Appendix C – evidence tables

Diagnosis

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Khuffash FA;Sethi SK;Shaltout AA; 1988{37994}	Study Type: Cross-sectional Evidence level: 3	595 children. 5 children with Aeromonas hydrophilia were excluded from the comparison because of the small number.	Children aged from under 1 year to 12 years presence of gastroenteritis hospitalised	Intervention: Clinical features of gastroenteritis Duration of gastroenteritis by aetiological agent Comparison: Comparisons of duration of diarrhoea are made between children with gastroenteritis due to different aetiological agents	Follow-up period: Clinical progress during hospitalisation and after discharge was recorded Outcome Measures: Duration of diarrhoea Frequency of clinical characteristics by aetiological pathogen	Mean Duration Rotavirus - 4.8 days Salmonellae 12.3 days E. Coli 6.8 days Campylobacter 7.4 days Shigellae 7.9 days Rotavirus & Salmonella 12.9 days Rotavirus & others 7.4 days No pathogen 5.6 days Overall mean 7.4 days Mortality 0.7% (all from salmonella group)	Gastroenteritis due to rotavirus follows a benign course both in the developing and developed world Althought the overall number of participants is large, some of the groups have small numbers of children. Because of the higher incidence of bacterial pathogens, the cases seem to have longer durations.
Deivanayagam N;Mala N;Ashok TP;Ratnam SR;Sankaranarayanan VS; 1993{41223}	Study Type: Case-control Evidence level: 2+	170 cases 340 controls 2 controls for each case, matched for age.	all participants were 1 - 23 months, admitted to the Institute of Child Health Madras for diarrhoea. CASES children with diarrhoea persisting more than 14 days at admission CONTROLS children with acute diarrhoea who had recovered within 7 days	Intervention: Risk factors for persistent diarrhoea are being investigated. They include: mother' literacy father's literacy diarrhoea within the past 3 months pre-admission feeding pattern container used for feeding method of cleaning the bottle nature of stool frequency of stool indiscriminate use of antimicrobials dehydration	Follow-up period: this is not reported Outcome Measures: Odds Ratios for mother' literacy father's literacy diarrhoea within the past 3 months pre-admission feeding pattern container used for feeding method of cleaning the bottle nature of stool frequency of stool indiscriminate use of antimicrobials dehydration persistence of	Mother's literacy OR 1.3; 95% CI 0.8 - 1.9; p value= 0.28 Mother's literacy excluding invasive diarrhoea OR 0.8; 95% CI 0.5 - 1.2; p value = 0.34 Father's literacy OR - 1.0; 95% CI 0.6 - 1.6; p value = 0.91 Diarrhoea wthin the past 3 months OR - 0.5; 95% CI 0.3 - 1.0; p value = 0.04 Preadmission feeding pattern OR 1.0; 95% CI 0.7 - 1.5; p value = 0.97 Container used for feeding OR 0.9; 95% CI 0.6 - 1.5; p value	The risk factors strongly associated with persistent diarrhoea are: malnutrition stools with blood / mucus stool frequency of > 10 / day indiscriminate use of antimicrobials for acute diarrhoeas associated illnesses like septicaemia, pneumonia and UTI, persistence of dehydration > 24 hrs with appropriate fluid therapy loss of weight during hospital stay The risk factors shown to be strongly associated with persistent diarrhoea can influence the natural history of diarrhoea and should be carefully considered in

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				persistence of dehydration for >24 hrs nutritional status vitamin A deficiency associated illness weight loss during study period Comparison: Comparisons are made between cases and controls for each of the risk factors listed	dehydration for >24 hrs nutritional status vitamin A deficiency associated illness weight loss during study period	= 0.79 Method of cleaning the feeding bottle OR 0.6; 95% CI 0.1 - 2.3; p value= 0.33 Method of cleaning the feeding bottle excluding invasive diarrhoea OR 0.3; 95% CI 0.03 - 1.7; p value = 0.11 Nature of stool OR 2.4; 95% CI 1.3 - 4.3; p value = 0.003 Adjusted OR 2.4; 95% CI 1.3 - 4.3; Frequency of stool OR 1.7; 95% CI 1.1 - 2.5; p value = 0.01 Adjusted OR 1.8; 95% CI 1.2 - 2.8 Frequency of stool excluding invasive diarrhoea OR 1.6; 95% CI 1.0 - 2.4; Adjusted OR 1.9; 95% CI 1.1 - 3.0 Indiscriminate use of antimicrobials OR 2.5; 95% CI 1.6 - 3.8; p value = <0.001 Adjusted OR 2.4; 95% CI 1.6 - 3.9 Indiscriminate use of antimicrobials excluding invasive diarrhoea OR 2.6; 95% CI 1.6 - 4.2	examination and history taking.

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						Adjusted OR 2.8; 95% CI 1.7 - 4.8 CLINICAL FEATURES Dehydration OR 0.7; 95% CI 0.9 - 2.4; p value = 0.78 Dehydration excluding invasive diarrhoea OR 0.9; 95% CI 0.2 - 3.9; p value = 0.54 Persistence of dehydration > 24 hrs OR 4.2; 95% CI 2.8 - 6.5; p value = <0.001 Adjusted OR 1.4; 95% CI 1.2 - 1.7 Persistence of dehydration > 24 hrs excluding invasive diarrhoea OR 3.8; 95% CI 2.4 - 5.9; p value = <0.001 Nutritional status OR 2.7; 95% CI 1.9 - 4.1; p value = <0.001 Adjusted OR 2.9; 95% CI 1.9 - 4.5 Nutritional status excluding invasive diarrhoea OR 2.9; 95% CI 1.6 - 3.9 adjusted OR 2.9; 95% CI 1.7 - 4.7 Vitamin A deficiency OR 2.3; 95% CI 1.0 - 5.2; p value = 0.06 Vitamin A deficiency excluding invasive diarrhoea	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
						OR 2.3; 95% CI 1.0 - 5.7 Associated illness OR 4.5; 95% CI 2.7 - 7.4; p value = < 0.001 Adjusted OR 2.1; 95 % CI 1.5 - 3.1; Associated illness excluding invasive diarrhoea OR 5.9; 95% CI 3.5 - 10.0; Adjusted OR 2.1; 95% CI 1.4 - 3.1 Weight loss during study period OR 15.6; 95% CI 6.5 - 39.1; p value = < 0.001 Weight loss during study period excluding invasive diarrhoea OR 11.3; 95% CI 5.3 - 24.2; p value = < 0.001 Adjusted OR 11.5; 95% CI 5.4 - 25.2	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Study Summary	Reviewer Comment
Cunliffe NA;Allan C;Lowe SJ;Sopwith W;Booth AJ;Nakagomi O;Regan M;Hart CA; 2007 Nov{40929}	Study Type: Survey Evidence Level: 3	Determination of the presence of rotavirus in stool samples by enzyme immunoassay	stool samples from an n=234 children	Children (age 1-168mths, median age 10 months) with acute gastroenteritis who had been hospitalised between January and May 2006	The presence of rotavirus	Rotavirus was detected in 17/91 cases (19%) of the healthcare - associated acute gastroenteritis and 54/152 cases (36%) of community acquired acute gastroenteritis	Rotavirus is an important cause of healthcare - associated acute gastroenteritis in a large paediatric hospital	This is survey data and thus is graded as evidence level 3. It is important to consider that this a small sample from one hospital and the data may not necessarily be extrapolated. The focus of the study was the healthcare-acquired rotavirus but this guideline is concerned with the community acquired rotavirus which was 36%
Froggatt PC;Vipond IB;Ashley CR;Lambden PR;Clarke IN;Caul EO; 2004{40923}	Study Type: Survey Evidence Level: 3	Intervention: Stool samples were tested using electron microscopy for viral pathogens Enzyme-Immuno Assay (EIA) and Polymerase Chain Reaction PCR for Norovirus EIA for rotavirus Comparison: Results of sporadic testing of stools and stools from outbreaks of gastroenteritis	n=3172 Sporadic stool samples (PHLS) from children under the age of seven with gastroenteritis n=1,360 stool samples from outbreaks of gastroenteritis	Clinical specimens (usually stool but sometimes vomit) from cases of gastroenteritis in children under the age of seven years and from sporadic outbreaks of gastroenteritis (unclear if all paediatric) All South west and South Wales region 1999-2000 winter season	Identification of causative agents focusing on norovirus	Results of sporadic cases rotavirus 21.6% norovirus 10.3% adenovirus 3.9% astrovirus 3.1% calcivirus 0.2% 62.3% were negative tests Results of the outbreaks rotavirus 3.9% norovirus 63.9% adenovirus 0.4% astrovirus 0.4% 32.6% were negative tests	Norovirus was second most common viral agent in sporadic childhood gastroenteritis indicating it has a significant role	This is a surveillance study thus is graded as evidence level 3. It must be considered that this a localised study which was conducted nearly 10 years ago. The funding of this study was not declared

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Study Summary	Reviewer Comment
Gomara MI;Simpson R;Perault AM;Redpath C;Lorgelly P;Joshi D;Mugford M;Hughes CA;Dalrymple J;Desselberger U;Gray J; 2008{40934}	Study Type: Survey Evidence Level: 3	Intervention: Stool samples were investigated for the presence of viruses by PCR for the detection of enteric adenovirus astrovirus norovirus Grp A & C rotavirus sapovirus Comparison: none	n=685 stool samples of which n=223 in a structured surveillance cohort (GP based) n=203 in a community cohort (referred to hospital from GP) n=259 in a hospital cohort (in patient)	Children under the age of 6 years with acute gastroenteritis in East Anglia UK between 2000 to 2003	presence of viral pathogens in the stool samples enteric adenovirus astrovirus norovirus Grp A & C rotavirus sapovirus	A viral agent was detected in 367/685 samples (53.6%) Rotavirus was the most common in all three groups followed by norovirus and enteric adenovirus Structured surveillance n(%) rotavirus A 106(47.5%) norovirus 31(13.9%) adenovirus 20 (9.0%) astrovirus 11(4.9%) sapovirus 2 (0.9%) rotavirus 1(0.4%) Community cohort n(%) rotavirus A 60(29.6%) norovirus 18(8.9%) adenovirus 26(12.8%) astrovirus 4(2.0%) sapovirus 8(3.9%) rotavirus 2(1.0%) Hospital cohort n(%) rotavirus A 59(22.8%) norovirus 36(13.9%) adenovirus 20 (7.7%) astrovirus 7(2.7%) sapovirus 5(1.9%) rotavirus 2(0.8%) Multiple viruses were found in 8% of cases	Rotavirus was the most common pathogen found in all three cohorts followed by norovirus and enteric adenovirus	This was a surveillance survey and was graded as evidence level 3. It should be considered that this is a localised small study although it is fairly recent data. The study was funded by the NHS executive Eastern Region, research and Development Directorate

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Study Summary	Reviewer Comment
Van DP;Giaquinto C;Maxwell M;Todd P;Van der WM;REVEAL Study Group.; 2007 May 1 {40927}	Study Type: Other Evidence Level: 3	Intervention: Identification of rotavirus by ELISA and PCR Comparison: none	n=1010 stool samples	Children under the age of 5 years with acute gastroenteritis seeking health care in UK hospitals during a 12 month period (part of multicentre pan European project)	results were presented from three setting: Hospital Emergency department Primary care setting % of samples positive for rotavirus given as observed and expected (if ELISA test was missing, same proportion of rotavirus was assumed)	No(%) of + rotavirus ELISA Hospital observed 39(60.9%) estimated 51(60.7%) Emergency department observed 22(59.5%) estimated 33(60%) Primary care setting observed 15 (31.9%) estimated 279(32%) Total estimated 363(35.9%)	Rotavirus is an important pathogen in acute gastroenteritis in children. The incidence rate of rotavirus is ~60% in secondary health care and ~30% in the primary care setting.	This is a surveillance study so is graded as evidence level 3. The focus of this multicentre pan European study was to look at rotavirus genotypes across Europe in view of vaccine development The incidence rate of rotavirus is ~60% in secondary health care and ~30% in the primary care setting. However it is important to note that the was a high proportion of estimated cases in the community data. This study was funded by Sanofi Pastuer MSD

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Study Summary	Reviewer Comment
Wheeler JG; Sethi D; Cowden JM; Wall PG; Rodriques LC; Tompkins DS; Hudson MJ; Roderick PJ 1999{40974}	Study Type: Survey Evidence Level: 3	Intervention: Incidence of infectious intestinal disease in community and reported to general practice Comparison: GP and community data is compared to the National Laboratory Surveillance data	n=459, 975 patients served by 70 general practices in England plus community surveillance of 9776 randomly selected patients	Patients (all ages) registered at a GP practice and who either attended the practice with an infectious intestinal disease or were surveyed in the community (dates unclear)	Main outcome measure: incidence of infectious intestinal disease at 70 GP practices and in the community No of cases with identified pathogen divided into bacterial, viral or protozoan	Community data : 781 cases Incidence of 19.4/100 person years GP: 8770 cases Incidence of 3.3/100 person years Types of pathogen Community One case sent to national surveillance for every: 6.2 stools send for lab investigation 1.4 laboratory identifications 23 cases in GP 136 community cases Community cases vs. national surveillance Salmonella 3.2 :1 Campylobacter 7.6 :1 Rotavirus 35 : 1 Round, structured viruses 1562 :1	Infectious intestinal disease occurs in 1 in 5 people each year of whom 1 in 6 presents to a GP Proportion of cases not reported by national surveillance is large and varies widely per organism	This study is described by the authors as a population based community cohort incidence study but is essentially survey data and is therefore graded as evidence level 3. The specific date of the data is unclear but is ~10 years old. Although incidence data is given for bacterial, viral and protozoan agents, the key result of this study is the disparity between the GP/community based incidence of infectious intestinal disease and that reported by the national laboratory surveillance. This study was funded by the Department of Health

Assessment for dehydration and shock

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Khuffash FA;Sethi SK;Shaltout AA; 1988 {37994}	Study Type: Cross-sectional Evidence level: 3	595 children. 5 children with Aeromonas hydrophilia were excluded from the comparison because of the small number.	Children aged from under 1 year to 12 years presence of gastroenteritis hospitalised	Intervention: Clinical features of gastroenteritis Duration of gastroenteritis by aetiological agent Comparison: Comparisons of duration of diarrhoea are made between children with gastroenteritis due to different aetiological agents	Follow-up period: Clinical progress during hospitalisation and after discharge was recorded Outcome Measures: Duration of diarrhoea Frequency of clinical characteristics by aetiological pathogen	Mean Duration Rotavirus - 4.8 days Salmonellae 12.3 days E. Coli 6.8 days Campylobacter 7.4 days Shigellae 7.9 days Rotavirus & Salmonella 12.9 days Rotavirus & others 7.4 days No pathogen 5.6 days Overall mean 7.4 days Mortality 0.7% (all from salmonella group)	Gastroenteritis due to rotavirus follows a benign course both in the developing and developed world Althought the overall number of participants is large, some of the groups have small numbers of children. Because of the higher incidence of bacterial pathogens, the cases seem to have longer durations.

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Bhattacharya SK;Bhattacharya MK;Manna B;Dutta D;Deb A;Dutta P;Goswami AG;Dutta A;Sarkar S;Mukhopadhaya A; 1995 Feb{39547}	Study Type: Case-control Evidence level: 2+ India	n= 243 cases n=136 controls	Infants with acute gastroenteritis (<24 hrs) with either moderate or severe dehydration (cases) or non or mild dehydration (controls) and admitted into hospital.	Univariate analysis for the following factors was carried out for both groups Aetiology Feeding practices Management of diarrhoea Hygiene practices Measles in previous 6 months Clinical features on admission Followed by multivariate analysis after controlling for confounding factors including age group gender religion nutritional status family income persons/room in family home	Univariate analysis showed presence of vibrios in stool, withdrawal of breastfeeding during diarrhoea, not giving fluids including ORS during diarrhoea , frequent purging (>8 per day) and frequent vomiting(>2 per day) and under nutrition to be associated with dehydration The following risk factors which were significantly associated with dehydration following multivariate analysis, controlling for confounders were Withdrawal of breastfeeding during diarrhoea OR 6.8 (95% CI 3.8 to 12.2) P<0.00001 Not giving ORS during diarrhoea OR 2.1 (95% CI 1.2 to 3.6) p=0.006 The confounding variables which also contributed significantly were: age (<12 months) OR 2.7 (95% CI 1.5 to 5.0) p=0.001 Frequency of stool OR 4.1 (95% CI 2.4 to 7.0) p<0.00001) Frequency of vomiting	Lack of fluid intake whether breast milk or other fluids by the infant during acute gastroenteritis is strongly associated with risk of dehydration. Age, severity of symptoms and nutritional status also play a part.	Well conducted case control study Good choice of control group- a source population that gave rise to the cases good structured univariate and multivariate analysis The funding of this study was undeclared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					OR 2.4 (95%CI 1.4 to 4.0) p=0.001 Severe under nutrition (≤60IAP classification) OR 3.1 (95% CI 1.6 to 5.9) p=0.001		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Zodpey SP;Deshpande SG;Ughade SN;Hinge AV;Shirikhande SN; 1998 Jul{40827}	Study Type: Case-control Evidence level: 2+ India	n=387 cases n= 387 controls	Children under the age of five with acute gastroenteritis (no details on duration) with severe or moderate dehydration (cases) or mild or no dehydration (controls) and admitted to hospital	Outcome Measures: Risk factors a) demographic factors e.g. age, sex b) nutritional status (IAP classification) c) hygiene practices e.g. hand washing d) clinical features on admission e.g. frequency of symptoms e) history of measles in the past 6 mths f) management of diarrhoea e.g. breast feeding	Data was subject to univariate analysis and multivariate analysis (shown below) Results were similar OR (95% CI) p value Age <12 mths 1.53 (1.02 to 2.28) p=0.038 Female sex 1.18 (0.8 to 1.73) p=0.389 Muslim religion 1.64 (1.01 to 2.7) p=0.048 Residence in rural/urban slum 0.98 (0.77 to 1.24) p=0.884) Severe under nutrition 1.56 (1.31 to 1.86) p<0.001) Non washing of mothers hands & food prep 1.45 (0.97 to 2.16) p=0.064 Non washing of mothers hands after defaecation 1.33 (0.9 to 1.97) p=0.144 Non washing of mothers hands after disposal of faeces 1.44 (0.97 to2.12) p=0.063 Freq of stool(>8/day) 8.76 (5.88 to 13.04) p<0.001	This study found a significant association of infancy, religion, severe under nutrition, clinical symptoms, withdrawal of breastfeeding during diarrhoea, history of measles, withdrawal of fluids during diarrhoea and not giving ORS, HAF or both during diarrhoea with the development of moderate or severe dehydration	Large case control study with appropriate control group Some of the significantly associated factors were very near the level of significance e.g. age, religion The funding of this study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					Freq of vomiting(>2day) 2.57 1.74 to 3.78 p<0.001 Temp (>99oC) 0.91 (0.47 to 1.76) p=0.797 History of measles 2.87 (1.47 to 5.56) p=0.001) Withdrawal of breastfeeding 3.61 (2.11 to 6.16) p<0.001 withdrawal of fluids 1.61 91.09 to 2.37) p=0.016 Not giving ORS 1.59 (1.08 to 2.34) p=0.018 Not giving home available fluids(HAF) 1.62 (1.09 to 2.4) p=0.015 Not giving either ORS of HAF 1.98 (1.34 to 2.91) p<0.001		
Victora CG;Fuchs SC;Kirkwood BR;Lombardi C;Barros FC; 1992{40852}	Study Type: Case-control Evidence level: 2+ Brazil	n=192 cases n=192 controls	Children (<2 years) with either gastroenteritis with moderate or severe dehydration (cases) or children without disease from the same neighbourhood	Prognostic factors for diarrhoea associated dehydration **Biological variables** Age Birth order birth interval	Relationship between prognostic factor & diarrhoea-associated dehydration (OR 95% CI adjusted for age & father's presence/education **Biological variables** *Age* Grp of infants under 12	This study found a wide range of contributing factors to dehydration but reported that child's age, birth weight (& associated measures), low body weight (whether due to age or malnutrition), birth interval and feeding mode were the most strongly associated. More complex anthropometric indices e.g.	Well conducted case control study Good choice of control group This study was funded by the WHO

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
				Maternal age Maternal race **Anthropometric variables** Birth weight Height for age weight for age weight for length post rehydration body weight **Dietary variables** Type of milk Feeding mode Breastfeeding status **Morbidity** previous hospitalisations Medicines used in last 2 weeks Antibiotics used in last two weeks	mths: OR (95% CI) 0-1mths 2.6 (1.3 to 5.5) 2-3mths 7.1 (3.0 to 16.5) 4-5mths 3.5 (1.6 to 7.5) 6-8mths 2.4 (1.2-4.8) 9-11mths 1.0 p<0.001 Grp of infants 12-23 mths 12-17mths 3.7 (1.0 to 13.1) 18-23mths 1.0 p=0.03 *birth order* was not related to diarrhoea-associated dehydration p=0.06 *Birth interval (mths)* <18: 1.0 >/=20-24:0.5 (0.2 to 1.2) >/=25-29:0.4 (0.2 to 1.1) >/=30:0.3 (0.1 to 0.7) p=0.01 *Maternal age* <20: 1.0 >/=20-24:0.5 (0.3 to 0.96) >/=25-29:1.4 (0.7 to 2.7) >/=30:0.7 (0.4 to 1.4) p=0.02 *Maternal race* white: 1.0 black: 1.4 (0.8 to 2.6) mixed: 3.3 (1.6 to 6.7) p=0.003 **anthropometric variables** *Birth weight (g)* <2500 1.0	length for age were less useful In addition, breast feeding reduces the risk of dehydration in terms of whether it is present, has been present and length of time since it has been practised. Signs and symptoms are less useful as determined by Sensitivity & specificity data (actual data not shown)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					>2500 0.4 (0.2 to 0.8) >3000 0.3 (0.1 to 0.5) >/=3500 0.3 (0.1 to 0.6) p<0.001 Height for age, Weight for age, Weight for length showed a similar relationship p<0.01, p<0.001,p<0.001 respectively **Dietary variables** *type of milk* Breast 1.0 Breast & cows 1.3 (0.5 to 3.3) Breast & powdered 0.9 (0.2 to 4.8) Cow's 2.5 (1.1 to 6.0) powdered 10.3 (2.6 to 40.1) p=0.002 *Feeding mode* Breast milk 1.0 Breast & non breast milk 1.2 (0.2 to 6.0) Breast & solids 0.2 (0.03 to 1.2) Breast & non breast & solids 0.3 (0.05 to 1.4) non breast milk 2.7 (0.7 to 10.4) Non breast & solids or solids only 0.9 (0.2 to 4.1) P<0.001 **Morbidity** Previous hospitalisations 0: 1.0 >/=1: 2.0 (1.15 to 3.4) p=0.01		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					Medicines used in past 2 weeks no 1.0 yes 2.3 (1.3 to 4.1) p=0.002 Antibiotics used in past 2 weeks was not associated p=0.5 Authors provide selected data on **specificity & sensitivity** Age (mths) <2 18%, 96% <4 46%, 79% Birth weight (<2500g) 24% 91% Breast feeding None: 73%, 38% None/mixed: 91% 15% Birth interval (<18mths) 27%, 85% Clinical symptoms: 6+ stools: 71% vs. 45% Reported fever 60% vs. 78% Vomiting 58% vs. 78% Fever or vomiting 75% vs. 66%		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Fuchs SC;Victora CG;Martines J; 1996 Aug 17 {40853}	Study Type: Case-control Evidence level: 2+	n=192 cases acute gastroenteritis with moderate or severe dehydration n=192 controls matched for age and neighbourhood without gastroenteritis	Children (up to 2 years old) matched for age and neighbourhood with or without dehydrating gastroenteritis	Associations between dehydrating diarrhoea and the risk factors of age type of milk consumed time since breast feeding stopped Breast feeding status	Risk factors Age Grp of infants under 12 mths: OR (95% CI) 0-1mths 2.6 (1.3 to 5.5) 2-3mths 7.1 (3.0 to 16.5) 4-5mths 3.5 (1.6 to 7.5) 6-8mths 2.4 (1.2-4.8) 9-11mths 1.0 p<0.001 Grp of infants 12-23 mths 12-17mths 3.7 (1.0 to 13.1) 18-23mths 1.0 p=0.03 Type of milk consumed OR (95% CI) adjusted for age, family income, father's presence or education, mother's education, mother's skin colour, type of housing, availability of water, number of children under 5 living in house, cleanliness of house, mothers age , presence of twins, birth weight, weight for age and previous hospitalisation Breast only 1.0 Breast & cow's 1.3 (0.3-4.9) Breast & formula 2.2 (0.3-17.2) Cows' only 6.0 (1.8 to 19.8) Formula only 6.9 (1.4 to 33.3)	These results suggest that age is related to the risk of dehydration with gastroenteritis and that breast feeding reduces the risk of dehydration in terms of whether it is present, has been present and length of time since it has been practiced.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					p=0.006 Breast feeding status OR (95% CI) adjusted as above Continuing 1.0 Stopped 6.4 (2.3 to17.3) Never breast fed 0.7 (0.1 to3.7) p<0.001 Interval since breast feeding stopped(mths) OR (95% CI) adjusted as above Still breastfeeding 1.0 </=2mths 8.4 (2.4-29.6) 3-5mths 7.3 (2.0 to 26.20 >/=6mths 3.9 (1.1 to 14.4) Never breast fed 0.7 (0.1 to 3.6) p<0.001		
Ahmed FU;Karim E; 2002 Oct{40831}	Study Type: Case-control Evidence level: 2+ India	n=80 cases n=160 controls	Children under the age of 2 years with acute gastroenteritis (<7 days) and either 'some' or severe dehydration (cases) or 'no signs' of dehydration (controls) attending hospital and having subsequent home visits	38 factors were studied for their influence on the development of dehydration which included sociodemographic e.g. age, working mother, number in family Clinical details: e.g. duration of	Bi-variant analysis showed that 17 factors were significantly associated with the development of dehydration OR (95% CI) p value Illiterate mother 2.53 (1.44 to 4.45) p<0.05 Illiterate father 2.45 (1.37 to 4.42) p<0.01 Father doing manual work 2.45 (1.37 to 4.42) p<0.01 Child death in family	Along with sociodemiographic and environmental factors; duration of diarrhoea, stool frequency, vomiting , receiving ORS at home before attendance, receiving drugs before attendance and body weight were significantly associated with development of dehydration	Good case control study with appropriate control group. Logistic regression analysis not explained in full. The funding of this study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
				diarrhoea, received ORS at home Environmental factors e.g. distance from hospital, clean water available	2.64 (1.25 to 5.58) p<0.01 Duration of diarrhoea at hospital attendance (>3 days) 1.88 (1.05 to 3.36) p<0.05 Stool frequency of more than 5 per day 6.22 (1.36 to 27.14) p<0.01 Vomited during 'episode' 58.14 (16.59 to 243.06) p<0.01 Received ORT at home 10.68 (3.05 to 44.64) p<0.01 Drugs received before attending hospital 3.97 (2.00 to 797) p<0.01 'wasted' child 3.84 (1.65 to 9.03) p<0.01 Distance from hospital (>3km) 5.13 (2.61 to 10.13) p<0.01 Thatched house 1.89 (1.02 to 3.49) p<0.05 Mothers dirty finger nails 3.67 (1.95 to 6.95) p<0.01 child's dirty finger nails 5.39 (2.59 to 10.40 p<0.01 no refrigerator 3.32 (1.16 to 10.23) p<0.05		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
					ate unsafe leftover food 2.36 (1.11 to 5.06) p<0.005 Followed by step wise logistic regression analysis (no detail for all factors) vomiting, ORS therapy at home , mother dirty fingernails and residing more than 3km away from hospital was the best for predicting the development of dehydration Sensitivity 77.5% Specificity 91.2 %		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Steiner MJ;DeWalt DA;Byerley JS; 2004{31541}	Study Type: Systematic review - meta-analysis Evidence level: II	13 diagnostic test studies were included	Studies that contained data on the precision or accuracy of findings for diagnosis of dehydration in children 1month to 5years old.	Intervention: 3 studies that made a independent, blind comparison of test with a valid gold standard; patients enrolled in a non-consecutive fashion, using a subset or smaller group who may have had the condition and generated definitive results on both test and gold standard. 10 studies with a non-independent comparison of a test with a valid gold	Follow-up period: Outcome Measures: Test sensitivity and specificity, positive LR and negative LR.	Prolonged capillary refill: LR+ (95% CI): 4.1 (1.7 to 9.8) LR-:(95% CI): 0.57 (0.39 to 0.82) Sensitivity (95% CI): 0.60 (0.29 to 0.91) Specificity (95% CI): 0.85 (0.72 to 0.98) Abnormal skin turgor: LR+ (95% CI): 2.5 (1.5 to 4.2) LR- (95% CI): 0.66 (0.57 to 0.75) Sensitivity (95% CI): 0.58 (0.40 to 0.75) Specificity (95% CI): 0.76 (0.59 to 0.93)	The initial assessment of dehydration in young children should focus on estimating capillary refill time, skin turgor, and respiratory pattern and using combinations of other signs. The relative imprecision and inaccuracy of available tests limit the ability of clinicians to estimate the exact degree of dehydration.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
				standard among a "grab" sample of patients believed to have the condition in question. Comparison: Test compared with a valid gold standard		Abnormal respiratory pattern: LR+ (95% CI): 2.0 (1.5 to 2.7) LR- (95% CI): 0.76 (0.62 to 0.88) Sensitivity (95% CI): 0.43 (0.31 to 0.55) Specificity (95% CI): 0.79 (0.72 to 0.86) Sunken eyes LR+ (95% CI): 1.7 (1.1 to 2.5) LR- (95% CI): 0.49 (0.38 to 0.63) Sensitivity (95% CI): 0.75 (0.62 to 0.88) Specificity (95% CI): 0.52 (0.22 to 0.81) Dry mucous membranes: LR+ (95% CI): 1.7 (1.1 to 2.6) LR- (95% CI): 0.41 (0.21 to 0.79) Sensitivity (95% CI): 0.86 (0.80 to 0.92) Specificity (95% CI): 0.44 (0.13 to 0.74) Cool extremity (range): LR+: 1.5, 18.8 LR- : 0.89, 0.97 Sensitivity: 0.10, 011 Specificity: 0.93, 1.00 Weak pulse (range): LR+: 3.1, 7.2 LR- : 0.66, 0.96 Sensitivity: 0.04, 0.25 Specificity: 0.86, 1.00 Absent tears: LR+ (95% CI): 2.3 (0.9 to		

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
						5.8) LR- (95% CI): 0.54 (0.26 to 1.13) Sensitivity (95% CI): 0.63 (0.42 to 0.84) Specificity (95% CI): 0.68 (0.43 to 0.94) Increased heart rate: LR+ (95% CI): 1.3 (0.8 to 2.0) LR- (95% CI): 0.82 (0.64 to 1.05) Sensitivity (95% CI): 0.52 (0.44 to 0.60) Specificity (95% CI): 0.58 (0.33 to 0.82) Sunken fontanelle: LR+ (95% CI): 0.9 (0.6 to 1.3) LR- (95% CI): 1.12 (0.82 to 1.54) Sensitivity (95% CI): 0.49 (0.37 to 0.60) Specificity (95% CI): 0.54 (0.22 to 0.87) Poor overall appearance: LR+ (95% CI): 1.9 (0.97 to 3.8) LR- (95% CI): 0.46 (0.34 to 0.61) Sensitivity (95% CI): 0.80 (0.57 to 1.04) Specificity (95% CI): 0.45 (-0.1 to 1.02)		

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients & Patient Characteristics	Population Characteristics	Outcome measures	Results & Comments	Study Summary	Reviewer Comment
Hill ID;Mann MD;Bowie MD; 1981 Mar 28 {38318}	Study Type: Other Prospective comparative study Evidence Level: 3	Intervention: Clinical features of hypernatreamic dehydration Comparison: Children with and without hypernatreamic dehydration.	Total N=197 147 children with hypernatraemia 50 children with non-hypernatreamic dehydration		Age, sex, weight, central nervous system dysfunction, underestimation of dehydration	Difference between groups: Age: Hypernatreamic group 63.9%; Non-hypernatreamic group 38.0% under the age of 6 months; p<0.01. Symptoms of CNS (Drowsy, but rousable, Jittery, hypertonic or hyperreflexic, Coma and/or convulsions): Hypernatreamic group n=56 (38%) Non-hypernatreamic group n=2 (4%) p<0.001 Underestimation of dehydration: Hypernatreamic group 72.5% Non-hypernatreamic group 36% p<0.001	The authors conclude that without checking serum sodium concentration a large number of hypernatreamic individuals will initially go undetected. The most useful signs for assessing hypernatreamia are those of CNS dysfunction, drowsiness being the most common abnormal finding. There are some diagnostic clinical features, but these are not specific, and without routine electrolyte estimations many with hypernatraemia would go undetected.	There are not many studies regarding hypernatreamia. This study is not of very good quality but the only study identified that reports clinical features for hypernatreamia.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Reid SR;Losek JD; 2005{41222}	Study Type: Other Evidence Level: 3	Intervention: Prevalence of hypoglycaemia among children among children with dehydration due to acute gastroenteritis Clinical variables associated with hypoglycaemia in these children Comparison: Comparisons are made between hypoglycaemic and non-hypoglycaemic children	Study population was 196 children	children aged 1 month to 5 years presented to hospital and received an ICD code -9 for acute gastroenteritis and dehydration	Duration of vomiting Duration of diarrhoea systolic blood pressure (mm Hg) Glucose (mg/dL) sodium (mEq/L) bicarbonate (mEq/L) BUN (mg/dL)	Duration of vomiting in days (hypoglycaemic children) 2.6 (SD = 1.5) Duration of vomiting in days (non -hypoglycaemic children) 1.6 (SD = 1.8) Duration of diarrhoea in days for hypoglycaemic children 3.3 (SD = 1.7) Duration of diarrhoea in days for non hypoglycaemic children 2.4 (SD = 2.6)	The authors conclusions are not relevant to the clinical question being addressed	While the study is limited by its retrospective design (duration of diarrhoea and vomiting were not recorded for a number of children), the figures presented are similar to those reported from other studies
Steiner MJ;DeWalt DA;Byerley JS; 2004{31541} [1]	Study Type: Systematic review - meta-analysis Evidence level: II	13 diagnostic test studies were included	Studies that contained data on the precision or accuracy of findings for diagnosis of dehydration in children 1month to 5years old.	Intervention: 3 studies that made a independent, blind comparison of test with a valid gold standard; patients enrolled in a non-consecutive fashion, using a subset or smaller group who may have had the condition and generated definitive results on both test and gold standard. 10 studies with a non-independent comparison of a test with a valid gold standard among a "grab" sample of	Follow-up period: Outcome Measures: Test sensitivity and specificity, positive LR and negative LR.	Prolonged capillary refill: LR+ (95% CI): 4.1 (1.7 to 9.8) LR-:(95% CI): 0.57 (0.39 to 0.82) Sensitivity (95% CI): 0.60 (0.29 to 0.91) Specificity (95% CI): 0.85 (0.72 to 0.98) Abnormal skin turgor: LR+ (95% CI): 2.5 (1.5 to 4.2) LR- (95% CI): 0.66 (0.57 to 0.75) Sensitivity (95% CI): 0.58 (0.40 to 0.75) Specificity (95% CI): 0.76 (0.59 to 0.93) Abnormal respiratory pattern: LR+ (95% CI): 2.0 (1.5 to 2.7) LR- (95% CI): 0.76 (0.62 to 0.88) Sensitivity (95% CI): 0.43 (0.31	The initial assessment of dehydration in young children should focus on estimating capillary refill time, skin turgor, and respiratory pattern and using combinations of other signs. The relative imprecision and inaccuracy of available tests limit the ability of clinicians to estimate the exact degree of dehydration.	

				patients believed to have the condition in question. Comparison: Test compared with a valid gold standard		to 0.55) Specificity (95% CI): 0.79 (0.72 to 0.86) Sunken eyes LR+ (95% CI): 1.7 (1.1 to 2.5) LR- (95% CI): 0.49 (0.38 to 0.63) Sensitivity (95% CI): 0.75 (0.62 to 0.88) Specificity (95% CI): 0.52 (0.22 to 0.81) Dry mucous membranes: LR+ (95% CI): 1.7 (1.1 to 2.6) LR- (95% CI): 0.41 (0.21 to 0.79) Sensitivity (95% CI): 0.86 (0.80 to 0.92) Specificity (95% CI): 0.44 (0.13 to 0.74) Cool extremity (range): LR+: 1.5, 18.8 LR- : 0.89, 0.97 Sensitivity: 0.10, 011 Specificity: 0.93, 1.00 Weak pulse (range): LR+: 3.1, 7.2 LR- : 0.66, 0.96 Sensitivity: 0.04, 0.25 Specificity: 0.86, 1.00 Absent tears: LR+ (95% CI): 2.3 (0.9 to 5.8) LR- (95% CI): 0.54 (0.26 to 1.13) Sensitivity (95% CI): 0.63 (0.42 to 0.84) Specificity (95% CI): 0.68 (0.43 to 0.94) Increased heart rate: LR+ (95% CI): 1.3 (0.8 to 2.0) LR- (95% CI): 0.82 (0.64 to 1.05) Sensitivity (95% CI): 0.52 (0.44 to 0.60)		

						Specificity (95% CI): 0.58 (0.33 to 0.82) Sunken fontanelle: LR+ (95% CI): 0.9 (0.6 to 1.3) LR- (95% CI): 1.12 (0.82 to 1.54) Sensitivity (95% CI): 0.49 (0.37 to 0.60) Specificity (95% CI): 0.54 (0.22 to 0.87) Poor overall appearance: LR+ (95% CI): 1.9 (0.97 to 3.8) LR- (95% CI): 0.46 (0.34 to 0.61) Sensitivity (95% CI): 0.80 (0.57 to 1.04) Specificity (95% CI): 0.45 (-0.1 to 1.02)		

Fluid Management

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Faruque AS; 1992{38599} Study population was located in India	Study Type: Case-control Evidence level: 2+	Total N=1013 Cases n=285 Cases with cholera n=29 (10.2%) Controls n=728 Controls with cholera n=19 (2.6%)	Children aged 1 and 35 months presenting with watery diarrhoea for six days or less. Only children who had been receiving breast feeding up to the time of onset of diarrhoea were included.	Intervention: Withdrawal of breastfeeding; giving ORT at home before admission to hospital Comparison: Withdrawal of breastfeeding versus continuation of breastfeeding Giving more than 250ml or less than 250ml of ORT solution at home versus not giving any ORT solution at home.	Follow-up period: Outcome Measures: Withdrawal of breastfeeding; Total volume of ORT before admission (ml)	Withdrawal of breastfeeding: OR 3.89 (95% CI 0.96 - 15.84) adjusted for confounding variables: OR 5.23 (95% CI 1.37 to 19.99) ORT at home: None: OR 1.34 (95% CI 0.93 to 1.92) compared to more than 250ml Adjusted: OR 1.57 (95% CI 1.08 to 2.29) Less than 251ml: OR 1.09 (95% 0.74 to 1.60) compared to more than 250 ml Adjusted: OR 1.18 (95% CI 0.84 to 1.66) Confounding variables were: Illiterate mother, history of vomiting, high stool frequency in any 24h period (11+), young age (1-9 months) and cholera (positive).	Withdrawal of breast feeding during diarrhoea was associated with a five times higher risk of dehydration compared with continued breast feeding during diarrhoea at home. Lack of ORT with either complete formula or a salt sugar solution at home was associated with a 57% higher risk of dehydration compared with receipt of a reasonable amount of ORT after controlling for several confounders.	The study does not report the number of children who were breast feed and given ORT at the same time. The use of ORT must be interpreted as start of rehydration therapy for the purpose of the guideline. 10.2% of cases and 2.6% of controls had cholera.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Hahn S;Kim Y;Garner P; 2007{38982} Egypt (2), Bangladesh (3), Mexico (1), Columbia (1), India (3), Panama (1), USA (1). Multicentre trial (1) conducted in Brazil, India, Mexico, Peru. A multicentre trial (1) conducted in Bangladesh, Brazil, India, Peru, Vietnam	Study Type: Systematic review - meta-analysis Evidence level: 1++	Reduced osmolarity ORS - 1004 children WHO standard ORS - 992 children the above figures refer to the outcome: need for unscheduled IV infusion	children with acute diarrhoea (history of less than 5 days). Three trials included cholera patients	Intervention: This is a systematic review of RCTs Comparison: Reduced osmolarity ORS compared with WHO standard ORS	Follow-up period: Different in individual studies Outcome Measures: Primary outcome : need for unscheduled IV fluid infusion during the course of treatment Secondary outcomes: Stool output children vomiting during rehydration asymptomatic hyponatremia (serum sodium less than 130 mmol/L) during follow up	need for unscheduled IV fluid infusion - OR (fixed) 0.59 (0.45 to 0.79) Stool output - SMD (fixed) -0.23 (-0.33 to -0.14) episode of vomiting during rehydration - OR (Peto) 0.71 (0.55 to 0.92) Presence of hyponatremia after rehydration - OR (Peto) 1.44 (0.93 to 2.24) Sensitivity Analysis: need for unscheduled IV fluid infusion - OR (fixed) 0.61 (0.46 to 0.82) stool output - SMD (fixed) -0.21 (-0.31 to -0.11) Stratified by sodium concentration: need for unscheduled IV fluid infusion - OR (fixed) 0.59 (0.44 to 0.78) stool output - SMD (fixed) -0.20 (-0.30 to -0.10) episodes of vomiting - OR (fixed) 0.70 (0.54 to 0.91) presence of hyponatremia - OR (fixed) 1.45 (0.93 to 2.26)	The review provides some evidence that dehydrated children given a solution of with a lower osmolarity were less likely to nedd an IV fluid infusion, than those given WHO standard ORS	This meta- analysis was very useful in answering this question

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Gavin N; 1996{37226} The studies were conducted in the US and in Canada. One of the US studies included children from a Panamanian hospital	Study Type: Systematic review - meta-analysis Evidence level: 1+	There was a total of 803 participants across the study. The review was not reported in a manner that allowed separation of those in the ORT arms from those in the IVT arms	Most studies enrolled children aged 3 months up to 3 years. One RCT enrolled children aged 1 month to 14 years. Most of the patients were mildly to moderately dehydrated whereas in RCTs with IVT armsseverely dehydrated children were included	Intervention: The efficacy of ORT in comparison to IVT ORS with high sodium content is being compared to ORS with low sodium content 13 RCTs were included in the review Comparison: Oral rehydration therapy vs. IV rehydration therapy High sodium glucose based ORS vs. low sodium glucose based ORS Effectiveness of ORT administered outpatient vs. inpatient	Follow-up period: Follow up period differed for individual studies. In a few studies rehydration phase lasted up to 48 hours before regular feeding schedules were re-introduced Outcome Measures: Outcome measures were: Treatment failure-defined as the persistence or recurrence of signs of dehydration beyond 24 hours of ORT and other clinical indications requiring the need to revert to IV therapy weight gain; volume, frequency and duration of diarrhoea; length of stay and hospitalization	Trials with IVT arms - Failure rate 5.7% (CI 1.8% to 9.6%) Trials without IVT arms - Failure rate 3.0% (CI 0.6% to 5.4%) Overall failure rate 3.6% (CI 1.4% to 5.8%) high sodium WHO formula - Failure rate 1.9% (CI 0% to 5.4%). Difference between low and medium groups was not statistically significant low sodium formula - Failure rate 3.6% (CI 0% to 7.3%) medium sodium formula - Failure rate 5.0% (CI 1.9% to 8.1%) Hyponatremia one trial with an IVT arm reported 3 cases of hyponatremia that corrected to normal after 24 hours of treatment one trial with no IVT arm reported 1 case in the high sodium group and 6 cases each in the medium and low sodium groups Hypernatremia - one study with no IVT arm (same as above) reported one case each in the low, medium and high sodium groups.	Over the counter ORS available in the US (45 - 70 mEq/L with a carbohydrate to sodium ration of less than 3) are appropriate and efficacious in treating well nourished children. Only 2 of the 13 studies showed that well nourished children rehydrated with medium to low sodium solutions (50 - 75 mmol/L and 26 - 45 mmo/L respectively) may be at higher risk of iatrogenic hyponatremia	The results of this review are consistent with other evidence that has been retreived to answer this question

Fontaine O; 2007{43498} Studies were conducted in Bangladesh, Indonesia, India, Pakistan, Mexico, Chile, Peru and Egypt.	Study Type: Systematic review - meta-analysis Evidence level: 1++		Children and adults with signs of dehydration due to acute diarrhoea	Intervention: Benefit of rice-based ORS and it's relation to age of patient and aetiology of diarrhoea in comparison to WHO ORS Comparison: Standard WHO ORS was compared to rice based ORS (50 - 80 g/l of rice powder with electrolyte concentrations remaining unchanged)	Follow-up period: Until cessation of diarrhoea Outcome Measures: Stool output during the first 24 hours total stool output from admission to study until cessation of diarrhoea duration of diarrhoea from admission to study until cessation of diarrhoea	24 hour stool otuput in cholera cases (4 trials children under 12) - WMD (g/kg) = -67.397 (95%CI -94.260 to -40.534) Total stool output (1 trial in children under 12) - WMD (g/kg) = -124.000 (95% CI -248.603 to 0.603) Duration of diarrhoea (1 trial in children under 12) - WMD (days) = -13.000 (95%CI -24.895 to -1.105) 24 hour stool output in non-cholera diarrhoea in children under 5 (15 trials) - WMD (g/kg) = -4.292 (95% CI -9.362 to 0.779) total stool output in non cholera diarrhoea in children under 5 (9 trials) - WMD (g/kg) = -28.162 (95% CI -52.381 to -3.944) Duration of diarrhoea in non-cholera diarrhoea in children under 5 (12 trials) - WMD (days) = -1.258 (95% CI -4.406 to 1.891)	Based on stool outputs within the first 24 hours, rice-based ORS may be more clinically effective than WHO ORS for patients with cholera. However, it has no advantage over standard ORS in children with non-cholera diarrhoea and as it is more expensive cannot be justified in this group.	These findings are consistent with those of similar research. Given that non cholera type diarrhoea is more likely to be experienced in the UK, careful consideration must be given to the benefit that may be enjoyed from use of rice-based ORS in this country.

Nutritional Management

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Bhattacharya SK;Bhattacharya MK;Manna B;Dutta D;Deb A;Dutta P;Goswami AG;Dutta A;Sarkar S;Mukhopadhaya A; 1995{39547} Study population was located in Burma	Study Type: Case-control Evidence level: 2+	Total N=379 Cases (moderate to severe dehydration) n=243 Cases having cholera n=65 (26.7%) Controls (no or mild dehydration) n=136 Contols having cholera n=29 (21.3%)	Children aged up to 2 years of age with acute watery diarrhoea for less than 24h duration.	Intervention: Withdrawal of breast feeding, Not giving ORS (WHO) Comparison: Withdrawal of breast feeding during diarrhoea versus continued breast feeding. Not giving ORS versus giving ORS during diarrhoea episode.	Follow-up period: Outcome Measures: Withdrawal of breast feeding, Not giving ORS during diarrhoea Confounding variables: Age, Frequency of stools and vomiting, severe under nutrition	MULTIVARIATE ANALYSIS: Withdrawal of breast feeding: OR 6.8 (95% CI 3.8 to 12.2) and not giving ORS: OR 2.1 (95% CI 1.2 to 3.6) adjusted for age (<12months), frequency of stool and vomiting and severe under nutrition. UNIVARIATE ANALYSIS: Stopping breast feeding compared with increased/continued breast feeding: OR 5.9 (95% CI 3.6 to 9.6) Not received ORS (WHO) versus received: OR 1.6 (95% CI 1.0 to 2.4) Not received home available fluid received versus received home available fluid: OR 1.1 (95% CI 0.9 to 2.0) Vibrios compared with Rota: OR 1.3 (95% CI 3.7 to 10.6)	Emphasis on the importance of continued breast feeding and use of oral rehydration therapy from the beginning of diarrhoea to prevent development of life-threatening dehydration and death.	The outcome is severe or moderate dehydration. The study includes cholera cases. The study investigates breast feeding and use of ORS as independent risk factors.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Khin MU;Nyunt NW;Myo K;Mu MK;Tin U;Thane T; 1985{39544} Study population was located in Bangladesh	Study Type: RCT Evidence level: 1+	ORS alone n=26 of which n=5 (19.2%) had Vibrio cholerae in stools ORS plus breast feeding n=26 of which n=4 (15.4%) had Vibrio cholerae in stools	Inclusion: Children aged less than 2 years with acute diarrhoea of less than 48h with moderate or severe dehydration who had been normally breastfeed. Exclusion: Children with a concomitant illness (such as bronchopneumonia, urinary tract infection, clinically evident malnutrition, or shock), bottle fed children, and children who had received antibiotics before admission.	Intervention: Breast feeding during rehydration with ORS Comparison: ORS alone for the first 24h versus ORS plus breast feeding thereafter ORS plus breast feeding in both comparison groups	Follow-up period: 48h Outcome Measures: Stool output No of times stools passed in hospital Vomitus volume Duration of diarrhoea in hospital (hours) Total ORS required for rehydration	Number of stools passed in hospital: ORS alone: mean 17.4 (SE 2.3) ORS plus breast feeding: mean 12.1 (SE 1.1) p<0.05 Non significant: Duration of diarrhoea in hospital (h) ORS alone: 45.7 (3.9) ORS plus breast feeding: 43.3 (5.0) Stool output ORS alone: (ml) 887.4 (116.0) ORS plus breast feeding: 640.9 (65.5) Vomitus volume (ml) ORS alone: 15.2 (8.5) ORS plus breast feeding: 22.9 (10.9) Total ORS (ml/patient) ORS alone: mean 2119.2 ml (SE 192.1) ORS plus breast feeding: mean 1570.4 ml (SE 112.5) p=0.02	There were no statistical significant differences between children receiving ORS only and those who received ORS plus breast feeding in stool and vomitus output, number of stools passed in hospital and duration of diarrhoea in hospital. The children who received ORS plus breast feeding had on average five fewer motions than those who where not breast fed and required on average 550 ml less ORS than those not breast fed during early acute phase of diarrhoea. Breast feeding exerts a beneficial effect on the course and outcome of acute diarrhoea by reducing the number and volume of diarrhoeal stools.	Children who required IVT where given IVT until rehydrated (usually within 4 hours of admission) and then randomly allocated. Given IVT: 8/26 (30.8%) of children receiving ORS alone and 7/26 (26.9%) of children receiving ORS and breast feeding required IVT..

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Faruque AS; 1992 {38599} Study population was located in India	Study Type: Case-control Evidence level: 2+	Total N=1013 Cases n=285 Cases with cholera n=29 (10.2%) Controls n=728 Controls with cholera n=19 (2.6%)	Children aged 1 and 35 months presenting with watery diarrhoea for six days or less. Only children who had been receiving breast feeding up to the time of onset of diarrhoea were included.	Intervention: Withdrawal of breastfeeding; giving ORT at home before admission to hospital Comparison: Withdrawal of breastfeeding versus continuation of breastfeeding Giving more than 250ml or less than 250ml of ORT solution at home versus not giving any ORT solution at home.	Follow-up period: Outcome Measures: Withdrawal of breastfeeding; Total volume of ORT before admission (ml)	Withdrawal of breastfeeding: OR 3.89 (95% CI 0.96 - 15.84) adjusted for confounding variables: OR 5.23 (95% CI 1.37 to 19.99) ORT at home: None: OR 1.34 (95% CI 0.93 to 1.92) compared to more than 250ml Adjusted: OR 1.57 (95% CI 1.08 to 2.29) Less than 251ml: OR 1.09 (95% 0.74 to 1.60) compared to more than 250 ml Adjusted: OR 1.18 (95% CI 0.84 to 1.66) Confounding variables were: Illiterate mother, history of vomiting, high stool frequency in any 24h period (11+), young age (1-9 months) and cholera (positive).	Withdrawal of breast feeding during diarrhoea was associated with a five times higher risk of dehydration compared with continued breast feeding during diarrhoea at home. Lack of ORT with either complete formula or a salt sugar solution at home was associated with a 57% higher risk of dehydration compared with receipt of a reasonable amount of ORT after controlling for several confounders.	The study does not report the number of children who were breast feed and given ORT at the same time. The use of ORT must be interpreted as start of rehydration therapy for the purpose of the guideline. 10.2% of cases and 2.6% of controls had cholera.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Sandhu BK;Isolauri E;Walker-Smith JA;Banchini G;van Caillie-Bertrand M;Dias JA;Guandalini S;Hoekstra JH;Juntunen M;Kolacek S;Marx D;Micetic-Turk D;Razenberg MC;Szajewska H;Taminiau J;Weizman Z;Zanacca C;Zetterstrom R; 1997 May {39581}	Study Type: Comparative RCT Evidence level: 1- Pan-European 12 hospitals	n= 134 early feeding Grp A n=96 late feeding Grp B n=8 excluded from Grp B as they were given food too early. N=4 in each grp were considered treatment failures as they required i.v. fluids by day 4	Infants (aged 12-17 mths, mean ~14mths) with acute gastroenteritis (<5 days) with mild (majority) to severe dehydration and admitted to hospital	Rehydration as appropriate for 4 hrs then randomised to Grp A: usual diet (no details) Grp B: ORS continued for 20 hrs followed by usual diet Extra ORS was given for each watery stool. If child was breast fed, it was continued Comparison: early vs. late feeding of normal diet	Follow-up period: 14 days Outcome Measures: Total duration of diarrhoea (hrs) mean weight gain (reducing sugars in stools)	Fluid intake was similar in both grps. Total duration of diarrhoea was measured by number of watery stools, there was no significant differences between the two grps (or for vomiting) (data expressed as graph, no detail) Mean weight gain Grp A vs. Grp B During rehydration phase: 85g vs. 77g p=0.76 After rehydration (4-24hr): 95g vs. 2g p=0.01 During hospitalisation No data (graph only) but higher in Grp A vs. Grp B p=0.001 overall weight gain was similar by day 5 and day 14 No infants had lactose intolerance on day 5 and diarrhoea and vomiting on day 14	The results show that early refeeding of infants with acute diarrhoea is of benefit in terms of higher weight gain whilst in hospital and did not worsen any symptoms of diarrhoea or vomiting compared with later feeding.	n=230 recruited from 12 different European countries i.e. very mixed population No details on usual diet very sparse data, lots of graphs and no detail appropriateness of randomisation unclear

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Brown KH;Gastanaduy AS;Saavedra JM;Lembcke J;Rivas D;Robertson AD;Yolken R;Sack RB; 1988 {39536}	Study Type: Comparative RCT Evidence level: 1- Peru	n=31 CSO-110 formula n=29 CSO-55 formula n=34 GES only for 2 days, CSO-55 for 2 days, CSO-110 for 2 days n=34 i.v. GES followed by the above diet n=138 were initially enrolled of which n=10 did not remain in study for at least 5 days and so were eliminated from analysis. Of the n=128 remaining, n=3 were withdrawn early by parents, n=3 developed measles, n=3 developed 2nd episode of diarrhoea/infection and n=1 was eliminated as procedure was not carried out correctly 93% of infants were successfully managed (n=27,	Male children (aged 3-36 mths, mean~10mths) with diarrhoea (<60hrs) and mild to severe dehydration (details unclear) and admitted to hospital	Rehydration was carried out according to WHO guidelines. Children in the 3 grps excluding the CSO-110 grp were rehydrated with oral GES. Children in the CSO-110 grp received i.v. GES almost always successful within the first 2-4 hrs of admission. Children then received either a) full strength formula (CSO-110) composed of casein, sucrose: dextrin with maltose, and soybean oil: cotton seed oil (1:1) with added vitamins Or b) half strength formula as for a) (CSO-55) for the first 48 hrs followed by full strength or c) GES-O for the first 48 hrs followed by CSO-55 for the next 48 hrs and CSO -110 for the following 48hrs. Or	Follow-up period: 14 days Outcome Measures: Duration of diarrhoea Mean increment on body weight (g)	Total energy absorbed was equal in grps by days 5-6 when therapies became equal. **Duration of diarrhoea** (hrs) in successful cases (93%) Gp1vs.Gp2 vs.Gp3 vs. Gp 4 143hrs+/- 67 vs. 127hrs +/- 85 vs. 123hrs +/-58 vs. 134hrs +/-59 (NS) Unsuccessful cases were also not significantly different between grps. **Mean increment on body weight (g)** (minimal data, graph presentation) Admission to day 8: Grp1 vs. Gp2 vs. GP3 vs. GP4 were stat. signif. different $p<0.005$ by ANOVA - Grp 1 & 2 increasing in weight, Grps 3 & 4 decreasing Admission to Day 15: Grp1 & 2 vs. Grp 3 & 4 was stat. signif. different $p<0.04$ with in the children in the former two grps gaining approximately 140g more than the latter grps	Increase in body weight was positively related to the amounts of dietary energy consumed thus supporting the case for continued oral feeding in the early refeeding period following rehydration post acute diarrhoea in infants.	Randomisation was appropriate and successful n=20 infants had Giardia lamblia (carried by 50% of Lima children asymptomatically) n=13 infants had C Jejuni (carried by 10% of Lima children asymptomatically) No information on the financial support of this study

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
		n=23, n=31, n=33), losses were equal across grps: treatment failures included recurring dehydration, hyononatremia and prolonged severe diarrhoea. There was one case of septicaemia with a positive blood culture for Alcaligenes faecalis		d) No oral fluids for first 48hrs, but GES-IV, then CSO-55 for the next 48 hrs and CSO -110 for the following 48hrs. Thus by day 5, all grps were on the same therapy CSO-110 provides a maximum of 110cal/kg BW/day Comparison: early vs. late feeding diluted vs. full strength refeeding				

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Shaikh S;Molla AM;Islam A;Billoo AG;Hendricks K;Snyder J; 1991 {39540}	Study Type: Comparative RCT Evidence level: 1- Pakistan	n=33 WHO-ORS (24 hrs) followed by khitchri & 1/2 strength formula (grp a) n= 36 WHO-ORS (4hr) followed by khitchri and 1/2 strength formula & WHO-ORS (grp b) n=6 did not complete due to infections or removal by parents n=19 were treatment failures	Male children (aged 9-48mth, mean age 22-23mths) with acute gastroenteritis(<72hrs) with moderate and severe dehydration and admitted to hospital	Children were randomised to either Grp a) WHO-ORS only for first 24 hrs followed by khitchri (rice, dal, cottonseed oil) and 1/2 strength formula freely or Grp b) WHO-ORS for 4hrs followed by khitchri and 1/2 strength formula freely Comparison: early vs. late feeding	Follow-up period: mean follow up of 3 days Outcome Measures: % weight gain tolerability	Energy intake was similar in both grps Weight gain % change Grp A (n=21) vs. Grp B (n=23) (successful cases only) After rehydration: 7.0%± 3.5 (vs. 7.1% ±4.1 24hrs post rehydration -1.4%±3.9 vs. -0.6%±4.8 72hrs post rehydration -0.9%±4.3 vs. -1.0%±5.0 (NS for all) Tolerability: both treatments were well tolerated	These data indicate that an early feeding of khitchri and WHO-ORS may be as tolerable as WHO-ORS alone in the first 24 hrs	30% failure rate due to severity of some infants at start, reducing the power of study randomisation appropriate No blinding Thus study was supported by the Applied Diarrhoeal Disease Research Project (Harvard) with the US Agency for International Development

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Gazala E;Weitzman S;Weizman Z;Gross J;Bearman JE;Gorodischer R; 1988 Mar {39747}	Study Type: Comparative RCT Evidence level: 1- Israel	n= 53 early feeding (6hr) n=37 late feeding (24hr) 30% were lost to follow up 11% at 24hr, 24% at 48hr, 30% at 2 wks.	Infants (mean age ~7mth) with acute infantile gastroenteritis (< 7 days duration) with mild dehydration (≤5%) who attended a primary care clinic.	**Early feeding:** Following an initial oral rehydration period with ORS-WHO (ORET) of 6hr (50ml/kg) infants were refed with either breast milk or cow's milk (parents were asked not to mix). For infants that received solids the BRAT diet was advised. Or **Late feeding:** Infants were given ORS only for the first 24hr (200ml/kg per day). After which they were fed in the same way as the early grp. In both grps, water supplementation was allowed Comparison: Early (6hrs) vs. late feeding (24hrs)	Follow-up period: Two weeks Outcome Measures: % weight gain State of hydration Duration of diarrhoea Hospital admissions All at 24hr & 2 wks.	**At 24 hrs:** (early vs. late) % weight gain 0.6% vs. 1.2% (NS) Infants with mild dehydration (≤5%) 9(20%) vs. 5(15%) (NS) **Hospital admissions** 2 (4.4%) vs. 3 (8.5% (NS) **At 2 wks:** % weight gain 2.1% vs. 2.4 % (NS) Duration of diarrhoea (d) 3.7± 1.9 vs. 3.6±2.2 (NS) Hospital admissions 3 vs. 4 (NS)	Short term clinical outcomes for infants with acute diarrhoea were not influenced by early or late refeeding. Authors advise early refeeding to prevent malnutrition between bouts of gastroenteritis (particularly relevant to developing countries)	There was a overall 30% loss to follow up Randomisation was inappropriate (flipping a coin) Adherence to 'treatment' was under the control of family and study relied on accurate reporting by families e.g. actual/ expected ORS intake for early vs. late was 67% vs. 63% No information on the financial support of this study

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Nanulescu M;Condor M;Popa M;Muresan M;Panta P;Ionac S;Popescu L;Sarb S;Suciu D;Corduneanu D;Rusu C; 1995{39765}	Study Type: Comparative RCT Evidence level: 1- Peru	n=73 early feeding (normal feeding reached within 2-3 days) n=49 late feeding (normal feeding reached within 4-6 days)	Infants (1-12 mths) with acute gastroenteritis (≤ 5 days) who were not severely dehydrated (WHO criteria) and were hospitalised.	**Early refeeding**: In breast-fed children, feeding was continued throughout illness For each watery stool 50-100ml of ORS were given For non breast fed children, regime was given adapted according to age Less than 5 yr: 75ml/kg ORS or rice water and after 3-6 hr milk formula was resumed. Ist day 1/2 dilution (35-45cal/kg/day), 2nd day 2/1 dilution (75-85cal/kg/day) and 3rd day full strength (110-130cal/kg/day) Greater than 5 yr: 75ml/kg ORS or rice water for the first 3-6 hr after which feeding resumed soft cheese, meat, cereals, rice, fruit and vegetables. Milk after 3 days, initially diluted, at 5 days undiluted. ORS or water given if any watery stools **Late refeeding** Breast feeding was discontinued for 24-36hrs first 6-12 hr ORS (100-150ml/kg) Within next 24hr carrot soup (150-200ml/kg) or rice water. After 24-36 hr: breast feeding resumed	Follow-up period: up to 7 days Outcome Measures: Weight measures Duration of diarrhoea	**After resolution of disease** (early vs. late) % weight change +1.2 ±1.1 vs. -0.01±0.9 p=0.01 Weight loss recorded in 6.2% vs. 37.2% (p<0.01) Weight gain recorded in 76.6% vs. 32.6% (p=0.01) i.e. difference relates to infants with constant weight Duration of diarrhoea (d) 5.6±2.7 vs. 4.9±1.8 p=0.1	Authors concluded that there is a favourable effect of early feeding on body weight in the management of infantile acute diarrhoea	Loss to follow up of n= 21 in early grp, n=13 in late grp. No comment made on this. Randomisation was inappropriate (used odd and even days) Both early and late grps contained sub grps e.g. early grp breast fed infants did not stop feeding in 1st 3-6hr, formula fed infants were. Timings of dietary management were ranges. No information on the financial support of this study

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				supplemented by carrot soup/rice water to ensure 150-200ml/kg with the amount of milk gradually being increased until normal feeding resumed at 4-6 days. For non-breast fed children The same rehydration (6-12hr) and transition (next 24 hr) was instituted. After 24-36 hr milk formula was reintroduced in graduated manner with fluid requirements met with carrot soup, rice water or water. The full milk diet resumed at 5-6 days. If older than 5mth, solid foods as listed before were introduced at 24-36 hr. Comparison: Early vs. late feeding adapted for age of child and whether breast or formula fed.				

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Chew F;Penna FJ;Peret Filho LA;Quan C;Lopes MC;Mota JA;Fontaine O; 1993 Jan 23 {39719}	Study Type: Comparative RCT Evidence level: 1- South America	n=80 full strength milk n=79 diluted milk	Infants (mean age ~4 mths) with acute gastroenteritis (<120hrs) and no or some signs of dehydration on admission	Intervention: Following assessment and rehydration if appropriate (4-6 hrs), infants were randomised to either a) Full strength milk formula immediately or b) graded feeding: 1/2 strength for 24 hrs, 2/3 for next 24 hrs and then full strength milk Other fluids ORS or water were given as appropriate Comparison: full strength vs. regraded feeding	Follow-up period: 5 days Outcome Measures: Diarrhoea duration (hrs) % Weight gain at discharge Treatment successes (diarrhoea stops before 5 days) and failures (recurrent dehydration & increased stools)	Duration of diarrhoea Full strength vs. diluted milk 92(50) vs. 92(50) hrs 95% CI 1.0 (07 to 1.3) % weight gain 0.89 (0.47) vs. 0.3 (4.4) at discharge 95% CI 1.0 (0.6 to 1.7) Treatment successes 51 (71%) vs. 50 (70%) NS Treatment failures: Recurrent dehydration 6(8%) vs. 6(9%) Increased stool output 8(11%) vs., 8(11%)	In infants of less than 6 months with diarrhoea whose main food is animal milk or formula, feeds should be given at full strength as soon as dehydration is corrected.	Randomisation was appropriate (block randomisation) Failures were reported This study was supported by the WHO (Diarrhoeal Diseases Control Programme)

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Valois S; 2005{38903}	Study Type: RCT Evidence level: 1++	90 children in total 30 - White Grape Juice 30 - Apple Juice 30 - coloured and flavoured water	Male infants aged 4-18 months with severe diarrhoea and moderate dehydration.	Intervention: The effect of juice consumption during diarrhoea is being assessed. Treatment arm 1 - Apple juice Treatment arm 2 - White grape juice control arm - coloured flavoured water Comparison: Comparisons are made between the arms of duration and severity of diarrhoea as well as fecal losses througout the study. Fluid intake and vomitus losses were also compared between groups.	Follow-up period: Infants were followed up for 1 week Outcome Measures: duration of illness severity of diarrhoea (assessed by number, type and consistency of stools) amount of fecal losses (g/kg/day) vomitus losses fluid intake required to maintain fluid balance body weight changes	Total duration of diarrhoea reported as mean hours (SD) Apple juice - 111.7 (48.2) White grape juice - 105.4 (44.9) Water - 80.0 (39.6) significance not reported duration of diarrhoea in hours after randomisation Apple juice - 49.4 (32.6) White grape juice - 47.5 (38.9) Water - 26.5 (27.4) P< 0.05 for water vs. juice groups number of patients vomiting during the first day of treatment apple juice - 22 White grape juice - 26 water - 19	All patients recovered with appropriate treatment without anyone developing persistent diarrhoea.	Even though the study was primarily designed to compare juices with water, the fact that none of the infants had diarrhoea for more than 14 days, attests to the fact that this data can be used to answer the clinical question

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Fox R;Leen CL;Dunbar EM;Ellis ME;Mandal BK; 1990 Sep {39698}	Study Type: Comparative RCT Evidence level: 1- UK	n=32 graded refeeding n=30 immediate full strength feeds n=4 were subsequently excluded for unrelated reasons	Infants (mean age ~11 mths) with acute gastroenteritis (<7 days) with mild or moderate dehydration and admitted to hospital.	Intervention: Following rehydration for 12 hours infants were randomised to either a) graded refeeding with cow's milk formula or breast milk at 1/4 strength for 12 hrs , 1/2 strength for the next 12 hrs followed by full strength or b) full strength cow's milk formula or breast milk immediately Comparison: graded vs. immediate full strength refeeding	Follow-up period: Until discharge (up to 7 days) Outcome Measures: Recurrence (numbers that don't) Mean % change in weight Mean length of hospital stay (days)	No recurrence graded vs. full strength 19 (60%) vs. 17 (57%) (NS) Mean % weight change No significant differences between grps although graded feeders lost more weight at start (data in graph form only). Mean hospital stay 4.3±1.7vs. 4.2±1.6 days (NS)	There was no difference in the incidence of recurrence of diarrhoea, effect on weight or duration of hospital stay between the graded and immediate full strength feeding groups.	Randomisation was stated but not described Dropouts were described Lack of relevant clinical data and brief description of those that were included Infants whom experienced recurrence of diarrhoea were settled on a lactose free formula The funding of the study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Rees L;Brook CG; 1979 Apr 7 {39657}	Study Type: Comparative RCT Evidence level: 1- UK	n=16 full strength milk n=16 clear fluids and full strength milk n=14 clear fluids and gradual reintroduction of full strength milk	Children (aged 6wks to 4 yrs) with gastroenteritis (<5 days duration) and mild dehydration admitted to hospital	Intervention: Children were randomly assigned to either a) full strength milk or b) Clear fluids (0.18% NaCl & 4% dextrose in water) until diarrhoea settles then full strength milk or c) Clear fluids (0.18% NaCl & 4% dextrose in water) until diarrhoea settles then milk given diluted then increased by 1/4 every 8 hrs until full strength achieved Comparison: using grps b) & c) Full strength vs. graded feeding	Follow-up period: ~4 days (length of hospital stay) Outcome Measures: Average length of hospital stay (days)	Average length of hospital stay Grp a vs. Grp b) vs. Grp c) 3.4±1.5 vs. 3.2±1.0 vs. 3.6± 1.4 days NS	There was no difference in hospital stay of children with acute diarrhoea receiving full strength or graded milk feeds.	Randomisation was stated but not described Lack of clinical outcomes e.g. weight, duration of diarrhoea The funding of the study was not declared

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Dugdale A; Lovell S; Gibbs V; Ball D; 1982{39901}	Study Type: Comparative RCT Evidence level: 1- Australia	n=28 rapid refeeding n=31 graduated feeding n=62 were initially enrolled but n=3 were immediately excluded as they were not age matched with the other grp	Infants (mean age ~22 mths) with acute gastroenteritis (<7 days) and mild or moderate dehydration, admitted into hospital	Intervention: After initial assessment and rehydration as appropriate infants were randomised to either a) Immediate resumption of normal milk and food. or b) Graduated feeding: half strength whole milk for 24 hrs followed by normal feeds Clear fluids were given if deemed appropriate Comparison: Graduated vs. immediate full strength feeding	Follow-up period: one week after discharge Outcome Measures: Total stay in hospital (days) Weight changes (kg) during first 24 hr of refeeding	Total stay in hospital immediate resumption vs. graduated feeding 4.7(3-7) vs. 5.4(3-9) days p>0.05 Weight changes (24 hrs) both were losses -0.02±0.25 vs.- 0.14±±0.2 kg P>0.05	The rapid refeeding group with full strength milk lost less weight and went home early than the group who had graduated feeding.	Randomisation was stated but not described Short term study with short term outcome measures i.e. 24 hrs although infants were checked at home a week later (no data). The funding of the study was not declared

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Ransome OJ; Roode H; 1984 {39708}	Study Type: Comparative RCT Evidence level: 1- South Africa	n=37 full strength cow's milk n=37 graduated milk n=8 and n=5 respectively were withdrawn from the groups because of lactose malabsorption	Children (3-36 mths) with acute gastroenteritis requiring i.v. therapy and at least 5% dehydrated	Intervention: Following assessment and rehydration, children were randomised to either a) full strength cow's milk or b) Ist day 1/2 strength 2nd day 2/3 strength 3rd day 2/3 strength 4th day full strength cow's milk Comparison: full strength vs. graded refeeding	Follow-up period: 4 days Outcome Measures: Mean duration of diarrhoea (days)	Duration of diarrhoea Full strength vs. graded refeeding 2.62±0.35 vs. 2.46±0.35 p=0.71	Early introduction of full strength cow's milk does not prolong the course of acute gastroenteritis	Randomisation was stated but not described Children with lactose intolerance were withdrawn assumably they would have not recovered so well. Lack of clinical outcomes e.g. weight The funding of the study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Valois S; 2005 {38903}	Study Type: RCT Evidence level: 1++	90 children in total 30 - White Grape Juice 30 - Apple Juice 30 - coloured and flavoured water	male infants aged 4-18 months with severe diarrhoea and moderate dehydration.	Intervention: The effects of juice consumption during diarrhoea is being assessed. Treatment arm 1 - Apple juice Treatment arm 2 - White grape juice control arm - coloured flavoured water Comparison: Comparisons are made between the arms of duration and severity of diarrhoea as well as fecal losses througout the study. Fluid intake and vomitus losses were also compared between groups.	Follow-up period: Infants were followed up for 1 week Outcome Measures: duration of illness severity of diarrhoea (assessed by number, type and consistency of stools) amount of fecal losses (g/kg/day) vomitus losses fluid intake required to maintain fluid balance body weight changes	Total duration of diarrhoea reported as mean hours (SD) Apple juice - 111.7 (48.2) White grape juice - 105.4 (44.9) Water - 80.0 (39.6) significance not reported duration of diarrhoea in hours after randomisation Apple juice - 49.4 (32.6) White grape juice - 47.5 (38.9) Water - 26.5 (27.4) P< 0.05 for water vs. juice groups number of patients vomiting during the first day of treatment apple juice - 22 White grape juice - 26 water - 19	All patients recovered with appropriate treatment without anyone developing persistent diarrhoea.	Even though the study was primarily designed to compare juices with water, the fact that none of the infants had diarrhoea for more than 14 days, attests to the fact that this data can be used to answer the clinical question

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Jan A;Rafi M;Mustafa S;Rasmussen ZA;Thobani S;Badruddin SH; 1997 Jan {39720}	Study Type: Comparative RCT Evidence level: 1- Pakistan	n=38 Dowdo grp n=38 Khitchri grp n=2 patients withdrew (one from each grp) due to short hospital stay and unwillingness parents to adhere n=3 treatment failures (could not adhere to diet)	Children (aged 6-36mths, mean 13-14mths) with acute gastroenteritis (<7 days duration) with a range of dehydration from 'none', 'some' and 'severe.' admitted to hospital	If dehydrated (see notes) mild cases with treated with ORS, severe with iv. For 4-5 hrs. Followed by randomisation to either **Dowdo diet:** atta (whole wheat flour), cow's milk, oil, salt, water cooked or **Khitchri diet:** rice, Mongdal (lentils), oil, salt, water cooked With a target intake of 110Kcal/kg/day, offering food at 3 hour intervals. Comparison: Dowdo vs. Khitchri diet	Follow-up period: 5 days Outcome Measures: Total weight change (g) Duration of hospitalisation	**Total weight change (g)** Dowdo vs. Khitchri median 150 vs. 140 range -500 to +640 vs. -440 to +920 **Duration of hospitalisation (days)** median 69.5 vs. 62 range 19-192 vs. 20-216	Author's concluded that feeding Dowdo was as effective as Khitchri in children with acute diarrhoea	Over 50% of children were not dehydrated on admission Randomisation appropriate Mothers reported that the children preferred dowdo the best and that they were more likely to use this approach at home. Financial support for his was project was received from the applied Diarrhoeal Disease Research project (Harvard)

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Alarcon P;Montoya R;Rivera J;Perez F;Peerson JM;Brown KH; 1992 Jul {39713}	Study Type: Comparative RCT Evidence level: 1- Peru	n=25 rice, beans and vegetable oil (RB) n= 21 rice, soy protein isolate, corn syrup solids and vegetable oil (RS) n=5 treatment failures were 8% RB vs. 14% RS (p=0.058) Further n=3 were eliminated from analysis due to intercurrent illness.	Infants (aged 6-24 mths, mean~11mths) with acute gastroenteritis (<96hrs) with a range of dehydration from mild to severe admitted to hospital	Rehydration therapy was provided according to WHO guidelines usually for the first 4 hours post admission and then the infants were randomised to either a) **RB diet:** rice, white beans (*Phaseolis vulgaris*, 'frijol canario') and soybean: cottonseed oils (55:45) or b) **RS diet:** rice, soy protein isolate, corn syrup solids and soybean: cottonseed oils, 55:45) both 80Kcal/100g and were offered *ad libitum* in 6 divided feeds A vitamin mix was also given to both grps. Comparison: Bean vs. soy component of a mixed food diet	Follow-up period: 6 days Outcome Measures: Change in body weight Duration of diarrhoea	Both grps consumed ~95kcal/BW for 1st day after that mean intakes rose. The RS grp levelled off at 140kCal/kg day at day 4 but Grp RB intake continued to rise. Energy consumption of RB compared to RS diet during days 4-6 was significantly greater (p<0.02). **Changes in body weight** Infants in both grps gained on average 100-200g in 1st day. After this RS grp weights did not change significantly, RB declined to towards their admission weights. Data is graph form only. Author's state that weight differences were only significant (p=0.047) due to day 1rehydration. **Duration of diarrhoea** The estimated median duration of illness was 60 hrs in grp Rb vs. 121hrs in grp RS (p=0.01) (survival analysis. Data in graph form only).	The duration of diarrhoea was significantly less in the bean diet compared to the soy diet but there were no significant difference in infant weight between the two groups.	Double-blinded study, food dye was added to diets. Randomisation was appropriate numbers of participants was small before dropouts/exclusions This study was financially supported by the Applied Diarrhoeal Disease Research project (Harvard) for the International Development Cooperation Agreement.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Mitra AK;Rahman MM;Mahalanabis D;Patra FC;Wahed MA; 1995{39717}	Study Type: Comparative RCT Evidence level: 1- Bangladesh	n=32 amylase of germinated wheat flour (ARF) treated porridge diet n=32 unaltered thick porridge n= 31 porridge diluted with extra water n=102 were enrolled, 7 dropped out before being assigned to treatment	Infants (aged 6-23 mths, mean ~12mths) with acute gastroenteritis (<72hrs) with 'some' (majority) or ' marked' dehydration and admitted into hospital	Infants were rehydrated with ORS or i.v solution as appropriate for 224 hrs before being assigned to a treatment a) ARF treated porridge b) unaltered thick porridge c) Porridge diluted with water each treatment was offered 4x daily (30 minute slots) Intake was monitored All infants received milk (breast or other) outside these periods Comparison: three porridge regimes with the assumption the ARF treated one as a test diet	Follow-up period: 5 days Outcome Measures: Weight changes (kg) Diarrhoea duration after admission (h)	The mean intake of porridge was (g/kg.d) ARS vs.thick vs. diluted 44 ±13 vs. 28 ±15 vs. 58±17 Total energy intake:(kJ/kg.d) 414 ±97 vs.355± 120 vs. 351± 73 ANOVA p<0.001 in favour of test diet **Weight changes (Kg)** (from admission to discharge, after 4 days of any diet) - -0.01±-0.3 vs. 0.00±0.27 vs. -0.06±-0.27 (NS) **Diarrhoea duration (hr)** 0.96±43 vs. 0.00±-47 vs. 94 ±44 (NS)	An ARS- treated porridge was more palatable (more was consumed) than the other porridge formats but this had no effect on weight of infant or length of illness	Majority of infants were mildly dehydrated and not malnourished Main result is that infants found ARS treated porridge easier to eat. Randomisation was appropriate This study was financially supported by the Swiss Development Cooperation and the International Centre for Diarrhoeal Disease Research Bangladesh.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Darling JC;Kitundu JA;Kingamkono RR;Msengi AE;Mduma B;Sullivan KR;Tomkins AM; 1995 Jul {39739}	Study Type: Comparative RCT Evidence level: 1- Tanzania	n= 26 normal corn porridge diet n=25 amylase digested (AMD) porridge diet n=24 fermented and amylase digested (FAD) porridge diet n=81 presented but n=6 were excluded due to dysentery and not satisfying the inclusion criteria n=4 left the study because they required nasogastric feeding There were 4 deaths during admission (5% mortality)	Children (aged 6-25mths, mean 9-11.5mths) with acute gastroenteritis (<14 days) severe enough to warrant admission with a range of dehydration including 'none', 'some' (majority) and 'severe'	Children were entered into the study following rehydration between 4-24hrs after admission randomised to a) Normal corn porridge b) AMD porridge c) FAD porridge Study foods were prepared by staff in 300g portions and served *ad libitum* 5 times a day. Intake was monitored Most infants were being breast fed and this was encouraged Further i.v. rehydration was required in n=6 infants and there was a systematic infection in n=23 infants spread across the grps Comparison: Three porridge diets	Follow-up period: 9 days Outcome Measures: Duration of diarrhoea (hr) Recurrence of diarrhoea Median weight changes	Over the 4 day period, the mean daily energy intake was significantly greater in the AMD (42% more, p=0.003) than the normal porridge grp. The energy intake of the FAD diet was not different from the other two at any point. **Duration of diarrhoea** (using survival analysis showed no significant differences between the grps p=0.54 No difference in recurrence of diarrhoea between the grps. **Median weight changes** (as a % of admission weights were between -0.5±1.0 percent) for the 4 days of study and were no difference between the grps.	The energy intake of the AMD diet was 42% greater than the normal porridge grp but this had no bearing on the clinical outcome of diarrhoea	Children as a grp were moderately malnourished at start of study and 31% were unwell during study (infections) the trial was not blinded the randomisation was appropriate 4 deaths and 4 dropouts reduced power of study. This study was financially supported with the Overseas Development Administration.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Alarcon P; Montoya R; Perez F; Dongo JW; Peerson JM; Brown KH; 1991 {39607}	Study Type: Comparative RCT Evidence level: 1- Peru	n= 29 soy-protein, lactose-free formula n=28 mixed food diet plus wheat n=28 mixed food diet plus potato n=88 were initially admitted to study from which n=3 were eliminated due to meningoencephalitis (n=1) and withdrawal by parents (n=2) n=5 were considered treatment failures (distributed 1, 2, 2 between grps) of which n=1 had severe diarrhoea on day 6 and n=5 had recurrent dehydration	Infants (aged 5-24mths, mean ~12mths) with acute gastroenteritis (<96hrs) with mild (majority) to severe dehydration and admitted into hospital	Rehydration therapy was provided according to WHO guidelines and this was usually completed within 4hrs. The infants were then randomised to either a) (Isomil) **soy formula** (lactose free) (SP) or b) wheat peas diet (toasted wheat flour, toasted pea flour, carrot flour, soybean oil: cotton seed oil 55:45) and cane sugar (WP) or c) **potato milk diet:** potato flour, dry whole milk, carrot flour, soybean oil: cotton seed oil 55:45) and cane sugar (PM) all diets were 73.3kcal/100ml. Formula fed by bottle. Solids by cup and spoon All diets were offered to a maximum intake of 110cal/kg of BW per day plus a vitamin mixture for both grps Comparison: Soy formula vs. solid food (wheat vs. solid food (potato)	Follow-up period: 7 days Outcome Measures: Median duration of diarrhoea (hrs) Mean cumulative increment in body weight from admission (Kg)	There were no significant differences in energy intake by dietary grp. **Median duration of diarrhoea (hrs)** Kaplan survival analysis PM vs. WP vs. SF 55hrs vs. 57hrs vs. 154hrs (p=0.005) calculated as unadjusted and adjusted. No details given. **Mean cumulative increment in body weight from admission (Kg)** There were no statistically significant differences between the 3 grps at any one point of the 7 day study. (data shown in graph form only)	Locally available, lost cost staple food mixtures (wheat & potato based) are a safe alternative to lactose free formula in the post rehydration phase following gastroenteritis in infants and in this study shortened the duration of diarrhoea.	Randomisation was appropriate Blinding was not achieved as formula was fed by bottle and solids by cup and spoon sparse description of duration of diarrhoea and weight data This study was financially supported by the Office of S & T Nutrition, US Agency for International Development and the local USAID Mission. Supplies of Isomil were provided by Ross

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Grange AO;Santosham M;Ayodele AK;Lesi FE;Stallings RY;Brown KH; 1994 Aug {39767}	Study Type: Comparative RCT Evidence level: 1- Nigeria	n= 36 maize-cowpea-palm oil diet (MCP) n= 38 soy-protein lactose-free formula diet (SF) n=5 did not remain in study of which n=2 had measles/septicaemia (both SF grp) and n=3 were withdrawn by parents (2 SF grp 1 MCP grp) n=9 were also either withdrawn later (4-6 days) in the study by parents(n=6), had recurrent diarrhoea (n=2) or developed measles (n=1) but their data was included in the analysis	Male infants (Aged 6-24mths, mean ~10mths) with acute gastroenteritis(<72hrs) of which 20% of the MCP grp and 42.4% of the SF grp were severely dehydrated and were admitted to hospital	Infants were rehydrated according to WHO guidelines and assessed at 4hrs and if still dehydrated treated for a further 4hrs to complete hydration Infants were then randomised to either a) **MCP grp:** fermented maize flour, toasted cowpea flour, palm oil and sugar or b) **SF grp**: lactose-free soy protein isolate formula (Isomil) Both diets were 67kcal/100ml a total of 150kcal/kg bodyweight/day was offered in 5/6 feeds per day for 6 days of hospitalisation. Consumption was monitored Water was offered to a maximum of 10ml/kg/period. A multivitamin was also given Comparison: MCP diet vs. SF diet	Follow-up period: 6 days Outcome Measures: Median duration of diarrhoea (hr) Mean weight change	Prior to interventions grps were not equal in terms of % severely dehydrated and this affected some of their clinical characteristics at baseline Infants on SF diet consumed significantly more than the MCP diet from day 1-6 (P<0.001) **Unadjusted estimated median duration of diarrhoea** in hospital was 42hrs in grp MCP vs. 104hrs in grp SF (p<0.001) Data presented as graph. It was stated that adjustment did not affect result but data not presented 'Infants in the SF grp gained weight consistently, with a final increment of approximately 40g at 6 days' 'Infants in the MCP had a less consistent weight gain with a slightly negative weight increment during the study.' These differences were stated to be statistically significant between grps at 3-6 days but data not shown (graph only)	Less MCP diet was consumed than SF diet but MCP diet resulted in a significantly reduced duration of diarrhoea but the SF diet resulted in more steady weight gain?	Grps were not equal to start in terms of their clinical condition Lots of graphs but not enough data Confusing results Randomisation appropriate Study not blinded This study was financially supported by the Office of S & T Nutrition and the US Agency for International Development.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Maulen-Radovan I;Brown KH;Acosta MA;Fernandez-Varela H; 1994 Nov{39737}	Study Type: Comparative RCT Evidence level: 1- Mexico	n=44 Mixed diet (MD) n=43 Soy formula (SF) n=6 treatment failures all in soy grp due to recurrent dehydration and severe diarrhoea followed by recurrent dehydration	Male children (aged 5-36mths, mean~11mths) with acute dehydration (<96hours) and a range of dehydration from mild to severe (WHO guidelines) and admitted in hospital	Rehydration therapy was provided according to WHO/UNICEF guidelines for the first 6 hours followed by either a) Mixed diet: rice, chicken, brown beans, carrots and vegetable oil blended into a puree. Feed with cup and spoon b) Soy formula fed by bottle 25kcal/kgBW was offered by carer at 4 hour intervals A maximum intake of 150kcal/kg was permitted per day Infants were also permitted plain boiled water Comparison: Mixed solid diet vs. soy formula	Follow-up period: 6 days Outcome Measures: Duration of diarrhoea (hrs) Weight change (g)	Energy consumption was similar in both grps. **Median duration of diarrhoea (survival analysis)** MD vs. SF 25 hrs(CI 21 to 29) vs. 67hrs (CI 56 to 79) p<0.001 **Cumulative weight During 6 days** 63±50g/kg BW vs. 37±60gm/kg BW (p=0.04) but if calculated from day 2 (post rehydration) to day 7 the weight changes were NS	Infants with acute diarrhoea improved quicker on a mixed solid diet as compared to soy formula diet	Impossible to blind treatments Randomisation appropriate No information on the financial support of this study.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Isolauri E; Vesikari T; Saha P; Viander M; 1986 {39899}	Study Type: Comparative RCT Evidence level: 1- Finland	n=38 milk containing diet n=27 milk free diet	Infants (mean age 14.7 mths) with acute gastroenteritis (<4 days) with mild or moderate dehydration and admitted to hospital	Intervention: Following assessment and appropriate rehydration for 6-10 hrs with ORS, infants were randomised to either a) Milk containing diet including plain milk, milk based gruel, sour milk, yoghurt and ice cream. Or b) Milk free diet (no details) plus both grps received an ordinary diet of broth, soup, mashed vegetable, potato, meat, porridge, strained and jellied berries, banana and juice. mean intake 800 kcal daily Comparison: lactose vs. lactose free diet	Follow-up period: 3 days Outcome Measures: Duration of (watery) diarrhoea (days) Length of hospital stay (days) Weight gain (g) at day 1 & 3	Duration of diarrhoea (n=8 infants had passed no stools once on ward) remaining infants lactose free vs. lactose 1.3+/-0.7 vs. 1.2+/-0.8 days NS Length of hospital stay 2.9+/-1.2 vs. 3.1+/-1.6 days NS Weight gain (g) day 1 +313 +/-476 vs. +181+/-173 NS day 3 +292+/-470 vs. +175+/-169 NS	There was no difference in the clinical recovery of infants with acute diarrhoea with either a milk free or milk diet therefore the authors recommend rapid reintroduction of feeding with no dietary restrictions in this age group.	Randomisation was stated but not described No details on dropouts Diet were under the control of parents and therefore may have deviated from the protocol The study was funded by the Finnish Foundation for Pediatric Research and the Sigrid Juselius Foundation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Lozano JM;Cespedes JA; 1994 Mar {39759}	Study Type: Comparative RCT Evidence level: 1- Columbia South America	n=29 lactose free formula n=28 lactose formula Of which n=2 in the lactose free grp were excluded due to their disease being secondary to *E. histolytica* & n=1 in the lactose grp due to referral to another hospital. A further n=1 from each grp dropped out.	Infants (aged 1-24mths, mean ~11-13mths) with acute gastroenteritis(<1 wk) with mild or moderate dehydration admitted into hospital.	All infants received parenteral fluids followed by ORS for on average the first 12 hrs and were stratified for age and nutritional status and randomised to either a) lactose free formula (AL-110) or b) lactose formula (NAN 1 for infant <6mths) (NAN 2 for infants>6mths) For both grps, the milk was administered at half strength for the first 24 hrs by the end of the 2nd day; all infants were on full strength milk. Comparison: lactose vs., non-lactose formula	Follow-up period: up to 2 days Outcome Measures: Mean duration of diarrhoea (hrs) Body weight increment (kg)	**Mean duration of diarrhoea (hrs)** lactose free vs., lactose 41.9±32 vs., 54.5±-40 p=0.247 **Body weight increment (kg)** **at third visit** (no details but mean follow up was 43hrs) 0.8kg ±0.5 vs. 0.82kg ±0.5 p=0.918	The results of this study suggest that using lactose free as opposed to a lactose formula for infants confers no benefit in the early refeeding period post acute diarrhoea.	Randomisation appropriate no blinding Small study with dropouts/withdrawals No information on the financial support of this study.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Simakachorn N;Tongpenyai Y;Tongtan O;Varavithya W; 2004 Jun {39724}	Study Type: Comparative RCT Evidence level: 1- Thailand	n=40 lactose free formula n= 40 lactose formula n=3 (n=2 lactose free, n=1 lactose dropped out of study. n=6 unscheduled i.v. infusions (n=2 lactose free, n=4 lactose)	Male infants (aged 3-24mths, mean 11-13mths) with acute gastroenteritis (<7 days) with mild or moderate dehydration and admitted into hospital.	After appropriate rehydration by WHO guidelines infants were randomised to either a) lactose free formula or b) lactose formula Both for 90ml/kg/day and alternated with 90ml/kg/day of ORS for the 4-24 and 24-48hrs period to give ~180ml/kg/day Infants were also fed rice gruel as tolerated and appropriate for age after 4 hrs of rehydration Comparison: lactose free vs. lactose formula	Follow-up period: 7 days Outcome Measures: Duration of diarrhoea (hrs) Weight change %	**Duration of diarrhoea (hrs)** lactose free vs. lactose Survival analysis median duration of diarrhoea 77 vs. 97.5hrs p=0.002 t-test 64.2hrs±39.9 vs. 92hrs±43.3hrs p=0.003 **Weight change %** Day 1: 1.51±1.71 vs. 0.31±1.98 p=0.005 On day 2 &5 there was no stat. signif. differences in % weight changes	The use of lactose free formula for infants with acute diarrhoea significantly shortened the duration of diarrhoea compared with lactose formula. Although there was a trend towards better weight gain, this was only significant at 24hrs. Infants receiving the lactose free formula tolerated it well.	Randomisation was appropriate No details on the tolerability assume it is extrapolated from low dropout described as double-blind and details given The International Nutritional Research Institute Denmark and Dumex Ltd Thailand supplied the formula. The international Nutrition Research Institute, Denmark provided the financial support for the present study.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Gabr M; Maraghi S; Morsi S; 1979 {39905}	Study Type: Comparative RCT Evidence level: 1- Egypt	n=29 milk based formula n=29 soy based lactose free formula	Well nourished infants (aged 3-18 mths) with their first attack of acute gastroenteritis (3-7 days) and moderately or severely dehydrated	Following assessment and rehydration, infants were randomised to either a) milk formula containing lactose or b) lactose free soy formula at half strength for 3-4 days followed by full strength Comparison: lactose vs. non lactose	Follow-up period: 2-8 weeks Outcome Measures: Recurrence of diarrhoea (%)	Recurrence of diarrhoea (n) Lactose vs. no-lactose day 1: 0 vs. 0 day 6 : 15 (21%) vs. 4.0 (21%) p<0.05	The author's suggest that due to the recurrence if diarrhoea in the lactose group compared to the soy group, infants with acute diarrhoea should be given lactose-free formula for at least 8 weeks.	Randomisation was stated but not described No details on dropouts No other relevant clinical outcome measures reported e.g. weight The funding of the study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Haffejee IE; 1990 {39537}	Study Type: Comparative RCT Evidence level: 1- South Africa	n=120 milk formula n= 79 breast milk n=35 breast & supplementation n=75 soy formula n=316 were initially enrolled but there n=2 deaths, n=5 on going diarrhoea spread across the groups	Children (age range 3 days to 28 mths (mean 5.5 mths) with acute gastroenteritis (< 7 days) and dehydration leading to being admitted to hospital	Following assessment and appropriate rehydration children were randomised to either a) cow's milk based formula or b) breast milk or c) breast milk plus supplementation or d) Soya formula Notes. Children on formula before study were randomised to one of two of the study formula. Breast feed children remained on breast milk Comparison: Cow's milk (lactose) vs. breast milk vs. soy formula (no-lactose)	Follow-up period: until recovery Outcome Measures: Duration of diarrhoea (hours)	Duration of diarrhoea Cows vs. breast vs. breast & sup vs. soy 70.5±60.3 vs.60.9±44.8 vs.64.8 ±43.4 vs. 61.4 ±43.5 hrs (NS) Sub analysis of age, duration of diarrhoea prior to admission and type of organism (rotavirus or other) did not influence duration of diarrhoea post admission	These data suggest that lactose free feeds are not required following hospital admission of children with acute gastroenteritis	Randomisation was not appropriate (sealed envelope- no details) and the feeding status of the children had to be taken into account prior to the procedure. Dropouts/exclusions were described Pragmatic study This study was funded by the South African MRC

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Santosham M;Goepp J;Burns B;Reid R;O'Donovan C;Pathak R;Sack RB; 1991 May {39712}	Study Type: Comparative RCT Evidence level: 1- USA	n=29 early feeding n= 27 late feeding (n=59 started of which 3 dropped out in the 1st 24hr due to non adherence)	Infants (aged 2-12 mths, mean~6mth) with acute diarrhoea (<7 days duration) and <7% dehydration (used standard criteria) under outpatient management	On presentation and following assessment infants were randomised to either Early feeding: Mothers were provided with a soy-based lactose-free formula (Nursoy) and an ORS to give their infant at ~100ml/kg per 24 hr of each. Mothers were asked to give alternate ad libitum feedings with each liquid during a 24 hr period or Late feeding: Mothers were provided with ORS only, to alternate with water for the first 24hr ad libitum. After 24 hr infants moved on to alternate half strength soy formula (as above) with ORS for the next 24hr and then full strength soy formula for the following 24 hrs both regimes continued until resolution of illness Comparison: Early vs. late feeding	Follow-up period: Two weeks after initial presentation Outcome Measures: % resolved illness at 24,48 or post 48hr Duration of diarrhoea (days) % weight gain at 24hr and resolution of diarrhoea, 2wks later	% resolved illness (early vs.late) at 24hr 13% (44.8) vs. 6%(22) (NS) at 48hr 21%(72) vs. 12%(44) (p=0.02) post 48hr 6%(20.7) vs. 15%(55.6) p<0.1 Duration of diarrhoea (days) 2.0 ±0.2 vs. 2.7±1.3 (p=0.02) % weigh gain at 24hr 1.5±3.5 vs. 2.5±3.7 (NS) at resolution 1.8±3.5 vs. 1.2±2.2 (NS) 2wks after therapy 3.0±6.2 vs. 3.4±2.9 (NS)	The authors concluded that the soy-based, lactose-free formula is safe and may shorten the duration of diarrhoea in infants.	Size effects on the duration of diarrhoea are small and % resolved illness data does not support the fact this formula produces clinically relevant outcomes Randomisation method is appropriate This study was supported by a grant from Wyeth laboratories (producers of soy formula & ORS)

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Bhan MK;Arora NK;Khoshoo V;Raj P;Bhatnager S;Sazawal S;Sharma K; 1988 Mar {39728}	Study Type: Comparative RCT Evidence level: 1- India	n=30 cows' milk formula n=30 lactose-free cereal based formula n=3 were treatment failures or which n=2 in the lactose free grp lost weight and cultures showed Salmonella and n=1 in the cow's milk grp showed intolerance. All three were excluded from analysis.	60 infants (mean age ~9 mths) with mild acute gastroenteritis (</=7 days) and no dehydration	Intervention: Following assessment, infants were randomised to either a) milk free formula (rice powder, mung bean powder, sugar, coconut oil) (Nestum, Nestle) or b) cow's milk formula (lactogen full protein, Nestle) For at least 7 days Both provide 77kcal/100ml ORS was given for each liquid stool passed. No other foods were allowed during the first 7 day period Comparison: Lactose free vs. lactose	Follow-up period: 11 days plus Outcome Measures: Duration of diarrhoea (days) Weight gain (g/kg admission weight/day) on day 4, 7 and recovery	Duration of diarrhoea Non-lactose vs. lactose 11.0+/-10.0 vs. 7.6 +/-10.8 days NS Weight gain day 4: 1.45+/-9.9 vs. 7.31+/-8.8 p<0.05 day 7: 2.2+/-6.1 vs. 5.4+/-7.9 NS Recovery: 2.0+/-4.2 vs. 5.8+/-7.8 p<0.05 (energy intake was less in the non-lactose grp vs. lactose grp at day 4 & 7, statistically significantly so at day 7 p<0.05)	Cow's milk formula was well tolerated by the infants, the infants who were fed the non-lactose feed showed less energy intake and gained weight less rapidly.	Randomisation was appropriate (block randomisation) Treatment failures were described Data suggests the non-lactose feed was less palatable The funding of the study was not declared

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient Characteristics	Intervention & Comparison	Follow-up & Outcome Measures	Effect Size	Study Summary	Reviewer Comments
Romer H;Guerra M;Pina JM;Urrestarazu MI;Garcia D;Blanco ME; 1991 Jul {39734}	Study Type: Comparative RCT Evidence level: 1+ Venezuela	n= 37 cow's milk n=36 chicken - based formula n=4 in cow's milk grp & n=2 in chicken formula grp did not have diarrhoea after admission to study. N=4 in cow's milk grp and n=1 in chicken formula grp did not tolerate their treatment n=2 (one in each grp) had antibiotics	Male infants (aged 3 to 14 months) with acute gastroenteritis (<96hrs) with mild or moderate dehydration and admitted into hospital	Intervention: Following assessment, infants were given WHO-ORS for 4hrs after which they were randomised to either a) Cow's milk at normal concentration for age (8.8% for 3-6mths old, 13.5% for >6 mths old) Or b) Experimental soup (59% green plantain hydrolysed with fungal alpha-amylase, 27% chicken meat with skin and 14% coconut oil (salt adjusted to same as cow's milk) at the same concentration according to age Infants also received WHO-ORS and unrestricted water as required. Breast feeding was continued as prior to study. Comparison: Cow's milk feeding versus chicken-based formula feeding	Follow-up period: 1 month Outcome Measures: Duration of diarrhoea (hrs) Weight increase after admission as % at 48 hrs and discharge	The only difference in dietary intake between the two grps was water consumed in which the cow's milk grp drank significantly more p</= 0.025 Diarrhoea duration (hrs) (cow's vs. chicken formula) 75.53 (9.73) vs. 55.59 (8.92) hrs (NS) Weight increase after admission as % at 48hrs 2.74 (0.69) vs. 5.53 (0.65) (NS) at discharge 3.39 (0.75) vs. 2.19 (0.55) (NS)	The infants on cow milk formula had a shorter duration of diarrhoea than those on chicken formula but this difference was not statistically significant. % weight changes were similar between both groups at 48hrs and on discharge.	Randomisation was appropriate (block randomisation) Dropouts were described. Although the authors high-light the 20 hr mean difference between the groups in terms of duration of diarrhoea, this figure is rended not statistically significant by the variation in the point data. This study was financially supported by CONICIT PC004 and ENGAST

Antibiotic therapy

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Cryptosporidium						
Abdel-Maboud 2000 {42816} Location : Egypt	**Study Type** RCT **Evidence Level** 1-	**Total number of participants** N = 150 Results for 73 children reported here Randomised into three treatment arms Group 1 Intervention : Nitrazoxanide n = 24 Group 2 Intervention : Co-trimoxazole n = 24 Group 3 Intervention : Placebo n = 25	**Inclusion criteria:** Adults and children with diarrhoea attending out-patients who had a stool examination (MZN and IFA tests) which was positive for Cryptosporidium **Exclusion criteria :** Patients with a stool examination (MZN and IFA tests) negative for Cryptosporidium None other stated **Withdrawal criteria :** Not stated	**Comparison** Nitazoxanide vs Co-trimoxazole vs Placebo Intervention details: **Group 1:** Nitazoxanide at 100mg/12hours for children<=4 yrs 200mg/12 hours for children >=4 yrs for 3 successive days **Group 2:** Co-trimoxazole (sulphamethoxazole 200mg + trimethoprim 70mg)/12hrs for children<=4 yrs 10ml/12hours for children >=4 yrs for 6 successive days **Group 3:** Placebo no further details given	**Follow up :** Samples obtained at day 7 and 10 from treatment start **Outcome measures:** ***- Proportion of individuals "cured" (presumed within 10 days)*** Group 1 = 21/24 Group 2 = 8/24 Group 3 = 9/25 Gp1 vs Gp 3 RR 2.43 [95% CI 1.41 to 4.19] p= 0.001 Gp 2 vs Gp 3 RR=0.93 [95% CI 0.43 to 2.00] p=0.84	**Funding :** Not stated Applicable to UK Baseline comparability Not stated Allocation concealment : Not stated Sequence generation : Not stated Blinding of outcome assessors : Not stated Loss to follow up 2/75 children in Intention to treat analysis : No Power calculation : Not stated
Campylobacter						
Robins-Browne 1983a {42834} Location : South Africa	**Study Type** RCT **Evidence Level** 1-	**Total number of participants** N = 25 C jejuni only N=8	**Inclusion criteria:** Children aged 1 to 24 months admitted to hospital with a history of diarrhoea of duration <96hrs, who had received no antimicrobial therapy for this illness.	**Comparison** Erythromycin vs placebo Intervention details:	**Follow up** Daily examination for 7 days **Outcome measures:** ***Mean duration of abnormal***	**Funding :** South African MRC University of Natal, Abbott Laboratories Applicable to UK

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
		Randomised into two treatment arms Group 1 Intervention : Erythromycin All participants n = 11 C jejuni infection only n = 4 Group 2 Intervention : Placebo All participants n = 14 C jejuni infection only n = 4	Confirmation of C jejuni and any other infection from microscopic and culture examination of stool samples. **Exclusion criteria :** No details **Withdrawal criteria :** No details	**Group 1:** Erythromycin ethylsuccinate oral suspension, 40mg/kg/day in divided doses for 5 days **Group 2:** Placebo oral suspension	***stool frequency*** All participants Group 1 = 0.77+-0.47 days Group 2 = 1.57+-1.59 days P = NS C jejuni only Group 1 = 0.8+-0.5 days Group 2 = 1.8+-2.5 days P = NS ***Mean duration of abnormal stool consistency*** All participants Group 1 = 5.27+-1.68 d Group 2 = 5.79+-1.25 d P=NS C jejuni only Group 1 = 5.3+-1.7 days Group 2 = 6.0+-1.2 days P=NS ***Mean duration of vomiting*** All participants Group 1 = 3.5+-0.71 d Group 2 = 3.8+-1.3 d P = NS C jejuni only Group 1 = 0 Group 2 = 3.0 d ***Mean duration of dehydration*** All participants Group 1 = 2.91+-1.81 d Group 2 = 2.79+-1.97 d P=NS C jejuni only Group 1 = 1.8+-1.5 days Group 2 = 2.3+-2.5 days	Baseline comparability Similar for age, sex, nutritional status, duration of illness, extent of dehydration Allocation concealment : Yes, pharmacy controlled Sequence generation : Code used Blinding of outcome assessors : Yes Loss to follow up 1/26 voluntarily withdrew Intention to treat analysis : Not stated Power calculation : None stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					P=NS ***Fever*** All participants Group 1 = 3.33+-1.63 d Group 2 = 3.6+-1.52 d P=NS C jejuni only Group 1 = 2.0 d Group 2 = 0 d	
Pai 1983 {42832} Location : Canada	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N =32, results for 27 participants with complete data presented Randomised into two treatment arms Group 1 Intervention : Erythromycin n = 15 Group 2 Intervention : No treatment n = 12	**Inclusion criteria:** Children up to 12 years with symptomatic enteritis and their household contacts. Recruitment when stool samples from children had positive culture of erythromycin sensitive campylobacter. **Exclusion criteria :** Presence of other enteric pathogens in the stool, antibiotic therapy in previous 2 weeks and patients with a positive culture who were no longer symptomatic **Withdrawal criteria :** Not stated	**Comparison** **Erythromycin vs no treatment** Intervention details: **Group 1:** Erythromycin ethylsuccinate oral suspension, 40mg/kg/day every 6 hours for 7 days **Group 2:** No treatment	**Follow up** All participants contacted until all of the household had three consecutive negative (weekly) stool samples Clinical symptoms assessed and reported daily by parent on telephone **Outcome measures:** ***Mean no of days with diarrhoea*** Group 1 = 3.2 +/- 1.7 Group 2 = 3.8 +/- 4.0 WMD -0.60 [95% CI -3.02 to 1.82] p=0.63 ***Range of no of days with diarrhoea*** Group 1 = 1-6 Group 2 = 1-15 ***Mean no of days until first negative culture*** Group 1 = 2.0 +-1.3 Group 2 = 16.8 +-12.5	**Funding :** Applicable to UK Baseline comparability Similar for age, sex, symptoms (diarrhoea, bloody diarrhoea, fever, vomiting), days ill prior to study entry. Allocation concealment : Not stated Sequence generation : Not stated Blinding of outcome assessors: No Loss to follow up 5/32 participants had incomplete data Intention to treat analysis : No details Power calculation : Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					P<0.01	
Salazar-Lindo 1986 {42837} **Location :** Peru	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 30 30 participants had C. jejuni positive stool culture 2/30 had concurrent Shigella infection Randomised into two treatment arms **Group 1** Intervention : Erythromycin n = 14 **Group 2** Intervention : Placebo n = 10	**Inclusion criteria:** Children aged 3-60months brought as outpatient for treatment of acute diarrhoea Five or more loose stools per day with mucous and gross blood or PMN leucocytes for no longer than 5 days, no antibiotic treatment for 7 days, no other illness necessitating antibiotics **Exclusion criteria :** Clinical signs of dehydration, separate episode of diarrhoea during 2 wks prior to coming to hospital, weight/height ratio <3rd percentile. Concurrent Campylobacter and Shigella infection **Withdrawal criteria :** Not stated Confirmation of Campylobacter by stool culture. Confirmation received after randomisation. If treatment failed, cotrimoxazole given as therapy for dysentery.	**Comparison** Intervention details: **Group 1:** Erythromycin ethylsuccinate oral suspension, 50mg/kg/day in 4 doses for 5 days **Group 2:** Placebo oral suspension	**Follow up** Daily stool cultures (except Sundays holidays and daily reporting of symptoms by parents for a period of 5 days Outcome measures: ***Mean duration of diarrhoea*** Group 1 = 2.4+-0.4 days Group 2 = 4.2+-0.3 days P<0.01 ***Number patients with normal stools at 5 days*** Group 1 = 13/14 Group 2 = 5/10 P<0.02 ***Mean days to last positive stool culture*** Group 1 = 0.5+-0.3 days Range 0-5 Group 2 = 2.2+-0.6 days Range 0-5 P<0.01 ***Number patients with positive stool culture at 5 days*** Group 1 = 1/11 Group 2 = 3/5 P <0.05	**Funding :** Abbott Laboratories Nestec Ltd Applicable to UK Baseline comparability Similar for age, sex, weight/length ratio, diarrhoea symptoms, fever, vomiting, infections concurrent with Campylobacter Allocation concealment : Pharmacy controlled Sequence generation : Pharmacy controlled Blinding of outcome assessors : Yes Loss to follow up 4/30 (two from each group) Intention to treat analysis : Partly Power calculation : Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Yersinia						
Pai 1984 {42833} Location : Canada	**Study Type** RCT **Evidence Level** 1-	**Total number of participants** N = 45 results for 34 participants with complete data presented Two treatment arms Group 1 Intervention : Trimethoprim/sulphamethoxazole n = 18 Group 2 Intervention : Placebo n = 16	**Inclusion criteria:** Children under 15 years with symptomatic enteritis and their household contacts. Prior to recruitment, stool samples from children had positive culture of yersinia (confirmation within 2 days of receipt of specimen) **Exclusion criteria :** Presence of other enteric pathogens in the stool, antibiotic therapy in previous 2 weeks and patients with a positive culture who were no longer symptomatic **Withdrawal criteria :** Not stated	**Comparison** Intervention details: **Group 1:** 10mg/kg/day trimethoprim + 50/mg/kg/day sulphamethoxazole oral suspension twice per day for 7 days **Group 2:** Placebo oral suspension	**Follow up** All participants contacted until all of the household had three consecutive negative (weekly) stool samples Clinical symptoms assessed and reported daily by parent on telephone Stool specimens obtained for first 7 days, then weekly. **Outcome measures:** ***Median duration of diarrhoea*** Group 1 = 3.0 Range 1-67 days Group 2 = 3.5 Range 1-27 P = NS **Diarrhoea for <7 days** Group 1 = 1 Group 2 = 1 P = NS ***Recurrence of diarrhoea*** Group 1 = 4 Group 2 = 2 P = NS ***Median no days until bacteriological cure*** Group 1 = 5.5 Range 2-53 Group 2 = 17.5 Range 3-62 P < 0.005	**Funding :** In part from National Health Research and Development (Project 605-1396-40) Drug and placebo supplied by Burroughs Wellcome Applicable to UK Baseline comparability Similar for age, sex, symptoms (diarrhoea, fever, vomiting, abdominal pain), days ill prior to study entry. Allocation concealment : Implied pharmacy controlled Sequence generation : Implied pharmacy controlled Blinding of outcome assessors : Yes Loss to follow up 11/45 Incomplete follow-up (5) Negative stool culture at admission to study (3) Appendectomy (2) Mixed infection (1) Intention to treat analysis : No Power calculation : No

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Positive stool culture at end of treatment Group 1 = 2 Group 2 = 13 P<,0.001 ***Bacteriologic relapse*** Group 1 = 7 Group 2 = 0 P <0.05	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Shigella						
Garcia de Olarte 1974 {42821} Location : Colombia	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 282 Randomised into two treatment arms Group 1 Intervention : Ampicillin n = 142 Group 2 Intervention : Placebo n = 140	**Inclusion criteria:** Infants and children admitted with diarrhoea as a major symptom. Subsequent culture confirmation of Shigella or Salmonella, or E Coli in under 2 years age required. 1 patient without recognised pathogens per 2 patients with Shigella, Salmonella, or E Coli were entered into study **Exclusion criteria :** Other illness requiring antibiotic therapy, age under 6 wks, history of allergy to penicillin or its derivatives **Withdrawal criteria :** Not stated Rectal swab and stool sample examined	**Comparison** Ampicillin vs placebo Intervention details: *Year 1* **Group 1:** IM ampicillin **Group 2:** Injection of sterile fructose *Year 2* **Group 1** Oral suspension of ampicillin 100/mg/kg in equally divided doses every six hours for 5 days (One half Salmonella patients given 100/mg/kg in equally divided doses every twelve hours for 5 days **Group 2 :** Oral suspension of placebo in doses every six hours for	**Follow up** Daily rectal swabs until 10 days, thereafter if still hospitalised, every three days. Daily clinical examination **Outcome measures:** ***Mean number of days until diarrhoea improved*** Shigella n=37 Group 1 = 2.4 Group 2 =4.6 Salmonella n=110 Group 1 = 2.9 Group 2 = 2.4 E coli n=35 Group 1 = 2.8 Group 2 = 4.9 No Pathogens n=96 Group 1 = 2.7 Group 2 = 2.9	**Funding :** Applicable to UK Baseline comparability Similar for sex, race, E Coli group younger than other groups. Blood and mucus present in stools, lethargy and convulsions found in greater proportion of shigella group than other groups. Allocation concealment : Random number table Sequence generation : Random number table Blinding of outcome assessors : Yes Loss to follow up 4/282

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
				5 days	***Mean number of days until diarrhoea ceased*** Shigella Group 1 = 4.4 Group 2 =6.8 Salmonella Group 1 = 5.2 Group 2 = 4.8 E coli Group 1 = 4.2 Group 2 = 6.4 No Pathogens Group 1 = 4.2 Group 2 = 4.2 ***Mean number of days until patient afebrile*** Shigella Group 1 = <0.5 Group 2 =1.6 P<0.05 Salmonella Group 1 = 0.8 Group 2 = 1.0 E coli Group 1 = 0.3 Group 2 = 0.9 No Pathogens Group 1 = 0.7 Group 2 = 0.8 ***Mean number of days until culture negative*** Shigella Group 1 = 0.9 Group 2 = 2	Intention to treat analysis : Not stated Power calculation : Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					P<0.05 Salmonella Group 1 = 1.8 Group 2 = 1.7 E coli Group 1 = 3.4 Group 2 = 3.0 No Pathogens – not rel	
Salmonella						
Nelson 1980 {42830} Location : USA	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 45 Randomised into three treatment arms Group 1 Intervention : Ampicillin n = 15 Group 2 Intervention : Amoxicillin n = 15 Group 3 Intervention : Placebo n = 14	**Inclusion criteria:** Children up to 8 yrs with acute diarrhoea seen in hospital with Salmonella species isolated in rectal swab cultures. **Exclusion criteria :** History of adverse drug reactions to penicillins, another focus of infection, under 6 wks age. **Withdrawal criteria :** Confirmation and serotyping of salmonella by rectal swab cultures. All isolates sensistive to amoxicillin and ampicillin	**Comparison** Intervention details: **Group 1:** Ampicillin 100mg/kg/day in 4 doses daily for 5 days **Group 2:** Amoxicillin 100/mg/kg/day in 4 doses daily for 5 days **Group 3:** Placebo in 4 doses daily for 5 days	**Follow up** Daily reporting of clinical symptoms and rectal swabs by parents. Seen in clinic at day2-3 and day 5-6, then every fortnight for 2 months **Outcome measures:** ***Mean no days until diarrhoea stopped*** Group 1 = 8.8+-3.0 Group 2 = 7.3+-1.0 Group 3 = 7.2+-1.8 P>0.20 ***Mean no days until diarrhoea improved*** Group 1 = 1.7+-0.3 Group 2 = 1.9+-0.3 Group 3 = 2.9+-0.8 P>0.20 ***Mean no days until 1st negative culture*** Group 1 = 18.5+-9.5	**Funding :** None stated Applicable to UK Baseline comparability Similar for sex, duration of illness prior to therapy, Salmonella serogroups. *Children in amoxicillin group younger than other groups and no white children in placebo group* Allocation concealment : Computer generated Sequence generation : Computer generated Blinding of outcome assessors : Yes Loss to follow up 1/45 (placebo group) due to short duration of Salmonella isolation Intention to treat analysis : No Power calculation :

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Group 2 = 20.9+-12.6 Group 3 = 28.5+-9.4 P >0.10 ***Days until last positive culture*** Group 1 = 41.3+-11.7 Group 2 = 37.0+-12.7 Group 3 = 20.9+-6.8 P>0.50	No
Chiu 1999 {42819} Location : Taiwan	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 42 Randomised into three treatment arms Group 1 Intervention : azithromycin n = 14 Group 2 Intervention : Cefixime n = 14 Group 3 Intervention : No treatment n = 14	**Inclusion criteria:** All children older than 6 months age presenting to hospital with suspected Salmonella enteritis – blood and/or mucoid diarrhoea with or without fever **Exclusion criteria :** Children with toxic appearance , vomiting, abdominal distension indicative of sepsis or ileus or who had taken antibiotics in 72 hours prior to admission. Negative Salmonella stool culture **Withdrawal criteria :** Not stated Confirmation and serotyping of salmonella by stool culture.	**Comparison** Intervention details: **Group 1:** Oral azithromycin 10mg/kg/day, in one dose daily for 5 days **Group 2:** Cefixime 10mg/kg/day, in 2 doses daily for 5 days **Group 3 :** No treatment	**Follow up** Weekly visits to clinic after completion of therapy until two consecutive normal stools noted **Outcome measures:** *Mean duration of diarrhoea post-treatment (days)* Group 1 = 2.5+-2.1 Group 2 = 5.8+-5.1 Group 3 = 3.5+-3.2 *Mean duration of fever post-treatment (days)* Group 1 = 1.5+-1.4 Group 2 = 2.1+-2.4 Group 3 = 1.2+-1.3 *Proportion of patients with positive cultures at week 3 post treatment* Group 1 = 3/14 Group 2 = 3/14 Group 3 = 4/14 P = NS	**Funding :** Applicable to UK Baseline comparability Similar for sex, duration of diarrhoea and fever prior to treatment, Salmonella subtypes. *Children receiving cefixime were younger that children in the other two groups (p<0.05)* Allocation concealment : Computer generated Sequence generation : Computer generated Blinding of outcome assessors : Loss to follow up None Intention to treat analysis: No Power calculation : No

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Kazemi 1973 {42825} Location : Canada	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 36 Randomised into three treatment arms Group 1 Intervention : Trimethoprim/sulphamethoxazole n = 14 Group 2 Intervention : Ampicillin n = 10 Group 3: Intervention : No treatment n = 12	**Inclusion criteria:** Children ages 10 months to 15 years with a history of diarrhoea and fever for 3 days or more and/or mucus and blood from diarrhoeal stools. Subsequent positive culture for Salmonella **Exclusion criteria :** Antibiotics in previous 5 days or renal or hepatic disease, blood dyscrasia, or salmonella bacteraemia **Withdrawal criteria :** Not stated Confirmation and serotyping of salmonella by stool culture and all isolates sensitive to trimethoprim/sulphamethoxazole and ampicillin	**Comparison** Intervention details: **Group 1:** 20mg/kg/day trimethoprim + 100/mg/kg/day sulphamethoxazole oral suspension 4times per day for 7 days **Group 2:** Ampicillin 100/mg/kg/day oral suspension or capsules 4times per day for 7 days **Group 3:** No treatment	**Follow up** During treatment once daily physical examination and stool cultures 2 or 3 consecutive daily stool cultures at 1 wk, 8 wks and 6 months post therapy (Family contacts also had stool cultures performed at admission and as above) **Outcome measures:** ***Mean duration of diarrhoea after start of therapy*** Group 1 = 2.8 Group 2 = 3.1 Group 3 = 3 P = NS ***Mean duration of hospitalisation after start of therapy*** Group 1 = 5.3 Group 2 = 5 Group 3 = 6 P = NS ***Mean duration of fever after start of therapy*** Group 1 = 3.2 Group 2 = 1.6 Group 3 = 2.6 P = NS	**Funding :** Partly Hoffman-LaRoche Applicable to UK Baseline comparability Similar for age, fever, vomiting, blood in stool, initiation of therapy in relation to onset of disease, Salmonella serotypes Allocation concealment : Not stated Sequence generation : Not stated Blinding of outcome assessors : Not stated Loss to follow up None Intention to treat analysis : No Power calculation : No

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Travellers Diarrhoea						
De Bruyn 2000 {42820} Location :	**Study Type** Cochrane systematic review **Evidence Level** 1+	**Total number of participants** Twelve trials included in total, nine relevant here N = 1174 Randomised into two treatment arms Group 1 Intervention : Antibiotic therapy n = 664 Group 2 Intervention : Placebo n = 510	**Inclusion criteria:** All trials in any language in which travellers older than 5 years were randomly allocated to treatment for acute non-bloody diarrhoea with antibiotics and where the causative organism is not known at allocation. To exclude dysentery and persistent diarrhoea at randomisation, acute bloody diarrhoea did not last more than 14 days **Exclusion criteria :** Diarrhoea lasting over 14 days **Withdrawal criteria :**	**Comparison** Antibiotic therapy vs placebo Intervention details: **Group 1:** **Antibiotics used** *Ofloxacin* Du Pont 1992 *Bicozamycin* Ericsson 1983 *Ciprofoxacin* Salam 1994 Wistrom 1992 *TMP, TMP-SMX* Du Pont 1982 *Norfloxacin* Mattila 1993 Wistrom 1989 *Fleroxacin* Steffen 1993 *Atreonam* Du Pont 1992 **Group 2:** Placebo	**Follow up** Not specified **Outcome measures:** *Mean duration of diarrhoea, as assessed by time to last unformed stool* 3 trials, 4 comparisons Group 1 n = 199 Range of means 24.8 - 39 hrs Group 2 n = 264 Range of means 53.5 - 63.7 WMD -25.86 [95% CI -32.58 to -19.14] Also Wistrom 1992 (poorly reported) Group 1 n = 8 Mean 26 h Group 2 n = 9 Mean 60h Pooled SD 27.989 *Number cured at 72 hrs* 6 trials included Group 1 n= 330 Group 2 n= 306 OR = 5.90 [95% CI 4.06 to 8.57] *Severity (no of unformed stools/24hour period)*	**Funding :** Applicable to UK

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Baseline 1 study WMD –0.10 [95%CI –0.81 to 0.61] 0-24h 2 studies Group 1 n=117 Group 2 n=106 WMD –1.59 [95% CI -2.66 to –0.52] 25-48h 2 studies Group 1 n=117 Group 2 n=106 WMD –2.10 [95%CI –2.78 to –1.42] 49-72h 2 studies Group 1 n=117 Group 2 n=106 WMD –1.38 [95%CI –1.94 to –0.82] *Tolerability* 5 studies Group 1 = 10/523 Group 2 =38/339 OR 2.37 [95%CI 1.50 to 3.75]	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Non-specific Gastroenteritis						
Wolfsdorf 1973 {42840} Location : South Africa	**Study Type** RCT **Evidence Level** 1-	**Total number of participants** N = 34 Randomised into two treatment arms Group 1 n = 18 Group 2 n = 26	**Inclusion criteria:** Children aged 5-30 months admitted to hospital for gastroenteritis **Exclusion criteria :** Not stated **Withdrawal criteria :** Not stated	**Comparison** Trimethoprim/sulphonamide vs placebo No further details	**Follow up** **Outcome measures:** ***Mean duration of diarrhoea (days)*** Group 1 = 5.250+-3.118 Group 2 = 6.607+-9.765 P = NS ***Mean duration of vomiting (days)*** Group 1 = 1.812+-3.505 Group 2 = 1.607+-2.998 P = NS ***Mean duration of pyrexia (days)*** Group 1 = 0.437+-0.6549 Group 2 =0.642+-0.9109 P = NS ***Mean duration of hospital stay (hours)*** Group 1 = 156.687+-93.672 Group 2 = 177071+-99.76 P = NS	**Funding :** Burroughs Wellcome Applicable to UK Baseline comparability Similar for age Allocation concealment : Code used Sequence generation : Code used Blinding of outcome assessors : Yes Loss to follow up None Intention to treat analysis : Not stated Power calculation : Not stated
Robins-Browne 1983 {42834} Location : South Africa	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 78 Randomised into two treatment arms	**Inclusion criteria:** Children aged 1m-2yrs admitted to hospital with a history of diarrhoea not exceeding 96hrs and who had received no antimicrobial therapy for the current illness	**Comparison** Erythromycin vs placebo Intervention details:	**Follow up** Daily examination for 7 days Distribution of pathogens similar between groups	**Funding :** South African MRC University of Natal, Abbott Laboratories

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
		Group 1 Intervention : Erythromycin n = 39 Data presented for 32 participants Group 2 Intervention : Placebo n = 39 Data presented for 33 participants	**Exclusion criteria :** Not stated **Withdrawal criteria :** Not stated	**Group 1:** Erythromycin ethylsuccinate oral suspension, 40mg/kg/day in divided doses for 5 days **Group 2:** Placebo oral suspension	**Outcome measures:** ***Mean duration of abnormal stool frequency*** Group 1 = 1.4+-1.7 days Group 2 = 1.8+-2.1 days P = 0.37 ***Mean duration of abnormal stool consistency*** Group 1 = 5.0+-1.4 days Group 2 = 5.8+-1.3 days WMD -0.80 [95% CI -1.46 to -0.14] P= 0.02 ***Mean duration of vomiting*** Group 1 = 3.4+-1.4 days Group 2 = 3.7+-1.2 days P = 0.35 ***Mean duration of dehydration*** Group 1 = 3.3+-1.8 days Group 2 = 3.3+-2.1 days P = 1.00 ***Fever*** Group 1 = 3.8+-1.6 days Group 2 = 3.3+-1.5 days P= 0.19	Applicable to UK No Baseline comparability Similar for age, sex, nutritional status, dehydration status, duration of current illness and severity of diarrhoea. Allocation concealment : Yes, pharmacy controlled Sequence generation : Code used Blinding of outcome assessors : Yes Loss to follow up : 13/78 **2 deaths (1 in each gp)** 6 infective complications requiring antibiotics(3 in each gp) 5 voluntary withdrawals (Gp 1=3, Gp 2 =2) Intention to treat analysis : No Power calculation : None stated
Rodriguez 1989 {42836} Location : Mexico	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 125 Randomised into three treatment arms Group 1 Intervention :	**Inclusion criteria:** Patients aged 2-59m brought to hospital with three or more watery stools in previous 24hrs, up to 5 days diarrhoea prior to admission, and presence of PMN leukocytes d blood in stool **Exclusion criteria :**	**Comparison** Intervention details: **Group 1:** 7.5mg/kg/day furazolidone in four equal doses a day for 5 days	**Follow up** Daily visits as outpatients to hospital. Clinical assessment at day 3, stool sample taken at days 1 and 6. **Outcome measures:**	**Funding :** Norwich Eaton Pharmaceuticals Inc, a Proctor & Gamble company Applicable to UK No Baseline comparability Similar for age, sex, height,

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
		Furazolidone n = 49 Group 2 Intervention : Trimethoprim/sulphamethoxazole n = 52 Group 3 Intervention : No treatment n = 24 Data presented for 22 participants	Presence of amoeba in stools, severe concomitant disease, intolerance of or allergy to study drugs, receipt of antimicrobials, antidiahorroeals, or other drugs affecting the disease course, within 48hrs prior to admission. **Withdrawal criteria :** Poor clinical response to treatment (treatment failures)	**Group 2:** 8mg/kg/day trimethoprim + 40/mg/kg/day sulphamethoxazole in two equal doses a day for 5 days **Group 3:** No treatment Oral rehydration, antipyretics and nutritional support given as needed to all groups Treatment success = clinical cure (absence of diarrhoea and alleviation of all symptoms) at day 3 and bacteriologic cure (negative stool culture) at day 6 For patients with negative culture: Treatment success = clinical cure (absence of diarrhoea and alleviation of symptoms) at day 3 Distribution of pathogens similar between groups. 48/125 had negative stool culture	***Clinical Cure at day 3*** All participants Group 1 = 43/49 Group 2 = 43/52 Group 3 = 10/22 Gp 1 vs Gp 3 RR = 1.93 [95% CI 1.21 to 3.09] Gp 2 vs Gp 3 RR = 1.82 [95% CI 1.13 to 2.92] Gps 1 + 2 vs Gp 3 RR = 1.87 [95% CI 1.18 to 2.98] ***Clinical Cure at day 3 pts with –ve stool cultures*** Group 1 = 13/14 Group 2 = 20/23 Group 3 = 5/9 Gp 1 vs Gp 3 RR = 1.67 [95% CI 0.92 to 3.05] Gp 2 vs Gp 3 RR = 1.57 [95% CI 0.85 to 2.87] Gps 1 + 2 vs Gp 3 RR = 1.61 [95% CI 0.89 to 2.91] ***Bacteriologic cure at day 6 pts with +ve stool cultures*** Group 1 = 20/34 Group 2 = 19/29 Group 3 = 4/12 Gp 1 vs Gp 3 RR = 1.76 [95% CI 0.76 to 4.12] Gp 2 vs Gp 3 RR = 1.97 [95% CI 0.85 to 4.56] Gps 1 + 2 vs Gp 3 RR = 2.33 [95% CI 1.04 to 5.25] ***Treatment cure at day 6*** Group 1 = 31/49 Group 2 = 36/52	weight, body temp and stools/day. Patients in Gp 1 had fewer days with diarrhoea compared to patients in either 2 treatment groups ($p<0.02$) Allocation concealment: Not stated Sequence generation : Not stated Blinding of outcome assessors: No Loss to follow up 2/24 in the control group voluntarily withdrawn Intention to treat analysis: No Power calculation: Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Group 3 = 5/22 Gp 1 vs Gp 3 RR = 2.78 [95% CI 1.25 to 6.19] Gp 2 vs Gp 3 RR = 3.05 [95% CI 1.38 to 6.72] Gps 1 + 2 vs Gp 3 RR = 2.92 [95% CI 1.33 to 6.39]	
Oberhelman 1987 {42831} Location : Mexico	**Study Type** RCT **Evidence Level** 1-	**Total number of participants** N = 141 Randomised into two treatment arms Group 1 Intervention : Trimethoprim/sulphamethoxazole n = 73 Group 2 Intervention : placebo n = 68	**Inclusion criteria:** Children aged 3-84 months seen in hospital with diarrhoea as chief complaint. Three or more unformed stools in previous 24hrs, <72 hours duration of diarrhoea, no antibiotic treatment in prior 7 days, absence of severe dehydration. **Exclusion criteria :** Not stated **Withdrawal criteria :** Not stated 74/141 had identifiable enteric pathogen 56/74 had a bacterial pathogen 6/31 ETEC mixed with others 25/31 ETEC only 7/10 patients had EPEC only 3/10 EPEC mixed with others 12 patients had Shigella 9 patients had Campylobacter 2 patients had Salmonella 4 patients had Cryptosporidium 6 patients had Giardia lablia	**Comparison** Intervention details: **Group 1:** 10mg/kg/day trimethoprim + 50/mg/kg/day sulphamethoxazole oral suspension in two divided doses per day for 5 days **Group 2:** Placebo oral suspension in two doses per day for 5 days	**Follow up** Daily assessments for 5 days except weight at day 5 and on assessment at 2 wks post-treatment **Outcome measures:** ***Mean time to last illness stool :*** All patients Group 1 = 58.2 Group 2 = 75.5 P = 0.021 Patients with fever Group 1 = 59.6 Group 2 = 94.6 P = 0.046 Patients with faecal leucocytes (3>HPF) Group 1 = 57.7 Group 2 = 106.5 P = 0.025 ***Mean no of unformed stools in 5 day period :*** All patients Group 1 = 9.8 Group 2 = 12.5 P = NS	**Funding :** Burroughs Wellcome Company Grant AI 23049 National Institutes of Health Applicable to UK Baseline comparability Similar for age, prior duration of illness, mean no stools in 24hrs prior to therapy, fever, dehydration, three faecal leukocytes per high-power field. Allocation concealment : Not stated Sequence generation : Not stated Blinding of outcome assessors : Daily assessments blinded – made by parents. Other assessments unclear Loss to follow up : None Intention to treat analysis : Not stated Power calculation : Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Patients with fever Group 1 = 9.1 Group 2 = 17.3 P = NS Patients with faecal leucocytes (3>HPF) Group 1 = 10.1 Group 2 = 18.1 P = 0.041 ***Post treatment no of unformed stools in wk1 and wk2*** All patients Patients with fever Patients with faecal leucocytes (3>HPF) Group 1 Group 2 P = NS	50/141 partipants had body weight <3rd percentile for age (Mexican standards)

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
E coli 0157:H7						
Wong 2000 {42940} USA	Study type: Prospective Cohort EL = 2+	Total no of patients N= 71/73 Cases : N = 10 HUS Controls : N = 61 no HUS	Inclusion criteria Children younger than 10 years who had diarrhoea caused by E coli 0157:H7 Exclusion criteria Definition HUS : A haemolytic anaemia (haematocrit < 30%, with evidence of destruction of erythrocytes on a peripheral blood-smear), thrombocytopaenia (platelet count <150,000/mm^3) and renal insufficiency (serum creatinine concentration that exceeded the upper limit of normal range for age)	Risk factors for HUS development antibiotics administered initial white blood cell count day stool culture obtained Follow up : Period of risk considered to be 14 days from the onset of diarrhoea.	**antibiotics administered** Yes 5/9 No 5/62 P= 0.001 Adjusted RR Within first 7 days after onset RR= 17.3 [95%CI 2.2 to 137] p=0.007 Within first 3 days after onset RR= 32.3 [95%CI 1.4 to 737] p= 0.03 **initial white blood cell count** 3200-8700/mm^3 0/18 8800–11,800/mm^3 1/18 11,900–14,200/mm^3 3/18 14,200–24,600/mm^3 6/17 Significant linear trend observed. P=0.005 Adjusted and analysed as a continuous outcome (RR = 1.5 [95%CI 1.1 to 2.1] p=0.02) Adjusted RR WBC count >= 13,000 RR= 6.0 [95%CI 1.2 to 29.8] p=0.03 **day stool culture obtained** Days 1-2 of illness 8/24 Day 2 of illness 2/22 Days 4-7 of illness 0/25 Significant linear trend observed P=0.01 Adjusted RR RR = 0.3 [95%CI 0.1 to 0.7] p=0.008 *Significant linear trend observed for positive E. coli 0157:H7 stool culture* P = 0.04 Days 2-4 of illness 6/24	Applicable to UK Funding : National Institutes of Health Baseline characteristics ; Similar for age, sex, bloody diarrhoea, fever, vomiting, initial temperature readings and lab test results (serum urea nitrogen or creatinine)

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Day 5 of illness 3/19 Days 6-10 of illness 1/28 Adjusted RR – not performed *Significant linear trend observed for day of initial white blood cell count obtained*. P=0.009 Days 1-3 of illness 7/25 Days 4-5 of illness 3/25 Days 6-10 of illness 0/21 Adjusted RR - NS *Significant linear trend observed for no of medications taken for E. coli infection* P=0.002 0 2/46 1 5/20 2 3/5 Adjusted RR – not performed	
Bell 1997 {42913} USA	Study type: retrospective cohort EL = 2+	Total no of patients N= 278/324 (46 children did not participate –reasons noted) Cases : N = 37 Controls : N = 241	Inclusion criteria Symptomatic, culture confirmed E. coli 0157:H7 infection or developed HUS in Jan-Feb 1993, <16 years old and resided in Washington State. Exclusion criteria Definitions Bloody diarrhoea = parental report of visible blood in stool Fever = temperature >= 38.5C at any site Treatment = 2 doses of therapy within first 3 days of first symptoms Complete HUS – platelet count <150,000/microL, haematocrit <30% with	Risk factors for HUS examined	Data collection from A telephone questionnaire by health dept staff of parents of participants within two weeks of their onset of illness. A second telephone questionnaire of parents 2-4 months later by research interviewers verifying previous data collected and collecting further data. Medical record examination Median age 6yrs (Range 0-15) **Clinical risk factors** *Vomiting* N = 278 HUS developed - 29/153 HUS did not develop – 8/125 (RR = 3.0 [95%CI 1.4 to 6.2]) *Bloody diarrhoea present* N= 271 HUS developed - 34/243 HUS did not develop – 2/28	Applicable to UK Funding : Children's Hospital Foundation (Seattle) American College of Gastroenterology Baseline characteristics ; Similar for age, sex, and annual family outcome

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
			evidence of intravascular haemolysis on peripheral blood smear and blood urea nitrogen >20mg/dL Incomplete HUS = two of criteria above		(RR= 2.0 [95%CI 0.5 to 7.7]) *Fever* N= 225 HUS developed – 11/56 HUS did not develop – 20/169 (RR= 1.8 [95% CI 0.8 to 4.1]) **Early Clinical risk factors** HUS development in: *Vomiting <=3days* – 22/127 *No vomiting <= 3days* – 13/140 RR = 1.9 [95% CI 1.0-3.5] *Children under 5.5yrs, vomiting <=3days* (RR = 3.5 [95%CI 1.4 – 9.4]) *Children over 5.5yrs, vomiting <=3days* (RR = 1.0 [95%CI 0.4 to 2.4]) **Medication risk factors** Antibiotic received N=50 Antibiotics given, TMP-SMZ = 31/50 Ampicillin/amoxicillin = 13/50 Cephalosporin = 6/50 Metronidazole = 4/50 Tetracycline, erythromycon, ciprofloxacin, gentamicin = 1 patient each received one drug More than one antibiotic = 11/50 Children receiving antibiotics were more likely to live in a household with annual income over $29,000 (RR=1.7 [95%CI 1.0 – 2.8]) Antimotility agent received N=34 **Early medication risk factors** HUS development in: *Antibiotic given* – 8/50 *No antibiotic given* – 28/218 P=0.56	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Antimotility agent given – 6/31 *No antimotility agent* – 20/234 P=0.10 *Adsorbant/antimotility given* – 8/43 *No adsorbant/antimotility agent* – 28/229 P=0.26 **Laboratory risk factors** Haematocrit, platelets, BUN, segmented neutrophils and band forms - no association with development of HUS . HUS development in: *WBC Count 3rd quartile (> 10,500/microL)* – 15/63 *WBC Count 1st,2nd or 4th quartile* – 3/65 P<0.01 *WBC Count 4th quartile (>= 13,000/microL)* – 13/34 *WBC Count 1st,2nd or 3rd quartile* – 5/94 P<0.01	
Non Specific Gastroenteritis						
Jonas 1982 {37988} Isreal	Study type: Prospective observational study EL=2+	Total no of patients N= 119/195 Salmonella = 24 Shigella = 47 E coli = 8 HRLA = 40 Unknown aetiology = 78/195	Inclusion criteria children admitted to paediatric wards for dehydration >= 5% and severe ongoing vomiting and diarrhoea Exclusion criteria Chronic gastrointestinal disease		Groups by age Salmonella = 24 <6m = 12 6-35m = 11 >= 36m = 1 Shigella = 47 <6m = 3 6-35m =15 >= 36m = 29 E coli = 8 <6m = 6 6-35m = 2	Applicable to UK Funding : Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					>= 36m = 0 HRLA = 40 <6m = 19 6-35m = 19 >= 36m =2 Unknown aetiology = 78/195 <6m = 35 6-35m = 33 >= 36m = 8 By specific clinical features : Vomiting Total Bacteria = 66% HRLA = 93% P<0.001 Signs of URTI Total Bacteria = 14% HRLA = 43% P<0.001 Signs of CNS Total Bacteria = 27% HRLA = 17% P<0.032 Dehydration Total Bacteria = 43 HRLA = 70 P<0.002 Contact with acute gastroenteritis, Fever>=37.5, Dehydration>10%, Stool exudates Total Bacteria vs HRLA All NS	
Ismail 1994{42928} Indonesia	Study type: Cross sectional, analytical study	Total no of patients N= 619/701 82 drop outs due to inaccessibility	Inclusion criteria Children aged 6 to 59 months seen in outpatients with who had had	Indications for antibiotic therapy	History and physical examination in OPD for demographic and clinical data. Stool sample or rectal swab for culture Follow-up – home visits	Applicable to UK Funding :

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
	EL=2+	Cases : N = Controls : One non-diarrhoeal pt from outpatients matched be age and sex for every 5 diarrhoeal pats N =	diarrhoea within prior 24h Exclusion criteria Need for hospitalization, chronic diarrhoea (>14d), antibiotic therapy required for a non-diarrhoeal disorder, pt not accessible for follow-up. Definition Diarrhoea = 3 or more watery stools with or without mucous or blood, or 3 or more loose stools with mucous and/or blood per day 3 categories of diarrhoea Watery diarrhoea, no blood and/or mucous Mucoid diarrhoea, mucous but no blood Bloody diarrhoea		Pathogens identified Shigella = 44 E histolytica – 32 C jejuni = 11 V cholera = 6 Salmonella = 3 A caviae, Aeromona, P. mirabilis, non-01 V cholerae – 1 each Invasive enteric pathogens considered to be Shigella, Salmonella, Campylobacter and Aeromonas (n=62) Significant positive linear trend between age and invasive pathogen (p=0.044) and Shigella infection (0.005) Non-significant linear trend between body weight and invasive pathogen (p=0.679) and Shigella infection (0.591) Mean duration of diarrhoea pre-OPD = 56.47 +/- 3.28 hrs Range 2-312 Watery stools = 365 patients Loose stools = 46 patients Mucoid stools = 177 patients Bloody stools = 77 patients Mean duration of vomiting pre-OPD = 35.25 hrs Range 2-240 Number participants with vomiting =199 Number participants with fever = 371 Significant positive predictive values greater than lower 85% estimate of CI for reported bloody stools – 20.8% Leucocytes >10/HPMF – 22.2 Microscopic erythrocyte positive – 19.6 Mucoid stools and Temperature >37.5 – 19.6	Not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Salmonella						
Lee 1998 {42930} Malaysia	Study type: Retrospective review	Total no of patients N= 131/148 (most exclusions because of a second enteropathogen)	Inclusion criteria Children with positive stool cultures for Salmonella species seen in an outpatients department Exclusion criteria Presence of a second enteropathogen Definition Invasive Salmonellosis = presence of bacteraemia or meningitis		Demographic, clinical (diarrhoea, vomiting, fever, hydration status), blood and stool outcome measures were recorded from case notes. Sex M = 69 F = 62 Age : Range 1m to 14 years 51/131 <6m 37/131 between 6 and 12 m 43/131 >12m Diarrhoea – 131/131 Fever – 60/131 Vomiting – 53/131 Bloody diarrhoea – 38/131 >5% dehydration 30/131 Abdominal colic 2/131 Fresh blood per rectum – 1/131 Risk factors for invasive complications Age<6m Non-invasive salmonellosis = 45/124 Invasive salmonellosis = 6/7 P<0.01 Fever > 38C Non-invasive salmonellosis = 53/124 Invasive salmonellosis = 7/7 P< 0.003 Dehydration >5% Non-invasive salmonellosis = 25/124 Invasive salmonellosis = 5/7 P<0.01 No significant differences between groups for breast feeding and bloody diarrhoea One fatality from bacteraemia	Applicable to UK Funding : No details

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Nelson 2002 {42932} Hong Kong	Study type: Retrospective review	Total no of patients N= 126 Salmonella n= 86 Rotavirus n=55 Not specified n=126	Inclusion criteria A sample of patients admitted to hospital with gastroenteritis subsequently identified as being of Salmonella, rotavirus or a non-specified aetiology Exclusion criteria Definition		Travel history Salmonella = 2/35 Rotavirus = 5/14 Not specified = 14/57 Salmonella vs rotavirus p=0.02 Blood in stool Salmonella = 44/86 Rotavirus = 6/53 Not specified = 19/118 Salmonella vs rotavirus p<0.0001 Salmonella vs non-specified p<0.05 Mucus in stool Salmonella =60/85 Rotavirus =26/54 Not specified = 31/117 Salmonella vs rotavirus p<0.0001 Rotavirus vs non-specified p<0.0001 Salmonella vs non-specified p<0.05 >1 episode of vomiting Salmonella =20/85 Rotavirus = 26/54 Not specified = 44/123 Salmonella vs rotavirus p<0.01 Fever during admission Salmonella = 77/86 Rotavirus = 46/55 Not specified = 80/124 Rotavirus vs non-specified p<0.0001 Salmonella vs non-specified p<0.05 Median Age (m) Salmonella = 7.05[3.9-13.6] Rotavirus = 14.3 [7.2-25.8] Not specified = 14.9[6.2-32.3] Salmonella vs rotavirus p<0.0001 Rotavirus vs non-specified p<0.0001 Median Hospital stay (d)	Applicable to UK Funding : Baseline characteristics ;

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					Salmonella = 3.4 [2.3-7.0] Rotavirus = 2.9[2-4] Not specified =1.8 [1.1-2.9] Rotavirus vs non-specified p<0.0001 Salmonella vs non-specified p<0.05 Stools (d) Salmonella = 6.2 [4.4-8.3] Rotavirus = 5.3 [3.8-7.6] Not specified = 3.6 [1.5-5.7] Rotavirus vs non-specified p<0.0001 Salmonella vs non-specified p<0.05 No significant differences between groups for sex, siblings at home, dehydration signs, abdominal pain, antihistamine treatment or no of infants <3m given antibiotic treatment	

Other therapies

Antiemetics

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Cubeddu 1997{44831} location: Venezuela	**Study Type** RCT **Evidence Level** 1-	**Total no. of patients** N= 36 Randomised in three arms: *ondansetron iv* N=12 *metoclopramide iv* N=12 *placebo* N=12	Children aged from 6 months to 8 years with GE with emesis, who had vomited twice within 1h. Patients were hospitalised for a minimum of 24h **Exclusion criteria** Severe dehydration, seizures, rectal T>= 39C, parenteral antiemetic medication in the 6h prior to the start of the study, parasite-induced GE	**Intervention1** *Iv ondansetron (0.3mg/kg)* ***Intervention2*** *iv metoclopramide (0.3mg/kg)* **Comparison 1** *Iv ondansetron* vs. pacebo **Comparison 2** *iv metoclopramide* vs. placebo **Comparison 3** *Iv ondansetron* vs. *iv metoclopramide*	**Follow-up** 24h **Outcome** Emesis Episodes of diarrhoea **Effect size** No emetic episodes 0-24h *Iv ondansetron 58%* *iv metoclopramide 33%* *placebo17%* diarrhoea 0-4 episodes *Iv ondansetron 4/12* *iv metoclopramide 2/12* placebo 8/12 >4 episodes *Iv ondansetron 8/12* *iv metoclopramide 10/12* placebo 4/12	**Funding** Glaxo Wellcome Research and Development **Comments** Baseline comparability between the two groups not adequate (only on gender and food intake) Method of randomisation: not reported blinding of outcome assessor: unclear power calculation: no *oral rehydration proceeded at 30min intervals for 4h (WHO rec) and was given after the 30min following the antiemetic/placebo administration.
Freedman 2006{36846} location: US	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=215 Randomised in two arms: Intervention group N= 108 Control group N=107	Children aged from 6 months to 10 years with GE (at least one episode of vomiting within the four hours preceding triage, at least one episode of diarrhoea and mild to moderate dehydration) **Exclusion criteria** Body weight<8Kg, severe dehydration, underlying disease that could affect the assessment of dehydration, history of abdominal surgery,	**Intervention** *oral ondansetron (tablets)* *from 8Kg to 15Kg: 2mg* *from 15Kg to 30Kg: 4mg* *>30Kg: 8mg* **Comparison** *oral ondansetron vs.* *placebo*	**Follow-up** Day 3 and day 7 after randomisation **Outcome** Cessation of vomiting (vomiting episodes) iv rehydration hospitalisation episodes of diarrhoea **Effect size** *Cessation of vomiting* *oral ondansetron 92/107* *placebo 70/107* iv rehydration *oral ondansetron 15/107*	**Funding** GlaxoSmithKline National Center for Research Resources of the National Institutes of Health **Comments** Method of randomisation and allocation concealment adequate. Loss to follow-up: 4/214 on day 3 8/214 on day 7

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
			hypersensitivity to ondansetron.		*placebo 33/107* hospitalisation *oral ondansetron 4/107* *placebo 5/107* *episodes of diarrhoea(mean)* *oral ondansetron 1.4* *placebo 0.5* p<0.001	baseline comparability: adequate *oral rehydration: 1h period of intense OR was initiated 15min after the administration of the medication, and then followed until disposition was determined (WHO rec).
Ramsook 2001{42032} Location: US	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=145 Randomised in two arms: Intervention group N= 74 Control group N=71	Children aged from 6 months to 12 years with GE presenting at least 5 episodes of vomiting in the preceding 24h and who did not receive antiemetics **Exclusion criteria** Underlying chronic conditions, possible appendicitis, UTI, severe GE requiring immediate IV fluids.	**Intervention** *Oral ondansetron every 8h.* *from 6 months to 1year:2mg* *from 1year to 3years:4mg* *from 4years to 12years:5ml* **Comparison** *Oral ondansetron* *vs.* *placebo*	**Follow-up** 48h **Outcome** Emesis (cessation of vomiting) Iv fluids administration Frequency of diarrhoea **Effect size** *Cessation of vomiting* *ED stay* *oral ondansetron 64/74* *placebo 46/71* *first 24h* *oral ondansetron 37/64* *placebo 30/56* *second 24h period* *oral ondansetron 43/62* *placebo 30/51* iv rehydration (*from histogram) *oral ondansetron 8%* *placebo 22.5%* *p=0.015* hospitalisation *oral ondansetron 2/74* *placebo 11/71* *episodes of diarrhoea(mean)* *oral ondansetron 1.4* *placebo 0.5* p<0.001	**Funding** GlaxoWellcome Research and Development **Comments** *rehydration protocol: pedyalite first choice (if not Gatorade) randomization and allocation concealment were adequate, the study was double-blind. Baseline comparability of the groups adequate. Power calculation: yes Loss to follow-up: none in the ED stay, 25/145 at 24h, 32/145 at 48h.
Roslund{44327}	**Study Type** RCT	**Total no. of participants**		**Intervention**		**Funding**

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
2008 Location : US	**Evidence Level** 1+	N=106 Randomised in two arms: Intervention group N= 51 Control group N=55	Children aged from 1 to 10 years with acute gastritis or gastroenteritis and mild to moderate dehydration who failed oral rehydration therapy in the emergency department. **Exclusion criteria** Anitemetics in previous 6 hours, underlying chronic illness, shock state requiring immediate IV fluids, severe (>=10%) dehydration, known sensitivity to 5-HT_3 antagonists	*Oral ondansetron.* *Under 15kg :2mg(0.5tablet)* *Between 15 – 30 kgs:4mg(1 tablet)* *Over 30kg :6mg (1.5 tablet)* **Comparison** *Oral ondansetron* *vs.* *placebo*	**Follow-up** Daily until symptoms resolved up to 6 days **Outcome** Emesis (cessation of vomiting) Iv fluids administration Frequency of diarrhoea **Effect size** receipt of iv hydration *oral ondansetron 9/48* *placebo 30/55* *RR= 0.34;95% CI 0.18 to 0.65* hospitalisation *oral ondansetron 3/51* *placebo 7/55* *RR = 0.46; 95% CI 0.13 to 1.69* *episodes of diarrhoea(mean)* *oral ondansetron 1.4* *placebo 0.5* p<0.001 *<3 episodes of vomiting post discharge* *oral ondansetron pts (n=48) 93%* *placebo pts (n=48) 88%* *median no of vomiting episodes* *oral ondansetron 0 (range 0-13)* *placebo 0 (range 0-4)* *mean no of vomiting episodes* *oral ondansetron 0.71* *placebo 0.5* *<3 episodes of vomiting post discharge* *oral ondansetron pts (n=48) 93%* *placebo pts (n=48) 80%* *median no of vomiting episodes* *oral ondansetron 0 (range 0-20)* *placebo 0 (range 0-6)*	GlaxoSmithKline supplied placebo tablets No other funding details **Comments** Randomisation and allocation concealment were adequate, the study was double-blind. Baseline comparability of the groups similar except significantly more children in the ondansetron group were "moderately" dehydrated. Hence more children were mildly dehydrated in the placebo group but this was not statistically significant Power calculation: yes Loss to follow-up: 9% did not participate in follow up telephone interviews Intention to treat analysis (3 patients in ondansetron group incorrectly diagnosed)

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					mean no of vomiting episodes *oral ondansetron 1.76* *placebo 0.45*	

Kaolin

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Watkinson 1982 41938} location: The Gambia	**Study Type** quasi-RCT **Evidence Level** 1-	**Total no. of patients** N= 97 Randomised in two arms: *Intervention group* N=45 *Control group* N=52	Children between 3 and 18 months with diarrhoea **Exclusion criteria** Diarrhoea associated with haematologically proven malaria or with a bacterial infection necessitating ABT	**Intervention** *Kaolin (5ml t.d.s.)* **Comparison** *GES + Kaolin vs. GES*	**Follow-up** Not stated **Outcome** Duration diarrhoea after treatment in days Mean number of stools/day **Effect size** Duration diarrhoea (mean+-SD) Intervention gp 5.8+-4.7 Control gp 4.7+-4.3 number of stools/day (mean+-SD) Intervention gp 3.7+-1.2 Control gp 3.7+-1	**Funding** none **Comments** Participants allocated in the groups by birth order Compliance with the doses of Kaolin was poor in 33% of the participants the two groups were slightly different according to age allocation concealment and loss to FU: n.s. blinding outcome assessor: no power calculation: no

Activated charcoal

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Sebodo 1982{41902} location: Indonesia	**Study Type** RCT **Evidence Level** 1-	**Total no. of patients** N= 39 Randomised in two arms: *Intervention group* N=16 *Control group* N=23	Children with acute GE and severe dehydration aged between 1 ½ months and 10 years **Exclusion criteria** Acute GE due to Entamoeba histolytica	**Intervention** *Activated charcoal* *3x166mg: up to 6m* *3x250mg: from 6 to 12m* *3x375mg:from 1 to 2y* *3x500mg: from 2 to 5y* *3x500mg: more than 5y* *The activated charcoal was given until a day after the cessation of the diarrhoea* **Comparison** *Ringer lactate solution + OGE + activated charcoal vs. ringer lactate solution + OGE*	**Follow-up** Not stated **Outcome** Duration diarrhoea Total ORS Total iv fluids **Effect size** (mean+-SD) Duration diarrhoea (days) Intervention gp 2.125+-0.8 Control gp 3+-1.17 Total ORS (pack) Intervention gp 3.25+-2.08 Control gp 5.43+-3.22 Total iv fluids (bottle) Intervention gp 3.19+-1.17 Control gp 3.74+-2.30	**Funding** none **Comments** Study poorly reported (Method of randomisation, allocation concealment, follow-up, baseline comparability of the two groups)

Racecadotril

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Salazar-Lindo 2000 {41934} Location : Peru	**Study Type** RCT **Evidence Level** 1+	**Total number of participants** N = 135 Randomised into two treatment arms Group 1 Racecadotril n = 68 Group 2 Placebo n = 67	**Inclusion criteria:** Boys aged between 3-35months admitted for dehydration, with watery diarrhoea for 5 days or less, had passed 3 or more diahorreic stools in 24 hrs prior to admission and had passed 1 diarrhoeic stool within 4-6hrs post-admission. **Exclusion criteria :** Blood in the stool, severe dehydration (inability to drink because of drowsiness), any serious concomitant illness **Withdrawal criteria :** Blood in stools during first 24 hrs, antibiotic treatment for concomitant illness, physician judged treatment ineffective, consent withdrawal, severe adverse events	**Comparison** racecadotril vs placebo **Group 1:** racecadotril 1.5mg/kg body weight every 8 hrs **Group 2:** placebo every 8 hrs Both treatments given as saccharose-containing powders of identical taste and appearance, with small amount of water to aid swallowing. Treatment given for 5 days or until diarrhoea stopped. Standard oral rehydration given as needed to all boys (111mmol glucose, 90mmol sodium, 20mmol potassium, 80mmol chloride, 10mmol citrate per litre)	**Follow up** every four hours for the first 48 hours then at 5 days or at the time of recovery if earlier **Outcome measures:** *- Mean stool output in first 48hrs* *- Hourly rate of stool production in first 48 hrs* *- Mean total stool output before recovery* *- Duration of diarrhoea* *- Cure rate at 5 days* *- Oral rehydration solution intake* Effects measured for all participants and for rotavirus positive boys **Effect size :** *Mean stool output in first 48hrs* All participants Group 1 = 92 +/- 12g/kg Group 2 = 170 +/- 15 g/kg P<0.001 Rotavirus +ve Group 1 = 105 +/- 17g/kg Group 2 = 195 +/- 20g/kg P<0.001 *Hourly rate of stool production in first 48 hrs* All participants Group 1 = 1.8 +/- 0.2g/kg/hr Group 2 = 3.1 +/- 0.3g/kg/hr P<0.001 Rotavirus +ve No details *Mean total stool output before recovery*	**Funding :** grant from Bioprojet Pharma (developers of racecadotril) Applicable to UK Baseline comparability Similar for age, weight, stools in previous 24hrs, stool consistency on previous 24hrs, diarrhoea duration pre-hospitalisation, bacteria and rotavirus detected in stool. 8 boys in racecadotril group had a respiratory illness compared to one in the placebo group Allocation concealment : not stated Sequence generation : not stated Blinding of outcome assessors : not stated Loss to follow up : 9 boys in group 1, 14 boys in group 2 Intention to treat analysis : yes Power calculation : not stated

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					All participants Group 1 = 157+/- 27g/kg Group 2 = 331 +/-39g/kg P<0.001 Rotavirus +ve Group 1 = 174+/-36g/kg Group 2 = 397+/-37g/kg P<0.001 *Duration of diarrhoea* Rotavirus +ve Group 1 = median 28 h Group 2 = median 72h Rotavirus –ve Group 1 = median 28h Group 2 = median 52 h *Cure rate at 5 days* All participants Group 1 = 57/68 Group 2 = 44/67 *Oral rehydration solution intake* @ Day 1 Group 1 = 439+/-49ml Group 2 = 658+/-59ml @Day 2 Group 1 = 414+/-68ml Group 2 = 640+/-68ml	
Cezard 2001 {41990} Location :France	Study Type RCT Evidence Level 1-	**Total number of participants** N= 172 Randomised into two treatment arms Group 1 Racecadotril n = 89	Inclusion criteria : 172 children hospitalised for severe acute diarrhoea aged between 3m to 4 yrs of both sexes. Participants had watery diarrhoea (3 watery stools/day or more) for a duration of less than 72 hrs and had passed one watery stool post-admission	**Comparison** racecadotril vs placebo **Group 1:** racecadotril 1.5mg/kg body weight 3 times daily **Group 2:** Placebo 3 times daily Both treatments given as	**Follow up for 5 days** **Outcome measures:** *-- Hourly rate of stool production in first 24 hrs - Hourly rate of stool production in first 48 hrs* Effects measured for all participants and for rotavirus positive boys	Applicable to UK **Funding** : no information supplied Baseline comparability Similar for age, weight, height, stools in previous 24hrs, diarrhoea duration prior to inclusion, IV rehydration prior to

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
		Group 2 Placebo n = 83	Exclusion criteria: Chronic diarrhoea, weight for age deficit of 20% or more of NCHS standard, systemic illness, antibiotic or antidiarrhoeal drug or acetylsalicylic acid usage in preceding 48hrs	granules of identical taste and appearance. Oral rehydration given to all children ad libitum each hour for first 24 hrs of study either orally or by gastric tube (111mmol glucose, 49mmol sodium, 25mmol potassium, 25mmol chloride, 24mmol carbonate, 58mmol saccharose per litre) Treatment given for 5 days or until diarrhoea stopped.	**Effect size :** *Hourly rate of stool production in first 24 hrs (read from graph)* Group 1 = 11g/hr Group 2 = 16 g/hr P<0.001 *Hourly rate of stool production in first 48 hrs (read from graph)* All participants Group 1 = 8g/hr Group 2 = 16 g/hr P<0.001 Rotavirus +ve Group 1 = 8g/hr Group 2 = 19g/hr P<0.001 Rotavirus –ve Group 1 = 6g/hr Group 2 = 13g/hr No evidence of difference between treatments depending on rotavirus status (p= 0.500)	inclusion, antidiarrhoeal treatment prior to inclusion, abdominal circumference and temperature. Allocation concealment : not stated Sequence generation : not stated Blinding of outcome assessors : not stated Loss to follow up : 28% data presented for full dataset and for per-protocol dataset Intention to treat analysis : yes Power calculation : yes

Bismuth subsalicylate

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Chowdhury 2001 {42052} location: Bangladesh	**Study Type** RCT **Evidence Level** 1+	**Total no. of patients** N= 451 Randomised in two arms: *Bismuth subsalicylate* N=226 *placebo* N=225	Children aged from 4 to 36months admitted in the Diarrhoea Hospital of the Matlab Health Research Programme and with a history of acute watery diarrhoea of less than 72h duration, with 3 or more watery stools in the last 24h. **Exclusion criteria** Use of antimicrobials within the previous 48h, blood in the stoll, severe malnutrition, other systemic illness, salicylates intake in the last 24h, allergy to salicylates, varicalla or measles in the last 3 months.	**Intervention** bismuth subsalicylate (100mg/Kg/d x 5 days) **Comparison** *bismuth subsalicylate* vs. placebo	**Follow-up** for the duration of the hospitalisation + 4 days **Outcome** Onset persistent diarrhoea Duration acute diarrhoea (median) total intake of oral rehydration solution total stool+urine output **Effect size** <u>Onset persistent diarrhoea</u> bismuth subsalicylate 8% placebo 11% <u>Duration acute diarrhoea in h (median)</u> bismuth subsalicylate 36 placebo 42 p<0.057 * in children with rotavirus diarrhoea (>50%) bismuth subsalicylate 56 placebo 72 p=0.03 <u>total intake of oral rehydration solution ml/Kg (median+-SD)</u> bismuth subsalicylate 291+-181 placebo 325+-218 p=0.072 <u>total stool+urine output g/Kg (median+-SD)</u> bismuth subsalicylate 386+-248 placebo 438+-272 p=0.037	**Funding** Centre for Health and Population Research, via the International Child Health Foundation which received a grant from Procter & Gamble. Aid Agencies of the Government of Australia, Bangladesh, Belgium, Canada, Japan, the Netherlands, Sweden, Sri Lanka, Switzerland, UK and US and international organizations including the UN Children's Fund. **Comments** Well conducted RCT Loss follow-up 8% (lost participants not included in the analysis, initially 489 patients enrolled) * Diarrhoea=3 or more liquid stools in 24h PD=diarrhoeal episodes for or more than 14 days
Figueroa-Quintanilla 1993 {41932} location: Peru	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=215 Randomised in three arms: <u>BSS 100mg/Kg/d group</u> N= 108 <u>BSS 150mg/Kg/d group</u> N= 108	Boys from 6 to 59 months that had presented 3 or more watery stools in the preceding 24h (acute diarrhoea). **Exclusion criteria** Blood in the stools, diarrhoea for more than 5 days, antibiotics or antidiarrhoeal medication or any treatment	**Intervention** BSS (bismuth subsalicylate) 100mg/Kg/d or 150mg/Kg/d, every 4h for 5 days or until the diarrhoea stopped. **Comparison1** *BSS (100mg/Kg/d) vs. placebo* **Comparison2**	**Follow-up** Hospital stay **Outcome** Duration of diarrhoea (proportion of patients with diarrhoea by day 5) Total stool output (ml/Kg) Total volume of vomitus (ml/Kg) Total intake of rehydration (ml/Kg) Hospital stay (days)	**Funding** Grant from the International Child Foundation and Procter&Gamble **Comments** Loss follow-up 8% (lost participants not included in the analysis, initially 275 patients enrolled)

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
		placebo group N=107	with AAS in the 72h before admission, clinical evidence of another illness requiring ABT, severe malnutrition, allergy to salicylate or bismuth, exclusively breastfed.	*BSS (150mg/Kg/d) vs. placebo* **Comparison3** *BSS (100mg/Kg/d) vs. BSS (150mg/Kg/d)*	**Effect size** Duration of diarrhoea BSS (100mg/Kg/d) 89% BSS (150mg/Kg/d) 88% placebo 74% Total stool output (mean+-SD) BSS (100mg/Kg/d) 182+-197 BSS (150mg/Kg/d) 174=-159 placebo 260+-254 Total volume of vomitus (mean+-SD) BSS (100mg/Kg/d) 11.6+- 19.6 BSS (150mg/Kg/d) 8.7+- 18.3 placebo 16.2+- 27 Total intake of rehydration (mean+-SD) BSS (100mg/Kg/d) 239+-177 BSS (150mg/Kg/d) 236+-152 placebo 314+- 234 Hospital stay (mean+-SD) BSS (100mg/Kg/d) 3.3+- 1.5 BSS (150mg/Kg/d) 3.4+- 1.5 placebo 4.1+- 2.1	Well conducted RCT (outcomes other than duration of diarrhoea might refer to the whole stay in hospital but not clear)
Soriano-Brucher 1991 {41908} location: Chile	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=142 Randomised in two arms: Intervention group N= 72 Control group N=70	Children 4-36months of age with diarrhoea and dehydration <72h and who needed hospitalisation for therapy and rehydration **Exclusion criteria** Symptoms >72h, blood in stools, severe malnutrition, antibiotics use in the previous 48h, salicylate intake>20mg/Kg in the previous 12h, allergy to bismuth/salicylate, acute illness not consistent with diarrhoeal state.	**Intervention** bismuth subsalicylate (100mg/Kg/d x 5 days) **Comparison** *bismuth subsalicylate* vs. placebo	**Follow-up** 8 days -patients were monitored in hospital for at least 5 days and then were followed for 3 more days (whether they remained in hospital or were discharged) **Outcome** Disease duration in h: time to last abnormal stool weight, time to last loose/watery stool, time until last unformed stool. Duration of hospital stay Iv fluids intake (mL/Kg) **Effect size** Disease duration: last loose/watery stool *bismuth subsalicylate 73.4* placebo 107.5 p<0.02 time until last unformed stool *bismuth subsalicylate 130.4* placebo 170 p<0.01	**Funding** Procter&Gamble Company **Comments** Patients lost in the follow-up (13.4%) were excluded from the analysis Method of randomisation not reported. *treatment regimes were in accordance with WHO recommendations, with initial iv fluids (for at least 8h) and followed by oral rehydration

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					Duration of hospital stay *bismuth subsalicylate 6.93* placebo 8.48 p<0.02 Iv fluids intake *The authors reported that the group receiving BSS required less iv fluids (day 3 and day 5). than the placebo group, the difference being statistically significant. No data but an histogram is provided.* Day 3 *bismuth subsalicylate ap. 30* mL/Kg placebo approx. 45mL/Kg day 5 *bismuth subsalicylate ap. 20*mL/Kg placebo *42*mL/Kg	

Loperamide

Bibliographic details	Study type & evidence level	Study details	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up and Results	Comments
Su-Ting TL 2007 US	**Study Type** Systematic Review **Evidence Level** 1+	13 RCTS included in the review Total number of participants 1788 randomised in two arms across all the studies: Intervention group: 975 Control group: 813 Prakash 1980 (location: India)- 472 patients Owens 1981 (location: Lybia)- 100 patients Kassem 1983 (location: Egypt)- 100 patients Anderson 1984 (location: Mexico)- 56 patients Anonymous 1984 (location: UK)- 303 patients Chavarria 1984 (location: Costa Rica)- 34 patients Vesikari 1985 (location: Finland)- 31 patients Cordier 1987 (location: France)- 50 patients Ghisolfi 1987 (location: France)- 63 patients Karrar 1987 (location: Saudi Arabia)- 59 patients Motala 1990 (location: South Africa)- patients 60 Bowie 1995 (location: South Africa)- 200 patients	Children aged between 0 to 132 months suffering from acute diarrhoea (inpatients -10 trials- and outpatients -3 trials-included).	**Intervention** Loperamide (daily doses varied across studies) **Comparison** *Loperamide vs. placebo*	**Follow-up** Varied among the studies **Outcome** Proportion of children with diarrhoea at 24 and 48 h Duration acute diarrhoea (median) Stool count (mean count at 24h) Adverse events **Results** <u>Diarrhoea at 24h</u> -4 trials- RR 0.66 [95%CI 0.57 to 0.78] -3 trials with same definition for diarrhoea resolution (=last unformed stool)- RR 0.66 [95%CI 0.56 to 0.77] <u>Diarrhoea at 48h</u> -4 trials- RR 0.59 [95%CI 0.45 to 0.78] <u>Duration diarrhoea (mean +- SD)</u> -6 trials- WMD -0.80 [95%CI -0.87 to -0.74] -5 trials with loperamide dose <= 0.25mg/Kg/d- WMD -0.7 [95%CI -0.6 to -0.8] <u>Stool count at 24h (mean +- SD)</u> -4 trials- count ratio 0.84 [95%CI 0.77 to 0.92] *The results reported favoured significantly the use of loperamide in shortening the duration of diarrhoea and reducing the number of stools <u>Adverse events</u> -12 trials- **ileus, lethargy, death** intervention group 8/927 control group 0/764	**Funding** No specific funding received **Comments** Well-conducted systematic review The authors concluded that in children under 3 years, malnourished, moderately/severely dehydrated or with blood in the stools the risk of adverse events from loperamide outweighs the benefits.

Bibliographic details	Study type & evidence level	Study details	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up and Results	Comments
		Kaplan 1999 (location: Mexico)- 258 patients			**ileus, abdominal distension, lethargy/sleepiness, death** intervention group 21/927 control group 4/764 * serious adverse events occurred among children under 3 years	

Smectite

Bibliographic details	Study type & evidence level	Study details	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up and Results	Comments
Szajewska 2006 {41959} Poland	**Study Type** Systematic Review **Evidence Level** 1+	9 RCTS included in the review Total number of participants 1238 randomised in two: Intervention group: 622 Control group: 616 Gilbert 1991 (location : France)- 36 patients Guarino 2001 (location : Italy)- 804 patients Lachaux 1986 (location : France)- 36 patients Lexomboon 1994 (location : Thailand)- 66 patients Madkour 1993 (location : Egypt)- 90 patients Narkeviciute 2002 (location : Lithuania)- 54 patients Osman 1992 (location : Egypt)- 60 patients Vivatvakin 1992 (location : Thailand)- 62 patients	Children between 1 to 60 months of age with acute diarrhoea and treated in hospitals or as outpatients.	**Intervention** Smectite (daily doses from 3 to 6 g per day) **Comparison** *Smectite vs. placebo or no additional treatment*	**Follow-up** Varied across studies: - not reported for three trials (Gilbert, Lachaux and Lexomboon) -3 days (Madkour) - 5 days (Guarino and Osman) -24h (Narkeviciute) -from to 48 to 120h (Vivatvakin) -3 to 6 days (Zong) **Outcome** duration of diarrhoea frequency of stools vomiting (number of episodes of vomiting and duration of vomiting) no symptoms by day 3 and by day 5 diarrhoea for >= 7days adverse events **Results** <u>Duration of diarrhoea (h)</u> -6 trials- WMD -22.7 [95%CI -24.80 to -20.61] <u>frequency of stools</u> <u>0 to 6h</u> -2 trials- WMD -0.07 [95%CI -0.6 to 0.4] <u>6 to 24h</u> -2 trials-	**Funding** Partially funded by a grant from the Medical University of Warsaw **Comments** Well-conducted systematic review

Bibliographic details	Study type & evidence level	Study details	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up and Results	Comments
		Zong 1997 (location : China)- 30 patients			WMD -0.33[95%CI -0.8 to 0.2] 24 to 48h -2 trials- WMD -0.62 [95%CI -1 to -0.2] vomiting number of episodes -2 trials- WMD -0.02 [95%CI -0.5 to 0.6] Duration of vomiting (h) -1 trial- WMD -0.1 [95%CI -0.15 to 0.3] no symptoms by day 3 -4 trials- RR 1.64 [95%CI 1.36 to 31.98] no symptoms by day 5 -4 trials- RR 1.19 (95%CI [0.93 to 1.53]) diarrhoea for > 7days -1 trial- RR 0.6 [95%CI 0.42 to 0.85] adverse events constipation -1 trial- RR 5.8 [95%CI 0.7 to 47.1] * three RCTs reported no adverse events associated with short-term treatment with smectite	

Micro-nutrients and fibre
Vitamin A

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Henning 1992 {41993} location: Bangladesh setting: Hospital	**Study Type** RCT **Evidence Level** 1+	**Total no. of patients** N=83 Randomised in two arms: *Intervention group* N=46 *Placebo group* N=37	Male children aged from 1 to 5 years with watery non-cholera diarrhoea for less than 48h. **Exclusion criteria** Children with cholera, those with serious illness (such as pneumonia or severe malnutrition) and those receiving vitamin A within the past 3 months were excluded. *Children with a history of night blindness or clinical signs of vitamin A deficiency were given high-dose vitamin A and excluded from further study.	**Intervention** *Vitamin A 200 000 UI + vitamin E 25 UI* ***placebo*** *vitamin E 25 IU* **Comparison** *Vitamin A vs. placebo* ** rehydration therapy and maintenance: rice-based oral rehydration solution* *iv fluids (5%dextrose) were administered if the child had excessive vomiting or inability to take fluids orally*	**Follow-up** Until discharge from hospital when cessation of diarrhoea occurred (= the last liquid stool after which two normal stools occurred or after no stool for 24h) **Outcome** 1.total duration of diarrhoea after start intervention (h) 2.total stool output (g/Kg/episode) 3.stool output 1st 24h (g/Kg/h) 4.emetic episodes 1st 24h (g/d) 5.Diarrhoea >10d 6.treatment failures (=children who needed iv fluids after initial rehydration) **Effect size** 1. total duration of diarrhoea * *intervention group 52.1(29.4)* *placebo group 54.6(41.7)* 2.total stool output * *intervention group 143(133.2)* *placebo group 143.6(160.7)* 3.stool output 1st 24h* *intervention group 5.8(4.2)* *placebo group 5.5(3.9)* 4.emetic episodes 1st *24h*	**Funding** Office of Health, the United States Agency for International Development, and the Institute for International Programs, the Johns Hopkins University and the International Centre for Diarrhoeal Diseases Research, Bangladesh **Comments** *the groups in the final analysis were of unequal sizes because more children in the placebo group had to be excluded after enrolment (reasons for exclusion after enrolment: development of other illnesses like pneumonia, meningitis, measles-, identification of Giardia lamblia, parental refusal to continue). - 9 children in the intervention group and 7 in the placebo group (15/83) withdrew from the study before the episode of diarrhoea was over. All withdrawals occurred when the subjects' clinical status had already improved. Total lost to follow-up: unclear -Method of randomisation: yes -allocation concealment yes -Power calculation: n.s. -Baseline comparability: yes

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					* *intervention group 24.9(59.8)* *placebo group 16.5(46.1)* 5. diarrhoea >10d *intervention group 0/46* *placebo group 1/37* 6.treatment failures *intervention group 5/46* *placebo group 4/37* *** (mean and SD)**	
Hossain 1998 {42018} location: Bangladesh setting: hospital	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=83 Randomised in two arms: Intervention group N= 42 Control group N=41	Children aged from 1 and 7 years with Shigella infection, bloody diarrhoea for < 72h (proved by culture of the stool or rectal swab) and with no other illnesses. **Exclusion criteria** Children with other acute or chronic illnesses, microscopic stool examination showing trophozoites of Entamoeba histolytica, antibiotic therapy, vitamin A administration within tha last 3 months, weight <=75% of the national health statistics growth reference median.	**Intervention** Single oral dose of vitamin A 200 000 IU plus 25 IU of vitamin E ***placebo*** *vitamin E 25 IU* **Comparison** *Vitamin A vs. placebo* * medical care: each child was given nalixidic acid (55mg/Kg every 6h). Children were admitted to hospital for 5 study days after receiving the trial treatment.	**Follow-up** Five days **Outcome** Clinical cure Bacteriological cure **Effect size** 1.Clinical cure *intervention group 19/42* *placebo group 8/41* 2.Bacteriological cure *intervention group 16/42* *placebo group 16/41*	**Funding** United States Agency for International Development with the International Centre for Diarrhoeal Disease Research, Bangladesh **Comments** Subjects were considered **clinically cured** when: 3 or < formed stools/d without blood or mucus, afebrile, no abdominal pain, no abdominal tenderness. **Bacteriological cure** was defined as: absence of Shigella spp in both stools and rectal swab samples from study day 3 onwards. Method of randomisation: adequate Allocation concealment: yes Power calculation: yes Baseline comparability: adequate Lost to follow-up: 7/90 (Seven subjects were excluded after enrolment: 3 in the control group and four in the intervention group).
Yurdakok 2000 {41953} Location: Turkey	**Study Type** quasi-RCT **Evidence Level** 1-	**Total no. of participants**	Children aged from 6 to 12 months with diarrhoea <5 days duration. **Exclusion criteria**	**Intervention** Single oral dose of vitamin A 100 000 IU	**Follow-up** until recovery from diarrhoea (=passage of	**Funding** Grant from the Scientific and Technical Research Council of

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Setting: community-based		N=120 Randomised in two arms: Intervention group N= 60 Control group N=60	Chronic diseases, malnutrition (<WFA 10th percentile according to NCHS), associated infectious disease, prior antibiotic use, dysentery.	**Comparison** *Vitamin A vs. placebo*	formed stool as described by the mother for at least 24h). Infants were then evaluated at 2 weeks and 1 month from the study enrolment. **Outcome** 1.total duration of diarrhoea after start intervention (d) 2.persistent diarrhoea **Effect size** 1.total duration of diarrhoea after start intervention (d)-mean(SD) *intervention group 3.8 (2.3)* *placebo group 3.9 (1.9)* 2.persistent diarrhoea *intervention group 2/60* *placebo group 2/60*	Turkey **Comments** *dehydration was assessed and treated according to WHO guidelines (G-ORS) -Method of randomisation: based on patients file numbers (odd or even) -allocation concealment: yes -baseline comparability: yes -power calculation: yes -double-blind -Lost to follow-up: none until cessation of diarrhoea, 19/120 at the 2nd assessment and 40/120 at the follow-up visit one month later

Glutamine

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Songul Yalcin 2004 Location: Turkey Setting: community-based	**Study Type** quasi-RCT **Evidence Level** 1-	**Total no. of participants** N=159 Randomised in two arms: Intervention group N= 79 Control group N=80	Children aged from 6 to 24 months with diarrhoea < 10 days duration. **Exclusion criteria** Chronic diseases, severe malnutrition (<60%WFA according to NSCHS), associated infectious disease, prior antibiotic or anti-diarrhoeal use, dysentery.	**Intervention** 0.3g/Kg/d of glutamine for 7d **Comparison** *Glutamine vs. placebo* *non compliant children were excluded (less than 3 days or less than ½ of the prescribed supplementation)	**Follow-up** until recovery from diarrhoeal episode and further assessments monthly for the next 3 months **Outcome** 1.mean duration of diarrhoea after treatment(d) 2. Proportion of persistent diarrhoea 3. total duration of diarrhoea (d) after start intervention in children with: -<8stools/d on admission >8stools/d on admission -<90%WFA ->90%WFA **Effect size** 1.mean (SD)duration of diarrhoea *intervention group 3.4 (1.96)* *placebo group 4.57 (2.48)* 2.mean (SD) total duration of diarrhoea *intervention group 6.90 (3.24)* *placebo group 8.29 (3.39)* 3. Proportion of persistent diarrhoea *intervention group 2/63* *placebo group 6/65*	**Funding** Supported by the Scientific and Technical Research Council of Turkey **Comments** **Clinical recovery**=the passage of a soft-formed stool as described by the mother for at least 24h. **Persistent diarrhoea**=an episode lasting 14 or more days. -Lost to follow-up: 31/159 Lost patients were not included in the final analysis -Method of randomisation: based on patients file numbers (odd or even) -allocation concealment: yes -power calculation: yes -double-blind -baseline comparability: yes

Folic acid

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Ashraf 1998 {42050} Location: Bangladesh Setting: hospital	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=106 Randomised in two arms: Intervention group N= 54 Control group N=52	Male children aged from 6 to 23 months with watery diarrhoea < 72h duration and with some signs of dehydration. **Exclusion criteria** n.s.	**Intervention** Folic acid in a dose of 5mg at 8h intervals for 5d. **Comparison** *Folic acid vs. placebo*	**Follow-up** 5 days **Outcome** 1. Total diarrhoea output g/kg 2. Total intake ORS g/kg 3. Duration of diarrhoea h 4. Proportion of patients with diarrhoea beyond 5d 5. Proportion of patients that received iv fluids **Effect size** 1.mean (SD) total diarrhoea output *intervention group 532 (476)* *placebo group 479 (354)* 2.mean (SD) total intake ORS *intervention group 511(457)* *placebo group 456 (355)* 3. mean (SD) duration of diarrhoea *intervention group 108 (68)* *placebo group 103 (53)* 4. proportion of patients with diarrhoea beyond 5d *intervention group 24/54* *placebo group 22/52* 5. proportion of patients that received iv fluids *intervention group 2/54* *placebo group 5/52*	**Funding** n.s. **Comments** Cessation of diarrhoea=the passage of a minimum of two soft stools or no stools in at least two consecutive 8h periods without recurrence of watery/liquid stool. * patients were rehydrated using a rice-based oral rehydration solution according to WHO guidelines -Method of randomisation: n. s. -Baseline comparability of the two groups at the start of the study adequate -Allocation concealment n.s. -Double-blinded -Power calculation done -Lost to follow-up: none

Zinc

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Al-Sonboli 2003 Location: Brazil Setting: hospital	**Study Type** RCT **Evidence Level** 1-	**Total no. of participants** N=74 Randomised in two arms: Intervention group N= 37 Control group N=37	Children aged from 3 to 60 months with acute diarrhoea for <7days or 1 or more loose stool with blood in the previous 24h and at least mild dehydration **Exclusion criteria** Severe systemic infection, antimicrobials/ anti-diarrhoeals in the 72h prior to admission, severe malnutrition (<60%WFA, NCHS).	**Intervention** Zinc sulfate - 22.5mg 3-6m - 45mg 7-60m **Control** Vitamin C - 250mg 3-6m - 500mg 7-60m **Comparison** *zinc vs. control*	**Follow-up** 5 days (or until resolution of diarrhoea, defined by clinical judgement) **Outcome** 1.mean duration of diarrhoea (d) 2.stool frequency (number of stools) **Effect size** 1.mean (SD) duration of diarrhoea *intervention group 1.2 (0.8)* *placebo group 2.5 (1.8)* *p<0.001* 2. mean (SD) number of stools *intervention group 4.1(4.1)* *placebo group 10 (10.2)* *p<0.01*	**Funding** n.s. **Comments** *all children in the trial received Ringer's lactate before ORS -Lost to follow-up:8.6% -Method of randomisation: random numbers -Baseline comparability of the two groups at the start of the study adequate -Double-blinded (assessor and patient) -Allocation concealment non stated -Power calculation n.s.
Fischer Walker 2006 {41958} Location: Ethiopia, India, Pakistan Setting: community-based	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=1110 Randomised in two arms: Intervention group N= 538 Control group N=536	infants from 1 to 5 months with acute diarrhoea for < 72h **Exclusion criteria** Severe malnutrition, pneumonia, required hospitalisation for any reason, major congenital malformation, or other serious pre-existent medical condition, live out or plan to move out of study area.	**Intervention** Zinc sulfate 10mg/day per 14 days **Comparison** *zinc vs. placebo*	**Follow-up** until the infant had passed <3 watery stools per 24h for at least 48h and until the mother confirmed the cessation of the diarrhoea * patients with diarrhoea>9d were referred to the HC facility for additional clinical assessment **Outcome** 1.mean duration of diarrhoea (h) 2.proportion of diarrhoea d7 3.stool frequency (mean number of stools/d) 4.hospitalisation 5.vomiting 6.death **Effect size**	**Funding** Johns Hopkins Family Health and Survival and Global Research Activity Cooperative Agreement with the US Agency for International Development **Comments** -Method of randomisation: adequate -Allocation concealment: yes

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					1.geometric mean (-1SD,+1SD) duration of diarrhoea *intervention group 3.80(1.84, 7.85)* *placebo group 3.59(1.82, 7.10)* 2.proportion (95%CI) of diarrhoea >7d *intervention group 25.1(21.5, 29.0)* *placebo group 20.3(17.0, 24,0)* 3. mean (SD) number of stools/d *intervention group 5(2.3)* *placebo group 5(2.4)* 4.hospitalisation, 1st 3d of study *intervention group 0/554* *placebo group 1/556* 5.vomiting *intervention group 8.7%* *placebo group 6.2%* 6.death (Ethiopia), 1st 3d of study *intervention group 1/554* *placebo group 1/556*	-power calculation: yes -Baseline comparability of the two groups at the start of the study was not adequate for gender and breast-feeding -Double-blinded (assessor and patient) -Lost to follow-up: 36/1074 during the 1st 3 days of the study (and were excluded from the analysis)
Bhatnagar 2004 {44021} Location: India Setting: hospital	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=287 Randomised in two arms: Intervention group N= 143 Control group N=144	boys aged from 3 to 36 months with acute diarrhoea for <72h with mild dehydration **Exclusion criteria** Severe malnutrition (<65% WFH, NCHS), visible blood in stool, severe systemic illness	**Intervention** Zinc sulfate per 14d - 15mg: <12 m - 30mg: > 12m **Comparison** *zinc vs. control* * both groups received multivitamin	**Follow-up** Until cessation of diarrhoea= time of the last abnormal stool before a 12h period when no stool had been passed or before the passage of two consecutive formed stools) **Outcome** 1. duration of diarrhoea (h) 2.diarrhoea at d5 3.diarrhoea at d7 4.stool output (g/Kg) 5.vomiting **Effect size** 1.mean (SD) duration of diarrhoea *intervention group 55.8 (37)* *placebo group 64.6 (45.6)* 2.diarrhoea at d5 *intervention group 17/132* *placebo group 27/134* 3.diarrhoea at d7	**Funding** WHO and the Indian Council of Medical Research **Comments** -Method of randomisation: random numbers -Allocation concealment yes -Power calculation: yes -Double-blinded (assessor and patient) -Baseline comparability of the two groups at the start of the study adequate -Lost to follow-up: 21/287 (7%), not included in the final analysis

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					intervention group 1/132 *placebo group 9/134* 4.total stool output GM (CI) *intervention group 111 (86,147)* *placebo group 148 (116,190)* 5.vomiting (at any time in the study) *intervention group 65%* *placebo group 59%*	
Brooks 2005 {42038} location: Bangladesh Setting: hospital	**Study Type** RCT **Evidence Level** 1+	**Total no. of patients** N=275 Randomised in two arms: *Intervention 1 group* N=91 *Intervention 2 group* N=91 *Placebo group* N=93	males aged from 1 to 6months with diarrhoea <72h and >=3 watery stools in the preceding 24h, some dehydration or >= 100ml of watery stool within 4h observation period **Exclusion criteria** Clinical signs of zinc deficiency, kwashiorkor, weight-to-age <60%WFA (NCHS), bloody stool, other comorbidity that required to be managed in another ward or proven or suspected cholera. * patients dehydration was corrected before enrolment: some (moderate) dehydration with 100ml/kg ORS for 4h; severe dehydration with initial iv fluid therapy and then ORS *Those who remained dehydrated were treated as cholera patients and therefore not enrolled in the study	**Intervention 1** 5mg zinc acetate/5ml **Intervention 2** 20mg zinc acetate/5ml ***placebo*** *5ml placebo* *treatment given for the duration of illness* **Comparison** *20mg zinc vs. placebo* *5mg zinc vs. placebo* *20mgzinc vs.5mg zinc*	**Follow-up** Duration of illness **Outcome** 1.total duration of diarrhoea after start intervention (d) 2.total stool output (ml) 3.frequency of diarrhoeal stools (number/d) 4. vomiting volume (ml) 5.total iv fluids (ml) 6.total fluid intake (ml) 1.total duration of diarrhoea after start intervention (d) Intervention1 gp 5 (4,6) Intervention2 gp 5 (4,6) Placebo gp 5 (4,6) 2.total stool output (ml) Intervention1 gp 229 (180,256) Intervention2 gp 240 (200,266) Placebo gp 202 (180,246) 3.frequency of diarrhoeal stools (number/d) Intervention1 gp 5 (5,6) Intervention2 gp 5 (5,6) Placebo gp 5 (4,6) 4. vomiting volume (ml) Intervention1 gp 26 (11.8,36.8) Intervention2 gp 18.5 (5.4,34.9) Placebo gp 37 (7.7,63.9)	**Funding** Supported by Johns Hopkins Family Health and Chld Survival Cooperative Agreement with the US Agency for International Development, by a cooperative agreement between the International Centre for Diarrhoeal Diseases Research, Bangladesh and US AID and by core donors to the ICDDR,B. **Comments** End of diarrhoea=formation of 3 soft stools or the absence of stools for >=12h -all the study members and patients were blinded to group assignment -adequate method of randomisation, baseline comparability

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					5.total iv fluids (ml) Intervention1 gp 300 (200,400) Intervention2 gp 240 (213,504) Placebo gp 300 (100,500) 6.total fluid intake (ml) Intervention1 gp 500 (500,527) Intervention2 gp 500 (500,500) Placebo gp 500 (500,572) *** There were no significant differences found between the groups**	between groups, power calculation done -allocation concealment unclear -15/275 lost at follow-up (95% of the enrolled participants included in the analysis)
Larson 2005 {41965} Location: Bangladesh Setting: outpatients and inpatients	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=1067 Randomised in two arms: Intervention group N= 534 Control group N=533	Children aged from 3 to 59 months with acute diarrhoea, having taken ORS as instructed, no vomiting reported in the past 2h for the short-stay ward or 30min in the outpatient clinic, and no longer dehydrated **Exclusion criteria** Returning to the hospital with an ongoing episode of diarrhoea, zinc supplementation	**Intervention** Zinc sulphate 20mg/day per 10 days **Control** placebo **Comparison** *zinc vs. placebo*	**Follow-up** 60 minutes from the administration of the study intervention (at the termination of the study observation period all children received zinc as per diarrhoea-management protocol of the hospital or clinic) **Outcome** Vomiting (=the forceful emptying of stomach contents) **Effect size** Short-stay ward treatment group 1.post-treatment vomiting *intervention group(N=267): 71 (26.6%)* *placebo group(N=266): 37 (13.9%)* outpatient clinic treatment group 1.post-treatment vomiting *intervention group (N=267): 68 (25.5%)* *placebo group (N=267): 27 (10.1%)*	**Funding** Bill and Melinda Gates Foundation-funded project **Comments** -All participants enrolled were included in the analysis (lost to follow-up reported 0%) -Method of randomisation: adequate -power calculation: yes -Baseline comparability of the two groups at the start of the study adequate -Double-blinded (assessor and patient) -Allocation concealment yes
Sachdev 1988 {41946}	**Study Type** RCT	**Total no. of participants**	Children aged from 6 to 18 months with dehydration secondary to acute diarrhoea	**Intervention** Zinc 20mg twice daily day	**Follow-up** Period of illness	**Funding** n.s.

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Location: India Setting: hospital	**Evidence Level** 1-	N=50 Randomised in two arms: Intervention group N= 25 Control group N=25	for < 4 days duration **Exclusion criteria** ABT, severe malnutrition, pneumonia, concomitant features (meningitis, pneumonia, liver disease, otitis media, fever>39C)	**Comparison** *zinc vs. placebo*	**Outcome** 1.mean duration of diarrhoea (h) 2.stool frequency (number of stools per 24h) 3.vomiting **Effect size** 1mean (SD) duration of diarrhoea *intervention group 82(42.9)* *placebo group 90.5(40)* 2.stool frequency (number of stools per 24h) *intervention group 7.6(4.0)* *placebo group 9.3(4.3)* 5.vomiting *none of the infants developed emesis secondary to zinc intake*	**Comments** -Method of randomisation: no details -no details on the proportion of the participants enrolled and included in the analysis -Baseline comparability of the two groups at the start of the study was adequate -Blinding: unclear -Allocation concealment unclear *AB were given after completion of the rehydration therapy
Sazawal 1995 {41933} Location: India Setting: community-based	**Study Type** RCT **Evidence Level** 1+	**Total no. of participants** N=947 Randomised in two arms: Intervention group N= 462 Control group N=485	Children aged from 6 to 35 months with four unformed stools in the previous 24h and with diarrhoea for <7d, with dehydration >7%, permanent resident of Kalkaji **Exclusion criteria** Second visit, malnutrition requiring hospitalisation	**Intervention** Zinc gluconate 20mg daily (until recovery?) **Comparison** *zinc vs. control* * both groups received multivitamin supplements * children who had diarrhoea for 10 days or more were given ABT	**Follow-up** Period of illness (cessation of diarrhoea= the last day of diarrhoea followed by a 72h diarrhoea-free period) **Outcome** 1.diarrhoea at d7 2.stool frequency **Effect size** 1.diarrhoea > d7 *intervention group(N=456): 15.4* *placebo group(N=481): 18.5* **children enrolled by day 4 of D* *intervention group (N=284) 10.2* *placebo group (N=285) 16.8* 2. mean (sd) watery stools/d *intervention group 3.1 (9.9)* *placebo group 5.1(14.9)*	**Funding** WHO, Diarrhoeal Disease Control Programme, the Thrasher Research Fund and the Indian Research Council for Medical Research **Comments** -Lost to follow-up: 10 children were excluded from all the final analysis of the study and 6 other the duration of diarrhoea was unknown (and were excluded from the analysis of duration of diarrhoea) -Method of randomisation: random numbers -Baseline

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
						comparability of the two groups: adequate -Double-blinded (assessor and patient) -Allocation concealment yes
Strand 2002 {41915} location: Nepal setting: community-based	**Study Type** RCT **Evidence Level** 1+	**Total no. of patients** N=891 *Zinc group* N=442 *Placebo group* N=449	children aged from 6 to 35 months with acute diarrhoea for <96h **Exclusion criteria** massive dose of vitamin A, had an illness requiring hospitalisation, family intended to leave Bhaktapur within 2 months	**Intervention** zinc gluconate: 15mg for infants and 30mg for older children (for +- 10d) until 7d after recovery **Comparison** *Zinc vs. placebo*	**Follow-up** 1 month **Outcome** 1.diarrhoea at day 3 2. diarrhoea at day 7 3. diarrhoea at day 14 (recovery from diarrhoea= the first of the first 2 consecutive diarrhoea-free days-<3 loose and no watery stools) **Effect size * (mean and 95%CI)** 1.diarrhoea at day 3 RR 0.75 (95%CI 0.61 to 0.91) *placebo gp 159/449 2. diarrhoea at day 7 RR 0.0.57 (95%CI 0.38 to 0.86) *placebo gp 58/449 3. diarrhoea at day 14 RR 0.0.55 (95%CI 0.20 to 1.47) *placebo gp 11/449	**Funding** EU-INCO-DC and NUFU **Comments** -Lost to follow-up:1% -Method of randomisation: adequate -Baseline comparability of the two groups: adequate -Double-blinded (assessor and patient) -Allocation concealment: yes -power calculation: yes *some of the children were enrolled twice or even three times (if >4monthd had lapsed from recovery from the previous enrolment episode)

Fibre

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Brown 1993 {38586} location: Peru setting: hospital	**Study Type** RCT **Evidence Level** 1-	**Total no. of patients** N=34 *Intervention group* N=19 *Control group* N=15	Male children aged from 2 to 24 months with acute diarrhoea for <96h **Exclusion criteria** systemic infection, dysentery, previous diarrhoea episode within the last 14d, breast-fed >1/day	**Intervention** Soy protein lactose free formula + added fibre **Control** Soy protein lactose free formula **Comparison** *Intervention vs. control*	**Follow-up** **Outcome** 1.mean duration of diarrhoea (h) 2. mean stool output 3. treatment failure **Effect size** <u>1.median duration of diarrhoea</u> intervention gp 43h control gp 163h p=0.003 <u>2. mean (sd) stool output 1st d hospitalisation</u> intervention gp 84 (70)g/kg control gp 77 (46) g/kg *stool output declined significantly in both groups during subsequent days of follow-up but there were no significant differences reported between the two groups <u>3. treatment failure</u> intervention gp 4/19 control gp 2/15	**Funding** Pediatric Nutrition Research and Development Division of Ross Laboratories UC Davis Clinical Nutrition Research Unit **Comments** *duration of diarrhoea=number of hours postadmission until excretion of the last liquid stool not followed by another abnormal stool within 24h *Treatment failure= recurring dehydration >5%, or electrolyte disorders after initial rehydration or faecal excretion >350g/Kg for 1d, >250g/Kg for 2 consecutive days, or >100g/Kg on day 6 of treatment -Lost to follow-up:6/40 -Method of randomisation: adequate -Baseline comparability of the two groups at the start of the study adequate -Allocation concealment unclear
Vanderhoof 1997 {42010} location: US setting: community-based	**Study Type** RCT **Evidence Level** 1+	**Total no. of patients** N=55 *Intervention group* N=30 *Control group* N=25	Infants <24m with acute diarrhoea (<=3d), >= watery stools/24h, or 3 times the normal number of stools in 24h **Exclusion criteria** Other GI disorders, infection disease	**Intervention** Soy-fibre supplemented formula for the first 10 days **Control** Soy formula without fibre For the first 10 days **Comparison** *Intervention vs. control*	**Follow-up** 24days (the study addressed first 10 days) **Outcome** 1.duration of diarrhoea **Effect size** <u>1. median duration of diarrhoea (h)</u> *Intervention group* 12.2	**Funding** n.s. **Comments** Lost to follow-up:19/74 *55 infants completed the study, the analysis included 67. Method of randomisation: random numbers

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					Control group 16.9 P>0.5 *infants > 6 months (N=44) *Intervention group* 9.7 *Control group* 23.1 P<0.5	Baseline comparability of the two groups at the start of the study adequate Double-blinded (assessor and patient) Allocation concealment unclear

PROBIOTICS
Systematic reviews

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Allen SJ 2003 {42007} UK	Study type Systematic review with meta-analysis Evidence Level 1++	23 trials were identified for inclusion (Total n=1917 participants) Quality varied but all the studies were RCTs	Participants were adults and children with acute diarrhoea (<14days), proven or presumed to be caused by an infectious agent. 18 trials reported exclusively on children (N=1449)	Any probiotic preparation regime vs placebo or no probiotic administration (Intervention and control arm to be otherwise treated identically in relation to other treatments and drugs)	**Outcomes** Diarrhoea lasting 3 or more days, 4 or more days Duration of diarrhoea Stool frequency Adverse events **Comparison 1** ***Probiotic vs. control*** <u>1.Diarrhoea lasting 3 or more days</u> significantly favoured probiotic 15 RCTs (N=1341): RR 0.66 [0.55 to 0.77] *infants and children 11 RCTs (N=1008): RR 0.68 [0.54 to 0.85] <u>2.Diarrhoea lasting 4 or more days</u> significantly favoured probiotic 13 RCTs (N=1228): RR 0.31 [0.19 to 0.50] *infants and children 9 RCTs (N=895): RR 0.41 [0.24 to 0.68] <u>3.Duration of diarrhoea</u> significantly favoured probiotic 12 RCTs (N=970): WMD -30.48 [-42.46 to -18.51] <u>4.Stool frequency on day 2</u>	**Sources of support** Department for International Development UK Medical Research Council Laboratories Gambia University of Oxford UK **Comments** Well-conducted systematic review Despite the great variability between studies (setting, participants recruited, probiotic tested, treatment regimens and definitions of outcome measures), nearly all trials reported that probiotics had a beneficial effect in reducing diarrhoea , and this was statistically significant in many studies.

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					significantly favoured probiotic 5 RCTs (N=417): WMD -1.51 [-1.85 to -1.17] *infants and children 4 RCTs (N=232): WMD -1.01 [-1.66 to -0.36] 5.Stool frequency on day 3 significantly favoured probiotic 4 RCTs (N=447): WMD -1.31 [-1.56 to -1.07] *infants and children 2 RCTs (N=170): WMD -1.12 [-1.79 to -0.46] **Comparison 2** ***Probiotic vs control, in children with rotavirus diarrhoea*** Duration of diarrhoea No statistically significant difference 4 RCTs (N=231): WMD -38.10[-68.10 to 8.10] **Comparison 3** ***Live Lactobacillus GG vs. control*** 1.Diarrhoea lasting 3 or more days No statistically significant difference 2 RCTs (N=329): RR 0.51 [0.14 to 1.83] 2.Diarrhoea lasting 4 or more days significantly favoured probiotic 1 RCT (N=287): RR 0.61 [0.43 to 0.85] 3.Duration of diarrhoea significantly favoured probiotic 5 RCTs (N=578): WMD -31.18[-51.62 to -10.75] 4.Stool frequency on day 2 significantly favoured probiotic 2 RCTs (N=62): WMD -1.50 [-2.83 to -0.17] **Comparison 4** ***Live Lactobacillus reuteri vs. control*** 1.Diarrhoea lasting 3 or more days significantly favoured probiotic 2 RCTs (N=106): RR 0.49 [0.26 to 0.94] 2.Diarrhoea lasting 4 or more days No statistically significant difference 2 RCTs (N=106): RR 0.29 [0.06 to 1.51] 3.Duration of diarrhoea significantly favoured probiotic 5 RCTs (N=86): WMD -25.33 [-40.70 to -9.95] 4.Stool frequency on day 2 significantly favoured probiotic	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					1 RCT (N=40): WMD -1.50 [-2.93 to -0.07] 5.Stool frequency on day 3 No statistically significant difference 1 RCT (N=40): WMD -1.2 [-2.60 to 0.20] **Comparison 5** ***Live Enterococcus LAB strain SF68 vs. control*** 1.Diarrhoea lasting 3 or more days significantly favoured probiotic 5 RCTs (N=372): RR 0.59 [0.47 to 0.74] 2.Diarrhoea lasting 4 or more days significantly favoured probiotic 5 RCTs (N=372): RR 0.23 [0.11 to 0.49] 3.Stool frequency on day 2 significantly favoured probiotic 1 RCT (N=185): WMD -1.70 [-2.10 to -1.30] 4.Stool frequency on day 3 significantly favoured probiotic 1 RCT (N=185): WMD -1.40 [-1.67 to -1.13] **Comparison 6** ***Live L. acidophilus and L. bifidus vs. control*** 1.Diarrhoea lasting 3 or more days No statistically significant difference 2 RCTs (N=164): RR 0.52 [0.21 to 1.28] 2.Diarrhoea lasting 4 or more days significantly favoured probiotic 2 RCTs (N=164): RR 0.06 [0.01 to 0.31] **Comparison 7** ***Live Streptococcus thermophilus and Lactobacillus. bulgaricus vs. control*** 1.Diarrhoea lasting 3 or more days No statistically significant difference 1 RCT (N=96): RR 1.08 [0.76 to 1.55] 2.Diarrhoea lasting 4 or more days No statistically significant difference 1 RCT (N=96): RR 1.04 [0.61 to 1.79] **Comparison 8** ***Killed Lactobacillus acidophilus LB vs. control*** 1.Diarrhoea lasting 3 or more days No statistically significant difference 2 RCTs (N=144): RR 0.77 [0.40 to 1.46] 2.Diarrhoea lasting 4 or more days significantly favoured probiotic 1 RCT (N=73): RR 0.11 [0.01 to 0.81] 3.Duration of diarrhoea	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					No statistically significant difference 1 RCT (N=73): WMD -13.60 [-28.10 to 0.90] **Comparison 9** ***Saccharomyces boulardii vs. control*** 1.Diarrhoea lasting 3 or more days significantly favoured probiotic 1 RCT (N=130): RR 0.71 [0.58 to 0.87] 2.Diarrhoea lasting 4 or more days significantly favoured probiotic 1 RCT (N=130): RR 0.41 [0.26 to 0.66] 3.Stool frequency on day 2 No statistically significant difference 1 RCT (N=130): WMD -0.62 [-1.49 to 0.25] 4.Stool frequency on day 3 significantly favoured probiotic 2 RCTs (N=222): WMD -0.92 [-1.52 to -0.32] **Comparison 10** ***Live Lactobacillus casei vs. control*** 1.Duration of diarrhoea significantly favoured probiotic 1 RCT (N=27): WMD -36.00 [-65.87 to -6.13] **Comparison 11** ***Live L. rhamnosus and L. reuteri vs. control*** 1.Duration of diarrhoea significantly favoured probiotic 2 RCTs (N=112): WMD -23.43 [-41.47 to -5.40] ***Adverse events** 12 RCTs reported that clinical observations of the participants revealed no adverse events, 8 did not collect or report information on adverse events and 3 studies reported that an adverse event occurred: Pant 1996, 1/19 children in the control group vomited one dose of the medication (0/20 in the probiotic group) Raza 1995, frequency of vomiting on the 2nd day of intervention was statistically significant less in children in the probiotic group than in the placebo group. Shornikova-a 1997, fewer children in the probiotic than in the control group had vomiting from the 2nd day of treatment (stat. sig. on day 2 and 4) No authors reported an adverse effect that they considered to be attributable to the probiotic	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Szajweska 2007 {42043} Poland	Study type Systematic review with meta-analysis Evidence Level 1+	5 RCTs were identified for inclusion (Total N=619 participants) The quality varied across the studies 2 RCTs were located in Pakistan, One in Mexico, one in Turkey and one in Argentina	Participants were children (from 2months to 12 years) with acute diarrhoea, inpatients and outpatients.	*S. boulardii* compared to placebo or no additional intervention in treating acute diarrhoea.	**Outcomes** Duration of diarrhoea Cure on day 2 and 8 Presence of diarrhoea at different time intervals Diarrhoea lasting > 7 days Frequency of stool output Vomiting Hospitalisation * definition criteria for resolution of the diarrhoea, when reported, was different across studies **Comparison** ***S.boulardii vs. control*** 1.Duration of diarrhoea (days) significantly favoured Sb 4 RCTs (N=473): WMD -1.1 [-1.3 to -0.83] 2. Cure on day 2 significantly favoured Sb 1 RCT (N=130): RR 4 [1.8 to 9.1] 3. Cure on day 8 significantly favoured Sb 1 RCT (N=130): RR 1.9 [1.4 to 2.8] 4.Diarrhoea on day 3	**Sources of funding** Medical University of Warsaw **Comments** All the studies included presented methodological limitations (only two RCTs reported an adequate method of randomisation, only one had an adequate allocation concealment, two were not blinded and three did not apply the ITT analysis). Duration of intervention: was between 4 and 6 days (and one study had 14d follow-up)

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
					significantly favoured Sb 1 RCT (N=101): RR 0.71 [0.56 to 0.9] 5.Diarrhoea on day 4 No statistically significant difference 1 RCT (N=88): RR 0.73 [0.5 to 1.1] 6.Diarrhoea on day 6 'significantly' favoured Sb 1 RCT (N=101): RR 0.49 [0.24 to 0.99] 7.Diarrhoea on day 7 significantly favoured Sb 1 RCT (N=88): RR 0.39 [0.20 to 0.75] 8.Diarrhoea > 7d significantly favoured Sb 1 RCT (N=88): RR 0.25 [0.08 to 0.83] 9.number of stools on day 1 No statistically significant difference 1 RCT (N=130): WMD -0.32 [-1.1 to 0.43] 10.number of stools on day 3 significantly favoured probiotic 3 RCTs (N=331): WMD -1.3 [-1.9 to -0.63] 11.number of stools on day 4 significantly favoured probiotic 2 RCTs (N=218): WMD -1.1 [-1.6 to -0.64] 12.number of stools on day 6 significantly favoured probiotic 2 RCTs (N=201): WMD -1.7 [-2.4 to -1] 13.number of stools on day 7 significantly favoured probiotic 1 RCT (N=88): WMD -0.9 [-1.4 to -0.62] 14.Hospitalisation (days) significantly favoured probiotic 1 RCT (N=200): WMD -1 [-1.4 to -0.62] 15.Duration of vomiting (days) No statistically significant difference 1 RCT (N=200): WMD -0.1 [-0.34 to 0.14] ***Adverse events** Adverse events associated with the administration of Sb were not reported in any of the trials	
Bibliographic Details	**Study Type & Evidence Level**	**Study Details**	**Patient Characteristics**	**Intervention & Comparisons**	**Outcome Measures, Follow Up & Effect Size**	

Bibliographic Details	Study Type & Evidence Level	Study Details	Patient Characteristics	Intervention & Comparisons	Outcome Measures, Follow Up & Effect Size	Comments
Szajweska 2007 {42045} Poland	Study type Systematic review with meta-analysis Evidence Level 1+	8 RCTs were included (Total N=988 participants) The quality varied across the studies 4 RCTs were located in Europe, 1 in Brazil, 1 in Uruguay, 1 in Peru and 1 in Pakistan.	Participants were children (from 1 to 36 months) with acute diarrhoea, inpatients and outpatients *5 trials included inpatients participants and 1 outpatient. 2 trials included inpatient and outpatient participants *The RCT located in Pakistan included undernourished children.	*L.* GG compared to placebo or no additional intervention. *The daily dose of the probiotic, preparation and the duration of the intervention varied across studies	**Outcomes** Duration of diarrhoea Total stool output Presence of diarrhoea at different time intervals hospitalisation * definition criteria for resolution of diarrhoea, when reported, was different across studies **Comparison** ***L. GG vs. control*** 1.Duration of diarrhoea (days) significantly favoured LGG 7 RCTs (N=876): WMD -1.08 [-1.87 to -0.28] * Duration diarrhoea rotavirus + children 3 RCTs (N=201): WMD -2.08 [-3.55 to -0.6] 2.total stool output ml/kg significantly favoured LGG 2 RCTs (N=303): WMD 24.2 [-86.26 to 104.2] 3. Diarrhoea on day 3 significantly favoured LGG 2 RCTs (N=329): RR 0.56 [0.4 to 0.78] 4.Diarrhoea >7d significantly favoured LGG 1 RCT (N=287): RR 0.25 [0.09 to 0.75] 5.Diarrhoea >10d No statistically significant difference 1 RCT (N=97): RR 0.23 [0.03 to 1.91] 6.Hospitalisation (days) No statistically significant difference (random EM) 3 RCTs (N=535): WMD -0.43 [-1.32 to 0.46]	**Sources of funding** Medical University of Warsaw **Comments** All the studies included presented methodological limitations and were significantly heterogenous. Only studies carried out in Europe consistently showed a beneficial effect of the administration of LGG Duration of intervention was not specified in two trials, was ad libitum in two others, was 2 days in one and five days in the remaining three.

Probiotics
RCTs

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
Henker 2007{44384} Location: Ukraine, Russia, Germany	**Study Type** Multicentre-RCT **Evidence Level** 1+ **Setting:** outpatient	**Total no. of participants** N=113 Randomised in two arms: Intervention group N= 55 Control group N=58	Children, aged between 2 and 47 months, treated for acute diarrhoea (< than 3 days of >3 watery-to-loose stools/day of non-bloody diarrhoea) in the paediatric outpatient wards of 11 centres **Exclusion criteria** Dehydration (>5% loss of BW), participation in another trial, intake of EcN within the previous 3 months, intake of food supplements or drugs with live micro-organisms, antibiotics, other antidiarrhoeal drugs, breast-feeding, premature birth, severe or chronic GI illness, other concomitant diseases.	**Intervention** Oral suspension E.coli Nissle Infants<1year: 1ml/d 1 to 3years:1ml x2/d 3 to 4years:1mlx3/d **Control** placebo **Comparison** *EcN vs. control*	**Follow-up** 10 days **Outcome** 1.median duration of diarrhoea (d) 2.patients with no diarrhoea d3 3.patients with no diarrhoea d10 4.adverse events **Effect size** 1.median duration of diarrhoea (d) *intervention group 2.5* *placebo group 4.8* *p<0.001* 2.patients with no diarrhoea d3 *intervention group 34/55* *placebo group 24/55* 3.patients with no diarrhoea d10 *intervention group 52/55* *placebo group 39/58* 4.adverse events *intervention group 2/55* **rhinitis and abdominal pain* *placebo group 2/58* *acute otitis media	**Funding** ARDEYPHARM . **Comments** Lost to follow-up: 12.3% Method of randomisation: random numbers Baseline comparability of the two groups at the start of the study adequate Double-blinded (assessor and patient) Allocation concealment yes ITT: yes
Salazar-Lindo 2007 {42023} Location: Peru	**Study Type** Multicentre-RCT **Evidence Level** 1+ **Setting** outpatients	**Total no. of participants** N=80 Randomised in two arms: Intervention group N= 40 Control group N=40	Children with acute diarrhoea presumed to be of infectious origin, <72h and with >=3 watery stools within the previous 24h. **Exclusion criteria** Signs of dehydration requiring hospitalisation according to WHO guidelines, bloody stools, chronic GI disease, chronic	**Intervention** 20 billion units of killed Lactobacillus LB 2 sachets/d x 4.5 days **Comparison** *L LB vs. placebo*	**Follow-up** 4.5 days **Outcome** 1.median duration of diarrhoea (h) 2.proportion of children with diarrhoea at the end of the study 3.total ORS intake 4.vomiting 5.adverse events	**Funding** Axcan Pharma SA **Comments** End of diarrhoea episode=time to the first normal stool followed by 2 consecutive normal stools or time to the last diarrhoeic stool followed by 12h without stool

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
			immunological condition, lactose or fructose intolerance, haemodynamic abnormalities, neurological disturbance, rectal body temperature >39C.		**Effect size** 1median duration of diarrhoea *intervention group 10(6/56.7)** *placebo group 16.6(7.1/50.3)** **(quartile1/quartile3)* 2.proportion of children with diarrhoea at the end of the study *intervention group 1/40* *placebo group 5/40* 3.total ORS intake reported as similar in both groups ➔the authors reported that the findings were non statistically significant 4.vomiting *intervention group 12/40* *placebo group 6/40* 5.adverse events *intervention group 1/40* *placebo group 1/40*	Lost to follow-up:3/80 Method of randomisation: n.s. Baseline comparability of the two groups at the start of the study was addequate Double-blinded (assessor and patient) Allocation concealment unclear
Sarker 2005 {41918} Location: Bangladesh	**Study Type** RCT **Evidence Level** 1+ **Setting:** hospital	**Total no. of participants** N=230 Randomised in two arms: Intervention group N= 115 Control group N=115	Male infants and young children aged from 4 to 24 months with acute diarrhoea (>=4liquid stools during 24h) for <48h **Exclusion criteria** Severe malnutrition, systemic infection requiring ABT, bloody diarrhoea, children whose stool sample resulted + (dark-field microscopy) to *Vibrio cholerae*, ABT within the previous 2 weeks	**Intervention** Lyophilized L. paracasei strain ST11 (5x10 9 CFU) twice daily for 5d **Comparison** *L.ST11 vs. placebo*	**Follow-up** 6 days or until cessation of diarrhoea **Outcome** 1. mean duration of diarrhoea (h) after first dose therapy 2.cessation of diarrhoea 3. total stool output (g/kg) 4.total ORS intake (ml/kg) 5.children requiring IV fluid therapy **Effect size** 1.mean (SD) duration of diarrhoea *intervention group 90.4 (45)* *placebo group 94.2 (43.3)* 2.cessation of diarrhoea *intervention group 81/115* *placebo group 73/115* 3.total stool output (g/kg) *intervention group 385(330)* *placebo group 389(259)* 4.total ORS intake (ml/kg) *intervention group 334 (280)*	**Funding** Swedish agency for research in developing countries, the Karolinska Institute, the Nestle Research Centre **Comments** *cessation of diarrhoea =passage of the last watery or loose stool before passage of 2 consecutive soft or formed stools or no stool in >2 consecutive 8h periods Lost to follow-up: 11.8% Method of randomisation: random numbers Baseline comparability of the two groups at the start of the study adequate

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					placebo group 343 (230) 5.children requiring IV fluid therapy *intervention group 1/115* *placebo group 4/115* ***children rotavirus-infected** 1.mean (SD) duration of diarrhoea *intervention group 94 (43)* *placebo group 95 (37.9)* 2.cessation of diarrhoea *intervention group 56/75* *placebo group 45/65* 3.total stool output (g/kg) *intervention group 421(345)* *placebo group 417(273)* 4.total ORS intake (ml/kg) *intervention group 370 (288)* *placebo group 366 (229)* ***children non rotavirus-infected** 1.mean (SD) duration of diarrhoea *intervention group 77 (48)* *placebo group 99 (51)* 2.cessation of diarrhoea *intervention group 19/27* *placebo group 17/18* 3.total stool output (g/kg) *intervention group 225(218)* *placebo group 318(240)* 4.total ORS intake (ml/kg) *intervention group 180 (207)* *placebo group 331 (236)*	Double-blinded (assessor and patient) Allocation concealment yes Power calculation
Szymanski 2006 {42042} location: Poland	**Study Type** RCT **Evidence Level** 1+ **Setting:** hospital	**Total no. of patients** N=87 Randomised in two arms: *Intervention group* N=49 *Placebo group* N=44	Children aged from 2m to 6y with acute diarrhoea treated either at the paediatric ward or at the outpatient department. **Exclusion criteria** Organic GI disease, underlying chronic disease, immuno-suppressive condition or treatment and exclusively breast-fed infants.	**Intervention 1** 1.2x10*10CFU L.rhamnosus strains (573L/1 ; 573L/2 ; 573L/3) **Comparison** *Probiotic vs placebo*	**Follow-up** 5 days **Outcome** 1.total duration of diarrhoea after start intervention (d) 2.diarrhoea lasting >7d 3.duration iv therapy (h) 4.adverse events **Effect size * (mean and 95%CI)** 1.total duration of diarrhoea after start	**Funding** Wellcome travel Award **Comments** diarrhoea= 3 or more bowel movements per day of stools that are looser than normal and may contain blood, pus or mucus, for more than 1 but less than 5 days

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
					intervention (h)* Intervention gp 83.6 (55.6) Placebo gp 96 (71.5) 2.diarrhoea lasting >7d Intervention gp 3/46 Placebo gp 7/41 3.duration iv therapy (h)* Intervention gp 16 (19.3) Placebo gp 24.3 (29.1) ***children with rotaviral diarrhoea** 1.total duration of diarrhoea after start intervention (h)* Intervention gp 77.5 (35.4) Placebo gp 115 (66.9) 2.diarrhoea lasting >7d Intervention gp 1/22 Placebo gp 1/17 3.duration iv therapy (h)* Intervention gp 14.9 (13.7) Placebo gp 37.7(32.9) 4.adverse events No adverse events were reported	study members and patients blinded to group assignment adequate method of randomisation, baseline comparability between groups, allocation concealment yes 6.5% lost at follow-up (<90% of the enrolled participants included in the analysis)
Berni Canani 2007 Location: Italy	**Study Type** RCT **Evidence Level** 1+ **Setting:** outpatient	**Total no. of participants** N=571 Randomised in six arms: Intervention group1 N= 92 Intervention group2 N= 100 Intervention group3 N= 91 Intervention group4 N= 100 Intervention group5	Children aged from 3 to 36 months visiting a family paediatrician for acute diarrhoea **Exclusion criteria** Returning to the hospital with an ongoing episode of diarrhoea, zinc supplementation	Interventions and placebo administered twice daily **Intervention1** LGG 6x10*9CFU/dose **Intervention2** S boulardii 5x10*9live micro-org. **Intervention3** Bacillus clausii 10*9CFU/dose **Intervention4** L bulgaricus 10*9CFU, L acidophilus 10*9CFU, S	**Follow-up** **Outcome** 1.duration of diarrhoea(h) 2.daily stool output 3.n. admitted to hospital 4.vomiting **Effect size** 1.median duration of diarrhoea (IQR) *intervention 1gp 78.5 (56.5-104.5)* **p<0.001* *intervention 2gp 105 (90-104.5)* *intervention 3gp 118 (95.2-128.7)*	**Funding** None` **Comments** *duration of diarrhoea= time in hours from the last abnormal (loose or liquid) stools preceding a normal stool output. Method of randomisation: computer generated sequence Allocation concealment yes Blinding: No

Bibliographic details	Study type & evidence level	No. of Participants	Participants characteristics	Intervention & comparison	Outcome measures, Follow-up, Effect size	Comments
		N= 97 Control group N=91		thermophilus 10*9CFU, B bifidum5X10*8/CFU **Intervention5** E faecium 7.5x10*7CFU/dose **Control** Placebo (ORS) **Comparison** *Intervention1 vs. placebo* *Intervention2 vs. placebo* *Intervention3 vs. placebo* *Intervention4 vs. placebo* *Intervention5 vs. placebo*	*intervention 4gp 70 (49-101)* **p<0.001* *intervention 5gp 115 (89-144)* *placebo gp 115.5 (95.2-127)* 2.median daily stool output(IQR) ***day2*** *intervention 1gp 4 (4-6)* **p<0.001* *intervention 2gp 5 (4-7)* *intervention 3gp 5 (4-7)* *intervention 4gp 4 (4-6)* **p<0.001* *intervention 5gp 5 (4-7)* *placebo gp 5 (4-7)* ***day5*** *intervention 1gp 2 (2-3) *p=0.003* *intervention 2gp 3 (2-4)* *intervention 3gp 3 (2-4)* *intervention 4gp 2 (2-3) *p=0.002* *intervention 5gp 3 (2-4)* *placebo gp 3 (2-4)* 3.n. admitted to hospital (%) *intervention 1gp 1 (1.0)* *intervention 2gp 4 (4.4)* *intervention 3gp 4 (4.0)* *intervention 4gp 2 (2.1)* *intervention 5gp 4 (4.4)* *placebo gp 4 (4.3)* ➔ reported as no statistically sig. 4.vomiting (%) *intervention 1gp 31 (31)* *intervention 2gp 24 (26.4)* *intervention 3gp 32 (32)* *intervention 4gp 34 (35.1)* *intervention 5gp 36 (39.6)* *placebo gp 34 (37)`* ➔ reported as no statistically sig.	Sample size power calculation yes