Management of acute gastroenteritis in children

SUMMARY OF THE ESPGHAN/ESPID 2014 UPDATE


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The objective of this document is to provide healthcare professionals with a quick access to essential information contained in the comprehensive Evidence-based Guidelines for the Management of Acute Gastroenteritis in Children in Europe, Update 2014. This document is an extract of each chapter that is fully detailed in the Guidelines, and as such, reflects the opinions of the Guidelines' authors. In particular, Biocodex holds no responsibility for its content.
Background

In 2008, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society of Paediatric Infectious Diseases (ESPID) jointly developed evidence-based guidelines for the management of acute gastroenteritis (AGE) in children for practitioners at all levels of health care – primary care physicians, pediatricians and family physicians – in Europe (Guarino et al. 2008).

These guidelines were updated in 2014 to take into account the evidence accumulated over the last years. The update differs from the original guidelines in that the quality of evidence and the weight of recommendations were rated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system. However, to reflect the changes that have occurred, the Muir Gray rating used five years ago has been retained, or where appropriate, revised.

Another novelty is a section on the management of children in hospital. This section addresses crucial issues in the management of diarrhea, namely, enteral and parenteral rehydration, correction of hydro-electrolyte imbalance, complications and monitoring the course of the disease.

Methods for guidelines update development

The approach used to develop the previous guidelines was used here. In brief, the process started with specifying clinical questions that define the population for search purposes. These were defined as: previously healthy children 5 years of age or younger with clinically diagnosed AGE (diarrhea and/or vomiting presumably of infectious origin), in- or outpatients living in geographic Europe. Children with at risk conditions, such as chronic disorders or immunodeficiency are not covered.

Recommendations were formulated and graded according to the Muir Gray and Cook (Table 1), and the GRADE system (Table 2).
**TABLE 1.** Strength of evidence and grade of recommendations in support of the recommendations formulated in the 2008 ESPGHAN/ESPID Guidelines for the Management of AGE in Children in Europe.

<table>
<thead>
<tr>
<th>Strength of evidence</th>
<th>I</th>
<th>Strong evidence from ≥1 systematic review(s) of well-designed randomized controlled trials (RCTs).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II</td>
<td>Strong evidence from ≥1 properly designed RCT(s) of appropriate size.</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Evidence from well-designed trials without randomization, single group pre-post, cohort, time series, or matched case-control studies.</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Evidence from well-designed trials, non-experimental studies from &gt;1 center or research group.</td>
</tr>
<tr>
<td></td>
<td>Va</td>
<td>Opinion of respected authorities.</td>
</tr>
<tr>
<td></td>
<td>Vb</td>
<td>Clinical evidence, descriptive studies, or reports of expert committees.</td>
</tr>
<tr>
<td>Grade of recommendation</td>
<td>A</td>
<td>Supported by level I evidence, highly recommended.</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Supported by level II evidence, recommended.</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>Supported by level III evidence, recommended.</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>Supported by level IV and V evidence; the consensus route would have to be adopted.</td>
</tr>
</tbody>
</table>

**TABLE 2.** The GRADE system.

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>High quality</th>
<th>Further research is unlikely to change our confidence in the estimate of effect.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate quality</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td></td>
<td>Low quality</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td></td>
<td>Very low quality</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
<tr>
<td>Grade of recommendation</td>
<td>Strong</td>
<td>When the desirable effects of an intervention clearly outweigh the undesirable effects, or they clearly do not.</td>
</tr>
<tr>
<td></td>
<td>Weak</td>
<td>When the trade-offs are less certain (either because of the low quality of evidence or because the evidence suggests that desirable and undesirable effects are closely balanced).</td>
</tr>
</tbody>
</table>
Epidemiology

Definition

Acute gastroenteritis is generally defined as a decrease in the consistency of stools (loose or liquid) and/or an increase in the frequency of evacuations (typically ≥ 3 in 24 hours), with or without fever or vomiting. However, a change in stool consistency versus previous stool consistency is more indicative of diarrhea than stool number, particularly in the first months of life. Acute diarrhea typically lasts less than 7 days and not longer than 14 days.

Epidemiology

The incidence of diarrhea ranges from 0.5 to 2 episodes per child per year in children younger than 3 years in Europe.

Gastroenteritis is a major reason for hospitalization in this range of age.

Rotavirus is the most frequent agent of AGE. However, norovirus is becoming the leading cause of medically attended AGE in countries with high rotavirus vaccine coverage.

The most common bacterial agent is either Campylobacter or Salmonella depending on country.

Intestinal infections are a major cause of nosocomial infection.
Risk factors for the severity and/or persistence of diarrhea

Etiology of diarrhea

Rotavirus is the most severe enteric pathogen of childhood diarrhea (III, C) (strong recommendation, moderate quality evidence).

In children with persistent diarrhea the main pathogens detected are:

- Rotavirus, norovirus, astrovirus, enteroaggregative *Escherichia coli* and atypical *E. coli* (III, C) (weak recommendation, low quality evidence).
- *Giardia* (I, A) (weak recommendation, moderate quality evidence)
- *Cryptosporidium* and *Entamoeba histolytica* (III, C) (weak recommendation, low quality evidence).

Host-related factors

- **Younger age**

  The high incidence of dehydration in infants younger than 6 months is related to a higher exposure to rotavirus (III, C) (weak recommendation, low quality evidence)

  In developing countries, a young age (<6 months) is related to the severity and persistence of diarrhea (II, B) (strong recommendation, low quality evidence).

- **Feeding practice**

  Predominant breastfeeding may reduce the risk of AGE in young European infants (III, C) (strong recommendation, moderate quality evidence).

  In developing areas early weaning may be associated with earlier onset of severe or prolonged diarrhea (III, C) (weak recommendation, low quality evidence).

- **Underlying chronic disease or immune deficiencies**

  Children with immune deficiencies have a higher risk of developing more prolonged and more severe disease (III, C) (weak recommendation, low quality evidence).

  Malnutrition and immunodeficiencies are risk factors for persistent parasitic diarrhea in developing countries (III C) (weak recommendation, low quality evidence).

  *Clostridium difficile* is a major agent of severe diarrhea in selected chronic diseases such as
inflammatory bowel disease and oncologic conditions (III,C) (weak recommendation, low quality evidence).

**Clinical condition of the patient**

Loss of appetite, fever, vomiting and mucus in stools are frequently associated with persistent diarrhea (III, C) (weak recommendation, very low quality evidence).

Fever, severe dehydration, and lethargy, which are more common in rotavirus infection, indicate systematic involvement and are associated with severe diarrhea (III, C) (weak recommendation, low quality evidence).

**Setting / socio-economic factors**

Children attending daycare centers have a greater risk of mild and severe diarrheal illness than children at home (III, C) (weak recommendation, low quality evidence).

In European countries, there is evidence, albeit weak, of a link between low socioeconomic status and the severity or persistence of diarrhea (III, C) (weak recommendation, very low quality evidence).
Clinical evaluation

Indications for a medical visit

A telephone triage can be appropriate in the management of uncomplicated AGE or to evaluate the need for a medical visit (Vb, D) (weak recommendation, low quality evidence).

Infants and toddlers with AGE should be referred for medical evaluation if any of the following are present:

- Age younger than 2 months (III, C) (strong recommendation, low quality evidence)
- Severe underlying disease (e. g., diabetes and renal failure) (Vb, D) (strong recommendation, very low quality evidence)
- Persistent vomiting (III, C) (strong recommendation, low quality evidence)
- High output diarrhea with elevated stool volumes (>8 episodes/day) (III, C) (strong recommendation, low quality evidence)
- Family-reported signs of severe dehydration (Vb, D) (strong recommendation, very low quality evidence).

Assessment of dehydration

The best measure of dehydration is the percentage loss of body weight (Vb, D) (weak recommendation, low quality evidence).

Historical points are moderately sensitive as a measure of dehydration (III, C) (weak recommendation, moderate quality evidence).

Classification into subgroups with no or minimal dehydration, mild to moderate dehydration, and severe dehydration is an essential basis for appropriate treatment (I, A) (strong recommendation, moderate quality evidence).

Parental reports of dehydration symptoms are so low in specificity that they may not be clinically useful. However, parental report of normal urine output decreases the likelihood of dehydration (Vb, C) (strong recommendation, low quality evidence).

Little is known about the severity of diarrhea and/or vomiting and dehydration in industrialized countries, therefore recommendations are largely based on data from developing countries. In the latter, infants and young children with frequent high output diarrhea and vomiting are most at risk (III, C) (weak recommendation, low quality evidence).

Clinical tests for dehydration are imprecise, generally showing only fair to moderate agreement among examiners (III, C) (weak recommendation; moderate quality evidence).
The best three individual examination signs for assessment of dehydration are prolonged capillary refill time, abnormal skin turgor, and abnormal respiratory pattern (III, C) (weak recommendation, moderate quality evidence).

Scoring systems to assess dehydration and severity of illness

• Clinical dehydration scales

The use of the Clinical Dehydration Scale (CDS) is supported by consistent evidence and it is easy to use in the assessment of dehydration (III, C) (weak recommendation, low quality evidence).

This scale should be used in combination with other criteria to guide the need of medical interventions in individual cases (III, C) (weak recommendation, low quality evidence).

**TABLE 3.** CDS for children (Total score from 0 to 8)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>General appearance</td>
<td>Normal</td>
<td>Thirsty, restless or lethargic but irritable when touched</td>
<td>Drowsy, limp, cold or sweaty +/- comatose</td>
</tr>
<tr>
<td>Eyes</td>
<td>Normal</td>
<td>Slightly sunken</td>
<td>Very sunken</td>
</tr>
<tr>
<td>Mucous membranes (tongue)</td>
<td>Moist</td>
<td>Sticky</td>
<td>Dry</td>
</tr>
<tr>
<td>Tears</td>
<td>Tears</td>
<td>Decreased tears</td>
<td>Absent tears</td>
</tr>
</tbody>
</table>

A score of 0 represents no dehydration; a score of 1 to 4, some dehydration; and a score of 5 to 8 moderate/severe dehydration.
• Severity scores

**TABLE 4. Modified Vesikari Score**

<table>
<thead>
<tr>
<th>Points</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea duration, h</td>
<td>0</td>
<td>1-96</td>
<td>97-120</td>
<td>≥121</td>
</tr>
<tr>
<td>Max number of diarrheal stools per 24-h period (in the course of the disease)</td>
<td>0</td>
<td>1-3</td>
<td>4-5</td>
<td>≥6</td>
</tr>
<tr>
<td>Vomiting duration, h</td>
<td>0</td>
<td>1-24</td>
<td>25-48</td>
<td>≥49</td>
</tr>
<tr>
<td>Max number of episodes per 24-h period (in the course of the disease)</td>
<td>0</td>
<td>1</td>
<td>2-4</td>
<td>≥5</td>
</tr>
<tr>
<td>Max recorded fever (°C)</td>
<td>&lt;37.0</td>
<td>37.1 to 38.4</td>
<td>38.5-38.9</td>
<td>≥39.0</td>
</tr>
<tr>
<td>Future health care visit</td>
<td>0</td>
<td>-</td>
<td>Primary care</td>
<td>Emergency department</td>
</tr>
<tr>
<td>Treatment</td>
<td>None</td>
<td>Intravenous rehydration</td>
<td>Hospitalization</td>
<td>-</td>
</tr>
</tbody>
</table>


**Clinical features that suggest a bacterial vs a viral etiology of diarrhea**

No clinical features can differentiate a bacterial from a viral etiology. However, high fever (>40°C), overt fecal blood, abdominal pain, and central nervous system involvement each suggests a bacterial pathogen. Vomiting and respiratory symptoms are associated with a viral etiology (III, C) (weak recommendation, low quality evidence).
Diagnosis

Acute gastroenteritis does not generally require a specific diagnostic work up (Vb, D) (strong recommendation, low quality evidence).

Microbiological investigations

Children presenting with AGE do not require routine etiological investigation. However, there may be particular circumstances in which microbiological investigations may be necessary for diagnosis and treatment (Vb, D) (strong recommendation, low quality evidence).

Microbiological investigations may be considered in children with underlying chronic conditions (e.g. oncologic diseases, inflammatory bowel diseases etc.), in those in very severe conditions, or in those with prolonged symptoms in whom specific treatment is considered. (Vb, D) (strong recommendation, very low quality evidence).

Hematological markers of bacterial diarrhea

The differentiation of a bacterial from non bacterial etiology is not likely to change treatment. C-reactive protein and procalcitonin measurements are not routinely recommended to identify a bacterial etiology (Vb, D) (weak recommendation, low quality evidence).

Stool markers of bacterial vs non bacterial agents

Based on available data we do not recommend the routine use of fecal markers to distinguish between viral and bacterial AGE in the clinical setting (Vb, D) (weak recommendation, low quality evidence).

Biochemical tests

Tests of dehydration are imprecise, and generally there is only fair to moderate agreement with the examiner’s estimate. (III, C) (weak recommendation, low quality evidence).

The only laboratory measurement that appears to be useful in decreasing the likelihood of >5% dehydration is serum bicarbonate (normal serum bicarbonate) (III, C) (weak recommendations, low quality evidence).

Electrolytes should be measured in hospital settings:

- In moderately dehydrated children whose history and physical examination findings are inconsistent with a severe diarrheal disease, and in all severely dehydrated children (Va, D) (strong recommendation, low quality evidence).
- In all children starting intravenous (IV) therapy, and during therapy, because hyper- or hyponatremia will alter the rate at which IV rehydration fluids will be given (Va, D) (strong recommendation, low quality evidence).

**Endoscopy and histology**

There is no indication for endoscopy except in selected circumstances or cases such as differential diagnosis with inflammatory bowel disease at its onset (Vb, D) (strong recommendation, low quality evidence).
Hospitalization

Indications for hospitalization

The recommendations for hospital admission are based on consensus and include any of the following conditions (Vb, D) (strong recommendation, low quality evidence):

- Shock
- Severe dehydration (> 9% of body weight)
- Neurological abnormalities (lethargy, seizures, etc)
- Intractable or bilious vomiting
- Failure of oral rehydration
- Suspected surgical condition
- Conditions for a safe follow-up and home management are not met.

Hygiene and isolation precautions

Contact precautions are advised in addition to standard precautions (hand hygiene, personal protective equipment, soiled patient-care equipment, environmental control including textiles, laundry and adequate patient placement). (Vb, D) (strong recommendation, very low quality evidence).

Indications for nasogastric rehydration

When oral rehydration is not feasible, enteral rehydration by the nasogastric route is the preferred method of rehydration and should be proposed before IV rehydration (I, A) (strong recommendation, moderate quality evidence).

Enteral rehydration is associated with significantly fewer major adverse events and a shorter hospital stay than IV rehydration and is successful in most children (I, A) (strong recommendation, moderate quality evidence).

The rapid (40-50 ml/kg within 3-6 hours) and standard (24 hours) nasogastric rehydration regimens are equally effective and may be recommended (II, B) (weak recommendation, moderate quality evidence).
Indications for intravenous rehydration

Intravenous fluids are required in the following cases (Vb, D) (strong recommendation, low quality evidence):

- Shock
- Dehydration with altered level of consciousness or severe acidosis
- Worsening of dehydration or lack of improvement despite oral or enteral rehydration therapy
- Persistent vomiting despite appropriate fluid administration orally or via a nasogastric tube
- Severe abdominal distension and ileus.

Administration of intravenous rehydration

• For children presenting with shock

Children presenting with shock secondary to AGE should receive rapid IV infusion of isotonic crystalloid solution (0.9% saline or lactated Ringer’s solution) with a 20 ml/kg bolus. (Vb, D) (strong recommendation, very low quality evidence).

If the blood pressure has not improved after the first bolus, a second (or even a third) bolus of 20 ml/kg should be administered over 10-15 min and other possible causes of shock should be considered. (Vb, D) (strong recommendation, very low quality evidence).

• For children with severe dehydration without shock

Children with severe dehydration requiring IV fluids may receive rapid rehydration with 20 ml/kg/h of 0.9% saline solution for 2-4 hours (II, B) (strong recommendation, moderate quality evidence).

In IV-rehydrated children, a dextrose-containing solution may be used for maintenance (III, C) (weak recommendation, low quality evidence).

A solution containing not less than 0.45% saline (at least 77 mEq/L [Na⁺]) is recommended during the first 24 hours of IV rehydration therapy to prevent hyponatremia (III, C) (weak recommendation, low quality evidence).

After the child starts to urinate and if serum electrolyte values are known, add 20 mEq/L of K⁺ chloride (Vb, D) (weak recommendation, low quality evidence).

• Intravenous rehydration rates

Rapid rehydration with 20 ml/kg/h for 2-6 hours followed by oral rehydration or continuous infusion of dextrose solution is adequate for initial rehydration of most patients requiring hospital assistance (II, B) (weak recommendation, low quality evidence).
More rapid IV rehydration may be associated with electrolyte abnormalities and is associated with long time to hospital discharge and therefore is not recommended. (II, B) (strong recommendation, low quality evidence).

• **Composition of fluids for rehydration**

Isotonic (0.9%) saline solution effectively reduces the risk of hyponatremia and is recommended for initial rehydration in most cases. In the rare but extremely severe cases of shock, Ringer’s lactate solution is recommended (III, C) (strong recommendation, low quality evidence).

Glucose may be added to saline solution once fluid volume has been restored in the subsequent phase of IV rehydration (“maintenance”) (III, C) (weak recommendation, low quality evidence).

• **Treatment of hypernatremia**

Oral or nasogastric rehydration with hypo-osmolar ORS is an effective and safe treatment and has fewer side effects than IV rehydration (III, C) (weak recommendation, very low quality evidence).

If the child is hypernatremic and needs IV rehydration:

- Use an isotonic solution (0.9% saline) for fluid deficit replacement and maintenance (III, C) (strong recommendation, very low quality evidence).

- Replace the fluid deficit slowly, typically over 48 hours, with the aim of reducing it to less than 0.5 mmol/L per hour (III, C) (weak recommendation, very low quality evidence).

- Monitor plasma sodium frequently (Vb, D) (weak recommendation, very low quality evidence).

**Therapies to reduce the length of hospitalization**

Administration of effective probiotic strains reduce the duration of hospital stay and may be considered in children admitted with AGE (II, B) (strong recommendation, low quality evidence).

Hospitalized children with severe rotavirus gastroenteritis may benefit from oral administration of serum immunoglobulins (III, C) (weak recommendation, very low quality evidence).

Lactose free formulas can be considered in the management of AGE in hospitalized children younger than 5 years of age (I,A) (weak recommendation, low quality evidence).
Discharging a child admitted because of acute gastroenteritis

Prompt discharge from hospital should be considered in children admitted for AGE when the following conditions are fulfilled (Vb, D) (weak recommendation, low quality evidence):

- Sufficient rehydration is achieved as indicated by weight gain and/or clinical status
- IV fluids are no longer required
- Oral intake equals or exceeds losses
- Medical follow-up is available via telephone or office visit.
Treatment

Rehydration

• Reduced osmolarity ORS

Reduced osmolarity ORS (50/60 mmol/L Na) should be used as first-line therapy for the management of children with AGE. (I, A) (strong recommendation, moderate quality evidence).

Reduced osmolarity ORS is more effective than full strength ORS as measured by such important clinical outcomes as reduced stool output, reduced vomiting and reduced need for supplemental intravenous therapy (I,A) (strong recommendation, moderate quality evidence).

The ESPGHAN solution has been used successfully in several RCTs and in a number of non-RCTs in European children. It may be used in children with AGE (II,A) (strong recommendation, moderate quality evidence).

• Modified ORS

There is insufficient evidence to recommend in favor or against the universal addition of enriched ORS (II, B) (weak recommendation, low quality evidence).

There is limited evidence for similar efficacy of ORS with standard taste and ORS with improved taste (II, B) (weak recommendation, moderate quality evidence).

Frozen fruit-flavored ORS is better tolerated than conventional ORS (III, C) (weak recommendation; very low quality evidence).

Nutritional management

Breastfeeding should be continued throughout rehydration, an age-appropriate diet should be started during or after initial rehydration (4-6 hours) and dilution of the formula or the use of a modified milk formula is usually unnecessary.

• Early versus Late Feeding of a Child With AGE

Early resumption of feeding after rehydration therapy is recommended. However, further studies are needed to determine whether the timing of refeeding affects the duration of diarrhea, total stool output, or weight gain in childhood acute diarrhea (I, A) (strong recommendation, low quality evidence).
• **Modified formulas**

The routine use of lactose-free feeds is currently not recommended in outpatient setting (I, A) (strong recommendation, low-quality evidence).

There is insufficient evidence to recommend in favor or against the use of diluted lactose-containing milk (I,A) (weak recommendation, low quality evidence).

• **Milk-free mixed diets, cereal-based milk/formulas, home available staple foods, and other types of food or drinks**

The bread, rice, apple, toast (BRAT) diet has not been studied and is not recommended (Vb, D) (strong recommendation, low quality evidence).

Beverages with a high sugar content should not be used (III, C) (strong recommendation, low quality evidence).

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**Pharmacological therapy**

• **Antiemetics**

Ondansetron, at the dosages used in the available studies and administered orally or intravenously, may be effective in young children with vomiting related to AGE. However, before a final recommendation is made, a clearance on safety in children is needed (II, B) (strong recommendation, low quality evidence).

There is no evidence to support the use of other antiemetics (II, B) (strong recommendation, low quality evidence).

• **Antimotility or Antiperistaltic Drugs (Loperamide)**

Loperamide is not recommended in the management of AGE in children (II, B) (strong recommendation, very low quality evidence).

• **Adsorbents**

Diosmectite can be considered in the management of AGE (II,B) (weak recommendation, moderate quality evidence).

Smectite plus *Lactobacillus GG* (LGG) and LGG alone are equally effective in the treatment of young children with AGE. Combined use of the two interventions is not justified (II, B) (weak recommendation, low quality evidence).

Other absorbents (namely, kaolin-pectin and attapulgite activated charcoal) are not recommended (III, C) (weak recommendation, very low quality evidence).
• Antisecretory Drugs

Raceladotril can be considered in the management of AGE (II, B) (weak recommendation, moderate quality evidence).

Bismuth subsalicylate is not recommended in the management of children with AGE (III, C) (strong recommendation, low quality evidence).

Children older than 6 months in developing countries may benefit from the use of zinc in the treatment of AGE. However, in regions where zinc deficiency is rare, no benefit from the use of zinc is expected (I, A) (strong recommendation, moderate quality evidence).

• Probiotics

Active treatment with probiotics, in adjunct to ORS, is effective in reducing the duration and intensity of symptoms of gastroenteritis. Selected probiotics can be used in children with AGE (I, A) (strong recommendation, moderate quality evidence).

New evidence has confirmed that probiotics are effective in reducing the duration of symptoms in children with AGE (I, A) (strong recommendation, moderate quality evidence).

The use of the following probiotics should be considered in the management of children with AGE as an adjunct to rehydration therapy: L. rhamnosus GG and S. boulardii (I,A) (strong recommendation, low quality evidence).

### TABLE 4. Probiotics for treating acute gastroenteritis (recommendations developed by the ESPGHAN Working Group on Probiotics/Prebiotics)

<table>
<thead>
<tr>
<th>PROBIOTICS WITH A POSITIVE RECOMMENDATION</th>
<th>Quality of evidence</th>
<th>Recommendation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactobacillus GG</td>
<td>Low</td>
<td>Strong</td>
<td>≥10^{10} CFU/day (typically 5-7 days)</td>
</tr>
<tr>
<td>Saccharomyces boulardii</td>
<td>Low</td>
<td>Strong</td>
<td>250 to 750 mg/day (typically 5-7 days)</td>
</tr>
<tr>
<td>Lactobacillus reuteri DSM 17938</td>
<td>Very low</td>
<td>Weak</td>
<td>10^8 to 4 x 10^8 (typically 5-7 days)</td>
</tr>
<tr>
<td>Heat-killed Lactobacillus acidophilus LB*</td>
<td>Very low</td>
<td>Weak</td>
<td>Min. 5 doses of 10^{10} CFU over 48 h Max. 9 doses of 10^{10} CFU for 4.5 days.</td>
</tr>
</tbody>
</table>

*This is not a probiotic strain being heat-killed.*
### PROBIOTICS WITH A NEGATIVE RECOMMENDATION

<table>
<thead>
<tr>
<th>Strain(s)</th>
<th>Quality of evidence</th>
<th>Recommendation</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecium (SF68 strain)</td>
<td>Low</td>
<td>Strong</td>
<td>Safety issues (a possible recipient of the vancomycin resistance genes)</td>
</tr>
</tbody>
</table>

### PROBIOTICS WITH A LACK OF RECOMMENDATION

<table>
<thead>
<tr>
<th>Strain(s)</th>
<th>Quality of evidence</th>
<th>Reason for a lack of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli Nissle 1917</td>
<td>Very low</td>
<td>Methodological issues</td>
</tr>
<tr>
<td>L. acidophilus</td>
<td>Very low</td>
<td>No strain identification</td>
</tr>
<tr>
<td>L. acidophilus rhamnosus 573L/1, 573L/2, 573L/3</td>
<td>Moderate</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>L. paracasei ST11</td>
<td>Moderate</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>L. acidophilus, L. rhamnosus, B. longum, S. boulardii</td>
<td>Moderate</td>
<td>Only 1 RCT available; no strain identification</td>
</tr>
<tr>
<td>L. helveticus R0052, L. rhamnosus R0011</td>
<td>Very low</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>Bacillus mesentericus, Clostridium butyricum, Enterococcus faecalis</td>
<td>Very low</td>
<td>Only 1 RCT available; no strain identification</td>
</tr>
<tr>
<td>L. delbrueckii var. bulgaricus, L. acidophilus, Str thermophiles, B bifidum (strains LMG-P17550, LMG-P 17549, LMG-P 17503, and LMG-P 17500)</td>
<td>Very low</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>Bifidobacterium lactis Bb12</td>
<td>No data</td>
<td>Lack of data</td>
</tr>
<tr>
<td>B. lactis Bb12, Str thermophiles TH3</td>
<td>Very low</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>Bacillus clausii (O/C84, N/R84, T84, SIN84)</td>
<td>Low</td>
<td>Only 1 RCT available</td>
</tr>
<tr>
<td>L. acidophilus, L. paracasei, L. bulgaricus, L. plantarum, B. breve, B. infantis, B. longum, Str thermophiles</td>
<td>Very low</td>
<td>Only 1 RCT available; no strain identification</td>
</tr>
<tr>
<td>L. acidophilus, B. infantis</td>
<td>Very low</td>
<td>No strain identification</td>
</tr>
<tr>
<td>L. acidophilus, B. bifidum</td>
<td>Very low</td>
<td>No strain identification</td>
</tr>
</tbody>
</table>
• **Synbiotics**

None of the synbiotics studied thus far can be recommended until confirmatory data are available (II, B) (weak recommendation, low quality evidence).

• **Prebiotics**

The use of prebiotics in the management of children with AGE is not recommended (II, B) (weak recommendation, low quality evidence).

• **Micronutrients**

Folic acid is not recommended for the management of children with AGE (II, B) (weak recommendation, very low quality evidence).

• **Gelatine tannate**

Gelatine tannate is not recommended for the management of children with AGE (III, C) (weak recommendation, very low quality evidence)

**Anti-inf ective therapy**

Anti-infective therapy should not be given to the vast majority of otherwise healthy children with acute gastroenteritis (Va, D) (strong recommendation, low quality evidence).

• **Antimicrobial Therapy of Bacterial Gastroenteritis**

Antibiotic therapy for acute bacterial gastroenteritis is not needed routinely but only for specific pathogens or in defined clinical settings (Va, D) (strong recommendation, low quality evidence).
### TABLE 5: Antibiotic therapy of bacterial gastroenteritis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Indication for antibiotic therapy</th>
<th>Drug of choicea</th>
<th>Alternative agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shigella spp</strong></td>
<td>Proven or suspected shigellosis</td>
<td>Oral: azithromycin (12 mg/kg on day 1, followed by 6 mg/kg for 4 days) Parenteral, IV, IM: ceftriaxone (50 mg/kg for 2-5 days)b</td>
<td>Cefixime (8 mg/kg/d) Ciprofloxacind PO (20-30 mg/kg/d). For a known susceptible strain: TMP/SMX (8 mg/kg/d of TMP) or ampicillin (100 mg/kg/d) or nalidixic acid (55 mg/kg/d)</td>
</tr>
<tr>
<td><strong>Salmonella spp (non-typhoidal)</strong></td>
<td>Antibiotic therapy is indicated only in high risk childrenc to reduce the risk of bacteremia and extra-intestinal focal infections</td>
<td>Ceftriaxone (50-100 mg/kg/d)</td>
<td>Azithromycin (10 mg/kg/d) Ciprofloxacind PO (20-30 mg/kg/d) For a known susceptible strain, TMP/SMX (8 mg/kg/d of TMP).</td>
</tr>
<tr>
<td><strong>Campylobacter spp</strong></td>
<td>Antibiotic therapy is recommended mainly for the dysenteric Campylobacter gastroenteritis and most efficacious when started within 3 days after onset of the disease</td>
<td>Azithromycin (10 mg/kg/d for 3 days, or a single dose of 30 mg/kg)</td>
<td>Doxycycline (&gt; 8 years) or ciprofloxacin (&gt; 17 years), when susceptible</td>
</tr>
<tr>
<td><strong>Shiga toxin-producing Escherichia coli</strong></td>
<td>Antibiotic therapy is not recommended</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Enterotoxigenic Escherichia coli</strong></td>
<td>Antibiotic therapy is recommended, mainly for traveler’s diarrhea</td>
<td>Azithromycin (10 mg/kg/d for 3 days)</td>
<td>Cefixime (8 mg/kg/d for 5 days) TMP/SMX (8 mg/kg/d of TMP) Ciprofloxacind PO (20-30 mg/kg/d) Rifaximin (&gt; 12 years, 600 mg/d, for 3 days)</td>
</tr>
<tr>
<td><strong>Vibrio cholerae</strong></td>
<td>Antibiotic therapy is recommended for confirmed or suspected case by travel history</td>
<td>Azithromycin (10 mg/kg/d for 3 days, or a single 20 mg/kg dose)</td>
<td>Doxycycline (&gt; 8 years), Ciprofloxacin (&gt; 17 years), or TMP/SMX (when susceptible)</td>
</tr>
<tr>
<td><strong>Clostridium difficile</strong></td>
<td>Antibiotic therapy is recommended for moderate and severe cases</td>
<td>Metronidazole (30 mg/kg/d for 10 days)</td>
<td>Vancomycin PO (40 mg/kg/d)</td>
</tr>
</tbody>
</table>

a Depends on local antibiotic susceptibility profile, which should be monitored
b TMP/SMX trimethoprim/sulfamethoxazole
c See text
d Can be used in children <17 years when an alternative is not feasible
Empiric Antibiotic Therapy in Sporadic Cases of AGE

The choice of the antimicrobial agent depends on the local prevalence of the three pathogens (Shigella spp, Campylobacter spp and Salmonella enterica) and the resistance patterns (Va, B) (strong recommendation, moderate quality evidence).

In children with watery diarrhea, antibiotic therapy is not recommended unless the patient has recently traveled or may have been exposed to cholera (Vb, D) (strong recommendation, moderate quality evidence).

Bloody diarrhea with low or no fever is typical of STEC (EHEC), but can be mild shigellosis or salmonellosis. Antibiotics are not recommended unless epidemiology suggests shigellosis (Vb, D) (weak recommendation, low quality evidence).

Parenteral rather than oral antibiotic therapy is recommended (Va, D) (Strong recommendation, low quality evidence) for:

1. Patients unable to take oral medications (vomiting, stupor, etc)
2. Patients with underlying immune deficiency who have AGE with fever
3. Severe toxemia, suspected or confirmed bacteremia
4. Neonates and young infants (<3 months) with fever. Sepsis work-up and antibiotics should be considered according to local protocols.

Antimicrobial therapy of systemic infections due to enteric pathogens or involvement of extraintestinal organs

Antibiotic therapy is recommended for the rare but potentially severe extraintestinal infections caused bacterial enteric pathogens (Vb, D) (strong recommendation, low quality evidence).

Antimicrobial therapy of parasite-induced gastroenteritis

Antiparasitic treatment is generally not needed in otherwise healthy children. However, it may be considered if symptoms are severe. (III,C) (strong recommendation, very low quality evidence).

Severe cases of giardiasis can be treated with metronidazole, nitazoxanide, albendazole or tinidazole (III, C) (weak recommendation, low quality evidence).

Cryptosporidiasis should be treated mainly in immunocompromised children with nitazoxanide (III, C) (strong recommendation, low quality evidence).

Amebic colitis should be treated with metronidazole (III, C) (strong recommendation, low quality evidence).
• Antiviral treatment

Specific antiviral treatment is usually not indicated in AGE (Vb, D) (strong recommendation, very low quality evidence).

Severe cytomegalovirus colitis, especially in an immunocompromised child, should be treated with ganciclovir (III, C) (strong recommendation, low quality evidence).

Oral immunoglobulin may be considered in children hospitalized with rotavirus gastroenteritis (III, C) (weak recommendation, very low quality evidence).

• Nitazoxanide for rotavirus diarrhea

There is not sufficient evidence to recommend nitazoxanide in the management of children with rotavirus AGE until confirmatory data are available (III, C) (strong recommendation, low quality evidence).