Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children (Review)

Hartling L, Bellemare S, Wiebe N, Russell KF, Klassen TP, Craig WR

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 1

http://www.thecochranelibrary.com

TABLE OF CONTENTS

[Intervention Review]

Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Lisa Hartling[2], Steven Bellemare[3], Natasha Wiebe[4], Kelly F Russell[5], Terry P Klassen[6], William Raine Craig[1]

[1]Pediatric Emergency, University of Alberta, Edmonton, Canada. [2]Department of Paediatrics, University of Alberta, Edmonton, Canada. [3]Department of Pediatrics, Dalhousie University, Halifax, Canada. [4]Medicine, University of Alberta, Edmonton, Canada. [5]Department of Paediatrics, Alberta Children's Hospital, Calgary, Canada. [6]Department of Pediatrics, University of Alberta, 8417 Aberhart Centre One, Edmonton, Canada

Contact address: William Raine Craig, Pediatric Emergency, University of Alberta, 7215 Aberhart Centre 1, 11402 University Ave, Edmonton, Alberta, T6G 2J3, Canada. William.Craig@albertahealthservices.ca.

Editorial group: Cochrane Infectious Diseases Group.
Publication status and date: Stable (no update expected for reasons given in 'What's new'), published in Issue 1, 2010.
Review content assessed as up-to-date: 28 March 2006.

Citation: Hartling L, Bellemare S, Wiebe N, Russell KF, Klassen TP, Craig WR. Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD004390. DOI: 10.1002/14651858.CD004390.pub2.

ABSTRACT

Background

Dehydration associated with gastroenteritis is a serious complication. Oral rehydration is an effective and inexpensive treatment, but some physicians prefer intravenous methods.

Objectives

To compare oral with intravenous therapy for treating dehydration due to acute gastroenteritis in children.

Search methods

We searched the Cochrane Infectious Diseases Group Specialized Register (March 2006), CENTRAL (*The Cochrane Library* 2006, Issue 1), MEDLINE (1966 to March 2006), EMBASE (1974 to March 2006), LILACS (1982 to March 2006), and reference lists. We also contacted researchers, pharmaceutical companies, and relevant organizations.

Selection criteria

Randomized and quasi-randomized controlled trials comparing intravenous rehydration therapy (IVT) with oral rehydration therapy (ORT) in children up to 18 years of age with acute gastroenteritis.

Data collection and analysis

Two authors independently extracted data and assessed quality using the Jadad score. We expressed dichotomous data as a risk difference (RD) and number needed to treat (NNT), and continuous data as a mean difference (MD). We used meta-regression for subgroup analyses.

Main results

Seventeen trials (1811 participants), of poor to moderate quality, were included. There were more treatment failures with ORT (RD 4%, 95% confidence interval (CI) 1 to 7, random-effects model; 1811 participants, 18 trials; NNT = 25). Six deaths occurred in the IVT group and two in the ORT groups (4 trials). There were no significant differences in weight gain (369 participants, 6 trials), hyponatremia (248 participants, 2 trials) or hypernatremia (1062 participants, 10 trials), duration of diarrhea (960 participants, 8 trials), or total fluid intake at six hours (985 participants, 8 trials) and 24 hours (835 participants, 7 trials). Shorter hospital stays were reported for the ORT group (WMD -1.20 days, 95% CI -2.38 to -0.02 days; 526 participants, 6 trials). Phlebitis occurred more often in the IVT group (NNT 50, 95% CI 25 to 100) and paralytic ileus more often in the ORT group (NNT 33, 95% CI 20 to 100, fixed-effect model), but there was no significant difference between ORT using the low osmolarity solutions recommended by the World Health Organization and IVT (729 participants, 6 trials).

Authors' conclusions

Although no clinically important differences between ORT and IVT, the ORT group did have a higher risk of paralytic ileus, and the IVT group was exposed to risks of intravenous therapy. For every 25 children (95% CI 14 to 100) treated with ORT one would fail and require IVT.

PLAIN LANGUAGE SUMMARY

Children with dehydration due to gastroenteritis need to be rehydrated, and this review did not show any important differences between giving fluids orally or intravenously

Dehydration is when body water content is reduced causing dry skin, headaches, sunken eyes, dizziness, confusion, and sometimes death. Children with dehydration due to gastroenteritis need rehydrating either by liquids given by mouth or a tube through the nose, or intravenously. The review of 17 trials (some funded by drug companies) found that the trials were not of high quality; however the evidence suggested that there are no clinically important differences between giving fluids orally or intravenously. For every 25 children treated with fluids given orally, one child would fail and require intravenous rehydration. Further, the results for low osmolarity solutions, the currently recommended treatment by the World Health Organization, showed a lower failure rate for oral rehydration that was not significantly different from that of intravenous rehydration. Oral rehydration should be the first line of treatment in children with mild to moderate dehydration with intravenous therapy being used if the oral route fails. The evidence showed that there may be a higher risk of paralytic ileus with oral rehydration while intravenous therapy carries the risk of phlebitis (ie inflammation of the veins).

BACKGROUND

Gastroenteritis is an illness characterized by the acute onset of diarrhea, which may or may not be accompanied by nausea, vomiting, fever, and abdominal pain (AAP 1996). It can be caused by a variety of infectious agents including bacteria and viruses (Armon 2000). Acute diarrhea refers to the passage of loose or watery stools, usually at least three times per 24 hours, and lasting less than 14 days; the consistency of stools being more important than the frequency.

Mild cases of gastroenteritis are usually self-limiting and may cause mild dehydration, which can be treated or prevented by continued feeding and drinking more fluids. Children who lose a large volume of liquid stool may develop moderate or severe dehydration; in the most severe cases this can lead to death. These children should be given rehydration therapy in order to restore the lost fluids and electrolytes.

Worldwide, 12% of deaths among children less than five years are due to diarrhea (WHO 2000). In low-income and middle-income countries, an estimated 1.8 million children below the age of five years die of diarrhea each year (Bern 1992). Almost 50% of these deaths are due to dehydration and most affect children less than one year of age (WHO 1996). Children in high-income countries are also affected by diarrhea. In the USA, for example, each year there are roughly 21.5 to 38 million episodes of diarrhea among the 16.5 million children under the age of five years (

Glass 1991). Diarrhea accounts for an estimated 2.1 to 3.7 million physician visits per year (Glass 1991) and 9% to 10% of all hospital admissions of children under the age of 5 years (Glass 1991; Gangarosa 1992). Approximately one per 15,000 children born in the USA or one per 500 children hospitalized with gastrointestinal illness will die of their illness (Glass 1991).

Widespread use of oral rehydration salt (ORS) solutions began in the 1970s as an effective and inexpensive method of treating diarrhea in low-income and middle-income countries (Duggan 1992). The basis for their use lies in the knowledge that glucose enhances sodium and water absorption in the bowel, even during diarrhea (Mackenzie 1988; Duggan 1992). There are a number of ORS solutions that vary in terms of their electrolyte and carbohydrate concentrations (Santosham 1991). The World Health Organization recommends a specific formulation of ORS solution for both rehydration and maintenance of hydration (WHO 2002). It has an osmolarity similar to that of plasma and contains citrate to correct metabolic acidosis and a glucose concentration that allows maximum absorption of sodium and water.

Despite its success and proven efficacy (Gavin 1996), and recommendations for use by the American Academy of Pediatrics and the Centers for Disease Control (Duggan 1992; AAP 1996), oral rehydration therapy (ORT) continues to be less frequently used by family physicians and pediatricians in North America, where intravenous therapy (IVT) is more in vogue (Snyder 1991; Ozuah 2002).

IVT, usually with normal saline or Ringer's lactate (AAP 1996), is familiar to physicians and is rapid and effective in promptly reversing cases of hypovolemic (low blood volume) shock. Since it must be administered in an outpatient or inpatient setting by specially trained staff, it is expensive in terms of money and human resources. In addition, IVT is a traumatic experience for most children and is known to have complications related to rapid over correction of electrolyte imbalances (WHO 1995), leaking of solutions into surrounding tissues (Garland 1992), and infection or inflammation (Garland 1992).

ORT is colloquially used in the literature as a substitute for the perhaps more appropriate term enteral rehydration therapy. It is important to note that rehydration can be provided enterally in two manners: orally or via nasogastric tube. Although ORT is not widely popular in developed countries because it is thought to take extra time and effort (Goepp 1993), it has many advantages. If administered by mouth, it is less traumatic to the child and can be administered by caregivers in a variety of settings including the home (Mackenzie 1988; AAP 1996). Research has shown ORT to be less expensive than IVT and to be associated with lower hospital admission rates and shorter lengths of stay (Listernick 1986; Gremse 1995). ORT is not recommended if the child has paralytic ileus or glucose malabsorption (Duggan 1992; WHO 1995), which are rare events. In both these clinical scenarios, fluid remains in the gut lumen rather than being absorbed into the intravascular space where the body can use it. Further delivery of fluid then just causes abdominal distention.

In 1996, Gavin and colleagues published the results of a meta-analysis that evaluated the efficacy of glucose-based ORT among well-nourished children in developed countries (Gavin 1996). The review included six studies that compared ORT with IVT and seven studies that compared ORS solutions with different sodium contents. They found that failure of ORT (defined as the need to revert to IVT) varied among trials, ranging from 0% to 18.8% with an overall failure rate of 3.6% (95% confidence interval 1.4 to 5.8). They found no significant difference in failure between different ORS solutions. They also found no higher risk of iatrogenic hypernatremia or hyponatremia with ORT compared with IVT and no significant differences in failure rates between inpatients and outpatients. The authors suggested that ORT may, in fact, be associated with more favourable outcomes such as increased weight gain and shorter duration of diarrhea.

The NHS Centre for Reviews and Dissemination (CRD) at the University of York, England critically appraised the Gavin 1996 review. While there was little detail in the paper on the individual studies reviewed and some aspects of the methods used for the review, the appraisal concluded that sufficient information was presented to suggest that the findings were likely reliable (DARE 2002). In addition, we evaluated the review by applying Oxman and Guyatt's index of the scientific quality of research overviews (Oxman 1991). The weaknesses identified by the Oxman and Guyatt index included the limited search (MEDLINE up to 1993 and contact with organizations and content experts; English language articles only) and the lack of assessment and consideration of the validity of the included studies. The purpose of the present review is to update and build on the work started by Gavin and colleagues by increasing the scope (countries of all income levels, method of administration of ORT) and comprehensiveness (broader search strategy, inclusion not limited by language of publication or publication status), and by assessing the risk of bias in the included studies.

OBJECTIVES

To compare oral with intravenous therapy for treating dehydration due to acute gastroenteritis in children.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized and quasi-randomized controlled trials.

Types of participants

Children up to 18 years of age with dehydration secondary to acute gastroenteritis.

We included hospital inpatients and outpatients.

Acute gastroenteritis was defined as the rapid onset of diarrhea (lasting less than 14 days) with or without nausea, vomiting, fever, or abdominal pain (AAP 1996). Diarrhea is the passage of loose or watery stools, usually with increased frequency and volume (Baldassano 1991). Dehydration due to diarrhea is a "deficiency of water and salt" (Santosham 1991), and is most often assessed in terms of the percentage of weight lost during the dehydrating episode (Armon 2000). The severity of dehydration can be classified as mild (3% to 5%), moderate (6% to 9%), or severe (10% or greater) (Duggan 1992; AAP 1996).

Types of interventions

Intervention

Oral rehydration therapy administered orally or via nasogastric tube.

Control

Intravenous therapy.

Types of outcome measures

Primary

- Failure of rehydration or failure to maintain hydration after initial rehydration (as defined in the trials).
- Death.

Secondary

- Weight gain.
- Length of hospital stay for inpatients.
- Hypernatremia (excessive concentration of sodium in the blood).
- Hyponatremia (reduced concentration of sodium in the blood).
- Duration of diarrhea.
- Total fluid intake.
- Sodium intake and sodium levels.
- Complications and adverse events.

Search methods for identification of studies

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

Databases

We searched the following databases using the search terms and strategy described in Appendix 1: Cochrane Infectious Diseases Group Specialized Register (March 2006);Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (2006, Issue 1); MEDLINE (1966 to March 2006); EMBASE (1974 to March 2006); and LILACS (1982 to March 2006).

Researchers, organizations, and pharmaceutical companies

We contacted the World Health Organization Division of Child and Adolescent Health, Technologies for Primary Health Care Project (sponsored by US Agency for International Development), International Child Health Foundation, International Children's Centre, International Center for Diarrhoeal Diseases Research, and individual researchers working in the field for unpublished data, confidential reports, and raw data of published trials. We also contacted the manufacturers of Pedialyte (Ross Products Division, Abbott Laboratories) and Gastrolyte (Aventis Pharma Inc.) for any unpublished information or studies they may have possessed information pertaining to the efficacy of ORT.

Reference lists

We also reviewed the citations of existing reviews (Gavin 1996; Fonseca 2004), and of all trials identified by the above methods.

Data collection and analysis

Selection of studies

Two authors (Steven Bellemare (SB) and Kelly Russell (KR)) independently screened the results of the literature search. The full text of all potentially relevant articles was retrieved. Two authors (KR, Don McConnell (DM), or Lisa Hartling (LH)) independently assessed the trials for inclusion in the review using predetermined inclusion criteria. We resolved any disagreements through discussion or by consulting a third party.

Data extraction and management

One author (SB or LH) extracted data from the included trials, and a second author (KR) checked the data for completeness and

accuracy. We requested unpublished data from authors where necessary. We used a standard data extraction form to extract data on trial characteristics including methods, participants, interventions, and outcomes. We also collected information on source of funding and intention-to-treat (whether an intention-to-treat analysis was planned and whether an intention-to-treat analysis was done). We resolved any disagreements by referring to the trial report and through discussion.

Assessment of risk of bias in included studies

Two authors (SB, William Craig (WC), or LH) evaluated each trial using the Jadad 5-point scale to assess randomization (0 to 2 points), double blinding (0 to 2 points), and withdrawals and dropouts (0 to 1 point) (Jadad 1996). SB, WC, or LH also assessed concealment of allocation as being adequate, inadequate, or unclear (Schulz 1995). We resolved any differences through consensus or by consulting a third party. We provided overall quality scores according to the Jadad scale. We also described and displayed the quality information by individual components — generation of random sequence, blinding, loss to follow up, and allocation concealment — which we classified as adequate, inadequate, or unclear.

Data synthesis

Since we had frequent zero event rates (per group, per trial), we expressed dichotomous data (eg failure of treatment) as a risk difference (RD) rather than using a relative measure that would force the trial data to be omitted or approximated (adding ½ to each 2 x 2 table cell) (Higgins 2005a). We also calculated the number needed to treat (NNT) to help clarify the degree of benefit for the baseline intravenous risk. We calculated baseline risks using the same weights calculated from the risk difference analyses. We converted continuous data to a mean difference and then calculated an overall mean difference. We analyzed the results in Review Manager 4.2 using a random-effects model and presented all estimates with 95% confidence intervals (CI). We analyzed the longitudinal outcome of total fluid intake for two time points: six and 24 hours. One trial assessed total fluid intake at four hours (Spandorfer 2005), while two trials assessed total fluid intake at eight hours (Santosham 1982i; Santosham 1982ii); these trials were included in the analysis for total fluid intake at six hours.

We quantified statistical heterogeneity using the I^2 statistic (Higgins 2003). We assessed possible sources of heterogeneity by subgroup analyses meta-regressing (using Stata 7.0) on the primary outcome measure (failure to rehydrate). We examined several participant subgroups: inpatient or outpatient status; participant age; state of nourishment; extent of dehydration; country's income status; route of administration (oral versus nasogastric); and type of ORS solution. We also examined several other subgroups: Jadad score; allocation concealment; funding source; and intention-to-treat analysis.

The relationship between the osmolarity of the ORT solution and failure to rehydrate was explored using a chi-square subgroup test (Deeks 2001). We calculated osmolarity based on the reported constituent concentrations in the solutions (Appendix 2). We also examined the choice of model for sensitivity to the results (eg Mantel-Haenszel fixed-effect model). We performed intention-to-treat analyses for our primary outcome measure (failure to rehydrate). After viewing the trials, we created a more homogeneous failure definition and applied it to each article in order to check the robustness of the primary results (ie using failure to rehydrate as defined in the trials). The decision to examine persistent vomiting as an exclusion criterion was selected post hoc for subgroup analysis; all other subgroups were specified a priori. We identified and explored all statistical outliers.

We tested for publication bias using the funnel plot visually and quantitatively using the rank correlation test (Begg 1994), weighted regression (Egger 1997), and the trim-and-fill method (Duval 2001) in Stata 7.0.

When standard deviations were not reported, we performed a sensitivity analysis by substituting both the minimum and maximum standard deviations from the other outcome-specific included studies to gauge whether these omitted studies might significantly alter our results.

RESULTS

Description of studies

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

We identified 466 unique references through the electronic databases and obtained the full text of 28 potentially relevant articles. We identified 11 additional studies via recommendations from authors and experts in the field and references. Seventeen of these met the inclusion criteria (see 'Characteristics of included studies'). One trial was conducted concurrently and slightly differently in two countries; we have analyzed this as two separate studies (Santosham 1982i; Santosham 1982ii). The reasons for excluding studies are noted in the 'Characteristics of excluded studies'.

Randomization

All trials compared an IVT arm with one or more ORT arms (oral or nasogastric). The trials varied widely in methodology and quality. They were published from 1982 to 2005 and though most were randomized, two trials were quasi-randomized (Singh 1982; Mackenzie 1991).

Location

The trials varied in their countries of origin. Nine were conducted in high-income countries: six in the USA (Tamer 1985; Listernick 1986; Gremse 1995; Atherly-John 2002; Nager 2002; Spandorfer 2005); one in Canada (Issenman 1993); one in Australia (Mackenzie 1991); and one in Finland (Vesikari 1987). The other trials were from lower income countries such as Puerto Rico (de Pumarejo 1990), Egypt (el-Mougi 1994), Mexico (Gonzalez 1988), Iran (Sharifi 1985), Afghanistan (Singh 1982), Colombia (Hernandez 1987), and Peru (Brown 1988). One trial was conducted in the USA and Panama simultaneously (Santosham 1982i; Santosham 1982ii).

Funding source

Of the trials that mentioned the source of funding, five received funding or sponsorship from the pharmaceutical industry (Ross or Abbott Laboratories) (Santosham 1982i; Listernick 1986; de Pumarejo 1990; Issenman 1993; Gremse 1995), one trial received funding from other external sources (Santosham 1982i), one trial received funding from Nestle, the World Health Organization, and the US government (Brown 1988), and two trials used Pedialyte in their protocol but did not specifically acknowledge Ross Laboratories (the manufacturer of Pedialyte) as a funding source (Nager 2002; Spandorfer 2005).

Inclusion and exclusion criteria

Most trials were similar in their inclusion and exclusion criteria except in the area of treatment of children with persistent vomiting and severe dehydration and shock. All trials excluded children in shock except for two (Santosham 1982i; Santosham 1982ii; Sharifi 1985), and three trials did not mention whether they included or excluded these children (Hernandez 1987; Vesikari 1987; Brown 1988). All children in the Santosham trials presenting in either severe dehydration or shock were first treated immediately with IVT to reverse the condition before being randomized to a treatment group.

Three trials enrolled children with only dehydration secondary to acute diarrhea and made no mention of vomiting in the inclusion criteria (Brown 1988; Vesikari 1987; el-Mougi 1994). Of the remaining trials, five excluded children with persistent or protracted vomiting (Singh 1982; de Pumarejo 1990; Issenman 1993; Atherly-John 2002; Nager 2002), while four trials included these children (Spandorfer 2005; Sharifi 1985; Listernick 1986; Gremse 1995). The remaining authors did not elaborate on the inclusion or exclusion of children with persistent vomiting (Santosham 1982i; Santosham 1982ii; Tamer 1985; Hernandez 1987; Gonzalez 1988; Mackenzie 1991).

Study population

The populations studied were similar: 1015 (56%) people were randomized to the ORT group and 796 (44%) people to the IVT group. Overall more people were randomized to ORT as some trials included more than one ORT group (Santosham 1982i; Santosham 1982ii; Hernandez 1987; Brown 1988; el-Mougi 1994). Most trials included children from three months to five years of age. The other trials included children from eight weeks to three years (Spandorfer 2005), children up to the age of 17 years (Atherly-John 2002), or neonates aged less than 14 days (Vesikari 1987; Gonzalez 1988; de Pumarejo 1990). One trial did not specify the age range (Singh 1982). Finally, Hernandez 1987 enrolled children less than five years but did not specify a lower age limit (15.3% of their population was $\leq$ 3 months).

ORS solutions: description and administration

All the trials used ORS solutions containing glucose (75 to 144 mEq/L) or dextrose (70 to 139 mEq/L), as well as sodium (45 to 90 mEq/L), potassium (13 to 30 mEq/L), and chloride (35 to 80 mEq/L) (Appendix 2). One trial used a combination of glucose and fructose as the carbohydrate component (Listernick 1986). All the trials used either citrate or bicarbonate in their ORS. Eight trials reported the osmolarity of the ORS solutions (Santosham 1982i; Santosham 1982ii; Singh 1982; Sharifi 1985; Hernandez 1987; de Pumarejo 1990; Issenman 1993; el-Mougi 1994; Nager 2002), which ranged from 210 to 390 mmol/L. One trial did not report on the makeup or osmolarity of the ORS used (Atherly-John 2002).

The route of administration of ORT differed. Some trials administered by mouth only (Santosham 1982i; Santosham 1982ii; Singh 1982; el-Moughi 1983; Tamer 1985; Listernick 1986; Brown 1988; de Pumarejo 1990; Issenman 1993; Atherly-John 2002; Spandorfer 2005), while others administered it by mouth, using an nasogastric tube only when required (Hernandez 1987; Vesikari 1987; Gonzalez 1988; Mackenzie 1991). Children randomized to the ORT arm received ORS exclusively via nasogastric tube in one trial (Gremse 1995); but before study enrolment children in both arms had failed a prior uncontrolled trial of ORS administered by mouth. One trial administered ORS exclusively via nasogastric tube (Nager 2002), while another gave ORS via nasogastric tube in the rehydration phase of the trial and by mouth in the maintenance phase (Sharifi 1985).

Outcomes

All trials reported on the primary outcome measure of interest: failure to rehydrate using ORT. However, the definition of failure of ORT varied. While some trials counted children taking ORS by mouth with persistent vomiting as treatment failures, others inserted nasogastric tubes in these children, thus giving ORT more chances of success in the process (Hernandez 1987; Vesikari 1987;

Gonzalez 1988; Mackenzie 1991). Only three trials reported data on deaths (Singh 1982; el-Mougi 1994; Sharifi 1985), while additional data were obtained from a fourth (Mackenzie 1991). Secondary outcome measures, when not determined a priori, were tabulated as they were reported in individual trials.

Risk of bias in included studies

The quality of the studies ranged from zero to three on the Jadad scale (median two). Since none of the trials could be double blind due to the nature of the intervention, the maximum Jadad score was three rather than the conventional five. Two trials scored a three (Atherly-John 2002; Spandorfer 2005). One trial scored a zero on the Jadad scale as it was described as randomized (one point) but used an inappropriate method of randomization (point deducted) (Singh 1982). Six trials scored a one on the Jadad score (Sharifi 1985; Hernandez 1987; Gonzalez 1988; de Pumarejo 1990; el-Mougi 1994; Gremse 1995). All received a point for randomization. The seven remaining trials scored a two: one point for randomization and one point for reporting withdrawals. The quality components for each trial are detailed in Appendix 3.

Two trials had adequately concealed allocation (Atherly-John 2002; Spandorfer 2005); it was unclear in the remaining trials. Although four trials had incomplete follow up and one other (Issenman 1993) counted a withdrawal as a failure (Tamer 1985; Brown 1988; Mackenzie 1991; Nager 2002), only two trials reported doing an intention-to-treat analysis (Atherly-John 2002; Spandorfer 2005).

Effects of interventions

Failure to rehydrate

There was a statistically significant difference in failure to rehydrate between treatment groups (RD 4%, 95% CI 1 to 7; 1811 participants, 18 trials, Analysis 1.1). The NNT was 25 (95% CI 14 to 100), and the failure risks were 4.9% for ORT and 1.3% for IVT. Failure definitions varied by trial and are discussed later. The results for failure to rehydrate were not sensitive to the choice of model, as the fixed-effect model also favoured IVT (RD 4%, 95% CI 2 to 6; NNT 25, 95% CI 17 to 50).

Gonzalez 1988 was a statistical outlier in this analysis because its risk difference was large given its sample size (RD 13%, 95% CI 6 to 20; 200 participants). An influence plot and the Galbraith plot show evidence to this effect (Figure 1 and Figure 2). Removing this trial shifted the overall risk difference closer to the null, but the result was still statistically significant (RD 2%, 95% CI 0.08 to 5; NNT 50, 95% CI 20 to 1250) and reduced the heterogeneity (from I^2 69.9% to 43.0%). The risk difference was also statistically significant using the fixed-effect model (RD 3%, 95% CI 1 to 5; NNT 33, 95% CI 20 to 100).

Figure 1. Influence plot: meta-analysis using random-effects model (linear form)

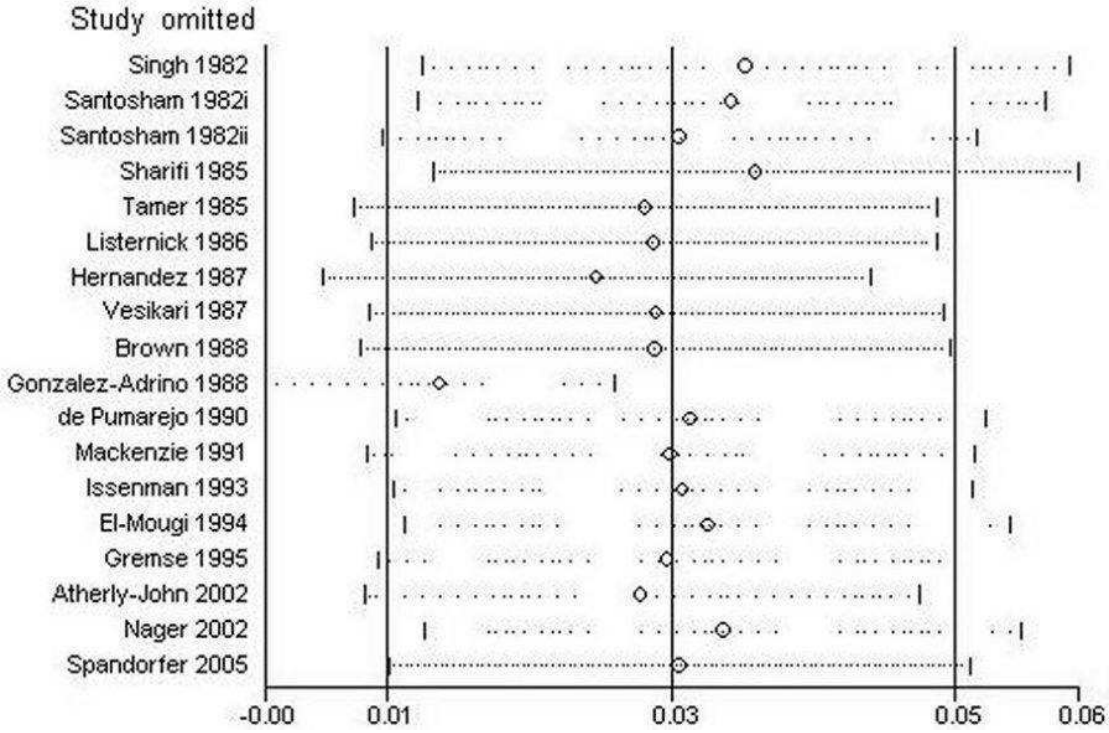
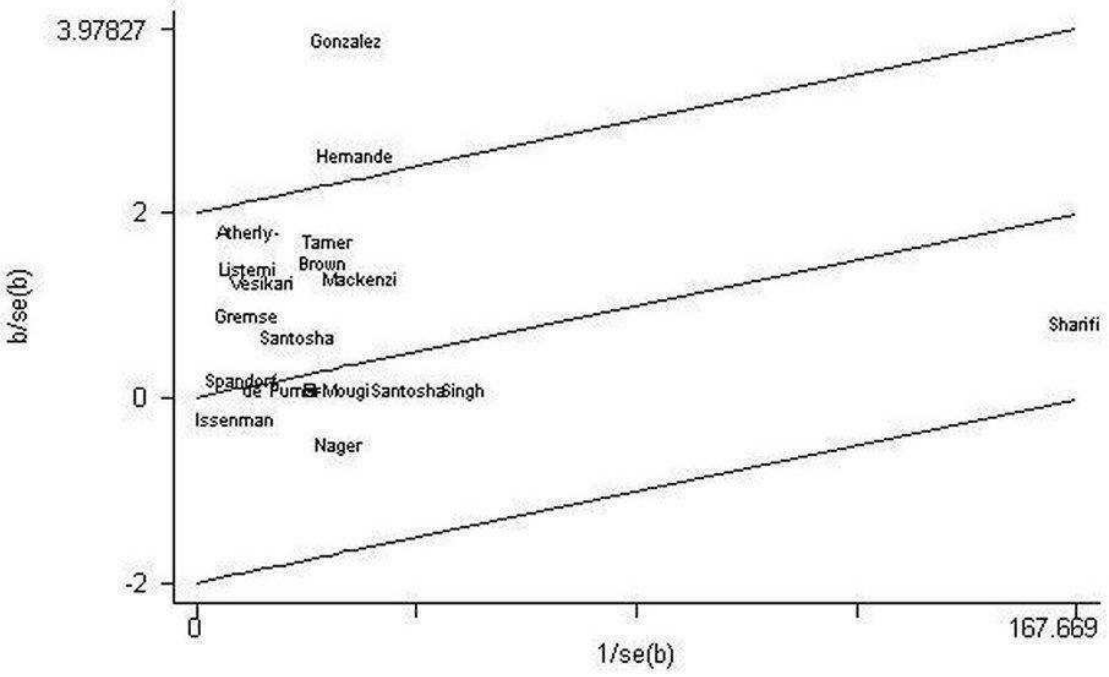


Figure 2. Galbraith plot



Gremse 1995 and Nager 2002 met all the inclusion criteria but randomized the participants to the nasogastric or intravenous route; this occurred after the participants had already failed an uncontrolled trial of ORT in Gremse 1995. These trials were neither outliers nor influential.

Death

Three trials reported deaths, and a fourth author provided supplemental data (Mackenzie 1991). Singh 1982 reported that all children were successfully rehydrated; however one participant succumbed to a "severe pyrogenic reaction". el-Mougi 1994 reported one death in the IVT group due to pneumonia and ileus. Sharifi 1985 reported seven deaths: two in the ORT group and five in the IVT group. The cause of death was not reported although four of the seven deaths occurred in participants below the third percentile weight class. Mackenzie 1991 reported that no deaths occurred. All reported deaths occurred in low-middle income countries (UN Statistics).

Weight gain at discharge

There was no statistically significant difference in weight gain between treatment groups (WMD -26.33 g, 95% CI -206.92 to 154.26; 369 participants, 6 trials, Analysis 1.2), but there was substantial heterogeneity (I^2 90.8%). Nager 2002 reported means but not standard deviations for weight gain; substituting the minimum and maximum standard deviation from the other trials did not greatly influence the results. There was no statistically significant difference in percent weight gain between groups (WMD -0.26%, 95% CI -1.56 to 1.05, I^2 90.9%; 767 participants, 5 trials, Analysis 1.3).

Length of hospital stay for inpatients

Children treated with ORT spent less time in hospital (WMD -1.20 days, 95% CI -2.38 to -0.02, I^2 95.1%; 526 participants, 6 trials, Analysis 1.4). This was no longer statistically significant when we removed the outlying study (Gonzalez 1988).

Hyponatremia

The combined estimate of the two trials reporting on this did not show a significant difference (RD 1%, 95% CI -13 to 15, I^2 67.2%; 248 participants, Analysis 1.5).

Hypernatremia

The number of cases of hypernatremia was not statistically different between treatments (RD 0%, 95% CI -1 to 1, I^2 0%; 1062 participants, 10 trials, Analysis 1.6).

Duration of diarrhea

The mean length of diarrhea was not statistically different between groups (WMD -5.90 h, 95% CI -12.70 to 0.89, I^2 76.3%; 960 participants, 8 trials, Analysis 1.7).

Total fluid intake

Total fluid intake did not differ significantly between the two groups at six hours after starting treatment (WMD 32.09 mL/kg, 95% CI -26.69 to 90.88, I^2 99.9%; 985 participants, 8 trials, Analysis 1.8) or at 24 hours (73.45 mL/kg, 95% CI -31.78 to 178.69; I^2 99.8%; 835 participants, 7 trials, Analysis 1.9). The total fluid intake as measured in milliliters was also not significantly different at six hours (152.00 mL, 95% CI -64.21 to 368.21;37 participants, 1 trial, Analysis 1.10).

Complications and adverse events

There were statistically significantly more children with paralytic ileus in the ORT group when analyzed using the fixed-effect model (RD 3%, 95% CI 1 to 5, IVT risk 0%; I^2 43.8%; 670 participants, 2 trials) but not the random-effects model (RD 2%, 95% CI 0 to 5; Analysis 1.11). Thirty-three children (95% CI 20 to 100) need to be treated with IVT rather than ORT to prevent one case of paralytic ileus. The occurrence of phlebitis in the IVT group was statistically significant (RD -2%, 95% CI -4 to -1, I^2 0%; 877 participants, 5 trials, Analysis 1.11). Fifty children (95% CI 25 to 100) need to be treated with ORT rather than IVT to prevent one case of phlebitis. The IVT risk for phlebitis was 2.5%. Incidences of peri-orbital edema, seizures, and abdominal distention were not statistically significantly different between groups (see Analysis 1.11).

Sodium intake and sodium levels

Sodium intake at six hours was not statistically significantly different between the ORT and IVT groups (WMD 5.80 mmol/kg, 95% CI -1.48 to 13.07, I^2 99%; 607 participants, 3 trials, Analysis 1.12). Sodium levels at 24 hours were also not statistically significantly different (WMD 1.25 mmol/kg, 95% CI -0.56 to 3.07, I^2 88.5%; 992 participants, 7 trials, Analysis 1.13).

Subgroup and sensitivity analyses

We explored participant status (inpatient versus outpatient), state of nourishment (well nourished versus some malnourished), country's income (low-middle income versus high-income; UN Statistics), funding source (funded versus not reported), allocation concealment (adequate versus unclear), and Jadad scores (0, 1, 2) in a meta-regression using failure to rehydrate as the dependent variable. None were found to be statistically significant (Appendix 4). The remaining a priori subgroup comparisons were not reported by subgroup (age and extent of dehydration) and could not be analyzed. Although two trials reported that more than 20% of participants were severely dehydrated (Singh 1982; Tamer 1985), neither was considered an outlier.

The definition of "failure" varied by study. We evaluated the sensitivity of a more homogeneous definition in which we limited failures to children with persistent vomiting, having some level of dehydration persisting, and experiencing shock or seizures. (We excluded children with paralytic ileus, intussusception, cerebral palsy, septicemia, urinary tract infection, and duodenal ulcer from this analysis.) This post hoc failure definition was statistically significant and favoured IVT for the fixed-effect model (RD 2%, 95% CI +0 to 4) but not for the random-effects model (RD 2%, 95% CI -0 to 4) (Analysis 2.1). The heterogeneity was also reduced using our homogeneous definition (from 70% to 37%). Subsequently participants who had withdrawn or dropped out (only ORT participants) were reclassified as failures, as in a worst-case intention-to-treat analysis. With this analysis, there were statistically significant differences in failure rate between treatment groups that favored the IVT group when analyzed using the fixed-effect model (RD 3%, 95% CI 1 to 5) and the random-effects model (RD 3%, 95% CI 0 to 5) (Analysis 2.2). Heterogeneity was also reduced using this intention-to-treat analysis (from 70% to 48.1%).

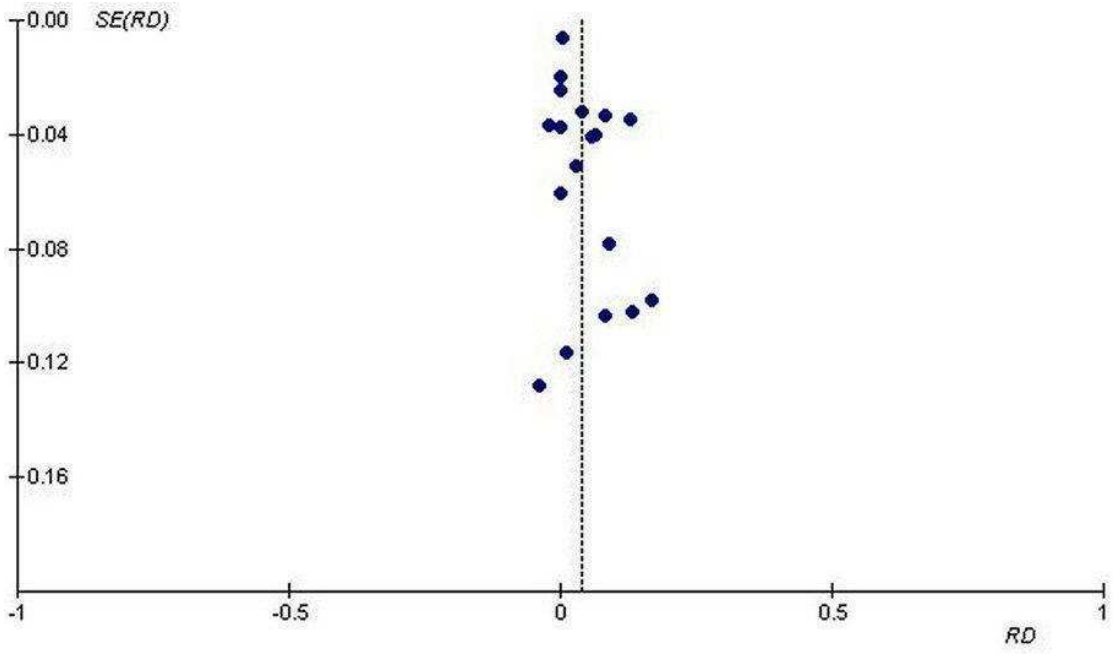
Since one of the assumptions for performing a meta-regression was not met (ie the constant variance assumption), we did not explore the osmolarity subgroups with this method. Instead, we divided the trials into low osmolarity (range 208 to 270 mOsmol/L) and high osmolarity (range 299 to 331 mOsmol/L) subgroups; these cut-offs were defined post hoc based on those used in another review (Hahn 2001). The difference found by the chi-square subgroup test (Deeks 2001) was statistically significant (P < 0.0001). The risk difference for the low osmolarity group was 1% (95% CI -1 to 2) and it was homogeneous (I^2 0%); for the high osmolarity group, the risk difference was 5% (95% CI 1 to 8) and had some heterogeneity (I^2 31.7%) (Analysis 2.3).

We used meta-regression to examine further subgroups: inclusion and exclusion criteria for participants with persistent vomiting (post-hoc) (Analysis 2.4) as well as the route of ORT administration (nasogastric versus oral versus a combination) (Analysis 2.5). Neither analysis resulted in statistically significant differences, although the analysis stratified by whether or not the trial excluded participants with persistent vomiting suggests that there may be differences given sufficient power.

Publication bias

The rank correlation test did not indicate any publication bias (r = 23, P = 0.41). The weighted regression analysis did show a significant indication of funnel plot asymmetry (bias = 0.9, P = 0.02). The trim-and-fill method indicated five missing studies; the adjustment to overall effect size rendered the new estimate non-significant by moving it closer to the null (RD 2%, 95% CI -1 to 4). The funnel plot appears somewhat asymmetrical (Figure 3); publication bias may be present suggesting that missing studies are more likely to favour ORT.

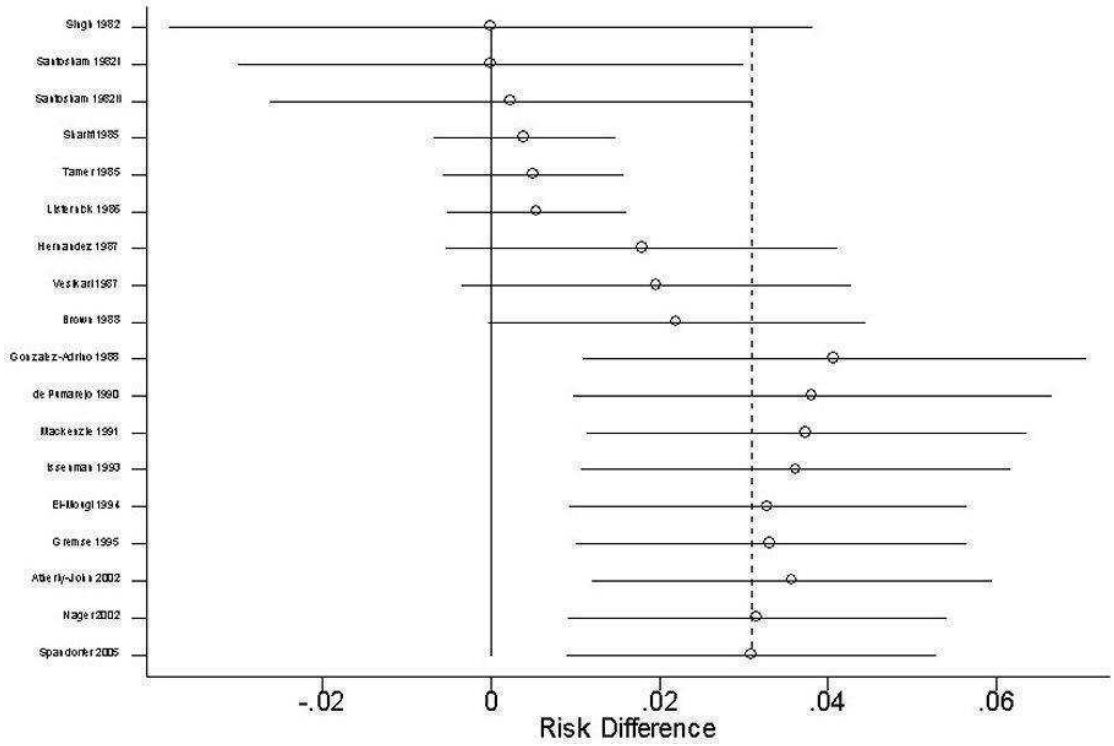
Figure 3. Funnel plot for primary outcome (failure to rehydrate) based on fixed-effect model



DISCUSSION

The most conservative model showed no important clinical differences in failure to rehydrate between ORT and IVT in terms of efficacy (RD 4%, fixed-effect model). For every 25 children treated with ORT, one would fail and require IVT (ie NNT = 25, CI 14 to 100). These overall findings are similar to those found in an earlier review (Gavin 1996). The results were consistent among different populations, such as children with different states of nourishment. Moreover the results for low osmolarity solutions, the currently recommended treatment by the World Health Organization, showed a lower failure rate for ORT that was not significantly different from the failure rate of IVT (RD 1%, NNT = 100). These results support existing practice guidelines recommending ORT with a low osmolarity solution as the first course of treatment in children with dehydration secondary to gastroenteritis. A cumulative meta-graph, which adds studies by ascending year, showed that the overall estimate is unlikely to change substantially with further trials (Figure 4). Overall we studied more than 1800 children providing adequate power to support the observed results.

Figure 4. Cumulative plot: failure cumulative by year



Most trials were small and of poor to moderate quality. The median quality score according to the Jadad scale was two. Because it is impossible to double blind studies on this topic, the quality of studies was limited to a maximum of three (rather than five). It is important to note that studies that are not double blind can lead to an overestimate of the treatment effect (Colditz 1989) and that this is an inherent limitation in this body of literature. While double blinding is probably not feasible in a trial comparing IVT and ORT, allocation can always be properly concealed. Allocation concealment was unclear in all but two trials; this can lead to an overestimate of treatment effects by as much as 40% (Schulz 1995). These factors could skew the results in favour of either ORT or IVT depending on the biases of the investigators.

Additionally, adverse events were not systematically sought in most of the trials. Though this meta-analysis had adequate power to support the efficacy of ORT, it lacks the power to detect serious but rare adverse events in either treatment group. However, analysis of the currently available data suggests that ORT and IVT are similar in safety profiles. Based on two trials, paralytic ileus occurred significantly more often in the ORT group (using the fixed-effect but not random-effects model); however it would not be deemed common enough to discourage the use of ORT. Further there was a statistically significant difference in the occurrence of phlebitis, but phlebitis cannot occur when an IV is not used, thus the statistical significance does not equate to a clinically important difference.

In applying the evidence to clinical practice, the objective output of the meta-analysis must be weighed with other less easily measured factors that support the use of ORT. On a theoretical basis, IVT should be able to replace the fluid already lost, as well as keep up with the ongoing losses even if those losses are through vomiting, diarrhea, or third spacing within the lumen of the gut. For IVT to be effective, the correct fluid and rate needs to be chosen, for errors in either of these parameters can lead to harm as severe as death. IVT is viewed as the gold standard for children in shock or with severe dehydration, and most of the papers reviewed excluded children from their studies on this basis. Besides the complication of IVT fluid type and rate, starting an intravenous intervention causes pain, the attempt can be unsuccessful, phlebitis (inflammation of the vein) can occur, a cellulitis can result and the intravenous can go interstitial resulting in the intravenous fluid going into the immediate surrounding tissue rather than into the vein and therefore the intravascular space. ORT can be performed by almost anyone with very little training and has the advantage that a child's thirst can moderate the quantity and rate of fluid administration. It does not work if the fluid is not being absorbed

by the gut (paralytic ileus), and in some cases, the rate of diarrhea increases as oral fluid rate increases so that the child remains in a net negative fluid balance. Once the ORT is administered via a nasogastric tube, some of the theoretical advantages of ORT disappear, and some theoretical disadvantages need to be considered. The child is no longer able to control the rate or amount of fluid intake and so operator errors may occur just as they do with IVT. Errors in placement of the nasogastric tube can occur; the most severe of these is passing the nasogastric tube into the trachea so that the fluid is going into the lungs rather than the stomach. The passing of a nasogastric tube can result in a bleeding nose and discomfort. The tube does not always pass easily on the first attempt. There is evidence to suggest that ORT is less costly than IVT and can be administered as rapidly (Nager 2002). A randomized controlled trial has demonstrated that the use of ORT in a high-income country pediatric emergency department resulted in statistically significantly lower costs, less time spent in the emergency department, and a more favorable impression of caregivers for this form of therapy (Atherly-John 2002).

Though there was little statistical heterogeneity between trials on failure to rehydrate when the outlying trial was omitted (Gonzalez 1988) (I^2 43%), there were important clinical variations and large heterogeneity in most of the secondary outcomes. Rehydration was accomplished at different rates, by different routes, and with various solutions in different populations. Comparisons of different oral rehydration solutions have been the subject of other reviews (Fontaine 2000; Hahn 2001). A meta-analysis comparing reduced osmolarity ORT (< 270 mOsmol/L) with the standard solution (311 mOsmol/L) showed that unscheduled intravenous infusion was statistically significantly less in the reduced osmolarity group (odds ratio 0.59, 95% CI 0.45 to 0.79) (Hahn 2001). Our post-hoc (between-study) analysis comparing low and high osmolarity solutions supported these findings.

Another source of variation was the definition of "treatment failure". We examined the effect of different treatment failure definitions through a post hoc refined definition analysis and found that it reduced heterogeneity and the therapeutic benefits of IVT as compared with ORT (from 4% to 2%). The intention-to-treat version of this model involved reclassifying seven ORT withdrawals as failures; this model also reduced heterogeneity and benefits for IVT (from 4% to 3%). If the seven withdrawals were systematically related to treatment benefit, then this intention-to-treat analysis is less biased.

One trial had a statistically significantly greater failure rate (Gonzalez 1988). The trial authors attributed it to the fact that many of the children who failed were younger than six months of age. (This trial was the only one to include neonates.) The authors argued that the burden of illness can be more severe in younger infants. Our data neither prove nor disprove this statement. When we removed this trial from the analysis, the remaining trial results were homogeneous and the overall risk difference shifted towards the null.

The results may not be generalizable to all children with dehydration secondary to gastroenteritis but may be generalizable only to those with dehydration secondary to diarrhea. The reader must also recognize that most of the trials excluded children in shock, severe dehydration, and paralytic ileus since IVT is the indicated treatment for these clinical scenarios. A post hoc look between trials with different inclusion and exclusion criteria suggests that there may be an important difference in response to ORT among participants that vomited and did not vomit. The risk difference for trials that excluded participants with persistent vomiting was 0% (95% CI -3 to 3) as compared with 4% (95% CI -5 to 13) in trials that did not exclude such participants (Analysis 01.17). The issue of how vomiting affects the efficacy of ORT needs further study. However, in practice treatment failure only means than one switches to IVT.

AUTHORS' CONCLUSIONS

Implications for practice

There were no important clinical differences between ORT and IVT for rehydration secondary to acute gastroenteritis in children. It seems reasonable that children presenting for medical care with mild to moderate dehydration secondary to acute gastroenteritis should initially be treated with ORT. Should treatment fail, then IVT may be used. In children who have persistent vomiting, ORT may be used, but the child must be closely observed for proof of successful treatment.

For every 25 children treated with ORT, one would fail and require IVT. Clinicians and families need to apply this evidence to individual situations in order to decide whether they are willing to accept this minimal risk.

Implications for research

Further research comparing ORT and IVT for children with dehydration secondary to gastroenteritis is not warranted and may be unethical. If undertaken, further research should focus on evaluating the efficacy of nasogastric rehydration in children who have persistent vomiting.

ACKNOWLEDGEMENTS

We thank Ellen Crumley, Marlene Dorgan, and Carol Friesen for their assistance with searching, Ben Vandermeer for assistance rerunning the statistical analysis, and Maria Ospina for assistance with interpretation of Spanish articles. The editorial base for the Cochrane Infectious Diseases Group is funded by the UK Department for International Development (DFID) for the benefit of developing countries.

REFERENCES

References to studies included in this review

Atherly-John 2002 *{published data only}*
Atherly-John YC, Cunningham SJ, Crain EF. A randomized trial of oral vs intravenous rehydration in a pediatric emergency department. *Archives of Pediatrics & Adolescent Medicine* 2002;**156**(12):1240–3.

Brown 1988 *{published data only}*
Brown KH, Gastanaduy AS, Saavedra JM, Lembcke J, Rivas D, Robertson AD, et al.Effect of continued oral feeding on clinical and nutritional outcomes of acute diarrhea in children. *Journal of Pediatrics* 1988;**112**(2):191–200.

de Pumarejo 1990 *{published data only}*
de Pumarejo MM, Lugo CE, Alvarez-Ruiz JR, Colon-Santini JL. Oral rehydration: experience in the management of patients with acute gastroenteritis in the emergency room at the Dr. Antonio Ortiz pediatric hospital [Rehidratacion oral: experiencia en el manejo de pacientes con gastroenteritis auguda en la sala de emergencia hospital pediatrico Dr. Antonio Ortiz]. *Boletin de la Asociacion Medica de Puerto Rico* 1990;**82**(5):227–33.

el-Mougi 1994 *{published data only}*
el-Mougi M, el-Akkad N, Hendawi A, Hassan M, Amer A, Fontaine O, et al.Is a low-osmolarity ORS solution more efficacious than standard WHO ORS solution?. *Journal of Pediatric Gastroenterology and Nutrition* 1994;**19**(1):83–6.

Gonzalez 1988 *{published data only}*
Gonzalez-Adriano SR, Valdes-Garza HE, Garcia-Valdes LC. Oral hydration versus intravenous hydration in patients with acute diarrhea. *Boletin Medico del Hospital Infantil de Mexico* 1988;**45**(3):165–72.

Gremse 1995 *{published data only}*
Gremse DA. Effectiveness of nasogastric rehydration in hospatilized children with acute diarrhea. *Jouranl of Pediatric Gastroenterology and Nutrition* 1995;**21**(2):145–8.

Hernandez 1987 *{published data only}*
Hernandez A, Jaramillo C, Ramirez R, Gomez G, Franco D. Treatment of acute diarrhea in children. Comparative study of three oral rehydration solutions and I.V. therapy in Colombia [Tratamiento de diarrea aguda en ninos. Estudio comparativo de tres soluciones de rehidratacion oral y venoclisis en Colombia]. *Boletin de la Oficina Sanitaria Panamericana* 1987;**102**(6):606–16.

Issenman 1993 *{published data only}*
Issenman RM, Leung AK. Oral and intravenous rehydration of children. *Canadian Family Physician* 1993;**39**:2129–36.

Listernick 1986 *{published data only}*
Listernick R, Zieserl E, Davis AT. Outpatient oral rehydration in the United States. *American Journal of Disease in Childhood* 1986;**140**(3):211–5.

Mackenzie 1991 *{published data only}*
Mackenzie A, Barnes G. Randomised controlled trial comparing oral and intravenous rehydration therapy in children with diarrhoea. *BMJ* 1991;**303**(6799):393–6.

Nager 2002 *{published data only}*
Nager AL, Wang VJ. Comparison of nasogastric and intravenous methods of rehydration in pediatric patients with acute dehydration. *Pediatrics* 2002;**109**(4):566–72.

Santosham 1982i *{published data only}*
Santosham M, Daum RS, Dillman L, Rodriguez JL, Luque S, Russell R, et al.Oral rehydration therapy of infantile diarrhea: a controlled study of well-nourished children hospitalized in the United States and Panama. *New England Journal of Medicine* 1982;**306**(18):1070–6.

Santosham 1982ii *{published data only}*
Santosham M, Daum RS, Dillman L, Rodriguez JL, Luque S, Russell R, et al.Oral rehydration therapy of infantile diarrhea: a controlled study of well-nourished children hospitalized in the United States and Panama. *New England Journal of Medicine* 1982;**306**(18):1070–6.

Sharifi 1985 *{published data only}*
Sharifi J, Ghavami F, Z Nowrouzi, Fouladvand B, Malek M, Rezaeian M, et al.Oral versus intravenous reheydration therapy in severe gastroenteritis. *Archives of Disease in Childhood* 1985;**60**(9):856–60.

Singh 1982 *{published data only}*
Singh M, Mahmoodi A, Arya LJ, Azamy S. Controlled trial of oral versus intravenous rehydration in the management of acute gastroenteritis. *Indian Journal of Medical Research* 1982;**75**:691–3.

Spandorfer 2005 *{published data only}*
Spandorfer PR, Alessandrini EA, Joffe MD, Localio R, Shaw KN. Oral versus intravenous rehydration of moderately dehydrated children: a randomized, controlled trial. *Pediatrics* 2005;**115**(2):295–301.

Tamer 1985 *{published data only}*
Ross MB. Erratum: Oral rehydration. *Journal of Pediatrics* 1986;**108**(1):160.
Tamer AM, Friedman LB, Maxwell SRW, Cynamon HA, Perez HN, Cleveland WW. Oral rehydration of infants in a large urban U.S. medical center. *Journal of Pediatrics* 1985; **107**(1):14–9.

Vesikari 1987 *{published data only}*
Vesikari T, Isolauri E, Baer M. A comparative trial of rapid oral and intravenous rehydration in acute diarrhoea. *Acta Paediatria Scandanavia* 1987;**76**(2):300–5.

References to studies excluded from this review

Alam 1987 *{published data only}*
Alam AN, Sarker SA, Molla AM, Rahaman MM, Greenough III WB. Hydrolysed wheat based oral rehydration solution for acute diarrhoea. *Archives of Disease in Childhood* 1987; **62**(5):440–4.

Carpenter 1982 *{published data only}*
Carpenter CC. Oral rehydration: is it as good as parenteral therapy?. *New England Journal of Medicine* 1982;**306**(18): 1103–4.

Gavin 1996 *{published data only}*
Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. *Pediatrics* 1996;**98**(1):45–51.

Hirschhorn 1972 *{published data only}*
Hirschhorn N, Cash RA, Woodward WE, Spivey GH. Oral fluid therapy of Apache children with acute infectious diarrhoea. *Lancet* 1972;**2**(7766):15–8.

Isolauri 1985 *{published data only}*
Isolauri E, Vesikari T. Oral rehydration, rapid feeding, and cholestyramine for treatment of acute diarrhea. *Journal of Pediatric Gastroenterology and Nutrition* 1985;**4**(3):366–74.

Jan 1997 *{published data only}*
Jan A, Rafi M, Mustafa S, Rasmussen ZA, Thobani S, Badruddin SH. Evaluation of dowdo (wheat-milk gruel) in children with acute diarrhoea. *Jouranl of Pakistan Medical Association* 1997;**47**(1):12–6.

Kist-van Holthe 1999 *{published data only}*
Kist-van Holthe JE, van der Heijden AJ. Dehydration due to gastroenteritis in children [Dehydratie ten gevolge van gastro–enteritis bij kinderen]. *Nederlands Tijdschrift Voor Geneeskunde* 1999;**143**(4):193–6.

Klish 1985 *{published data only}*
Klish WJ. Use of oral fluids in treatment of diarrhea. *Pediatrics in Review* 1985;**7**(1):27–30.

Lexomboon 1994 *{published data only}*
Lexomboon U, Harikul S, Lortholary O. Control randomized study of rehydration/rehydration with dioctahedral smectite in ambulatory Thai infants with acute diarrhea. *Southeast Asian Journal of Tropical Medicine and Public Health* 1994;**25**(1):157–62.

Mackenzie 1988 *{published data only}*
Mackenzie A, Barnes G. Oral rehydration in infantile diarrhoea in the developed world. *Drugs* 1988;**36 Suppl 4**: 48–60.

Mackenzie 1989 *{published data only}*
Mackenzie A, Barnes G, Shann F. Clinical signs of dehydration in children. *Lancet* 1989;**2**(8663):605–7.

Mahalanabis 1972 *{published data only}*
Mahalanabis P, Brayton JB, Mondal A, Pierce NF. The use of Ringer's lactate in the treatment of children with cholera and acute noncholera diarrhoea. *Bulletin of the World Health Organization* 1972;**46**(3):311–9.

Orenstein 1986 *{published data only}*
Orenstein SR. Enteral versus parenteral therapy for intractable diarrhea of infancy: a prospective, randomized trial. *The Journal of Pediatrics* 1986;**109**(2):277–86.

Patra 1989 *{published data only}*
Patra FC, Sack DA, Islam A, Alam AN, Mazumder RN. Oral rehydration formula containing alanine and glucose for treatment of diarrhoea: a controlled trial. *BMJ* 1989; **298**(6684):1353–6.

Rautanen 1993 *{published data only}*
Rautanen T, el-Radhi S, Vesikari T. Clinical experience with a hypotonic oral rehydration solution in acute diarrhoea. *Acta Paediatricia* 1993;**82**(1):52–4.

Reid 1996 *{published data only}*
Reid SR, Bonadio WA. Outpatient rapid intravenous rehydration to correct dehydration and resolve vomiting in children with acute gastroenteritis. *Annals of Emergency Medicine* 1996;**28**(3):318–23.

Samadi 1983 *{published data only}*
Samadi AR, Islam R, Huq MI. Replacement of intravenous therapy by oral rehydration solution in a large treatment centre for diarrhoea with dehydration. *Bulletin of the World Health Organization* 1983;**61**(3):471–6.

Sarker 1995 *{published data only}*
Sarker SA, Majid N, Mahalanabis D. Alanine- and glucose-based hypo-osmolar oral rehydration solution in infants with persistent diarrhoea: a controlled trial. *Acta Paediatria* 1985;**84**(7):775–80.

Srivastava 1985 *{published data only}*
Srivastava VK, Arya H, Uppal SS, Rath B, Laisram N. Comparison of oral and intravenous rehydration among hospitalized children with acute diarrhoea. *Journal of Diarrhoea Disease Research* 1985;**3**(2):92–5.

Tripp 1980 *{published data only}*
Tripp JH, Harries JT. UNICEF/W.H.O. glucose electrolyte solution not always appropriate. *Lancet* 1980;**2**(8198):793.

Weizman 1983 *{published data only}*
Weizman Z, Schmueli A, Deckelbaum RJ. Continuous nasogastric drip elemental feeding. Alternative for prolonged parenteral nutrition in severe prolonged diarrhea. *American Journal of Disease in Childhood* 1983;**137**(3): 253–5.

Additional references

AAP 1996
American Academy of Pediatrics, Provisional committee on quality improvement, Subcommittee on acute gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics* 1996;**97** (3):424–35.

Armon 2000
Armon K, Elliott EJ. Acute gastroenteritis. In: Moyer VA, Elliott EJ, Davis RL, Gilbert R, Klassen T, Logan S, Mellis C, Williams K editor(s). *Evidence based pediatrics and child health*. 1st Edition. London: BMJ Books, 2000:273–86.

Baldassano 1991
Baldassano RN. Chronic diarrhea. A practical approach for the pediatrician. *Pediatric Clinics of North America* 1991;**38** (3):667–86.

Begg 1994
Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;**50**(4): 1088–101.

Bern 1992
Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bulletin of the World Health Organization* 1992;**70** (6):705–14.

Colditz 1989
Colditz GA, Miller JN, Mosteller F. How study design affects outcomes in comparisons of therapy. I: Medical. *Statistics in Medicine* 1989;**8**(4):411–54.

DARE 2002
Efficacy of glucose-based oral rehydration therapy. [Abstract 961213] Database of Abstracts of Reviews of Effectiveness. Abstract of Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. Pediatrics. 1996. 98(1). 45-51. *The Cochrane Library* 2004, Issue 1.

Deeks 2001
Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG editor(s). *Systematic reviews in health care: meta-analysis in context*. 2nd Edition. London: BMJ Books, 2001:300.

Duggan 1992
Duggan C, Santosham M, Glass RI. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. Centers for Disease Control and Prevention. *MMWR. Recommendations and reports* 1992;**41** (RR-16):1–20.

Duval 2001
Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2001;**56**(2):455–63.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

Fonseca 2004
Fonseca BK, Holdgate A, Craig JC. Enteral vs intravenous rehydration therapy for children with gastroenteritis: a meta-analysis of randomized controlled trials. *Archives of Pediatrics & Adolescent Medicine* 2004;**158**(5):483–90.

Fontaine 2000
Fontaine O, Gore SM, Pierce NF. Rice-based oral rehydration solution for treating diarrhoea. *Cochrane Database of Systematic Reviews* 2000, Issue 2. [DOI: 10.1002/14651858.CD001264.pub2]

Gangarosa 1992
Gangarosa RE, Glass RI, Lew JF, Boring JR. Hospitalizations involving gastroenteritis in the United States, 1985: the special burden of the disease among the elderly. *American Journal of Epidemiology* 1992;**135**(3):281–90.

Garland 1992
Garland FS, Dunne WM Jr, Havens P, Hintermeyer M, Bozzette MA, Wincek J, et al.Peripheral intravenous catheter complications in critically ill children: a prospective study. *Pediatrics* 1992;**89**(6 Pt 2):1145–50.

Glass 1991
Glass RI, Lew JF, Gangarosa RE, LeBaron CW, Ho MS. Estimates of morbidity and mortality rates for diarrheal diseases in American children. *Journal of Pediatrics* 1991; **118**(4 (Pt 2)):S27–33.

Goepp 1993
Goepp JG, Katz SA. Oral rehydration therapy. *American Family Physician* 1993;**47**(4):843–51.

Hahn 2001
Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration due to diarrhoea in children: systematic review. *BMJ* 2001;**323** (7304):81–5.

Higgins 2003
Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327** (7414):557–60.

Higgins 2005a
Higgins JPT, Green S, editors. Measures of relative effect: the risk ratio and odds ratio. Cochrane Handbook for Systematic Reviews of Interventions 8.2.1.2 [updated May 2005]; Section 8. www.cochrane.org/resources/handbook/hbook.htm. Chichester, UK: John Wiley & Sons, Ltd., (accessed 14 February 2006).

Higgins 2005b
Higgins J, Green S, editors. Highly sensitive search strategies for identifying reports of randomized controlled trials in MEDLINE. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]; Appendix 5b. www.cochrane.org/resources/handbook/hbook.htm (accessed 1 March 2006).

Jadad 1996
Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al.Assessing the quality of reports of randomized clinical trials: is blinding necessary?. *Controlled Clinical Trials* 1996;**17**(1):1–12.

Oxman 1991
Oxman A, Guyatt GH. Validation of an index of the quality of review articles. *Journal of Clinical Epidemiology* 1991;**44** (11):1271–8.

Ozuah 2002
Ozuah PO, Avner JR, Stein RE. Oral rehydration, emergency physicians, and practice parameters: a national survey. *Pediatrics* 2002;**109**(2):259–61.

Review Manager 4.2
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 4.2 for Windows. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2003.

Santosham 1991
Santosham M, Greenough WB 3rd. Oral rehydration therapy: a global perspective. *Journal of Pediatrics* 1991;**4**(4 (Pt 2)):S44–51.

Schulz 1995
Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**(5):408–12.

Snyder 1991

Snyder JD. Use and misuse of oral therapy for diarrhea: comparison of US practices with American Academy of Pediatrics recommendations. *Pediatrics* 1991;**87**(1):28–33.

Stata 7.0

Stata Corporation. Intercooled Stata 7.0. for Windows 98/95/NT. College Station, Texas: Stata Corporation.

UN Statistics

United Nations Statistics Division. Economic trade and other groupings of countries or areas. New York, NY: United Nations Statistics Division. www.un.org/Depts/unsd/methods/m49groupe.htm#ldcs (accessed 14 November 14 2001).

WHO 1996

World Health Organization. The challenge of diarrhoeal and acute respiratory disease control. *Point of Fact No 77*. Geneva: World Health Organization, 1996:1–4.

WHO 2000

World Health Organization, Child and Adolescent Health and Development. Child health epidemiology. www.who.int/child-adolescent-health/overview/child_health/child_epidemiology.htm (accessed 6 May 2002).

WHO 2002

World Health Organization, Dept. of Child and Adolescent Health and Development. *Reduced osmolarity : oral rehydration salts (ORS) formulation : a report from a meeting of experts jointly organised by UNICEF and WHO : UNICEF house, New York, USA, 18 July 2001 [WHO/FCH/CAH/01.22]*. Geneva: World Health Organization, 2002.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Atherly-John 2002

Methods	Randomized controlled trial Length of follow up: 2 to 4 days Withdrawals: none Described as an intention-to-treat study Score on Jadad scale: 3
Participants	Number of participants: 34 Inclusion criteria: previously healthy patients aged 3 months to 17 years with acute gastroenteritis for < 1 week with associated dehydration (children must meet > = 4 standard criteria for moderate dehydration); children presented to a pediatric emergency department Exclusion criteria: patients with protracted vomiting, severe dehydration, or shock; chronic illness; and those requiring IV access for other reasons
Interventions	1. IV (16 participants): initial bolus 20 mL/kg isotonic sodium chloride solution over 30 minutes, second bolus of isotonic sodium chloride solution if necessary; followed by IV solution of 5% dextrose in 0.45% saline for children > = 2 years and 5% dextrose in 0.33% saline in children < 2 years at rate of 1.5 x daily maintenance 2. ORT (18 participants): commercially prepared oral maintenance electrolyte solutions at rate of 5 mL every 5 mins if < 4 years and 10 mL every 5 mins if > = 4 years
Outcomes	1. Duration of stay in emergency department (primary outcome) 2. Staff time 3. Hospital admission rate 4. Relapse after discharge 5. Parental satisfaction Failure of ORT defined as having vomited > = 3 times after initiation of ORT
Notes	Trial location: USA Source of funding: not stated

Brown 1988

Methods	Randomized controlled trial Length of follow up: 14 days Withdrawals and losses to follow up: 10 participants withdrew before 5 days (3 participants withdrawn by parents, 3 developed measles after admission, 3 developed second episode of diarrhea or other infection, 1 protocol violation) Withdrawals not included in analysis Score on Jadad scale: 2
Participants	Number of participants: 138 Inclusion criteria: males 3 to 36 months with diarrhea for < 60 h (> 3 liquid stools during previous 24 h) Exclusion criteria: females; > 1 dose of antibiotics; > 1 breastfeeding/day; diarrhea in previous 3 weeks; poor nutritional status

Brown 1988 (*Continued*)

Interventions	Rehydration: 1. IV (34 participants) 2 to 4. ORT (94 participants) (GES) Initial fluid deficit administered within first 2 to 4 h, then additional solution given to replace volume for volume losses orally or intravenously depending on group Maintenance: 1. GES-IV to maximum 120 mL/kg/day for days 1 and 2; days 3 to 4 offered CSO half strength; days 5 to 6 CSO full strength 2. Full strength CSO formula to maximum of 110 kcal/kg body weight/day 3. Half strength CSO formula to maximum of 55 kcal/kg/day for days 1 to 2 then full-strength formula 4. GES formula 150 mL/kg/day for days 1 to 2, half-strength CSO days 3 to 4, full strength CSO days 5 to 6
Outcomes	1. Therapeutic failure (recurring dehydration; worsening electrolyte abnormalities; prolonged severe diarrhea) 2. Speed of rehydration 3. Severity of diarrhea (fecal weight, serum electrolytes) 4. Duration of diarrhea 5. Absorption of macronutrients and retention of nitrogen 6. Weight gain Outcomes 3 to 6 presented only for participants "successfully managed according to their original dietary groups"
Notes	Trial location: Peru Source of funding: WHO, Nestle, US Agency for International Development

de Pumarejo 1990

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals or losses to follow up: none Score on Jadad scale: 1
Participants	Number of participants: 31 Inclusion criteria: outpatients aged 2 weeks to 4 years with acute diarrhea of rapid onset lasting for less than 7 days and clinical signs of dehydration; all patients were well nourished; in the IV group, 12/14 had a history of vomiting and 10/17 in the ORT group; in the IV group, 12/14 were mildly and 2/14 were moderately dehydrated; in the ORT group, 14/17 were mildly and 3/17 were moderately dehydrated Exclusion criteria: intractable vomiting; shock; malnutrition; paralytic ileus
Interventions	1. "Conventional IV" (14 participants): 1/5 parts of total volume in 2 h (isotonic); 2/5 parts/volume over 10 h then received remaining 2 parts over 12 h 2. ORT (17 participants): rate of 20 cc/kg/h for 2 h orally; 10 cc/kg/h in periods of 6 h, administered every 2 h or as wanted; after first 6 to 12 h, rehydrated participants went to a maintenance solution of Pedialyte (45 mEq sodium) and then soy milk (30 cal/oz)
Outcomes	1. Failures of ORT (not defined) 2. Complications 3. Sodium concentration 4. Weight gain 5. Total fluid intake at 6 and 24 h

de Pumarejo 1990 (*Continued*)

Notes	Trial location: Puerto Rico (USA) Source of funding: Ross Laboratories supplied Pedialyte and Rehydralyte

el-Mougi 1994

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Score on Jadad scale: 1
Participants	Number of participants: 61 Inclusion criteria: 61 males aged 3 to 24 months; not explicitly stated as inpatients; all patients fully weaned, well nourished, and had diarrhea for < 72 h; all participants moderately dehydrated Exclusion criteria: those without dehydration and those with severe dehydration, bloody diarrhea, or other severe infections
Interventions	1. IV (20 participants): get IV for 24 h then ORT (standard WHO solution) 2. ORT: standard WHO solution (21 participants) with 1 L water 3. ORT: diluted WHO solution (20 participants) diluted with 1.5 L water Appropriate diet started after rehydration (~4 to 6 h); those receiving standard WHO solution were allowed to drink plain water after rehydration; route of administration of ORT: oral
Outcomes	1. Duration of diarrhea 2. Stool volume 3. Weight gain 4. Total fluid intake at 6 and 24 h (6 h data provided by authors) 5. Failure (not defined)
Notes	Trial location: Egypt Source of funding: not stated

Gonzalez 1988

Methods	Randomized controlled trial Length of follow up: 24 h Withdrawals and losses to follow up: none Score on Jadad scale: 1
Participants	Number of participants: 200 Inclusion criteria: inpatients aged 1 day to 5 years with diarrhea for < 15 days and signs of dehydration; in the IV group, 78/100 were mildly and 22/100 were moderately dehydrated; in the ORT group, 85/100 were mildly, 14/100 were moderately, and 1 was severely dehydrated Exclusion criteria: received previous treatment; referrals from other institutions; shock; septicemia; paralytic ileus; and abdominal distension
Interventions	1. IV (100 participants): mildly dehydrated get 150 to 180 mL/kg/24 h; moderately dehydrated get IV for 1 h at 20 to 30 mL/kg, then 200 to 250 mL/kg/24 h

Gonzalez 1988 (*Continued*)

	2. ORT (100 participants): WHO/UNICEF solution; mildly dehydrated received 75 mL/kg for 6 h; moderately dehydrated received 150 mL/kg for 6 h ORS administered orally, and nasogastric if required
Outcomes	1. Duration of diarrhea 2. Complications 3. Sodium concentration 4. Failures (not defined)
Notes	Trial location: Mexico Source of funding: not stated

Gremse 1995

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Score on Jadad scale: 1
Participants	Number of participants: 24 Inclusion criteria: inpatients aged 2 to 24 months with diarrhea for < 5 days; oral rehydration had been attempted in all patients in the emergency department or clinic prior to enrollment in study; all patients were moderately dehydrated; vomiting was present in all patients Exclusion criteria: those in hypovolemic shock; sepsis; ileus; seizures; metabolic disease; or intestinal obstruction
Interventions	1. IV (12 participants): IV fluid contained 5% dextrose and 77 mEq/L sodium chloride; after child voided, 20 mEq/L potassium chloride was added to the IV fluid 2. ORT (12 participants): Rehydralyte was administered by continuous nasogastric infusion at a rate sufficient to replace participant's estimated fluid deficit within 6 h, at which time the nasogastric tube was removed Following rehydration, participants in both groups received Pedialyte to replace ongoing stool losses and lactose-free formula; decision to initiate formula feeding at the discretion of individual physician
Outcomes	1. Failure (participants required IVT due to persistent vomiting) 2. Duration of rehydration 3. Duration of vomiting after admission (h) 4. Duration of diarrhea after admission (h) 5. Formula volume (mL/kg/day) 6. Duration of hospitalization 7. Cost of hospitalization 8. Daily cost of hospitalization
Notes	Trial location: USA Source of funding: Ross Labs

Hernandez 1987

Methods	Randomized controlled trial Length of follow up: 96 h Withdrawals and losses to follow up: none reported Score on Jadad scale: 1
Participants	Number of participants: 144 Inclusion criteria: < 5 years of age; acute diarrhea; dehydration grades I and II; severe pathology associated with diarrhea (sepsis, severe cardio-respiratory disorder, consciousness disorders) Exclusion criteria: none reported
Interventions	1. IV (36 participants): administered according to hospital protocol based on Snyder method (no other details provided) 2 to 4. ORT (144 participants): 100 mL/kg given in 12 portions offered every 1/2 hour for 6 h (grade I dehydration) ; 200 mL/kg given in 12 portions offered every 1/2 h over 6 h (grade II dehydration) For all groups, after hydration, breastfeeding and use of formula were allowed; for cases with lactose intolerance, lactose-free and/or soy milk were used
Outcomes	1. Failure of oral rehydration: profuse vomiting or diarrhea with loss superior to ingestion or inadequate hydration after 24 h of ORT 2. Relapse: dehydration within 72 h once hydrated 3. Time to rehydration 4. Hyponatremia and hypernatremia
Notes	Trial location: Colombia Source of funding: not stated

Issenman 1993

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Intention-to-treat analysis (though not reported as such) Score on Jadad scale: 2
Participants	Number of participants: 42 randomized; 1 from each group later excluded because antibiotics were prescribed after entry Inclusion criteria: inpatients, 6 to 31 months, well nourished, with mild to moderate dehydration; 8 in each group had rotavirus; history of vomiting existed in 16/18 of the IV group and 22/22 in the ORT group; acute diarrhea defined as more than 3 stools/day for < 5 days (stool takes shape of container) Exclusion criteria: chronic disease; chronic diarrhea; those with continuous forceful vomiting; shock; hypernatremia or severe dehydration
Interventions	1. IV (18 participants): 20 cc/kg bolus x 1 h, then IV fluids to replace fluid deficit and maintain fluid requirements for 8 to 12 h; if rehydrated in 8 to 12 h, IV discontinued and maintenance solution freely fed 2. ORT (22 participants): 20 cc/kg bolus orally x 1 h, replacement and maintenance over next 8 to 12 h. ORT ad lib if fully rehydrated at 12 h Neither group received food or beverages during therapy

Issenman 1993 (*Continued*)

Outcomes	1. Failures (participant refused ORT solution, failed to return to normal hydration by 24 h after entry, or failed to achieve adequate maintenance oral intake) 2. Weight gain 3. Side effects 4. Total fluid intake at 24 h
Notes	Trial location: Canada Source of funding: Ross Labs

Listernick 1986

Methods	Randomized controlled trial Length of follow up: 48 h after study conclusion Withdrawals and losses to follow up: none Score on Jadad scale: 2 2 children had urinary tract infections and were the failures
Participants	Number of participants: 29 Inclusion criteria: outpatients aged 3 to 24 months; all patients were well nourished, dehydrated, and had acute diarrhea for < 5 days; 10/14 in IV group and 11/15 in ORT group had rotavirus; history of vomiting was present in all of the patients; acute diarrhea defined as < 5 days increased frequency or more liquid consistency (stool takes shape of container) Exclusion criteria: those requiring intensive care, or having a serum sodium concentration of > 160 mEq/L
Interventions	1. IV (14 participants): 20 cc/kg for 1 h then rehydrated over 8 h 2. ORT (15 participants): 20 cc/kg of 60-GES via orally for 1 h then ad lib for 8 h One child in ORT group got IV prior to ORT
Outcomes	1. Failures (failed to achieve normal state of hydration by 12 h or adequate oral intake due to vomiting or refusal to drink) 2. Time to rehydrate 3. Weight gain 4. Complications 5. Side effects 6. Sodium concentration 7. Total fluid intake at 24 h
Notes	Trial location: USA Source of funding: Ross Labs

Mackenzie 1991

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: 7 Not intention-to-treat analysis (7 withdrawals not accounted for in analysis) Score on Jadad scale: 2
Participants	Number of participants: 111 enrolled; 104 analyzed Inclusion criteria: previously healthy children aged 3 to 36 months admitted with diarrhea for 7 days or less, clinical signs of dehydration, not in shock; 7 were later withdrawn: 2 had intussusception (IV), 2 had sepsis (ORT), 1 had urinary tract infection (ORT), 1 had an ulcer (ORT), and 1 due to parental request (ORT); 32/52 in IV and 27/52 in the ORT group had rotavirus; all patients had acute gastroenteritis; in the IV group, 36/52 were mildly and 16/52 were moderately dehydrated; in the ORT group, 31/52 were mildly and 21/52 were moderately dehydrated; history of vomiting was present in 49/52 in the IV group and 45/52 of the ORT group Exclusion criteria: severe dehydration and shock, and chronic illness
Interventions	1. IV (52 participants): deficit replaced over 24 h; patients allowed to drink oral rehydration solution 2. ORT (52 participants): deficit replaced over 6 h; 14 refused orally, thus administered via nasogastric route Breastfeeding was continued, but no solids until rehydrated
Outcomes	1. Failures (if pediatric gastroenterologist thought the persistent vomiting was severe enough to prevent rehydration or weight loss of 2% after admission or impending circulatory failure) 2. Time to rehydrate 3. Number of stools 4. Frequency of stools 5. Complications 6. Side effects 7. Sodium concentration 8. Total fluid intake at 6 and 24 h
Notes	Trial location: Australia Source of funding: not stated

Nager 2002

Methods	Randomized controlled trial Length of follow up: 24 hours after discharge Not an intention-to-treat analysis (6 withdrawals from secondary outcomes, none for the primary) Score on Jadad scale: 2
Participants	Number of participants: 96 randomized; 90 analyzed (completed trial) Inclusion criteria: outpatients; aged 3 to 36 months; all mild to moderate dehydration; diarrhea < = 7 days; vomiting and/or diarrhea; 3 diagnosed with urinary tract infections Exclusion criteria: those with severe dehydration (> 10%), intractable vomiting, shock, suspected intussusception, appendicitis, malrotation, recent trauma, meningitis, congestive heart failure, or if evidence of these diagnoses appeared as the study progressed; those with chronic disease were also excluded
Interventions	1. IV (48 participants randomized, 44 analyzed): continuous infusion of 50 mL/kg of normal saline over 3 h 2. Nasogastric (48 participants randomized, 46 analyzed): continuous infusion of 50 mL/kg of Pedialyte over 3 h

Nager 2002 (*Continued*)

Outcomes	1. Failures: those unable to tolerate oral fluid challenge after 3 h therapy, have normal vital signs, and an average urine output of 0.5 mL/kg; those who vomited 3 times after institution of nasogastric hydration were also considered failures 2. Weight gain 3. Percent weight gain 4. Sodium levels at discharge
Notes	Trial location: USA Source of funding: Abbott Lab

Santosham 1982i

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Score on Jadad scale: 2
Participants	Number of participants: 94 Inclusion criteria: those hospitalized for less than 5 days with dehydration > = 5% secondary to acute diarrhea; length and weight of the children had to be above the third percentile; any child who was considered to be severely dehydrated or have signs of shock was given IV Ringers lactate before being assigned to the study Exclusion criteria: none stated
Interventions	1. IV (31 participants): replace deficit over 8 h with 0.45% saline containing 5% glucose and 20 mmol/L of potassium chloride, then maintained with oral Pedialyte 2. ORT (66 participants): replace deficit over 8 h; 33 participants received ORT of 50 mmol/L sodium and 30 received strawberry-flavored ORT of 90 mmol/L sodium; route of administration: oral Patients allowed rice, bananas, and apple sauce with water after first 8 h; all severely dehydrated patients given Ringer's lactate (20 mL/kg/h) until blood pressure and pulse returned to normal prior to being assigned to a treatment group; subsequently rehydration and maintenance therapy completed according to randomly assigned intervention
Outcomes	1. Failures (refused ORT; initial signs of dehydration after 8 h; dehydration returned during maintenance phase) 2. Frequency of stools 3. Weight gain 4. Complications 5. Side effects 6. Duration of diarrhea 7. Sodium concentration 8. Total fluid intake at 8 h and for duration of illness
Notes	Trial location: Panama Source of funding: Pennwalt Corp., Ross Labs, Pan American Health Org., and the NIH

Santosham 1982ii

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Score on Jadad scale: 2
Participants	Number of participants: 52 Inclusion criteria: those hospitalized for less than 5 days with dehydration > = 5% secondary to acute diarrhea; length and weight of the children had to be above the third percentile; any child who was considered to be severely dehydrated or have signs of shock was given IV Ringers lactate before being assigned to the study Exclusion criteria: none stated
Interventions	1. IV (31 participants): replace deficit over 8 h with 0.45% saline containing 5% glucose and 20 mmol/L of potassium chloride, then maintained with oral Pedialyte 2. ORT (66 participants): replace deficit over 8 h; 33 participants received ORT of 50 mmol/L sodium and 30 received strawberry-flavored ORT of 90 mmol/L sodium; route of administration: oral Patients were not allowed additional water within 24 h if diarrhea had not stopped within the 24 h; ORT patients were given a soy-based lactose-free formula (Isomil) diluted 1:1 with water after diarrhea stopped, followed by a regular diet 24 h later; IV patients were given Pedialyte for 12 h after diarrhea stopped then Isomil followed by regular diet; all severely dehydrated patients were given Ringer's lactate (20 mL/kg/h) until blood pressure and pulse returned to normal prior to be assigned to a treatment protocol; subsequently rehydration and maintenance therapy completed according to randomly assigned intervention
Outcomes	1. Failures (refused ORT; initial signs of dehydration after 8 h; dehydration returned during maintenance phase) 2. Frequency of stools 3. Weight gain 4. Complications 5. Side effects 6. Duration of diarrhea 7. Sodium concentration 8. Total fluid intake at 8 h and for duration of illness
Notes	Trial location: USA Source of funding: Pennwalt Corp., Ross Labs, Pan American Health Org., and the NIH

Sharifi 1985

Methods	Randomized controlled trial Length of follow up: random follow up at 1 to 7 months on 334 patients Withdrawals and losses to follow up: none Score on Jadad scale: 1
Participants	Number of participants: 470 Inclusion criteria: inpatients aged 1 to 18 months; 33% of the IV group and 36% of the ORT group were malnourished; in the IV group, 152/234 were moderately and 61/234 severely dehydrated; in the ORT group, 151/236 were moderately and 49/236 severely dehydrated; 215/234 in the IV group had a history of vomiting and 212/236 in the ORT group; acute diarrhea defined as > 10 cc/kg/h Exclusion criteria: none stated

Sharifi 1985 (*Continued*)

Interventions	1. IV (234 participants): received a range of Ringer's solution (not a standard IV solution); 20 to 30 cc/kg push or, if less sick, over 1 h 2. ORT (236 participants): rehydration solution (nasogastric) of 40 mL/kg/h until no longer dehydrated administered orally; maintenance solution (orally) of 250 mL/kg/day unless diarrhea > 10 cc/kg/h; if diarrhea > 10 cc/kg/h, return to rehydration solution
Outcomes	1. Duration of diarrhea 2. Weight gain 3. Complications 4. Side effects 5. Failures (signs of dehydration worse or unchanged within first 2 h) 6. Sodium concentration 7. Total fluid intake at 6 and 24 h, and for duration of illness 8. Death
Notes	Trial location: Iran Source of funding: not stated

Singh 1982

Methods	Randomized controlled trial (by inpatient registration number) Length of follow up: hospital discharge Withdrawals or losses to follow up: not stated Score on Jadad scale: 0
Participants	Number of participants: 100 Inclusion criteria: children admitted with acute diarrhea and dehydration; most children had mild to moderate dehydration; diarrhea not defined Exclusion criteria: those with shock, acidosis, severe abdominal distension and persistent vomiting
Interventions	1. IV (50 participants): 200 cc/kg/day of N/2 glucose saline for deficit and N/5 for maintenance 2. ORT (50 participants): 1 package of UNICEF salt mixed in 1 L of water for 15 to 30 min orally, then orally ad lib All participants received 50 mg/kg of chloramphenicol syrup per day
Outcomes	1. Failures (not defined) 2. Duration of diarrhea 3. Volume of stools 4. Complications 5. Side effects
Notes	Trial location: Afghanistan Source of funding: not stated

Spandorfer 2005

Methods	Randomized controlled trial Length of follow up: all outcomes assessed at 4 h, except emergency department revisits at 72 h Withdrawals and losses to follow up: none Score on Jadad scale: 3
Participants	Number of participants: 73 Inclusion criteria: children between 8 weeks and 3 years with diagnosis of probable viral gastroenteritis (>= 3 loose or watery stools in past 24 h); moderate dehydration (dehydration scores of >= 3 and < 7 corresponding to 5% to 10% dehydration); parent or guardian to stay with child; could be contacted for 72-h follow up Exclusion criteria: hypotension; sick for > 5 days; chronic illness that influences fluid status; malnutrition; impaired oromotor skills; received treatment at an emergency department in the previous 12 h
Interventions	1. IV (37 participants): 2 x 20 cc/kg in the first h of normal saline; oral fluids thereafter at child's request 2. ORT (36 participants): 50 cc/kg of Pedialyte given every 5 minutes over 4 h if dehydration score 3 to 5; 75 cc/kg given every 5 minutes over 4 h if dehydration score = 6
Outcomes	1. Success of treatment (resolution of moderate dehydration, weight gain, urine output, no severe emesis) 2. Time to initiate therapy 3. Improved dehydration after 2 h 4. Rate of hospitalizations 5. Parent preference of therapy at 4 h 6. 72-h revisit to emergency department 7. Fluid parameters (ie oral fluid intake, IV fluid input, and total input at 4 h; urine output; emesis; diarrhea; weight gain)
Notes	Trial location: USA Source of funding: not stated

Tamer 1985

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawal and losses to follow up: 3 (protocol deviation) Not intention-to-treat (3 participants in ORT group withdrew) Score on Jadad scale: 2
Participants	Number of participants: 100 Inclusion criteria: previously healthy inpatients aged 3 to 33 months with acute enteritis and dehydration of <= 10%; participants in the IV group (47/50) and the ORT group (42/50) had a history of vomiting; in the IV group, 6 were mildly, 27 moderately, and 17 severely dehydrated; in the ORT group, 15 were mildly, 14 were moderately, and 15 were severely dehydrated; acute diarrhea not defined Exclusion criteria: shock, ileus, or unconsciousness
Interventions	1. IV (50 participants): 20 cc/kg/h of Ringer's solution for 1 h; then 0.45% saline and 5% glucose solution for 7 h 2. ORT (50 participants): rehydrated via orally in hour intervals for 6 h then maintained ad lib; ORT delivered orally Soya bean or casein hydrolyte formula after rehydration was adequate

Tamer 1985 (*Continued*)

Outcomes	1. Days on ward 2. Volume of stools 3. Frequency of stools 4. Weight gain 5. Complications 6. Failures (not defined) 7. Sodium concentration 8. Total fluid intake at 6 and 24 h
Notes	Trial location: USA Source of funding: not stated

Vesikari 1987

Methods	Randomized controlled trial Length of follow up: hospital discharge Withdrawals and losses to follow up: none Score on Jadad scale: 2
Participants	Number of participants: 37 Inclusion criteria: inpatients (< 60 months of age) with acute diarrhea; 12/15 in IV group and 16/22 in ORT group had rotavirus; 1 in ORT group withdrew due to diarrhea > 7 days; in the IV group, 1 was mildly and 14 were moderately dehydrated; in the ORT group, 1 was mildly, 19 were moderately, and 2 were severely dehydrated; acute diarrhea not defined Exclusion criteria: none mentioned
Interventions	1. IV (15 participants): modified Ringer's solution used; 2/3 of estimated fluid deficit corrected over first 6 h; remaining solution over next 6 h 2. ORT (22 participants): 2 x 2/3 x estimated fluid deficit over 6 h and then 30 cc/kg for the next 6 h; 9 received ORT via orally and 13 via nasogastric route IV and ORT groups allowed normal full diet and choice of drink at 12 h (providing those in ORT tolerated orally)
Outcomes	1. Days on ward 2. Duration of diarrhea (last appearance of watery stool) 3. Volume of stools 4. Weight gain 5. Complications 6. Failures (not defined) 7. Sodium concentration 8. Total fluid intake at 6 and 12 h
Notes	Trial location: Finland Source of funding: not stated

CSO: casein, sucrose, dextrin with maltose, and vegetable oil; GES: glucose-electrolyte rehydration solution; IV: intravenous; IVT, intravenous therapy; ORT: oral rehydration therapy; UNICEF, United Nations Children's Fund; WHO, World Health Organization; NIH, National Institutes of Health.

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

Study	Reason for exclusion
Alam 1987	Study did not include treatment group with an intravenous treatment arm; all patients initially received IV then randomized to 3 ORT treatment arms
Carpenter 1982	A review
Gavin 1996	A systematic review
Hirschhorn 1972	Study design not randomized; intervention did not include an IV treatment arm and no diagnosis of dehydration amongst the study population
Isolauri 1985	Study design not randomized; the physician ordered some patients to go to IV and others to ort based on clinical judgment
Jan 1997	Interventions did not include intravenous or oral rehydration therapy
Kist-van Holthe 1999	A review
Klish 1985	A review
Lexomboon 1994	Interventions did not include intravenous or oral rehydration therapy
Mackenzie 1988	A review
Mackenzie 1989	A review that only looks at dehydration
Mahalanabis 1972	Study did not include a treatment group with an intravenous treatment arm; results presented as a function of the non-randomized treatment groups
Orenstein 1986	Duration of diarrhea was greater than 14 days
Patra 1989	Study did not include a treatment group with an intravenous treatment arm
Rautanen 1993	Patients not randomized to their treatment groups; no diagnosis of dehydrations amongst the study population; study did not include a treatment group with an intravenous treatment arm
Reid 1996	Study design not randomized; a cohort with convenience sampling
Samadi 1983	Study design not randomized
Sarker 1995	Duration of diarrhea > 14 days
Srivastava 1985	Study design not randomized
Tripp 1980	Letter to the editor

(*Continued*)

Weizman 1983	Duration of diarrhea > 14 days; study design not randomized

DATA AND ANALYSES

Comparison 1. Oral rehydration therapy (any solution) versus intravenous therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to rehydrate (by inpatient/outpatient)	18	1811	Risk Difference (M-H, Random, 95% CI)	0.04 [0.01, 0.07]
1.1 Inpatient	13	1551	Risk Difference (M-H, Random, 95% CI)	0.04 [0.00, 0.07]
1.2 Outpatient	5	260	Risk Difference (M-H, Random, 95% CI)	0.03 [-0.05, 0.10]
2 Weight gain (g) at discharge (by inpatient/outpatient)	6	369	Mean Difference (IV, Random, 95% CI)	-26.33 [-206.92, 154.26]
2.1 Inpatient	3	177	Mean Difference (IV, Random, 95% CI)	69.16 [-119.80, 258.12]
2.2 Outpatient	3	192	Mean Difference (IV, Random, 95% CI)	-189.90 [-419.40, 39.59]
3 Per cent weight gain (g) at discharge (by inpatient/outpatient)	5	767	Mean Difference (IV, Random, 95% CI)	-0.26 [-1.56, 1.05]
3.1 Inpatient	4	677	Mean Difference (IV, Random, 95% CI)	0.02 [-1.39, 1.42]
3.2 Outpatient	1	90	Mean Difference (IV, Random, 95% CI)	-1.37 [-2.35, -0.39]
4 Length of hospital stay (days)	6	526	Mean Difference (IV, Random, 95% CI)	-1.20 [-2.38, -0.02]
5 Incidences of hyponatremia	2		Risk Difference (M-H, Random, 95% CI)	Subtotals only
5.1 Inpatient	2	248	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.13, 0.15]
6 Incidences of hypernatremia (by inpatient/outpatient)	10	1062	Risk Difference (M-H, Random, 95% CI)	Not estimable
6.1 Inpatient	8	1002	Risk Difference (M-H, Random, 95% CI)	Not estimable
6.2 Outpatient	2	60	Risk Difference (M-H, Random, 95% CI)	Not estimable
7 Duration of diarrhea (h) (by inpatient/outpatient)	8	960	Mean Difference (IV, Random, 95% CI)	-5.90 [-12.70, 0.89]
7.1 Inpatient	8	960	Mean Difference (IV, Random, 95% CI)	-5.90 [-12.70, 0.89]
8 Total fluid intake (mL/kg) at 6 h (by inpatient/outpatient)	8	985	Mean Difference (IV, Random, 95% CI)	32.09 [-26.69, 90.88]
8.1 Inpatient	6	881	Mean Difference (IV, Random, 95% CI)	42.23 [-27.52, 111.97]
8.2 Outpatient	2	104	Mean Difference (IV, Random, 95% CI)	1.45 [-38.78, 41.67]
9 Total fluid intake (mL/kg) at 24 h (by inpatient/outpatient)	7	835	Mean Difference (IV, Random, 95% CI)	73.45 [-31.78, 178.69]
9.1 Inpatient	5	775	Mean Difference (IV, Random, 95% CI)	81.03 [-47.37, 209.43]
9.2 Outpatient	2	60	Mean Difference (IV, Random, 95% CI)	53.64 [-39.44, 146.72]
10 Total fluid intake (mL) at 6 h (by inpatient/outpatient)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 Inpatient	1		Mean Difference (IV, Random, 95% CI)	Not estimable
11 Complications	10		Risk Difference (M-H, Random, 95% CI)	Subtotals only
11.1 Paralytic ileus	2	670	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.00, 0.05]
11.2 Phlebitis	5	877	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.04, -0.01]

11.3 Peri-orbital edema	7	844	Risk Difference (M-H, Random, 95% CI)	Not estimable
11.4 Abdominal distention	1	470	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.00, 0.04]
11.5 Seizures	6	877	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.03, 0.01]
12 Sodium intake (mmol/kg) at 6 h (by inpatient/outpatient)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 Inpatient	3	607	Mean Difference (IV, Random, 95% CI)	5.80 [-1.48, 13.07]
13 Sodium levels (mmol/kg) at 24 h (by inpatient/outpatient)	7	992	Mean Difference (IV, Random, 95% CI)	1.25 [-0.56, 3.07]
13.1 Inpatient	5	932	Mean Difference (IV, Random, 95% CI)	1.57 [-0.91, 4.05]
13.2 Outpatient	2	60	Mean Difference (IV, Random, 95% CI)	0.59 [-0.89, 2.07]

Comparison 2. Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to rehydrate: review authors' definition	18	1792	Risk Difference (M-H, Random, 95% CI)	Not estimable
1.1 Inpatient	13	1534	Risk Difference (M-H, Random, 95% CI)	Not estimable
1.2 Outpatient	5	258	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.05, 0.05]
2 Failure to rehydrate: intention-to-treat analysis	18	1799	Risk Difference (M-H, Random, 95% CI)	0.03 [0.00, 0.05]
2.1 Inpatient	13	1541	Risk Difference (M-H, Random, 95% CI)	0.03 [0.00, 0.06]
2.2 Outpatient	5	258	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.05, 0.05]
3 Failure to rehydrate: by osmolarity	16		Risk Difference (M-H, Random, 95% CI)	Subtotals only
3.1 Low	6	729	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.01, 0.02]
3.2 High	14	955	Risk Difference (M-H, Random, 95% CI)	0.05 [0.01, 0.08]
4 Failure to rehydrate: by vomiting	18		Risk Difference (M-H, Random, 95% CI)	Subtotals only
4.1 Excluding children who vomited	5	298	Risk Difference (M-H, Random, 95% CI)	Not estimable
4.2 Including children who vomited	4	596	Risk Difference (M-H, Random, 95% CI)	0.04 [-0.05, 0.13]
4.3 Not stated	9	917	Risk Difference (M-H, Random, 95% CI)	0.05 [0.02, 0.09]
5 Failure to rehydrate: by route	18		Risk Difference (M-H, Random, 95% CI)	Subtotals only
5.1 Oral	11	739	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.01, 0.04]
5.2 Oral and nasogastric	5	955	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.03, 0.16]
5.3 Nasogastric	2	117	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.08, 0.06]

Analysis 1.1. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 1 Failure to rehydrate (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 1 Failure to rehydrate (by inpatient/outpatient)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Inpatient					
Sharifi 1985	1/236	0/234		11.2 %	0.00 [-0.01, 0.02]
Mackenzie 1991	2/52	0/52		7.7 %	0.04 [-0.02, 0.10]
Singh 1982	0/50	0/50		9.7 %	0.0 [-0.04, 0.04]
Tamer 1985	3/47	0/50		6.5 %	0.06 [-0.01, 0.14]
Santosham 1982i	0/63	0/31		8.9 %	0.0 [-0.05, 0.05]
el-Mougi 1994	0/41	0/20		6.9 %	0.0 [-0.07, 0.07]
Vesikari 1987	2/22	0/15		2.9 %	0.09 [-0.06, 0.24]
Santosham 1982ii	1/35	0/17		5.1 %	0.03 [-0.07, 0.13]
Issenman 1993	4/22	4/18		1.3 %	-0.04 [-0.29, 0.21]
Gremse 1995	1/12	0/12		1.9 %	0.08 [-0.12, 0.29]
Brown 1988	8/94	1/34		6.4 %	0.06 [-0.02, 0.14]
Gonzalez 1988	13/100	0/100		7.3 %	0.13 [0.06, 0.20]
Hernandez 1987	9/108	0/36		7.5 %	0.08 [0.02, 0.15]
Subtotal (95% CI)	**882**	**669**		**83.3 %**	**0.04 [0.00, 0.07]**
Total events: 44 (ORT), 5 (IVT)					
Heterogeneity: Tau² = 0.00; Chi² = 52.96, df = 12 (P<0.00001); I² =77%					
Test for overall effect: Z = 2.17 (P = 0.030)					
2 Outpatient					
Atherly-John 2002	3/18	0/16		2.1 %	0.17 [-0.03, 0.36]
de Pumarejo 1990	0/17	0/14		4.2 %	0.0 [-0.12, 0.12]
Listernick 1986	2/15	0/14		1.9 %	0.13 [-0.07, 0.33]
Nager 2002	1/47	2/46		7.0 %	-0.02 [-0.09, 0.05]
Spandorfer 2005	16/36	16/37		1.6 %	0.01 [-0.22, 0.24]
Subtotal (95% CI)	**133**	**127**		**16.7 %**	**0.03 [-0.05, 0.10]**
Total events: 22 (ORT), 18 (IVT)					

(*Continued . . .*)

(. . . *Continued*)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Heterogeneity: Tau^2 = 0.00; Chi^2 = 5.37, df = 4 (P = 0.25); I^2 =26%					
Test for overall effect: Z = 0.71 (P = 0.48)					
Total (95% CI)	**1015**	**796**	◆	**100.0 %**	**0.04 [0.01, 0.07]**
Total events: 66 (ORT), 23 (IVT)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 56.42, df = 17 (P<0.00001); I^2 =70%					
Test for overall effect: Z = 2.36 (P = 0.018)					

-0.5 -0.25 0 0.25 0.5

Favours ORT Favours IVT

Analysis 1.2. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 2 Weight gain (g) at discharge (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 2 Weight gain (g) at discharge (by inpatient/outpatient)

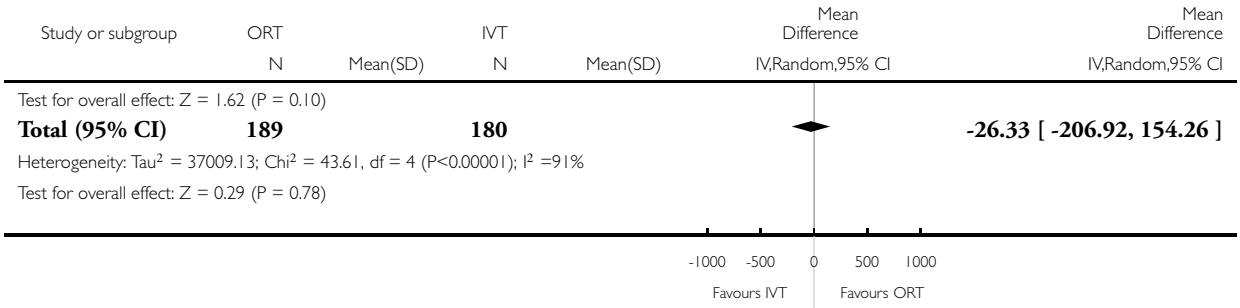
Study or subgroup	ORT N	Mean(SD)	IVT N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Inpatient						
Issenman 1993	22	282 (73)	18	290 (158)		-8.00 [-87.11, 71.11]
Tamer 1985	50	217 (349)	50	288 (326)		-71.00 [-203.37, 61.37]
Vesikari 1987	22	314 (315)	15	-16 (253)		330.00 [146.37, 513.63]
Subtotal (95% CI)	**94**		**83**		◆	**69.16 [-119.80, 258.12]**
Heterogeneity: Tau^2 = 23195.60; Chi^2 = 13.24, df = 2 (P = 0.001); I^2 =85%						
Test for overall effect: Z = 0.72 (P = 0.47)						
2 Outpatient						
Listernick 1986	15	520 (300)	14	570 (290)		-50.00 [-264.77, 164.77]
Nager 2002	44	220 (0)	46	350 (0)		0.0 [0.0, 0.0]
Spandorfer 2005	36	154 (192.81)	37	441.9 (192.81)		-287.90 [-376.37, -199.43]
Subtotal (95% CI)	**95**		**97**		◆	**-189.90 [-419.40, 39.59]**
Heterogeneity: Tau^2 = 21275.93; Chi^2 = 4.03, df = 1 (P = 0.04); I^2 =75%						

-1000 -500 0 500 1000

Favours IVT Favours ORT

(*Continued* . . .)

(. . . *Continued*)

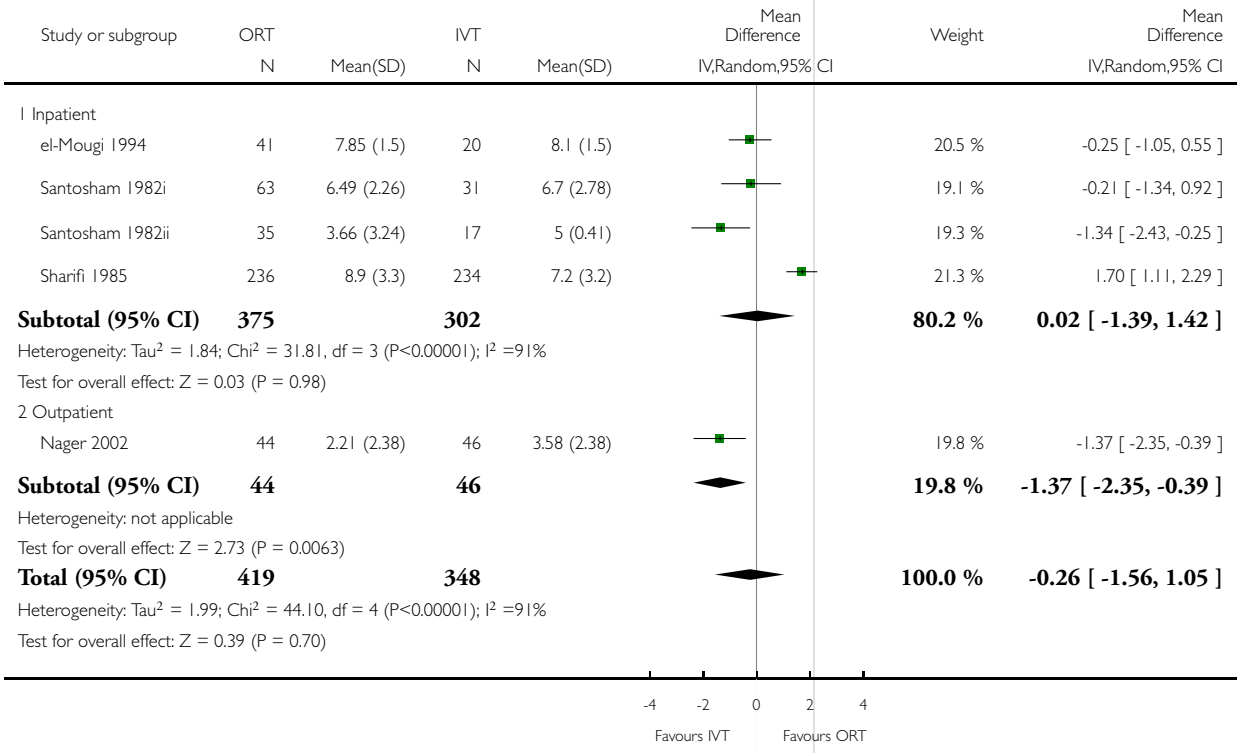


Analysis 1.3. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 3 Per cent weight gain (g) at discharge (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 3 Per cent weight gain (g) at discharge (by inpatient/outpatient)



Analysis 1.4. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 4 Length of hospital stay (days).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

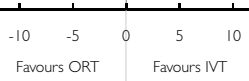
Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 4 Length of hospital stay (days)

Study or subgroup	ORT N	Mean(SD)	IVT N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
el-Mougi 1994	41	1.47 (0.78)	20	1.49 (0.82)		17.7 %	-0.02 [-0.45, 0.41]
Gonzalez 1988	100	2.1 (1.4)	100	6.86 (4.4)		16.3 %	-4.76 [-5.66, -3.86]
Gremse 1995	12	1.8 (1.04)	12	2.8 (1.39)		16.1 %	-1.00 [-1.98, -0.02]
Mackenzie 1991	52	2 (1)	52	2 (0.71)		17.8 %	0.0 [-0.33, 0.33]
Tamer 1985	50	4.1 (2.2)	50	4.5 (2.9)		16.0 %	-0.40 [-1.41, 0.61]
Vesikari 1987	22	2.7 (1)	15	3.9 (1.7)		16.2 %	-1.20 [-2.16, -0.24]
Total (95% CI)	**277**		**249**			**100.0 %**	**-1.20 [-2.38, -0.02]**

Heterogeneity: $Tau^2 = 2.00$; $Chi^2 = 101.51$, df = 5 ($P<0.00001$); $I^2 = 95\%$

Test for overall effect: Z = 2.00 (P = 0.046)



Analysis 1.5. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 5 Incidences of hyponatremia.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 5 Incidences of hyponatremia

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Inpatient					
Hernandez 1987	15/108	7/36		40.1 %	-0.06 [-0.20, 0.09]
Mackenzie 1991	3/52	0/52		59.9 %	0.06 [-0.01, 0.13]
Subtotal (95% CI)	**160**	**88**		**100.0 %**	**0.01 [-0.13, 0.15]**
Total events: 18 (ORT), 7 (IVT)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.05$, df = 1 (P = 0.08); $I^2 = 67\%$					
Test for overall effect: Z = 0.17 (P = 0.86)					

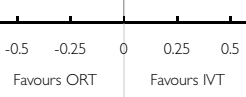
Analysis 1.6. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 6 Incidences of hypernatremia (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 6 Incidences of hypernatremia (by inpatient/outpatient)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Inpatient					
el-Mougi 1994	0/41	0/20		1.9 %	0.0 [-0.07, 0.07]
Hernandez 1987	0/108	0/36		6.7 %	0.0 [-0.04, 0.04]
Issenman 1993	0/22	0/18		1.2 %	0.0 [-0.09, 0.09]
Mackenzie 1991	0/52	0/52		7.6 %	0.0 [-0.04, 0.04]
Santosham 1982i	0/63	0/31		4.5 %	0.0 [-0.05, 0.05]
Santosham 1982ii	0/35	0/17		1.4 %	0.0 [-0.08, 0.08]
Sharifi 1985	1/236	1/234		74.4 %	0.00 [-0.01, 0.01]
Vesikari 1987	0/22	0/15		1.0 %	0.0 [-0.10, 0.10]
Subtotal (95% CI)	**579**	**423**		**98.6 %**	**0.00 [-0.01, 0.01]**
Total events: 1 (ORT), 1 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 7 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.01 (P = 1.0)					
2 Outpatient					
de Pumarejo 1990	0/17	0/14		0.7 %	0.0 [-0.12, 0.12]
Listernick 1986	0/15	0/14		0.7 %	0.0 [-0.12, 0.12]
Subtotal (95% CI)	**32**	**28**		**1.4 %**	**0.0 [-0.09, 0.09]**
Total events: 0 (ORT), 0 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 1 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.0 (P = 1.0)					
Total (95% CI)	**611**	**451**		**100.0 %**	**0.00 [-0.01, 0.01]**
Total events: 1 (ORT), 1 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 9 (P = 1.00); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.01 (P = 1.0)					



Analysis 1.7. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 7 Duration of diarrhea (h) (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 7 Duration of diarrhea (h) (by inpatient/outpatient)

Study or subgroup	ORT N	ORT Mean(SD)	IVT N	IVT Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Inpatient							
Brown 1988	88	135.53 (69.59)	34	135.41 (58.68)		5.7 %	0.12 [-24.38, 24.62]
el-Mougi 1994	41	39.71 (27.1)	20	37 (19)		13.1 %	2.71 [-9.04, 14.46]
Gremse 1995	12	23.3 (24.25)	12	43.9 (28.41)		7.0 %	-20.60 [-41.73, 0.53]
Santosham 1982i	63	34 (11.24)	31	34 (11.14)		19.5 %	0.0 [-4.80, 4.80]
Santosham 1982ii	35	33 (22.74)	17	34 (20.62)		12.6 %	-1.00 [-13.36, 11.36]
Sharifi 1985	236	115.2 (50.4)	234	132 (69.6)		13.8 %	-16.80 [-27.79, -5.81]
Singh 1982	50	40.56 (6.96)	50	38.16 (7.92)		20.8 %	2.40 [-0.52, 5.32]
Vesikari 1987	22	24 (12)	15	62.4 (38.4)		7.5 %	-38.40 [-58.47, -18.33]
Total (95% CI)	**547**		**413**			**100.0 %**	**-5.90 [-12.70, 0.89]**

Heterogeneity: $Tau^2 = 55.58$; $Chi^2 = 29.50$, df = 7 (P = 0.00012); $I^2 = 76\%$

Test for overall effect: Z = 1.70 (P = 0.089)

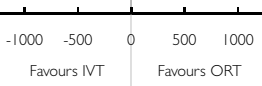
Analysis 1.8. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 8 Total fluid intake (mL/kg) at 6 h (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 8 Total fluid intake (mL/kg) at 6 h (by inpatient/outpatient)

Study or subgroup	ORT N	ORT Mean(SD)	IV N	IV Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Inpatient							
el-Mougi 1994	41	117.89 (36.43)	20	94 (2.8)		12.7 %	23.89 [12.67, 35.11]
Mackenzie 1991	52	63 (4.47)	52	47 (3)		12.8 %	16.00 [14.54, 17.46]
Santosham 1982i	63	97.38 (51.42)	31	192 (72.38)		12.4 %	-94.62 [-123.09, -66.15]
Santosham 1982ii	35	271 (163.31)	17	163 (49.48)		11.3 %	108.00 [49.00, 167.00]
Sharifi 1985	236	222 (14)	234	81 (10)		12.8 %	141.00 [138.80, 143.20]
Tamer 1985	50	130.8 (58)	50	68.2 (15.1)		12.6 %	62.60 [45.99, 79.21]
Subtotal (95% CI)	**477**		**404**			**74.7 %**	**42.23 [-27.52, 111.97]**
Heterogeneity: Tau^2 = 7406.61; Chi^2 = 8744.86, df = 5 (P<0.00001); I^2 =100%							
Test for overall effect: Z = 1.19 (P = 0.24)							
2 Outpatient							
de Pumarejo 1990	17	81 (34)	14	58 (21)		12.6 %	23.00 [3.45, 42.55]
Spandorfer 2005	36	43 (17.57)	37	61.1 (17.57)		12.7 %	-18.10 [-26.16, -10.04]
Subtotal (95% CI)	**53**		**51**			**25.3 %**	**1.45 [-38.78, 41.67]**
Heterogeneity: Tau^2 = 786.40; Chi^2 = 14.51, df = 1 (P = 0.00014); I^2 =93%							
Test for overall effect: Z = 0.07 (P = 0.94)							
Total (95% CI)	**530**		**455**			**100.0 %**	**32.09 [-26.69, 90.88]**
Heterogeneity: Tau^2 = 7038.74; Chi^2 = 9052.50, df = 7 (P<0.00001); I^2 =100%							
Test for overall effect: Z = 1.07 (P = 0.28)							



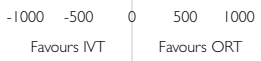
Analysis 1.9. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 9 Total fluid intake (mL/kg) at 24 h (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 9 Total fluid intake (mL/kg) at 24 h (by inpatient/outpatient)

Study or subgroup	ORT N	ORT Mean(SD)	IVT N	IVT Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Inpatient							
el-Mougi 1994	41	338.9 (114.07)	20	269 (47)		14.1 %	69.90 [29.36, 110.44]
Issenman 1993	22	188.12 (40.73)	18	130.67 (14.86)		14.4 %	57.45 [39.10, 75.80]
Mackenzie 1991	52	94 (5.61)	52	122 (5.34)		14.4 %	-28.00 [-30.11, -25.89]
Sharifi 1985	236	432 (54)	234	228 (35)		14.4 %	204.00 [195.78, 212.22]
Tamer 1985	50	281.4 (98.7)	50	179.6 (33)		14.3 %	101.80 [72.95, 130.65]
Subtotal (95% CI)	**401**		**374**			**71.6 %**	**81.03 [-47.37, 209.43]**
Heterogeneity: Tau^2 = 21309.42; Chi^2 = 3004.65, df = 4 (P<0.00001); I^2 =100%							
Test for overall effect: Z = 1.24 (P = 0.22)							
2 Outpatient							
de Pumarejo 1990	17	145 (58)	14	138 (33)		14.2 %	7.00 [-25.54, 39.54]
Listernick 1986	15	243 (75)	14	141 (30)		14.1 %	102.00 [60.92, 143.08]
Subtotal (95% CI)	**32**		**28**			**28.4 %**	**53.64 [-39.44, 146.72]**
Heterogeneity: Tau^2 = 4155.02; Chi^2 = 12.62, df = 1 (P = 0.00038); I^2 =92%							
Test for overall effect: Z = 1.13 (P = 0.26)							
Total (95% CI)	**433**		**402**			**100.0 %**	**73.45 [-31.78, 178.69]**
Heterogeneity: Tau^2 = 19971.81; Chi^2 = 3035.49, df = 6 (P<0.00001); I^2 =100%							
Test for overall effect: Z = 1.37 (P = 0.17)							



Analysis 1.10. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 10 Total fluid intake (mL) at 6 h (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 10 Total fluid intake (mL) at 6 h (by inpatient/outpatient)

Study or subgroup	ORT N	Mean(SD)	IVT N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Inpatient						
Vesikari 1987	22	823 (399)	15	671 (272)		152.00 [-64.21, 368.21]

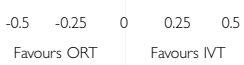
Analysis 1.11. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 11 Complications.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 11 Complications

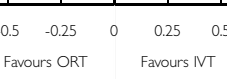
Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Paralytic ileus					
Gonzalez 1988	1/100	0/100		46.9 %	0.01 [-0.02, 0.04]
Sharifi 1985	8/236	0/234		53.1 %	0.03 [0.01, 0.06]
Subtotal (95% CI)	**336**	**334**		**100.0 %**	**0.02 [0.00, 0.05]**
Total events: 9 (ORT), 0 (IVT)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.78$, df = 1 (P = 0.18); $I^2 = 44\%$					
Test for overall effect: Z = 1.83 (P = 0.068)					
2 Phlebitis					
el-Mougi 1994	0/41	0/20		5.5 %	0.0 [-0.07, 0.07]
Gonzalez 1988	0/100	5/100		13.6 %	-0.05 [-0.10, 0.00]



(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Santosham 1982i	0/63	1/31		5.0 %	-0.03 [-0.11, 0.04]
Santosham 1982ii	0/35	0/17		4.1 %	0.0 [-0.08, 0.08]
Sharifi 1985	0/236	5/234		71.8 %	-0.02 [-0.04, 0.00]
Subtotal (95% CI)	**475**	**402**		**100.0 %**	**-0.02 [-0.04, -0.01]**
Total events: 0 (ORT), 11 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.15$, df = 4 (P = 0.71); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.72 (P = 0.0064)					
3 Peri-orbital edema					
el-Mougi 1994	0/41	0/20		9.1 %	0.0 [-0.07, 0.07]
Issenman 1993	4/18	1/16		1.0 %	0.16 [-0.07, 0.39]
Listernick 1986	1/15	0/14		1.8 %	0.07 [-0.10, 0.24]
Mackenzie 1991	1/52	5/52		6.4 %	-0.08 [-0.17, 0.01]
Santosham 1982i	0/63	0/31		19.5 %	0.0 [-0.05, 0.05]
Santosham 1982ii	2/35	0/17		4.0 %	0.06 [-0.06, 0.17]
Sharifi 1985	4/236	4/234		58.2 %	0.00 [-0.02, 0.02]
Subtotal (95% CI)	**460**	**384**		**100.0 %**	**0.00 [-0.02, 0.02]**
Total events: 12 (ORT), 10 (IVT)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.48$, df = 6 (P = 0.37); $I^2 = 7\%$					
Test for overall effect: Z = 0.01 (P = 0.99)					
4 Abdominal distention					
Sharifi 1985	4/236	0/234		100.0 %	0.02 [0.00, 0.04]
Subtotal (95% CI)	**236**	**234**		**100.0 %**	**0.02 [0.00, 0.04]**
Total events: 4 (ORT), 0 (IVT)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.81 (P = 0.070)					
5 Seizures					
el-Mougi 1994	0/41	0/20		5.9 %	0.0 [-0.07, 0.07]
Santosham 1982i	0/63	0/31		13.5 %	0.0 [-0.05, 0.05]
Santosham 1982ii	0/35	1/17		1.8 %	-0.06 [-0.19, 0.07]
Sharifi 1985	2/236	6/234		57.2 %	-0.02 [-0.04, 0.01]
Singh 1982	0/50	1/50		10.8 %	-0.02 [-0.07, 0.03]
Tamer 1985	1/50	0/50		10.8 %	0.02 [-0.03, 0.07]
Subtotal (95% CI)	**475**	**402**		**100.0 %**	**-0.01 [-0.03, 0.01]**
Total events: 3 (ORT), 8 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.48$, df = 5 (P = 0.78); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.20 (P = 0.23)					



Analysis 1.12. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 12 Sodium intake (mmol/kg) at 6 h (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

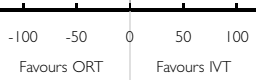
Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 12 Sodium intake (mmol/kg) at 6 h (by inpatient/outpatient)

Study or subgroup	ORT N	Mean(SD)	IVT N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Inpatient							
Sharifi 1985	236	17.8 (1.1)	234	6.6 (0.13)		43.7 %	11.20 [11.06, 11.34]
Tamer 1985	50	9.36 (3.9)	50	6.09 (1.1)		43.3 %	3.27 [2.15, 4.39]
Vesikari 1987	22	49 (24)	15	53 (27)		13.0 %	-4.00 [-20.95, 12.95]
Subtotal (95% CI)	**308**		**299**			**100.0 %**	**5.80 [-1.48, 13.07]**

Heterogeneity: $Tau^2 = 31.48$; $Chi^2 = 191.54$, df = 2 (P<0.00001); $I^2 = 99\%$

Test for overall effect: Z = 1.56 (P = 0.12)



Analysis 1.13. Comparison 1 Oral rehydration therapy (any solution) versus intravenous therapy, Outcome 13 Sodium levels (mmol/kg) at 24 h (by inpatient/outpatient).

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy

Outcome: 13 Sodium levels (mmol/kg) at 24 h (by inpatient/outpatient)

Study or subgroup	ORT N	ORT Mean(SD)	IVT N	IVT Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Inpatient							
el-Mougi 1994	41	137.25 (6.33)	17	135.4 (7.9)		9.0 %	1.85 [-2.38, 6.08]
Gonzalez 1988	100	132.1 (6)	100	127 (6.4)		15.2 %	5.10 [3.38, 6.82]
Mackenzie 1991	52	137 (1.41)	52	138 (1.41)		17.3 %	-1.00 [-1.54, -0.46]
Sharifi 1985	234	138.8 (8.6)	236	138.5 (8.7)		15.6 %	0.30 [-1.26, 1.86]
Tamer 1985	50	140 (6.58)	50	138 (2.83)		14.5 %	2.00 [0.01, 3.99]
Subtotal (95% CI)	**477**		**455**			**71.6 %**	**1.57 [-0.91, 4.05]**
Heterogeneity: Tau^2 = 6.84; Chi^2 = 50.88, df = 4 (P<0.00001); I^2 =92%							
Test for overall effect: Z = 1.24 (P = 0.21)							
2 Outpatient							
de Pumarejo 1990	17	138 (2)	14	137 (3.2)		14.7 %	1.00 [-0.93, 2.93]
Listernick 1986	15	137 (3.9)	14	137 (2.3)		13.7 %	0.0 [-2.31, 2.31]
Subtotal (95% CI)	**32**		**28**			**28.4 %**	**0.59 [-0.89, 2.07]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.42, df = 1 (P = 0.51); I^2 =0.0%							
Test for overall effect: Z = 0.78 (P = 0.43)							
Total (95% CI)	**509**		**483**			**100.0 %**	**1.25 [-0.56, 3.07]**
Heterogeneity: Tau^2 = 4.89; Chi^2 = 52.33, df = 6 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 1.35 (P = 0.18)							

Analysis 2.1. Comparison 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses, Outcome 1 Failure to rehydrate: review authors' definition.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome: 1 Failure to rehydrate: review authors' definition

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Inpatient					
Sharifi 1985	3/236	6/226		15.2 %	-0.01 [-0.04, 0.01]
Mackenzie 1991	2/52	0/52		7.6 %	0.04 [-0.02, 0.10]
Singh 1982	0/50	0/50		12.2 %	0.0 [-0.04, 0.04]
Tamer 1985	2/46	0/50		6.7 %	0.04 [-0.03, 0.11]
Santosham 1982i	0/63	0/31		10.1 %	0.0 [-0.05, 0.05]
el-Mougi 1994	0/41	0/20		6.3 %	0.0 [-0.07, 0.07]
Vesikari 1987	2/22	0/15		1.9 %	0.09 [-0.06, 0.24]
Santosham 1982ii	1/35	1/17		2.7 %	-0.03 [-0.15, 0.09]
Issenman 1993	1/19	2/18		1.5 %	-0.06 [-0.23, 0.12]
Gremse 1995	1/12	0/12		1.1 %	0.08 [-0.12, 0.29]
Brown 1988	7/93	1/34		5.7 %	0.05 [-0.03, 0.12]
Gonzalez 1988	9/96	0/100		7.9 %	0.09 [0.03, 0.15]
Hernandez 1987	9/108	0/36		7.3 %	0.08 [0.02, 0.15]
Subtotal (95% CI)	**873**	**661**		**86.0 %**	**0.03 [0.00, 0.05]**
Total events: 37 (ORT), 10 (IVT)					
Heterogeneity: Tau² = 0.00; Chi² = 23.36, df = 12 (P = 0.02); I² =49%					
Test for overall effect: Z = 1.92 (P = 0.055)					
2 Outpatient					
Atherly-John 2002	3/18	0/16		1.3 %	0.17 [-0.03, 0.36]
de Pumarejo 1990	0/17	0/14		3.0 %	0.0 [-0.12, 0.12]
Listernick 1986	0/13	0/14		2.4 %	0.0 [-0.13, 0.13]
Nager 2002	1/47	2/46		6.4 %	-0.02 [-0.09, 0.05]
Spandorfer 2005	16/36	16/37		0.9 %	0.01 [-0.22, 0.24]
Subtotal (95% CI)	**131**	**127**		**14.0 %**	**0.00 [-0.05, 0.05]**
Total events: 20 (ORT), 18 (IVT)					

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Heterogeneity: Tau^2 = 0.0; Chi^2 = 3.63, df = 4 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 0.05 (P = 0.96)					
Total (95% CI)	**1004**	**788**		**100.0 %**	**0.02 [0.00, 0.04]**
Total events: 57 (ORT), 28 (IVT)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 26.92, df = 17 (P = 0.06); I^2 =37%					
Test for overall effect: Z = 1.90 (P = 0.058)					

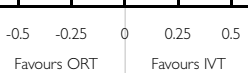
Analysis 2.2. Comparison 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses, Outcome 2 Failure to rehydrate: intention-to-treat analysis.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome: 2 Failure to rehydrate: intention-to-treat analysis

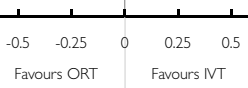
Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Inpatient					
Sharifi 1985	3/236	6/226		13.1 %	-0.01 [-0.04, 0.01]
Mackenzie 1991	3/53	0/52		7.0 %	0.06 [-0.01, 0.13]
Singh 1982	0/50	0/50		11.3 %	0.0 [-0.04, 0.04]
Tamer 1985	5/49	0/50		5.2 %	0.10 [0.01, 0.19]
Santosham 1982i	0/63	0/31		9.8 %	0.0 [-0.05, 0.05]
el-Mougi 1994	0/41	0/20		6.8 %	0.0 [-0.07, 0.07]
Vesikari 1987	2/22	0/15		2.4 %	0.09 [-0.06, 0.24]
Santosham 1982ii	1/35	1/17		3.3 %	-0.03 [-0.15, 0.09]
Issenman 1993	4/22	2/18		1.3 %	0.07 [-0.15, 0.29]
Gremse 1995	1/12	0/12		1.4 %	0.08 [-0.12, 0.29]



(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Brown 1988	7/93	1/34		6.3 %	0.05 [-0.03, 0.12]
Gonzalez 1988	9/96	0/100		8.2 %	0.09 [0.03, 0.15]
Hernandez 1987	9/108	0/36		7.7 %	0.08 [0.02, 0.15]
Subtotal (95% CI)	**880**	**661**		**83.8 %**	**0.03 [0.00, 0.06]**
Total events: 44 (ORT), 10 (IVT)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 29.50$, df = 12 (P = 0.003); $I^2 = 59\%$					
Test for overall effect: Z = 2.24 (P = 0.025)					
2 Outpatient					
Atherly-John 2002	3/18	0/16		1.6 %	0.17 [-0.03, 0.36]
de Pumarejo 1990	0/17	0/14		3.6 %	0.0 [-0.12, 0.12]
Listernick 1986	0/13	0/14		3.0 %	0.0 [-0.13, 0.13]
Nager 2002	1/47	2/46		6.9 %	-0.02 [-0.09, 0.05]
Spandorfer 2005	16/36	16/37		1.2 %	0.01 [-0.22, 0.24]
Subtotal (95% CI)	**131**	**127**		**16.2 %**	**0.00 [-0.05, 0.05]**
Total events: 20 (ORT), 18 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.63$, df = 4 (P = 0.46); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.05 (P = 0.96)					
Total (95% CI)	**1011**	**788**		**100.0 %**	**0.03 [0.00, 0.05]**
Total events: 64 (ORT), 28 (IVT)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 32.75$, df = 17 (P = 0.01); $I^2 = 48\%$					
Test for overall effect: Z = 2.21 (P = 0.027)					



Analysis 2.3. Comparison 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses, Outcome 3 Failure to rehydrate: by osmolarity.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

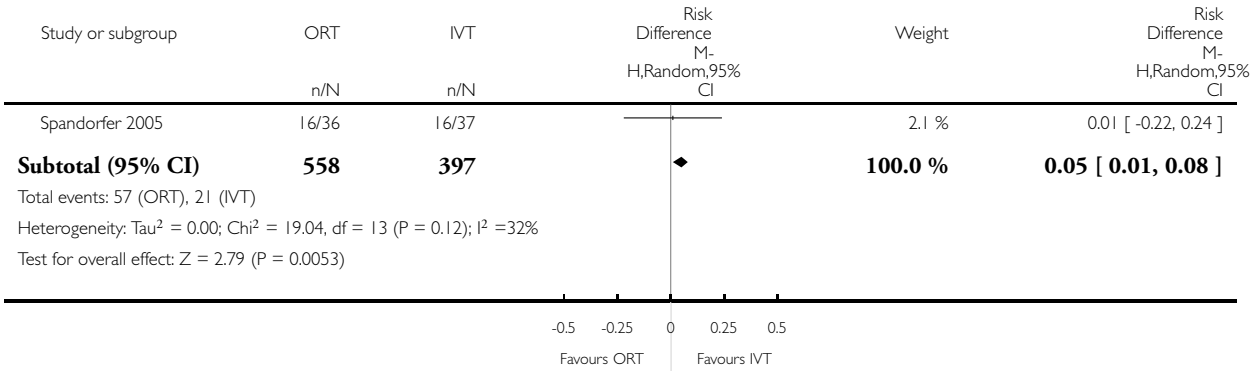
Comparison: 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome: 3 Failure to rehydrate: by osmolarity

Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
1 Low					
Sharifi 1985	1/236	0/234		93.2 %	0.00 [-0.01, 0.02]
Mackenzie 1991	2/52	0/52		3.2 %	0.04 [-0.02, 0.10]
Santosham 1982i	0/33	0/15		1.4 %	0.0 [-0.09, 0.09]
el-Mougi 1994	0/20	0/10		0.7 %	0.0 [-0.14, 0.14]
Santosham 1982ii	0/15	0/8		0.4 %	0.0 [-0.17, 0.17]
Hernandez 1987	2/36	0/18		1.1 %	0.06 [-0.05, 0.16]
Subtotal (95% CI)	**392**	**337**		**100.0 %**	**0.01 [-0.01, 0.02]**
Total events: 5 (ORT), 0 (IVT)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.18$, df = 5 (P = 0.67); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.01 (P = 0.31)					
2 High					
Singh 1982	0/50	0/50		19.9 %	0.0 [-0.04, 0.04]
Tamer 1985	3/47	0/50		11.1 %	0.06 [-0.01, 0.14]
Santosham 1982i	0/30	0/16		9.1 %	0.0 [-0.09, 0.09]
el-Mougi 1994	0/21	0/10		5.0 %	0.0 [-0.14, 0.14]
Vesikari 1987	2/22	0/15		4.2 %	0.09 [-0.06, 0.24]
Santosham 1982ii	1/20	0/9		3.4 %	0.05 [-0.12, 0.22]
Issenman 1993	4/22	4/18		1.7 %	-0.04 [-0.29, 0.21]
Gremse 1995	1/12	0/12		2.6 %	0.08 [-0.12, 0.29]
Brown 1988	8/94	1/34		10.8 %	0.06 [-0.02, 0.14]
de Pumarejo 1990	0/17	0/14		6.3 %	0.0 [-0.12, 0.12]
Gonzalez 1988	13/100	0/100		13.0 %	0.13 [0.06, 0.20]
Hernandez 1987	7/72	0/18		8.1 %	0.10 [0.00, 0.20]
Listernick 1986	2/15	0/14		2.6 %	0.13 [-0.07, 0.33]

(*Continued* . . .)

(. . . *Continued*)

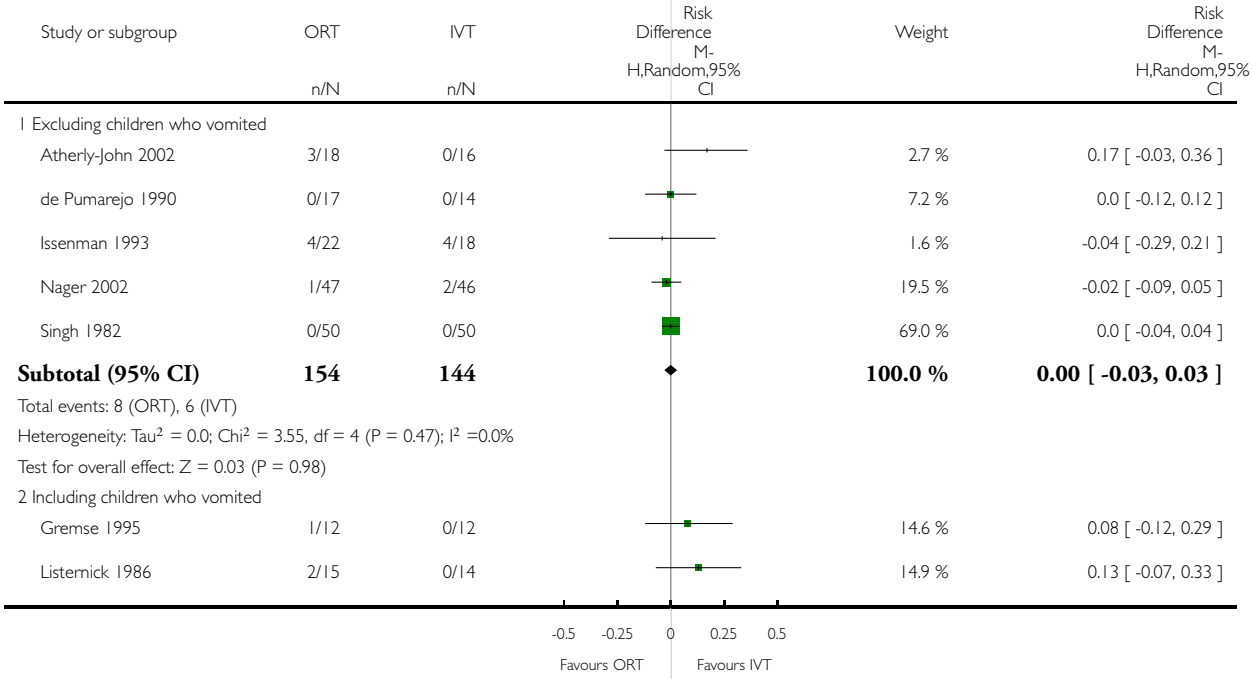


Analysis 2.4. Comparison 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses, Outcome 4 Failure to rehydrate: by vomiting.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Comparison: 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome: 4 Failure to rehydrate: by vomiting



(*Continued* . . .)

(. . . *Continued*)

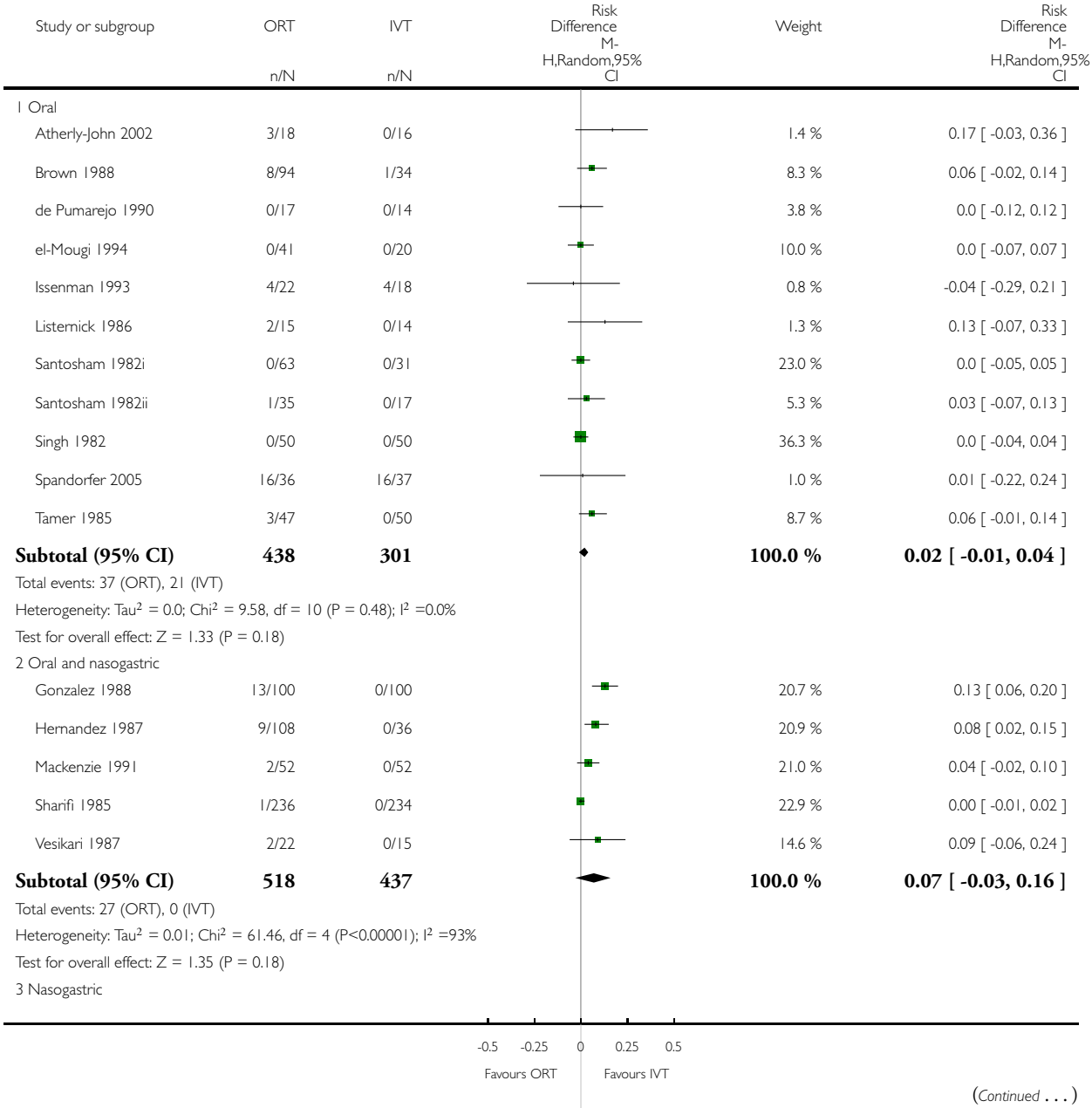
Study or subgroup	ORT n/N	IVT n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Sharifi 1985	1/236	0/234		58.3 %	0.00 [-0.01, 0.02]
Spandorfer 2005	16/36	16/37		12.2 %	0.01 [-0.22, 0.24]
Subtotal (95% CI)	**299**	**297**		**100.0 %**	**0.04 [-0.05, 0.13]**
Total events: 20 (ORT), 16 (IVT)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 4.85, df = 3 (P = 0.18); I^2 =38%					
Test for overall effect: Z = 0.79 (P = 0.43)					
3 Not stated					
Brown 1988	8/94	1/34		10.5 %	0.06 [-0.02, 0.14]
el-Mougi 1994	0/41	0/20		11.6 %	0.0 [-0.07, 0.07]
Gonzalez 1988	13/100	0/100		12.4 %	0.13 [0.06, 0.20]
Hernandez 1987	9/108	0/36		13.0 %	0.08 [0.02, 0.15]
Mackenzie 1991	2/52	0/52		13.4 %	0.04 [-0.02, 0.10]
Santosham 1982i	0/63	0/31		16.3 %	0.0 [-0.05, 0.05]
Santosham 1982ii	1/35	0/17		8.0 %	0.03 [-0.07, 0.13]
Tamer 1985	3/47	0/50		10.7 %	0.06 [-0.01, 0.14]
Vesikari 1987	2/22	0/15		4.2 %	0.09 [-0.06, 0.24]
Subtotal (95% CI)	**562**	**355**		**100.0 %**	**0.05 [0.02, 0.09]**
Total events: 38 (ORT), 1 (IVT)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 15.76, df = 8 (P = 0.05); I^2 =49%					
Test for overall effect: Z = 2.88 (P = 0.0040)					

Analysis 2.5. Comparison 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses, Outcome 5 Failure to rehydrate: by route.

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

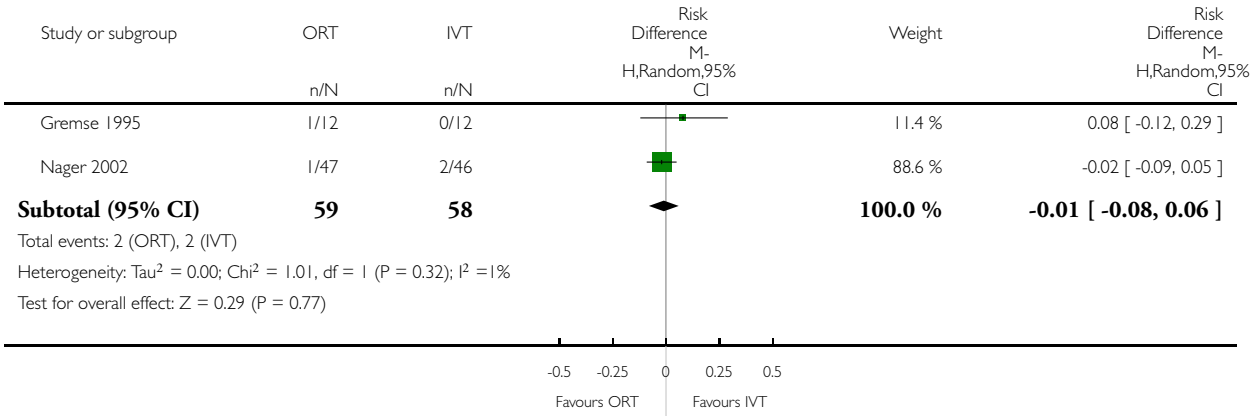
Comparison: 2 Oral rehydration therapy (any solution) versus intravenous therapy: subgroup analyses

Outcome: 5 Failure to rehydrate: by route



(*Continued . . .*)

(. . . *Continued*)



APPENDICES

Appendix 1. Search methods: detailed search strategies

Search set	CIDG SR[a]	CENTRAL	MEDLINE[b]	EMBASE[b]	LILACS[b]
1	gastroenteritis	gastroenteritis	gastroenteritis	GASTROENTERITIS	gastroenteritis
2	diarrhea	diarrhea	diarrhea	ACUTE-GASTROENTERITIS	diarrhea
3	1 or 2	1 or 2	1 or 2	INFANTILE-GASTROENTERITIS	1 or 2
4	rehydration	rehydration	FLUID THERAPY	DIARRHEA	rehydration
5	intravenous feeding	intravenous feeding	WATER-ELECTROLYTE BALANCE	1 or 2 or 3 or 4	intravenous feeding
6	intravenous administration	intravenous administration	WATER-ELECTROLYTE IMBALANCE	REHYDRATION	intravenous administration
7	fluid therapy	fluid therapy	REHYDRATION SOLUTIONS	ORAL- REHYDRATION- SOLUTION	fluid therapy

(*Continued*)

8	4 or 5 or 6 or 7	4 or 5 or 6 or 7	rehydrat*	INTRAVENOUS-FEEDING	4 or 5 or 6 or 7
9	3 and 8	3 and 8	INFUSIONS, INTRAVENOUS	FLUID-THERAPY	3 and 8
10	-	-	FEEDING METHODS	INTRAVENOUS-FEEDING	-
11	-	-	nose feed*	intravenous administration	-
12	-	-	nasogastric feed*	NOSE-FEEDING	-
13	-	-	naso-gastric feed*	NASOGASTRIC-TUBE	-
14	-	-	ng feed*	nasogastric feed$	-
15	-	-	ng tube	nose feed$	-
16	-	-	nasogastric tube	ng feed$	-
17	-	-	4-16/or	ng tube	-
18	-	-	3 and 17	6-17/or	-
19	-	-	Limit 18 to human	5 and 18	-
20	-	-	-	Limit 19 to human	-

[a] Cochrane Infectious Diseases Group Specialized Register.
[b] Search terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Higgins 2005b); upper case: MeSH or EMTREE heading; lower case: free text term.

Appendix 2. Description of oral rehydration solutions

Trial	Sodium	Potassium	Chloride	Sugar	Bicarbonate	Citrate	Osmolarity reported	Osmolarity calculated	Notes
Atherly-John 2002	-	-	-	-	-	-	-	-	Commercially prepared oral maintenance elec-

(*Continued*)

									trolyte solution (no further details)
Brown 1988 (rehydration)	90 mEq	20 mEq	80 mEq	Glucose 111 mmol/L	30 mEq	-	-	331 mOsmol/L	-
Brown 1988 (maintenance)	60 mEq	20 mEq	60 mEq	Glucose 20 g	20 mEq	-	-	-	-
de Pumarejo 1990	75 mEq/L	20 mEq/L	65 mEq/L	Glucose 139 mmol/L[a]	-	30 mEq/L	305 mmol/L	329 mOsmol/L	Rehydralyte (Ross Lab)
el-Mougi 1994 (standard ORS)	90 mM	20 mM	80 mM	Glucose 111 mm	-	10 mM	311 mOsmol/L	-	-
el-Mougi 1994 (diluted ORS)	60 mM	13 mM	53 mM	Glucose 75 mm	-	6.6 mM	210 mOsmol/L	207.6 mOsmol/L	-
Gonzalez 1988	90 mmol/L	20 mmol/L	80 mmol/L	Glucose 111 mmol/L	30 mmol/L	-	-	331 mOsmol/L	World Health Organization solution
Gremse 1995	75 mmol/L	20 mmol/L	65 mmol/L	Glucose 139 mmol/L[a]	-	10 mmol/L	-	309 mOsmol/L	-
Hernandez 1987 (Group 1)	30 mEq/L	20 mEq/L	30 mEq/L	Glucose 277 mmol/L	30 mEq/L	31 mEq/L	338 mOsmol/L	-	Pedialyte
Hernandez 1987 (Group 2)	90 mEq/L	20 mEq/L	80 mEq/L	Glucose 111 mmol/L	30 mEq/L	-	331 mOsmol/L	-	World Health Organization solution
Hernandez 1987 (Group 3)	60 mEq/L	20 mEq/L	40 mEq/L	Glucose 111 mmol/L	30 mEq/L	-	261 mOsmol/L	-	-

(*Continued*)

Issenman 1993 (rehydration)	75 mEq/L	20 mEq/L	65 mEq/L	Dextrose 139 mmol/L[a]	-	30 mEq/L	305 mOsmol/L	329 mOsmol/L	-
Issenman 1993 (maintenance)	45 mEq/L	20 mEq/L	35 mEq/L	Dextrose 139 mmol/L[a]	-	30 mEq/L	250 mOsmol/L	269 mOsmol/L	-
Listernick 1986	60 mEq/L	20 mEq/L	50 mEq/L	Glucose 111 mmol/L and fructose 28 mmol/L	-	30 mEq/L	-	299 mOsmol/L	-
Mackenzie 1991	50 mmol/L	20 mmol/L	40 mmol/L	Glucose 111 mmol/L (2% glucose)	-	10 mmol/L	-	231 mOsmol/L	-
Nager 2002[b]	45 mEq/L	20 mEq/L	35 mEq/L	Glucose 139 mmol/L	-	30 mEq/L	390 mmol/L	-	Pedialyte
Santosham 1982i and Santosham 1982ii (group A)	90 mmol/L	20 mmol/L	80 mmol/L	Glucose 111 mmol/L	30 mmol/L	-	333 mOsmol/L	331 mOsmol/L	-
Santosham 1982i and Santosham 1982ii (group B)	50 mmol/L	20 mmol/L	40 mmol/L	Glucose 111 mmol/L	30 mmol/L	-	251 mOsmol/L	-	-
Sharifi 1985 (rehydration)	80 mmol/L	20 mmol/L	65 mmol/L	Dextrose 70 mmol/L	35 mmol/L	-	270 mOsmol/L	-	-
Sharifi 1985 (maintenance)	40 mmol/L	30 mmol/L	45 mmol/L	Dextrose 130 mmol/L	25 mmol/L	-	270 mOsmol/L	-	-

(*Continued*)

Singh 1982	90 mmol/L	20 mmol/L	80 mmol/L	Glucose 111 mmol/L	30 mmol/L	-	333 mOsmol/L	331 mOsmol/L	-
Spandorfer 2005[b]	45 mEq/L	20 mEq/L	35 mEq/L	Glucose 139 mmol/L	-	30 mEq/L	390 mmol/L	-	Pedialyte
Tamer 1985 (rehydration)	75 mEq/L	30 mEq/L	75 mEq/L	Dextrose 111 mmol/L[a]	30 mEq/L	-	-	321 mOsmol/L	-
Tamer 1985 (maintenance)	50 mEq/L	30 mEq/L	50 mEq/L	Dextrose 166 mmol/L[a]	30 mEq/L	-	-	326 mOsmol/L	-
Vesikari 1987	60 mmol/L	20 mmol/L	50 mmol/L	Glucose 144 mmol/L	30 mmol/L	-	-	304 mOsmol/L	-

[a] Units converted from those reported in the published paper.
[b] Components not reported in the paper (taken from another source).

Appendix 3. Risk of bias (methodological quality)

Trial	Randomization		Double blinding		Describe withdrawals	Overall Jadad score	Allocation concealment
	Stated	Method	Stated	Method			
Atherly-John 2002	Yes	Adequate	No	N/A	Adequate	3	Adequate
Brown 1988	Yes	Unclear	No	N/A	Adequate	2	Unclear
de Pumarejo 1990	Yes	Unclear	No	N/A	Inadequate	1	Unclear
el-Mougi 1994	Yes	Unclear	No	N/A	Inadequate	1	Unclear
Gonzalez 1988	Yes	Unclear	No	N/A	Inadequate	1	Unclear
Gremse 1995	Yes	Unclear	No	N/A	Inadequate	1	Unclear

(*Continued*)

Hernandez 1987	Yes	Unclear	No	N/A	Inadequate	1	Unclear
Issenman 1993	Yes	Unclear	No	N/A	Adequate	2	Unclear
Listernick 1986	Yes	Unclear	No	N/A	Adequate	2	Unclear
Mackenzie 1991	Yes	Unclear	No	N/A	Adequate	2	Unclear
Nager 2002	Yes	Unclear	No	N/A	Adequate	2	Unclear
Santosham 1982i; Santosham 1982ii	Yes	Unclear	No	N/A	Adequate	2	Unclear
Sharifi 1985	Yes	Unclear	No	N/A	Inadequate	1	Unclear
Singh 1982	Yes	Inadequate	No	N/A	Inadequate	0	Unclear
Spandorfer 2005	Yes	Adequate	No	N/A	Adequate	3	Adequate
Tamer 1985	Yes	Unclear	No	N/A	Adequate	2	Unclear
Vesikari 1987	Yes	Unclear	No	N/A	Adequate	2	Unclear

Appendix 4. Meta-regression results

Variable	Values	Coefficient	P value
Allocation concealment	0 = unclear; 1 = adequate	0.15	0.12
Funding source	0 = not stated; 1 = stated	-0.0033	0.63
Participant status	0 = inpatient; 1 = outpatient	-0.0050	0.86
Quality score	Value of Jadad score	0.015	0.18
State of nourishment	0 = well nourished; 1 = some malnourished	0.0091	0.59

(*Continued*)

Country income	0 = high income; 1 = low-middle income	-0.027	0.14
Persistent vomiters	0 = excluded; 1 = included	0.0054	0.76
ORT route	Oral: 0 = yes; 1 = no	0.00094	0.95
ORT route	Nasogastric: 0 = yes; 1 = no	-0.028	0.43
ORT route	Combination of oral and nasogastric: 0 = yes; 1 = no	0.0040	0.77

WHAT'S NEW

Last assessed as up-to-date: 28 March 2006.

Date	Event	Description
10 November 2009	Review declared as stable	Given the current evidence new trials are unlikely to change the results, and further research on this question is not warranted. Therefore, the authors do not plan to update the current review

HISTORY

Protocol first published: Issue 3, 2003

Review first published: Issue 3, 2006

Date	Event	Description
10 November 2008	Amended	Converted to new review format with minor editing.

CONTRIBUTIONS OF AUTHORS

L Hartling provided overall project coordination and contributed to protocol development, literature searching, screening of articles for relevance and inclusion, assessment of study quality, data extraction, data analysis, and preparation of completed review. S Bellemare contributed to protocol development, literature searching, relevance screening of articles, assessment of study quality, data extraction, data analysis, and preparation of completed review. N Wiebe conducted the statistical analysis and contributed to the protocol development and preparation of completed review. K Russell contributed to screening of articles for relevance and inclusion, data extraction and entry, and preparation of completed review. T Klassen contributed to protocol development and preparation of completed review, and provided methodological and content expertise. W Craig contributed to protocol development, quality assessment, preparation of completed review, and provided content expertise.

DECLARATIONS OF INTEREST

None declared.

SOURCES OF SUPPORT

Internal sources

- Alberta Research Centre for Child Health Evidence, Canada.

External sources

- Alberta Heritage Foundation for Medical Research, Canada.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

2006, Issue 3 (deviations from protocol).

- We used risk difference for our primary outcome instead of risk ratio because we have too many trials with zeros in both treatment groups; we did say how we would calculate baseline risk in the protocol, and we are simply expanding upon this.

- Our primary analysis changed from using the fixed-effect model to the random-effects model before we looked at the data; this change was based on the comments from statisticians in Cochrane's Statistical Methods Group.

- We chose to use the I-squared statistic rather than the chi-square test for heterogeneity based on comments from statisticians in Cochrane's Statistical Methods Group.

- Heterogeneity is always present, but it may not always be quantifiable (too small). We used the fixed-effect model in the sensitivity analyses to give a sense of whether the treatment effect may ever be significant, because the random-effects model may be biased when there is funnel plot asymmetry, and for a conservative approach to an equivalence hypothesis if there could be one.

- Omitting the trim-and-fill method from the protocol was an oversight.

- We added the participant subgroup inpatient/outpatient status before looking at the data, but after the protocol was published.

- We added 'sodium intake and sodium levels' as an outcome measure; since hyponatremia and hypernatremia were part of the protocol, this makes sodium levels and intake relevant, and we therefore chose to include this outcome measure post-hoc as it was frequently reported in the included trials.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Oral; Dehydration [etiology; *therapy]; Fluid Therapy [*methods]; Gastroenteritis [*complications]; Infusions, Intravenous; Randomized Controlled Trials as Topic; Rehydration Solutions [*administration & dosage]

MeSH check words

Child; Humans