Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review)

Gregorio GV, Gonzales MLM, Dans LF, Martinez EG

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Polymer-based oral rehydration solution for treating acute watery diarrhoea

Germana V Gregorio¹, Maria Liza M Gonzales¹, Leonila F Dans², Elizabeth G Martinez¹

¹Department of Pediatrics, College of Medicine-Philippine General Hospital, University of the Philippines, Manila, Philippines.
²Departments of Pediatrics and Clinical Epidemiology, Philippine General Hospital, University of the Philippines, Manila, Philippines

Contact address: Germana V Gregorio, Department of Pediatrics, College of Medicine-Philippine General Hospital, University of the Philippines, Taft Avenue, Manila, National Capital Region, 1000, Philippines. germana1@hotmail.com.

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A B S T R A C T

Background
Acute diarrhoea is one of the principal causes of morbidity and mortality among children in low-income countries. Glucose-based ORS helps replace fluid and prevent further dehydration from acute diarrhoea. Since 2004, the World Health Organization has recommended the osmolarity < 270 mOsm/L (ORS ≤ 270) over the > 310 mOsm/L formulation (ORS ≥ 310). Glucose polymer-based ORS (eg prepared using rice or wheat) slowly releases glucose and may be superior.

Objectives
To compare polymer-based ORS with glucose-based ORS for treating acute watery diarrhoea.

Search methods
In September 2008, we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (The Cochrane Library 2008, Issue 3), MEDLINE, EMBASE, LILACS, and mRCT. We also contacted researchers, organizations, and pharmaceutical companies, and searched reference lists.

Selection criteria
Randomized controlled trials of people with acute watery diarrhoea (cholera and non-cholera associated) comparing polymer-based and glucose-based ORS (with identical electrolyte contents).

Data collection and analysis
Two authors independently assessed the search results and risk of bias, and extracted data. In multiple treatment arms with two or more treatment groups, we combined outcomes as appropriate and compared collectively with the control group.

Main results
Thirty-four trials involving 4214 participants met the inclusion criteria: 27 in children, five in adults and two in both. Twelve trials used adequate methods to conceal allocation. Most compared polymer-based ORS with ORS ≥ 310. There were fewer unscheduled intravenous infusions in the polymer-based ORS group compared with glucose-based ORS (ORS ≥ 310 and ≤ 270 groups combined) (RR 0.75, 95% CI 0.59 to 0.95; 2235 participants, 19 trials). Adults positive for Vibrio cholerae had a shorter duration of diarrhoea
with polymer-based ORS than with ORS ≤ 270 (MD -7.11 hours, SD -11.91 to -2.32; 228 participants, 4 trials). Wheat-based ORS resulted in lower total stool output in the first 24 hours compared with ORS ≤ 270 (MD -119.85 g/kg, SD -114.73 to -124.97; 129 participants, 2 trials). Adverse effects were similar for polymer-based ORS and glucose-based ORS.

Authors’ conclusions
Polymer-based ORS shows some advantages compared to ORS ≥ 310 for treating all-cause diarrhoea, and in diarrhoea caused by cholera. Comparisons favoured the polymer-based ORS over ORS ≤ 270, but the analysis was underpowered. If specialists consider a potential role for polymer-based ORS, further trials against the current standard (ORS ≤ 270) will be required.

Plain Language Summary
Polymer-based oral rehydration solution (ORS) ORS for acute diarrhoea

Acute diarrhoea is a common cause of death and illness in developing countries. Oral rehydration solutions (ORS) have had a massive impact worldwide in reducing the number of deaths related to diarrhoea.

Most ORS is in the form of a sugar-salt solution, but over the years people have tried adding a variety of compounds ('glucose polymers') such as whole rice, wheat, sorghum, and maize. The aim is to slowly release glucose into the gut and improve the absorption of the water and salt in the solution. This review updates and expands on a 1998 Cochrane Review of rice-based ORS, and assesses the available evidence on the use of polymer-based ORS (both rice and non-rice based) in comparison with the glucose-based ORS.

The original ORS was based on glucose and had an osmolarity of ≥ 310 mOsm/L (ORS ≥ 310). Glucose-based ORS with a lower osmolarity was later introduced in attempts to improve efficacy, and is considered better at reducing the amount and duration of diarrhoea.

Thirty-four trials involving 4214 participants met the inclusion criteria: 27 in children; five in adults; and two in both. Most trials compared polymer-based ORS with a sugar-salt ORS with a particular strength (ORS ≥ 310), which is slightly more salty than the currently agreed best formula (≤ 270 mOsm/L). The trials’ methodological quality was variable.

Fewer people in the polymer-based ORS group needed a drip to be rehydrated compared with those in the glucose-based ORS group. Adverse events were similar for polymer-based ORS and glucose-based ORS.

The authors conclude that polymer-based ORS show some advantages compared to glucose-based ORS for treating diarrhoea of any cause and in diarrhoea caused by cholera. Limited evidence favoured the polymer-based ORS over ORS ≤ 270.

Further trials should compare the efficiency of ORS ≤ 270 with a polymer-based ORS.

Background
Acute diarrhoea, which is defined as three or more loose bowel movements in a 24-hour period (WHO/ICDDRB 1995), is one of the principal causes of morbidity and mortality among children in low-income countries. A 2003 review of 27 prospective studies from 20 countries published from 1990 to 2000 estimated the incidence of diarrhoea as 3.8 episodes per child per year for children less than 11 months of age and 2.1 episodes per child per year for children aged one to four years (Kosek 2003). It has a negative impact on quality of life and can result in considerable healthcare costs. Most of these diarrhoeal illnesses occur in low-income countries and are largely caused by infection. The cause is mainly viral in children aged less than five years, while both bacterial and viral pathogens are implicated in adults (Casburn-Jones 2004). Other causes of acute diarrhoea are disordered motility, such as irritable bowel syndrome, intake of certain drugs, or ileal bile acid malabsorption.

Since the 1980s, efforts to decrease the number of deaths from diarrhoea have been based on several interventions, including the improvement of water quality and sanitation, promotion of breastfeeding, and the introduction of treatment programmes that in-
clude oral rehydration therapy (Claeson 1990). Oral rehydration solution (ORS) was introduced in 1979 by the World Health Organization (WHO), and it rapidly became the cornerstone of programmes for the control of diarrhoeal diseases (Claeson 1990). The osmolarity of the original formulation is 310 mOsm/L (referred to as ORS ≥ 310) and consists of glucose (111 mmol/L), sodium (90 mmol/L), potassium (20 mmol/L), chloride (80 mmol/L), and citrate (10 mmol/L) or bicarbonate (30 mmol/L). The ORS was shown to improve signs of dehydration, including thirst, sunken eyeballs, sunken fontanelles, poor skin turgor, or a decreased or absence of urine output (WHO/ICDDRB 1995). It is considered as both safe and effective (Santosham 1991), and, since its introduction, it has been considered to be mainly responsible for the decrease in case-fatality rates from acute dehydrating diarrhoea (Victora 2000).

The physiological basis for the use of ORS ≥ 310 was the co-transport of glucose and sodium across the intestinal membrane (Santosham 1991). While this glucose-based ORS is effective in replacing the fluid from acute diarrhoea thus preventing further dehydration, it neither reduces stool loss nor shortens the duration of illness (Santosham 1991). Increasing the glucose concentration to greater than 111 mmol/L increases the osmotic load of the solution, which may further aggravate the fluid loss and induce hypernatraemia (Hunt 1992). In 2004, the WHO recommended a different formulation in which the glucose and sodium content were each reduced to 75 mmol/L to give a total osmolarity of 245 mOsm/L (referred to as ORS ≤ 270) (WHO 2004). ORS ≤ 270 reduces stool volume, shortens the duration of diarrhoea, and decreases the need for unscheduled intravenous therapy compared with ORS ≥ 310 (Hahn 2002).

New ORS formulations have been evaluated in attempts to improve the efficacy of ORS ≥ 310. Glucose polymer-based ORS (referred to as polymer-based ORS) may contain whole rice (amylopectins), as in rice-based ORS or rice syrups (maltodextrins). The difference is that the latter contains only a small amount of amino acids and protein. Other sources of polymers are wheat, sorghum, and maize (high amylase-resistant starch). In these polymer-based solutions, the glucose is slowly released after digestion and is absorbed in the small bowel, enhancing the reabsorption of water and electrolyte secreted into the bowel lumen during diarrhoea (Carpenter 1988; Pizarro 1991). Although ORS ≥ 310 is no longer recommended it remains unknown whether a polymer-based ORS is indeed more effective than a glucose-based ORS (ie ORS ≥ 310 or ORS ≤ 270).

A 1998 Cochrane Review of rice-based ORS for treating diarrhoea concluded that it significantly reduced the mean 24-hour stool output in adults and children with cholera or cholera-like diarrhoea, but results were inconclusive for infants and children with non-cholera diarrhoea (Fontaine 1998). Our Cochrane Review has updated the evidence on the use of polymer-based ORS (both rice and non-rice based) and expanded the primary outcome measures to include the number of participants who required unscheduled use of intravenous fluid therapy. Other primary outcome measures focus on the duration of diarrhoea and the stool output in the first 24 hours since these are considered crucial in the management of these patients and the first 24 hours is the period of greatest stool loss. Our Cochrane Review also aims to provide more insights into whether polymer-based ORS is more effective than glucose-based ORS, and to inform future research.

Patients are dehydrated during the first six to eight hours, but once rehydrated, feeding is initiated and stool losses are replaced volume per volume with the ORS. The effect of feeding a rice-based or starch-based food as soon as the participants are rehydrated could confound the effects of glucose polymer-based ORS (Alam 1992).

OBJECTIVES
To compare polymer-based oral rehydration solution (ORS) with glucose-based ORS for treating acute watery diarrhoea.

METHODS
Criteria for considering studies for this review

Types of studies
Randomized controlled trials.

Types of participants
Infants, children, and adults with acute watery diarrhoea (cholera and non-cholera associated) and mild, moderate, or severe dehydration, as defined by trial authors. We excluded trials enrolling patients who were unable to drink or take in oral fluids, those in shock, and those with bloody diarrhoea or dysentery.

Types of interventions

Intervention: polymer-based ORS
ORS in which glucose was replaced by a commercial or a local preparation of a polymer (eg rice, wheat, maltodextrins, maize, sorghum, or corn), the electrolyte composition remaining unchanged between the two solutions.
Control: glucose-based ORS
ORS that contains glucose as a carbohydrate source with either 90 or 60 to 75 mmol/L of sodium.

Types of outcome measures

Primary
- Total stool output (g/kg) during the first 24 hours after randomization.
- Total stool output (g/kg) from randomization to cessation of diarrhoea.
- Duration of diarrhoea (hours) from randomization until cessation of diarrhoea.

Secondary
- Unscheduled intravenous fluid therapy.
- Cases of vomiting.

Adverse events
- All adverse events including hyponatraemia (serum sodium level ≤ 130 mmol/L) (low sodium), hypokalaemia (≤ 3 mol/L) (low potassium), and development of persistent diarrhoea.

Search methods for identification of studies
All relevant trials regardless of language or publication status (published, unpublished, in press, and ongoing).

Databases
We searched the following databases using the search terms and strategy described in Appendix 1: Cochrane Infectious Diseases Group Specialized Register (September 2008); Cochrane Central Register of Controlled Trials (CENTRAL), published in The Cochrane Library (2008, Issue 2); MEDLINE (1966 to September 2008); EMBASE (1974 to September 2008); and LILACS (1982 to September 2008). We also searched the metaRegister of Controlled Trials (mRCT) using ‘diarrhoea’ and ‘oral rehydration solution’ as search terms.

Researchers, organizations, and pharmaceutical companies
To help identify unpublished and ongoing trials, we conducted a communications or website search (May 2006 to September 2008) with individual researchers working in the field of general paediatrics and gastroenterology, and the following organizations who may be funding a similar study: WHO - Dr. Kevin Palmer, Regional Adviser, Waterborne and Parasitic Diseases, WHO Regional Office for the Western Pacific, Manila, Philippines; INCLEN (www.inclen.org); USAID (www.usaid.gov); Asian Development Bank (www.adb.org); and World Bank (www.worldbank.org). We also searched United Laboratories Philippines (www.unilab.com.ph) and Abbott International (www.abbott.com.ph) (pharmaceutical companies who manufacture oral rehydration solution) for any unpublished or ongoing trials.

Reference lists
We checked the reference lists of all studies identified by the above methods.

Data collection and analysis

Selection of studies
Two authors (GV Gregorio and LF Dans) independently assessed the results of the literature search to determine whether the title or abstract cited a randomized controlled trial. We retrieved the full reports of clinical trials considered by one or both authors to be potentially relevant as well as trials with unclear treatment allocation. We independently assessed the inclusion criteria of these trials using a standard eligibility form. We resolved any disagreements through discussion, or if this failed, by consulting another author (MLM Gonzales). We scrutinized trial reports to ensure multiple publication would be detected. We listed the excluded studies and the reasons for the exclusion.

Data extraction and management
Two authors (GV Gregorio and EG Martinez or MLM Gonzales) independently extracted the data from the trials using pre-tested data extraction forms. We extracted the number of participants who were randomized and the number analysed for all outcomes for each treatment arm in each trial to determine loss to follow up, whether loss was comparable across treatments, and to determine the type of analysis used. Since the primary outcome measures were continuous, we extracted arithmetic means and standard deviations for each treatment group and noted the number of participants in each group. In trials with multiple interventions (two or more different polymer-based ORS that were used as treatment groups) we pooled the means and standard deviations of the different polymer-based ORS across the treatment arms.

For dichotomous outcome measures, we recorded the number(s) experiencing the event and the numbers analysed in each treatment group. In the meta-analysis, for multiple treatment arms, we combined the numbers experiencing the outcome in two or more
experimental interventions as appropriate and compared collectively with the control group. We resolved any disagreements about data extracted by referring to the trial report and through discussion, or, if that failed, by consulting with another author. Where data were insufficient or missing, we attempted to contact the trial authors. GV Gregorio entered the data into Review Manager 5.

Assessment of risk of bias in included studies
Two authors (GV Gregorio and LF Dans or MLM Gonzales) independently assessed the risk of bias (methodological quality) of each trial using a prepared assessment form. We assessed the generation of allocation sequence and allocation concealment as adequate, inadequate, or unclear according to Juni 2001. We also noted who was blinded, such as the trial participants, care providers, or outcome assessors, and classified the inclusion of randomized participants in the analysis as adequate if greater than 90% or inadequate if 90% or less. We used the results of the assessment to perform a sensitivity analysis. In the case of unclear or missing information, we made attempts to contact the authors. We resolved disagreements by discussion between review authors.

Assessment of reporting biases
We assessed the presence of publication bias by looking for asymmetry in the funnel plots. We also assessed asymmetry of the funnel plots using StatsDirect and considered a P value < 0.05 on Egger's bias test as significant.

Data synthesis
GV Gregorio analysed the data using Review Manager 5 and presented the results with 95% confidence intervals (CI). We determined and reported the percentage lost to follow up for all trials from the numbers randomized and the numbers analysed in each treatment group. Analyses were based on a complete-case approach. For the participants who did not adhere to the study protocol, their outcome was based on what was reported by the author (if an intention-to-treat analysis was done) or on data sought from the trial authors (if there was no intention-to-treat analysis). We presented risk ratios (RR) for dichotomous outcomes. We determined continuous outcomes summarized as arithmetic means and standard deviations data using the mean difference (MD). We checked the normality of the data by calculating the ratio of the mean over the standard deviation. If the ratio (mean/SD) was less than two, then it was likely that the data were skewed and therefore were not combined in the meta-analysis.

Subgroup analysis and investigation of heterogeneity
We evaluated the presence of statistical heterogeneity among the interventions by inspecting the forest plot and by performing a Chi² test for heterogeneity using a P value of 0.10 to determine statistical significance. Also, we used a I² value of 50% as an indication of moderate heterogeneity. If there was statistically significant heterogeneity, we used the random-effects model (DerSimonian and Laird method) to combine data, otherwise we applied a fixed-effect model. We investigated heterogeneity using subgroup analyses. We subgrouped trials according to the osmolarity of glucose ORS (ORS ≥ 310 or ORS ≤ 270) and type of polymer (rice, wheat, maltodextrins, and sorghum). We also evaluated the effect of the participant age (< 19 years (paediatric) and ≥ 19 years (adult)) and of cholera as a pathogen. When there was substantial statistical heterogeneity (ie I² = 100%), we did not combine the trials in the meta-analysis.

Sensitivity analysis
We performed sensitivity analyses to assess the robustness of the meta-analysis by excluding trials of a low methodological quality, that is, those that used an inadequate method of randomization, uncontrolled allocation, and inadequate inclusion of randomized participants in the analysis.

RESULTS

Description of studies

Search results
Of the 212 clinical trials included in the primary search until 26 September 2008, 69 were assessed for inclusion in the review (none were multiple publications). Thirty-five trials met the inclusion criteria (see 'Characteristics of included studies'). We excluded the remaining 35 trials for the following reasons (see also 'Characteristics of excluded studies'): electrolyte composition of the intervention and the control group were not identical or not known (11); composition of treatment group was either unknown or not a polymer (eight); not a clinical trial on ORS but on the use of drugs in acute diarrhoea (four); control group used an oral saline solution (one) or an ORS that did not contain either a 90 or 310 or ORS ≤ 270) and type of polymer (rice, wheat, maltodextrins, and sorghum). We also evaluated the effect of the participant age (< 19 years (paediatric) and ≥ 19 years (adult)) and of cholera as a pathogen. When there was substantial statistical heterogeneity (ie I² = 100%), we did not combine the trials in the meta-analysis.

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Sensitivity analysis
We performed sensitivity analyses to assess the robustness of the meta-analysis by excluding trials of a low methodological quality, that is, those that used an inadequate method of randomization, uncontrolled allocation, and inadequate inclusion of randomized participants in the analysis.
Setting
Most trials were conducted in India (10) and Bangladesh (nine). Other study centres were in Egypt (three) (El-Mougi 1988; Fayad 1993; El-Mougi 1996), Chile (two) (Guiraldes 1995a; Guiraldes 1995b), Mexico (two) (Maulen-Radovan 1994; Maulen-Radovan 2004), and one trial each was done in Australia (Wall 1997), Colombia (Bernal 2005), Madagascar (Razafindrakoto 1993), Malaysia (Iyngkaran 1998), Pakistan (Islam 1994), Philippines (Santos Ocampo 1993), Romania (Nanulescu 1999), and Sudan (Mustafa 1995). Only two trials were not done in a hospital setting. One was done in a paediatric clinic (Nanulescu 1999) and one in a rural treatment centre (Zaman 2007).

Participants
The 34 eligible trials included 4214 participants: 2269 used polymer-based ORS and 1945 used glucose-based ORS. In the individual trials, there was no statistically significant difference in the baseline characteristics between the two groups.

Age
Twenty-seven trials included children only (26 in children < five years old), five included adults only (Alam 1992; Bhattacharya 1998; Ramakrishna 2000; Hussain 2003), and two included both adults and children (Molla 1985; Dutta 1998). The two trials that included both adults and children randomized and reported the outcomes separately for each group.

Pathogen
In terms of the aetiology of diarrhoea, only eight trials randomized exclusively Vibrio cholerae positive patients (Molla 1989a; Alam 1992; Bhattacharya 1998; Ramakrishna 2000; Hussain 2003), while 21 included participants with mixed pathogens (both cholera and non-cholera), and five did not report the pathogen (El-Mougi 1988; Molla 1989b; Fayad 1993; Mustafa 1995; Sharma 1998).

Interventions
Twenty-eight trials compared two interventions (polymer versus glucose-based ORS), five trials compared three interventions (rice ORS versus non-rice ORS versus glucose-based ORS) (Alam 1987; Dutta 1988; Mustafa 1995; Ramakrishna 2000), and one trial ≤ (Molla 1989b) compared six interventions (rice, millet, maize, potatoes, sorghum, and wheat ORS versus glucose-based ORS). Only five trials used an ORS ≤ 270 mOsm/L (Bhattacharya 1998; Iyngkaran 1998; Nanulescu 1999; Dutta 2000; Maulen-Radovan 2004), while 29 used ORS ≥ 310 mOsm/L. Twenty-five trials used a variety of rice (uncooked, cooked, powdered, and pop rice) as a source of polymer, three utilized maltodextrins (Akbar 1991; Santos Ocampo 1993; El-Mougi 1996), two trials used amylase-resistant starch (Ramakrishna 2000; Ramakrishna 2008), and one trial each employed plain flour (Bernal 2005), mung beans (Bhan 1987) (with another arm of the trial using pop rice), and wheat (Alam 1987) (another arm using rice). One trial compared the efficacy of glucose ORS with several polymers in the form of wheat, millet, maize, rice, sorghum, and potatoes (Molla 1989b).

The polymer was prepared locally in 23 trials and obtained commercially in eight trials (Santos Ocampo 1993; Maulen-Radovan 1994; Guiraldes 1995a; Guiraldes 1995b; El-Mougi 1996; Faruque 1997; Zaman 2001; Maulen-Radovan 2004). The source was not reported in three trials (Akbar 1991; Nanulescu 1999; Hussain 2003). Only one trial withheld feeding in the first 24 hours (Molla 1989). In another trial (Alam 1992), the patients were randomized into the rice- and glucose-based ORS and further stratified as with and without food intake (Alam 1992). In this, only the data on participants with food intake were used in the review. Feeding was immediately started after hydration in 25 trials, while in seven the onset of refeeding was unclear (Patra 1982; Molla 1985; Bhattacharya 1998; Dutta 1998; Iyngkaran 1998; Dutta 2000; Ramakrishna 2000).

Outcomes reported
Most of the 34 trials reported the total stool output in the first 24 hours (25), total stool output from randomization to discharge (18), duration of diarrhoea (26), and unscheduled use of intravenous fluid (19). However, some of these outcomes were measured and reported in different units by the different studies and therefore not all the data could be used in the meta-analysis. Furthermore, we did not include the data in the meta-analyses if they were skewed: data for total stool output in 24 hours (Molla 1989a; Santos Ocampo 1993; Maulen-Radovan 2004; Bernal 2005); data on duration of diarrhoea (Santos Ocampo 1993; Mustafa 1995; Wall 1997); and data on total stool output from randomization to discharge (Santos Ocampo 1993).

There were a few trials that reported the number of participants with vomiting (nine) (Patra 1982; Bhan 1987; El-Mougi 1988; Mohan 1988; Alam 1992; Islam 1994; Mustafa 1995; Dutta 1998; Iyngkaran 1998), hyponatraemia (six) (Dutta 1988; Guiraldes 1995a; Bhattacharya 1998; Dutta 2000; Zaman 2001; Ramakrishna 2008), hypokalaemia (two) (Bhan 1987; Zaman 2007), and development of persistent diarrhoea (two) (Fayad 1993; Faruque 1997).

Risk of bias in included studies
See Appendix 2 for a summary of the assessment and the characteristics of included studies for details of each trial’s methods.

Of the 34 trials, the methods used to generate the allocation sequence were adequate (computer-generated or random-numbers table) in 24 trials and unclear in the remaining 10 trials (Patra 1982; Bhan 1987; Mohan 1988; Molla 1989a; Razafindrakoto...
Less than half of the trials (12) used an adequate method to conceal allocation. The method was unclear in the other 22 trials. Blinding of the participants, providers, and assessors was only done in three trials (Akbar 1991; Santos Ocampo 1993; El-Mougi 1996). Blinding was difficult or impossible in most trials because of the difference in the appearance of the ORS formulation after reconstitution. All but two trials included an adequate (> 90%) number of randomized participants in the analysis. The number was assessed as inadequate in two trials (Akbar 1991; Nanulescu 1999).

Effects of interventions

There were two trials that reported the effects on adults and children separately (Molla 1985; Dutta 1998). Thus, in the following results, there are some analyses that have more comparison groups than the number of trials reported.

Type of glucose ORS

Five trials compared polymer-based ORS with ORS ≤ 270, and 30 trials with ORS ≥ 310. Overall, the stool volume during the first 24 hours was lower in the polymer-based ORS group (1375 participants, 12 trials, Analysis 1.1). There was substantial, significant heterogeneity (Chi² test P < 0.00001, I² = 100%). One trial with ORS ≤ 270 also showed lower stool volume (99 participants, Nanulescu 1999, Analysis 1.1). The duration of diarrhoea varied from 30 to 81 and 34 to 91 hours in the polymer-based ORS and glucose-based ORS groups, respectively.

For ORS ≥ 310, overall duration was shorter in the polymer-based ORS group (977 participants, 12 trials, Analysis 1.2) (Chi² test P < 0.00001, I² = 100%). For ORS ≤ 270, there was a similar difference (MD -5.98 g/kg, 95% CI -2.08 to -9.89; 194 participants, 3 trials, Analysis 1.2), but we observed significant heterogeneity when we excluded Nanulescu 1999, the one trial with incomplete outcome data (Chi² test P < 0.10, I² = 63%). There was a trend toward slightly fewer unscheduled intravenous infusions in the polymer-based ORS group compared with both the ORS ≥ 310 and ≤ 270 groups; neither was significant, but when both ORS groups were combined the difference was significant in favour of the polymer-based ORS (RR 0.75, 95% CI 0.59 to 0.95; 2235 participants, 19 trials, Analysis 1.3, Figure 1). There was no statistically significant difference between the polymer-based and glucose-based ORS groups in the number of participants with vomiting (Analysis 1.4), hyponatraemia (Analysis 1.5), hypokalaemia (Analysis 1.6), and development of persistent diarrhoea (Analysis 1.7).
Type of polymer

Stratification by types of polymer showed that participants in the rice-based ORS group had a lower stool output (1262 participants, 12 trials, \textit{Analysis 2.1}: subgroup 1) and duration of diarrhoea (1097 participants, 15 trials, \textit{Analysis 2.2}: subgroup 1) (Chi$^2$ test $P < 0.00001$, I$^2$ = 100%). Results with wheat-based ORS were consistent with this (MD -119.85 g/kg, 95% CI -114.73 to -124.97; 129 participants, 2 trials; \textit{Analysis 2.1}; subgroup 2). For sorghum (1 trial) and maltodextrin ORS (1 trial) the data were clearly skewed (mean/SD > 2) so the results are difficult to interpret. A sensitivity analysis showed similar results.

There was a decrease in the number of participants requiring intravenous fluid for those given rice-based ORS (RR 0.75, 95% CI 0.58 to 0.98; 1962 participants, 16 trials, \textit{Analysis 2.3}), but not for those given wheat-based ORS and maltodextrin-based ORS.

Effects of age and pathogen

The effects of age and type of pathogen were evaluated using trials that compared rice-based ORS with glucose-based ORS. In children, there was a significant decrease in the total stool output (\textit{Analysis 3.1}) and duration of diarrhoea (\textit{Analysis 3.2}) (Chi$^2$ test, $P < 0.00001$, I$^2$ = 100%). Among the adults, there was a significant decrease in the duration of diarrhoea (MD -7.11 hours, 95% CI -2.32 to -11.91; 228 participants, 4 trials, \textit{Analysis 3.2}; subgroup 2, \textit{Figure 2}). All four trials were conducted with participants positive for \textit{V. cholerae}.
Participants positive for *V. cholerae* had a lower stool output (Analysis 3.3) when given a rice-based ORS. These effects were not seen among participants with non-cholera diarrhea (Chi² test, P < 0.00001, I² = 100%). The duration of diarrhea was significantly shorter among those given rice-based ORS, regardless of the pathogen (Analysis 3.4) (Chi² test, P < 0.00001, I² = 100%). Sensitivity analysis of the above outcomes showed similar results.

**Publication bias**

We observed substantial, significant heterogeneity in the primary outcomes and therefore decided to use a funnel plot for the secondary outcome, where the data were homogenous. We constructed a funnel plot of 19 trials comparing polymer-based ORS, and glucose-based ORS and measuring the outcome of unscheduled use of intravenous fluid (Figure 3). The funnel plot is asymmetric due to the absence of smaller trials at the base and to the right of the pooled estimate. This was confirmed by the test for funnel plot asymmetry, which indicated significant asymmetry (Egger: bias = -0.856208 (95% = -1.699023 to -0.013393, P = 0.0469)). Asymmetry in the funnel plot could result from possible selection bias where smaller studies reporting greater treatment benefit for the experimental group were published (publication bias). The gap in the bottom corner of the graph suggests that smaller studies without statistically significant effects remain unpublished. Differences in inclusion criteria (e.g. cholera positive versus any pathogen) and method of assessment of unscheduled use of intravenous fluid may also account for the asymmetry.
Figure 3. Funnel plot on the trials of polymer-based ORS vs glucose-based ORS, measuring the outcome of unscheduled use of intravenous fluid.

DISCUSSION

The biochemical basis for the use of a polymer-based ORS is the presence of starch in rice, wheat, sorghum, and some fruits and vegetables (Carpenter 1988; Pizarro 1991). Even during diarrhoea, the digesting enzyme (amylase) is present in large amounts in the small intestine, so this starch is slowly broken down into glucose molecules. This glucose in turn provides the carrier molecules for co-transport of sodium and water across the intestinal epithelium, without the corresponding osmotic penalty that results if the quantity of glucose is further increased by the use of ORS ≥ 310.

There are three significant findings in this systematic review of 34 randomized controlled trials. First, there was a decrease in the need for unscheduled intravenous fluid among the participants given polymer-based ORS and in the subgroup of participants who were given rice-based ORS as compared with a glucose-based ORS. This indicates a decrease in the failure rate of oral rehydration when patients are given a polymer-based as compared to a glucose-based oral rehydration therapy. These results remained significant when a sensitivity analysis was carried out. However, the risk difference between the two ORS formulations is only 3%, with 34 patients needing treatment with a polymer-based ORS to prevent one episode of oral rehydration therapy failure. Is this result clinically important? While the use of polymers, such as rice, wheat, maize or potatoes, may be more acceptable as a treatment for diarrhoea, being foods that are familiar and readily available in the household, the preparation of the solution is more tedious. Polymers from local sources require cooking and have to be consumed within eight hours, especially in humid countries, to prevent bacterial growth and contamination. This is in contrast to the glucose-based ORS whose preparation only requires mixing the sachet of glucose and electrolytes in boiled water, and the solution may be consumed up to 12 hours in room temperature. It also has to be borne in mind that the clinical trials that were included in this meta-analysis do not allow one to conclude whether polymer-based ORS is indeed physiologically better than glucose-based ORS, as most of the trials immediately re-fed the patients after hydration. Patients with diarrhoea are dehydrated during the first six to eight hours, but once rehydrated, feeding is initiated. The effect of feeding a rice-based or starch-based food as soon as the participants are rehydrated could confound the effects of poly-
mer-based ORS (Alam 1992) and may have led to an underestimate of the effect of glucose-based ORS (Molla 1989a). In a large multicentre trial, the use of a reduced osmolarity ORS (ORS ≤ 270) compared to a glucose-based ORS (ORS ≥ 310) was shown to decrease the need for unscheduled use of intravenous fluid by 33% (Choice 2001). In this review, most of the included clinical trials used ORS ≥ 310 compared to the newer ORS ≤ 270, which has a lower osmolarity. Whether polymer-based ORS is as effective as, or more effective than the reduced osmolarity ORS, which is presently recommended, remains a subject for investigation.

A second observation of this meta-analysis is the decrease in the duration of diarrhoea among V. cholerae positive adults who were given polymer-based ORS, which was not seen when the analysis was limited to participants with non-cholerae or mixed pathogens. This positive result was not demonstrated in children. The efficacy of rice-based ORS has previously been reported to decrease the stool output in the first 24 hours among V. cholerae positive patients, in both adults and children (Fontaine 1998). These findings, however, were not confirmed in the present review, possibly due to the marked heterogeneity of the pooled data. Moreover, in some of the trials, the data were skewed and could not be used in the meta-analysis. Nonetheless, the efficacy of polymer-based ORS in reducing the duration of diarrhoea among cholera-positive patients but not in patients with other types of pathogens maybe due to the difference in the diarrhoeal mechanisms between the two groups (Casburn-Jones 2004). In cholera, which is an enterotoxin-mediated diarrhoea, intestinal secretory processes are activated by the bacteria, leading to massive fluid and electrolyte losses, without any macro- or micro-damage to the intestinal mucosa. On the other hand, commonly encountered enteric pathogens in childhood diarrhoea, such as rotavirus, Salmonella spp, and Shigella spp cause injury to the intestinal mucosa leading to a decrease in intestinal absorption of fluid, electrolytes, and nutrients.

Lastly, an interesting finding of this meta-analysis is the decrease in the total stool output during the first 24 hours in patients given wheat-based ORS who were enrolled in two trials (Alam 1987, wheat; Molla 1989b, wheat). Apart from its carbohydrate content, the proteins present in wheat may also help in the transport of salt and water across the intestinal mucosa, further decreasing the stool output and duration of diarrhoea (Dagher 1996). The available data in this review, however, are only derived from two trials. The chemical quality and digestibility of wheat-based ORS, as well as its clinical efficacy and safety, warrants further research. The ultimate goal is to find an ORS that is cheap, readily available, acceptable, and effective in all types of diarrhoea.

A major limitation of this review is the substantial heterogeneity in the clinical trials, despite statistically significant results in the primary outcomes. Heterogeneity in the treatment effect may have been affected by the way the outcomes have been measured (methodological diversity). Ideally, measurement of stool output should be made by taking the difference in the weight of the diaper before and after use. In some studies in which both males and females were included (especially in the paediatric group) the urine output may have been inadvertently mixed with the stool, giving an erroneously higher stool output. In adults, three trials used a cholera cot to measure stool output (Bhattacharya 1998; Dutta 2000; Ramakrishna 2000), while one trial did not state the measurement method used (Alam 1992). The cholera cot has a bucket underneath to measure the stool output more accurately. It was also unclear in most of the trials whether the duration of diarrhoea was measured from the initial onset of the disease, before admission to the study, or only from admission up to the time of discharge. Different trials may also have used different criteria to define patients who warrant an unscheduled use of intravenous fluid. Despite these limitations, however, sensitivity analyses did not change the results when trials with unclear randomization, unclear allocation, and inadequate numbers of patients analysed were excluded, suggesting that the results of this review are robust.

Authors’ conclusions

Implications for practice

Polymer-based ORS decreases the duration of diarrhoea among adults positive for V. cholerae and lowers the risk of unscheduled use of intravenous fluid, compared with a glucose-based ORS ≥ 310. Trial participants who were given a wheat-based ORS were also shown to have a decrease in total stool output in the first 24 hours; however, the data on wheat ORS were only derived from two trials. Glucose-based ORS, when accompanied by early feeding, may be just as effective.

Implications for research

The rationale for the use of polymer-based ORS is the slow release of glucose from starch, which provides the carrier molecules for sodium without the osmotic penalty that results if the quantity of glucose is increased by the use of ORS ≥ 310. Since the ORS presently recommended already has a reduced osmolarity (ORS ≤ 270), it will be of interest to compare the efficacy of ORS ≤ 270 with a polymer-based ORS in reducing the total stool output, the total volume of ORS intake, the duration of diarrhoea, and the risk of unscheduled intravenous fluid therapy. There is also a need for more trials on the efficacy of wheat-based ORS.

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Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review) 15

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* Indicates the major publication for the study.
## Characteristics of included studies  [ordered by study ID]

### Akbar 1991

| Methods | Randomized controlled trial  
| **Generation of allocation sequence:** block randomization  
| **Allocation concealment:** code broken at the end of the study  
| **Blinding:** participants, providers, outcome assessors  
| Inclusion of participants in analysis: 81% (maltodextrin group 33/43, 77%; glucose group 36/43, 84%)  
| Duration: 20 months, from January 1987 to August 1988 |

| Participants | Number: 86 enrolled  
| Inclusion criteria: male; 4 to 36 months; diarrhoea < 3 days; mild to moderate dehydration  
| Exclusion criteria: bloody diarrhoea; antibiotic treatment in the last 3 days; severe malnutrition; presence of systemic illness |

| Interventions | 1. Glucose oral rehydration solution (ORS): 43 participants  
| 2. Maltodextrin ORS: 43 participants |

| Outcomes | 1. Total stool output in first 24 hours  
| 2. Total stool output from randomization to discharge  
| 3. Duration of diarrhoea  
| 4. Number with unscheduled use of intravenous fluid |

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |

| Setting | Hospital-based trial  
| Location: Dhaka, Bangladesh |

| Notes | - |

### Alam 1987

| Methods | Randomized controlled trial  
| **Generation of allocation sequence:** permuted block design  
| **Allocation concealment:** not reported  
| **Blinding:** none  
| Inclusion of participants in analysis: > 90%  
| Duration: 13 months, from April 1983 to April 1984 |

| Participants | Number: 72 enrolled  
| Inclusion criteria: age 1 to 8 years; watery diarrhoea < 3 days; presence of moderate to severe dehydration  
| Exclusion criteria: antibiotic treatment before admission; severe malnutrition; presence of systemic illness |
### Alam 1987

**Interventions**
- 1. Glucose oral rehydration solution (ORS): 24 participants
- 2. Wheat ORS: 24 participants
- 3. Rice ORS: 24 participants

**Outcomes**
- 1. Total stool output in first 24 hours
- 2. Duration of diarrhoea
- 3. Number of participants with unscheduled use of intravenous fluid
- 4. Number of participants with vomiting

**Glucose-based ORS osmolarity** \( \geq 310 \text{ mOsm/L} \)

**Setting**
- Hospital-based trial
  - Location: Dhaka, Bangladesh

**Notes**
- Participants who were given rice ORS were less dehydrated compared to those given glucose ORS, but the difference was not statistically significant

### Alam 1987, rice

**Methods**
- Rice arm of Alam 1987

**Participants**
- -

**Interventions**
- 1. Glucose oral rehydration solution (ORS): 30 participants
- 2. Rice ORS: 30 participants

**Outcomes**
- -

**Glucose-based ORS osmolarity**
- -

**Setting**
- -

**Notes**
- -

### Alam 1987, wheat

**Methods**
- Wheat arm of Alam 1987

**Participants**
- -

**Interventions**
- 1. Glucose oral rehydration solution (ORS): 30 participants
- 2. Wheat ORS: 30 participants

**Outcomes**
- -

**Glucose-based ORS osmolarity**
- -
Alam 1987, wheat  (Continued)

| Setting | - |
| Notes | - |

Alam 1992

Methods  Randomized controlled trial  
*Generation of allocation sequence:* random numbers  
*Allocation concealment:* not reported  
*Blinding:* none  
*Inclusion of participants in analysis:* > 90%  
*Duration:* 30 months, from July 1986 to December 1988

Participants  
*Number:* 182 enrolled  
*Inclusion criteria:* age 15 to 60 years; acute watery diarrhoea; presence of dehydration; positive for *Vibrio cholerae*  
*Exclusion criteria:* history of antidiarrhoeal or antimicrobial intake before admission

Interventions  
1. Glucose oral rehydration solution (ORS) with no food intake: 47 participants  
2. Rice ORS with no food intake: 46 participants  
3. Glucose ORS with food intake: 42 participants  
4. Rice ORS with food intake: 47 participants

Outcomes  
1. Total stool output in first 24 hours  
2. Total stool output from randomization to discharge  
3. Duration of diarrhoea  
4. Number of participants with unscheduled use of intravenous fluid  
5. Number of participants with vomiting

Glucose-based ORS osmolarity  ≥ 310 mOsm/L

Setting  Hospital-based trial  
*Location:* Dhaka, Bangladesh

Notes  
Analysed separately with or without food intake

Bernal 2005

Methods  Randomized controlled trial  
*Generation of allocation sequence:* permuted blocks of variable length  
*Allocation concealment:* sealed, opaque envelopes  
*Blinding:* unclear  
*Inclusion of participants in analysis:* > 90%  
*Duration:* 17 months, from March 2001 to July 2002
### Bernal 2005

**Participants**
- **Number:** 101 enrolled
- **Inclusion criteria:** age 1 to 48 months; acute watery diarrhoea < 7 days; presence of dehydration but without hypovolaemic shock
- **Exclusion criteria:** malnourished, kwashiorkor type; presence of paralytic ileus

**Interventions**
1. Glucose oral rehydration solution (ORS): 54 participants
2. Plain flour ORS: 47 participants

**Outcomes**
1. Total stool output in first 24 hours

**Glucose-based ORS osmolarity**\(\geq 310\) mOsm/L

**Setting**
- Hospital-based trial
  - **Location:** Medellin, Colombia

**Notes**
Data on total stool output in first 24 hours are skewed

### Bhan 1987

**Methods**
- Randomized controlled trial
  - **Generation of allocation sequence:** randomly assigned using sealed envelopes
  - **Allocation concealment:** sealed envelopes
  - **Blinding:** none
  - **Inclusion of participants in analysis:** > 90%
  - **Duration:** not specified; only stated that trial was done for 10 consecutive months

**Participants**
- **Number:** 93 enrolled
- **Inclusion criteria:** males; age 3 months to 5 years; watery diarrhoea < 5 days; presence of dehydration; weight for height > 70% of 50th centile of reference standard
- **Exclusion criteria:** female; persistent vomiting; bloody diarrhoea; temperature > 39 °C; other associated medical illness; intake of antibiotics during illness

**Interventions**
1. Glucose oral rehydration solution (ORS): 33 participants
2. Pop rice ORS: 31 participants
3. Mung bean ORS: 29 participants

**Outcomes**
1. Total stool output in first 24 hours
2. Total stool output from randomization to discharge
3. Duration of diarrhoea
4. Number of participants with unscheduled use of intravenous fluid
5. Number of participants with vomiting

**Glucose-based ORS osmolarity**\(\geq 310\) mOsm/L

**Setting**
- Hospital-based trial
  - **Location:** New Delhi, India
Participants who were given glucose ORS were more malnourished as compared to the treatment groups, but the difference was not statistically significant.

### Bhan 1987, mung bean

| Methods | Mung bean ORS arm of Bhan 1987 |
|---------|--------------------------------|
| Participants | - |
| Interventions | 1. Glucose oral rehydration solution (ORS): 33 participants  
2. Mung bean ORS: 29 participants |
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |

### Bhan 1987, rice

| Methods | Pop rice ORS arm of Bhan 1987 |
|---------|--------------------------------|
| Participants | - |
| Interventions | 1. Glucose oral rehydration solution (ORS): 33 participants  
2. Pop rice ORS: 31 participants |
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |
### Bhattacharya 1998

| Methods | Randomized controlled trial |
|---------|-----------------------------|
| Generation of allocation sequence: | permuted block of random numbers |
| Allocation concealment: | not reported |
| Blinding: | none |
| Inclusion of participants in analysis: | > 90% |
| Duration: | 32 months, from August 1993 to March 1996 |

| Participants | Number: 123 enrolled |
|--------------|----------------------|
| Inclusion criteria: | adult males; acute watery diarrhoea; presence of severe dehydration; no antibiotic or intravenous fluid intake; no systemic illness |
| Exclusion criteria: | presence of systemic illness; use of intravenous fluid before admission |

| Interventions | 1. Glucose oral rehydration solution (ORS) ≥ 310: 30 participants |
|----------------|------------------------------------------------------------|
|                | 2. Glucose ORS ≤ 270: 33 participants |
|                | 3. Rice ORS with electrolytes as glucose ORS ≥ 310: 27 participants |
|                | 4. Rice ORS with electrolytes as glucose ORS ≤ 270: 33 participants |

| Outcomes | 1. Total stool output in first 24 hours |
|----------|----------------------------------------|
|          | 2. Total stool output from randomization to discharge |
|          | 3. Duration of diarrhoea |

Glucose-based ORS osmolarity ≥ 310 mOsm/L and ≤ 270 mOsm/L.

| Setting | Hospital-based trial |
|---------|----------------------|
| Location: | Calcutta, India |

| Notes | - |

### Dutta 1988

| Methods | Randomized controlled trial |
|---------|-----------------------------|
| Generation of allocation sequence: | random-numbers table |
| Allocation concealment: | not reported |
| Blinding: | unclear |
| Inclusion of participants in analysis: | > 90% |
| Duration: | not stated |

| Participants | Number: 105 enrolled |
|--------------|----------------------|
| Inclusion criteria: | age 4 months to 4 years; males; acute watery diarrhoea; presence of severe dehydration |
| Exclusion criteria: | presence of systemic illness; antibiotic intake before admission |

| Interventions | 1. Glucose oral rehydration solution (ORS): 33 participants |
|----------------|------------------------------------------------------------|
|                | 2. Rice ORS: 35 participants |
|                | 3. Pop rice ORS: 37 participants |

| Outcomes | 1. Total stool output in first 24 hours |
|----------|----------------------------------------|
|          | 2. Total stool output from randomization to discharge |
|          | 3. Duration of diarrhoea |
### Dutta 1988 (Continued)

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
| Setting                      | Hospital-based trial |
|                             | Location: Calcutta, India |
| Notes                       | Results of rice ORS and pop rice ORS were combined both for the continuous and dichotomous outcomes, and compared with glucose ORS. These were all reported as rice-based ORS |

### Dutta 1998

| Methods | Randomized controlled trial |
|         | Generation of allocation sequence: permuted block of random numbers |
|         | Allocation concealment: not reported |
|         | Blinding: none |
|         | Inclusion of participants in analysis: > 90% |
|         | Duration: 14 months, from May 1995 to June 1996 |
| Participants | Number: 50 adults and 20 children enrolled |
|             | Inclusion criteria: age 3 to 12 years for children, and 18 to 55 years for adults; acute watery diarrhoea; severe dehydration |
|             | Exclusion criteria: presence of systemic illness; with intake of drug or intravenous fluid before admission |
| Interventions | Adults: |
|              | 1. Glucose oral rehydration solution (ORS): 25 participants |
|              | 2. Rice ORS: 25 participants |
|              | Children: |
|              | 1. Glucose ORS: 10 participants |
|              | 2. Rice ORS: 10 participants |
| Outcomes | 1. Total stool output from randomization to discharge |
|          | 2. Duration of diarrhoea |
|          | 3. Number of participants with unscheduled use of intravenous fluid |
|          | 4. Number of participants with vomiting |
| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
| Setting | Hospital-based trial |
|         | Location: Calcutta, India |
| Notes | Children and adults were randomized separately |
### Dutta 1998, adults

| Methods | Adult arm of Dutta 1998 |
|---------|-------------------------|
| Participants | 1. Glucose oral rehydration solution (ORS): 25 participants  
2. Rice ORS: 25 participants |
| Interventions | - |
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |

### Dutta 1998, children

| Methods | Children arm of Dutta 1998 |
|---------|---------------------------|
| Participants | 1. Glucose oral rehydration solution (ORS): 10 participants  
2. Rice ORS: 10 participants |
| Interventions | - |
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |

### Dutta 2000

| Methods | Randomized controlled trial  
*Generation of allocation sequence:* permuted blocks of random numbers  
*Allocation concealment:* not reported  
*Blinding:* none  
*Inclusion of participants in analysis:* > 90%  
*Duration:* 34 months, from August 1995 to May 1998 |
|---------|-------------------------------------------------|
| Participants | *Number:* 58 enrolled  
*Inclusion criteria:* age 2 to 10 years; acute watery diarrhoea; presence of severe dehydration; positive for *Vibrio cholerae*  
*Exclusion criteria:* presence of systemic illness; with intake of drug or intravenous fluid before admission |
### Dutta 2000 (Continued)

| Interventions | 1. Glucose oral rehydration solution (ORS) ORS ≥ 310: 20 participants  
|               | 2. Glucose ORS ≤ 270: 19 participants  
|               | 3. Rice ORS with electrolyte content of glucose ORS ≤ 270: 19 participants  
| Outcomes      | 1. Total stool output from randomization to discharge  
|               | 2. Duration of diarrhoea  
|               | 3. Number of participants with hypo- or hypernatraemia  
| Glucose-based ORS osmolarity | ≥ 310 mOsm/L and ≤ 270 mOsm/L  
| Setting       | Hospital-based trial  
|               | Location: Calcutta, India  
| Notes         | Only the data on glucose ORS ≤ 270 were used as this is the one with same electrolyte composition as the rice ORS  

### El-Mougi 1988

| Methods | Randomized controlled trial  
|         | Generation of allocation sequence: random permuted blocks  
|         | Allocation concealment: not reported  
|         | Blinding: none  
|         | Inclusion of participants in analysis: > 90% of randomized participants included in the final analysis  
|         | Duration: not stated  
| Participants | Number: 60 enrolled  
|              | Inclusion criteria: age 4 months to 4 years; males; acute watery diarrhoea; presence of moderate to severe dehydration; on milk formula intake  
|              | Exclusion criteria: presence of bloody diarrhoea; severe dehydration; febrile (temperature > 38.5 °C); marasmic-kwashiorkor malnutrition  
| Interventions | 1. Glucose oral rehydration solution (ORS): 30 participants  
|               | 2. Rice ORS: 30 participants  
| Outcomes      | 1. Total stool output in first 24 hours  
|               | 2. Duration of diarrhoea  
|               | 3. Number of participants with vomiting  
|               | 4. Number of episodes of vomiting  
| Glucose-based ORS osmolarity | ≥ 310 mOsm/L  
| Setting       | Hospital-based trial  
|               | Location: Cairo, Egypt  
| Notes         | -  

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Polymer-based oral rehydration solution for treating acute Watery diarrhoea (Review)  
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### El-Mougi 1996

**Methods**
- Randomized controlled trial
- **Generation of allocation sequence:** random blocks of fixed length
- **Allocation concealment:** serially numbered identical oral rehydration solution (ORS) packets
- **Blinding:** participants, providers, outcome assessors
- **Inclusion of participants in analysis:** > 90%
- **Duration:** not stated

**Participants**
- **Number:** 89 enrolled
- **Inclusion criteria:** age 3 to 24 months; acute watery diarrhoea; presence of mild to moderate dehydration; non-cholera diarrhoea
- **Exclusion criteria:** presence of bloody diarrhoea; severe malnutrition; with no or severe dehydration

**Interventions**
1. Glucose ORS: 44 participants
2. Maltodextrin ORS: 45 participants

**Outcomes**
1. Total stool output in first 24 hours
2. Duration of diarrhoea
3. Number of participants with unscheduled intravenous fluid

**Glucose-based ORS osmolarity** \( \geq 310 \text{ mOsm/L} \)

**Setting**
- Hospital-based trial
- **Location:** Cairo, Egypt

**Notes**
- 

### Faruque 1997

**Methods**
- Randomized controlled trial
- **Generation of allocation sequence:** randomized
- **Allocation concealment:** not reported
- **Blinding:** none
- **Inclusion of participants in analysis:** > 90%
- **Duration:** 17 months, from August 1990 to December 1991

**Participants**
- **Number:** 471 enrolled
- **Inclusion criteria:** age 3 to 35 months; acute watery diarrhoea; presence of mild and moderate dehydration
- **Exclusion criteria:** presence of severe dehydration; severe malnutrition; intercurrent illness or chronic disease

**Interventions**
1. Glucose oral rehydration solution (ORS): 235 participants
2. Rice ORS: 236 participants

**Outcomes**
1. Total stool output in first 24 hours
2. Duration of diarrhoea
3. Number of episodes of vomiting
4. Number of participants who developed persistent diarrhoea
### Faruque 1997

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
|------------------------------|--------------|
| Setting                      | Hospital-based trial |
| Location:                    | Dhaka, Bangladesh |
| Notes                        | -             |

### Fayad 1993

| Methods                                      | Randomized controlled trial |
|----------------------------------------------|------------------------------|
| Generation of allocation sequence:          | random permuted blocks of variable length |
| Allocation concealment:                     | sealed, serially numbered envelopes |
| Blinding:                                    | unclear                       |
| Inclusion of participants in analysis:       | > 90%                         |
| Duration:                                    | not stated                    |

| Participants                               | Number: 441 enrolled |
|--------------------------------------------|----------------------|
| Inclusion criteria:                        | age 3 to 18 months, acute watery diarrhoea < 7 days; presence of dehydration |
| Exclusion criteria:                        | bloody diarrhoea; severe malnutrition; presence of systemic illness; exclusively or mostly breastfed |

| Interventions                              | 1. Glucose oral rehydration solution (ORS): 222 participants |
|--------------------------------------------|-------------------------------------------------------------|
|                                            | 2. Rice ORS: 219 participants                               |

| Outcomes                                   | 1. Total stool output in first 24 hours |
|                                            | 2. Duration of diarrhoea during the maintenance phase (not from the time of admission) |
|                                            | 3. Number of participants with unscheduled use of intravenous fluid |
|                                            | 4. Number of participants with diarrhoea > 7 days            |

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
|------------------------------|--------------|
| Setting                      | Hospital-based trial |
| Location:                    | Cairo, Egypt   |
| Notes                        | -             |

### Guiraldes 1995a

| Methods                                      | Randomized controlled trial |
|----------------------------------------------|------------------------------|
| Generation of allocation sequence:          | permuted block randomization |
| Allocation concealment:                     | code was kept                |
| Blinding:                                    | none                         |
| Inclusion of participants in analysis:       | > 90%                        |
| Duration:                                    | not stated                   |
### Guiralde 1995a (Continued)

| Participants | Number: 100 enrolled  
|              | Inclusion criteria: age 3 to 18 months; acute watery diarrhoea; presence of moderate dehydration; non-breastfed  
|              | Exclusion criteria: presence of systemic illness; presence of moderate to severe malnutrition  
| Interventions | 1. Glucose oral rehydration solution (ORS): 49 participants  
|              | 2. Rice ORS: 51 participants  
| Outcomes | 1. Total stool output in first 24 hours  
| | 2. Total stool output from randomization to discharge  
| | 3. Duration of diarrhoea  
| | 4. Number of participants with unscheduled use of intravenous fluid  
| | 5. Number of participants with hypo- or hypernatraemia  
| Glucose-based ORS osmolarity | $\geq 310 \text{ mOsm/L}$  
| Setting | Hospital-based trial  
| Location: Santiago, Chile  
| Notes | -  

### Guiralde 1995b

| Methods | Randomized controlled trial  
| Generation of allocation sequence: block randomization  
| Allocation concealment: code was kept until end of trial  
| Blinding: none  
| Inclusion of participants in analysis: $> 90\%$  
| Duration: not stated  
| Participants | Number: 48 enrolled  
| Inclusion criteria: age 3 to 24 months; acute watery diarrhoea; presence of moderate dehydration; non-breastfed  
| Exclusion criteria: presence of systemic illness; moderate to severe malnutrition  
| Interventions | 1. Glucose oral rehydration solution (ORS): 24 participants  
| | 2. Rice ORS: 24 participants  
| Outcomes | 1. Total stool output in first 24 hours  
| | 2. Duration of diarrhoea  
| | 3. Number of participants with unscheduled use of intravenous fluid  
| Glucose-based ORS osmolarity | $\geq 310 \text{ mOsm/L}$  
| Setting | Hospital-based trial  
| Location: Santiago, Chile  

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### Hossain 2003

| **Methods**                                                                 |  
|-----------------------------------------------------------------------------|
| Randomized controlled trial                                                |
| *Generation of allocation sequence*: computer-generated randomization      |
| *Allocation concealment*: sealed envelopes                                  |
| *Blinding*: none                                                            |
| *Inclusion of participants in analysis*: > 90%                              |
| *Duration*: not stated                                                      |

| **Participants**                                                            |
|---                                                                         |
| *Number*: 113 enrolled                                                     |
| *Inclusion criteria*: adult males 18 to 60 years old; acute watery diarrhoea; presence of severe dehydration; positive for *Vibrio cholerae* |
| *Exclusion criteria*: presence of concomitant illness; received antibiotic and oral rehydration solution (ORS) before admission |

| **Interventions**                                                          |
|---                                                                         |
| 1. Glucose ORS: 56 participants                                            |
| 2. Rice ORS: 57 participants                                               |

| **Outcomes**                                                               |
|---                                                                         |
| 1. Total stool output in first 24 hours                                    |
| 2. Duration of diarrhoea                                                   |
| 3. Number of participants with unscheduled use of intravenous fluid      |

| **Glucose-based ORS osmolarity**                                           |
|---                                                                         |
| ≥ 310 mOsm/L                                                              |

| **Setting**                                                                |
|---                                                                         |
| Hospital-based trial                                                      |
| *Location*: Dhaka, Bangladesh                                             |

| **Notes**                                                                 |
|---                                                                         |
| Data for primary outcomes reported as median (range)                      |

### Islam 1994

| **Methods**                                                               |
|---                                                                         |
| Randomized controlled trial                                              |
| *Generation of allocation sequence*: permuted block randomization        |
| *Allocation concealment*: not reported                                   |
| *Blinding*: none                                                          |
| *Inclusion of participants in analysis*: > 90%                           |
| *Duration*: 14 months, from March 1989 to April 1990                     |

| **Participants**                                                          |
|---                                                                         |
| *Number*: 52 enrolled                                                     |
| *Inclusion criteria*: age < 6 months; acute watery diarrhoea; presence of mild to moderate dehydration; weight for height > 75% of 50th centile |
| *Exclusion criteria*: presence of bloody diarrhoea; systemic illness; unable to take oral rehydration solution (ORS); intake of antibiotic |

---
### Islam 1994  *(Continued)*

| Interventions          | 1. Glucose ORS: 25 participants  
|                        | 2. Rice ORS: 27 participants |
|------------------------|---------------------------------|
| Outcomes               | 1. Total stool output in first 24 hours  
|                        | 2. Duration of diarrhoea (but only in those who were successfully treated)  
|                        | 3. Number of participants with unscheduled use of intravenous fluid, number of participants with vomiting |
| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
| Setting                | Hospital-based trial (diarrhoea training unit)  
| Location               | Karachi, Pakistan |
| Notes                  | Participants who were given rice ORS were younger compared to those given glucose ORS, but the difference is not statistically significant |

### Iyngkaran 1998

| Methods      | Randomized controlled trial  
|--------------|------------------------------|
|             | *Generation of allocation sequence:* randomized  
|             | *Allocation concealment:* not reported  
|             | *Blinding:* none  
|             | *Inclusion of participants in analysis:* > 90%  
|             | *Duration:* not stated |
| Participants | *Number:* 63 enrolled  
|             | *Inclusion criteria:* age < 6 months; loose stools < 7 days' duration  
|             | *Exclusion criteria:* presence of systemic illness; intake of antibiotic/anti-diarrhoeal before admission; severe dehydration |
| Interventions| 1. Glucose oral rehydration solution (ORS): 32 participants  
|             | 2. Rice ORS: 31 participants |
| Outcomes    | 1. Duration of diarrhoea  
|             | 2. Number of episodes of vomiting |
| Glucose-based ORS osmolarity | ≤ 270 mOsm/L |
| Setting     | Hospital-based trial  
| Location    | Kuala Lumpur, Malaysia |
| Notes       | - |
### Maulen-Radovan 1994

| Methods | Randomized controlled trial  
| Generation of allocation sequence: randomly assigned permuted blocks  
| Allocation concealment: serially numbered sealed envelopes  
| Blinding: none  
| Inclusion of participants in analysis: > 90%  
| Duration: not stated |

| Participants | Number: 97 enrolled  
| Inclusion criteria: age 1 to 6 months; acute watery diarrhoea < 5 days; presence of mild to moderate dehydration  
| Exclusion criteria: presence of bloody diarrhoea; systemic illness; severe malnutrition; history of diarrhoea in the last 2 weeks |

| Interventions | 1. Glucose oral rehydration solution (ORS): 48 participants  
| 2. Rice ORS: 49 participants |

| Outcomes | 1. Total stool output in first 24 hours  
| 2. Duration of diarrhoea  
| 3. Number of participants with unscheduled intravenous fluid |

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |

| Setting | Hospital-based trial (emergency department)  
| Location: Mexico City, Mexico |

| Notes | Results for primary outcome skewed |

### Maulen-Radovan 2004

| Methods | Randomized controlled trial  
| Generation of allocation sequence: block randomization  
| Allocation concealment: serially numbered sealed envelopes  
| Blinding: none  
| Inclusion of participants in analysis: > 90%  
| Duration: not stated |

| Participants | Number: 189 enrolled  
| Inclusion criteria: age 3 to 24 months; males; acute watery diarrhoea; presence dehydration  
| Exclusion criteria: presence of bloody diarrhoea; systemic illness; severe malnutrition |

| Interventions | 1. Glucose oral rehydration solution (ORS): 92 participants  
| 2. Rice ORS: 97 participants |

| Outcomes | 1. Total stool output in first 24 hours during the maintenance phase only  
| 2. Duration of diarrhoea  
| 3. Number of participants with unscheduled use of intravenous fluid |

| Glucose-based ORS osmolarity | ≤ 270 mOsm/L |
### Maulen-Radovan 2004

**Setting**
- Hospital-based trial
  - Location: Mexico City, Mexico

**Notes**
- 

### Mohan 1988

**Methods**
- Randomized controlled trial
  - Generation of allocation sequence: randomized
  - Allocation concealment: not reported
  - Blinding: none
  - Inclusion of participants in analysis: > 90%
  - Duration: not stated

**Participants**
- Number: 50 enrolled
  - Inclusion criteria: age 3 to 36 months, acute watery diarrhoea, presence of dehydration
  - Exclusion criteria: none reported

**Interventions**
1. Glucose oral rehydration solution (ORS): 23 participants
2. Rice ORS: 23 participants

**Outcomes**
1. Total stool output in first 24 hours
2. Number of participants with unscheduled use of intravenous fluid
3. Number of participants with vomiting

**Glucose-based ORS osmolarity**
- ≥ 310 mOsm/L

**Setting**
- Hospital-based trial
  - Location: New Delhi, India

**Notes**
- 

### Molla 1985

**Methods**
- Randomized controlled trial
  - Generation of allocation sequence: predetermined random numbers
  - Allocation concealment: not reported
  - Blinding: none
  - Inclusion of participants in analysis: > 90%
  - Duration: 4 months, from December 1982 to March 1983

**Participants**
- Number: 342 enrolled
  - Inclusion criteria: children aged < 10 years and adults; acute watery diarrhoea; presence of moderate and severe dehydration
  - Exclusion criteria: presence of systemic illness; intake of antibiotics and oral rehydration solution (ORS) before admission
| Interventions | Adults: |
|---------------|---------|
|               | 1. Glucose ORS: 72 participants |
|               | 2. Rice ORS: 85 participants |
| Children:     | 1. Glucose ORS: 101 participants |
|               | 2. Rice ORS: 84 participants |

| Outcomes      | 1. Total stool output in first 24 hours |
|---------------|----------------------------------------|
|               | 2. Number of participants with unscheduled use of intravenous fluid |

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
|------------------------------|-------------|

| Setting | Hospital-based trial |
|---------|----------------------|
| Location: | Dhaka, Bangladesh |

| Notes | Separate analysis for children and adults |
|-------|-----------------------------------------|

### Molla 1985, adults

| Methods | Adult arm of Molla 1985 |
|---------|-------------------------|
| Participants | - |

| Interventions | 1. Glucose oral rehydration solution (ORS): 72 participants |
|---------------|----------------------------------------------------------|
|               | 2. Rice ORS: 85 participants |

| Outcomes | - |
|----------|---|

| Glucose-based ORS osmolarity | - |
|------------------------------|---|

| Setting | - |
|---------|---|

| Notes | - |
|-------|---|

### Molla 1985, children

| Methods | Children arm of Molla 1985 |
|---------|----------------------------|
| Participants | - |

| Interventions | 1. Glucose oral rehydration solution (ORS): 101 participants |
|---------------|----------------------------------------------------------|
|               | 2. Rice ORS: 84 participants |

| Outcomes | - |
|----------|---|

| Glucose-based ORS osmolarity | - |
|------------------------------|---|

| Setting | - |
|---------|---|

| Notes | - |
### Molla 1985, children (Continued)

| Setting | - |
| Notes | - |

### Molla 1989a

| Methods | Randomized controlled trial  
Generation of allocation sequence: randomly assigned  
Allocation concealment: not reported  
Blinding: unclear  
Inclusion of participants in analysis: > 90%  
Duration: not stated |
| Participants | Number: 93 enrolled  
Inclusion criteria: children aged < 5 years; acute watery diarrhoea; presence of moderate and severe dehydration; positive for *Vibrio cholerae*  
Exclusion criteria: breastfed; those with previous treatment |
| Interventions | 1. Glucose oral rehydration solution (ORS): 46 participants  
2. Rice ORS: 47 participants |
| Outcomes | 1. Total stool output in first 24 hours  
Glucose-based ORS osmolarity \( \geq 310 \text{ mOsm/L} \) |
| Setting | Hospital-based trial  
Location: Dhaka, Bangladesh |
| Notes | Data on total stool output in first 24 hours are skewed |

### Molla 1989b

| Methods | Randomized controlled trial  
Generation of allocation sequence: permuted block design  
Allocation concealment: not reported  
Blinding: participants and providers not blinded; outcome assessors unclear  
Inclusion of participants in analysis: > 90%  
Duration: not stated |
| Participants | Number: 276 enrolled  
Inclusion criteria: age 1 to 5 years; acute watery diarrhoea < 48 hours; presence of moderate to severe dehydration; no complications  
Exclusion criteria: none reported |
| Interventions | 1. Glucose oral rehydration solution (ORS): 42 participants  
2. Rice ORS: 37 participants  
3. Maize ORS: 38 participants |
### Molla 1989b (Continued)

| Participant Groups | Details |
|--------------------|---------|
| 4. Sorghuma ORS | 35 participants |
| 5. Millet ORS | 39 participants |
| 6. Wheat ORS | 39 participants |
| 7. Potatoes ORS | 36 participants |

#### Outcomes

1. Total stool output in first 24 hours

#### Glucose-based ORS osmolarity

≥ 310 mOsm/L

#### Setting

Hospital-based trial  
Location: Dhaka, Bangladesh

#### Notes

Study with 6 treatment groups vs 1 control group

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### Molla 1989b, rice

#### Methods

Rice arm of Molla 1989b

#### Participants

- 1. Glucose oral rehydration solution (ORS): 42 participants  
  2. Rice ORS: 37 participants

#### Interventions

1. Glucose oral rehydration solution (ORS): 42 participants  
2. Rice ORS: 37 participants

#### Setting

-  

#### Notes

-  

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### Molla 1989b, sorghum

#### Methods

Sorghum arm of Molla 1989b

#### Participants

-  

#### Interventions

1. Glucose oral rehydration solution (ORS): 42 participants  
2. Sorghum ORS: 35 participants

#### Setting

-  

#### Notes

-  

---
**Molla 1989b, sorghum (Continued)**

| Notes | - |
|-------|---|

**Molla 1989b, wheat**

| Methods | Wheat arm of Molla 1989b |
|---------|--------------------------|
| Participants | - |

| Interventions | 1. Glucose oral rehydration solution (ORS): 42 participants  
2. Wheat ORS: 39 participants |
|----------------|----------------------------------------------------------|
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |

**Mustafa 1995**

| Methods | Randomized controlled trial  
*Generation of allocation sequence: randomly assigned*  
*Allocation concealment: not reported*  
*Blinding: unclear*  
*Inclusion of participants in analysis: > 90%*  
*Duration: 9 months, from April to December 1990* |
|---------|-----------------------------------------------------------------|
| Participants | Number: 96 enrolled  
*Inclusion criteria: males aged < 5 years; acute watery diarrhoea; presence of moderate and severe dehydration*  
*Exclusion criteria: presence of bloody diarrhoea; no systemic illness* |
| Interventions | 1. Glucose oral rehydration solution (ORS): 30 participants  
2. Rice ORS: 32 participants  
3. Sorghum ORS: 34 participants |
| Outcomes | 1. Duration of diarrhoea  
2. Number of episodes of vomiting  
3. Number of participants with vomiting |
| Glucose-based ORS osmolarity | $\geq 310$ mOsm/L |
| Setting | Hospital-based trial  
*Location: Khartoum, Sudan* |
Study with 3 treatment arms: 2 polymer-based ORS vs 1 control group. Data on duration of diarrhoea are skewed

**Mustafa 1995, rice**

| Methods          | Rice arm of Mustafa 1995 |
|------------------|--------------------------|
| Participants     | -                        |
| Interventions    | 1. Glucose oral rehydration solution (ORS): 30 participants  
                    2. Rice ORS: 32 participants |
| Outcomes         | -                        |
| Glucose-based ORS osmolarity | -                  |
| Setting          | -                        |
| Notes            | -                        |

**Mustafa 1995, sorghum**

| Methods          | Sorghum arm of Mustafa 1995 |
|------------------|-----------------------------|
| Participants     | -                           |
| Interventions    | 1. Glucose oral rehydration solution (ORS): 30 participants  
                    2. Sorghum ORS: 34 participants |
| Outcomes         | -                           |
| Glucose-based ORS osmolarity | -                  |
| Setting          | -                           |
| Notes            | -                           |
### Nanulescu 1999

| Methods | Randomized controlled trial |
|---------|-----------------------------|
| Generation of allocation sequence: randomly assigned |
| Allocation concealment: not reported |
| Blinding: none |
| Inclusion of participants in analysis: 88% (rice group, 48/56, 86%; glucose group, 51/57, 89%) |
| Duration: 12 months, from 1 May 1995 to 1 May 1996 |

| Participants | Number: 113 enrolled |
|--------------|---------------------|
| Inclusion criteria: age 1 to 12 months; acute watery diarrhoea; presence of mild or moderate dehydration; weight for age > 80% of 50th centile |
| Exclusion criteria: newborn; presence of bloody diarrhoea; systemic illness; intake of antibiotics; severe dehydration; moderate to severe malnutrition |

| Interventions | 1. Glucose oral rehydration solution (ORS): 48 participants |
|---------------|----------------------------------------------------------|
|               | 2. Rice ORS: 51 participants |

| Outcomes | 1. Total stool output in first 24 hours |
|----------|----------------------------------------|
|          | 2. Duration of diarrhoea |
|          | 3. Number of participants with unscheduled use of intravenous fluid |

| Glucose-based ORS osmolarity | $\leq 270$ mOsm/L |

| Setting | Paediatric clinic |
|---------|-------------------|
| Location: | Cluj-Napoca, Romania |

| Notes | - |

### Patra 1982

| Methods | Randomized controlled trial |
|---------|-----------------------------|
| Generation of allocation sequence: randomly assigned |
| Allocation concealment: sealed envelopes |
| Blinding: none |
| Inclusion of participants in analysis: > 90% |
| Duration: not stated |

| Participants | Number: 52 participants |
|--------------|------------------------|
| Inclusion criteria: age 3 months to 5 years; acute watery diarrhoea; presence of moderate to severe dehydration |
| Exclusion criteria: none reported |

| Interventions | 1. Glucose oral rehydration solution (ORS): 24 participants |
|---------------|----------------------------------------------------------|
|               | 2. Rice ORS: 24 participants |

| Outcomes | 1. Total stool output in first 24 hours |
|----------|----------------------------------------|
|          | 2. Duration of diarrhoea |
|          | 3. Number of participants with unscheduled intravenous fluid |
|          | 4. Number of participants with vomiting |
### Patra 1982 (Continued)

| Glucose-based ORS osmolarity | ≥ 310 mOsm/L |
|-----------------------------|--------------|

#### Setting
**Hospital-based trial**
- **Location:** Calcutta, India

#### Notes
- 

### Ramakrishna 2000

#### Methods
- **Randomized controlled trial**
- **Generation of allocation sequence:** block randomization
- **Allocation concealment:** not reported
- **Blinding:** participants and providers partially blinded; outcome assessors unclear
- **Inclusion of participants in analysis:** > 90%
- **Duration:** 27 months, from May 1994 to July 1996

#### Participants
- **Number:** 48 enrolled
- **Inclusion criteria:** age 14 to 58 years old; acute watery diarrhoea < 72 hours; positive for *Vibrio cholerae*
- **Exclusion criteria:** presence of systemic illness; intake of antibiotics

#### Interventions
1. Glucose oral rehydration solution (ORS): 16 participants
2. Rice ORS: 16 participants
3. Amylase-resistant starch ORS: 16 participants

#### Outcomes
- **1. Total stool output in first 24 hours (measured in g and not in g/kg), duration of diarrhoea**

#### Glucose-based ORS osmolarity
- ≥ 310 mOsm/L

#### Setting
**Hospital-based trial**
- **Location:** Vellore, India

#### Notes
- *Study with 3 treatment arms:* 2 polymer-based ORS vs glucose ORS

### Ramakrishna 2000, amylase

#### Methods
- Amylase arm of *Ramakrishna 2000*

#### Participants
- 

#### Interventions
1. Glucose oral rehydration solution (ORS): 16 participants
2. Amylase-resistant starch ORS: 16 participants

#### Outcomes
- 

#### Glucose-based ORS osmolarity
- 

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*Note: The text is a part of a Cochrane review on Polymer-based oral rehydration solution for treating acute watery diarrhoea.*

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### Ramakrishna 2000, amylase

*(Continued)*

| Setting | - |
| Notes | - |

### Ramakrishna 2000, rice

| Methods | Rice arm of Ramakrishna 2000 |
| Participants | - |
| Interventions | 1. Glucose oral rehydration solution (ORS): 16 participants  
2. Rice ORS: 16 participants |
| Outcomes | - |
| Glucose-based ORS osmolarity | - |
| Setting | - |
| Notes | - |

### Ramakrishna 2008

| Methods | Randomized controlled trial  
*Generation of allocation sequence:* table of random numbers  
*Allocation concealment:* serially numbered oral rehydration solution (ORS) packages  
*Blinding:* assessors but not the participants or providers were blinded because of the nature of the study  
*Inclusion of participants in analysis:* 100%  
*Duration:* not stated |
| Participants | Number: 50 enrolled  
*Inclusion criteria:* males; 18 to 65 years old; acute watery diarrhoea  
*Exclusion criteria:* presence of bloody diarrhoea; presence of systemic illness |
| Interventions | 1. Glucose ORS: 25 participants  
2. High amylose maize starch ORS: 25 participants |
| Outcomes | 1. Total stool output (g) in first 24 hours  
2. Duration of diarrhoea  
3. Unscheduled use of intravenous fluid  
4. Number of participants with hyponatraemia |
| Glucose-based ORS osmolarity | ≤ 270 mOsm/L |
| Setting | Hospital-based trial  
*Location:* Vellore, India |
### Ramakrishna 2008

(Continued)

| Notes |
|-------|
| - |

### Razafindrakoto 1993

| Methods |
|---------|
| Randomized controlled trial  
*Generation of allocation sequence:* randomized  
*Allocation concealment:* not reported  
*Blinding:* none  
*Inclusion of participants in analysis:* > 90%  
*Duration:* 27 months, from January 1988 to March 1990 |

| Participants |
|--------------|
| Number: 150 enrolled  
*Inclusion criteria:* age 6 to 36 months; males; acute watery diarrhoea; mild to moderate dehydration; severe malnutrition < 70% of reference standard  
*Exclusion criteria:* presence of bloody diarrhoea; presence of systemic illness; patients in shock |

| Interventions |
|---------------|
| 1. Glucose oral rehydration solution (ORS): 68 participants  
2. Rice ORS: 82 participants |

| Outcomes |
|----------|
| 1. Total stool output in first 24 hours  
2. Duration of diarrhoea |

| Glucose-based ORS osmolarity |
|-----------------------------|
| ≥ 310 mOsm/L |

| Setting |
|---------|
| Hospital-based trial  
*Location:* Antananarivo, Madagascar |

| Notes |
|-------|
| - |

### Santos Ocampo 1993

| Methods |
|---------|
| Randomized controlled trial  
*Generation of allocation sequence:* table of random numbers  
*Allocation concealment:* code was kept until the end of trial  
*Blinding:* participants, providers, outcome assessors  
*Inclusion of participants in analysis:* > 90%  
*Duration:* not stated |

| Participants |
|--------------|
| Number: 120 enrolled  
*Inclusion criteria:* age 3 to 36 months; males; acute diarrhoea < 5 days; mild to moderate dehydration  
*Exclusion criteria:* presence of bloody diarrhoea; systemic illness; intake of antibiotics; severe dehydration; severe malnutrition; history of diarrhoea in the last 2 weeks |

| Interventions |
|---------------|
| 1. Glucose oral rehydration solution (ORS): 60 participants  
2. Maltodextrin ORS: 60 participants |
### Santos Ocampo 1993 (Continued)

| Outcomes | 1. Total stool output in first 24 hours  
2. Total stool output from randomization to discharge  
3. Duration of diarrhoea |
|-----------|--------------------------------------------------------------------------------|
| Glucose-based ORS osmolarity | $\geq 310 \text{ mOsm/L}$ |
| Setting | Hospital-based trial  
*Location*: Manila, Philippines |
| Notes | Results of total stool output in first 24 hours, total stool output from randomization to discharge, and duration of diarrhoea are skewed |

### Sharma 1998

| Methods | Randomized controlled trial  
*Generation of allocation sequence*: randomized  
*Allocation concealment*: not reported  
*Blinding*: none  
*Inclusion of participants in analysis*: $> 90\%$  
*Duration*: not stated |
|-----------|--------------------------------------------------------------------------------|
| Participants |  
*Number*: 100 enrolled  
*Inclusion criteria*: age 7 to 36 months; acute diarrhoea; some dehydration; non-cholerae; weight $> 80\%$ of reference standard  
*Exclusion criteria*: presence of bloody diarrhoea; presence of systemic illness; severe dehydration; malnutrition; abdominal distension |
| Interventions | 1. Glucose oral rehydration solution (ORS): 50 participants  
2. Rice ORS: 50 participants |
| Outcomes | 1. Total stool output (g, not in g/kg) in first 24 hours  
2. Duration of diarrhoea  
3. Number of participants with unscheduled intravenous fluid |
| Glucose-based ORS osmolarity | $\geq 310 \text{ mOsm/L}$ |
| Setting | Hospital-based trial  
*Location*: Rohtak, India |
| Notes | - |
### Wall 1997

**Methods**
- Randomized controlled trial
  - *Generation of allocation sequence:* table of random numbers
  - *Allocation concealment:* not reported
  - *Blinding:* participants and providers not blinded; outcome assessors unclear
  - *Inclusion of participants in analysis:* > 90%
  - *Duration:* not stated

**Participants**
- *Number:* 100 enrolled
  - *Inclusion criteria:* age 4 weeks to 5 years old; acute diarrhoea; mild to moderate dehydration
  - *Exclusion criteria:* presence of systemic illness; intake of antibiotics/antidiarrhoeals; severe dehydration; previous surgery

**Interventions**
1. Glucose oral rehydration solution (ORS): 50 participants
2. Rice ORS: 50 participants

**Outcomes**
1. Duration of diarrhoea

**Glucose-based ORS osmolarity**
- $\geq 310$ mOsm/L

**Setting**
- Hospital-based trial
  - *Location:* Brisbane, Australia

**Notes**
- Data on duration of diarrhoea are skewed

### Zaman 2001

**Methods**
- Randomized controlled trial
  - *Generation of allocation sequence:* table of random numbers
  - *Allocation concealment:* not specified whether envelope is opaque and sealed
  - *Blinding:* none
  - *Inclusion of participants in analysis:* > 90% of randomized participants included in the final analysis
  - *Duration:* September 1996 to May 1997

**Participants**
- *Number:* 167 enrolled
  - *Inclusion criteria:* age 5 to 15 years; acute diarrhoea; moderate to severe dehydration; purging rate $> 2$ mL/kg/hour
  - *Exclusion criteria:* presence of bloody diarrhoea; systemic illness; intake of antibiotics; malnutrition $< 65\%$ weight for age

**Interventions**
1. Glucose oral rehydration solution (ORS): 82 participants
2. Rice ORS: 85 participants

**Outcomes**
1. Total stool output in first 24 hours
2. Duration of diarrhoea
3. Number of unscheduled use of intravenous fluid
4. Number of participants with hyponatraemia and hypokalaemia

**Glucose-based ORS osmolarity**
- $\geq 310$ mOsm/L
### Setting

| Location | Rural treatment centre

| Location: Matlab, Bangladesh |

### Notes

- 

### Characteristics of excluded studies  

| Study                        | Reason for exclusion                                                                 |
|------------------------------|---------------------------------------------------------------------------------------|
| Agustina 2007                | Not a clinical trial on oral rehydration solution                                      |
| Alam 2008                    | Guar gum, a soluble fibre and not a polymer, was added to the oral rehydration solution |
| Ansaldi 1990                 | Different electrolyte composition of the 2 groups                                      |
| Barclay 1995                 | Different electrolyte composition of the 2 groups                                      |
| Barragan-Guzman 1998         | Control group given oral saline solution, not oral rehydration solution                |
| Bhandari 2008                | Not a clinical trial on oral rehydration solution                                      |
| Cohen 1995                   | Different electrolyte composition of the 2 groups                                      |
| Gutierrez 2007               | L-glutamine, an amino acid and not a polymer was added in the oral rehydration solution |
| Hoekstra 2004                | Investigated the use of non-digestible carbohydrates, which are not polymers          |
| Jirapinyo 1996               | Different electrolyte composition of the 2 groups                                      |
| Kassaye 1994                 | Composition of home-made oral rehydration solution is not known                        |
| Kenya 1989                   | The 2 groups have different sources of bicarbonate: polymer-based oral rehydration solution used sodium bicarbonate and glucose oral rehydration solution, trisodium citrate dihydrate |
| Lebenthal 1995               | Polymer-based oral rehydration solution has an additional amino acid                   |
| Molina 1995                  | Glucose-based oral rehydration solution contained 50 mmol/L sodium. The inclusion criteria of the review specified 90 or 60 to 75 mmol/L of sodium |
| Molla 1982                   | Used a sucrose and not a glucose-based oral rehydration solution as a control group   |
| Molla 2000                   | Not an efficacy study. The study compared the biochemical analysis of home-made rice oral rehydration solution vs glucose-based oral rehydration solution |
| Study Reference    | Key Finding                                                                                           |
|--------------------|-------------------------------------------------------------------------------------------------------|
| Mota-Hernandez 1991| Different electrolyte composition of the 2 groups                                                      |
| Murphy 1996        | Unknown electrolyte composition of the wheat-based oral rehydration solution                          |
| Patra 1984         | Treatment group used an amino acid-based oral rehydration solution, not a polymer-based oral rehydration solution |
| Pelleboer 1990     | Not a randomized trial, alternate allocation of participants in the 2 interventions was done          |
| Pizarro 1991       | Different electrolyte composition of the 2 groups                                                      |
| Prasad 1993        | The primary outcome of interest relevant to the study was not evaluated                               |
| Rabbani 2005       | Study has no control group that uses glucose-based oral rehydration solution. The control group contains L-histidine, an amino acid |
| Raghupathy 2006    | Polymer was not used in place of glucose. Instead, the amylase-resistant starch was added to the glucose-based oral rehydration solution |
| Roslund 2008       | Not a clinical trial on oral rehydration solution                                                    |
| Sabchareon 1992    | Different electrolyte content of rice oral rehydration solution and glucose-based oral rehydration solution |
| Sarker 2001        | Participants with persistent diarrhoea (> 14 days)                                                    |
| Sirivichayakul 2000| Different electrolyte composition of the 2 groups                                                      |
| Teferedegn 1993    | Not an efficacy but an effectiveness study                                                            |
| Yang 2007          | A clinical trial on the use of reduced osmolarity oral rehydration solution in acute diarrhoea. Not a clinical trial on the use of polymer-based oral rehydration solution |
| Yartev 1995        | Different electrolyte composition of the 2 groups                                                      |
| Yurdakok 1995      | Patients were only observed during the rehydration phase. The primary outcome of interest relevant to the study was not evaluated |
| Zaman 2007         | Not a clinical trial on oral rehydration solution                                                    |
| Zavaleta 2007      | Different electrolyte composition of the 2 groups                                                      |
## DATA AND ANALYSES

### Comparison 1. Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---------------------------|----------------|---------------------|--------------------|-------------|
| 1 Total stool output: during first 24 hours | 13 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 1.1 ORS ≥ 310 | 12 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.2 ORS ≤ 270 | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2 Duration of diarrhoea | 15 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 2.1 ORS ≥ 310 | 12 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2.2 ORS ≤ 270 | 3 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 3 Unscheduled use of intravenous fluid | 21 | 2235 | Risk Ratio (M-H, Fixed, 95% CI) | 0.75 [0.59, 0.95] |
| 3.1 ORS ≥ 310 | 18 | 1909 | Risk Ratio (M-H, Fixed, 95% CI) | 0.78 [0.60, 1.01] |
| 3.2 ORS ≤ 270 | 3 | 326 | Risk Ratio (M-H, Fixed, 95% CI) | 0.62 [0.36, 1.08] |
| 4 Vomiting (no. participants) | 10 | 617 | Risk Ratio (M-H, Fixed, 95% CI) | 0.83 [0.65, 1.05] |
| 4.1 ORS ≥ 310 | 9 | 554 | Risk Ratio (M-H, Fixed, 95% CI) | 0.87 [0.68, 1.11] |
| 4.2 ORS ≤ 270 | 1 | 63 | Risk Ratio (M-H, Fixed, 95% CI) | 0.56 [0.24, 1.34] |
| 5 Hyponatraemia (no. participants) | 6 | 480 | Risk Ratio (M-H, Fixed, 95% CI) | 1.03 [0.52, 2.01] |
| 5.1 ORS ≥ 310 | 3 | 335 | Risk Ratio (M-H, Fixed, 95% CI) | 2.25 [0.34, 14.92] |
| 5.2 ORS ≤ 270 | 3 | 145 | Risk Ratio (M-H, Fixed, 95% CI) | 0.88 [0.43, 1.82] |
| 6 Hypokalaemia (no. participants) | 2 | 260 | Risk Ratio (M-H, Fixed, 95% CI) | Subtotals only |
| 6.1 ORS ≥ 310 | 2 | 205 | Risk Ratio (M-H, Fixed, 95% CI) | 1.29 [0.74, 2.25] |
| 7 Developed persistent diarrhoea (no. participants) | 2 | 885 | Risk Ratio (M-H, Fixed, 95% CI) | Subtotals only |
| 7.1 ORS ≥ 310 | 2 | 885 | Risk Ratio (M-H, Fixed, 95% CI) | 1.28 [0.68, 2.41] |

### Comparison 2. Type of polymer: polymer-based ORS vs glucose-based ORS

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---------------------------|----------------|---------------------|--------------------|-------------|
| 1 Total stool output during the first 24 hours | 17 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 1.1 Rice-based ORS | 13 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.2 Wheat-based ORS | 2 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.3 Sorghum-based ORS | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.4 Maltodextrin-based ORS | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2 Duration of diarrhoea | 18 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 2.1 Rice-based ORS | 15 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2.2 Wheat-based ORS | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2.3 Sorghum-based ORS | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 2.4 Maltodextrin-based ORS | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
3 Unscheduled use of intravenous fluid

| Condition                        | No. of studies | No. of participants | Statistical method                        | Effect size       |
|----------------------------------|----------------|---------------------|-------------------------------------------|-------------------|
| 3.1 Rice-based ORS               | 18             | 1962                | Risk Ratio (M-H, Fixed, 95% CI)           | 0.75 [0.58, 0.98] |
| 3.2 Wheat-based ORS              | 1              | 48                  | Risk Ratio (M-H, Fixed, 95% CI)           | 1.0 [0.15, 6.53]  |
| 3.3 Maltodextrin-based ORS       | 2              | 158                 | Risk Ratio (M-H, Fixed, 95% CI)           | 0.79 [0.31, 2.02] |

Comparison 3. Effects of age and pathogen: rice-based ORS vs glucose-based ORS

| Outcome or subgroup title                              | No. of studies | No. of participants | Statistical method                        | Effect size       |
|--------------------------------------------------------|----------------|---------------------|-------------------------------------------|-------------------|
| 1 Total stool output during the first 24 hours, by age group | 13             |                     | Mean Difference (IV, Random, 95% CI)       | Totals not selected |
| 1.1 Paediatric                                         | 11             |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 1.2 Adults                                             | 2              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 2 Duration of diarrhoea, by age group                  | 15             | 998                 | Mean Difference (IV, Random, 95% CI)       | -7.19 [-11.80, -2.58] |
| 2.1 Paediatrics                                        | 11             | 770                 | Mean Difference (IV, Random, 95% CI)       | -6.81 [-12.10, -1.52] |
| 2.2 Adults                                             | 4              | 228                 | Mean Difference (IV, Random, 95% CI)       | -7.11 [-11.91, -2.32] |
| 3 Total stool output during the first 24 hours, by pathogen | 11             |                     | Mean Difference (IV, Random, 95% CI)       | Totals not selected |
| 3.1 Cholera                                            | 3              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 3.2 Non-cholera                                        | 4              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 3.3 Mixed pathogens                                    | 5              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 4 Duration of diarrhoea, by type of pathogen           | 12             |                     | Mean Difference (IV, Random, 95% CI)       | Totals not selected |
| 4.1 Cholera                                            | 7              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 4.2 Non-cholera                                        | 3              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
| 4.3 Mixed pathogens                                    | 2              |                     | Mean Difference (IV, Random, 95% CI)       | 0.0 [0.0, 0.0]    |
### Analysis 1.1. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 1 Total stool output: during first 24 hours.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

Outcome: 1 Total stool output: during first 24 hours

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Mean Difference | 95% CI |
|-------------------|-------------------|-------------------|----------------|-------|
| Alam 1987         | 52 148.85 (18.75) | 24 238.9 (27.53) | -90.05 | [-102.19, -77.91] |
| Alam 1992         | 47 223 (128)      | 42 366 (174)      | -143.00 | [-207.10, -78.90] |
| Dutta 1988        | 72 91.2 (8.85)    | 33 103.2 (9.6)    | -12.00  | [-15.86, -8.14]   |
| El-Mougi 1988     | 30 163.2 (21.8)   | 30 245 (25.3)     | -81.80  | [-93.75, -69.85]  |
| Islam 1994        | 27 101 (60.5)     | 25 137.1 (14.6)   | -36.10  | [-59.63, -12.57]  |
| Mohan 1988        | 23 88.56 (11.52)  | 23 110.16 (14.4)  | -21.60  | [-29.14, -14.06]  |
| Molla 1985, adults| 85 115 (10)       | 72 158.7 (12.8)   | -43.70  | [-47.34, -40.06]  |
| Molla 1985, children | 84 155 (13)     | 101 204 (13.9)    | -49.00  | [-52.88, -45.12]  |
| Molla 1989b       | 224 208.59 (109.56)| 42 343 (151)      | -134.41 | [-182.28, -86.54] |
| Patra 1982        | 24 97 (3.28)      | 24 166 (4.69)     | -69.00  | [-71.29, -66.71]  |
| Razafindrakoto 1993 | 68 91 (6)       | 56 81 (5)         | 10.00   | [8.06, 11.94]     |
| Zaman 2001        | 85 195 (1.58)    | 82 227.3 (1.99)   | -32.30  | [-32.85, -31.75]  |

### Study or subgroup | 2 ORS ≤ 270 | Polymer-based ORS | Glucose-based ORS | Mean Difference | 95% CI |
|-------------------|-------------|-------------------|-------------------|----------------|-------|
| Nanulescu 1999    | 48 77.4 (47)| 51 102 (33)       | -24.60            | [-40.69, -8.51] |

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*Favours polymer-based ORS*  *Favours glucose-based ORS*
### Analysis 1.2. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 2 Duration of diarrhoea.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

Outcome: 2 Duration of diarrhoea

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Mean Difference | Mean Difference |
|-------------------|-------------------|-------------------|-----------------|-----------------|
| N | Mean (SD) | N | Mean (SD) | IV (Random), 95% CI | IV (Random), 95% CI |
| 1 ORS ≥ 310 | | | | | |
| Dutta 1998, children | 10 | 30.65 (4.21) | 10 | 35.95 (7.37) | -5.30 [-10.56, -0.04] |
| Dutta 1988 | 72 | 75.33 (8.29) | 33 | 79.2 (6.4) | -3.87 [-6.77, -0.97] |
| El-Mougi 1988 | 30 | 28.4 (5.2) | 30 | 34.3 (2.3) | -5.90 [-7.93, -3.87] |
| Sharma 1998 | 25 | 33.9 (8.03) | 25 | 38.8 (8.03) | -4.90 [-9.35, -0.45] |
| Patra 1982 | 24 | 30 (0.82) | 24 | 43 (0.92) | -13.00 [-13.49, -12.51] |
| Alam 1987 | 48 | 79 (1.65) | 24 | 90 (1.78) | -11.00 [-11.85, -10.15] |
| Dutta 1998, adults | 25 | 41.32 (6.08) | 25 | 45.68 (6.91) | -4.36 [-7.97, -0.75] |
| Zaman 2001 | 85 | 35.3 (0.22) | 82 | 35.8 (0.23) | -0.50 [-0.57, -0.43] |
| Ramakrishna 2000 | 32 | 63.75 (20.4) | 16 | 90.9 (29.5) | -27.15 [-43.24, -11.06] |
| Alam 1992 | 47 | 81.1 (23.8) | 42 | 85.2 (19.9) | -4.10 [-13.18, 4.98] |
| Rasafindrakoto 1993 | 68 | 68 (4) | 56 | 89 (6) | -21.00 [-22.84, -19.16] |
| Guiraldes 1995b | 24 | 72 (10) | 24 | 77 (12) | -5.00 [-12.25, 2.25] |
| 2 ORS ≤ 270 | | | | | |
| Bhattacharya 1998 | 27 | 36.5 (12.8) | 30 | 46.9 (11.9) | -10.40 [-16.84, -3.96] |
| Dutta 2000 | 19 | 29.34 (4.83) | 19 | 33.9 (3.77) | -4.56 [-7.32, -1.80] |
| Nanulescu 1999 | 48 | 51 (24) | 51 | 54 (40) | -3.00 [-15.91, 9.91] |

Favours polymer-based ORS Favours glucose-based ORS
### Analysis 1.3. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 3 Unscheduled use of intravenous fluid.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

Outcome: 3 Unscheduled use of intravenous fluid

| Study or subgroup | Polymer-based ORS n/N | Glucose-based ORS n/N | Risk Ratio M-H,Fixed,95% CI | Weight | Risk Ratio M-H,Fixed,95% CI |
|------------------|-----------------------|-----------------------|----------------------------|--------|-----------------------------|
| 1 ORS ≥ 310      |                       |                       |                            |        |                             |
| Akbar 1991       | 1/33                  | 4/36                  | 3.1 %                      | 0.27   | 0.03, 2.32                  |
| Alam 1987        | 4/48                  | 2/24                  | 2.1 %                      | 1.00   | 0.20, 5.08                  |
| Alam 1992        | 20/47                 | 20/42                 | 16.9 %                     | 0.89   | 0.56, 1.41                  |
| Bhan 1987        | 0/60                  | 3/33                  | 3.6 %                      | 0.08   | 0.00, 1.50                  |
| Dutta 1998, adults | 0/25              |                       |                            |        |                             |
| Dutta 1998, children | 0/10            |                       |                            |        |                             |
| El-Mougi 1996    | 6/45                  | 5/44                  | 4.0 %                      | 1.17   | 0.39, 3.57                  |
| Fayad 1993       | 2/210                 | 6/204                 | 4.9 %                      | 0.32   | 0.07, 1.59                  |
| Guiraldes 1995a  | 5/51                  | 6/49                  | 4.9 %                      | 0.80   | 0.26, 2.45                  |
| Guiraldes 1995b  | 4/24                  | 7/24                  | 5.6 %                      | 0.57   | 0.19, 1.70                  |
| Hassain 2003     | 12/57                 | 14/56                 | 11.3 %                     | 0.84   | 0.43, 1.66                  |
| Islam 1994       | 5/27                  | 3/25                  | 2.5 %                      | 1.54   | 0.41, 5.80                  |
| Maulen-Radovan 1994 | 11/49             | 12/48                 | 9.7 %                      | 0.90   | 0.44, 1.84                  |
| Mohan 1988       | 1/23                  | 1/23                  | 0.8 %                      | 1.00   | 0.07, 15.04                 |
| Molla 1985, adults | 0/85              | 2/72                  | 2.2 %                      | 0.17   | 0.01, 3.48                  |
| Molla 1985, children | 0/84              | 4/101                 | 3.3 %                      | 0.13   | 0.01, 2.44                  |
| Patra 1982       | 2/24                  | 2/24                  | 1.6 %                      | 1.00   | 0.15, 6.53                  |
| Zaman 2001       | 7/85                  | 5/82                  | 4.1 %                      | 1.35   | 0.45, 4.09                  |
| **Subtotal (95% CI)** | **987**              | **922**               | **80.6 %**                 | **0.78** | **0.60, 1.01**              |

Total events: 80 (Polymer-based ORS), 96 (Glucose-based ORS)

Heterogeneity: Chi$^2$ = 10.37, df = 15 (P = 0.80); I$^2$ =0.0%

Test for overall effect: Z = 1.89 (P = 0.059)

2 ORS ≤ 270

| Study or subgroup | Polymer-based ORS n/N | Glucose-based ORS n/N | Risk Ratio M-H,Fixed,95% CI | Weight | Risk Ratio M-H,Fixed,95% CI |
|------------------|-----------------------|-----------------------|----------------------------|--------|-----------------------------|
| Maulen-Radovan 2004 | 1/93              | 8/84                  | 6.7 %                      | 0.11   | 0.01, 0.88                  |
| Nanulescu 1999   | 5/48                  | 4/51                  | 3.1 %                      | 1.33   | 0.38, 4.66                  |
| Ramakrishna 2008  | 9/25                  | 12/25                 | 9.6 %                      | 0.75   | 0.39, 1.46                  |

(Continued . . .)
### Analysis 1.4. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 4 Vomiting (no. participants).

#### Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea.

#### Comparison: 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

#### Outcome: 4 Vomiting (no. participants)

| Study or subgroup | Polymer-based ORS n/N | Glucose-based ORS n/N | Risk Ratio M-H,Fixed 95% CI | Weight | Risk Ratio M-H,Fixed 95% CI |
|-------------------|-----------------------|-----------------------|-----------------------------|--------|-----------------------------|
| **Subtotal (95% CI)** | 166/160 | 19.4 % | 0.62 [0.36, 1.08] | 1153/1082 | 100.0 % | 0.75 [0.59, 0.95] |
| Total events: 15 (Polymer-based ORS), 24 (Glucose-based ORS) | | Heterogeneity: Chi² = 4.35, df = 2 (P = 0.11); I² = 54% | Test for overall effect: Z = 1.68 (P = 0.093) | Total events: 95 (Polymer-based ORS), 120 (Glucose-based ORS) | Heterogeneity: Chi² = 14.83, df = 18 (P = 0.67); I² = 0.0% | Test for overall effect: Z = 2.42 (P = 0.016) |

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(Continued...)
### Study or subgroup

| Polymer-based ORS | Glucose-based ORS | Risk Ratio | Weight |
|-------------------|-------------------|------------|--------|
| n/N               | n/N               | M-H,Fixed,95% CI | M-H,Fixed,95% CI |
| **Subtotal (95% CI)** | | | |
| Total events: 78 (Polymer-based ORS), 69 (Glucose-based ORS) | | | |
| Heterogeneity: Chi$^2$ = 7.84, df = 6 ($P = 0.25$); I$^2$ = 23% | | | |
| Test for overall effect: $Z = 1.15$ ($P = 0.25$) | | | |
| 2 ORS ≤ 270 | | | |
| Iyngkaran 1998 | 6/31 | 11/32 | 12.5 % | 0.56 [ 0.24, 1.34 ] |
| **Subtotal (95% CI)** | | | |
| Total events: 6 (Polymer-based ORS), 11 (Glucose-based ORS) | | | |
| Heterogeneity: not applicable | | | |
| Test for overall effect: $Z = 1.30$ ($P = 0.19$) | | | |
| **Total (95% CI)** | | | |
| Total events: 84 (Polymer-based ORS), 80 (Glucose-based ORS) | | | |
| Heterogeneity: Chi$^2$ = 9.05, df = 7 ($P = 0.25$); I$^2$ = 23% | | | |
| Test for overall effect: $Z = 1.55$ ($P = 0.12$) | | | |

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**Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review)**

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### Analysis 1.5. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 5 Hyponatraemia (no. participants).

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS

Outcome: 5 Hyponatraemia (no. participants)

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Risk Ratio | Weight | Risk Ratio |
|-------------------|-------------------|-------------------|------------|--------|------------|
|                   | n/N               | n/N               | n/N        | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| 1 ORS ≥ 310       |                   |                   |            |        |            |
| Dutta 1988        | 0/35              | 0/33              |            |        |            |
| Guiraldes 1995a   | 2/51              | 1/49              | 7.2 %      | 1.92 [0.18, 20.52] |            |
| Zaman 2001        | 1/85              | 0/82              | 3.6 %      | 2.90 [0.12, 70.07] |            |
| **Subtotal (95% CI)** | **171** | **164** | **10.7 %** | **2.25 [0.34, 14.92]** |            |
| Total events: 3 (Polymer-based ORS), 1 (Glucose-based ORS) |
| Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0.0% |
| Test for overall effect: Z = 0.84 (P = 0.40) |
| 2 ORS ≤ 270       |                   |                   |            |        |            |
| Bhattacharya 1998 | 4/27              | 5/30              | 33.2 %     | 0.89 [0.27, 2.97] |            |
| Dutta 2000        | 4/19              | 6/19              | 42.1 %     | 0.67 [0.22, 1.99] |            |
| Ramakrishna 2008  | 3/25              | 2/25              | 14.0 %     | 1.50 [0.27, 8.22] |            |
| **Subtotal (95% CI)** | **71** | **74** | **89.3 %** | **0.88 [0.43, 1.82]** |            |
| Total events: 11 (Polymer-based ORS), 13 (Glucose-based ORS) |
| Heterogeneity: Chi² = 0.63, df = 2 (P = 0.73); I² = 0.0% |
| Test for overall effect: Z = 0.34 (P = 0.73) |

**Total (95% CI)**

| Total events: 14 (Polymer-based ORS), 14 (Glucose-based ORS) |
| Heterogeneity: Chi² = 1.52, df = 4 (P = 0.82); I² = 0.0% |
| Test for overall effect: Z = 0.08 (P = 0.94) |
### Analysis 1.6. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 6 Hypokalaemia (no. participants).

**Review:** Polymer-based oral rehydration solution for treating acute watery diarrhoea  
**Comparison:** 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS  
**Outcome:** 6 Hypokalaemia (no. participants)

| Study or subgroup | Polymer-based ORS n/N | Glucose-based ORS n/N | Risk Ratio M-H,Fixed 95% CI | Weight | Risk Ratio M-H,Fixed 95% CI |
|-------------------|-----------------------|-----------------------|-----------------------------|--------|-----------------------------|
| I ORS ≥ 310       |                       |                       |                             |        |                             |
| Bhan 1987         | 4/60                  | 3/33                  | 21.4 % 0.73 [0.17, 3.08]    |        |                             |
| Zaman 2001        | 21/85                 | 14/82                 | 78.6 % 1.45 [0.79, 2.65]    |        |                             |
| **Subtotal (95% CI)** | **145**              | **115**              | **100.0 % 1.29 [0.74, 2.25]** |        |                             |

**Total events:** 25 (Polymer-based ORS), 17 (Glucose-based ORS)  
**Heterogeneity:** Chi² = 0.73, df = 1 (P = 0.39); I² = 0.0%  
**Test for overall effect:** Z = 0.92 (P = 0.36)

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### Analysis 1.7. Comparison 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS, Outcome 7 Developed persistent diarrhoea (no. participants).

**Review:** Polymer-based oral rehydration solution for treating acute watery diarrhoea  
**Comparison:** 1 Type of glucose ORS: any polymer-based ORS vs glucose-based ORS  
**Outcome:** 7 Developed persistent diarrhoea (no. participants)

| Study or subgroup | Polymer-based ORS n/N | Glucose-based ORS n/N | Risk Ratio M-H,Fixed 95% CI | Weight | Risk Ratio M-H,Fixed 95% CI |
|-------------------|-----------------------|-----------------------|-----------------------------|--------|-----------------------------|
| I ORS ≥ 310       |                       |                       |                             |        |                             |
| Faruque 1997      | 5/236                 | 4/235                 | 24.8 % 1.24 [0.34, 4.58]    |        |                             |
| Fayad 1993        | 16/210                | 12/204                | 75.2 % 1.30 [0.63, 2.67]    |        |                             |
| **Subtotal (95% CI)** | **446**              | **439**              | **100.0 % 1.28 [0.68, 2.41]** |        |                             |

**Total events:** 21 (Polymer-based ORS), 16 (Glucose-based ORS)  
**Heterogeneity:** Chi² = 0.00, df = 1 (P = 0.96); I² = 0.0%  
**Test for overall effect:** Z = 0.77 (P = 0.44)
Analysis 2.1. Comparison 2 Type of polymer: polymer-based ORS vs glucose-based ORS, Outcome 1 Total stool output during the first 24 hours.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 2 Type of polymer: polymer-based ORS vs glucose-based ORS

Outcome: 1 Total stool output during the first 24 hours

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Mean Difference | IV, Random | 95% CI |
|-------------------|------------------|------------------|----------------|------------|--------|
|                   | N    | Mean(SD) | N    | Mean(SD) | IV, Random | 95% CI |        |
| 1 Rice-based ORS  |      |          |      |          |            |        |        |
| Alam 1987, rice   | 24   | 130 (6.12) | 24   | 290 (12.2) | -160.00   | [-165.46, -154.54] |        |
| Alam 1992         | 47   | 223 (128)  | 42   | 366 (174)  | -143.00   | [-207.10, -78.90] |        |
| Dutta 1988        | 72   | 75.33 (8.29) | 33   | 103.2 (9.6) | -27.87    | [-31.66, -24.08] |        |
| El-Mougi 1988     | 30   | 163.2 (21.8) | 30   | 245 (25.3)  | -81.80    | [-93.75, -69.85] |        |
| Islam 1994        | 27   | 101 (60.5)  | 25   | 137.1 (14.6) | -36.10    | [-59.63, -12.57] |        |
| Mohan 1988        | 23   | 88.56 (11.52) | 23   | 110.16 (14.4) | -21.60    | [-29.14, -14.06] |        |
| Molla 1985, adults| 85   | 115 (10)    | 72   | 159 (13)    | -44.00    | [-47.68, -40.32] |        |
| Molla 1985, children | 84  | 155 (13)    | 101  | 204 (13.9)  | -49.00    | [-52.88, -45.12] |        |
| Molla 1989b, rice  | 37   | 162 (56)    | 42   | 343 (151)   | -181.00   | [-230.10, -131.90] |        |
| Nanelescu 1999    | 48   | 77.4 (47)   | 51   | 102 (33)    | -24.60    | [-40.69, -8.51] |        |
| Patra 1982        | 24   | 97 (3.27)   | 24   | 166 (23)    | -69.00    | [-78.29, -59.71] |        |
| Razafindrakaoto 1993 | 68 | 91 (6)     | 56   | 81 (5)      | 10.00     | [8.06, 11.94]    |        |
| Zaman 2001        | 85   | 195 (1.58)  | 82   | 227.3 (1.99) | -32.30    | [-32.85, -31.75] |        |
| 2 Wheat-based ORS |      |          |      |          |            |        |        |
| Alam 1987, wheat  | 24   | 170 (4.08)  | 24   | 290 (12.2)  | -120.00   | [-125.15, -114.85] |        |
| Molla 1989b, wheat | 39  | 240 (96)    | 42   | 343 (151)   | -103.00   | [-157.71, -48.29] |        |
| 3 Sorghum-based ORS |      |          |      |          |            |        |        |
| Molla 1989b, sorghum | 35 | 215 (197)   | 42   | 343 (151)   | -128.00   | [-207.66, -48.34] |        |
| 4 Maltodextrin-based ORS |      |          |      |          |            |        |        |
| Santos Ocampo 1993 | 58  | 162.8 (138.2) | 59   | 135.4 (107.9) | 27.40    | [-17.58, 72.38]    |        |
### Analysis 2.2. Comparison 2: Type of polymer: polymer-based ORS vs glucose-based ORS, Outcome 2: Duration of diarrhoea.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: Type of polymer: polymer-based ORS vs glucose-based ORS

Outcome: Duration of diarrhoea

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Mean Difference | Mean Difference |
|------------------|-------------------|-------------------|----------------|----------------|
|                  | N Mean(SD)        | N Mean(SD)        | IV,Random,95% CI | IV,Random,95% CI |
| Rice-based ORS   |                   |                   |                |                |
| Alam 1987, rice  | 24 78 (1.43)      | 24 90 (1.78)      | 12.00 [-12.91, -11.09] |                |
| Alam 1992        | 47 81.1 (23.8)    | 42 85.2 (19.9)    | 4.10 [-13.18, 4.98] |                |
| Bhattacharya 1998| 27 36.5 (12.8)    | 30 46.9 (11.9)    | 10.40 [-16.84, -3.96] |                |
| Dutta 1988       | 72 75.33 (8.29)   | 33 79.2 (6.4)     | -3.87 [-6.77, -0.97] |                |
| Dutta 1998, adults | 25 41.32 (6.08)  | 25 45.68 (6.91)   | -4.36 [-7.97, -0.75] |                |
| Dutta 1998, children | 10 30.65 (4.21) | 10 35.95 (7.37) | -5.30 [-10.56, -0.04] |                |
| Dutta 2000       | 19 29.34 (4.83)   | 19 33.9 (3.77)    | -4.56 [-7.32, -1.80] |                |
| El-Mougi 1988    | 30 28.4 (5.2)     | 30 34.3 (2.3)     | 5.90 [-7.93, -3.87] |                |
| Guiraldez 1995b  | 24 72 (10)        | 24 77 (12)        | 5.00 [-11.25, 1.25] |                |
| Nanulescu 1999  | 48 51 (24)        | 51 54 (40)        | -3.00 [-15.91, 9.91] |                |
| Patra 1982       | 24 30 (0.82)      | 24 43 (0.92)      | -13.00 [-13.49, -12.51] |                |
| Ramakrishna 2000, rice | 16 70.8 (20.2) | 16 90.9 (29.5) | -20.10 [-37.62, -2.58] |                |
| Razafindrakoto 1993 | 68 68 (4) | 56 89 (6) | -21.00 [-22.84, -19.16] |                |
| Sharma 1998     | 25 33.9 (8.03)    | 25 38.8 (8.03)    | -4.90 [-9.35, -0.45] |                |
| Zaman 2001      | 85 35.3 (0.22)    | 82 35.8 (0.23)    | -0.50 [-0.57, -0.43] |                |
| Wheat-based ORS  |                   |                   |                |                |
| Alam 1987, wheat | 24 80 (1.22)      | 24 90 (1.78)      | -10.00 [-10.86, -9.14] |                |
| Sorghum-based ORS|                   |                   |                |                |
| Mustafa 1995, sorghum | 34 46.7 (35.97) | 32 63.1 (35.2) | -16.40 [-33.57, 0.77] |                |
| Maltodextrin-based ORS |     |                   |                |                |
| Santos Ocampo 1993 | 58 52.6 (32.2) | 58 57.2 (37.3) | -4.60 [-17.28, 8.08] |                |

Favours polymer-based ORS Favours glucose-based ORS

Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review)

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**Analysis 2.3. Comparison 2 Type of polymer: polymer-based ORS vs glucose-based ORS, Outcome 3 Unscheduled use of intravenous fluid.**

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 2 Type of polymer: polymer-based ORS vs glucose-based ORS

Outcome: 3 Unscheduled use of intravenous fluid

| Study or subgroup | Polymer-based ORS | Glucose-based ORS | Risk Ratio | Weight | Risk Ratio |
|-------------------|-------------------|-------------------|------------|--------|------------|
|                   | n/N               | n/N               | M-H,Fixed,95% CI |        | M-H,Fixed,95% CI |
| Rice-based ORS    |                   |                   |             |        |             |
| Alam 1987, rice   | 1/12              | 2/24              | 1.2 % 1.00 [ 0.10, 9.96 ] |        |             |
| Alam 1992         | 20/47             | 20/42             | 18.8 % 0.89 [ 0.56, 1.41 ] |        |             |
| Bhan 1987, rice   | 0/31              | 3/33              | 3.0 % 0.15 [ 0.01, 2.82 ] |        |             |
| Dutta 1998, adults| 0/25              | 0/25              |             |        |             |
| Dutta 1998, children | 0/10             | 0/10              |             |        |             |
| Fayad 1993        | 2/210             | 6/204             | 5.4 % 0.32 [ 0.07, 1.59 ] |        |             |
| Guiraldes 1995a   | 5/51              | 6/49              | 5.4 % 0.80 [ 0.26, 2.45 ] |        |             |
| Guiraldes 1995b   | 4/24              | 7/24              | 6.2 % 0.57 [ 0.19, 1.70 ] |        |             |
| Hossain 2003      | 12/57             | 14/56             | 12.6 % 0.84 [ 0.43, 1.66 ] |        |             |
| Islam 1994        | 5/27              | 3/25              | 2.8 % 1.54 [ 0.41, 5.80 ] |        |             |
| Maulen-Radovan 1994 | 11/49         | 12/48             | 10.8 % 0.90 [ 0.44, 1.84 ] |        |             |
| Maulen-Radovan 2004 | 1/93            | 8/84              | 7.5 % 0.11 [ 0.01, 0.88 ] |        |             |
| Mohan 1988        | 1/23              | 1/23              | 0.9 % 1.00 [ 0.07, 15.04 ] |        |             |
| Molla 1985, adults| 0/85              | 2/72              | 2.4 % 0.17 [ 0.01, 3.48 ] |        |             |
| Molla 1985, children | 0/84            | 4/101             | 3.6 % 0.13 [ 0.01, 2.44 ] |        |             |
| Nanulescu 1999    | 5/48              | 4/51              | 3.4 % 1.33 [ 0.38, 4.66 ] |        |             |
| Patra 1982        | 2/24              | 2/24              | 1.8 % 1.00 [ 0.15, 6.53 ] |        |             |
| Zaman 2001        | 7/85              | 5/82              | 4.5 % 1.35 [ 0.45, 4.09 ] |        |             |

Subtotal (95% CI): 985 977 90.3 % 0.75 [ 0.58, 0.98 ]

Total events: 76 (Polymer-based ORS), 99 (Glucose-based ORS)

Heterogeneity: Chi^2 = 12.15, df = 15 (P = 0.67); I^2 = 0.0%

Favours polymer-based ORS  Favours glucose-based ORS

(Continued...)

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Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review)

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| Subtotal (95% CI) | 24 | 24 | 1.8% | 1.00 [0.15, 6.53] |
|------------------|----|----|------|------------------|

Total events: 2 (Polymer-based ORS), 2 (Glucose-based ORS)
Heterogeneity: not applicable
Test for overall effect: Z = 2.14 (P = 0.033)

| Subtotal (95% CI) | 78 | 80 | 7.9% | 0.79 [0.31, 2.02] |
|------------------|----|----|------|------------------|

Total events: 7 (Polymer-based ORS), 9 (Glucose-based ORS)
Heterogeneity: Chi² = 1.44, df = 1 (P = 0.23); I² = 31%
Test for overall effect: Z = 0.50 (P = 0.62)

Total (95% CI) 1087 1081 100.0% 0.76 [0.59, 0.97]
Total events: 85 (Polymer-based ORS), 110 (Glucose-based ORS)
Heterogeneity: Chi² = 13.61, df = 18 (P = 0.75); I² = 0.0%
Test for overall effect: Z = 2.16 (P = 0.031)

---

0.001 0.01 0.1 1 10 100 1000
Favours polymer-based ORS  Favours glucose-based ORS
### Analysis 3.1. Comparison of Effects of age and pathogen: rice-based ORS vs glucose-based ORS, Outcome 1

Total stool output during the first 24 hours, by age group.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea

Comparison: 3 Effects of age and pathogen: rice-based ORS vs glucose-based ORS

Outcome: 1 Total stool output during the first 24 hours, by age group

| Study or subgroup | Rice-based ORS | Glucose-based ORS | Mean Difference | Mean Difference |
|-------------------|----------------|-------------------|----------------|----------------|
|                   | N   | Mean(SD) | N   | Mean(SD) | IV,Random,95% CI | IV,Random,95% CI |
| 1 Paediatric      |     |          |     |          |                |                |
| Alam 1987, rice   | 24  | 130 (6.12) | 24  | 290 (12.2) | -160.00 [-165.46, -154.54] |                |
| Dutta 1988        | 72  | 91.2 (8.85) | 33  | 103.2 (9.6) | -12.00 [-15.86, -8.14] |                |
| El-Mougi 1988     | 30  | 163.2 (21.8) | 30  | 245 (25.3) | -81.80 [-93.75, -69.85] |                |
| Islam 1994        | 27  | 101 (60.5) | 25  | 137.1 (14.6) | -36.10 [-59.63, -12.57] |                |
| Mohan 1988        | 23  | 88.56 (11.52) | 23  | 110.16 (14.4) | -21.60 [-29.14, -14.06] |                |
| Molla 1985, children | 84 | 155 (13) | 101 | 204 (13.9) | -49.00 [-52.88, -45.12] |                |
| Molla 1989a, rice  | 37  | 162 (56) | 42  | 343 (151) | -181.00 [-230.10, -131.90] |                |
| Nanulescu 1999    | 48  | 77.4 (47) | 51  | 102 (33) | -24.60 [-40.69, -8.51] |                |
| Patra 1982        | 24  | 97 (3.28) | 24  | 166 (4.69) | -69.00 [-71.29, -66.71] |                |
| Razafindraroko 1993 | 68  | 91 (6) | 56  | 81 (5) | 10.00 [8.06, 11.94] |                |
| Zaman 2001        | 85  | 195 (1.58) | 82  | 227.3 (1.99) | -32.30 [-32.85, -31.75] |                |
| 2 Adults          |     |          |     |          |                |                |
| Alam 1992         | 47  | 223 (128) | 42  | 366 (174) | -143.00 [-207.10, -78.90] |                |
| Molla 1985, adults | 85  | 115 (10) | 72  | 158.7 (12.8) | -43.70 [-47.34, -40.06] |                |
### Analysis 3.2. Comparison of age and pathogen: rice-based ORS vs glucose-based ORS, Outcome 2

**Duration of diarrhoea, by age group.**

**Review:** Polymer-based oral rehydration solution for treating acute watery diarrhoea

**Comparison:** 3 Effects of age and pathogen: rice-based ORS vs glucose-based ORS

**Outcome:** 2 Duration of diarrhoea, by age group

| Study or subgroup | Rice-based ORS | Glucose-based ORS | Mean Difference | Weight | Mean Difference |
|------------------|---------------|------------------|----------------|--------|----------------|
|                  | N  | Mean(SD)      | N  | Mean(SD)      | IV, Random, 95% CI | IV, Random, 95% CI |
| Alam 1987, rice  | 24 | 78 (1.43)     | 24 | 90 (1.78)     | 7.5 % -12.00 [-12.91, -11.09] |
| Dutta 1988       | 35 | 81.5 (6.3)    | 33 | 79.2 (6.4)    | 7.3 % 2.30 [0.72, 5.32] |
| Dutta 1998, children | 10 | 30.6 (4.21)   | 10 | 35.95 (7.37)  | 6.8 % -5.30 [-10.56, -0.04] |
| Dutta 2000       | 19 | 29.34 (4.83)  | 19 | 33.9 (3.77)   | 7.3 % -4.56 [-7.32, -1.80] |
| El-Mougi 1988    | 30 | 28.4 (5.2)    | 30 | 34.3 (2.3)    | 7.4 % -5.90 [-7.93, -3.87] |
| Guinaldes 1995b  | 24 | 72 (10)       | 24 | 77 (12)       | 6.6 % -5.00 [-11.25, 1.25] |
| Nanulescu 1999  | 48 | 51 (24)       | 51 | 54 (40)       | 4.7 % -3.00 [-15.91, 9.91] |
| Patra 1982       | 24 | 30 (0.82)     | 24 | 43 (0.92)     | 7.5 % -7.50 [-13.49, -12.51] |
| Razafindrakoto 1993 | 68 | 68 (4)      | 56 | 89 (6)       | 7.4 % -21.00 [-22.84, -19.16] |
| Sharma 1998     | 25 | 33.9 (8.03)   | 25 | 38.8 (8.03)   | 7.0 % -4.90 [-9.35, -0.45] |
| Zaman 2001      | 82 | 35.3 (0.22)   | 82 | 35.8 (0.23)   | 7.5 % -0.50 [-0.57, -0.43] |
| **Subtotal (95% CI)** | 392 | 378 | 76.9 % -6.81 [-12.10, -1.52] |

Heterogeneity: Tau² = 74.94; Chi² = 3510.56, df = 10 (P<0.00001); I² =100%

Test for overall effect: Z = 2.52 (P = 0.012)

- **2 Adults**
  - Alam 1992 | 47 | 81.1 (23.8) | 42 | 85.2 (19.9) | 5.8 % -4.10 [-13.18, 4.98] |
  - Bhattacharya 1998 | 27 | 36.5 (12.8) | 30 | 46.9 (11.9) | 6.5 % -10.40 [-16.84, -3.96] |
  - Dutta 1998, adults | 25 | 41.32 (6.08) | 25 | 45.68 (6.91) | 7.2 % -4.36 [-7.97, -0.75] |
  - Ramakrishna 2000 | 16 | 70.8 (20.2) | 16 | 90.9 (29.5) | 3.6 % -20.10 [-37.62, -2.58] |
| **Subtotal (95% CI)** | 115 | 113 | 23.1 % -7.11 [-11.91, -2.32] |

Heterogeneity: Tau² = 9.86; Chi² = 5.24, df = 3 (P = 0.15); I² =43%

Test for overall effect: Z = 2.91 (P = 0.0037)

- **Total (95% CI)** | 507 | 507 | 100.0 % -7.19 [-11.80, -2.58] |

Heterogeneity: Tau² = 73.85; Chi² = 3527.85, df = 14 (P<0.00001); I² =100%

Test for overall effect: Z = 3.06 (P = 0.0022)
Analysis 3.3. Comparison of Effects of age and pathogen: rice-based ORS vs glucose-based ORS, Outcome 3
Total stool output during the first 24 hours, by pathogen.

Review: Polymer-based oral rehydration solution for treating acute watery diarrhoea
Comparison: 3 Effects of age and pathogen: rice-based ORS vs glucose-based ORS
Outcome: 3 Total stool output during the first 24 hours, by pathogen

| Study or subgroup | Rice-based ORS | Glucose-based ORS | Mean Difference | 95% CI | IV, Random |
|------------------|----------------|-------------------|----------------|--------|------------|
| Alam 1987, rice  | 24 130 (6.12)  | 24 290 (12.2)     | -160.00        | -165.46, -154.54 |
| Alam 1992        | 47 223 (128)   | 42 366 (174)      | -143.00        | -207.10, -78.90  |
| Zaman 2001       | 85 195 (1.58)  | 82 227.3 (1.99)   | -32.30         | -32.85, -31.75  |
| Alam 1987, rice  | 24 140 (2.04)  | 24 100 (5.1)      | 40.00          | 37.80, 42.20   |
| Mohan 1988       | 23 88.56 (11.52)| 23 110.16 (14.4)| -21.60         | -29.14, -14.06 |
| Nanulescu 1999  | 48 77.4 (47)   | 51 102 (33)       | -24.60         | -40.69, -8.51  |
| Razafindrakoto 1993 | 68 91 (6)     | 56 81 (5)         | 10.00          | 8.06, 11.94    |
| Dutta 1988       | 35 96.6 (6.9)  | 33 103.2 (9.6)    | -6.60          | -10.59, -2.61  |
| Islam 1994       | 27 101 (60.5)  | 25 137.1 (14.6)   | -36.10         | -59.63, -12.57 |
| Molla 1985, adults | 85 115 (10)   | 72 158.7 (12.8)   | -43.70         | -47.34, -40.06 |
| Molla 1985, children | 84 155 (13)  | 101 204 (13.9)    | -49.00         | -52.88, -45.12 |
| Patra 1982       | 24 97 (3.28)   | 24 166 (4.69)     | -69.00         | -71.29, -66.71 |

Favours rice-based ORS   Favours glucose-based ORS
### Analysis 3.4. Comparison 3 Effects of age and pathogen: Rice-based ORS vs Glucose-based ORS, Outcome 4 Duration of diarrhoea, by type of pathogen

**Review:** Polymer-based oral rehydration solution for treating acute watery diarrhoea

**Comparison:** 3 Effects of age and pathogen: Rice-based ORS vs glucose-based ORS

**Outcome:** 4 Duration of diarrhoea, by type of pathogen

| Study or subgroup | Rice-based ORS | Glucose-based ORS | Mean Difference | Mean Difference |
|-------------------|----------------|-------------------|----------------|----------------|
|                   | N   | Mean (SD) | N   | Mean (SD) | IV, Random, 95% CI | IV, Random, 95% CI |
| 1 Cholera         |     |           |     |           |                      |                      |
| Alam 1992         | 47  | 81.1 (23.8)| 42  | 85.2 (19.9)| -4.10 [-13.18, 4.98] |                      |
| Bhattacharya 1998 | 27  | 36.5 (12.8)| 30  | 46.9 (11.9)| -10.40 [-16.84, -3.96] |                      |
| Dutta 1998, adults| 25  | 41.32 (6.08)| 25  | 45.68 (6.91)| -4.36 [-7.97, -0.75] |                      |
| Dutta 1998, children | 10 | 30.65 (4.21)| 10  | 35.95 (7.37)| -5.30 [-10.56, -0.04] |                      |
| Dutta 2000        | 19  | 29.34 (4.83)| 19  | 33.9 (3.77)| -4.56 [-7.32, -1.80] |                      |
| Ramakrishna 2000  | 16  | 70.8 (20.2)| 16  | 90.9 (29.5)| -20.10 [-37.62, -2.58] |                      |
| Zaman 2001        | 85  | 35.3 (0.22)| 82  | 35.8 (0.23)| -0.50 [-0.57, -0.43] |                      |
| 2 Non-cholera     |     |           |     |           |                      |                      |
| Guiraldes 1995b   | 24  | 72 (10)   | 24  | 77 (12)   | -5.00 [-11.25, 1.25] |                      |
| Nanulescu 1999    | 48  | 51 (24)   | 51  | 54 (40)   | -3.00 [-15.91, 9.91] |                      |
| Razafindrakoto 1993 | 68 | 68 (4)    | 56  | 89 (6)    | -21.00 [-22.84, -19.16] |                      |
| 3 Mixed pathogens |     |           |     |           |                      |                      |
| Dutta 1988        | 35  | 81.5 (6.3)| 33  | 79.2 (6.4)| 2.30 [0.72, 5.32] |                      |
| Patra 1982        | 24  | 30 (0.82)| 24  | 43 (0.92)| -13.00 [-13.49, -12.51] |                      |

-100 -50 0 50 100
Favours rice-based ORS Favours glucose-based ORS

Polymer-based oral rehydration solution for treating acute watery diarrhoea (Review)

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### Appendix 1. Search methods: detailed search strategies

| Search set | MEDLINE<sup>b</sup> | EMBASE<sup>b</sup> | OTHER<sup>b</sup> |
|------------|-----------------------|---------------------|------------------|
| 1          | REHYDRATION SOLUTIONS | FLUID THERAPY       | oral rehydration |
| 2          | FLUID THERAPY          | ORAL REHYDRATION THERAPY | fluid therapy    |
| 3          | oral rehydration solution | oral rehydration solution | ORS             |
| 4          | ORS                   | ORS                 | 1 or 2 or 3      |
| 5          | 1 or 2 or 3 or 4      | 1 or 2 or 3 or 4    | glucose          |
| 6          | STARCH                | GLUCOSE-POLYMER     | rice             |
| 7          | glucose               | STARCH              | amylase          |
| 8          | rice                  | glucose             | amylopectin      |
| 9          | amylase               | rice                | corn             |
| 10         | amylopectins          | amylase             | sorghum          |
| 11         | corn                  | amylopectins        | maize            |
| 12         | sorghum               | corn                | 6-11/or          |
| 13         | maize                 | sorghum             | 4 and 12         |
| 14         | 6-13/or               | maize               | -                |
| 15         | 5 and 14              | 6-14                | -                |
| 16         | Limit 15 to human     | 5 and 15            | -                |
| 17         | -                     | Limit 16 to human   | -                |

<sup>a</sup>Search terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Lefebvre 2008); upper case: MeSH or EMTREE heading; lower case: free text term.

<sup>b</sup>Used for Cochrane Infectious Diseases Group Specialized Register, CENTRAL, and LILACS.
### Appendix 2. Risk of bias assessment

| Trial             | Allocation sequence | Allocation concealment | Blinding                          | Inclusion of randomized participants in analysis |
|-------------------|---------------------|------------------------|-----------------------------------|--------------------------------------------------|
| Akbar 1991        | Adequate            | Adequate               | Participants, providers, outcome assessors | Inadequate                                      |
| Alam 1987         | Adequate            | Unclear                | None                              | Adequate                                         |
| Alam 1992         | Adequate            | Unclear                | None                              | Adequate                                         |
| Bernal 2005       | Adequate            | Adequate               | Unclear                           | Adequate                                         |
| Bhan 1987         | Unclear             | Unclear                | None                              | Adequate                                         |
| Bhattacharya 1998 | Adequate            | Unclear                | None                              | Adequate                                         |
| Dutta 1988        | Adequate            | Unclear                | Unclear                           | Adequate                                         |
| Dutta 1998        | Adequate            | Unclear                | None                              | Adequate                                         |
| Dutta 2000        | Adequate            | Unclear                | None                              | Adequate                                         |
| El-Mougi 1988     | Adequate            | Unclear                | None                              | Adequate                                         |
| El-Mougi 1996     | Adequate            | Adequate               | Participants, providers, outcome assessors | Adequate                                         |
| Faruque 1997      | Unclear             | Unclear                | None                              | Adequate                                         |
| Fayad 1993        | Adequate            | Adequate               | Unclear                           | Adequate                                         |
| Guiraldes 1995a   | Adequate            | Adequate               | None                              | Adequate                                         |
| Guiraldes 1995b   | Adequate            | Adequate               | None                              | Adequate                                         |
| Hossain 2003      | Adequate            | Adequate               | None                              | Adequate                                         |
| Islam 1994        | Adequate            | Unclear                | None                              | Adequate                                         |
| Iyngkaran 1998    | Unclear             | Unclear                | None                              | Adequate                                         |
| Maulen-Radovan 1994 | Adequate             | Adequate               | None                              | Adequate                                         |
| Maulen-Radovan 2004 | Adequate             | Adequate               | None                              | Adequate                                         |
| Authors          | Allocation | Blinding | Outcome Assessment | Overall Quality |
|------------------|------------|----------|--------------------|-----------------|
| Mohan 1988       | Unclear    | Unclear  | None               | Adequate        |
| Molla 1985       | Adequate   | Unclear  | None               | Adequate        |
| Molla 1989a      | Unclear    | Unclear  | Unclear            | Adequate        |
| Molla 1989b      | Adequate   | Unclear  | Participants and providers not blinded; outcome assessors unclear | Adequate |
| Mustafa 1995     | Unclear    | Unclear  | Unclear            | Adequate        |
| Nanulescu 1999   | Unclear    | Unclear  | None               | Inadequate      |
| Patra 1982       | Unclear    | Adequate | None               | Adequate        |
| Ramakrishna 2000 | Adequate   | Unclear  | Participants and providers partially blinded; outcome assessors unclear | Adequate |
| Ramakrishna 2008 | Adequate   | Adequate | Assessors but not the participants or providers were blinded because of the nature of the study | Adequate |
| Razafindrakoto 1993 | Unclear    | Unclear  | None               | Adequate        |
| Santos Ocampo 1993 | Adequate   | Adequate | Participants, providers, outcome assessors | Adequate |
| Sharma 1998      | Unclear    | Unclear  | None               | Adequate        |
| Wall 1997        | Adequate   | Unclear  | Participants and providers not blinded; outcome assessors unclear | Adequate |
| Zaman 2001       | Adequate   | Unclear  | None               | Adequate        |
CONTRIBUTIONS OF AUTHORS

GV Gregorio was the principal investigator, wrote the protocol, carried out the risk of bias (methodological quality) assessment, data extraction and analysis, and wrote the final manuscript.

MLM Gonzales helped in writing the protocol, carried out the risk of bias (methodological quality) assessment and data extraction, and commented on the final manuscript.

LF Dans carried out the risk of bias (methodological quality) assessment.

EG Martinez carried out the data extraction and commented on the final manuscript.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources
- Effective Health Care Research Programme Consortium, UK.

External sources
- Department for International Development (DFID), UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- Change in title: The title was changed to highlight the fact that this is a review of polymer-based ORS (not glucose-based ORS).
- New author: EG Martinez joined the author team after the protocol was published.
- Data extraction: We originally planned to extract count data by determining the total number of episodes in each group (if the episode is rare) or the number of person years in each group for each treatment arm (if the episode is common). However, during the assessment of the trials, the trials reported the number of participants with unscheduled use of intravenous fluid, and thus it was considered to be a dichotomous rather than a count outcome. Similarly, in the data extraction for number of episodes of vomiting, there were only four trials that reported this outcome, while nine clinical trials reported the number of participants with vomiting. It was decided that the latter would be reported. Other adverse effects that were reported in the trials, including number of participants with hypokalaemia (low potassium levels) and those with development of persistent diarrhoea (diarrhoea of more than 10 days’ duration from onset), were also included in the review.
- Data analysis: In multiple treatment arms with two or more polymer-based ORS as treatment groups, the outcomes were combined as appropriate and compared collectively with the control group. Most of the trials included both cholera and non-cholera cases, and this group was collectively termed as having mixed pathogens rather than non-cholera related diarrhoea.
- Subgroup analyses: These were limited to the osmolarity of the glucose ORS, the type of polymer, and the effects of participant’s age and pathogen. The source of the polymer and the effect of feeding were no longer evaluated as most of the polymers were locally prepared and all but two trials withheld feeding after hydration.
- Publication bias: The presence of publication bias was confirmed with StatsDirect, a statistical software program.
INDEX TERMS

Medical Subject Headings (MeSH)
Acute Disease; Cholera [complications]; Dehydration [etiology; *therapy]; Diarrhea [complications; *therapy]; Fluid Therapy [*methods]; Polymers [therapeutic use]; Randomized Controlled Trials as Topic; Rehydration Solutions [chemistry; *therapeutic use]

MeSH check words
Adult; Child; Humans; Infant