations in developing nations.

The travellers in these studies were students (10 studies), military personnel (5 studies), "package" tourists (2 studies), resort guests (1 study), independent travellers (1 study), or volunteers recruited for the purpose of the study (1 study).

Inclusion criteria were fairly uniform across the studies, with all of the studies but three (Christensen 1988, Salam 1994, Steffen 1993) requiring participants to have a minimum of three loose stools per 24 hours before presentation or a smaller number of stools in a shorter period, such as two stools in 8 hours, and have evidence of an enteric illness, such as abdominal cramps, nausea, vomiting, and low grade fever. Inclusion criteria were not explicitly stated in one study (Christensen 1988), and a single loose stool was sufficient for inclusion in two studies (Salam 1994, Steffen 1993).

The agents evaluated in these trials included an oral flouroquinolone (ciprofloxacin, norfloxacin, or ofloxacin) in 12 studies (DuPont 1992b, Ericsson 1987, Ericsson 1997, Kuschner 1995, Mattila 1993, Petrucelli 1992, Salam 1994, Steffen 1993, Wistrom 1989, Wistrom 1992), trimethoprim/ sulfamethoxazole in six studies (DuPont 1982, Ericsson 1986, Ericsson 1987, Ericsson 1990, Ericsson 1992, Thornton 1992), and in one study each for the following agents: ampicillin (DuPont 1984), azithromycin (Kuschner 1995), aztreonam (DuPont 1992), bicozamycin (Ericsson 1983), furazolidone (DuPont 1984), pivmecillinam (Christensen 1988), and trimethoprim alone (DuPont 1982).

Risk of bias in included studies

Allocation

All of the studies were randomised studies. Only one study reported on the method of randomisation used (DuPont 1982).

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Blinding

Eighteen studies were double-blinded, with one being single blinded (Ericsson 1997), and one study (Christensen 1988) not reporting whether blinding was used.

Inclusion of all randomised patients

Included trials had losses to follow up or excluded patients from efficacy analysis that were less than 10% of randomised participants in all cases. Few studies reported an intention to treat analysis (Ericsson 1990, Ericsson 1992, Ericsson 1997).

Effects of interventions

Data from studies comparing antibiotic treatment with placebo are presented in the summary analysis and in Table 1. A total of 1474 patients were included in placebo-controlled studies.

A meta-analysis of the primary outcome, duration of diarrhoea after initiation of antibiotic treatment, or time to last unformed stool, was not performed. Of 12 placebo-controlled studies identified, 10 studies (DuPont 1982, DuPont 1992, DuPont 1992b, Ericsson 1983, Ericsson 1987, Ericsson 1990, Mattila 1993, Salam 1994, Steffen 1993, Wistrom 1989) reported data for this outcome. However, only three of these (DuPont 1992b, Ericsson 1983, Salam 1994) reported mean and standard deviation (SD) time to last unformed stool. One other study reported mean and a P value for a statistical test from which an imputed pooled SD could be derived (Wistrom 1992). The remaining six studies reported statistical comparisons that used non-parametric tests. In five cases, trials used the Wilcoxon test and one used the Mann-Whitney test.

In all 10 trials, a statistically significant reduction in time to last unformed stool was reported for participants receiving antibiotic treatment when compared with placebo, with the exception of the five day ofloxacin arm in DuPont 1992b. The data from the trials from which mean and SD could be obtained or imputed are presented in Table 1.

For the secondary efficacy endpoint of number of patients cured by 72 hours after randomisation, data from six trials (DuPont 1982, Ericsson 1983, Mattila 1993, Salam 1994, Steffen 1993, Wistrom 1989) were available. Treatment with antibiotics resulted in a greater number of participants being cured of diarrhoea by 72 hours (OR 5.90, 95% CI 4.06 to 8.57, Analysis 1.1).

For the secondary endpoint of change in severity (number of unformed stools per 24 hour time interval), two trials (Ericsson 1983,Salam 1994) demonstrated a small reduction for antibiotic treated patients in the number of unformed stools passed per each 24 hour period from randomisation up to 72 hours (see Analysis 1.2). For the first 24 hours after randomisation, the difference was -1.59 stools (95% CI -2.66 to 0.52). For the period 25-48 hours, the difference was -2.10 stools (95% CI -2.78 to -1.42). For the third post-randomisation day, the difference was -1.38 stools (95% CI -1.94 to -0.82).

For the secondary endpoint of prevalence of any reported side effect of treatment, data from five trials (DuPont 1982, DuPont 1992, DuPont 1992b, Ericsson 1983, Steffen 1993) were available. There were more side effects reported by persons taking antibiotics than those taking placebo (OR 2.37, 95% CI 1.50 to 3.75, Analysis 1.3). There was significant variation in the incidence of side effects reported in different trials. Elimination of trials with the largest weight did not affect the overall result. Side effects reported were all noted to be not clinically serious, or resolved on withdrawal of the drug. Studies did not report examination for Clostridium difficile exotoxin in participants with recurrent diarrhoea. No studies reported fatalities or participants needing to be hospitalised after randomisation.

DISCUSSION

We examined the use of oral antibiotics for acute episodes of diarrhoea in travellers. The principal finding of this review was that a meta-analysis of the primary outcome was not feasible. The pooled results of the secondary endpoints demonstrate a significant beneficial effect of antibiotic treatment in terms of the proportion of persons taking antibiotics who were cured of diarrhoea by 72 hours of treatment, and in reducing the severity of illness. There were significantly more adverse effects reported in those taking antibiotics than those taking placebo. However, most of these side effects were minor, and resolved either spontaneously or on stopping the antibiotic.
The planned analyses of data for comparative trials of antibiotics and combination treatment were not carried out, principally because of concerns that the skewed nature of published data would imply a revision of the review methods.

Ten eligible trials reported summary measures based on mean, but only three reported both mean and SD. The ratios of mean and SD in these three trials also suggested that data for the primary outcome might be skewed; mean < 1.6 SD. In one trial, a pooled SD could be calculated. The other six trials used non-parametric tests to compare the means from treatment and control groups. From this we infer that this was also because the data were not normally distributed, yet it was not stated clearly in any trials. For these reasons meta-analysis for the primary outcome data was not feasible.

One major problem with the analyses presented in these trials was that the primary outcome was not treated as a time-to-event outcome. The proper analysis of such data would require time to event analysis, such as Kaplan-Meier life table methods, comparing groups using the log rank test. If such an analysis can be undertaken, it would strengthen the reliability of the conclusions.

The trials examined in this systematic review used similar entry criteria, with three exceptions (Christensen 1988, Salam 1994, Steffen 1993). Participants could be regarded as having had "classic travellers' diarrhoea" (Steffen 1999), or moderate to severe diarrhoeal illness to have been included in these studies. Part of the reason for this uniformity is that many of the studies were performed in the same geographic location, using similar protocols, in consistent participant populations.

AUTHORS' CONCLUSIONS

Implications for practice

Available trial data demonstrate that antibiotic treatment is effective in reducing the duration of post-treatment diarrhoea, and severity of diarrhoea. However, this is at the price of an increased chance of side effects from antibiotic treatment.

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Implications for research

The quality of information included in reports of therapeutic trials must meet certain minimum criteria. It is no longer accepted practice for authors to omit confidence interval data or measures of variation of the mean from reports of statistical testing. It is also crucial that data be appropriately analysed. The primary outcome for this review is ideally represented in a time-to-event analysis. Thorough statistical review of papers before publication should prevent such errors.

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Dr Paul Garner for general guidance, and Dr Paula Williamson for statistical advice. Dr HL DuPont provided access to unpublished trials, which are awaiting further analysis.

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CHARACTERISTICS OF STUDIES

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

Christensen 1988

Methods	Randomised, placebo-controlled trial
Participants	65 Danish tourists on a 2 week trip to India
Interventions	Treatment: Pivmecillinam 400 mg orally three times daily for 3 days Comparison: Matching placebo
Outcomes	Duration of post-treatment diarrhoea
Notes	Stool cultures were not obtained by investigators

DuPont 1982

Methods	Randomised, double-blind, placebo-controlled trial Patients sequentially allocated to one of three preparations, which had been randomly ordered using procedure PLAN of the Statistical Analysis System Patients kept daily diary of symptoms and medication doses They were seen daily in the study clinic
Participants	110 US students attending summer school in Guadalajara, Mexico during the summer of 1981 Entry criteria: four or more unformed stools per 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 48 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, or dysentery
Interventions	Treatment: 1. Trimethoprim/ sulfamethoxazole 160/800 mg twice daily for 5 days 2. Trimethoprim 200 mg twice daily for 5 days Comparison: 3. Placebo twice daily for 5 days
Outcomes	1. Number of unformed stools passed 2. Number of hours to last unformed stool 3. Failure: Diarrhoea persisting longer than the 5 day treatment period or with clinical evidence of worsening illness while on treatment
Notes	83 participants (75%) had positive stool cultures

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DuPont 1982 *(Continued)*

	Major pathogenic organisms: ETEC - (58%), Shigella - 23 (21%), Salmonella - 5 (5%) No pre- or post-treatment antibiotic sensitivities reported

DuPont 1984

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	100 US students attending summer school in Guadalajara, Mexico Entry criteria: four or more unformed stools pers 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 60 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, fever
Interventions	Treatment: Furazolidone 100 mg orally four times daily for 5 days Comparison: Ampicillin 500 mg orally four times daily for 5 days
Outcomes	Time from initiation of treatment to passage of last unformed stool
Notes	

DuPont 1992

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	191 US students attending summer school in Guadalajara, Mexico during the summers of 1989 and 1990 Entry criteria: four or more unformed stools pers 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 72 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, fever
Interventions	Treatment: Aztreonam 100 mg three times a day for 5 days Placebo: Matching placebo
Outcomes	1. Clinical recovery: duration of post-treatment diarrhoea, proportion of each group with clinical recovery by time interval post initiation of treatment 2. Treatment failures 3. Adverse events
Notes	81 participants (42%) had positive stool cultures Major pathogenic organisms: ETEC - 61 (32%), Shigella - 7 (4%). Others: Aeromonas, Edwardsiella, Plesiomonas, Salmonella

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DuPont 1992 *(Continued)*

	100% of pretreatment stools sensitive to aztreonam and norfloxacin. Reduced sensitivity to TMP/SMX: ETEC 91%, Shigella 91%, Salmonella 60%

DuPont 1992b

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Two patients were assigned ofloxacin for every patient assigned placebo Patients kept daily diary of symptoms and medication doses Patients were seen daily and questioned by investigators
Participants	232 US students attending summer school in Guadalajara, Mexico during the period from June 1986 and December 1988 Entry criteria: four or more unformed stools pers 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 60 hours' duration; other abdominal complaints, such as abdominal discomfort, urgency; or fever
Interventions	Treatment groups: 1. Ofloxacin 300 mg orally twice daily for three days 2. Ofloxacin 300 mg orally twice daily for five days Placebo groups: 3. Placebo orally twice daily for three days 4. Placebo orally twice daily for five days
Outcomes	1. Clinical response 2. Cure: complete resolution of illness 3. Duration of post treatment diarrhoea 4. Failure: Deterioration of clinical status during treatment or diarrhoea persisting 5 days or longer after treatment was begun
Notes	103 participants (44%) had 124 pathogens isolated Major pathogenic organisms: ETEC - 66 (28%), Shigella - 24 (10%), Plesiomonas -14 (6%) Others: Aeromonas, Campylobacter, ETEC, Salmonella Pre- and post-treatment antibiotic sensitivities not reported

Ericsson 1983

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	148 US students attending summer school in Guadalajara, Mexico during the summer of 1980 Entry criteria: four or more unformed stools pers 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 48 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, fever

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Ericsson 1983 *(Continued)*

Interventions	Treatment: Bicozamycin 500 mg orally 4 times daily for 3 days Comparison: Placebo orally 4 times daily for 3 days
Outcomes	1. Time from initiation of treatment to passage of last unformed stool 2. Number of unformed stools passed per 24 hour interval from initiation of treatment 3. Failed: Moderate to severe illness with more than 6 unformed stools per day and moderate cramps, nausea or vomiting
Notes	97 participants (66%) had positive stool cultures Major pathogenic organisms: ETEC - 49 (33%), Shigella - 25 (17%), Salmonella - 6 (4%), Rotavirus - 5 (3%) Data on pre- and post-treatment antibiotic sensitivities not reported

Ericsson 1986

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses, and were observed daily at the clinic site
Participants	134 US students attending summer school in Guadalajara, Mexico during the summer of 1983 Entry criteria: four or more unformed stools per 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 48 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, fever Participants with a temperature above 38.9 centigrade or with frank blood in the stools were excluded
Interventions	Groups and initial doses: 1. BW942 C 20 mg orally and placebo TMP/SMX 2. TMP/SMX 160/800 mg orally plus placebo BW942C 3. Both active formulations as above 4. Both placebo as above Subsequent doses: 1. BW924C 10 mg orally five times daily and one placebo morning and night for 3 days 2. TMP/SMX 160/800 mg orally twice daily and placebo BW942C five times daily for 3 days 3. Both active formulations as above 4. Both placebo formulations as above All groups: no dietary restrictions. Other antidiarrhoeal agents were prohibited
Outcomes	1. Time to last unformed stool 2. Passage of half or less than half the number of unformed stools in a given interval compared with the numbers passed in a corresponding pre-treatment interval 3. Relapse: recurrence of symptoms at least 24 hours after what was thought to be the last unformed stool 4. Failure: worsening clinically within or after the 3-day treatment period or diarrhoea persisting beyond day 5
Notes	

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Ericsson 1987

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	191 US students attending summer school in Guadalajara, Mexico during the summer of 1984 Entry criteria: four or more unformed stools pers 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 72 hours' duration; at least one of: abdominal pain, cramps, nausea, vomiting, fever Passage of frank blood or fever above 38.9 centigrade were exclusion criteria
Interventions	Treatment: 1. Ciprofloxacin 500 mg orally twice daily for 5 days 2. TMP/SMX 160/800 mg orally twice daily for 5 days Comparison: 3. Placebo twice daily for 5 days All groups: no specific dietary restrictions. Use of other antidiarrhoeal medication was prohibited
Outcomes	1. Time to last unformed stool 2. Well: Total diarrhoeal index score (defined in text) less than 1 or 0 3. Improvement: Passage of half or less than half the number of unformed stools in a given interval compared with the number in a corresponding pretreatment interval; Total diarrhoeal index half or less than half the enrollment index 4. Relapse: rise in patients' diarrhoeal index 24 or more hours after passage of what appeared to be the last unformed stool 5. Failed: Diarrhoea worsened clinically within the 5 day treatment period; diarrhoea persisting beyond day 5 of the study
Notes	Results of pretreatment stool cultures not presented Pretreatment antibiotic sensitivity patterns not disclosed

Ericsson 1990

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses. Intention to treat analysis performed
Participants	227 US students attending summer school in Guadalajara, Mexico Entry criteria: three or more unformed stools pers 24 hours; diarrhoea of no more than 14 days' duration; at least one of: abdominal cramps, nausea, or vomiting Patients with frankly bloody stools or temperature above 39 centigrade were excluded
Interventions	1. Single oral dose sulfamethoxazole 1600 mg/trimethoprim 320 mg 2. SMX/TMP 800/160 twice daily for 3 days 3. Loperamide hydrochloride orally, 4 mg given as a loading dose, and 2 mg after each loose bowel movement (daily dose not to exceed 16 mg/ day) 4. Combination SMX/TMP and loperamide as in 2. and 4. above 5. Placebo

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Ericsson 1990 *(Continued)*

	The medications were reformulated into two different colour capsules. White capsules contained 80 mg Trimethoprim/ 400 mg sulfamethoxazole or placebo. Yellow capsules contained 2 mg of loperamide or placebo. All subjects received a loading dose of 4 white and 2 yellow capsules All groups received advice about fluid replacement and dietary adjustments
Outcomes	1. Duration of diarrhoea: number of hours from enrollment to passage of last unformed stool 2. Treatment failure: Passing more than half the number of stools in a 24-hour period that qualified them for enrollment, so long as that number exceeded three
Notes	90 participants (40%) had positive stool cultures Major pathogenic organisms: ETEC - 46 (20%), Shigella - 18 (8%), Aeromonas - 8 (4%), Campylobacter - 7 (3%), Plesiomonas - 7 (3%), Salmonella - 2 (1%) No pre- or post-treatment antibiotic sensitivities reported

Ericsson 1992

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses Patients were seen daily at the clinic site. Intention to treat analysis used
Participants	190 US students attending summer school in Guadalajara, Mexico during the summers of 1988 and 1989 Entry criteria: three or more unformed stools per 24 hour period; diarrhoea of no more than 14 days' duration; at least one of: abdominal cramps, nausea, vomiting, or fever Patients with frankly bloody stools or temperature above 39 centigrade were excluded
Interventions	1. TMP/SMX 160/800 twice daily for 6 doses 2. TMP/SMX 320/1600 single dose with remaining doses of placebo 3. TMP/SMX 320/1600 single dose then 160/800 for 5 doses All groups: Open label loperamide 4 mg loading dose and 2 mg following each loose stool (not exceeding 16 mg /day) Information regarding fluid replacement and dietary adjustments
Outcomes	Duration of diarrhoea: number of hours from enrollment to passage of the last unformed stool, followed by at least 24 hours free of all symptoms
Notes	

Ericsson 1997

Methods	Randomised, single-blind, placebo-controlled trial Randomisation was performed using a table of random numbers Patients kept daily diary of symptoms and medication doses The primary outcome parameter was determined by a blinded evaluator

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Ericsson 1997 *(Continued)*

	Intention to treat analysis used
Participants	166 US students attending summer school in Guadalajara, Mexico during the summers of 1992-1994 Entry criteria: three or more unformed stools per 24 hours and at least one of: abdominal cramps, nausea, vomiting, or fever
Interventions	1. Ofloxacin 400 mg orally single dose 2. Ofloxacin 200 mg orally twice daily for 3 days 3. Ofloxacin 400 mg orally single dose plus loperamide for up to 3 days (4 mg loading dose, followed by 2 mg after each loose stool to a maximum of 16 mg/24 hour period)
Outcomes	Time from initiation of treatment to passage of last unformed stool
Notes	

Kuschner 1995

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept a daily diary of symptoms and timing of medication doses Patients were seen daily for at least 3 days and then on day 10
Participants	79 US military personnel participating in a military exercise in Thailand during May 1993 Entry criteria: three or more liquid bowel movements per 24 hour period; or two liquid stools plus cramps, nausea, vomiting, or fever; diarrhoea of no more than 48 hours' duration
Interventions	Treatment: Azithromycin 500 mg orally daily for three days Comparison: Ciprofloxacin 500 mg orally daily for three days Both groups: Doxycycline daily as malaria prophylaxis
Outcomes	1. Clinical cure: resolution of diarrhoea and all symptoms within 72 hours after taking first dose of study medication 2. Treatment failure: persistency of diarrhoea or any symptom for longer than 72 hours after treatment was initiated
Notes	

Mattila 1993

Methods	Randomised, double-blind, placebo-controlled study Efficacy analysis based on assigned treatment, i.e. not per intention to treat
Participants	106 Finnish tourists visiting Agadir, Morocco in 1989 Entry criteria: four or more unformed stools per 24 hours or three unformed stools per 8 hours; at least one of: abdominal pain or spasms, nausea, vomiting, fever
Interventions	Treatment: Norfloxacin 400 mg by mouth twice daily for three days

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Mattila 1993 *(Continued)*

	Control: Identical-looking placebo twice daily for three days Both groups: No specific dietary restrictions, use of other antidiarrhoeal medication was prohibited, oral rehydration solution provided if required
Outcomes	1. Duration of diarrhoea: time to the passage of last unformed stool 2. Full recovery: cessation of all symptoms and signs by the fourth day after beginning treatment 3. Treatment failure: passage of at least one unformed stool during the day after the treatment period or deterioration on treatment 4. Relapse: diarrhea recurring at least 24 hours after the 3-day treatment period and after apparent recovery 5. Adverse effects
Notes	This study spanned two seasons, namely Jan - February (winter) and October - November (fall) 67 participants (63%) had positive stool cultures, 21 cases with more than one pathogen Major pathogenic organisms: ETEC - 27 (25%), Salmonella - 23 (22%), Campylobacter - 22 (21%), Aeromonas - 9 (8%), EPEC - 6 (6%), Rotavirus - 3 (3%), Shigella - 2 (2%) 100% of pretreatment stools sensitive to norfloxacin

Petrucelli 1992

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	142 US military personnel participating in a military exercise in Thailand during May 1990 Entry criteria: three or more liquid bowel movements per 24 hour period; or two liquid stools plus cramps, nausea, or vomiting; diarrhoea of no more than 4 days duration Patients were excluded if they had grossly bloody stools or high fever (38.3 centigrade)
Interventions	1. Ciprofloxacin 750 mg orally plus placebo 2. Ciprofloxacin 750 mg plus loperamide 4 mg followed by 2 mg after each liquid bowel movement (maximum 16 mg/day) 3. Ciprofloxacin 500 mg twice daily for three days plus loperamide 4 mg followed by 2 mg after each liquid bowel movement (maximum 16 mg/day) All groups: Daily doxycycline for malaria prophylaxis
Outcomes	1. Duration of illness: Last unformed stool Last liquid stool 2. Complete recovery from all symptoms 3. Severity: Cumulative number of liquid bowel movements at 24, 48, and 72 hours after enrollment 4. Number of loperamide caplets taken after the loading dose
Notes	

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Salam 1994

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept daily diary of symptoms and medication doses
Participants	88 British marines on military exercises in Belize and within 8 weeks of arrival Inclusion criteria: one or more unformed stools Participants with blood in their stools, fever > 38.5 centigrade, or volume depletion requiring intravenous fluid therapy were excluded
Interventions	Treatment: Ciprofloxacin 500 mg orally as a single dose Comparison: Identical placebo orally as a single dose Both groups: Chloroquine weekly and proguanil daily for malaria prophylaxis
Outcomes	1. Duration of illness: Time to last liquid stool Time to last unformed stool (semi-solid or soft) 2. Severity: Cumulative numbers of liquid and unformed stools at 24, 48, and 72 hours after enrolment
Notes	Stool cultures were not obtained by investigators

Steffen 1993

Methods	Randomised, double-blind, placebo-controlled trial Randomisation by computer-generated list Patients were seen daily by a physician who also administered the dose of medication Patients kept a daily diary of symptoms
Participants	195 hotel guests at a resort in The Gambia Diarrhoea of less than 6 days duration defined as at least one watery stool; one soft stool with abdominal cramps, vomiting, or nausea
Interventions	Treatment: 1. Fleroxacin 400 mg orally single dose day one, placebo day 2 2. Fleroxacin 400 mg orally for two days Placebo: 3. Placebo orally for two days
Outcomes	Cure: Passage of a formed stool unless followed thereafter by unformed stool; no stools passed within 24 hours
Notes	44 participants excluded from efficacy analysis, but 190 analysed for safety 79 participants (52%) had positive stool cultures Major pathogenic organisms: ETEC - 44 (29%), Salmonella - 12 (8%), Plesiomonas - 4 (3%), Aeromonas - 2 (1%)

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Steffen 1993 *(Continued)*

	Pre- and post-treatment antibiotic sensitivities not reported

Taylor 1991

Methods	Randomised, double-blind trial Method of randomisation not stated Patients kept daily diary of symptoms, time and form of stool, and medication doses
Participants	162 military personnel participating in field training exercises in Egypt from October to November 1989 Inclusion criteria were three or more liquid stools in 24 hours; or one or two liquid stools accompanied by abdominal cramps, or vomiting Participants with fever >38.3 degrees centigrade, grossly bloody diarrhoea, or diarrhoea for longer than 60 hours were excluded
Interventions	Intervention: Ciprofloxacin 500 mg by mouth twice daily for three days plus loperamide, 4 mg initial dose followed by 2 mg with each unformed stool (to a maximum of 16 mg per 24 hours) Comparison: ciprofloxacin 500 mg by mouth twice daily for three days plus placebo, taken in the same manner as loperamide
Outcomes	1. Improvement: 50% decrease in daily number of stools compared to the previous 24 hours 2. Recovery: Total relief from all symptoms 3. Length of time lost from duty
Notes	First dose observed, subsequent doses self- administered

Thornton 1992

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients were seen daily in clinic and at follow-up visits at one and four weeks following onset of illness
Participants	142 male military personnel participating in 1986 and 1987 UNITAS/WATC shipboard exercises or 1986 Blue Horizon land-based exercise Entry criteria: four or more unformed stools per 24 hours or three unformed stools per 8 hours; diarrhoea of no more than 48 hours' duration; at least one other sign of gastrointestinal illness
Interventions	Treatment: Norfloxacin 400 mg orally twice daily for 5 days Comparison: TMP/SMX 160/800 orally twice daily for 5 days
Outcomes	1. Duration of post-treatment diarrhoea 2. Cure: resolution of diarrhoea after 5 days of treatment 3. Failure: continued diarrhoea after treatment 4. Non-evaluable
Notes	

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Wistrom 1989

Methods	Randomised, double-blind, placebo-controlled multi-centre trial Method of randomisation not stated Patients kept daily diary of symptoms, signs, and medication doses
Participants	447 Swedish travellers on short duration trips (1-6 weeks) to developing countries who visited three participating travel clinics for pre-travel immunisations between December 1986 and April 1988 Entry criteria: four or more loose stools per 24 hours; two loose stools/24 hours plus any of the following: abdominal cramps, nausea, vomiting, or fever (> 38 centigrade rectal temperature)
Interventions	Self treatment Treatment: Norfloxacin 400 mg twice daily orally for three days Comparison: Identical placebo twice daily orally for three days Both: Written and verbal instructions regarding the conduct of the trial. Sealed envelopes containing the randomisation code to be opened in the event of a medical emergency and returned to the investigators if not opened
Outcomes	1. Cure: one or fewer loose stools per 24 hours without additional symptoms Improving: two or three loose stools/24 hours without additional symptoms; one loose stool/24 hours with accompanying symptoms 2. Recurrence: return to inclusion criteria within 7 days after the last treatment dose 3. Failed
Notes	24 participants excluded initially 106 travellers developed diarrhoea meeting entry criteria 12 pathogens isolated on post-travel stool cultures

Wistrom 1992

Methods	Randomised, double-blind, placebo-controlled trial Method of randomisation not stated Patients kept a daily diary of symptoms and timing of medication doses Patients were seen daily for at least 3 days and then on day 10
Participants	42 US volunteers taken to a hotel in Puerto Vallarta, Mexico for 11 days Entry criteria: four or more unformed stools in a 24 hour period; two loose stools in a 24 hour period plus any of: abdominal cramps, vomiting, fever > 38 centigrade oral temperature
Interventions	Treatment: Ciprofloxacin 250 mg twice daily orally for three days Comparison: Placebo twice daily for three days
Outcomes	1. Cure: one or fewer loose stools per 24 hours without additional symptoms Improving: two or three loose stools/24 hours without additional symptoms; one loose stool/24 hours with accompanying symptoms 2. Failed

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Wistrom 1992 *(Continued)*

Notes	17 participants developed diarrhoea Major pathogenic organism: ETEC - 7 (41%) 100% of pretreatment stools sensitive to ciprofloxacin ETEC found with in vitro resistance on pretreatment stools: Ampicillin - 63%, Doxycycline - 47%, chloramphenicol - 32%, SMX/TMP 17%

ETEC, enterotoxigenic Escherichia coli; TMP, trimethoprim; SMX, sulfamethoxazole.

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

Study	Reason for exclusion
Bouree 1987	This was a study of prophylaxis not treatment of travellers' diarrhoea. In this double-blind, placebo-controlled study, 75 French adults participating in a car and motorcycle rally were randomised to nifuroxazide 400 mg per day or placebo as prophylaxis against travellers' diarrhoea
Chagnon 1996	This was a review article and not a clinical trial
Hill 1961	This unblinded trial allocated in rotation patients with acute onset of diarrhoea to one of four treatment groups: 1. "Empiric treatment" with magnesium sulphate and chlorodyne 2. Oxytetracycline 500 mg loading dose followed by 250 mg 6-hourly for 5 days 3. Sulfonamide (phthalylsulfathiazole) 4 g five times daily plus oral streptomycin 1 g four times daily for 6 days 4. Sulfonamide alone - phthalylsulfathiazole 4 g five times daily for 6 days No inclusion criteria for frequency of stools, stool consistency, or other symptoms were defined in the report. Allocation was done before obtaining culture results. Results for patients with dysentery were considered separately to those with no identified pathogens
Richards 1970	This study was a single-blind, non-randomised, placebo-controlled trial of prophylaxis with cloquinol 250 mg by mouth three or four times daily. The participants were British footballers playing abroad in the off season
Steffen 1988	This was a randomised, double-blind, placebo-controlled study of self-treatment of travellers' diarrhoea. The 2580 participants were Swiss residents visiting the Zurich University Vaccination Centre before travel to developing countries between July 1984 and December 1986. They were randomised, with stratification by destination, to one of seven regimens: 1. Bismuth subsalicylate 262.5 mg, 2 every 30 mins (total 8 doses per 24 hours) 2. Doxycycline 100 mg twice daily 3. Loperamide 4 mg loading dose and 2 mg after each unformed stool (max 16 mg per 24 hours) 4. Mecillinam 400 mg three times daily 5. Streptococcus faecium 75 x 10E6 SF68 three times daily 6. Trimethoprim/sulfamethoxazole 160/800 mg twice daily 7. Placebo Participants were instructed to commence self-treatment with the development of any of the following symptoms: at least one watery stool; a pasty stool accompanied by cramps, nausea, vomiting, or fever In this study, 482 participants were considered drop outs (18.9%) prior to travel. Of the 2098 who travelled, 798 developed diarrhoea, and 654 took the study medication (82% of eligible participants), but a further 115 were excluded for protocol violations, 35 for taking concurrent medications, and 17 for unspecified reasons. A total of 530 participants were analysed for drug efficacy (66% of eligible participants). Because of the high drop out rate the trial was excluded

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

Anonymous 1995

Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

Bruns 1995

Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

DuPont 1994

Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

DuPont 1994b

Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

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DuPont 1997	
Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

Ziegenhagen 1992	
Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	—

DATA AND ANALYSES

Comparison 1. Antibiotic versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number cured at 72 hours	6	697	Odds Ratio (M-H, Fixed, 95% CI)	5.90 [4.06, 8.57]
2 Severity (number of unformed stools / 24 hour period)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Baseline	1	83	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.81, 0.61]
2.2 0 - 24 hours	2	223	Mean Difference (IV, Fixed, 95% CI)	-1.59 [-2.66, -0.52]
2.3 25 - 48 hours	2	223	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-2.78, -1.42]
2.4 49 - 72 hours	2	223	Mean Difference (IV, Fixed, 95% CI)	-1.38 [-1.94, -0.82]
3 Side effects	5	862	Odds Ratio (M-H, Fixed, 95% CI)	2.37 [1.50, 3.75]

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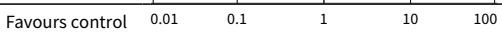
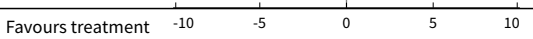
Analysis 1.1. Comparison 1 Antibiotic versus placebo, Outcome 1 Number cured at 72 hours.

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
DuPont 1982	67/75	18/48		10.01%	13.96[5.47,35.65]
Ericsson 1983	68/72	42/68		10.26%	10.52[3.43,32.28]
Mattila 1993	36/51	23/55		27.84%	3.34[1.49,7.48]
Salam 1994	43/45	30/38		6.18%	5.73[1.14,28.92]
Steffen 1993	82/102	23/49		26.05%	4.63[2.2,9.75]
Wistrom 1989	34/46	18/48		19.65%	4.72[1.96,11.39]
Total (95% CI)	**391**	**306**		**100%**	**5.9[4.06,8.57]**
Total events: 330 (Treatment), 154 (Control)					
Heterogeneity: Tau²=0; Chi²=6.83, df=5(P=0.23); I²=26.8%					
Test for overall effect: Z=9.31(P<0.0001)					



Analysis 1.2. Comparison 1 Antibiotic versus placebo, Outcome 2 Severity (number of unformed stools / 24 hour period).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.2.1 Baseline							
Ericsson 1983	45	3 (2)	38	3.1 (1.2)		100%	-0.1[-0.81,0.61]
Subtotal ***	**45**		**38**			**100%**	**-0.1[-0.81,0.61]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.28(P=0.78)							
1.2.2 0 - 24 hours							
Ericsson 1983	72	4.6 (3.7)	68	5.8 (5.2)		50.91%	-1.2[-2.7,0.3]
Salam 1994	45	3.8 (3.4)	38	5.8 (3.7)		49.09%	-2[-3.53,-0.47]
Subtotal ***	**117**		**106**			**100%**	**-1.59[-2.66,-0.52]**
Heterogeneity: Tau²=0; Chi²=0.53, df=1(P=0.46); I²=0%							
Test for overall effect: Z=2.91(P=0)							
1.2.3 25 - 48 hours							
Ericsson 1983	72	1.2 (1.8)	68	3.3 (3.6)		51.52%	-2.1[-3.05,-1.15]
Salam 1994	45	1.1 (2)	38	3.2 (2.5)		48.48%	-2.1[-3.08,-1.12]
Subtotal ***	**117**		**106**			**100%**	**-2.1[-2.78,-1.42]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=1); I²=0%							
Test for overall effect: Z=6.03(P<0.0001)							
1.2.4 49 - 72 hours							
Ericsson 1983	72	0.6 (1.2)	68	1.9 (2.8)		59.7%	-1.3[-2.02,-0.58]
Salam 1994	45	0.5 (1.3)	38	2 (2.5)		40.3%	-1.5[-2.38,-0.62]
Subtotal ***	**117**		**106**			**100%**	**-1.38[-1.94,-0.82]**
Heterogeneity: Tau²=0; Chi²=0.12, df=1(P=0.73); I²=0%							
Test for overall effect: Z=4.86(P<0.0001)							
Test for subgroup differences: Chi²=16.74, df=1 (P=0), I²=82.08%							



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Analysis 1.3. Comparison 1 Antibiotic versus placebo, Outcome 3 Side effects.

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H, Fixed, 95% CI	Weight	Odds Ratio M-H, Fixed, 95% CI
DuPont 1982	1/75	0/35		2.67%	1.43[0.06,35.97]
DuPont 1992	18/98	12/93		40.34%	1.52[0.69,3.36]
DuPont 1992b	7/152	0/79		2.51%	8.2[0.46,145.38]
Ericsson 1983	6/72	1/68		3.78%	6.09[0.71,51.98]
Steffen 1993	78/126	25/64		50.7%	2.54[1.37,4.7]
Total (95% CI)	**523**	**339**		**100%**	**2.37[1.5,3.75]**
Total events: 110 (Treatment), 38 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.81, df=4(P=0.59); I^2=0%					
Test for overall effect: Z=3.7(P=0)					

Favours treatment

Favours control

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ADDITIONAL TABLES

Table 1. Duration of post-treatment diarrhoea (hours)

Study	Treatment			Control			Pooled SD
	N	Mean	SD	N	Mean	SD	
DuPont 1992b (Ofloxacin 3-days)	81	28	30	79	56	48	—
DuPont 1992b (Ofloxacin 5-days)	66	39	36	79	56	48	—
Ericsson 1983	72	28.2	27.3	68	63.7	46.1	—
Salam 1994	45	24.8	25.49	38	53.5	27.12	—
Wistrom 1992	8	26	—	9	60	—	27.989

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WHAT'S NEW

Date	Event	Description
5 January 2012	Amended	The CIDG is piloting a new classification system for reviews. The classification for this has now been added; description included in "Published notes" section of review

HISTORY

Protocol first published: Issue 3, 1998
Review first published: Issue 3, 2000

Date	Event	Description
5 August 2008	Amended	Converted to new review format with minor editing.
8 September 2003	New search has been performed	New studies found but not yet included or excluded.

CONTRIBUTIONS OF AUTHORS

Not stated.

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

- Liverpool School of Tropical Medicine, UK.

External sources

- Department for International Development, UK.

NOTES

2012, Issue 2: Review status: Current question - update pending. New studies have been identified; a new author team is required for this review.

The Cochrane Infectious Diseases Group assesses Review Status using a pilot system to help the reader understand whether the review concerns a current question, and is up to date. We report on:

1. The question the review addresses. Is it a:

- **Historical question**, where the intervention or policy has been superseded by new medical developments (such as a new drug); or a
- **Current question**, which is still relevant to current policy or practice.

2. Whether the review is up to date. Is the review:

- **Up to date**;
- **Update pending**; or
- **No update intended**.

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We then provide comment of the review status, to help explain the categories selected.

INDEX TERMS

Medical Subject Headings (MeSH)

*Travel; Acute Disease; Administration, Oral; Anti-Bacterial Agents [*therapeutic use]; Diarrhea [*drug therapy]

MeSH check words

Adult; Child; Humans

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