NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG84) – Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years

1. Background information

Guideline issue date: 2009
3 year review: 2012
National Collaborating Centre: Women's and Children's Health

2. Consideration of the evidence

Literature search

Through an assessment of abstracts from a high-level randomised controlled trial (RCT) search, new evidence was identified relating to the following clinical areas within the guideline:

- Fluid management
- Other therapies

Through this stage of the process, a sufficient number of studies (n=33) relevant to the above clinical areas were identified to allow an assessment for a proposed review decision. These are summarised in Table 1 below.

From initial intelligence gathering, qualitative feedback from other NICE departments, the views expressed by members of the Guideline Development

Group, as well as the high-level RCT search, an additional focused literature search was conducted for the following clinical area:

- Is there a systematic scoring approach to the assessment of dehydration in children under 5 years of age?

The result of the focused search is summarised in Table 2 below. All references identified through the high-level RCT search, initial intelligence gathering and the focused searches can be viewed in Appendix 1

Table 1: Summary of articles from the high level search

Clinical area 1: Fluid management		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q4: What is the most effective composition of ORS (oral rehydration salt) solution? Q8: During rehydration with IVT, how much fluid is required, and how quickly should it be given? Is there a place for 'rapid rehydration therapy'? **Relevant section of the guideline** 5.3 Optimal composition and administration of oral fluids 5.4 Intravenous fluid therapy (IVT)	Through an assessment of the abstracts from the high-level RCT search, 4 studies relevant to the clinical questions were identified. *Composition of ORS solution (2 studies)* • One RCT[1] conducted in Egypt investigated whether the addition of honey in oral rehydration solution (ORS) could affect the duration of symptoms of acute gastroenteritis in infants and children. Babies in the control group received ORS for rehydration while those in the intervention group received ORS with honey. Results showed that in the honey-treated group the frequencies of vomiting and diarrhoea were significantly reduced compared to the control group. Also, the recovery time, defined as the number of hours from initiation of treatment to when normal soft stools are passed, with the patient showing normal hydration and satisfactory weight gain,	No new evidence was identified which would invalidate current guideline recommendation(s).

	was significantly shortened after honey ingestion. The authors concluded that honey added to ORS promoted rehydration of the body and sped recovery from vomiting and diarrhoea • One small RCT[2] conducted in Bangladesh investigated whether the addition of L-isoleucine to ORS would reduce stool output and/or duration of acute diarrhoea in children and induce antimicrobial peptides in intestine. Children aged 6 to 36 months with acute diarrhoea and some dehydration were included. The authors concluded that L-isoleucine-supplemented ORS might be beneficial in reducing stool output and ORS intake in children with acute watery diarrhoea but that a further study is warranted to substantiate the therapeutic effect of L-isoleucine. *Rapid rehydration therapy (2 studies)* • One RCT[3] conducted in Canada aimed to determine if rapid (60 mL/kg) rather than standard intravenous (IV) rehydration (20 mL/kg) over one hour results in improved hydration and clinical outcomes when administered to children with gastroenteritis. Included children were those who had not	

	responded to oral rehydration and had been prescribed IV rehydration. Results showed no evidence of a difference between the rapid and standard rehydration groups in the proportions of participants who were rehydrated at two hours; the rates of prolonged treatment were similar and the median time to discharge was longer in the rapid group. The authors concluded that there were no relevant clinical benefits from the administration of rapid rather than standard intravenous rehydration. • One pilot randomised trial[4] conducted in the USA tested the efficacy of ultra-rapidly infused hydration (50 mL/kg normal saline for 1 hour) compared to rapidly infused IV hydration (50 mL/kg normal saline for 3 hours) in 3-to-36-month-old babies with acute gastroenteritis and moderate dehydration who had failed an oral fluid challenge. The authors concluded that preliminary results suggest ultra-rapid hydration for 1 hour appears to be an efficacious alternative to standard rapid hydration for 3 hours and improves emergency department transition time	

	Summary In summary, the identified studies relate to the composition of ORS solution and rapid rehydration therapy and the findings are in line with current guideline recommendations	
Clinical area 2: Other therapies		
Clinical questions	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Which interventions (other than fluid therapy and antibiotic treatment) are effective and safe? **Relevant section of the guideline** 8.1 Anti-emetics 8.2 Antidiarrhoeal agents 8.3 Micronutrients and fibre 8.5 Probiotics	Through an assessment of the abstracts from the high-level search, 29 studies relevant to the clinical questions were identified. *Anti-emetics (6 studies)* • One Cochrane review[5] assessed the safety and effectiveness of antiemetics on gastroenteritis induced vomiting in children and adolescents. Pooled data from three studies comparing oral ondansetron with placebo showed that oral ondansetron increased the proportion of patients who had ceased vomiting and reduced the number needing intravenous rehydration and immediate hospital admission. The authors concluded that intravenous ondansetron and metoclopramide reduced the	Potential new evidence was identified that may change current recommendation(s).

	number of episodes of vomiting and hospital admission, and dimenhydrinate as a suppository reduced the duration of vomiting. • One systematic review and meta-analysis[6] assessed whether taking antiemetic drugs reduces vomiting and decreases the need for further intervention in children with gastroenteritis without causing significant adverse effects. Six studies on ondansetron were identified and meta-analysis demonstrated a decreased risk of further vomiting and immediate hospital admission, as well as a reduced need for intravenous fluid. However, there was an increase in diarrhoeal episodes in ondansetron-treated patients and its use did not significantly affect return to care. • One RCT[7] investigated potential beneficial effects of ondansetron in treating vomiting during acute gastroenteritis. Children 5 months to 8 years were randomized to receive either ondansetron or placebo at 8-hour intervals. Results showed that compared with the children who received placebo, children who received ondansetron were less likely to vomit	

	both during the first 8-hour follow-up in the emergency department and during the next 24-hour follow-up. The authors concluded that ondansetron may be an effective and efficient treatment that reduces the incidence of vomiting from gastroenteritis and is probably a useful adjunct to oral rehydration • One RCT[8] on the efficacy of intravenous ondansetron to prevent vomiting episodes in acute gastroenteritis was found. Children 3 months to 15 years with acute gastroenteritis were enrolled and randomly assigned to an ondansetron or a placebo group. Results showed that ondansetron significantly induced vomiting cessation compared to placebo; length of hospital stay and oral rehydration fluid volume were similar in the two groups, and no adverse effects were noticed. The authors concluded that the safety, low cost, and overall benefit of ondansetron treatment suggests that the drug can be administered successfully to children with acute gastroenteritis. • One double-blind RCT [9] investigated the efficacy and safety of ondansetron compared to metoclopramide in the treatment of	

	children with persistent vomiting with acute gastroenteritis. The primary efficacy outcome was the proportion of patients in each group with cessation of vomiting shortly after completion of the study medication infusion. The authors concluded that in their study population, intravenous metoclopramide therapy did not differ from ondansetron in the treatment of persistent vomiting for children with gastroenteritis admitted for intravenous fluid hydration. • One German multicentre RCT[10] investigated the efficacy and safety of rectal dimenhydrinate compared to placebo in children with acute gastroenteritis. Children with no or mild dehydration were included and all children received oral rehydration therapy. The authors concluded that dimenhydrinate reduces the frequency of vomiting in children with mild dehydration; however, the overall benefit is low because it does not improve oral rehydration and clinical outcome. Overall, the identified studies on anti-emetics mainly relate to ondansetron, and although the studies indicate that ondansetron	

	decreased the risk of further vomiting, concerns about adverse effects of the drug such as worsening diarrhoea remain. Hence, the findings of the above studies would not change the current guideline recommendations on the use of anti-emetics. *Anti-diarrhoeal agents (3 studies)* • An individual patient data (IPD) meta-analysis[11] assessed the efficacy of racecadotril as an adjunct to oral rehydration solution, against oral rehydration solution alone or with placebo in childhood acute gastroenteritis. The authors concluded that as an adjunct to oral rehydration solution, racecadotril has a clinically relevant effect in reducing diarrhoea (duration, stool output and stool number) irrespective of baseline conditions (dehydration, rotavirus or age), treatment conditions (inpatient or outpatient studies) or cultural environment. • One RCT[12] conducted in Spain compared the efficacy of racecadotril plus oral rehydration versus oral rehydration alone in children with gastroenteritis in an outpatient care setting. Results revealed no significant differences in the number of bowel movements between the 2 groups 48 hours after	

	initiating treatment or the average duration of gastroenteritis. The incidence of adverse events was similar in both groups. The authors concluded that the use of racecadotril did not improve the symptoms of diarrhoea compared with standard rehydration therapy. • One article[13] reported the results of two parallel, double-blind studies of diosmectite efficacy on stool reduction that were conducted in children 1 to 36 months old in Peru and Malaysia. Babies with the need for intravenous rehydration, gross blood in stools, fever higher than 39 degrees C, or current treatment with antidiarrhoeal or antibiotic medications were excluded. Results showed that diosmectite significantly decreased stool output in children with acute watery diarrhoea, especially those who were rotavirus-positive. The identified studies on anti-diarrhoeal agents indicate that racecadotril and diosmectite may be useful in the management of children with diarrhoea. The recommendation in the guideline is to not use antidiarrhoeal medications.	

	Micronutrients and fibre *Zinc (2 studies)* • One RCT[14] evaluated the efficacy and safety of zinc in the treatment of acute gastroenteritis in children in Poland. Children aged 3 to 48 months with acute gastroenteritis received zinc sulfate or placebo for 10 days. Results showed no significant difference between the two groups in the duration of diarrhoea, stool frequency, vomiting frequency, intravenous fluid intake, and the number of children with diarrhoea lasting >7 days. The authors concluded that children living in a country where zinc deficiency is rare do not appear to benefit from the use of zinc in the treatment of acute gastroenteritis. • One RCT[15] evaluated the effect of oral zinc sulfate on the management of acute gastroenteritis in Iranian children. Results showed that the frequency of diarrhoea was less and weight gain after 10 days was more, in the intervention group than the control group. There was no significant difference in duration of diarrhoea or hospitalisation. The authors concluded that there is a meaningful relationship between the frequency	

	of diarrhoea and weight gain in children with acute gastroenteritis receiving oral zinc sulphate and suggested that zinc sulfate be prescribed for babies with acute diarrhoea for a period of 10 to 14 days *Probiotics* *<u>Products or formulations containing only probiotics (4 studies)</u>* • One double blinded case-control clinical trial[16] conducted in Iran compared traditional yogurt and probiotic yogurt in improving acute non-inflammatory gastroenteritis in children aged 6 months to 12 years. Results showed statistically significant differences between the case and control groups in the reduction as well as discontinuation of diarrhoea. The authors concluded that acute non-inflammatory gastroenteritis improvement is accelerated by probiotic yogurt consumption. • One RCT[17] evaluated the efficacy and tolerability of a probiotic mixture (VSL[sharp]3 (CD Pharma India)) or placebo in the treatment of acute rotavirus diarrhoea in children. Results showed that overall recovery rates were significantly better in the intervention group compared with placebo. No side effects	

	were noted with the use of the probiotic mixture. The authors concluded that the use of the probiotic mixture (VSL[sharp]3) in acute rotavirus diarrhoea resulted in earlier recovery and reduced frequency of ORS administration, reflecting decreased stool volume losses during diarrhoea. • One RCT[18] compared the effect of two probiotic products in the treatment of diarrhoea in Bolivian children less than 2 years of age hospitalized for acute rotavirus diarrhoea. Children were randomly assigned to receive one of three treatments: ORT plus placebo; ORS solution plus Saccharomyces boulardii; or ORS solution plus a compound containing Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacterium longum and Saccharomyces boulardii. Results showed that both products decreased the duration of diarrhoea compared to ORS solution alone. However, the decrease was significant only for the single species product which also decreased the duration of fever. With the multiple species product there was no vomiting subsequent to the initiation of treatment. The authors concluded that the quantity of probiotic bacteria	

	needed for optimum treatment of gastroenteritis remains to be determined, particularly when multiple species are included in the product. • One RCT[19] evaluated the clinical, microbiologic, and immunologic effects of probiotics in acute infectious diarrhoea. Children aged 3 months to 6 years hospitalised for acute diarrhoea were randomised to receive Bio-three (a mixture of Bacillus mesentericus, Enterococcus faecalis, and Clostridium butyricum) or placebo orally 3 times daily for 7 days. The authors concluded that the probiotics mixture reduced the severity of diarrhoea and length of hospital stay in children with acute diarrhoea. They posited that in addition to restoring beneficial intestinal flora, probiotics may enhance host protective immunity such as down-regulation of pro-inflammatory cytokines and up-regulation of anti-inflammatory cytokines. *Probiotics in combination with other substances (4 studies)* • One RCT[20] evaluated the effectiveness of zinc, Saccharomyces boulardii (S. boulardii) (probiotic bacteria),	

	lactose-free formula as well as their different combinations in the treatment of rotavirus diarrhoea in young children. Results only showed statistically significant reduction in the duration of diarrhoea and hospitalization in babies who received zinc and zinc plus S. boulardii compared to those who received only oral and/or parenteral rehydration solutions. The authors concluded that different combinations of adjunct therapies did not bring additional value to rehydration therapy in children with rotavirus diarrhoea except for in those receiving only zinc and zinc plus S. boulardii. They suggested that further studies are required to determine the optimal protocol of adjunct therapy use in children with rotavirus diarrhoea. • One RCT[21]tested the efficacy of a new synbiotic formulation containing Lactobacillus paracasei B21060, arabinogalactan and xilooligosaccharides in children with acute diarrhoea. Results showed that the resolution rate of diarrhoea at 72 h was significantly higher in the synbiotic group compared to the placebo group. Also, children in the synbiotic group showed a significant reduction in the duration of diarrhoea, daily stool	

	outputs and stool consistency compared to placebo group. Rate of parents that missed at least one working day, rate of children that needed adjunctive medications or hospitalisation after the first 72 h of treatment, were reduced in the synbiotic group. The authors concluded that the synbiotic formulation was effective in children with acute diarrhoea. • One RCT[22] tested the efficacy of the synbiotic food supplement Probiotical (Streptoccoccus thermophilus, Lactobacillus rhamnosus, Lactobacillus acidophilus, Bifidobacterium lactis, Bifidobacterium infantis, fructo-oligosaccharides) in children with acute diarrhoea. The primary end-points were duration of diarrhoea and the number of children that had a normalised stool consistency. The authors concluded that median duration of diarrhoea was significantly 1 day shorter in the synbiotic group than in the placebo group, which was associated with decreased prescription of additional medications. • One RCT[23] evaluated the efficacy and safety of a pre & probiotic formulation (Bifilac) in children three months to three years of age, with acute rotaviral diarrhoea. Results showed a	

	statistically significant reduction in the frequency and duration of diarrhoea and rotavirus shedding was observed in those children treated with Bifilac along with ORS solution. The duration and volume of ORS solution and intravenous fluid therapy were also significantly reduced in those children treated with Bifilac. The authors concluded that Bifilac was safe for children in their study population. *Lactobaccilus (6 studies)* • One meta-analysis[24] on the effects of Lactobacillus rhamnosus GG supplementation for the prevention of healthcare-associated diarrhoea in children was found. The authors concluded that in hospitalised children, the administration of Lactobacillus rhamnosus GG compared with placebo has the potential to reduce the overall incidence of healthcare-associated diarrhoea, including rotavirus gastroenteritis. • One RCT[25] evaluated the efficacy of lactobacillus rhammosus GG in babies hospitalized for acute diarrhoea in rural India. Babies were given a 10-day course of Lactobacillus rhammosus GG (minimum dose, 10 degrees bacteria) or	

	placebo. Results showed that there was no difference in the two groups in the duration of diarrhoea or numbers of stool on days 3, 6, or 10 of treatment. • One RCT[26] conducted in Iran investigated the effects of Lactobacillus acidophilus yogurt and supplement in children with acute non-bloody diarrhoea. Standard fluid therapy was administered in all patients. The authors concluded that L.acidophilus yogurt and L.acidophilus supplement would diminish the seventy of acute non-bloody diarrhoea in children. • One RCT[27] assessed the efficacy of Lactobacillus GG in Australian Aboriginal children admitted to hospital with diarrhoeal disease. Children received either oral Lactobacillus GG (5 x 10(9) CFU 3 times per day for 3 days) or placebo. The authors concluded that Lactobacillus GG did not appear to enhance short-term recovery following acute diarrhoeal illness in their setting. • One small open-label trial [28] investigated the dose-dependent effect of Lactobacillus rhamnosus 35 (Lcr35) on reduction of faecal rotavirus shedding in children with acute rotaviral	

	gastroenteritis. Children were randomly allocated to receive one of the three regimens for 3 days: Lcr35 with 2x 10(8) colony-forming units (CFU) per day (low-dose group), 6x 10(8) CFU per day (high-dose group) or Lcr35 with no CFU per day (control group). Faecal samples were collected before and after the 3-day regimen for measurements of rotavirus concentrations by ELISA. Results showed no statistically significant change in faecal rotavirus concentrations in either the control group or the low-dose group. However, faecal rotavirus concentrations in the high-dose group declined by 86% after 3 days when compared with those before Lcr35 administration. • One RCT[29] assessed the clinical efficacy of Lactobacillus sporogenes (Bacillus coagulans) in children aged 6 to 24 months who had diarrhoea with some dehydration. Children received tablets of L. sporogenes (B. coagulans) or placebo, and ORS for correction of initial dehydration as well as maintenance therapy. The authors concluded that L. sporogenes (B. coagulans), as an adjunct to ORS, had no	

	therapeutic impact on management of acute dehydrating diarrhoea of diverse aetiology including rotavirus associated diarrhoea in children. *Saccharomyces boulardii (1 Study)* • One RCT[30] conducted in Brazil determined whether oral treatment with Saccharomyces boulardii (S. boulardii) would reduce the duration of diarrhoea in children with acute diarrhoea. Children 6 to 48 months old and hospitalised within 72hours after the onset of acute diarrhoea were randomly assigned to receive twice per day for 5 days 200mg of a commercial pharmaceutical product containing 4x10 viable cells of S. boulardii or a placebo. Results showed a reduction in diarrhoea duration when S. boulardii was given to children within 72hours after the onset of acute diarrhoea. *Bifidobacteria (1 Study)* • One RCT[31] assessed the effect of a lactose-free milk formula supplemented with bifidobacteria and streptococci on the recovery from acute diarrhoea in Chinese babies 6 to 36	

	months of age and free from moderate or severe malnutrition. After oral or parenteral rehydration, babies were allocated to one of three groups: a lactose-free formula (Control); the same formula but with viable 10(8)CFU Bifidobacterium lactis Bb12 and 5x 10(7)CFU Streptococcus thermophilus TH4 per gram of powder and, the same formula with the same microorganisms, but with 10(9)CFU/g and 5x 10(8)CFU, respectively. Results showed that the duration of diarrhoea was not influenced by the intake of the probiotics. However, a decrease of rotavirus shedding was observed in infants fed the formula with 10(9)CFU B. lactis Bb12/g The identified studies on the use of probiotics indicate that probiotics may be useful in the management of children with diarrhoea. The current guideline does not recommend the use of probiotics. *Other therapies not included in the original guideline (2 studies)* • One Cochrane Review [32] aimed to determine the effectiveness and safety of oral immunoglobulin preparations for the	

	treatment of rotavirus diarrhoea in hospitalised low birth weight babies. However, no randomised controlled trials that assessed the effectiveness or safety of oral immunoglobulin preparations for the treatment of rotavirus diarrhoea in hospitalised low birth weight babies was found. The authors concluded that clinical trials that address the issue of oral immunoglobulin treatment of rotavirus infection are needed. • One single-blind RCT[33] on the effectiveness of nitazoxanide in Bolivian children was found. Children aged from 28 days to 24 months, with rotavirus diarrhoea, were randomly assigned to receive either oral nitazoxanide (15 mg/kg/day) twice a day for three days, a combination of oral probiotics, 1 g twice a day for five days, or only oral or systemic rehydration solutions. Results showed that the median duration of hospitalisation was significantly shorter in patients who received nitazoxanide and probiotics compared to patients who received oral rehydration solution alone. Similarly, the median duration of diarrhoea was significantly reduced in children who received nitazoxanide and probiotics compared to the control group. The authors	

	concluded that both nitazoxanide and probiotics are effective in the management of children with acute rotavirus diarrhoea but small differences in favour of nitazoxanide were found in comparison with probiotics. They recommended that nitazoxanide is an important treatment option for rotavirus diarrhoea. <u>Summary</u> In summary, the identified studies relate to the use of anti-emetics, anti-diarrhoeal agents, Zinc and probiotics in children with gastroenteritis and were mostly in line with current guideline recommendations. However, new evidence on the use of antidiarrhoeal agents (racecadotril and diosmectite), probiotics and nitazoxanide was identified.	

Table 2: Summary of articles from focused search

Clinical area 1: Is there a systematic scoring approach to the assessment of dehydration in children under 5 years of age?		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Is there a systematic scoring approach to the assessment of dehydration in children under 5 years of age? **Relevant section of guideline** 4.1 Clinical assessment	Through an assessment of abstracts from a focused search, 6 publications (3 from the same author groups in Canada) relevant to the clinical question were identified. • One Canadian prospective cohort study[34] aimed to validate the Clinical Dehydration Scale (CDS) with a new cohort of patients with acute gastroenteritis assessed in a tertiary emergency department in Canada. Children 1 month to 5 years of age with symptoms of acute gastroenteritis were enrolled consecutively during a 4-month period. The authors concluded that the scoring system was valuable in predicting a longer length of stay and the need for intravenous fluid rehydration for children with symptoms of acute gastroenteritis. • One Canadian prospective cohort study[35] validated the clinical dehydration scale (CDS) for children with gastroenteritis in a	No new evidence was identified which would invalidate current guideline recommendation(s).

	different paediatric emergency department from where it was initially derived and validated. The authors concluded that the scale is a good predictor of length of stay in the emergency department after being seen by a physician. • One study[36] evaluated the clinical and laboratory assessment of dehydration severity in children, 1 to 36 months, with acute gastroenteritis, using the Clinical Dehydration Scale (CDS) and other laboratory measures. The authors concluded that clinicians may find it useful to incorporate the CDS and laboratory measures into clinical decision-making algorithms to assess dehydration severity in children with acute gastroenteritis. • One study[37] conducted in Canada evaluated the internal reliability, construct validity, and ease of administration of a gastroenteritis disease severity score, the modified Vesikari score (MVS), which does not require in-person assessment. The authors concluded that the MVS seemed to effectively measure the global severity of disease in children with acute gastroenteritis and that the data support the use of the MVS as	

	an outcome measure in future clinical trials. • One prospective cohort study[38] conducted in Rwanda compared the diagnostic accuracy of three popular clinical dehydration scales (the World Health Organization (WHO) scale, the Gorelick scale, and the Clinical Dehydration Scale (CDS)) in children with diarrhoea to determine whether these clinical scales can accurately assess dehydration status in children when performed by nurses or general physicians in a low-income country. Results showed that the WHO scale had sensitivities of 79% and 50% and specificities of 43% and 61% for severe and moderate dehydration, respectively; the 4- and 10-point Gorelick scale had sensitivities of 64% and 21% and specificities of 69% and 89%, respectively, for severe dehydration, while the same scales had sensitivities of 68% and 82% and specificities of 41% and 35% for moderate dehydration; the CDS had a sensitivity of 68% and specificity of 45% for moderate dehydration. The authors concluded that in their sample of children, the WHO scale, Gorelick scale, and CDS did not provide an accurate assessment of dehydration	

	status when used by general physicians and nurses in a developing world setting. • One UK study[39] aimed to determine if a scoring system based on standardised clinical signs would reduce the variability between doctors' assessment of dehydration. A clinical scoring system was developed using seven physiological variables based on previously published research. Three doctors of different seniority recorded the estimated percentage dehydration and severity scores for children presenting with symptoms of gastroenteritis and dehydration. Agreement was measured using intra-class correlation coefficient for percentage ratings and total clinical scores and kappa for individual characteristics. The authors concluded that the clinical scoring system used did not reduce the variability of assessment of dehydration compared to doctors' conventional methods. They suggested that in order to reduce variability, improving education may be more important than the production of a scoring system, as experience is a key determinant in the assessment of a potentially dehydrated child.	

	Summary In summary, the identified studies related to the use of scoring systems to assess dehydration in children under 5 years of age with gastroenteritis. Variability between the identified studies in terms of the different scoring systems was apparent. As such, there is insufficient consistent new evidence to update the current guideline recommendation(s).	

Ongoing clinical trials

13 clinical trials were identified focusing on the following areas:

- Electrolyte Maintenance Solution (EMS) in low-risk children with gastroenteritis (currently recruiting participants, expected completion date August 2012)
- Efficacy and safety of a new oral rehydration solution (Hipp ORS 200 Apple) in children with acute gastroenteritis (final data collection date for primary outcome measure November 2011, publication date unknown)
- Intravenous fluids with dextrose for dehydration and ketosis in children with gastroenteritis and dehydration (study completed July 2011, publication date unknown)
- Addition of dextrose to IV fluids in the treatment of acute dehydration due to gastroenteritis in children (study completed March 2012, publication date unknown)
- Efficacy and safety of multiple electrolyte solution for the treatment of moderate to severe dehydration in children with gastroenteritis (final data collection date for primary outcome measure April 2012, publication date unknown)
- Oral ondansetron vs domperidone for symptomatic treatment of vomiting during acute gastroenteritis in children (currently recruiting participants, estimated completion date March 2013)
- Oral dimenhydrinate versus placebo in children with moderate vomiting due to acute gastroenteritis (study completed September 2011, publication date unknown)
- Efficacy and safety of Filtrum-STI (lignin hydrolytic) in children with viral gastroenteritis (final data collection date for primary outcome measure December 2010, publication date unknown, no further information on the clinicaltrials.gov website)
- Oral zinc for the treatment of acute diarrhoea in US children (currently recruiting participants, expected completion date November 2012)

- Impact of emergency department probiotic treatment of paediatric gastroenteritis (study not yet open for participant recruitment, expected completion date July 2014)
- Impact of emergency department probiotic treatment of diarrheal illness on daycare attendance (currently recruiting participants, expected completion date December 2013)
- Probiotics for infectious diarrhea in children in South India (final data collection date for primary outcome measure December 2011, publication date unknown)
- Effect of Bio-Three® (a probiotic containing three independent probiotics) on children with enteritis due to salmonella or rotavirus or any unknown reason (study completed December 2010, publication date unknown, no further information on the clinicaltrials.gov website)

Guideline Development Group perspective

A questionnaire was distributed to GDG members to consult them on the need for an update of the guideline. Seven responses were received with five respondents stating that they do not think the guideline needs to be updated at this point in time and one respondent stating that the guideline should be updated; one respondent was unsure.

Three respondents highlighted that since the publication of the guideline, there has been relevant new literature on the following topics:

- use of zinc, oral rehydration solution and pre/probiotics
- rapid or ultra-rapid IV hydration
- ondansetron (and other antiemetics including metoclopramide and domperidone) for gastroenteritis
- assessment of dehydration (using a systematic scoring approach)
- racecadotril to control diarrhoea in gastroenteritis

One respondent highlighted that there is a now a national, HPA led, British Paediatric Allergy, Immunology and Infectious Diseases Group endorsed guideline on the management of acute bloody diarrhoea in children.

With regard to ongoing research relevant to the guideline, one respondent stated that their group is planning an analysis of data comparing clinical assessment of hydration with urine dipstick specific gravity in pre-school children presenting with any illness to primary care and hope to make this available by mid 2013. Another respondent stated that they were aware of two trials in development in London and Wales but that they were at an early stage.

This feedback contributed towards the development of the clinical question for the focused search.

Implementation and post publication feedback

The NICE implementation team identified one study from published literature relating to the guideline. Kunnath et al. (2010)[1] reviewed case notes of children under 5 with gastroenteritis admitted in two district general hospitals in the West Midlands. 23% of cases had clinical dehydration. 19% were found to have received IV fluids of which 50% did not have clinical dehydration. 35% had stool culture done of which 50% had reason to. Only a minority of case notes were found to have recorded flagged signs of dehydration.

Qualitative input from the field team also highlighted the following:

- One person commented that the guideline has been very helpful for a group of health visitors in advising mothers of young children and in ensuring they are given consistent advice.
- Another person commented that the guideline was straightforward to implement.
- A third person commented that the guideline is “heavily” used by NHS Direct nurses and health advisors.

[1] Kunnath MS et al (2010) A review of the practice of diagnosis and management of gastroenteritis in children below years in two district general hospitals *Archives of Disease in Childhood* 95 Suppl 1

In total 23 enquiries were received from post-publication feedback, most of which were routine. Key themes emerging from more complex post-publication feedback all related to fluid management and included:

- calculation of fluid deficit in relation to the weight of the child during fluid management (in children under 5 with diarrhoea and vomiting)
- clarification of dosage recommendations relating to fluid replacement for a non-shocked child
- clarification of recommendation on the rate of intravenous rehydration/rate of fluid deficit replacement

No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

Relationship to other NICE guidance

The following NICE guidance is related to CG84:

Guidance	**Review date**
CG116: Food allergy in children and young people: Diagnosis and assessment of food allergy in children and young people in primary care and community settings. February 2011.	Review date not stated
CG99: Constipation in children and young people: Diagnosis and management of idiopathic childhood constipation in primary and secondary care. May 2010.	May 2013
CG89: When to suspect child maltreatment. July 2009.	July 2012
CG86: Coeliac disease: Recognition and assessment of coeliac disease. May 2009.	May 2012
Related NICE guidance in progress	
The management of Crohn's disease (due October 2012)	To be confirmed

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The guideline addresses the diagnosis, assessment and management of children younger than 5 years with acute diarrhoea and vomiting caused by gastroenteritis in England and Wales.

Conclusion

The evidence and intelligence identified through the process suggests that two minor areas of the guideline may need updating at this stage:

- anti-diarrhoeal agents
- probiotics

However as these are minor areas and there are a number of ongoing trials identified which will be published in the next two to three years, it is considered to be premature to update the guideline at this time

3. Review recommendation

The guideline should not be considered for an update at this time.

Centre for Clinical Practice
May 2012

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