

Office of Evidence Based Practice (EBP) – Critically Appraised Topic: Choice of Oral Rehydration Solution (ORS) of Patients with Acute Gastroenteritis

Specific Care Question

For the usually healthy patient greater than two months of age with acute gastroenteritis (AGE), what is the best fluid for oral rehydration therapy (ORT)?

Question Originator

Acute Gastroenteritis in the Emergency Department (ED) and Urgent Care Center (UCC) Clinical Practice Guideline (CPG) Team

Literature Summary

Background. AGE is a common illness among infants and children. Over 10,000 patients may be seen per year in the EDs and UCCs of Children’s Mercy (Children’s Mercy data, May 22, 2018). Oral rehydration is the primary intervention for the medical management of patients who present to the ED/UCC with AGE (King et al., 2003). Problems persist with administration of the ORS due to vomiting, and taste of the ORS.

In developing countries where moderate and severe diarrhea from diseases like cholera is prevalent, the formula for ORS recommended by World Health Organization (WHO) and United Nations Children’s Fund (UNICEF) in treating moderate to severe dehydration is a low carbohydrate, high electrolyte solution, see Table 1 (King et al. 2003). The concentration of electrolytes, both sodium and potassium, along with a low concentration of glucose is necessary for optimal ORT because the coupled transport of sodium and glucose across the intestinal epithelial cell wall is the mechanism for efficient absorption of salt and water. (Granado-Villar, Cunill-De Sautu, & Granados, 2012). In the US, The American Academy of Pediatrics (AAP) endorses the WHO guidelines for mild and moderate diarrhea, specifically commercial rehydration products are recommended (Granado-Villar et al., 2012). However, the taste of the ORS is a barrier to successful administration. The flavor of ORS, such as Enfalyte® or Pedialyte® is perceived as unpleasant due to the high electrolyte concentration of the products (King et al., 2003). Fluid choices such as juice or soda pop are not recommended. They taste better but have higher osmolarity and electrolyte concentrations that do not support the coupled transport of sodium and glucose at the intestinal brush border (King et al., 2003). Even though ORS is the best fluid, the problems with vomiting and solution taste permit the question should other fluids can be used for ORS therapy?

Study characteristics. The search for suitable studies was completed on April 11, 2018. Jeff Michael, DO reviewed the 68 titles and abstracts found in the search and identified nine articles believed to answer the question. An ancestry search of included articles yielded an additional article. After an in-depth review, one article asked the question.

Key results. Based on low quality evidence, in children with mild dehydration, fluids other than commercial ORS such as dilute apple juice or preferred fluids may be used if commercial ORS is not tolerated (Freedman et al. (2016). When half-strength apple juice was compared to ORS in patients with mild dehydration there was no difference in unscheduled healthcare visits after the initial ED visit.

Summary by Outcome

Outcome 1. Hospitalization.

Freedman et al. (2016) is a randomized control trial, was performed in a single center, and was a non-blinded, non-inferiority study. It included 647 subjects that were mild dehydration, with Clinical Dehydration Scale (CDS) scores ≤ 5 and capillary refill time of < 2 seconds. The group treated with half- strength apple juice was compared to those treated with commercially available ORS. Both groups were discharged with the 2 liters of the fluid assigned at randomization. If more fluid was required, those in the half strength



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apple juice group were allowed to drink a preferred beverage, while those in the ORS group were to purchase and have the subject drink the ORS. There was no difference for the unscheduled health care visit outcome unscheduled health care visit, *OR* = 0.76, 95% CI [0.49, 1.18] (see Figure 3). Thereby showing half-strength apple juice followed by preferred beverage was not inferior to ORS in children with mild dehydration. Although risk of bias was low across all bias domains, it is the only study identified, and only included subjects with mild dehydration.

Search Strategy and Results ([see PRISMA diagram](#))

("gastroenteritis"[tw] OR "diarrhea"[tw] OR "diarrhoea"[tw]) AND (((("Rehydration Solutions"[Mesh] OR "Electrolytes/therapeutic use"[Mesh] OR "Fluid Therapy"[tw] OR rehydration[tw]) AND ("Administration, Oral"[MeSH] OR "Oral therapy"[tw])) OR "Fruit and Vegetable Juices"[Mesh] OR "oral solutions"[tw] OR "oral solution"[tw] OR "oral rehydration"[tw] OR "oral therapy"[tw]) AND (pediatr* OR child OR children OR childhood OR paediatr*)) AND (("2013/01/01"[PDat] : "2018/12/31"[PDat])) AND ((Meta-Analysis[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb])). 68 articles were sent to Jeff Michael, DO.

Studies Included in this Review (in Alphabetical Order)

Freedman et al., (2016)

Studies Not Included in this Review with Exclusion Rationale (in Alphabetical Order)

Authors	Reason for exclusion
Freedman et al. (2015)	Does not answer the question; compared intravenous vs. oral rehydration
Freedman, Ali, Oleszczuk, Gouin, & Hartling (2013)	Does not answer the question; compared intravenous vs. oral rehydration
Geurts, de Vos-Kerkhof, et al. (2017)	Does not answer the question; reports on the use of a clinical decision tool
Geurts, Streyerberg, et al. (2017)	Does not answer the question: reports on prognostic factors or ORS failure
Grisaru, Xie, Samuel, & Freedman (2017)	Compares rates of intravenous rehydration solutions
Jabbour et al. (2013)	Reported protocol only
Kumar, Kumar, Aneja, Kumar, & Rehan (2015)	Population is children with severe acute malnutrition, WHO definition, weight for length z score < -3
Passariello et al. (2015)	Does not answer the question; compares ORS with gel replacement with zinc

Method Used for Appraisal and Synthesis

The Cochrane Collaborative computer program, Review Manager (Higgins & Green, 2011)^a was used to synthesize the included study. [GRADEpro GDT \(Guideline Development Tool\)](#) is the tool used to create the Summary of Findings Tables for this analysis.

^aHiggins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cochrane Collaboration, 2011.



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Acronyms Used in this Document

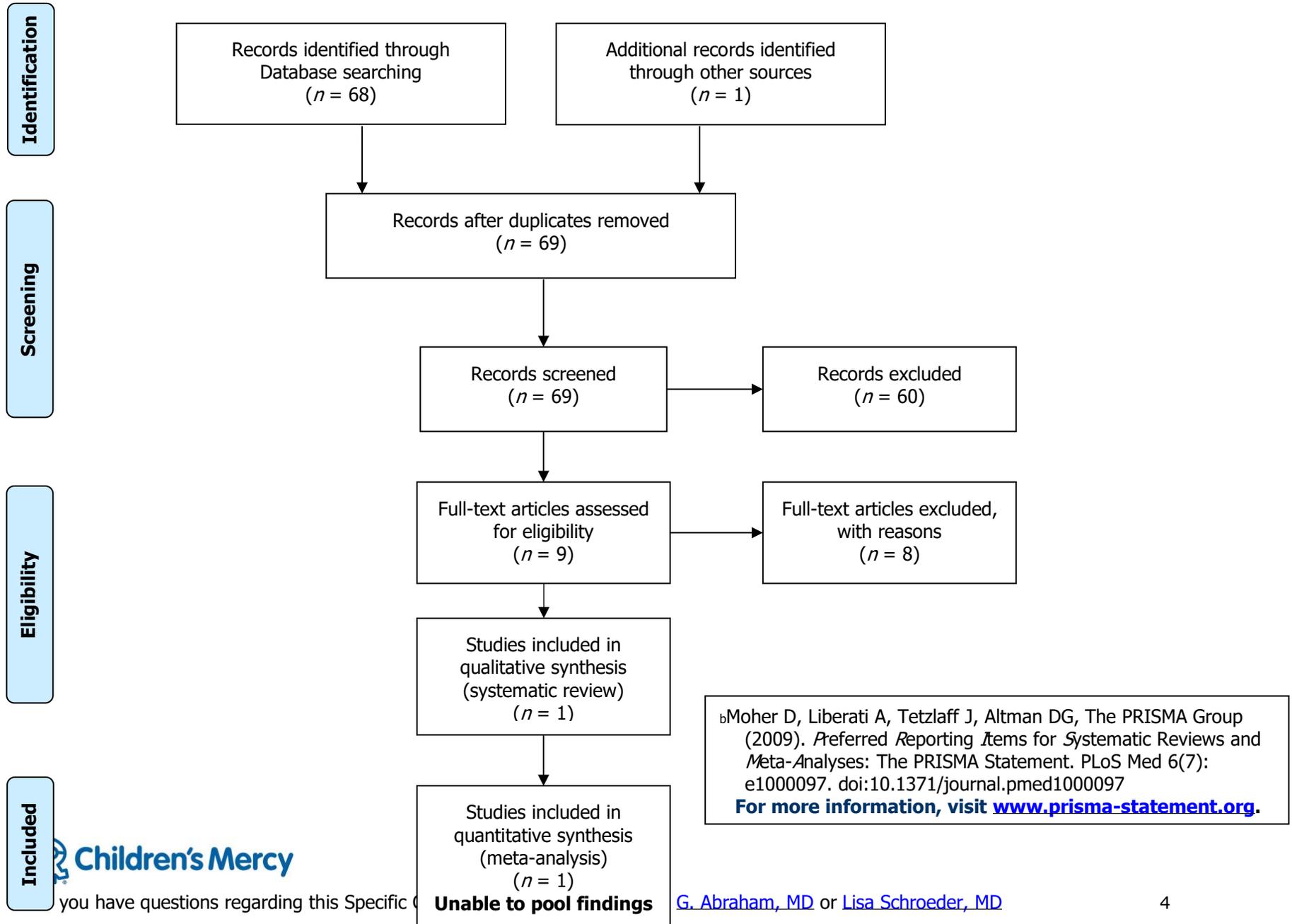
Acronym	Explanation
AGE	Acute Gastroenteritis
CDS	Clinical Decision Support
CPG	Clinical Practice Guideline
ED	Emergency Department
EMS	Electrolyte Maintenance Solution
OR	Odds Ratio
ORS	Oral Rehydration Solution
UCC	Urgent Care Center

Date Developed September 4, 2018, September 18 2018



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Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)^b



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Figure 2
Risk of Bias Summary

	Random sequence generation (selection bias)						
	Allocation concealment (selection bias)						
	Blinding of participants and personnel (performance bias)						
	Blinding of outcome assessment (detection bias)						
	Incomplete outcome data (attrition bias)						
	Selective reporting (reporting bias)						
	Other bias						
Freedman_2016							

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Table 1
Composition of Oral Rehydration Solutions and Commonly Used Rehydration Beverages

Solution	Carbohydrate (g/L)	Sodium (mMol/L)	Potassium (mMol/L)	Chloride (mMol/L)	Base ^a (mMol/L)	Osmolarity mOsm/L
ORS						
World Health Organization (2002)	13.5	75	20	65	30	245
Enfalyte ^b	30	50	25	45	34	160
Pedialyte Classic	25	45	20	35	30	250
Commonly used beverages						
Apple juice ^d	117	2.6	44	45	N/A	730
Coca-cola ^d	108	1.6	N/A	N/A	13.4	650

Note. Adapted from (King et al., 2003). ^a Actual or potential bicarbonate (e.g. lactate, citrate, or acetate) ^b Mead-Johnson Laboratories, ^c Ross Laboratories, ^d USDA Branded Food Products Database

Table 2
Characteristics of Studies

Freedman 2016

Methods	RCT, a single center, single-blind non-inferiority trial
Participants	<p>Setting: tertiary care pediatric ED in Toronto, Ontario, Canada, between October and April of each calendar year 2010 to 2015</p> <p>Randomized into study: <i>N</i> = 647</p> <ul style="list-style-type: none"> • Group 1: Fluid as Tolerated (FAT), <i>n</i> = 323 • Group 2: Electrolyte Maintenance solution therapy (EMS), <i>n</i> = 324 <p>Completed study:</p> <ul style="list-style-type: none"> • Group 1: <i>n</i> = 322 • Group 2: <i>n</i> = 322 <p>Gender, males: number (%)</p> <ul style="list-style-type: none"> • Group 1: 173 (53.6%) • Group 2: 158 (48.8%) <p>Age (mean, SD), months</p> <ul style="list-style-type: none"> • Group 1: 28.0 (15.4) • Group 2: 29.0 (16.5) <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • Age 6 to 60 months • 3 or more episodes of vomiting or diarrhea in the preceding 24 hours • < 96 hours of symptoms



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	<ul style="list-style-type: none"> • Weight of 8 kg or higher • Minimal dehydration (minimal dehydration was defined as obtaining a score of ≤ 5 using the validated Clinical Dehydration Scale and cap refill <2 seconds) • Ontario resident <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • History of <ul style="list-style-type: none"> ○ Chronic gastrointestinal disease (such as inflammatory bowel disease, celiac disease) ○ Other diseases (such as diabetes mellitus, inborn errors of metabolism) that complicated the clinical picture • Prematurity with corrected postnatal age < 30 weeks • Bilious vomiting • Hematemesis • Hematochezia • Clinical concern for acute abdomen • Had a need for immediate IV rehydration <p>Power analysis: To achieve 80% power to reject the null hypothesis that apple juice/preferred fluid is inferior to electrolyte maintenance solution, 624 subjects were necessary.</p>
<p align="center">Interventions</p>	<p>Both groups:</p> <ul style="list-style-type: none"> • Patients who vomited received oral ondansetron (dose not disclosed) • If patient failed ORT, physician could continue ORT with same or crossover drink or switch to IV hydration • Amount of ORT fluid administered: 5ml every 2-5 minutes, PO <ul style="list-style-type: none"> ○ 10mL/kg replacement for each watery stool and 2mL/kg replacement for each episode of emesis until resolution of symptoms • Caregivers were contacted daily by a research nurse <ul style="list-style-type: none"> ○ RN was blinded to treatment assignment until study participant had been symptom free for 24 hours. ○ Protocol had seven criteria for RN to recommend an ED return visit • Caregivers were provided a diary to record FU visits and vomiting and diarrhea frequency. These were returned at final in-person visit or by mail. <p>Group 1: Fluid As Tolerated (FAT)</p> <ul style="list-style-type: none"> • 2 L of half strength apple juice were provided to the family for ED use and at home • If > 2 L were needed, parents were encouraged to administer any fluid as tolerated • If the patient did not tolerate the apple juice solution, children were permitted to consume beverages with high content sugars or sports beverages <p>Group 2: Electrolyte Maintenance Solution (EMS)</p> <ul style="list-style-type: none"> • 2 L of apple-flavored, sucralose-sweetened Pediatric Electrolyte (Pharmascience), an electrolyte maintenance solution



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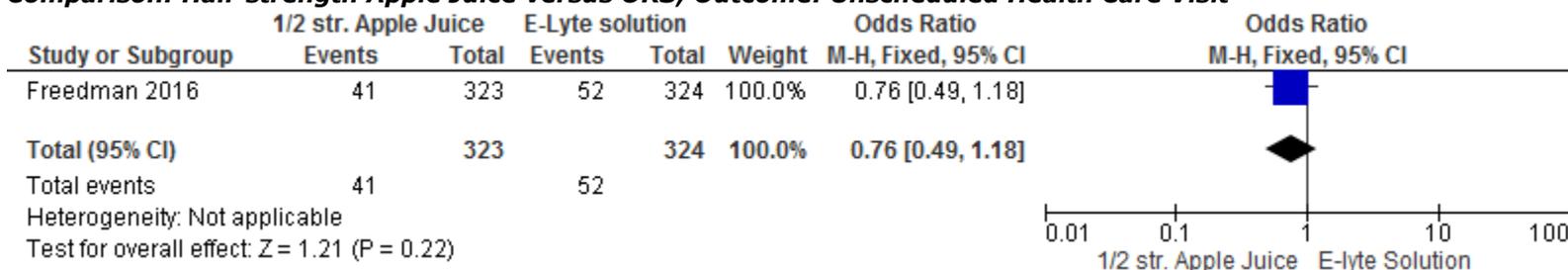
	<ul style="list-style-type: none"> • The solution tinted to match color of Group 1. • If > 2 L were needed, parents were encouraged to purchase Pediatric Electrolyte Solution®
Outcomes	<p>Primary Outcome:</p> <ul style="list-style-type: none"> • Treatment failure defined as any of the following occurring within seven days of enrollment: • Hospitalization • Unscheduled physician encounter in an office, urgent care or ED setting for the same episode of vomiting / diarrhea (episode was terminated when the patient was symptom free for 24 hours) • Protracted symptoms (such as \geq three episodes of vomiting or diarrhea within a 24-hour period occurring > 7 days after encounter) • Physician request to administer a solution representing treatment allocation crossover at the initial visit • 3% or greater weight loss or a Clinical Dehydration Scale score of 5 or higher at in-person follow-up <p>Secondary a priori outcomes:</p> <ul style="list-style-type: none"> • IV rehydration at initial ED visit • IV rehydration during follow-up within 7d of initial visit • Hospitalization at initial visit • Hospitalization at follow-up within 7d of initial visit • Frequency of diarrhea and vomiting • Percentage weight change at the 72- to 84-hour assessment
Notes	If the null hypothesis was rejected, the conclusion would be apple juice followed by preferred fluids was not inferior and could be considered a therapeutic option.

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Risk of bias table

Bias	Scholars' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Computer generated in blocks of 8
Allocation concealment (selection bias)	Low risk	The study team was unaware of block sizes. Identical, opaque, sealed envelopes were consecutively numbered on outside and stored in locked cabinet.
Blinding of participants and personnel (performance bias)	Low risk	The research support pharmacy staff was not responsible for patient selection. Drinks were mixed as color-matched, refrigerated study solutions in identical bottles. At time of discharge from ED, the caregiver will be given an "Unblinding" envelope that states what liquids their child should receive once they run out of the 2 L of study supplied liquid.
Blinding of outcome assessment (detection bias)	Low risk	The research nurses responsible for data collection did not participate in the preparation of randomization envelopes. The caregivers were asked not to disclose in the follow-up phone calls which solution the patient was given.
Incomplete outcome data (attrition bias)	Low risk	Used intention to treat analysis
Selective reporting (reporting bias)	Low risk	All outcome data reported; ITT analysis occurred
Other bias	Unclear risk	

Figure 3
Comparison: Half-strength Apple Juice versus ORS, Outcome: Unscheduled Health Care Visit



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