VIRAL GASTROENTERITIS

CHI Formulary Indication Review

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INDICATION UPDATE

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ADDENDUM to the CHI Original Viral Gastroenteritis Clinical Guidance- Issued March 2020

Table of Contents

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

List of Tables

List of Figures

Abbreviations

AAFP	American Academy of Family Physicians
AGE	Acute Gastroenteritis
AIDS	Acquired Immunodeficiency Syndrome
CDC	Centers for Disease Control and Prevention
CHI	Council of Health Insurance
CPG	Clinical Practice Guideline
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
FISPGHAN	Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition
HIV	Human Immunodeficiency Virus
IDF	CHI Drug Formulary
IDSA	Infectious Diseases Society of America
IV	Intravenous
LGG	Lactobacillus rhamnosus GG (a probiotic strain)
N/A	Not Available
ORS	Oral Rehydration Solution
ORT	Oral Rehydration Therapy
SFDA	Saudi Food and Drug Authority
STEC	Shiga Toxin-producing Escherichia coli
WG	Working Group
WHO	World Health Organization

Executive Summary

Viral gastroenteritis is an inflammation of the gastrointestinal tract, primarily the stomach and intestines, caused by viral infections. It is characterized by symptoms such as diarrhea, vomiting, abdominal pain, and sometimes fever. It is typically a self-limiting condition and can be caused by various viruses, including rotavirus, norovirus, adenovirus, and astrovirus, among others. It is often highly contagious and spreads through the ingestion of contaminated food or water, direct contact with infected individuals, or contact with contaminated surfaces. The condition is usually acute and resolves within a few days to a week, with supportive care and hydration being the primary treatment[1].

Risk factors associated with viral gastroenteritis include:

- **Age:** Infants, young children, and the elderly are more vulnerable to complications.
- **Weakened immune system:** Individuals with compromised immune systems, such as those with HIV/AIDS or undergoing chemotherapy, are at higher risk.
- **Close contact:** Living in crowded or institutional settings can increase the risk of exposure.
- **Consumption of contaminated food or water:** Eating or drinking contaminated food or water, especially in areas with poor sanitation, is a common mode of transmission.
- **Travel:** Travelers to regions with poor sanitation may be at risk of "traveler's diarrhea"[2].

Complications associated with viral gastroenteritis include dehydration, electrolyte imbalances, malnutrition, secondary infections due to weakened immune defenses and persistent symptoms: some individuals may experience prolonged or recurring symptoms, known as post-infectious irritable bowel syndrome[2].

Acute viral gastroenteritis is the leading cause of diarrheal disease worldwide, affecting both genders equally. Among the viral agents responsible, norovirus stands out as the most prevalent, contributing to 90% of global epidemic diarrheal cases and approximately 50% of all instances of viral gastroenteritis. Norovirus annually causes an estimated 685 million cases. About 200 million cases are seen among children under 5 years old, leading to an estimated 50,000 child deaths every year, mostly in developing countries. However, norovirus illness is a problem in both low- and high-income countries. Every year, norovirus is estimated to cost $60 billion worldwide due to healthcare costs and lost productivity[3].

The burden of viral gastroenteritis refers to the physical, emotional, social, and economic impact that the condition holds. Viral gastroenteritis has a significant economic impact due to healthcare costs, including hospitalization and treatment, as well as productivity losses from missed work and school days. The economic burden can be substantial both for individuals and healthcare systems. Moreover, it is a leading cause of morbidity and mortality, particularly in developing countries with limited access to clean water and proper sanitation. Norovirus imposes an annual economic burden of $60.3 billion on a global scale, with the highest regional cost of $23.5 billion being attributed to the Americas, as per the World Health Organization's breakdown[4].

Drug therapy is **not** an integral component for the management of viral gastroenteritis. Management of viral gastroenteritis is based on **symptomatic support.**

The objectives of treatment for viral gastroenteritis include symptom relief, prevention of dehydration, nutritional support, preventing complications and minimizing transmission.

The treatment of Viral Gastroenteritis is a combination of relieving symptoms, preventing dehydration, and minimizing the spread of the virus. Here are some key aspects of viral gastroenteritis management:

- **Fluid replacement**
- **Dietary adjustments**
- **Rest**
- **Medications:** Most cases of viral gastroenteritis do not require medication. Antibiotics are ineffective against viral infections, so they are not typically prescribed. Anti-diarrheal medications may be considered in some cases, but they should be used with caution.
- **Isolation and hygiene:** Since viral gastroenteritis is highly contagious, individuals with symptoms should practice good hygiene, including frequent handwashing with soap and water.
- **Vaccination:** In some regions, vaccines are available to protect against specific viral causes of gastroenteritis[5].

CHI issued viral gastroenteritis clinical guidance after thorough review of renowned international and national clinical guidelines in March 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI viral gastroenteritis clinical guidance and seeks to offer guidance for the effective management of viral

gastroenteritis. It provides an **update on the viral gastroenteritis guidelines** for CHI formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of new versions guidelines** namely AAFP Guidelines on Gastroenteritis in Children **(2019)**; Infection & Chemotherapy Guideline for the Antibiotic Use in Acute Gastroenteritis **(2019);** Journal of Hospital Infection Guidelines for the management of norovirus outbreaks in acute and community health and social care settings **(2023)**, CDC Guideline for the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings **(2017)**; Journal of Pediatric Health Care Clinical Practice Guideline for the Treatment of Pediatric Acute Gastroenteritis in the Outpatient Setting **(2016)**, Endocrinology Universal Recommendations for the Management of Acute Diarrhea in Nonmalnourished Children **(2018)**, AAFP Acute Diarrhea in Adults **(2022).**

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there has been **one withdrawal**: Rotavirus Vaccine.

Moreover, there have been **no newly approved drugs** for the treatment of Viral Gastroenteritis. Additionally, there have been **updates** regarding previously mentioned drugs in terms of drug information and prescribing edits since March 2020. **Dimenhydrate** does not need PA as a prescribing edit and it has an AGE prescribing edit: not for use in children < 2 years old. **Granisetron** does not need PA as a prescribing edit. **Loperamide** does not need PA/MD as a prescribing edit and it has an AGE prescribing edit: contraindicated in children < 2 years of age. **Valganciclovir** does not need PA as a prescribing edit. **Vitamins, folic acid, pantothenic acid, calcium, lactic ferments (lactobacillus acidophilus & sporogenes, bifidobacterium bifidum, longum & infantis)** do not need PA as a prescribing edit. **Zinc** does not need PA as a prescribing edit.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the Viral Gastroenteritis therapeutic management.

Below is a table summarizing the major changes based on the different Viral Gastroenteritis guidelines used to issue this report:

Table 1. General Recommendations for the Management of Viral Gastroenteritis

Management of Viral Gastroenteritis		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
ORT is recommended for children with mild to moderate dehydration from acute gastroenteritis. It is as effective as intravenous rehydration in preventing hospitalizations and return emergency department visits.	Category B[6]	AAFP[6]
The mainstay of therapy for children with mild or moderate dehydration should focus on ORT with an emphasis on replacing deficits and preventing ongoing fluid losses. ORS is the first-line treatment of acute gastroenteritis (AGE), with reduced osmolality ORS recommended as the first-line treatment. IV rehydration may be indicated for children who fail ORT.	No grade[7,8]	National Association of Pediatric Nurse Practitioners[7] FISPGHAN[8]
Children with mild dehydration should receive half-strength apple juice followed by preferred fluids (regular juices, milk) to reduce the need for eventual intravenous rehydration compared with a formal oral rehydration solution.	Category B[6]	AAFP[6]
During outbreaks of norovirus gastroenteritis, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. Handwashing with soap is an effective method for preventing episodes of gastroenteritis,	Category A[6] No grade[9] Category IB[10]	AAFP[6] Healthcare Infection Society[9] CDC[10]

although it does not prevent rotavirus infection.		
All children should receive an oral live, attenuated rotavirus vaccine to reduce the incidence of hospitalization, severe gastroenteritis, and death from rotavirus infection.	Category A[6]	AAFP[6]
Breastfeeding reduces the incidence of acute gastroenteritis and hospitalization from diarrheal disease in young children.	Category B[6]	AAFP[6]
Antibiotic treatment is generally not recommended for most cases of acute watery diarrhea, except in specific cases. Antibiotics may be considered in specific cases, including immune-suppressed patients with bloody diarrhea, Campylobacter infections, shigellosis, and suspected infections with non-invasive bacteria.	No grade[8] Strong recommendation, low quality of evidence[11]	FISPGHAN[8] Korean Society of Infectious Diseases/Korean Society for Antimicrobial Therapy[11]
For infectious diarrhea caused by Campylobacter, the use of azithromycin is recommended	Strong recommendation, high quality of evidence[11]	Korean Society of Infectious Diseases/Korean Society for Antimicrobial Therapy[11]
Azithromycin, ciprofloxacin, or ceftriaxone is recommended for shigellosis. Doxycycline is recommended for Vibrio cholerae infections, and ciprofloxacin, azithromycin, and ceftriaxone may also be used.	Strong recommendation, high quality of evidence[11]	Korean Society of Infectious Diseases/Korean Society for Antimicrobial Therapy[11]
Antibiotics can be considered for travelers' diarrhea and empiric antibiotics are recommended in moderate to severe cases of	Category B[12]	AAFP[12]

travelers' diarrhea.		
Ondansetron may be considered to facilitate oral rehydration in the acute care setting for children with persistent vomiting.	No grade[7,8]	National Association of Pediatric Nurse Practitioners[7] FISPGHAN[8]
Loperamide is helpful in shortening the duration of symptoms of acute watery diarrhea in otherwise healthy adults. Loperamide may improve symptoms in traveler's diarrhea with appropriate antibiotic treatment.	Strong recommendation, moderate quality of evidence[11]	Korean Society of Infectious Diseases/Korean Society for Antimicrobial Therapy[11]
In combination, loperamide and simethicone may provide relief for acute watery diarrhea and abdominal discomfort.	Grade B[12]	AAFP[12]
The use of ethanol-based hand sanitizers is recommended during outbreaks of norovirus gastroenteritis.	Category II[10]	CDC[10]
Probiotics may decrease the symptoms and duration of acute infectious diarrhea in otherwise healthy adult and pediatric patients but are not recommended to prevent traveler's diarrhea. Probiotics, including Lactobacillus rhamnosus GG (LGG) and Saccharomyces boulardii, can be considered in children with AGE as an adjunct to ORS.	No grade[7,8] Weak recommendation, moderate quality of evidence[11]	National Association of Pediatric Nurse Practitioners[7] FISPGHAN[8] Korean Society of Infectious Diseases/Korean Society for Antimicrobial Therapy[11]
Infants younger than 6 months should continue breastfeeding during AGE. Lactose-free formula may be considered in hospitalized children and those with prolonged diarrhea.	No grade[8]	FISPGHAN[8]
Early refeeding with a simple, age-	No grade[7]	National Association

appropriate diet is recommended once initial rehydration is achieved.		of Pediatric Nurse Practitioners[7]
Once a child is able to eat, a zinc supplement may be started to help reduce the severity and duration of symptoms. Zinc has also been associated with reduced incidence of diarrhea for 2 to 3 months.	No grade[7,8]	National Association of Pediatric Nurse Practitioners[7] FISPGHAN[8]
Food handlers should perform hand hygiene before contact with food items and beverages to prevent food-related outbreaks of norovirus gastroenteritis.	Category IC[10]	CDC[10]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Viral Gastroenteritis clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts; the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Viral Gastroenteritis report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

The following segment contains the updated versions of the guidelines mentioned in the March 2020 CHI Viral Gastroenteritis Report and the corresponding recommendations:

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
1.1 IDSA; Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea **(2017)**	N/A*
1.2 European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: **(Update 2014)**	N/A*

**: no new updates are available*

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Viral Gastroenteritis report, along with their recommendations.

Table 3. List of Additional Guidelines

Additional Guidelines
AAFP; Guidelines on Gastroenteritis in Children **(2019)**
Korean Society of Infectious Diseases and Korean Society for Antimicrobial Therapy Guideline for the Antibiotic Use in Acute Gastroenteritis **(2019)**

National Association of Pediatric Nurse Practitioners Clinical Practice Guideline for the Treatment of Pediatric Acute Gastroenteritis in the Outpatient Setting **(2016)**
Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN) Universal Recommendations for the Management of Acute Diarrhea in Nonmalnourished Children **(2018)**
AAFP; Acute Diarrhea in Adults **(2022)**
Healthcare Infection Society Guidelines for the management of norovirus outbreaks in acute and community health and social care settings **(2023)**
CDC; Guideline for the prevention and control of norovirus gastroenteritis outbreaks in healthcare settings **(2017)**

1.2.1 American Academy of Family Physicians (AAFP) Guidelines on Gastroenteritis in Children (2019)

The 2019 AAFP guidelines[6] have opted for the following Grading Scheme/Level of Evidence:

Table 4. AAFP Evidence Rating

Evidence Rating	Definition
A	Consistent, good-quality patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series

The review published by the AAFP focuses on acute gastroenteritis in children in industrialized nations, where viruses account for 75% to 90% of childhood acute infectious gastroenteritis. The main recommendations are detailed below[6]:

- Oral rehydration therapy is recommended for children with mild to moderate dehydration from acute gastroenteritis. It is as effective as intravenous rehydration in preventing hospitalizations and return emergency department visits (Category B).
- Children with mild dehydration should receive half-strength apple juice followed by preferred fluids (regular juices, milk). This approach reduces the need for eventual intravenous rehydration compared with a formal oral rehydration solution (Category B).

- Handwashing with soap is an effective method for preventing episodes of gastroenteritis. Handwashing and hygiene alone, however, do not prevent rotavirus infection (Category A).
- All children should receive an oral live, attenuated rotavirus vaccine to reduce the incidence of hospitalization, severe gastroenteritis, and death from rotavirus infection (Category A).
- Breastfeeding reduces the incidence of acute gastroenteritis and hospitalization from diarrheal disease in young children (Category B).

Table 5. WHO Guidelines for Administering Oral Rehydration Solution (ORS) in Children

Weight*	Age*	Approximate amount of ORS (mL) to give in the first four hours
Less than 5 kg (11 lb)	Younger than four months	200 to 400
5 to 7.9 kg (11 lb to 17 lb, 7 oz)	Four to 11 months	200 to 400
8 to 10.9 kg (17 lb, 10 oz to 24 lb)	12 to 23 months	600 to 800
11 to 15.9 kg (24 lb, 4 oz to 35 lb)	Two to four years	800 to 1,200
16 to 29.9 kg (35 lb, 4 oz to 65 lb, 15 oz)	Five to 14 years	1,200 to 2,200
30 kg (66 lb, 2 oz) or more	15 years or older	2,200 to 4,000

**Use the patient's age only if the weight is not known. The approximate amount of ORS required (in mL) can also be calculated by multiplying the patient's weight in kg by 75.*

WHO Guidelines for IV Rehydration Therapy in Children

- Start IV fluids immediately; if the patient can drink, give oral rehydration solution until the IV infusion is established; give 100 mL per kg of Ringer solution* divided as follows:

  → **Infants (younger than 12 months):** First give 30 mL per kg over one hour,† then give 70 mL per kg in five hours

  → **Older children:** First give 30 mL per kg in 30 minutes,† then give 70 mL per kg in 2.5 hours.
- Reassess the patient every one to two hours; if hydration is not improving, give the IV drip more rapidly.

- After six hours (infants) or three hours (older patients), assess the patient to determine the next steps in treatment.

**—If Ringer solution is not available, normal saline may be used.*
†—Repeat once if radial pulse is still very weak or not detectable.

1.2.2 Korean Society of Infectious Diseases and Korean Society for Antimicrobial Therapy Guideline for the Antibiotic Use in Acute Gastroenteritis (2019)

The 2019 Korean Society of Infectious Diseases and Korean Society for Antimicrobial Therapy Guidelines[11] have opted for the following Grading Scheme/Level of Evidence:

Table 6. Korean Society of Infectious Diseases and Korean Society for Antimicrobial Therapy Grading of Recommendations

Level of Evidence	
High	Almost no other study will change the level of trust in the estimates of the effects.
Moderate	Other studies may influence the committee's trust in the estimates of the effects, and the level of trust may also change.
Low	Other studies may significantly influence the committee's trust in the estimates of the effects, and the level of trust may also change.
Very low	The committee does not trust the calculated estimates of the effects.
Expert opinion	Although there is no supporting evidence, the committee has determined through official expert meetings that the recommendation is clinically appropriate at present.
Strength of Recommendations	
Strong	It is best that most or all individuals receive the services outlined in the recommendation. The benefit clearly outweighs the cost or risk, or the cost or risk clearly outweighs the benefit.
Conditional	It may not be best for all individuals to receive the services outlined in the recommendation. The decision should be made based on patient value, preference, and circumstances. The level of evidence is low, or there is no clear difference in risks and benefits.

This guideline was developed as an update to the 2010 clinical guidelines published by the Korean Society for Antimicrobial Therapy in order to provide clinical recommendations based on the newest evidence on empirical antibiotic therapy for suspected acute gastroenteritis, which is commonly seen in clinic, and on targeted antibiotic treatment for cases with confirmed bacterial growth. The ultimate aim is

to decrease antibiotic misuse and to prevent the rise of antibiotic resistant bacterial strains. The main recommendations are summarized below[11]:

- In general, antibiotic treatment is not recommended for most cases of acute watery diarrhea (Strong recommendation, low quality of evidence)
- Empirical antibiotic therapy can be considered in the following cases:
    - If bloody or mucoid stool and fever, or Shigellosis symptoms (frequent scant bloody stools, fever, cramping abdominal pain, and tenesmus) are present (Weak recommendation, expert opinion) and
    - in traveler's diarrhea accompanied by high fever above 38.5°C or septic findings (Low recommendation, low quality of evidence).
- Antibiotic treatment is recommended for immune-suppressed patients with bloody diarrhea (Strong recommendation, low quality of evidence).
- For empirical antibiotic therapy, use fluoroquinolone antibiotics or azithromycin upon consideration of the distribution and antibiotic sensitivity of pathogens in local communities or areas where the patient traveled (Strong recommendation, high quality of evidence).
- Rifaximin may be used for suspected infection with non-invasive bacteria without bloody diarrhea (Low recommendation, low quality of evidence).
- The use of antibiotics is not recommended for patients with suspected STEC infection (Strong recommendation, moderate quality of evidence).
- When the bacteria and antimicrobial susceptibility results are identified, antibiotics should be modified accordingly (Strong recommendation, high quality of evidence).
- For infectious diarrhea caused by *Campylobacter*, the use of azithromycin is recommended (Strong recommendation, high quality of evidence).
- For nontyphoidal salmonellosis, antibiotic treatment is not recommended with the exception of infants less than 3 months of age, patients over 50 with suspected atherosclerosis, immune-suppressed patients, patients with valvulopathy, and patients with significant joint diseases (Weak recommendation, low quality of evidence).
- Azithromycin, ciprofloxacin, or ceftriaxone is recommended for shigellosis (Strong recommendation, high quality of evidence).
- Doxycycline is recommended for Vibrio cholerae infections, and ciprofloxacin, azithromycin, and ceftriaxone may also be used (Strong recommendation, high quality of evidence).

- Bismuth subsalicylates provide symptomatic improvement by regulating the amount of stool in mild or moderate acute diarrhea (Strong recommendation, high quality of evidence).
- Loperamide is helpful in shortening the duration of symptoms of acute watery diarrhea in otherwise healthy adults (Weak recommendation, moderate quality of evidence).
- Loperamide should not be used for children below the age of 18 (Strong recommendation, moderate quality of evidence).
- Loperamide should be avoided when there is a possibility of toxic megacolon or when fever continues (Strong recommendation, low quality of evidence).
- Loperamide may improve symptoms in traveler's diarrhea with appropriate antibiotic treatment (Strong recommendation, moderate quality of evidence).
- Probiotics decrease the symptoms and duration of acute infectious diarrhea in otherwise healthy adult and pediatric patients (Weak recommendation, moderate quality of evidence).
- Probiotics are not recommended to prevent traveler's diarrhea (Weak recommendation, low quality of evidence).

1.2.3 National Association of Pediatric Nurse Practitioners Clinical Practice Guideline for the Treatment of Pediatric Acute Gastroenteritis in the Outpatient Setting (2016)

The purpose of the clinical practice guideline published by the National Association of Pediatric Nurse Practitioners is to describe current evaluation and management of pediatric patients with acute gastroenteritis (AGE) children older than 6 months with symptoms for fewer than 7 days in the outpatient setting. The main recommendations are summarized below[7]:

- The outpatient treatment of pediatric patients with AGE should be guided by a dehydration assessment or pre-illness weight that indicates total volume loss.
- The mainstay of therapy for children with mild or moderate dehydration should focus on ORT with an emphasis on replacing deficits and preventing ongoing fluid losses.

Table 7. Treatment Principles for Management of Dehydration

Dehydration Status	Management
Mild dehydration (<5%)	Continue hydration ORT with teaching on frequent small volumes of liquid. Encourage regular diet (unrestricted breastfeeding). Replace ongoing losses (assume 1 diarrheal stool/emesis equals 2 oz liquid or 10 ml/kg).
Moderate dehydration (5-10%)	Needs ORT. Defer solids until rehydrated May continue unrestricted breastfeeding with oral rehydration solution adjunct. Replace ongoing losses (assume 1 diarrheal stool/ emesis equals 2 oz liquid or 10 ml/kg).
Severe dehydration (>10%)	Needs IV rehydration. Place saline lock IV catheter and give 0.9% sodium chloride 20 ml/kg bolus IV push; repeat if warranted and patient is responding to fluid bolus. Recommend point of care glucose and electrolytes if patient is listless and lethargic. Measure intake and output. Initiate ORT with teaching on frequent small volumes of liquid once IV access obtained. May need maintenance IV fluids; hold potassium-containing fluids until patient has voided.

- Providers should minimize unnecessary medications and tests that increase costs and may potentially cause harm.
- Drugs that alter intestinal motility or secretion, anticholinergic agents, opiates, and antibiotics are not recommended.

1. Ondansetron

Ondansetron is a safe and effective antiemetic medication to facilitate oral rehydration in the acute care setting Although reliance on pharmacologic intervention shifts the therapeutic focus away from fluid and electrolyte replacement and can result in adverse effects, shared decision making should occur between the provider and family to consider ondansetron use in the outpatient setting when persistent vomiting impedes ORT. Although the CDC may remain in opposition to antiemetic agents in its recommendations, recent research has shown

that ondansetron is a safe and effective method of encouraging ORT in the acute care setting.

Dosing:

For age > 6 months: 0.15 mg/kg, maximum 8 mg as a single dose to aid in tolerance of ORT for rehydration; additional doses are associated with an increased risk of diarrhea.

Alternative dosing by weight range:

- < 8 kg: not recommended
- 8-15 kg: 2 mg
- 15-30 kg: 4 mg
- 30 kg: 8 mg

2. **Fluid replacement**

Oral rehydration therapy

→ Goal fluid intake: 15 ml/kg/1 hour or 60 ml/kg/ 4 hours

→ Add 10ml/kg for every episode of diarrhea or vomiting

Oral rehydration solution

Only clear liquids should be offered for oral rehydration. Fluids with a high sugar content may increase the osmotic pull of water into the intestinal lumen, which causes hypernatremia and exacerbates diarrhea. Water causes hyponatremia from the hypotonic osmotic gradient, which may result in seizure. Suitable oral rehydration solutions include:

- WHO oral rehydration solution packets
- Commercial electrolyte solutions for pediatric patients (e.g., Pedialyte and Infalyte)
- Sports drinks (e.g., Gatorade and Powerade) or low-calorie sports drinks (e.g., Gatorade G2) with ½ tsp salt per 32-oz bottle
- Salted rice water, salted yogurt drink, soup with salt

3. **Feeding**

Breastfed infants should continue unrestricted feeding. National guidelines recommend the reintroduction of nutrition within the first 24 hours of illness once initial rehydration is achieved. Early realimentation of an age-appropriate diet containing simple starches, fruits and vegetables, lean meats, and yogurt aids co-transport molecules, thereby increasing fluid and electrolyte uptake while reducing

stool losses. Although the BRAT diet of bananas, rice, applesauce, and toast is no longer promoted because of the low energy density and lack of protein or fat, these foods can still be added to the reintroduction diet to add bulk to diarrheal stool.

4. **Adjunct therapy**

Probiotics

Probiotics are microorganisms that can be beneficial when administered in adequate doses. Despite a lack of consensus regarding treatment of pediatric patients who have AGE with probiotics, findings from clinical trials support the use of probiotics to decrease the duration and intensity of AGE.

The quality of evidence on probiotics is low, and additional research should be conducted to strengthen evidence.

Lactobacillus rhamnosus GG (LGG) and Saccharomyces boulardii have strong recommendations for use by international practice guidelines, although the strength of evidence in these recommendations was low.

Most importantly, probiotics were not associated with any adverse events. Probiotics are considered a supplement that is not regulated by federal quality and safety standards, and therefore product differences may result in varying efficacy, which should be discussed with families before treatment begins.

Doses:

- LGG, 10 billion colony-forming units/day for 5 to 7 days
- S. boulardii, 250 to 750 mg/day for 5 to 7 days

Zinc

Once a child is able to eat, a zinc supplement may be started to help reduce the severity and duration of symptoms. Zinc has also been associated with reduced incidence of diarrhea for 2 to 3 months.

Dose: 10 to 20 mg/day for 10 to 14 days.

1.2.4 Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN) Universal Recommendations for the Management of Acute Diarrhea in Nonmalnourished Children (2018)

The Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN) Working Group (WG) selected care protocols on the management of acute diarrhea in infants and children aged between 1 month and 18 years. A core of recommendations including definition, diagnosis, nutritional

management, and active treatment of AGE was developed with an overall agreement of 91%. Recommendations on the use of antidiarrheal drugs and antiemetics received the lowest level of agreement and need to be tailored at local level. Oral rehydration and probiotics were the only treatments recommended.

Main recommendations are summarized below[8]:

Rehydration

- ORS is the first-line treatment of AGE. Knowledge, attitude, and practice about oral rehydration by health service providers are essential and should be promoted.
- Reduced osmolality ORS (60 – 75 mmol/L Na^+) is recommended as first-line treatment of AGE. In case of cholera, 75 mmol/L Na^+ is the standard rehydration regimen.
- ReSoMal (Rehydration Solution for Malnutrition) containing 45 mmol/L Na^+ and 40 mmol/L K^+ may be indicated for malnourished children, although there are no conclusive data on its efficacy compared to standard reduced osmolality ORS.
- In children who fail on oral rehydration, administration of rehydration fluids either by nasogastric tube or intravenously (IV) is effective and should be recommended. IV rehydration should be avoided where possible in severely malnourished children.
- Enteral administration of ORS through a nasogastric tube is effective in rehydrating children with AGE and it is associated with fewer side effects than IV rehydration, especially in malnourished children. Its knowledge, attitude, and practice should be promoted among health workers as well as families and local workers.

Nutritional management

- Infants younger than 6 months should neither interrupt breast-feeding nor introduce diluted or modified formula. Where there is not the possibility to breast-feed, routine dilution of milk and routine use of lactose-free milk formula are not usually necessary.
- Children should be re-fed early during the course of AGE. Regular oral feeding should be reintroduced no later than 4 to 6 hours after the onset of rehydration.
- Lactose-free formula is generally not necessary in AGE episodes. However, lactose-restricted diets may be considered in hospitalized children and in

children with prolonged diarrhea (>7 days). Lactose-free formula should be recommended in children with chronic diarrhea (>14 days).

- Elimination diet is usually not indicated for children with AGE and it may further impair the child's nutritional status.
- Zinc is recommended as an adjunct to oral rehydration therapy in children older than 6 months living in low-income countries or in settings with medium or high risk of zinc deficiency. Its efficacy is not supported by solid evidence in well-nourished children living in high-income countries. In infants younger than 6 months zinc is not effective regardless of the nutritional status.

Active treatment of diarrhea

- Active treatment of diarrhea with the administration of probiotics and/or drugs may be considered where there is solid proof of efficacy in reducing the intensity and duration of symptoms. To maximize efficacy, active treatment should be administered early in the course of the disease.
- However, administration of any product should not replace oral rehydration therapy and should always be used as an adjunct to ORS treatment.
- Because investigation of active therapies is rapidly evolving, the choice of best treatment should be always made along recommendations of evidence-based guidelines and in compliance with well-done randomized controlled trials.
- Probiotics are effective in reducing the duration and intensity of symptoms of AGE. If available and in agreement with caregivers, selected probiotic strains (including Lactobacillus rhamnosus GG, Saccharomyces boulardii, and L reuteri DSM 17938) can be considered in children with AGE, as an adjunct to ORS.
- Loperamide and other antimotility drugs are not recommended in the treatment of AGE.
- Metoclopramide, although effective, has significant side effects and is therefore not recommended for children with vomiting owing to AGE. The efficacy of domperidone is not supported by randomized controlled trials.
- Ondansetron administered either orally or intravenously is effective in reducing vomiting and may avoid hospital admission. A single dose at the dosages used in the available studies may be considered in young children presenting to an emergency department with vomiting to ensure oral rehydration and reduce hospital admis- sion. However, the use of ondansetron has been associated with QT prolongation and severe cardiac arrhythmias

and the drug carries a warning label by both the Food and Drug Administration and the European Medicines Agency that should be taken into account by health care providers.

- Routine use of antibiotics is not recommended for the treatment of AGE.
- The use of antibiotics should be started immediately and may be considered in specific situations, including:
    1. infants younger than 3 months
    2. children with underlying chronic conditions, including those with sickle cell anemia or immunodeficiency and those at risk for developing severe or extraintestinal dissemination
    3. isolation of specific pathogens such as Shigella, enterotoxigenic (but not Shiga-like toxin-producing) Escherichia coli, V cholerae, Yersinia enterocolitica, and Entamoeba histolytica.
- Campylobacter colitis can be treated with antibiotics, but treatment is effective only if administered within the first 2 days from the onset of symptoms.

1.2.5 American Academy of Family Physicians (AAFP); Acute Diarrhea in Adults (2022)

Evidence rating for recommendations stated below follow the definitions detailed in table 4 above.

The recommendations issued by the AAFP for the management of acute diarrhea is adults are summarized below[12]:

- Stool culture or multiplex polymerase chain reaction testing should be reserved for patients with evidence of invasive disease, immunocompromise, prolonged illness, or increased risk of involvement in an outbreak (Grade C).
- Rehydration is the first-line treatment for acute diarrhea, with oral rehydration being the preferred method for fluid replacement (Grade A).
- In combination, loperamide (Imodium) and simethicone may provide faster and more complete relief of acute watery diarrhea and abdominal discomfort than either medication alone (Grade B).
- When using antibiotics for travelers' diarrhea, adjunct loperamide shortens the duration of symptoms and increases the likelihood of a cure (Grade A).
- Empiric antibiotics can lessen the duration and severity of symptoms in moderate to severe cases of travelers' diarrhea (Grade A).

1.2.6 Healthcare Infection Society Guidelines for the Management of Norovirus Outbreaks in Acute and Community Health and Social Care Settings (2023)

The Healthcare Infection Society guidelines have issued the recommendations below[9]:

- During norovirus outbreaks, encourage all individuals to perform hand hygiene as per defined technique using soap and water.
- Consider monitoring whether appropriate handwashing takes place.
- Use gloves and aprons when caring for symptomatic patients with norovirus.
- Do not screen the environment routinely for norovirus, neither during outbreaks nor in non-outbreak situations.
- Ensure that appropriate cleaning, including the removal of organic soiling, precedes disinfection.
- Ensure that all staff involved in environmental cleaning are trained to achieve appropriate cleaning standards.
- Ensure that appropriate decontamination is performed on any re-usable cleaning equipment following the cleaning of contaminated areas.
- Consider excluding symptomatic staff with norovirus infection for a minimum of 48 h after symptom resolution.
- During norovirus outbreaks, undertake continuous risk assessment to establish which good practice points need to be introduced to minimize transmission.
- Provide staff with sufficient information and training so they are able to recognize and act quickly when a norovirus outbreak occurs.

1.2.7 CDC Guideline for the Prevention and Control of Norovirus Gastroenteritis Outbreaks in Healthcare Settings (2017)

The CDC[10] have opted for the following Grading Scheme/Level of Evidence:

Table 8. CDC Recommendation Categories

Rating	Definition
Category IA	A strong recommendation supported by high to moderate quality evidence suggesting net clinical benefits or harms.
Category IB	A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low to very low-

	quality evidence.
Category IC	A strong recommendation required by state or federal regulation.
Category II	A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms.
Recommendation for further research	An unresolved issue for which there is low to very low-quality evidence with uncertain tradeoffs between benefits and harms.

The CDC has issued the recommendations below[10]:

- Avoid exposure to vomitus or diarrhea. Place patients on Contact Precautions in a single occupancy room if they have symptoms consistent with norovirus gastroenteritis. (Category IB)
- Consider longer periods of isolation or cohorting precautions for complex medical patients (e.g., those with cardiovascular, autoimmune, immunosuppressive, or renal disorders) as they can experience protracted episodes of diarrhea and prolonged viral shedding. Patients with these or other comorbidities have the potential to relapse and facilities may choose longer periods of isolation based on clinical judgment. (Category II)
- Consider the development and adoption of facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection while implementing prompt control measures to reduce the magnitude of a potential norovirus outbreak. (Category II)
- To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers must perform hand hygiene prior to contact with or the preparation of food items and beverages (Category IC)
- Personnel who work with, prepare, or distribute food must be excluded from duty if they develop symptoms of acute gastroenteritis. Personnel should not return to these activities until a minimum of 48 hours after the resolution of symptoms or longer as required by local health regulations (Category IC)
- If norovirus infection is suspected, adherence to PPE use according to Contact and Standard Precautions is recommended for individuals entering the patient care area (i.e., gowns and gloves upon entry) to reduce the likelihood of exposure to infectious vomitus or fecal material. (Category IB)
- During outbreaks, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. (Category IB)

- Consider ethanol-based hand sanitizers (60-95%) as the preferred active agent compared to other alcohol or non-alcohol-based hand sanitizer products during outbreaks of norovirus gastroenteritis. (Category II)
- Use a surgical or procedure mask and eye protection or a full-face shield if there is an anticipated risk of splashes to the face during the care of patients, particularly among those who are vomiting. (Category IB)
- Exclude ill personnel from work for a minimum of 48 hours after the resolution of symptoms. Once personnel return to work, the importance of performing frequent hand hygiene should be reinforced, especially before and after each patient contact. (Category IB)
- Consider minimizing patient movements within a ward or unit during norovirus gastroenteritis outbreaks. (Category II)

Section 2.0 Drug Therapy in Viral Gastroenteritis

This section comprises three subsections: the first contains the newly recommended drugs, the second covers drug modifications, and the third outlines the drugs to delist due to withdrawal from the market among others.

2.1 Additions

No new drugs have been approved by the FDA or EMA for the treatment of Viral Gastroenteritis since March 2020.

2.2 Modifications

The following modifications and adjustments have been implemented since the 2020 report:

Table 9. Prescribing Edits (PE) Modifications for Viral Gastroenteritis Medications

Drugs	PE modifications
Dimenhydrate	"Prior Authorization (PA)" removed; "AGE" added: not for use in children < 2 years old.
Granisetron	"PA" removed.
Loperamide	"AGE": contraindicated in children < 2 years of age; Removed "PA", "MD".
Valganciclovir	"PA" removed.
Vitamins, folic acid, pantothenic acid, calcium, lactic ferments (lactobacillus acidophilus & sporogenes, bifidobacterium bifidum, longum & infantis)	"PA" removed.
Zinc	"PA" removed.

2.3 Delisting

One vaccine is no longer registered by the SFDA for the treatment of Viral Gastroenteritis since March 2020.

- Rotavirus Vaccine

However, other forms of the rotavirus vaccine are still registered by the SFDA and include the pentavalent oral form (RotaTeq®) and the monovalent oral form (Rotarix®).

Section 3.0 Key Recommendations Synthesis

- Viral Gastroenteritis is an inflammation of the gastrointestinal tract, primarily the stomach and intestines, caused by viral infections. It is characterized by symptoms such as diarrhea, vomiting, abdominal pain, and sometimes fever. It is typically a self-limiting condition and can be caused by various viruses, including rotavirus, norovirus, adenovirus, and astrovirus, among others. It is often highly contagious and spreads through the ingestion of contaminated food or water, direct contact with infected individuals, or contact with contaminated surfaces. The condition is usually acute and resolves within a few days to a week, with supportive care and hydration being the primary treatment[1].
- ORT is recommended for children with mild to moderate dehydration from acute gastroenteritis. It is as effective as intravenous rehydration in preventing hospitalizations and return emergency department visits[6].
- The mainstay of therapy for children with mild or moderate dehydration should focus on ORT with an emphasis on replacing deficits and preventing ongoing fluid losses. ORS is the first-line treatment of AGE, with reduced osmolality ORS recommended as the first-line treatment. IV rehydration may be indicated for children who fail ORT [7,8].
- Children with mild dehydration should receive half-strength apple juice followed by preferred fluids (regular juices, milk) to reduce the need for eventual intravenous rehydration compared with a formal oral rehydration solution[6].
- During outbreaks of norovirus gastroenteritis, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. Handwashing with soap is an effective method for preventing episodes of gastroenteritis, although it does not prevent rotavirus infection [6, 910, 10].
- All children should receive an oral live, attenuated rotavirus vaccine to reduce the incidence of hospitalization, severe gastroenteritis, and death from rotavirus infection[6].
- Breastfeeding reduces the incidence of acute gastroenteritis and hospitalization from diarrheal disease in young children[6].

- Antibiotic treatment is generally not recommended for most cases of acute watery diarrhea, except in specific cases. Antibiotics may be considered in specific cases, including immune-suppressed patients with bloody diarrhea, Campylobacter infections, shigellosis, and suspected infections with non-invasive bacteria[8, 11].
- For infectious diarrhea caused by Campylobacter, the use of azithromycin is recommended[11].
- Azithromycin, ciprofloxacin, or ceftriaxone is recommended for shigellosis. Doxycycline is recommended for Vibrio cholerae infections, and ciprofloxacin, azithromycin, and ceftriaxone may also be used[11].
- Antibiotics can be considered for travelers' diarrhea and empiric antibiotics are recommended in moderate to severe cases of travelers' diarrhea[12].
- Ondansetron may be considered to facilitate oral rehydration in the acute care setting for children with persistent vomiting[7,8].
- Loperamide is helpful in shortening the duration of symptoms of acute watery diarrhea in otherwise healthy adults. Loperamide may improve symptoms in traveler's diarrhea with appropriate antibiotic treatment[11].
- In combination, loperamide and simethicone may provide relief for acute watery diarrhea and abdominal discomfort mainly in adults[12].
- The use of ethanol-based hand sanitizers is recommended during outbreaks of norovirus gastroenteritis[10].
- Probiotics may decrease the symptoms and duration of acute infectious diarrhea in otherwise healthy adult and pediatric patients but are not recommended to prevent traveler's diarrhea. Probiotics, including Lactobacillus rhamnosus GG (LGG) and Saccharomyces boulardii, can be considered in otherwise healthy children with AGE as an adjunct to ORS[7,8].
- Infants younger than 6 months should continue breastfeeding during AGE. Lactose-free formula may be considered in hospitalized children and those with prolonged diarrhea[8].
- Early refeeding with a simple, age-appropriate diet is recommended once initial rehydration is achieved[7].
- Once a child is able to eat, a zinc supplement may be started to help reduce the severity and duration of symptoms. Zinc has also been associated with reduced incidence of diarrhea for 2 to 3 months[7,8].
- Food handlers should perform hand hygiene before contact with food items and beverages to prevent food-related outbreaks of norovirus gastroenteritis[10].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Viral Gastroenteritis report** and aims to provide recommendations to aid in the management of Viral Gastroenteritis. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Viral Gastroenteritis. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

1. Orenstein R. Gastroenteritis, Viral. In: *Encyclopedia of Gastroenterology, Second Edition*. Elsevier; 2019:652-657. doi:10.1016/B978-0-12-801238-3.65973-1
2. Gastroenteritis - Better Health Channel. Accessed September 25, 2023. https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/gastroenteritis#
3. CDC. Norovirus Burden and Trends | CDC. Published 2023. Accessed September 19, 2023. https://www.cdc.gov/norovirus/burden.html#
4. Bartsch SM, O'shea KJ, Lee BY. The Clinical and Economic Burden of Norovirus Gastroenteritis in the United States. *J Infect Dis*. 2020;222(11):1910. doi:10.1093/INFDIS/JIAA292
5. NIDDK. Treatment of Viral Gastroenteritis ("Stomach Flu") - NIDDK. Published 2018. Accessed September 19, 2023. https://www.niddk.nih.gov/health-information/digestive-diseases/viral-gastroenteritis/treatment#
6. AAFP. Gastroenteritis in Children. Published online 2019.
7. Carson RA, Mudd SS, Madati PJ. Clinical Practice Guideline for the Treatment of Pediatric Acute Gastroenteritis in the Outpatient Setting. *Journal of Pediatric Health Care*. 2016;30(6):610-616. doi:10.1016/j.pedhc.2016.04.012
8. Guarino A, Vecchio A Lo, Dias JA, et al. Universal recommendations for the management of acute diarrhea in nonmalnourished children. *J Pediatr Gastroenterol Nutr*. 2018;67(5):586-593. doi:10.1097/MPG.0000000000002053
9. Chadwick PR, Trainor E, Marsden GL, et al. Guidelines for the management of norovirus outbreaks in acute and community health and social care settings. *Journal of Hospital Infection*. 2023;136:127-191. doi:10.1016/j.jhin.2023.01.017

10. Maccannell T, Umscheid CA, Rajender ;, et al. *GUIDELINE FOR THE PREVENTION AND CONTROL OF NOROVIRUS GASTROENTERITIS OUTBREAKS IN HEALTHCARE SETTINGS*.; 2017.

11. Kim YJ, Park KH, Park DA, et al. Guideline for the antibiotic use in acute gastroenteritis. *Infect Chemother*. 2019;51(2):217-243. doi:10.3947/ic.2019.51.2.217

12. AAFP. Acute Diarrhea in Adults. Published 2022. Accessed September 20, 2023. https://www.aafp.org/pubs/afp/issues/2022/0700/acute-diarrhea.html

Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

Appendix B. Viral Gastroenteritis Scope

<table>
<tr><th>Section</th><th>Rationale/Updates</th></tr>
<tr><td>Addition of a new section:
AAFP; Guidelines on Gastroenteritis in Children (2019)[6]</td><td>Oral rehydration therapy is recommended for children with mild to moderate dehydration from acute gastroenteritis. It is as effective as intravenous rehydration in preventing hospitalizations and return emergency department visits (Category B).

Children with mild dehydration should receive half-strength apple juice followed by preferred fluids (regular juices, milk). This approach reduces the need for eventual intravenous rehydration compared with a formal oral rehydration solution (Category B).

Handwashing with soap is an effective method for preventing episodes of gastroenteritis. Handwashing and hygiene alone, however, do not prevent rotavirus infection (Category A).

All children should receive an oral live, attenuated rotavirus vaccine to reduce the incidence of hospitalization, severe gastroenteritis, and death from rotavirus infection (Category A).

Breastfeeding reduces the incidence of acute gastroenteritis and hospitalization from diarrheal disease in young children (Category B).

Table 10: WHO Guidelines for Administering ORS in Children
<table><tr><th>Weight</th><th>Age</th><th>Approximate amount of ORS (mL) to give in the first four hours</th></tr><tr><td>Less than 5 kg (11 lb)</td><td>Younger than four months</td><td>200 to 400</td></tr><tr><td>5 to 7.9 kg (11 lb to 17 lb, 7 oz)</td><td>Four to 11 months</td><td>200 to 400</td></tr><tr><td>8 to 10.9 kg (17 lb, 10 oz to 24 lb)</td><td>12 to 23 months</td><td>600 to 800</td></tr><tr><td>11 to 15.9 kg (24 lb, 4 oz to 35 lb)</td><td>Two to four years</td><td>800 to 1,200</td></tr><tr><td>16 to 29.9 kg (35 lb, 4 oz to 65 lb, 15 oz)</td><td>Five to 14 years</td><td>1,200 to 2,200</td></tr></table></td></tr>
</table>

	30 kg (66 lb, 2 oz) or more	15 years or older	2,200 to 4,000

—Use the patient's age only if the weight is not known. The approximate amount of ORS required (in mL) can also be calculated by multiplying the patient's weight in kg by 75.

ORS = oral rehydration solution; WHO = World Health Organization.

WHO Guidelines for IV Rehydration Therapy in Children
Start IV fluids immediately; if the patient can drink, give oral rehydration solution until the IV infusion is established; give 100 mL per kg of Ringer solution* divided as follows:
→ **Infants (younger than 12 months):** First give 30 mL per kg over one hour,† then give 70 mL per kg in five hours
→ **Older children:** First give 30 mL per kg in 30 minutes,† then give 70 mL per kg in 2.5 hours.

Reassess the patient every one to two hours; if hydration is not improving, give the IV drip more rapidly.

After six hours (infants) or three hours (older patients), assess the patient to determine the next steps in treatment.

—If Ringer solution is not available, normal saline may be used.
†—Repeat once if radial pulse is still very weak or not detectable.

Addition of a new section: Infection & Chemotherapy; Guideline for the Antibiotic Use in Acute Gastroenteritis **(2019)**[11]	In general, antibiotic treatment is not recommended for most cases of acute watery diarrhea (Strong recommendation, low quality of evidence) Empirical antibiotic therapy can be considered in the following cases: o If bloody or mucoid stool and fever, or Shigellosis symptoms (frequent scant bloody stools, fever, cramping abdominal pain, and tenesmus) are present (Weak recommendation, expert opinion) and o in traveler's diarrhea accompanied by high fever above 38.5°C or septic findings (Low recommendation, low quality of evidence). Antibiotic treatment is recommended for immune-suppressed patients with bloody diarrhea (Strong recommendation, low quality of evidence). For empirical antibiotic therapy, use fluoroquinolone antibiotics or azithromycin upon consideration of the

	distribution and antibiotic sensitivity of pathogens in local communities or areas where the patient traveled (Strong recommendation, high quality of evidence). Rifaximin may be used for suspected infection with non-invasive bacteria without bloody diarrhea (Low recommendation, low quality of evidence). The use of antibiotics is not recommended for patients with suspected STEC infection (Strong recommendation, moderate quality of evidence). When the bacteria and antimicrobial susceptibility results are identified, antibiotics should be modified accordingly (Strong recommendation, high quality of evidence). For infectious diarrhea caused by *Campylobacter*, the use of azithromycin is recommended (Strong recommendation, high quality of evidence). For nontyphoidal salmonellosis, antibiotic treatment is not recommended with the exception of infants less than 3 months of age, patients over 50 with suspected atherosclerosis, immune-suppressed patients, patients with valvulopathy, and patients with significant joint diseases (Weak recommendation, low quality of evidence). Azithromycin, ciprofloxacin, or ceftriaxone is recommended for shigellosis (Strong recommendation, high quality of evidence). Doxycycline is recommended for Vibrio cholerae infections, and ciprofloxacin, azithromycin, and ceftriaxone may also be used (Strong recommendation, high quality of evidence). Bismuth subsalicylates provide symptomatic improvement by regulating the amount of stool in mild or moderate acute diarrhea (Strong recommendation, high quality of evidence). Loperamide is helpful in shortening the duration of symptoms of acute watery diarrhea in otherwise healthy adults (Weak recommendation, moderate quality of evidence). Loperamide should not be used for children below the age of 18 (Strong recommendation, moderate quality of evidence). Loperamide should be avoided when there is a possibility of toxic megacolon or when fever continues (Strong

	recommendation, low quality of evidence). Loperamide may improve symptoms in traveler's diarrhea with appropriate antibiotic treatment (Strong recommendation, moderate quality of evidence). Probiotics decrease the symptoms and duration of acute infectious diarrhea in otherwise healthy adult and pediatric patients (Weak recommendation, moderate quality of evidence). Probiotics are not recommended to prevent traveler's diarrhea (Weak recommendation, low quality of evidence).
Addition of a new section: Journal of Hospital Infection; Guidelines for the management of norovirus outbreaks in acute and community health and social care settings **(2017** [9]	During norovirus outbreaks, encourage all individuals to perform hand hygiene as per defined technique using soap and water. Consider monitoring whether appropriate handwashing takes place. Use gloves and aprons when caring for symptomatic patients with norovirus. Do not screen the environment routinely for norovirus, neither during outbreaks nor in non-outbreak situations. Ensure that appropriate cleaning, including the removal of organic soiling, precedes disinfection. Ensure that all staff involved in environmental cleaning are trained to achieve appropriate cleaning standards. Ensure that appropriate decontamination is performed on any re-usable cleaning equipment following the cleaning of contaminated areas. Consider excluding symptomatic staff with norovirus infection for a minimum of 48 h after symptom resolution. During norovirus outbreaks, undertake continuous risk assessment to establish which good practice points need to be introduced to minimize transmission. Provide staff with sufficient information and training so they are able to recognize and act quickly when a norovirus outbreak occurs.
Addition of a new section: CDC; Guideline for the	Avoid exposure to vomitus or diarrhea. Place patients on Contact Precautions in a single occupancy room if they have

prevention and control of norovirus gastroenteritis outbreaks in healthcare settings **(2017)**[10]	symptoms consistent with norovirus gastroenteritis. (Category IB) Consider longer periods of isolation or cohorting precautions for complex medical patients (e.g., those with cardiovascular, autoimmune, immunosuppressive, or renal disorders) as they can experience protracted episodes of diarrhea and prolonged viral shedding. Patients with these or other comorbidities have the potential to relapse and facilities may choose longer periods of isolation based on clinical judgment. (Category II) Consider the development and adoption of facility policies to enable rapid clinical and virological confirmation of suspected cases of symptomatic norovirus infection while implementing prompt control measures to reduce the magnitude of a potential norovirus outbreak. (Category II) To prevent food-related outbreaks of norovirus gastroenteritis in healthcare settings, food handlers must perform hand hygiene prior to contact with or the preparation of food items and beverages (Category IC) Personnel who work with, prepare or distribute food must be excluded from duty if they develop symptoms of acute gastroenteritis. Personnel should not return to these activities until a minimum of 48 hours after the resolution of symptoms or longer as required by local health regulations (Category IC) If norovirus infection is suspected, adherence to PPE use according to Contact and Standard Precautions is recommended for individuals entering the patient care area (i.e., gowns and gloves upon entry) to reduce the likelihood of exposure to infectious vomitus or fecal material. (Category IB) During outbreaks, use soap and water for hand hygiene after providing care or having contact with patients suspected or confirmed with norovirus gastroenteritis. (Category IB) Consider ethanol-based hand sanitizers (60-95%) as the preferred active agent compared to other alcohol or non-alcohol based hand sanitizer products during outbreaks of norovirus gastroenteritis. (Category II) Use a surgical or procedure mask and eye protection or a full face shield if there is an anticipated risk of splashes to the face during the care of patients, particularly among those who are vomiting. (Category IB) Exclude ill personnel from work for a minimum of 48 hours

<table>
<tr><td></td><td>after the resolution of symptoms. Once personnel return to work, the importance of performing frequent hand hygiene should be reinforced, especially before and after each patient contact. (Category IB)

Consider minimizing patient movements within a ward or unit during norovirus gastroenteritis outbreaks. (Category II)</td></tr>
<tr><td>Addition of a new section:
Journal of Pediatric Health Care; Clinical Practice Guideline for the Treatment of Pediatric Acute Gastroenteritis in the Outpatient Setting (2016)[7]</td><td>Table 11: Treatment principles for management of dehydration
<table>
<tr><td>Mild dehydration (<5%)</td><td>Continue hydration
ORT with teaching on frequent small volumes of liquid

Encourage regular diet (unrestricted breastfeeding)

Replace ongoing losses (assume 1 diarrheal stool/emesis equals 2 oz liquid or 10 ml/kg)</td></tr>
<tr><td>Moderate dehydration (5-10%)</td><td>Needs ORT

Defer solids until rehydrated May continue unrestricted breastfeeding with oral rehydration solution adjunct

Replace ongoing losses (assume 1 diarrheal stool/ emesis equals 2 oz liquid or 10 ml/kg)</td></tr>
<tr><td>Severe dehydration (>10%)</td><td>Needs IV rehydration

Place saline lock IV catheter and give 0.9% sodium chloride 20 ml/kg bolus IV push; repeat if warranted and patient is responding to fluid bolus

Recommend point of care glucose and electrolytes if patient is listless and lethargic

Measure intake and output
Initiate ORT with teaching on frequent small volumes of liquid once IV access obtained</td></tr>
</table></td></tr>
</table>

	May need maintenance IV fluids; hold potassium-containing fluids until patient has voided

The outpatient treatment of pediatric patients with AGE should be guided by a dehydration assessment or pre-illness weight that indicates total volume loss.

The mainstay of therapy for children with mild or moderate dehydration should focus on ORT with an emphasis on replacing deficits and preventing ongoing fluid losses.

Providers should minimize unnecessary medications and tests that increase costs and may potentially cause harm.

Drugs that alter intestinal motility or secretion, anticholinergic agents, opiates, and antibiotics are not recommended

Ondansetron is a safe and effective antiemetic medication to facilitate oral rehydration in the acute care setting Although reliance on pharmacologic intervention shifts the therapeutic focus away from fluid and electrolyte replacement and can result in adverse effects, shared decision making should occur between the provider and family to consider ondansetron use in the outpatient setting when persistent vomiting impedes ORT. Although the CDC may remain in opposition to antiemetic agents in its recommendations, recent research has shown that ondansetron is a safe and effective method of encouraging ORT in the acute care setting.

Oral rehydration therapy

- Goal fluid intake: 15 ml/kg/1 hour or 60 ml/kg/ 4 hours
- Add 10ml/kg for every episode of diarrhea or vomiting

Oral rehydration solution

Only clear liquids should be offered for oral rehydration. Fluids with a high sugar content may increase the osmotic pull of water into the intestinal lumen, which causes hypernatremia and exacerbates the diarrhea. Water causes hyponatremia from the hypotonic osmotic gradient, which may result in seizure. Suitable oral rehydration solutions include:

- WHO oral rehydration solution packets
- Commercial electrolyte solutions for pediatric patients (e.g., Pedialyte and Infalyte)
- Sports drinks (e.g., Gatorade and Powerade) or low-calorie sports drinks (e.g., Gatorade G2) with *1*⁄2 tsp salt per 32-oz bottle
- Salted rice water, salted yogurt drink, soup with

	salt **Ondansetron:** For age > 6 months: 0.15 mg/kg, maximum 8 mg as a single dose to aid in tolerance of ORT for rehydration; additional doses are associated with an increased risk of diarrhea Alternative dosing by weight range: < 8 kg: not recommended 8-15 kg: 2 mg 15-30 kg: 4 mg > 30 kg: 8 mg **Feeding:** Breastfed infants should continue unrestricted feeding. National guidelines recommend the reintroduction of nutrition within the first 24 hours of illness once initial rehydration is achieved. Early realimentation of an age-appropriate diet containing simple starches, fruits and vegetables, lean meats, and yogurt aids co-transport molecules, thereby increasing fluid and electrolyte uptake while reducing stool losses. Although the BRAT diet of bananas, rice, applesauce, and toast is no longer promoted because of the low energy density and lack of protein or fat, these foods can still be added to the reintroduction diet to add bulk to diarrheal stool. **Adjunct therapy** **Probiotics:** Probiotics are microorganisms that can be beneficial when administered in adequate doses. Despite a lack of consensus regarding treatment of pediatric patients who have AGE with probiotics, findings from clinical trials support the use of probiotics to decrease the duration and intensity of AGE. The quality of evidence on probiotics is low, and additional research should be conducted to strengthen evidence. Lactobacillus rhamnosus GG (LGG) and Saccharomyces boulardii have strong recommendations for use by international practice guidelines, although the strength of evidence in these recommendations was low (Szajewska et al., 2014). Most importantly, probiotics were not associated with any adverse events. Probiotics are considered a supplement that is not regulated by federal quality and safety standards, and therefore product differences may result in varying efficacy, which should be discussed with families before treatment begins.

	Doses: ○ LGG, 10 billion colony-forming units/day for 5 to 7 days (Szajewska et al., 2014) ○ S. boulardii, 250 to 750 mg/day for 5 to 7 days (Szajewska et al., 2014) **Zinc** Once a child is able to eat, a zinc supplement may be started to help reduce the severity and duration of symptoms. Zinc has also been associated with reduced incidence of diarrhea for 2 to 3 months. **Dose.** 10 to 20 mg/day for 10 to 14 days (WHO, 2011)
Addition of a new section: Journal of Pediatric Gastroenterology and Nutrition; Universal Recommendations for the Management of Acute Diarrhea in Nonmalnourished Children **(2018)**[8]	**Rehydration** ORS is the first-line treatment of AGE. Knowledge, attitude, and practice about oral rehydration by health service providers are essential and should be promoted. Reduced osmolality ORS (60 – 75 mmol/L Naþ) is recom- mended as first-line treatment of AGE. In case of cholera, 75 mmol/L Na^+ is the standard rehydration regimen. ReSoMal (Rehydration Solution for Malnutrition) containing 45 mmol/L Na^+ and 40 mmol/L K^+ may be indicated for malnourished children, although there are no conclusive data on its efficacy compared to standard reduced osmolality ORS. In children who fail on oral rehydration, administration of rehydration fluids either by nasogastric tube or intra- venously (IV) is effective and should be recommended. IV rehydration should be avoided where possible in severely malnourished children. Enteral administration of ORS through a nasogastric tube is effective in rehydrating children with AGE and it is associated with fewer side effects than IV rehydration, especially in malnourished children. Its knowledge, atti- tude, and practice should be promoted among health workers as well as families and local workers. **Nutritional management** Infants younger than 6 months should neither interrupt breast-feeding nor introduce diluted or modified for- mula. Where there is not the possibility to breast-feed, routine dilution of milk and routine use of lactose-free milk formula are not usually necessary. Children should be re-fed early during the course of AGE.

	Regular oral feeding should be reintroduced no later than 4 to 6 hours after the onset of rehydration. Lactose-free formula is generally not necessary in AGE episodes. However, lactose-restricted diets may be considered in hospitalized children and in children with prolonged diarrhea (>7 days). Lactose-free formula should be recommended in children with chronic diar- rhea (>14 days). Elimination diet is usually not indicated for children with AGE and it may further impair the child's nutritional status. Zinc is recommended as an adjunct to oral rehydration therapy in children older than 6 months living in low- income countries or in settings with medium or high risk of zinc deficiency. Its efficacy is not supported by solid evidence in well-nourished children living in high- income countries. In infants younger than 6 months zinc is not effective regardless of the nutritional status. **Active treatment of diarrhea** Active treatment of diarrhea with the administration of probiotics and/or drugs may be considered where there is solid proof of efficacy in reducing the intensity and duration of symptoms. To maximize efficacy, active treatment should be administered early in the course of the disease. However, administration of any product should not replace oral rehydration therapy and should be always used as an adjunct to ORS treatment. Because investigation of active therapies is rapidly evolving, the choice of best treatment should be always made along recommendations of evidence-based guidelines and in compliance with well-done randomized controlled trials. Probiotics are effective in reducing the duration and intensity of symptoms of AGE. If available and in agreement with caregivers, selected probiotic strains (including Lactobacillus rhamnosus GG, Saccharomyces boulardii, and also L reuteri DSM 17938) can be considered in children with AGE, as an adjunct to ORS. Loperamide and other antimotility drugs are not recommended in the treatment of AGE. Metoclopramide, although effective, has significant side effects and is therefore not recommended for children with vomiting owing to AGE. The efficacy of domperidone is not supported by randomized controlled trials.

	Ondansetron administered either orally or intravenously is effective in reducing vomiting and may avoid hospital admission. A single dose at the dosages used in the available studies may be considered in young children presenting to an emergency department with vomiting to ensure oral rehydration and reduce hospital admis- sion. However, the use of ondansetron has been associated with QT prolongation and severe cardiac arrhythmias and the drug carries a warning label by both the Food and Drug Administration and the European Medicines Agency that should be taken into account by health care providers. Routine use of antibiotics is not recommended for the treatment of AGE. The use of antibiotics should be started immediately and may be considered in specific situations, including: 4. infants younger than 3 months 5. childrenwithunderlyingchronicconditions,including those with sickle cell anemia or immunodeficiency and those at risk for developing severe or extraintestinal dissemination 6. isolation of specific pathogens such as Shigella, enterotoxigenic (but not Shiga-like toxin-producing) Escherichia coli, V cholerae, Yersinia enterocolitica, and Entamoeba histolytica. 7. Campylobacter colitis can be treated with antibiotics, but treatment is effective only if administered within the first 2 days from the onset of symptoms.
Addition of a new section: AAFP; Acute Diarrhea in Adults **(2022)**[12]	Stool culture or multiplex polymerase chain reaction testing should be reserved for patients with evidence of invasive disease, immunocompromise, prolonged illness, or increased risk of involvement in an outbreak (Grade C) Rehydration is the first-line treatment for acute diarrhea, with oral rehydration being the preferred method for fluid replacement (Grade A) In combination, loperamide (Imodium) and simethicone may provide faster and more complete relief of acute watery diarrhea and abdominal discomfort than either medication alone (Grade B) When using antibiotics for travelers' diarrhea, adjunct loperamide shortens the duration of symptoms and increases the likelihood of a cure (Grade A) Empiric antibiotics can lessen the duration and severity of

	symptoms in moderate to severe cases of travelers' diarrhea (Grade A)

Appendix C. PubMed Search Methodology Terms

The following PubMed Search Methodology was opted:

Query	Filters	Search Details	Results
(Gastroenteritis[MeSH Terms]) OR (Gastroenteritides[Title/Abstract])	Guideline, in the last 5 years	("gastroenteritis"[MeSH Terms] OR "Gastroenteritides"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	107

Appendix D. Viral Gastroenteritis Treatment Algorithms

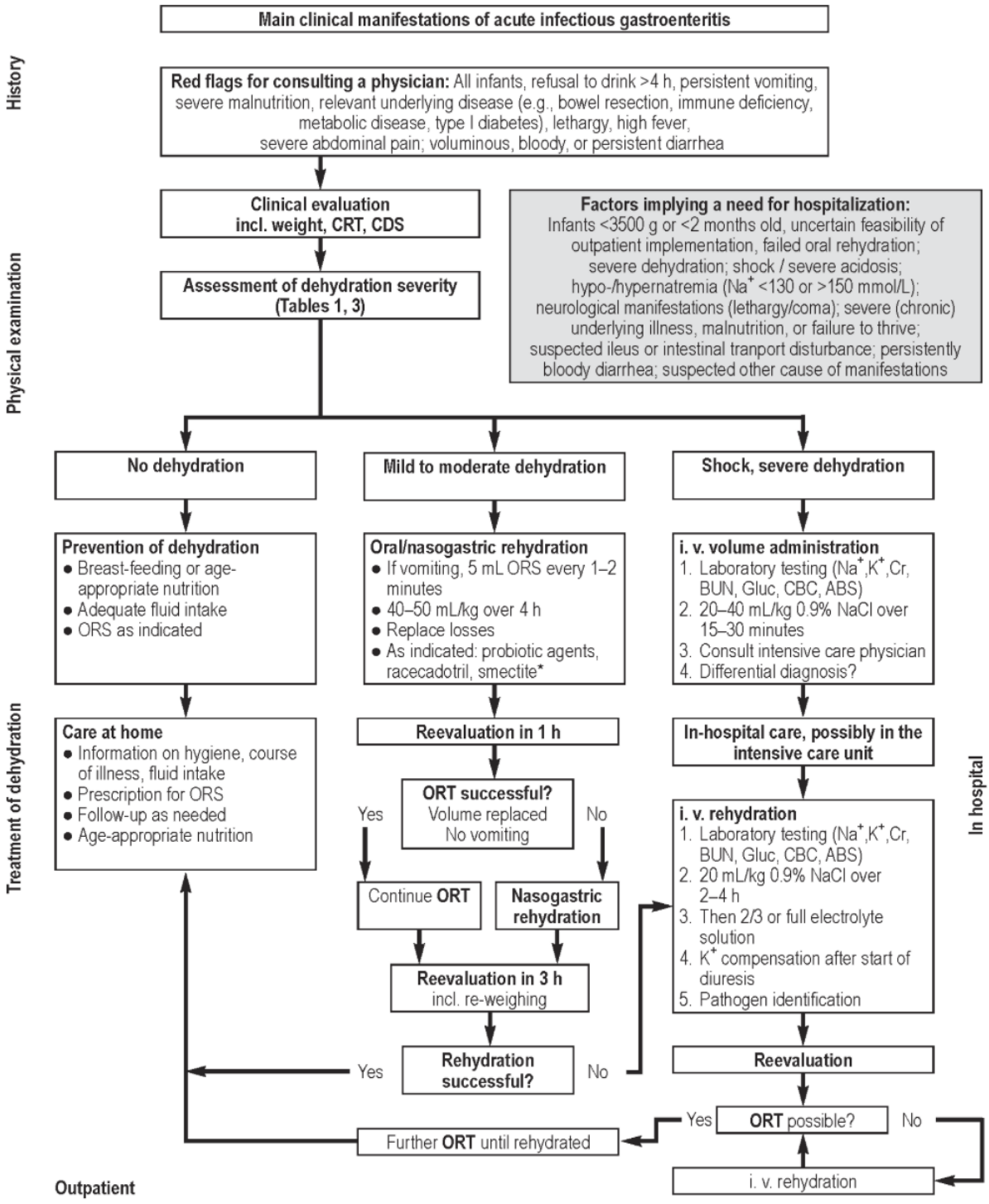

Figure 1. Treatment Algorithm for Viral Gastroenteritis in Infants and Children

Attention: the threshold values for percentage weight loss as an index of the degree of dehydration differ in infants and young children.

ABS: acid-base status; BUN: blood urea nitrogen; CBC: complete blood count, CDS: Clinical Dehydration Score; CRT: capillary refilling time; Cl: chloride: Cr: creatinine; i. v.; intravenous; K+: potassium; Na+: sodium; ORS: oral rehydration solution; ORT: oral rehydration therapy.

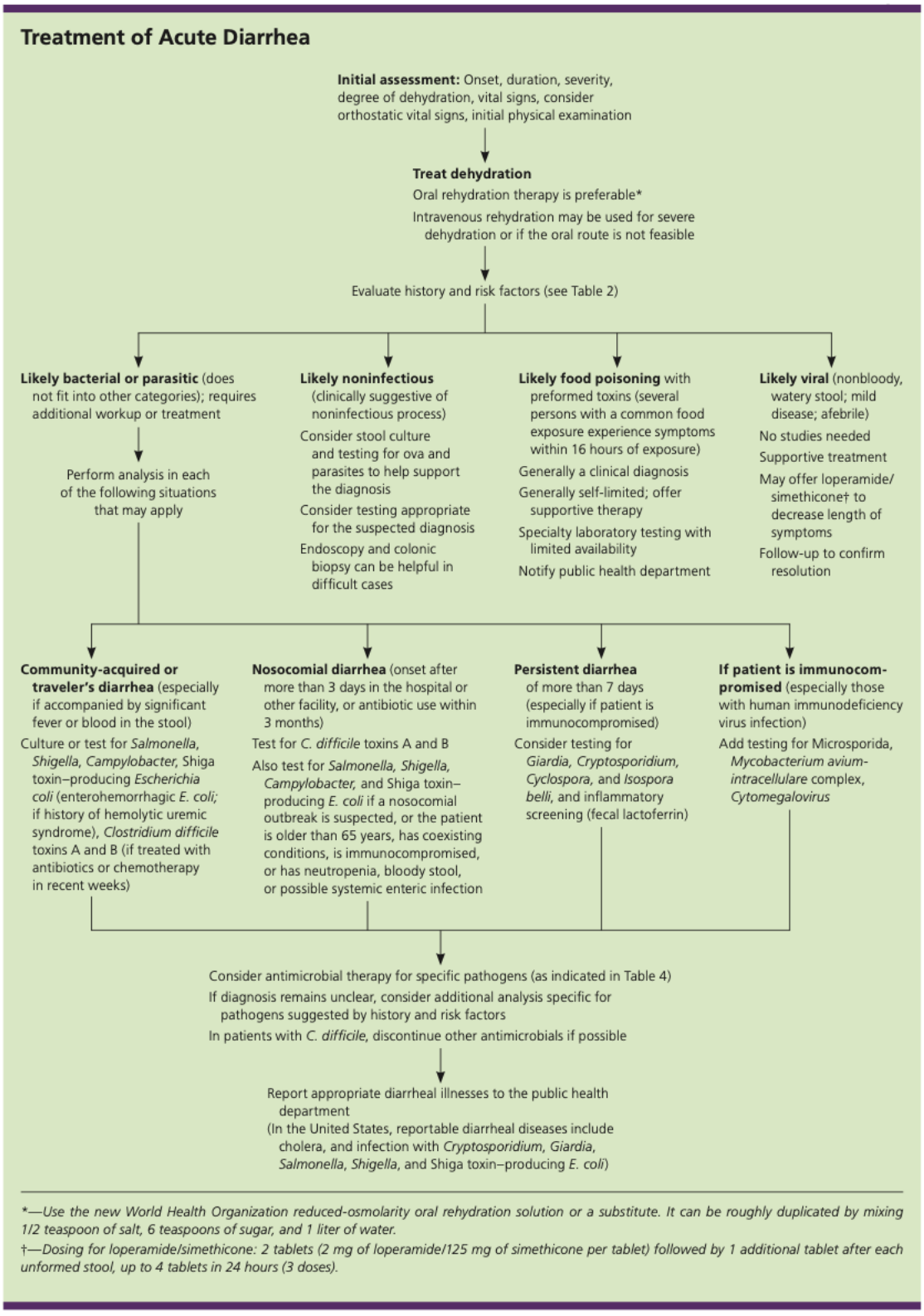

Figure 2. Treatment Algorithm for Viral Gastroenteritis in Adults