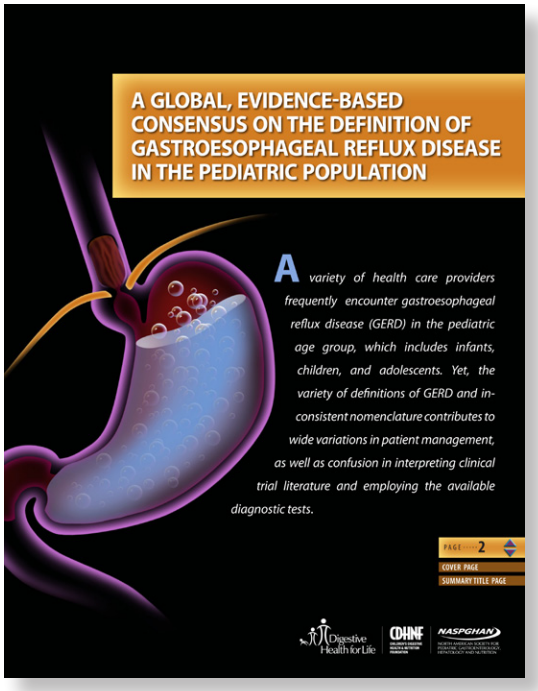
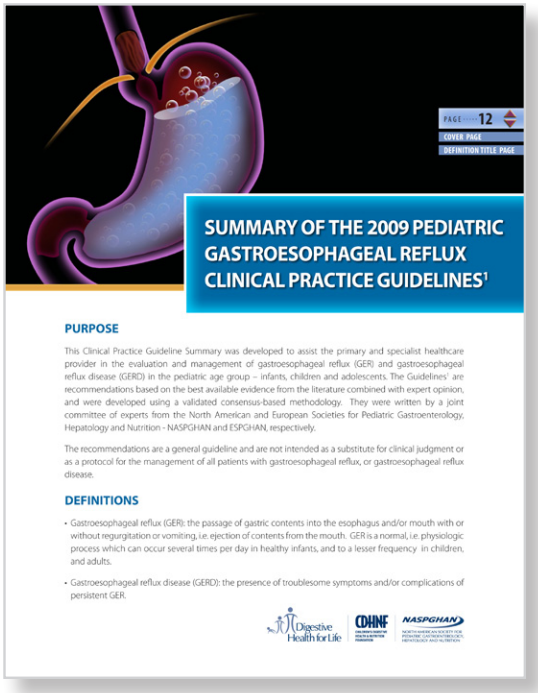
Gastroesophageal Reflux Disease in the Pediatric Population

A summary of two key 2009 publications which provide important guidance for the physician in regard to the diagnosis and management of gastroesophageal reflux disease in the pediatric population



A Global, Evidence-Based Consensus on the Definition of Gastroesophageal Reflux Disease in the Pediatric Population

Sherman P, Hassall E, Fagundes-Neto U, Gold BD, Kato S, Koletzko S, Orenstein S, Rudolph C, Vakil N, Vandeplas Y. Amer J Gastroenterol. 2009;104:1278-1295.



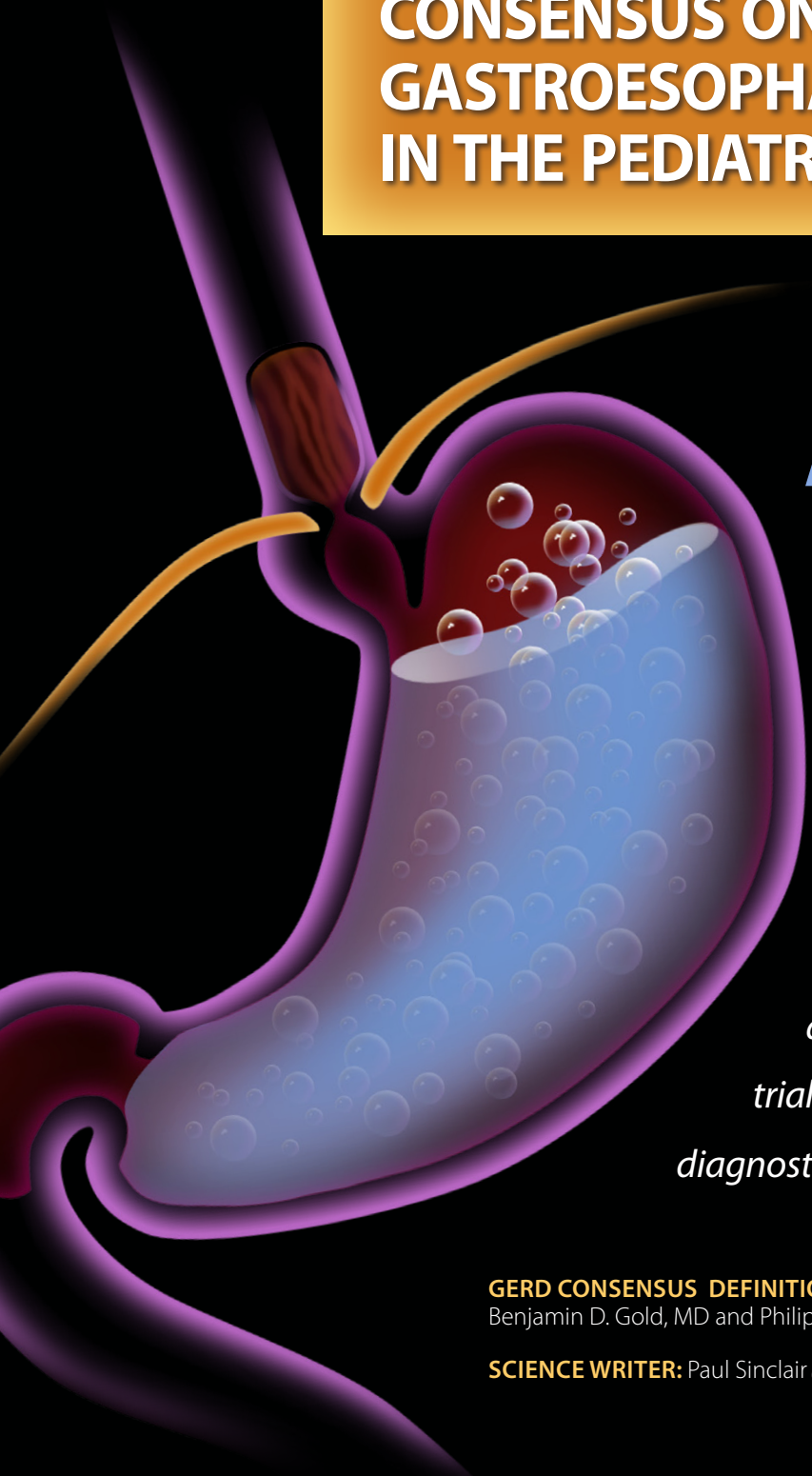
Summary of the 2009 Pediatric Gastroesophageal Reflux Clinical Practice Guidelines

Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition

Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L, Sondheimer J, Staiano A, Thomson M, Veereman-Wauters G, Wenzl TG. J Pediatr Gastroenterol Nutr. 2009;49:498-547.

CDHNF CHILDREN'S DIGESTIVE HEALTH & NUTRITION FOUNDATION | Digestive Health for Life | NASPGHAN NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

A GLOBAL, EVIDENCE-BASED CONSENSUS ON THE DEFINITION OF GASTROESOPHAGEAL REFLUX DISEASE IN THE PEDIATRIC POPULATION



A variety of health care providers frequently encounter gastroesophageal reflux disease (GERD) in the pediatric age group, which includes infants, children, and adolescents. Yet, the variety of definitions of GERD and inconsistent nomenclature contributes to wide variations in patient management, as well as confusion in interpreting clinical trial literature and employing the available diagnostic tests.

GERD CONSENSUS DEFINITION SUMMARY FACULTY:
Benjamin D. Gold, MD and Philip Sherman, MD

SCIENCE WRITER: Paul Sinclair *(INSINC Consulting Inc. Guelph, Ontario, Canada)*

PAGE ····· 2

COVER PAGE

SUMMARY TITLE PAGE

CDHNF CHILDREN'S DIGESTIVE HEALTH & NUTRITION FOUNDATION | Digestive Health for Life | NASPGHAN NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

This summary of the Evidence-Based Consensus on the Definition of Gastroesophageal Reflux Disease in the Pediatric Population – based on the Montreal Definition of GERD[1] (i.e., in adults) and the process used to develop it – was developed to provide pediatric health care providers, general pediatricians and subspecialists with a uniform definition of GERD that could be employed in these age groups. These consensus statements are intended to be used for the development of future clinical practice guidelines and as a basis for clinical trials. This document is different from the revised GERD clinical practice guidelines[2] which provide management recommendations.

GENERAL CONCEPTS

A patient-centered definition – based on symptoms becoming sufficiently troublesome so as to have a measurable impact on the quality of life of the patient – was used with certain caveats. These important caveats make the Global Consensus Definition quite distinct from the adult-based Montreal Definition of GERD.

Although the verbal child can communicate pain, descriptions of the intensity, location, and severity may be unreliable until at least eight years of age, and in some children even later. Younger children are generally more suggestible; so queries from parents or clinicians regarding a specific symptom may be biased toward affirmative responses. Thus, in younger patients, reliance on a parent or caregiver is generally necessary, although symptom reporting by these surrogates may decrease the validity of diagnosis. Validated symptom questionnaires related to specific age groups are needed for achieving reliability in the child at any age, as well as for diagnostic and evaluative validity related to symptom reporting in pediatrics.

Gastroesophageal reflux (GER) refers to the passage of gastric contents into the esophagus or oropharynx; with or without vomiting. GER can be a daily, normal physiological occurrence in infants, children and adolescents. Most episodes of GER in healthy individuals last <3 minutes, occur in the postprandial period, and cause few or no troublesome symptoms. Regurgitation or spitting up is the most obviously visible symptom to caregivers and pediatricians, particularly in the very young child, occurring daily in about 50% of infants <3 months of age. Regurgitation resolves spontaneously in most healthy infants by 12-14 months of age[3,4,5]. Gastroesophageal reflux disease (GERD) refers to the symptoms and complications that may develop secondary to persistent GER. Differentiating GER from GERD is critical for the clinician in order to avoid unnecessary diagnostic testing and exposure to medications.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

DEFINITIONS RELATED TO GERD IN PEDIATRICS

GERD:	Reflux of gastric contents causes troublesome symptoms and/or complications
Troublesome symptoms:	When GER symptoms have an adverse effect on the well-being of the pediatric patient
Troublesome dysphagia:	When older children and adolescents need to alter eating patterns or report food impaction
Regurgitation:	The passage of refluxed contents into the pharynx, mouth, or from the mouth
Heartburn:	In older children and adolescents, a burning sensation in the retrosternal area
Non-erosive reflux disease:	The presence of troublesome symptoms caused by the reflux of gastric contents and by the absence of mucosal breaks during endoscopy
Reflux esophagitis:	Endoscopically visible breaks of the distal esophageal mucosa
Reflux stricture:	A persistent luminal narrowing of the esophagus caused by GERD
Endoscopically Suspected Esophageal Metaplasia (ESEM):	Endoscopic findings consistent with Barrett's esophagus that await histological confirmation

SYMPTOMS

- **Symptoms of GERD Vary by Age**

  In infants, there is uncertainty as to whether regurgitation, food refusal, and crying represent acid reflux, presenting a problem in symptom-based diagnosis. For 1 to 11 year olds, there are relatively few data on presenting symptoms. Toddlers and young children (1–6 years) tend to present with food refusal, regurgitation, and abdominal pain. In contrast, the predominant symptoms in children 6–17 years are regurgitation or vomiting, cough and epigastric pain, or heartburn. The older the child, the more heartburn and regurgitation become predominant presenting symptoms, as in adults.

- **Pediatric population-based studies of reflux symptoms are insufficient and are a priority for further research.**

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

Troublesome Symptoms

To be defined as GERD, reflux symptoms must be troublesome to the infant, child, or adolescent, and not simply be troublesome to the caregiver. In addition, patients may be asymptomatic or unable to report "troublesome" symptoms (e.g., infants or neurologically impaired children), but still have complications of reflux and thereby meet the criteria for the definition of GERD.

- **Otherwise healthy newborns (age: 1 – 30 days) and infants (age: >30 days to < 1 year) with reflux symptoms that are not troublesome and are without complications should not be diagnosed with GERD.**

- Up to 70 % of completely healthy newborns and infants have regurgitation that is physiologic, resolving without intervention in 95 % of the individuals by 12–14 months of age. Crying is also common in infants; the issue of unexplained crying is complicated and must also incorporate patterns and characteristics of crying and parental responses to crying. Consequently, in infants, normal regurgitation and normal crying, or abnormal crying due to a cause other than GERD, may be mistaken for GERD.

- **Reflux symptoms that are not troublesome**
  - **in toddlers and children (age: 1–10 years), or**
  - **in adolescents (age: 11–17 years)**

  should not be diagnosed as GERD.

- **In clinical practice, adolescents are generally able to describe specific GERD symptoms and to determine whether those symptoms are troublesome.**

Heartburn

- **GER (i.e. reflux) in older children and adolescents is the most common cause of heartburn.**

- **Heartburn in older children and adolescents can have a number of non-reflux-related causes.**

Regurgitation vs. Rumination and Vomiting

- **Regurgitation is a characteristic symptom of reflux in infants, but is neither necessary nor sufficient for a diagnosis of GERD, because it is not sensitive or specific.**

  The specificity of regurgitation for diagnosing GERD is hampered by the frequency of its occurrence in normal infants, and by difficulties in distinguishing it from vomiting as well as a myriad of conditions that cause vomiting in infants.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

- **When assessing GERD, rumination should be distinguished from regurgitation.**

  Rumination refers to the effortless regurgitation of recently ingested food into the mouth with subsequent mastication and re-swallowing of food. Rumination is common in infants and children with neurological impairment, but it can also occur in subjects without obvious neurologic deficits. Rumination is increasingly recognized among older children, especially adolescent females, and is considered by some to lie within the spectrum of eating disorders.

- **Bilious vomiting should not be diagnosed as GERD**

  Bilious vomiting is an alarm signal that warrants further investigations to rule out anatomic abnormalities, such as intestinal malrotation, or acute illnesses causing intestinal obstruction.

"Typical Reflux Syndrome"

- **The Typical Reflux Syndrome is characterized by heartburn with or without regurgitation.**
- **"Typical Reflux Syndrome" cannot be diagnosed in infants and children who lack the cognitive ability to reliably report symptoms.**
- **Heartburn and regurgitation in older children and adolescents, with cognitive development sufficient to reliably report symptoms, are characteristic.**
- **In neurologically intact adolescents, the Typical Reflux Syndrome can be diagnosed on the basis of the characteristic symptoms, without additional diagnostic testing.**

Other Symptoms

- **GERD may be associated with sleep disturbances in newborns and infants, toddlers and children, and adolescents.**

  Although GERD may be associated with sleep disturbance, a cause-and-effect relationship and the direction of any causality remain to be proved.

- **Symptoms of GERD, particularly in infants, may be indistinguishable from those of food allergy.**

  In infants, GERD and milk protein (cow or soy) allergy may both manifest as regurgitation or as vomiting; crying, fussing, or irritability related to food intake; or as failure to thrive. Distinguishing the two on clinical presentations alone is difficult, thus, instituting a protein hydrolysate diet may resolve symptoms that are suggestive of GERD.

- **Epigastric pain in older children and adolescents can be a major symptom of GERD.**
- **Physical exercise in toddlers and children, and in adolescents, may induce troublesome symptoms of GERD in individuals who have no or minimal symptoms at other times (exercise-induced reflux).**

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

Exercise-induced GERD is well recognized in adults, and may be related to strain-induced reflux that is caused by increases in intra-abdominal pressure. Evidence for the existence of exercise-induced GERD in children is sparse and primarily anecdotal.

Conditions predisposing pediatric patients to severe, chronic GERD

- Neurologic impairment *(cerebral palsy, genetic disorders)*
- Congenital esophageal abnormalities (e.g., esophageal atresia, congenital diaphragmatic hernia)
- Cystic fibrosis
- Hiatal hernia
- Obesity
- Family history of severe GERD or Barrett's esophagus or esophageal adenocarcinoma

FIGURE 1: *Conditions predisposing to severe, chronic GERD. Adapted from Sherman, et al*[1].

SYNDROMES WITH ESOPHAGEAL INJURY

- **In pediatric patients, esophageal complications of GERD are reflux esophagitis, hemorrhage, stricture, Barrett's esophagus, and, rarely, adenocarcinoma.**

  Erosive esophagitis is more prevalent and severe in pediatric-age patients with underlying GERD-promoting disorders, such as neurologic impairment or esophageal atresia. In addition, stricture, Barrett's esophagus, and adenocarcinoma are also more common in this group of patients with GERD-promoting disorders.

- **Insufficient data exist for recommending histology as a tool to diagnose or to exclude GERD in children.**

- **A primary role for esophageal histology is to rule out other conditions in the differential diagnosis.**

  The main role for esophageal histology in clinical practice is to either diagnose or rule out other causes of esophagitis that have specific histologic findings, including: eosinophilic esophagitis, Barrett's esophagus, Crohn's disease, infection, and graft-versus-host disease.

- **When reflux-related erosions are present during endoscopy, the grade should be described according to one of the recognized classifications of erosive esophagitis.**

  The presence and severity of reflux esophagitis determined at diagnostic upper endoscopy supports clinical management decision-making and assessment of treatment outcomes. The endoscopic classification of Hetzel and Dent and the Los Angeles classification have been the commonly used ones in pediatric studies.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

- **In otherwise healthy pediatric patients, reflux esophagitis may not be chronic or recurrent after treatment.**

- **Reflux esophagitis in pediatric patients with chronic neurologic impairment, repaired esophageal atresia, hiatal hernia, or chronic respiratory diseases is usually chronic and recurrent.**

- **The characteristic symptom of a stricture in pediatric patients is persistent troublesome dysphagia.**

- **Dysphagia in older children and adolescents is a perceived impairment of the passage of food from the mouth into the stomach.**

  In a minority of pediatric patients, GERD leads to the narrowing of the esophageal lumen causing persistent dysphagia. Persistent, progressive, or troublesome dysphagia is a warning symptom for esophageal stricture warranting additional investigation. Endoscopy with esophageal biopsies is indicated to distinguish it from the other causes of esophageal narrowing, particularly eosinophilic esophagitis which also presents with dysphagia.

- **In the pediatric age group, Barrett's esophagus mainly occurs in individuals with hiatal hernia, and in those with certain underlying disorders that predispose to severe GERD.**

- **Documentation of esophogastric landmarks together with multiple biopsies are necessary to characterize Endoscopically Suspected Esophageal Metaplasia (ESEM).**

- **When biopsies from Endoscopically Suspected Esophageal Metaplasia (ESEM) show columnar epithelium, it should be called Barrett's esophagus and the presence or absence of the intestinal metaplasia specified.**

  The term "endoscopically suspected esophageal metaplasia" acknowledges that the endoscopic appearance may not be diagnostic and requires histologic confirmation. Even a rigorous biopsy protocol for the detection of intestinal-type metaplasia has imperfect sensitivity, and additionally, there is now some doubt whether only mucosa containing goblet cell metaplasia is premaligant.

EXTRAESOPHAGEAL SYNDROMES

- **Sandifer's syndrome (torticollis) is a specific manifestation of GERD in pediatric patients.**

- **There is insufficient evidence that GERD causes or exacerbates sinusitis, pulmonary fibrosis, pharyngitis, and serous otitis media in the pediatric population.**

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

- **Chronic cough, chronic laryngitis, hoarseness, and asthma may be associated with GERD.**
- **In the absence of heartburn or regurgitation, unexplained asthma is less likely to be related to GERD.**
- **Chronic cough, chronic laryngitis, hoarseness, and asthma are multifactorial disease processes and acid reflux can be an aggravating cofactor.**
- **GERD may cause dental erosions in pediatric patients.**
- **At present, no single diagnostic test can prove or exclude extraesophageal presentations of GERD in pediatrics.**

  Clinicians employ laryngoscopy, bronchoscopy and alveolar lavage, endoscopy, esophageal and laryngeal biopsies, pH monitoring in the hypopharynx, and multi-channel intraluminal impedance monitoring to diagnose GERD in pediatric patients presenting with extraesophageal symptoms. However, none of these tools independently establishes the diagnosis of GERD with extraesophageal symptoms.

Neonates and Infants

- **There is an association between GERD and bronchopulmonary dysplasia in neonates and infants, but the cause-and-effect relationship is uncertain.**

  As most studies have been cross sectional or case – control in design, it remains to be determined whether GERD is, in fact, a causal factor predisposing infants to the development of bronchopulmonary dysplasia (BPD), propagates the condition, or BPD in fact causes GERD. For this reason, the above statement is located under "possible associations" in the Figure 2.

- **In premature infants, a relationship between GER (i.e. reflux) and pathologic apnea and/or bradycardia has not been established.**

  Despite a lack of convincing evidence, if pathological apnea occurs in the face of pre-existing reflux, then the following two statements are the most common features:

- **Although reflux causes physiologic apnea, it causes pathologic apneic episodes in only a very small number of newborns and infants.**
- **When reflux causes pathological apnea, the infant is more likely to be awake and the apnea is more likely to be obstructive in nature.**
- **A diagnosis of an acute life-threatening event (ALTE) warrants consideration of causes other than GER (i.e. reflux).**

  Reflux of gastric acid seems to be related to ALTEs (episodes of combinations of apnea, color change, change in muscle tone, choking, and gagging) in < 5 % of infants with ALTE.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

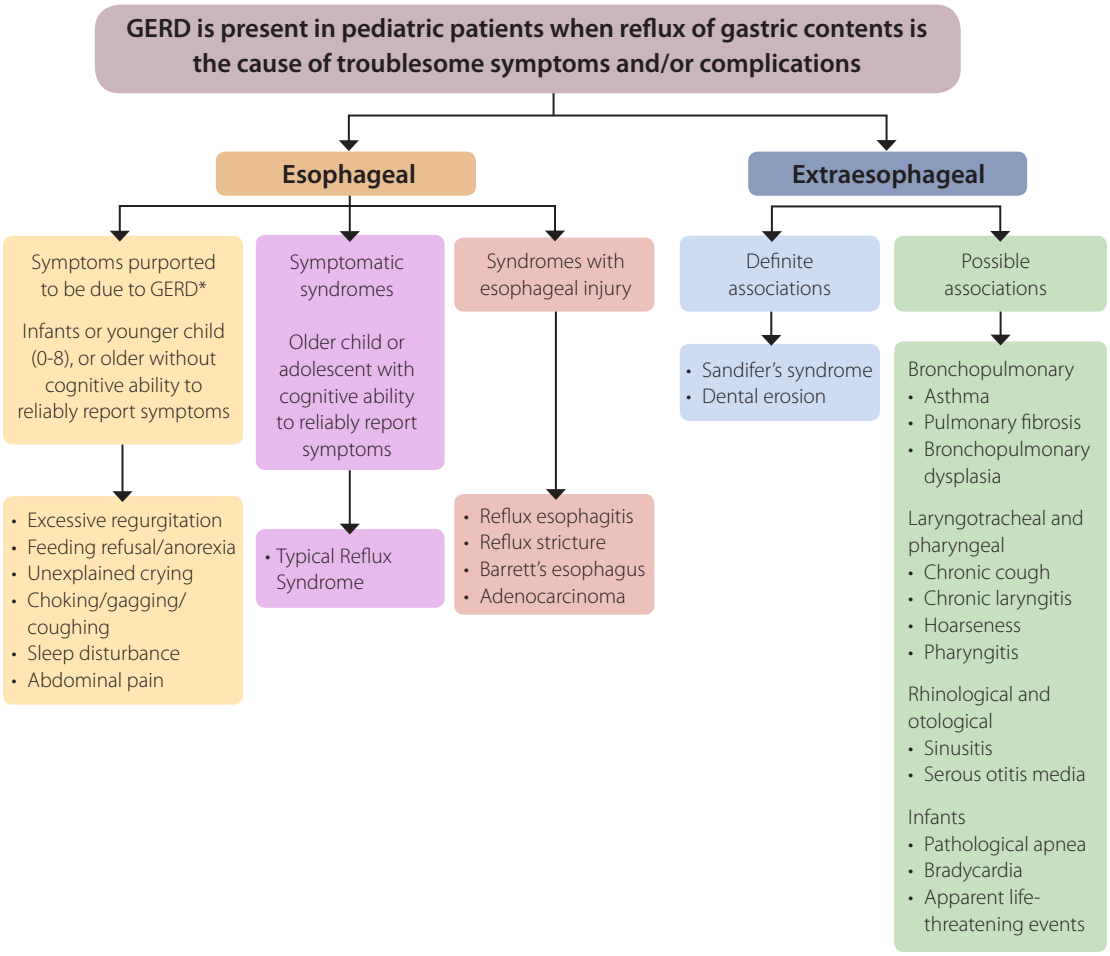


FIGURE 2: *Global definition of GERD in the pediatric population*[1].

1 Sherman PM, Hassall E, Fagundes-Neto U, Gold BD, Kato S, Koletzko S et al. A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. Am J Gastroenterol 2009;104:1278-95.

2 Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2009;49:498-547.

3 Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during infancy. A pediatric practice-based survey. Pediatric Practice Research Group. Arch Pediatr Adolesc Med 1997;151(6): 569-572.

4 Martin AJ, Pratt N, Kennedy JD, Ryan P, Ruffin RE, Miles H, et al. Natural history and familial relationships of infant spilling to 9 years of age. Pediatrics 2002;109(6): 1061-1067.

5 Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, et al. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr 2001;32(Suppl 2): S1-31.

Support: Support for this Summary of the Global Definition was provided by AstraZeneca L.P. and Takeda North America Pharmaceuticals Inc. This work was sponsored by CDHNF.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

Newborn *(1-30 days) /* **Infant** *(>30 days-1 yr)*	**Toddlers/Children** *(1-10 yr)*	**Adolescents** *(11-17 yr)*
Reflux symptoms that are not troublesome and are without complications should not be diagnosed as GERD	Reflux symptoms that are not troublesome should not be diagnosed as GERD	Reflux symptoms that are not troublesome should not be diagnosed as GERD
Regurgitation is characteristic of reflux but not necessary/sufficient to diagnose GERD	Heartburn is defined as a burning sensation in the retrosternal area (older children)	Heartburn is defined as a burning sensation in the retrosternal area
GERD symptoms may be indistinguishable from those of food allergy		Generally able to describe specific GERD symptoms and to determine whether those symptoms are troublesome
Typical Reflux Syndrome cannot be diagnosed if the cognitive ability to reliably report symptoms is lacking	Typical Reflux Syndrome cannot be diagnosed if the cognitive ability to reliably report symptoms is lacking	Typical Reflux Syndrome can be diagnosed on the basis of the characteristic symptoms, without additional diagnostic testing (neurologically intact adolescents)
An association between GERD and bronchopulmonary dysplasia exists but cause-and-effect is uncertain	Heartburn and regurgitation are characteristic if cognitive development is sufficient to reliably report symptoms	Heartburn and regurgitation are characteristic if cognitive development is sufficient to reliably report symptoms
GERD may be associated with sleep disturbances	GERD may be associated with sleep disturbances	GERD may be associated with sleep disturbances
In premature infants, a relationship between GER (i.e. reflux) and pathologic apnea and/or bradycardia has not been established	GER (i.e. reflux) in older children is the most common cause of heartburn	GER (i.e. reflux) is the most common cause of heartburn
Although reflux causes physiologic apnea, it causes pathologic apneic episodes in only a very small number	Heartburn can have a number of non-reflux-related causes (older children)	Heartburn can have a number of non-reflux-related causes
When reflux causes pathological apnea, the infant is more likely to be awake and the apnea is more likely to be obstructive	Epigastric pain can be a major symptom of GERD (older children)	Epigastric pain can be a major symptom of GERD
	Physical exercise may induce troublesome symptoms of GERD in individuals who have no or minimal symptoms at other times	Physical exercise may induce troublesome symptoms of GERD in individuals who have no or minimal symptoms at other times
	Dysphagia is a perceived impairment of the passage of food from the mouth into the stomach (older children)	Dysphagia is a perceived impairment of the passage of food from the mouth into the stomach.
	Troublesome dysphagia is present when older children need to alter eating patterns or report food impaction	Troublesome dysphagia is present when adolescents need to alter eating patterns or report food impaction

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

SUMMARY OF THE 2009 PEDIATRIC GASTROESOPHAGEAL REFLUX CLINICAL PRACTICE GUIDELINES[1]

GERD GUIDELINE SUMMARY FACULTY: Benjamin D. Gold, MD, Philip Sherman, MD and Eric Hassall, MD
SCIENCE WRITER: Paul Sinclair *(INSINC Consulting Inc. Guelph, Ontario, Canada)*

PURPOSE

This Clinical Practice Guideline Summary was developed to assist the primary and specialist healthcare provider in the evaluation and management of gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD) in the pediatric age group – infants, children and adolescents. The Guidelines[1] are recommendations based on the best available evidence from the literature combined with expert opinion, and were developed using a validated consensus-based methodology. They were written by a joint committee of experts from the North American and European Societies for Pediatric Gastroenterology, Hepatology and Nutrition - NASPGHAN and ESPGHAN, respectively.

The recommendations are a general guideline and are not intended as a substitute for clinical judgment or as a protocol for the management of all patients with gastroesophageal reflux, or gastroesophageal reflux disease.

DEFINITIONS

- Gastroesophageal reflux (GER): the passage of gastric contents into the esophagus with or without regurgitation or vomiting, i.e. ejection of contents from the mouth. GER is a normal, i.e. physiologic process which can occur several times per day in healthy infants, and to a lesser frequency in children, and adults.

- Gastroesophageal reflux disease (GERD): the presence of troublesome symptoms and/or complications of persistent GER.

CDHNF CHILDREN'S DIGESTIVE HEALTH & NUTRITION FOUNDATION | Digestive Health for Life | NASPGHAN NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

CLINICAL MANIFESTATIONS OF GERD IN CHILDREN

SYMPTOMS
• Recurrent regurgitation with/without vomiting
• Weight loss or poor weight gain
• Irritability in infants
• Ruminative behavior
• Heartburn or chest pain
• Hematemesis
• Dysphagia, odynophagia
• Wheezing
• Stridor
• Feeding refusal
• Cough
• Hoarseness

SIGNS
• Erosive esophagitis
• Esophageal stricture
• Barrett's esophagus
• Laryngeal/pharyngeal inflammation
• Recurrent pneumonia
• Anemia
• Dental erosions
• Wheezing
• Stridor
• Feeding refusal
• Dystonic neck posturing , back arching (Sandifer's syndrome)
• Apnea spells: rarely due to GERD
• Apparent life threatening events (ALTE): rarely due to GERD

WARNING SIGNALS IN INFANTS AND CHILDREN:

Suggesting DISORDERS OR CONDITIONS other than GERD

- Bilious vomiting
- Gastrointestinal (GI) bleeding
  - Hematemesis
  - Hematochezia
- Persistently forceful vomiting
- New onset of vomiting after age 6 months
- Failure to thrive
- Diarrhea
- Constipation
- Fever
- Lethargy
- Hepatosplenomegaly
- Bulging fontanelle
- Macro/microcephaly
- Seizures
- Abdominal tenderness or distension
- Documented/suspected genetic/metabolic syndrome
- Abdominal tenderness or distension

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

DIAGNOSTIC APPROACHES

History and Physical Examination

- In infants and toddlers, no symptom or group of symptoms can reliably diagnose GERD or predict treatment response
- In older children and adolescents a history and physical examination are often sufficient to reliably diagnose GERD and initiate management

Esophageal pH Monitoring

- A valid and reliable measure of esophageal acid exposure only
- The severity of pathologic acid reflux does not correlate consistently with symptom severity or complications
- Useful for evaluating the efficacy of anti-secretory therapy
- May be useful to correlate symptoms (e.g. cough, chest pain) with acid reflux episodes, and to identify those patients with wheezing or respiratory symptoms in whom reflux is a causative or aggravating factor

Combined Multiple Intraluminal Impedance (MII) and pH Monitoring

- MII measures the movement of fluids, solids and air to detect acid, weakly acid and non-acid reflux events
- MII and pH monitoring is superior to pH monitoring alone for evaluation of reflux-related symptom association

Endoscopy and Biopsy

- Reflux-induced esophageal damage is defined endoscopically as visible breaks (erosions) of the distal esophageal mucosa
- Esophageal biopsy cannot determine whether esophageal inflammation, if present, is due to reflux
- Absence of histological changes does not rule out reflux disease
- When endoscopy is performed, esophageal biopsies are recommended to diagnose Barrett's esophagus and causes of esophagitis other than reflux (e.g. eosinophilic esophagitis)

Barium Contrast Radiography (Upper GI Series)

- Not useful for the diagnosis of GERD
- Useful for the diagnosis of upper gastrointestinal tract anatomic abnormalities such as esophageal stricture, hiatal hernia, intestinal malrotation, achalasia, tracheoesophageal fistula, pyloric stenosis

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

Nuclear Scintigraphy

- May have a role in patients with chronic or refractory respiratory symptoms, to diagnose pulmonary aspiration of refluxed gastric contents
- Not routinely recommended in patients with other potentially reflux-related symptoms

Tests on Ear, Lung and Esophageal Fluids

- Pepsin in bronchoalveolar lavage fluid is an indicator of reflux-related aspiration, but its clinical utility remains to be established
- Lipid-laden-macrophages lack specificity and sensitivity for diagnosing reflux-related aspiration

Other Tests

- Esophageal manometry is not a diagnostic test for GERD but may identify motor disorders (e.g. achalasia) that may present with symptoms similar to those of GERD
- Esophageal and gastric ultrasonography are not recommended for the routine evaluation of GERD

Empiric Trial of Acid Suppression as a Diagnostic Test

- In the older child or adolescent with symptoms suggesting GERD, an empiric trial with a proton pump inhibitor (PPI) is justified for up to 4 weeks. Improvement following treatment does not confirm a diagnosis of GERD because symptoms may improve spontaneously or respond by a placebo effect
- There is no evidence to support an empiric trial of pharmacologic treatment in infants and young children as a diagnostic test of GERD

TREATMENT

Diet

- There is evidence to support a 2 to 4 week trial of an extensively hydrolyzed protein formula in formula-fed infants with symptoms suggestive of reflux disease
- Thickening of formula results in decreased visible reflux (regurgitation)
- In adults, obesity and late night eating are associated with symptoms of GERD

Positioning

- In infants (birth to 12 months of age), the risk of sudden infant death syndrome (SIDS) outweighs the potential benefits of prone sleeping. Therefore, supine positioning during sleep is generally recommended, although it may promote regurgitation.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

- Prone positioning may be beneficial in children over 1 year of age with GER or GERD whose risk of SIDS is negligible
- In adolescents with GERD, left side sleeping positioning and elevation of the head of the bed may decrease symptoms of GERD

Acid-Suppressant Therapy

- Histamine2-receptor antagonists (H_2RAs) produce relief of symptoms and mucosal healing
- PPIs are superior to H_2RAs in relieving symptoms and healing esophagitis
- When acid suppression is required, the smallest effective dose should be used
- Most patients require only once-daily PPI; routine use of twice-daily doses is not indicated
- No PPI is approved for use in infants younger than 1 year of age

Prokinetic and Other Therapy

- The potential benefits (i.e. reduction of reflux-related symptoms, in particular, regurgitation or vomiting) of currently available prokinetic agents are outweighed by their potential side effects
- There is insufficient evidence to support the routine use of metoclopramide, erythromycin, bethanechol or domperidone for GERD
- Since more effective alternatives (H_2RAs and PPIs) are available, chronic therapy with buffering agents, alginates and sucralfate is not recommended for GERD

Surgery

- Should be considered only in children with an established diagnosis of GERD and failure of optimized medical therapy; or long-term dependence on medical therapy where compliance or patient preference preclude ongoing use; or life-threatening complications of GERD

EVALUATION AND MANAGEMENT OF INFANTS AND CHILDREN WITH SUSPECTED GERD

1. The Infant with Uncomplicated Recurrent Regurgitation ("Happy Spitter")

- **Diagnosis**
  - A history and physical examination with absence of alarm signs or symptoms is generally sufficient to establish a clinical diagnosis of GER, i.e. physiologic reflux
  - Upper GI series or other diagnostic tests are not required unless diagnoses other than GERD are suspected, e.g. gastrointestinal obstruction

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

• **Management**
  - Parental education, reassurance and anticipatory guidance
  - Thickened formula (or anti-regurgitation formula)
  - If symptoms worsen or do not resolve by 12 to 18 months of age or alarm signs or symptoms develop, referral to a pediatric gastroenterologist is recommended

2. The Infant with Recurrent Regurgitation and Poor Weight Gain

• **Diagnosis**
  - If caloric intake is adequate, initial evaluation should include:
    - Diet history
    - Urinalysis
    - Complete blood count
    - Serum electrolytes
    - Blood urea nitrogen
    - Serum creatinine
    - Celiac screening
    - Upper GI series

• **Management**
  - A 2-week trial of extensively hydrolyzed/amino acid formula, thickened formula, or increased caloric density
  - If dietary management fails and/or if the investigations reveal no abnormalities, referral to a pediatric gastroenterologist is recommended

3. The Infant with Unexplained Crying and/or Distressed Behavior

  - Reflux is an uncommon cause of irritability or unexplained crying in otherwise healthy infants
  - There is no evidence to support the empiric use of acid suppression in such infants

4. The Child Over 18 Months with Chronic Regurgitation or Vomiting

• **Diagnosis**
  - While physiologic regurgitation and episodic vomiting are frequent in infants they are less common in children greater than 18 months of age
  - Although these symptoms are not unique to GERD, evaluation to diagnose possible GERD and to rule out alternative diagnoses is recommended
  - Testing may include upper gastrointestinal endoscopy, and/or esophageal pH/MII and/or barium upper GI series

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

5. *Heartburn in Older Children or Adolescents*

- **Management**
  - Lifestyle changes with a 4-week PPI trial are recommended
  - If symptoms resolve, continue PPI for 3 months
  - Heartburn that persists on PPI therapy or recurs after treatment should be investigated by a pediatric gastroenterologist

6. *Reflux Esophagitis*

- **Management**
  - Initial treatment consists of lifestyle changes and PPI therapy for 3 months
  - In most cases, efficacy of therapy can be monitored by the degree of symptom relief
  - Not all reflux esophagitis is chronic or relapsing, therefore trials of tapering the dose and then withdrawal of PPI therapy should be performed at intervals

7. *Barrett's Esophagus (BE)*

- **Diagnosis**
  - Acquisition of multiple biopsies documented in relation to endoscopically-identified esophagogastric landmarks is required to confirm or rule out the diagnosis of BE and dysplasia
  - Intestinal metaplasia is not a sine qua non for the diagnosis of BE. The new terminology is; BE with or without intestinal metaplasia

- **Management**
  - Aggressive acid suppression is advised for most cases
  - Dysplasia is managed according to adult guidelines

8. *Food Refusal, Dysphagia and Odynophagia*

- **Diagnosis and Management**
  - In the infant with feeding refusal, acid suppression without prior diagnostic evaluation is not recommended
  - In the child with dysphagia or odynophagia, a barium esophagram is recommended, generally followed by an upper endoscopy
  - Acid suppression without prior diagnostic evaluation is not recommended

9. *The infant with apnea or apparent life threatening event (ALTE)*

- **Diagnosis**
  - In the great majority of cases of pathologic apnea or ALTE, reflux is not the cause, although a clear temporal relationship exists in the occasional case
  - If this relationship is suspected or if symptoms recur, impedance pH recording in combination with polysomnographic recording may aid in establishing cause and effect

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

10. Asthma

- **Management**
  - Patients with asthma and heartburn should be treated for the heartburn
  - Despite a high frequency of reflux events in asthmatic patients, only a select group with nocturnal asthma symptoms, or with steroid- dependent, difficult to control asthma will benefit from long-term medical anti-reflux therapy or surgery

11. Recurrent Pneumonia

- Recurrent pneumonia and interstitial lung disease may be complications of reflux, due to aspiration of gastric contents
- No test can determine whether reflux is causing recurrent pneumonia
- Diagnostic evaluation may include:
  - A trial of nasogastric feeding to exclude aspiration during swallowing
  - A trial of nasojejunal therapy to determine if surgical antireflux therapy may be beneficial

12. Upper Airway Symptoms

- Chronic hoarseness, chronic cough, sinusitis, chronic otitis media, erythema and cobblestone appearance of the larynx have not been proved to be associated as there is insufficient evidence demonstrating causality from persistent reflux

13. Dental Erosions

- An association between GERD and dental erosions is well established; young children and children with neurologic impairment appear to be at greatest risk

14. Sandifer's Syndrome

- A spasmodic torsional dystonia with arching of the back and opisthotonic posturing, mainly involving the neck
- An uncommon but specific manifestation of GERD that resolves with antireflux treatment

GROUPS AT HIGH RISK FOR GERD

Certain conditions predispose to severe, chronic GERD. These conditions include neurologic impairment, obesity, repaired esophageal atresia or other congenital esophageal disease, cystic fibrosis, hiatal hernia, repaired achalasia, lung transplantation, and a family history of GERD, BE, or esophageal adenocarcinoma.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

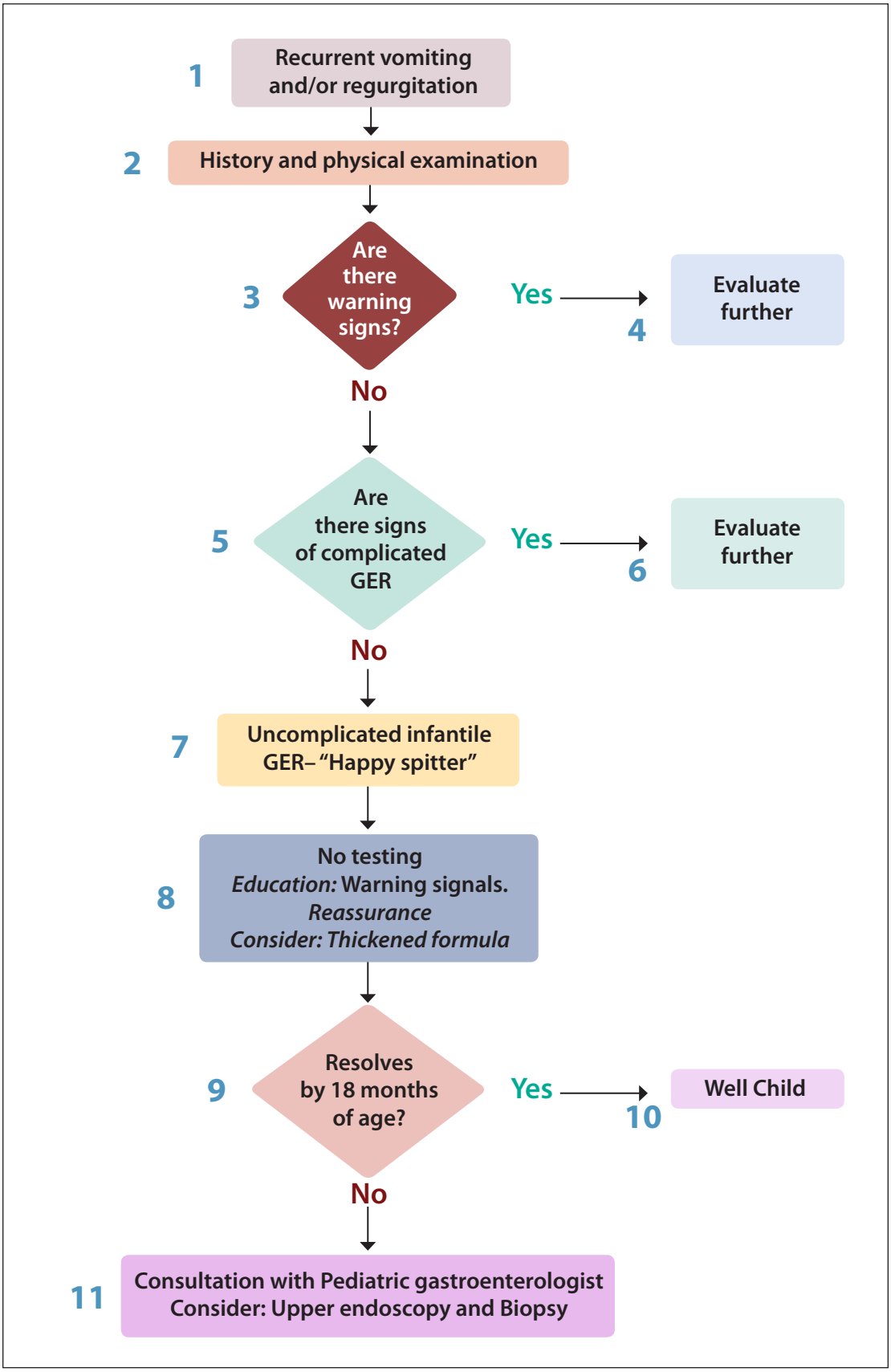


FIGURE 1: *Approach to the Infant with Uncomplicated Recurrent Regurgitation (Happy Spitter)*

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

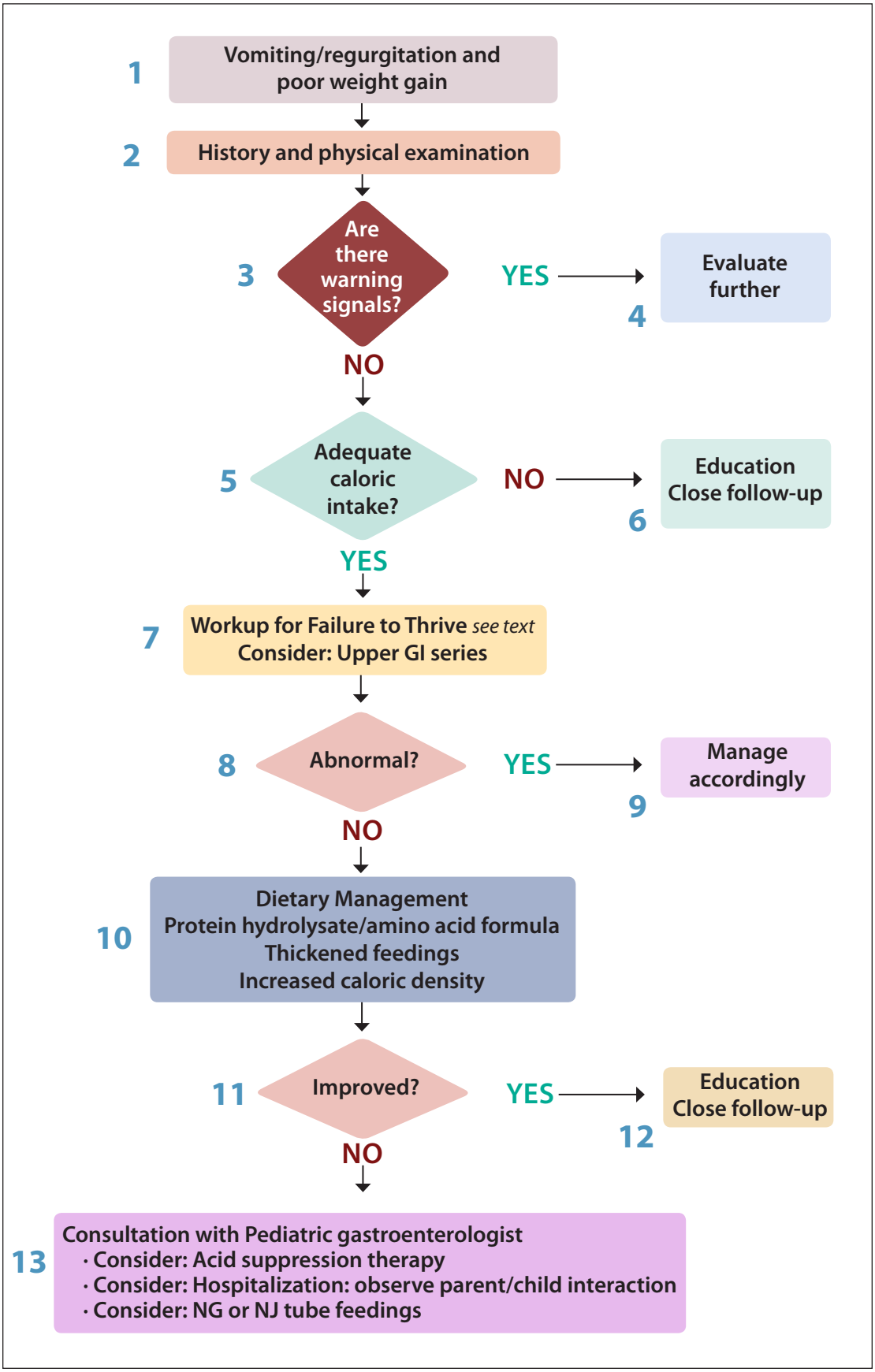


FIGURE 2: *Approach to the Infant with Recurrent Regurgitation and Poor Weight Gain*

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

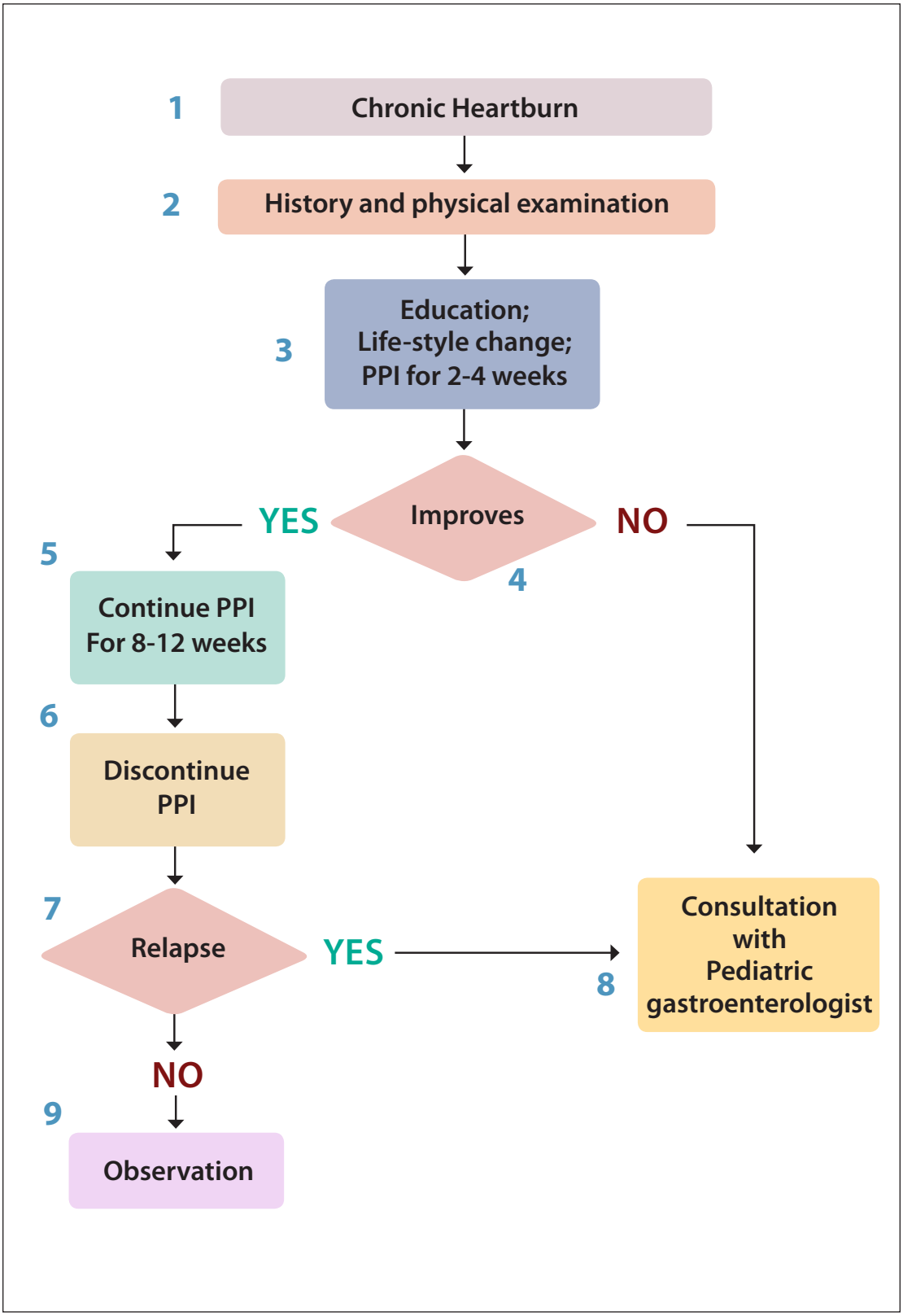


FIGURE 3: *Approach to the Older Child or Adolescent with Heartburn*

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

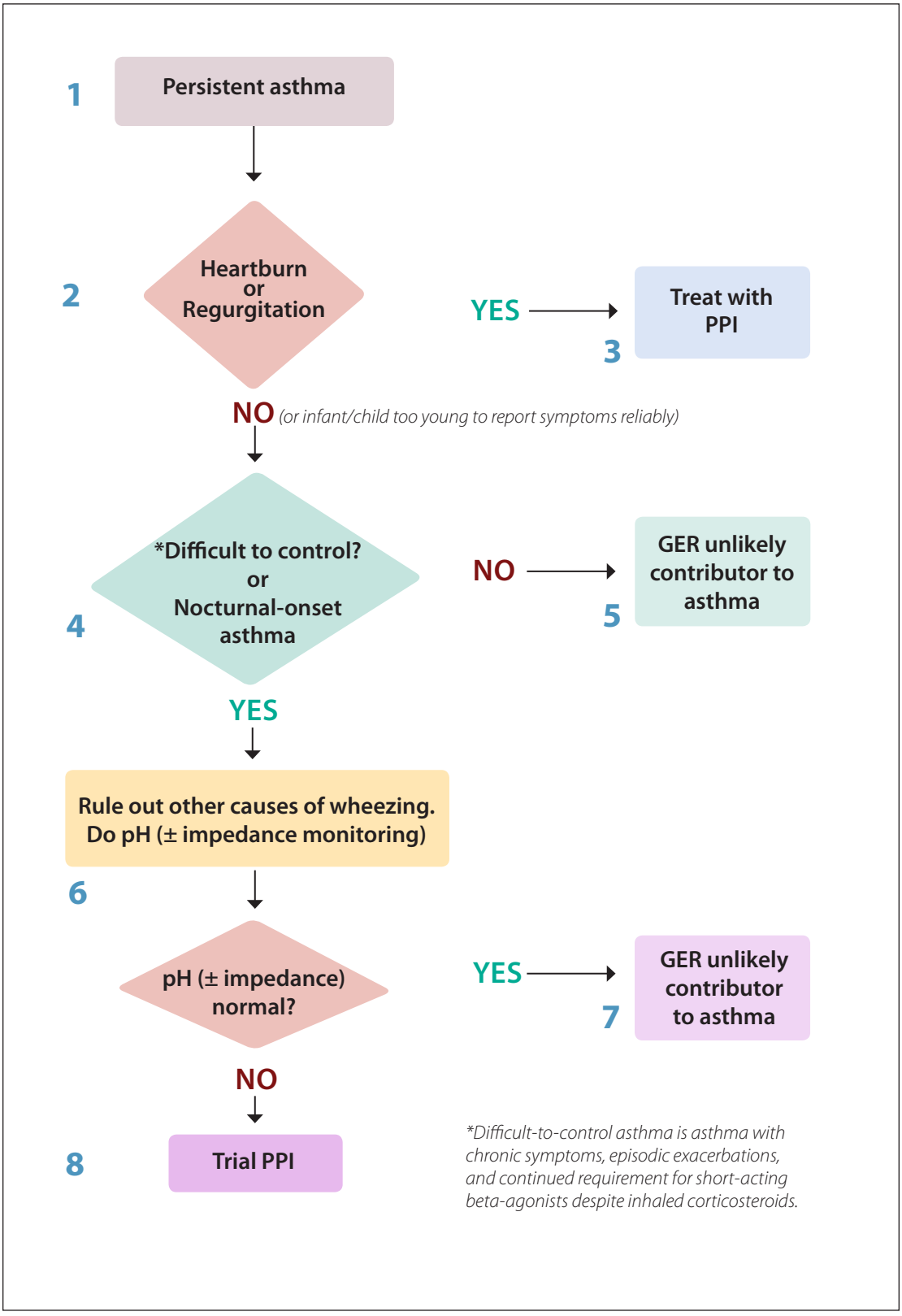


FIGURE 4: *Approach to the child with asthma that may be worsened by GERD*

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE

REFERENCES:

1. Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L, Sondheimer J, Staiano A, Thomson M, Veereman-Wauters G, Wenzl TG. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2009;49:498-547.

   Complete guidelines can also be found on the following websites: www.cdhnf.org *or* www.naspghan.org.

2. Sherman P, Hassall E, Fagundes-Neto U, Gold BD, Kato S, Koletzko S, Orenstein S, Rudolph C, Vakil N, Vandeplas Y. A Global, Evidence-Based Consensus on the Definition of Gastroesophageal Reflux Disease in the Pediatric Population. Am J Gastroenterol. 2009;104:1278-1295.

The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) represents more than 1400 pediatric gastroenterologists, predominantly in 46 states, the District of Columbia, Puerto Rico, Mexico and 8 provinces in Canada. NASPGHAN strives to improve the care of infants, children and adolescents with digestive disorders by promoting advances in clinical care, research and education.

The Children's Digestive Health and Nutrition Foundation (CDHNF) was established by NASPGHAN to promote research and education that will improve the health of children with digestive and nutritional disorders.

Support: Support for this Guideline Summary was provided by AstraZeneca L.P. and Takeda North America Pharmaceuticals Inc. This work was sponsored by CDHNF.

COVER PAGE
DEFINITION TITLE PAGE
SUMMARY TITLE PAGE