

FUNCTIONAL CONSTIPATION (FC) AND IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) IN PEDIATRIC PATIENTS

ABBVIE MEDICAL AFFAIRS + HEALTH IMPACT

abbvie

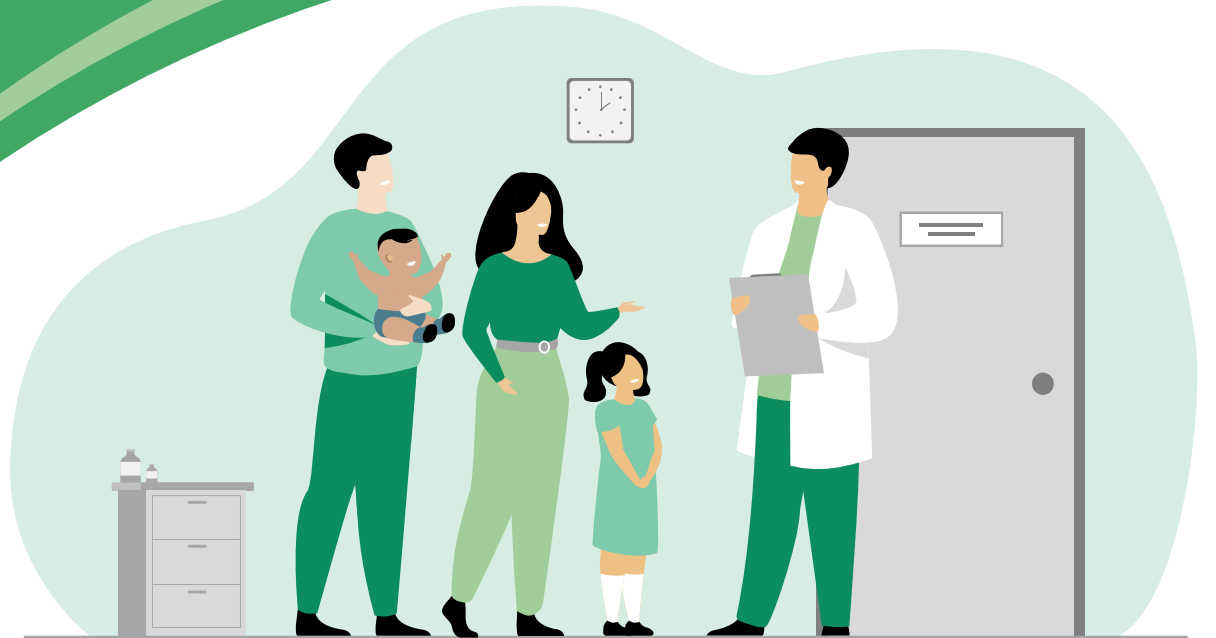


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Epidemiology
and burden

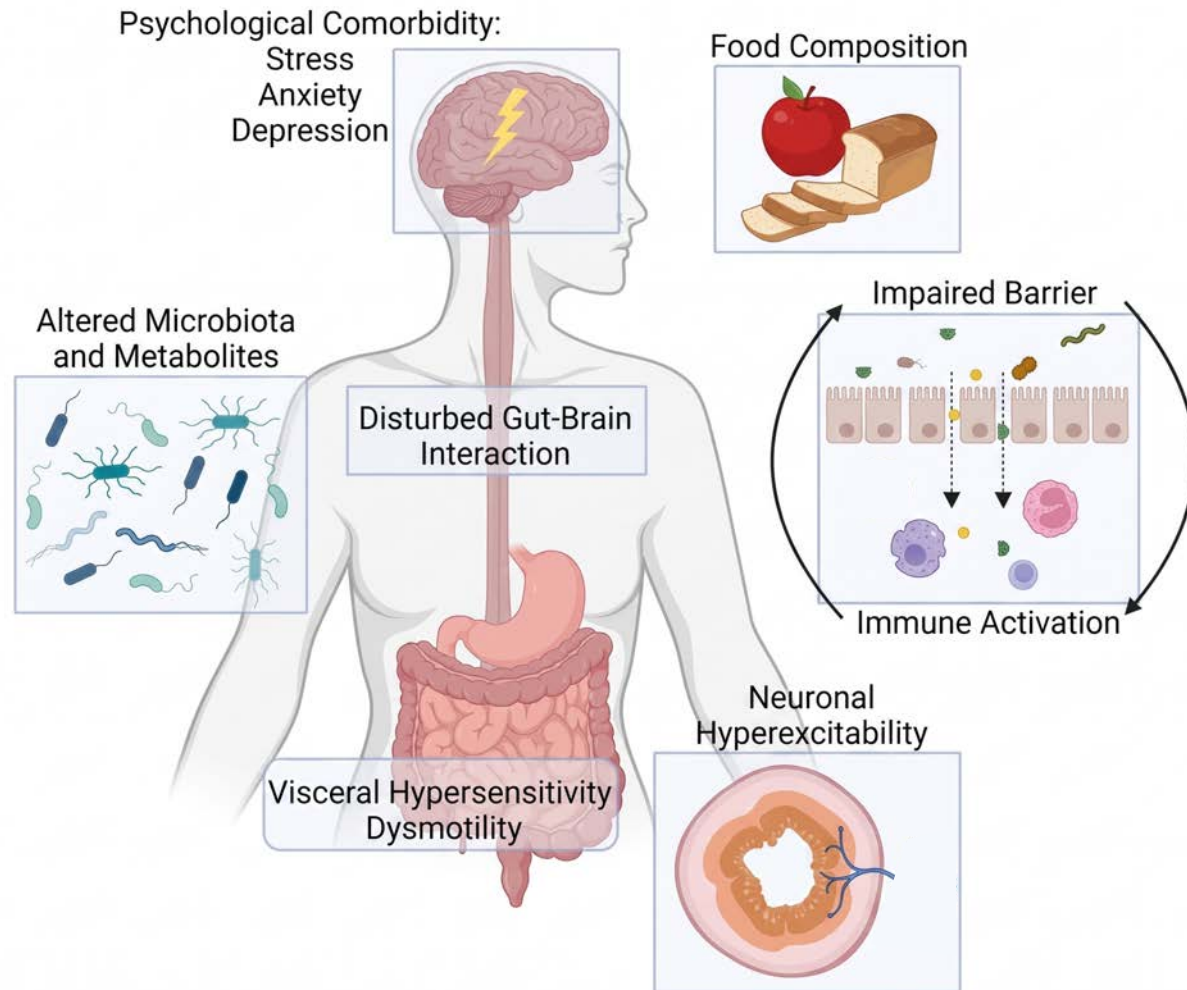
Pathophysiology

Diagnostic
criteria

Key Takeaways

DISORDERS OF GUT-BRAIN INTERACTIONS (DGBIs)¹

DGBIs Involve Dysfunction in How the Brain Interprets Signals from the Gut.



Pathophysiological Mechanisms In DGBIs Include:

- Food composition
- Psychological comorbidity
- Visceral hypersensitivity
- Altered microbiota and metabolites
- Neuronal hyperexcitability
- Impaired Barrier/Immune activation

1. Vamuytsel J, et al. BMJ 2023;72:787-798.

FUNCTIONAL CONSTIPATION IN PEDIATRIC PATIENTS



PEDIATRIC FC IS A COMMON GI DISORDER

Pediatric FC is characterized by the presence of infrequent bowel movements, painful defecation, fecal incontinence, stool withholding behavior, and occasional passage of large-diameter stools.^{1,2}



Age and sex were not found to be associated with the prevalence of pediatric FC



Pediatric FC has a higher prevalence in the Americas and Europe, and lower prevalence in Asia



GLOBAL
PREVALENCE³

9.5%



US
PREVALENCE⁴

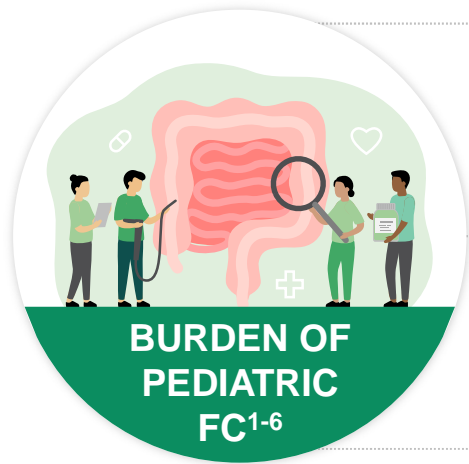
14.1%
≥4 Years Old

17.2%
<4 Years Old

FC=Functional Constipation; GI=Gastrointestinal;

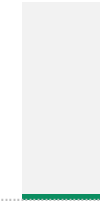
1. Rajindrajith S, et al. *World J Clin Pediatr.* 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385 2. Koppen IJN, et al. *Paediatr Drugs.* 2015;17(5):349-360. doi:10.1007/s40272-015-0142-4 3. Koppen IJN, et al. *J Pediatr.* 2018;198:121-130.e6. doi:10.1016/j.jpeds.2018.02.029 4. Data on file, AbbVie Inc. Pediatric functional constipation prevalence.

PEDIATRIC FC IS ASSOCIATED WITH SUBSTANTIAL DISEASE BURDEN



PEDIATRIC FC ACCOUNTS FOR:

~**3%** of general pediatrician visits



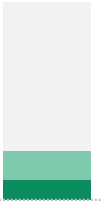
PEDIATRIC FC IN THE UNITED STATES:

Represents **\$3.9** billion/year additional cost attributable to children with constipation

PATIENTS WITH PEDIATRIC FC:

- Have more outpatient and emergency room visits vs those without constipation
- Have lower school functioning HRQoL scores vs healthy children

10–25% of pediatric GI visits



In a study of children younger than 5 years, FC was reported to have the highest number of first-time medical visits compared to other chronic GI disorders, including abdominal pain and GERD.



Children with FC have significantly lower QoL scores compared with IBD and GERD, and equal QoL scores with IBS.




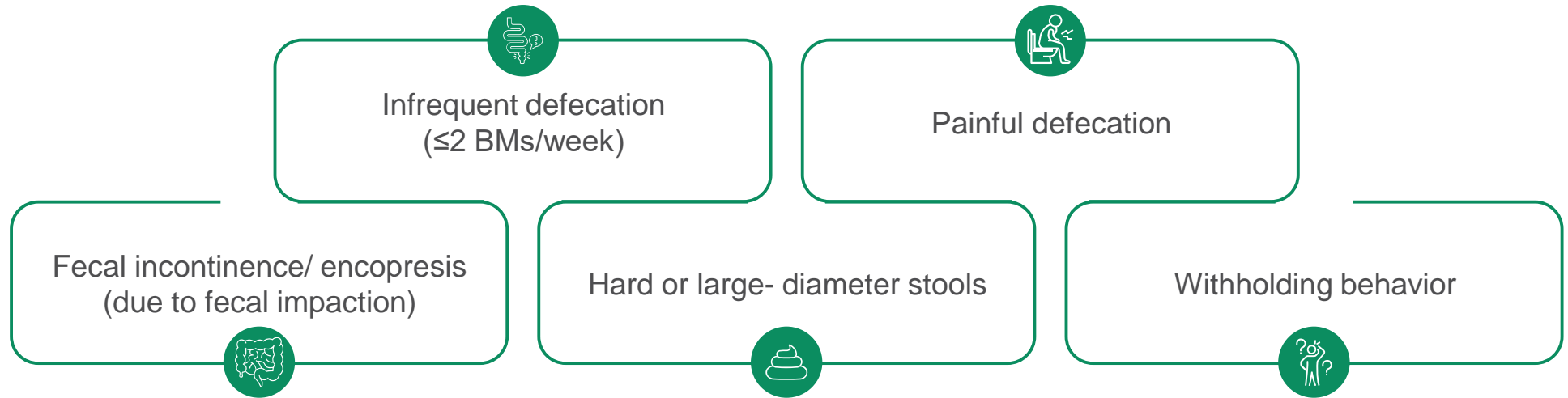
One-fourth to one-third of children with FC continue to have constipation into adulthood despite having tried multiple treatments.



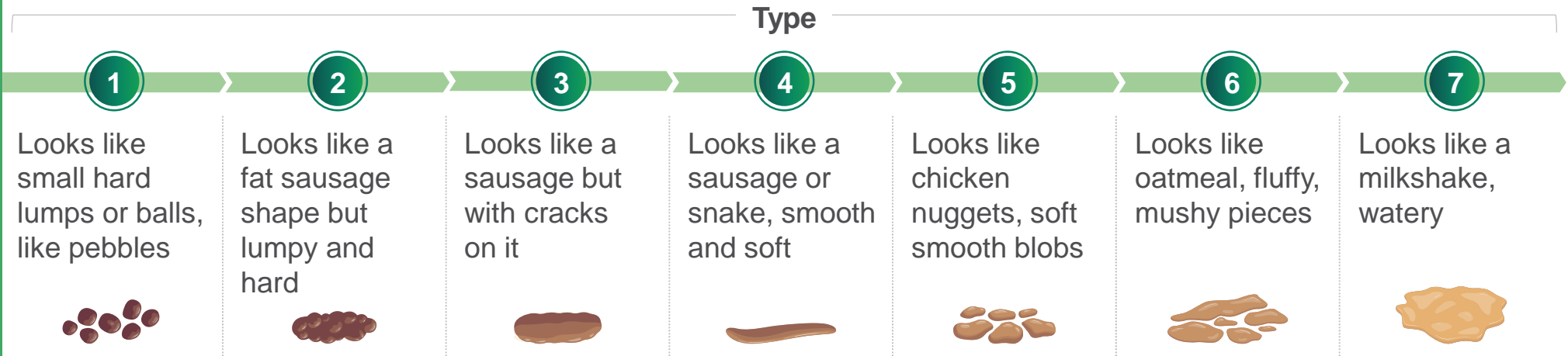
FC=Functional Constipation; GERD=Gastroesophageal Reflux Disease; GI=Gastrointestinal; HRQoL=Health-related quality of life; IBD=Inflammatory Bowel Disease; QoL=Quality of life.
 1. Koppen IJN, et al. *Paediatr Drugs*. 2015;17(5):349-360. doi:10.1007/s40272-015-0142-4 2. Liem O, et al. *J Pediatr*. 2009;154(2):258-262. doi:10.1016/j.jpeds.2008.07.060 3. Vriesman MH, et al. *J Pediatr*. 2019;214:141-150. doi:10.1016/j.jpeds.2019.06.059 4. Wang C, et al. *PLoS One*. 2013;8(10):e77273. doi:10.1371/journal.pone.0077273 5. Bongers ME, et al. *Pediatrics*. 2010;126(1):e156-e162. doi:10.1542/peds.2009-1009 6. Rajindrajith S, et al. *World J Clin Pediatr*. 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385 7.

PEDIATRIC FC CLINICAL PRESENTATION

PATIENT SYMPTOM OVERVIEW^{1,2}

PEDIATRIC BRISTOL STOOL FORM SCALE^{3*}

*The p-BSFS is a 7-point ordinal scale used to measure stool consistency developed by the sponsors for AbbVie clinical trials based on the original BSFS and refined based on qualitative research. BM=Bowel movement; BSFS=Bristol Stool Form Scale; FC=Functional Constipation.

1. Rajindrajith S, et al. *World J Clin Pediatr.* 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385 2. Koppen IJN, et al. *Paediatr Drugs.* 2015;17(5):349-360. doi:10.1007/s40272-015-0142-4 3. Linaclotide safety and efficacy in pediatric participants, 6 to 17 years of age, with irritable bowel syndrome with constipation (IBS-C) or functional constipation (FC). ClinicalTrials.gov identifier: NCT04026113. Updated May 3, 2023. Accessed May 9, 2023. <https://www.clinicaltrials.gov/ct2/show/nct04026113>

FECAL INCONTINENCE IS COMMON IN PEDIATRIC FC

Fecal Incontinence is Almost Always Associated with Constipation¹

FECAL INCONTINENCE CHARACTERISTICS²



80%



Large-diameter Stools

77.8%



Retentive Posturing

75.6%



Painful Defecation

75.6%



Straining

55.6%



Blood in Stools

FC=Functional Constipation; 1. Ali SR, et al. *Oman Med J.* 2011;26(5):376-378. doi:10.5001/omj.2011.94 2. Rajindrajith S, et al. *J Pediatr Gastroenterol Nutr.* 2010;51(4):472-476. doi:10.1097/MPG.0b013e3181d33b7d

= 10%

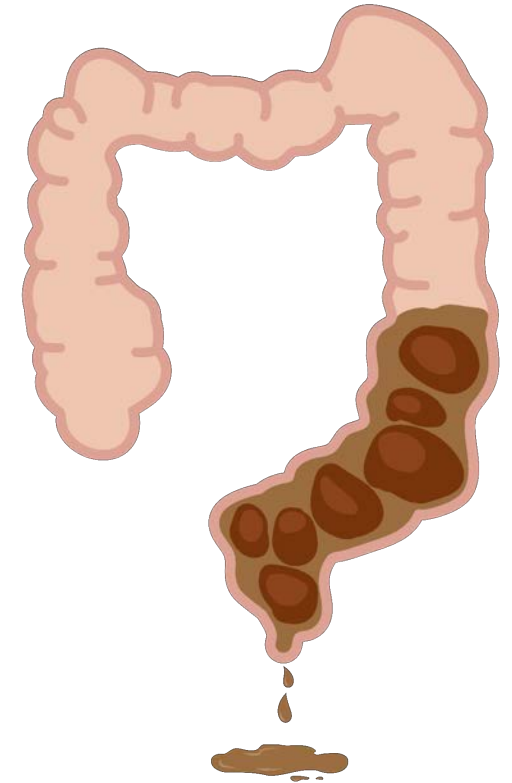
FECAL INCONTINENCE IS COMMON IN PEDIATRIC FC

Constipation in children is a vicious cycle of painful evacuation of hard, large stools that often leads to stool withholding, accumulated stool in a distended lower colonic segment, and an irregular urge to defecate due to decreased rectal sensation¹

Most cases of constipation and related fecal incontinence are secondary to functional disorders rather than organic causes¹

Fecal incontinence results when softer stool from the more proximal colon cannot be held in the distended rectum and leaks around the bolus of hard stool¹

- Due to lack of sensation in the distended distal colon, the child is not aware of softer stool passage until clothing is soiled¹
 - This leads to marked loss of self-esteem and behavioral problems that affect quality of life for the child and family¹

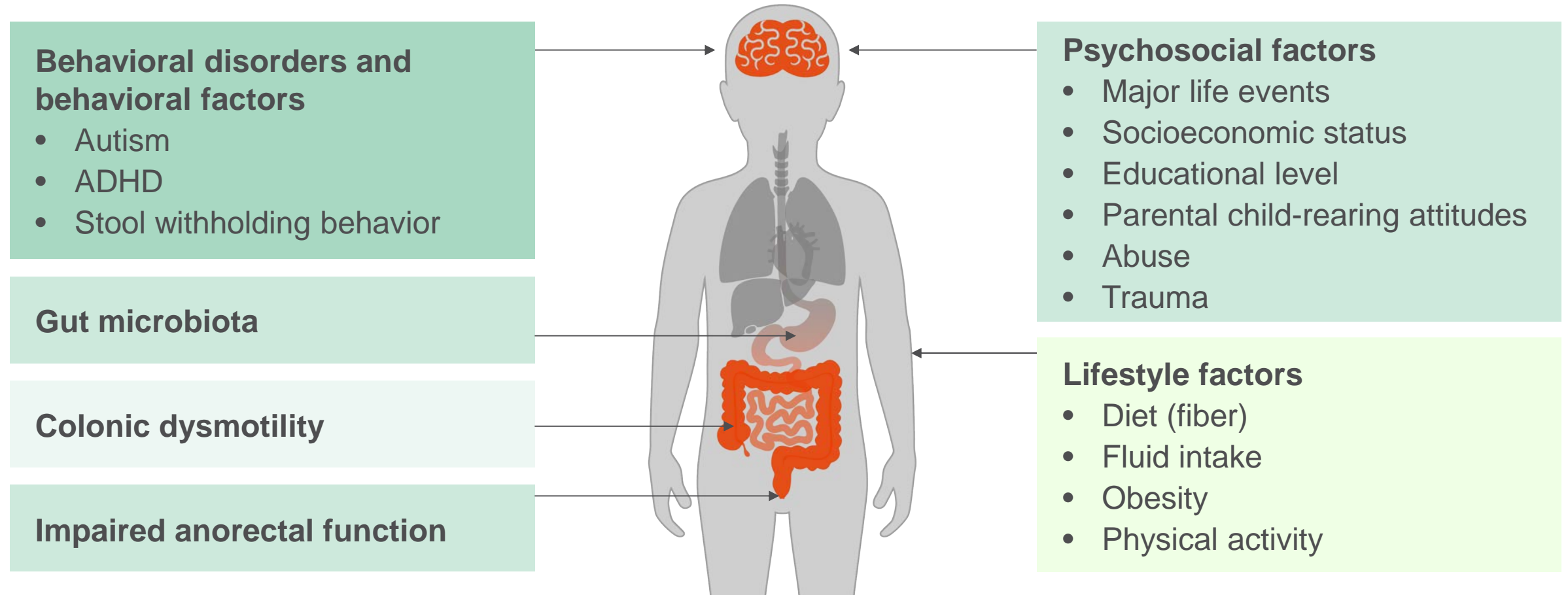


FC=Functional Constipation.

1. Ali SR, et al. *Oman Med J*. 2011;26(5):376-378. doi:10.5001/omj.2011.94 2. Rajindrajith S, et al. *J Pediatr Gastroenterol Nutr*. 2010;51(4):472-476. doi:10.1097/MPG.0b013e3181d33b7d

PEDIATRIC FC PATHOPHYSIOLOGY¹⁻⁴

The Etiology of Functional Constipation in Children is Largely Unknown but it is Believed to Be Multifactorial



1. Rajindrajith S, et al. *World J Clin Pediatr.* 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385; 2. Koppen IJN, et al. *Paediatr Drugs.* 2015;17(5):349-360. doi:10.1007/s40272-015-0142-4; 3. Olaru C, et al. *Gastroenterol Res Pract.* 2016;2016:3989721. doi:10.1155/2016/3989721; 4. Boilesen SN, et al. *Eur J Nutr.* 2021;60(8):4647-4655. doi:10.1007/s00394-021-02657-2
ADHD=Attention-Deficit/Hyperactivity Disorder; FC=Functional Constipation.



PSYCHOSOCIAL FACTORS INVOLVED IN THE PATHOPHYSIOLOGY OF FC IN CHILDREN¹



MAJOR LIFE EVENTS

- Stressful events
 - Separation from best friend
 - Failure in exam or bullied in school
 - Divorce/separation of parents
 - A parent's loss of a job
 - Severe illnesses in the family



ABUSE

- Physical, emotional, and sexual abuse
- Psychological trauma associated with abuse and maltreatment



PARENT-CHILD ATTITUDES

- Parents' rearing style during toilet training
- Authoritative parenting resulting in overprotective and rigid attitudes





TOILET TRAINING


- Poor toilet training
 - Toilet training/potty training should be started between **18-30 months**
- 18 months** > **30 months**
- Timing influenced by socioeconomic factors and cultural norms
 - Toileting refusal may be due to fear of defecation, using the toilet, or strained family dynamics
 - This enhances withholding behavior


FC=Functional Constipation. 1. Rajindrajith S et al. *World J Clin Pediatr.* 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385

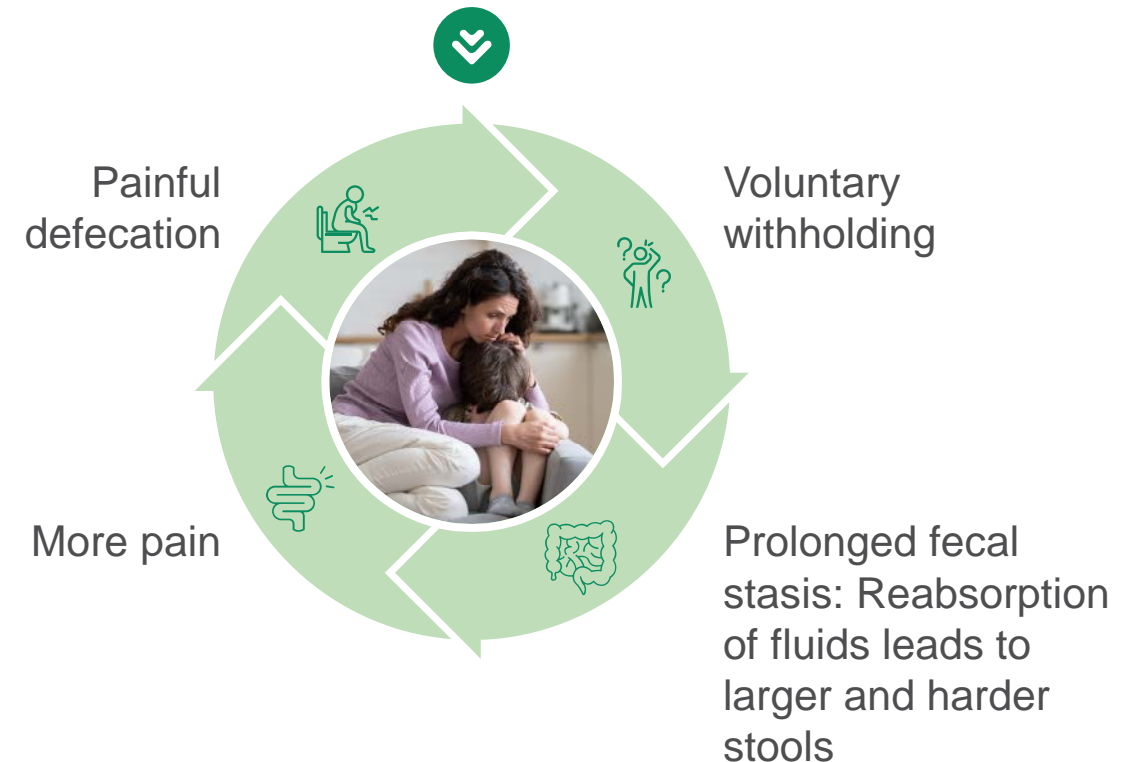
IMPACT OF STOOL WITHHOLDING ON CHILDREN WITH FC ^{1,2}

 Most common pathophysiological mechanism in young children

 Faulty toilet training and painful defecation due to passage of hard and large fecal masses lead children to withhold stools

 Rectal mucosa absorb water in feces, and the fecal mass becomes rock hard and difficult to evacuate; occasional passage of the fecal mass causes pain in the perianal region, which further aggravates withholding

 Stretched rectal walls may lose normal contractility, which is necessary to propel feces



1. Rajindrajith S, et al. World J Clin Pediatr. 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385 2. Poddar U, Indian Pediatr. 2016;53(4):319-327. doi:10.1007/s13312-016-0845-9

ROME IV CONSTIPATION DIAGNOSTIC CRITERIA



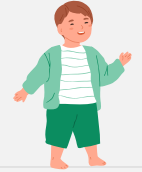
INFANTS AND TODDLERS (<4 YEARS OLD)

ONE MONTH OF AT LEAST TWO OF THE FOLLOWING:

- **2** or fewer bowel movements per week
- History of excessive stool retention
- History of painful or hard bowel movements
- History of large-diameter stools
- Presence of a large fecal mass in the rectum

In toilet trained children:

- At least **1** episode/week of fecal incontinence
- History of large diameter stools that may obstruct the toilet



OLDER CHILDREN (≥4 YEARS OLD)

TWO OR MORE OF THE FOLLOWING ONCE PER WEEK OVER ONE MONTH:

- **2** or fewer bowel movements per week
- History of excessive stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- At least **1** episode/week of fecal incontinence
- History of large diameter stools that may obstruct the toilet

CLINICAL EVALUATION BASED ON GUIDELINES FOR THE EVALUATION AND TREATMENT OF THE CHILD WITH FC BY ESPGHAN AND NASPGHAN¹

HISTORY AND PHYSICAL



- Rome criteria is the recommended definition of FC for all age groups
- Diagnosis of FC:
 - Based on history and physical examination
 - If only one Rome criterion is present and the diagnosis of FC is uncertain, a digital examination of the anorectum is recommended
- Identification of underlying disease:
 - Alarm signs/symptoms and diagnostic clues

IMAGING



- Abdominal X-ray
 - No role for routine use in diagnosis
 - May be used if fecal impaction is suspected but physical examination is unreliable/not possible

LABS



- The following are not recommended for testing in the absence of alarm symptoms
 - Routine allergy testing for cow's milk allergy
 - Hypothyroidism
 - Celiac disease
 - Hypercalcemia

PROCEDURES



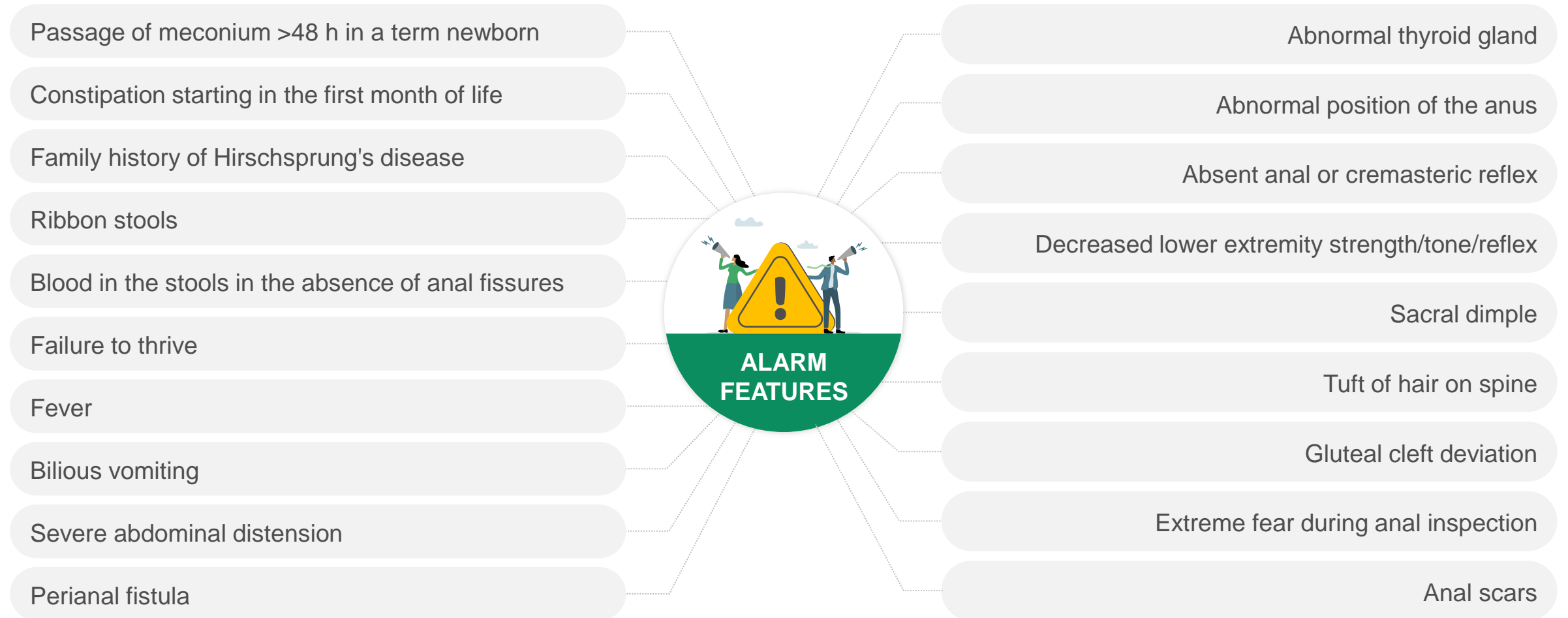
- Colonic manometry
 - May be indicated in the evaluation of intractable constipation before surgical intervention is considered
- Rectal biopsy
 - Gold standard for diagnosing Hirschsprung disease*
- Barium enema
 - Not used as an initial diagnostic tool

*Hirschsprung disease is a birth defect in which some nerve cells are missing in the large intestine, so a child's intestine can't move stool and becomes blocked.²

ESPGHAN=European Society for Pediatric Gastroenterology, Hepatology, and Nutrition; FC=Functional Constipation; NASPGHAN=North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

1. Tabbers MM et al. *J Pediatr Gastroenterol Nutr.* 2014;58(2):258-274. doi:10.1097/MPG.000000000000266 2. Hirschsprung disease. <https://www.niddk.nih.gov/health-information/digestive-diseases/hirschsprung-disease>

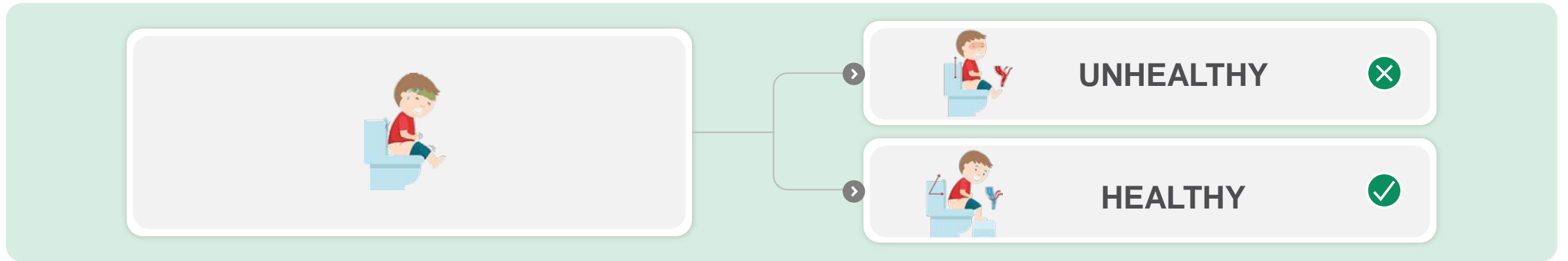
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ESPGHAN=European Society for Pediatric Gastroenterology, Hepatology, and Nutrition; FC=Functional Constipation. NASPGHAN=North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

1. Hyams JS, et al. Gastroenterology. 2016;150(6):1456-1468.e2. doi:10.1053/j.gastro.2016.02.015

NON-PHARMACOLOGICAL INTERVENTIONS



BEHAVIORAL AND PHYSICAL INTERVENTION¹⁻³

- Children should **sit on the potty or toilet for 5 min after waking and after each meal** to take advantage of the gastrocolic reflex
- **Relaxed posturing should be encouraged** by providing foot support
- Parents should be encouraged to **reinforce positive behavior**, potentially with incentives for passing stools
- **Pelvic physiotherapy** may help improve constipation and fecal incontinence.

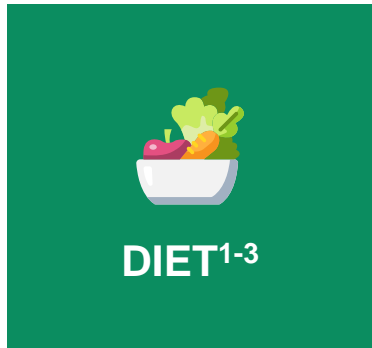


BEHAVIORAL AND PSYCHOLOGICAL INTERVENTIONS¹

- Mental health services should be utilized for children with behavioral problems (**toilet refusal, stress, fear of defecation**)

1. Rajindrajith S. *World J Clin Pediatr.* 2022;11:385-404; 2. Vriesman.MH, et al. *Nat Rev Gastroenterol Hepatol.* 2020;17:21-39; 3. van Engelenburg-van Lonkhuyzen ML, et al. *Gastroenterology.* 2017;152(1):82-91.

NON-PHARMACOLOGICAL INTERVENTIONS





ESPGHAN/
NASPGHAN **recommends normal amount of fiber** for children with FC



ESPGHAN/
NASPGHAN **does not recommend probiotics** for children with FC

Dietary Need
Recommendation

Dietary fiber 
<ul style="list-style-type: none">• Age (yrs) + 5 or 10 g/day• 7 to 15 g/day for ages 2 to 5 y

Hydration 
32 to 64 ounces of water and nondairy liquids per day



- Instrument-based and **neuromuscular conditioning techniques train relevant muscles** to promote regular BMs
- RCT reported significant difference **favoring pelvic physiotherapy** vs standard medical care in children ages 5 to 17 years^{4a}
- ESPGHAN/NASPGHAN **does not recommend behavioral therapy or biofeedback** for children with FC

^aRCT compared "successful treatment" defined as absence of FC according to Rome III criteria; AHF, American Health Foundation; 1. Koppen IJN. *Pediatr Drugs*. 2015; 17:349-360.; 2. Rajindrajith S. *World J Clin Pediatr*. 2022;11:385-404.; 3. Tabbers MM et al. *JPGN*. 2014;58:258-274.; 4. van Engelenburg-van Lonkhuyzen ML et al. *Gastroenterol*. 2017;152:82-91.



PRINCIPLES OF PHARMACOLOGICAL TREATMENT¹

DISIMPACTION



- Fecal impaction is defined as the presence of a large fecal mass in the rectum or abdomen
- Disimpaction recommended prior to initiation of maintenance

MAINTENANCE



- Recommended to prevent re-accumulation of feces
- Effect of treatment should be evaluated 1 to 2 weeks after initiation
- Treatment should be continued for at least 2 months
 - Symptoms should be resolved for at least 1 month before weaning is initiated

WEANING



- 50% of children with FC on maintenance can stop using treatment within 6–12 months after initiation
- Maintenance treatment should be gradually reduced, to prevent relapse
- Weaning can be considered when child maintains defecation frequency of ≥ 3 times per week



PEDIATRIC FC KEY TAKEAWAYS



PED FC EPIDEMIOLOGY^{2,3}

Estimated global prevalence of **9.5%**

Prevalence in the US is **14.1%** in children **≥4** years old

PED FC CHARACTERISTICS¹

Common pediatric disorder characterized by infrequent defecation, hard or large diameter stools, painful defecation, withholding behavior and fecal incontinence.

Ped FC is associated with significant disease burden for patients and caregivers

DIAGNOSIS AND MANAGEMENT^{4,5}

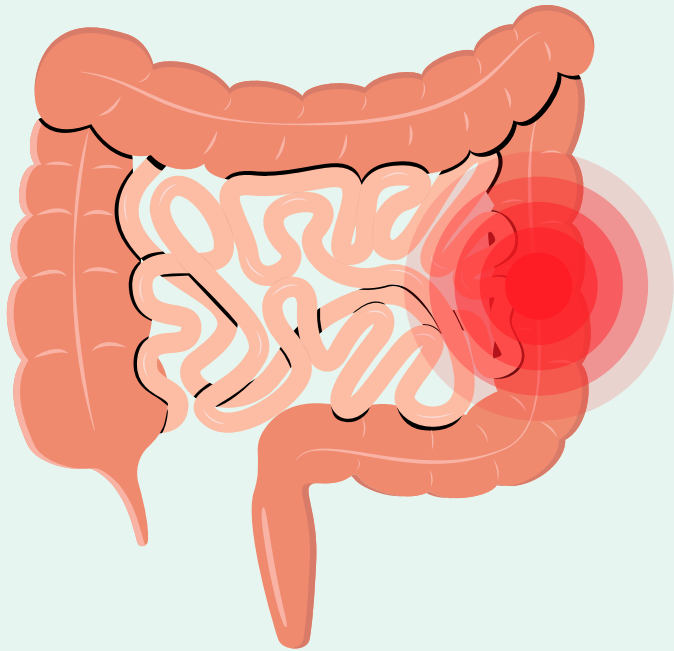
Ped FC can be diagnosed by using the Rome IV criteria with minimal lab testing and imaging

Management consists of 3 stages:

- ✓ Disimpaction
- ✓ Maintenance
- ✓ Weaning

1. Koppen IJN, et al. *J Pediatr.* 2018;198:121-130.e6. doi:10.1016/j.jpeds.2018.02.029 2. Data on file, AbbVie Inc. Pediatric functional constipation prevalence. 3. Rajindrajith S, et al. *World J Clin Pediatr.* 2022;11(5):385-404. doi:10.5409/wjcp.v11.i5.385 4. Hyams JS, et al. *Gastroenterology.* 2016;150(6):1456-1468.e2. doi:10.1053/j.gastro.2016.02.015 5. Koppen IJN, et al. *Paediatr Drugs.* 2015;17(5):349-360. doi:10.1007/s40272-015-0142-4

IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) IN PEDIATRIC PATIENTS





IBS-C IS ONE OF THE MOST COMMONLY DIAGNOSED MEDICAL PROBLEMS IN PEDIATRICS¹



IBS PREVALENCE IN CHILDREN²

Estimated global prevalence of **8.8%** (95% CI, **6.2-11.9**)^{*}

Reported US prevalence has ranged **1.6%-24.0%**^{*}



IBS SUBTYPES IN CHILDREN³



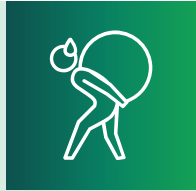
■ IBS-C ■ IBS-D ■ Mixed IBS ■ Unsubtyped IBS

IBS-C was the most common subtype in children[†]

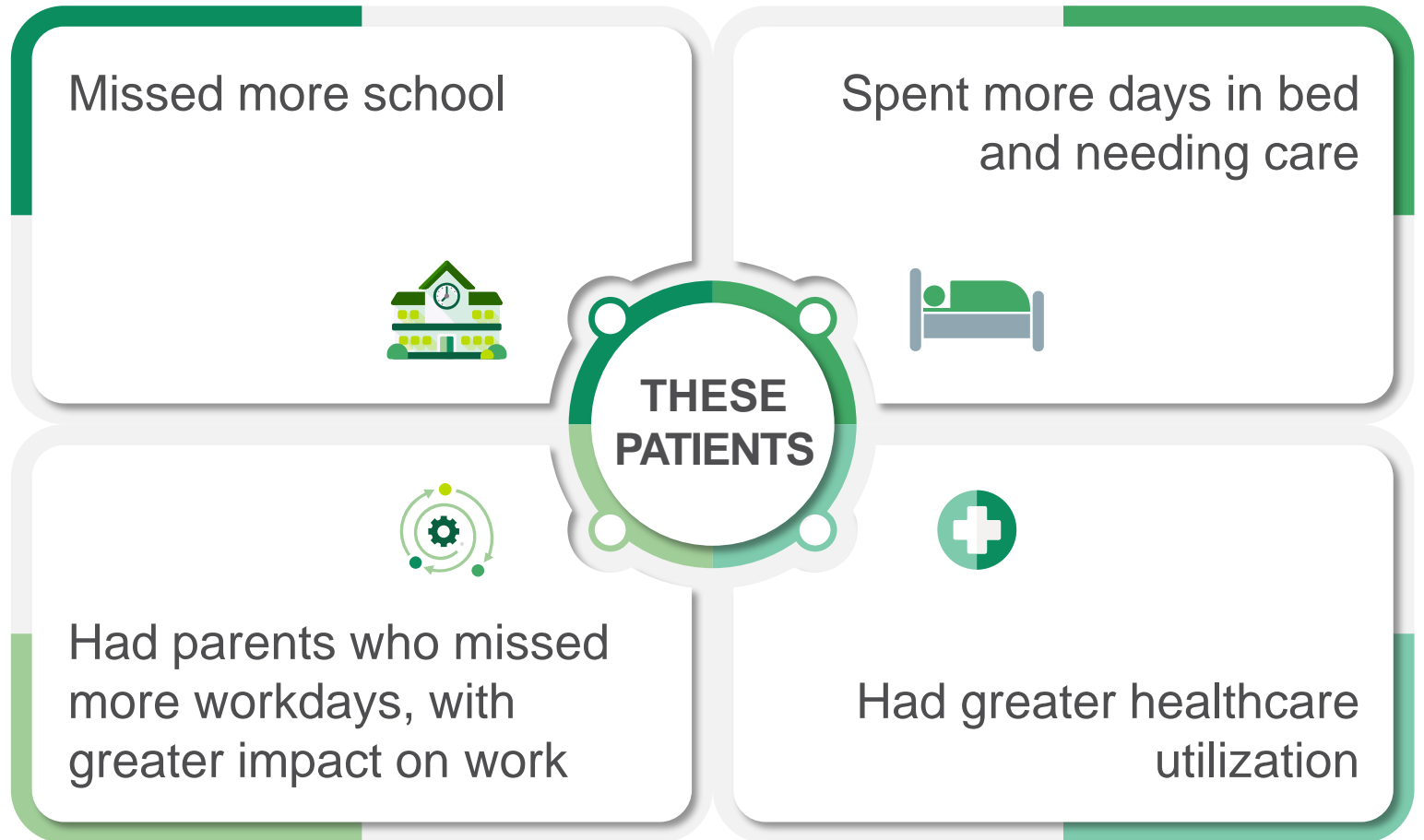
^{*}Based on a meta-analysis of 58 articles published by February 2014 that included 196,472 children ages 4-18 years with functional abdominal pain disorder. [†]Based on a prospective study of 129 patients ages 7-18 years who met pediatric Rome III IBS criteria and were part of larger studies of children with functional GI disorders, recruited from primary and tertiary centers. Participants were assigned IBS subtypes based on their reported stool information per adult Rome III criteria. IBS=irritable bowel syndrome; IBS-C=irritable bowel syndrome with constipation; IBS-D=irritable bowel syndrome with diarrhea.

1. Chiou E, Nurko S. *Expert Rev Gastroenterol Hepatol*. 2010;4(3):293-304. doi:10.1586/egh.10.28 2. Korterink JJ, et al. *PLoS One*. 2015;10(5):e0126982. doi:10.1371/journal.pone.0126982 3. Self MM, et al. *Clin Gastroenterol Hepatol*. 2014;12(9):1468-73. doi:10.1016/j.cgh.2014.01.031

IBS BURDEN IN CHILDREN¹



Pediatric patients with GI disorders, including IBS, reported lower HRQoL vs healthy controls[‡]

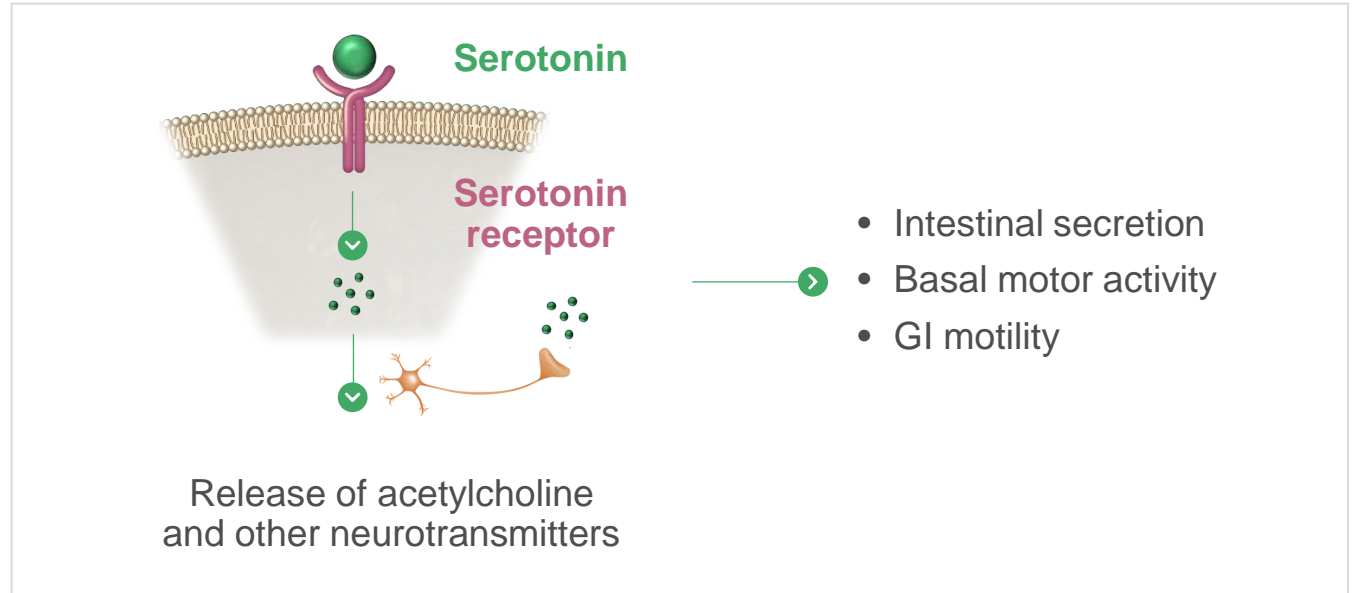
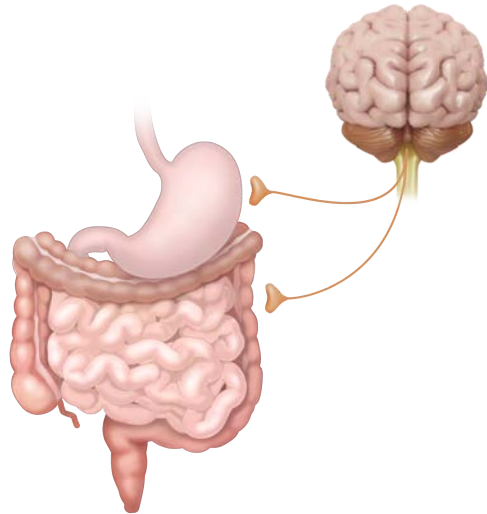


[‡]Based on results from 689 families completing the Pediatric Quality of Life Inventory 4.0 Generic Core Scales. Patients had 1 of 7 physician-diagnosed GI disorders, including IBS. The healthy control sample included 1114 families. GI=gastrointestinal; HRQoL=health-related quality of life

1. Varni JW, et al. *J Pediatr.* 2015;166(1):85-90. doi:10.1016/j.jpeds.2014.08.022



THE PRECISE CAUSE OF IBS IS UNKNOWN, BUT A COMBINATION OF FACTORS MAY CONTRIBUTE TO IBS DEVELOPMENT



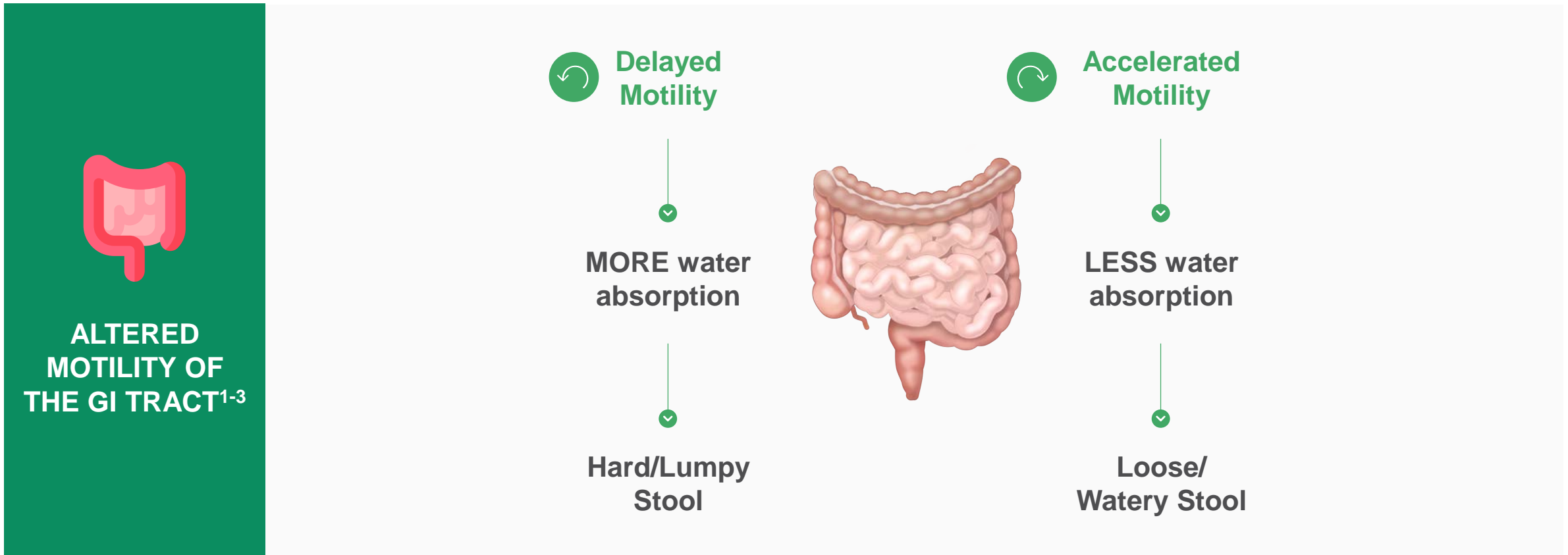
Food, hunger, emotions, and stress impact the bidirectional communication between the GI tract and the nervous system. The neurotransmitter serotonin is a key mediator, and alteration of serotonergic signaling has been implicated in IBS.

GI=Gastrointestinal; IBS=Irritable Bowel Syndrome.; 1. Fichna J et al. *Front Pharmacol.* 2012;3(127):1-12. doi:10.3389/fphar.2012.00127

2. Pathophysiology of irritable bowel syndrome. <https://www.uptodate.com/contents/pathophysiology-of-irritable-bowel-syndrome>



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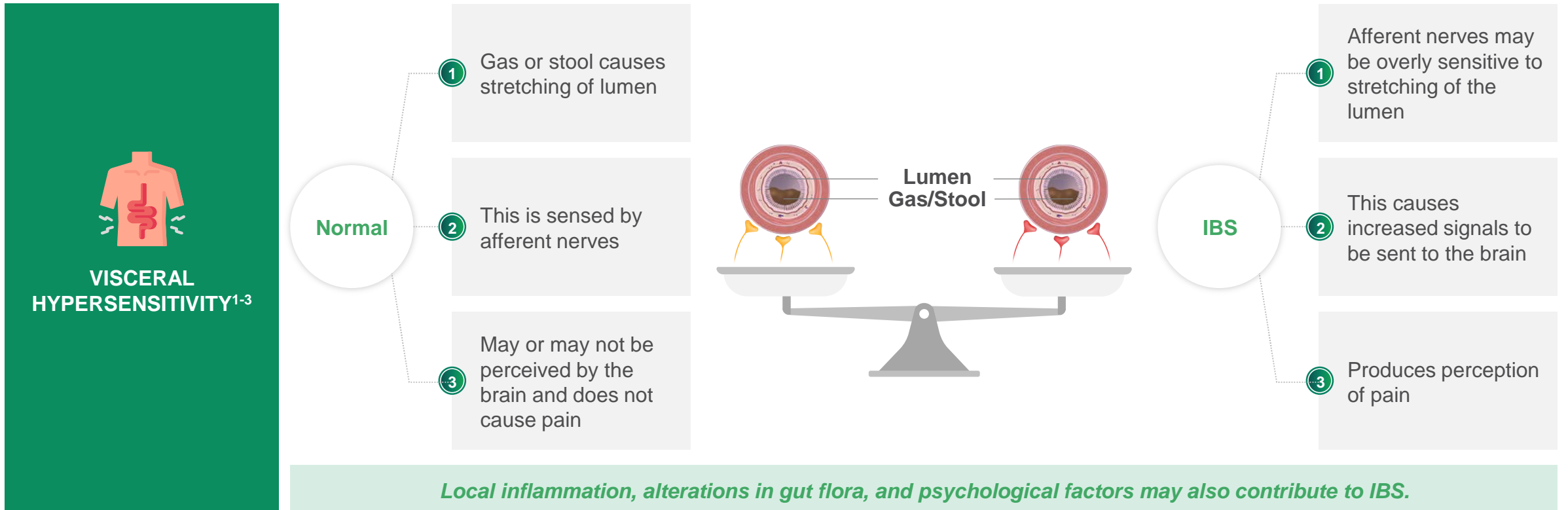


GI=Gastrointestinal; IBS=Irritable Bowel Syndrome

1. Pathophysiology of irritable bowel syndrome. <https://www.uptodate.com/contents/pathophysiology-of-irritable-bowel-syndrome> 2. Feldman M et al. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 9th ed. 2010. 3. Chey WD et al. *Curr Gastroenterol Rep*. 2006;8(4):273-281. doi:10.1007/s11894-006-0047-z



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2. Delvaux M. *Gut*. 2002;51(suppl 1):i67-i71. doi:10.1136/gut.51.suppl_1.i67 3. Karantanos T et al. *Gut Pathog*. 2010;2(1):3. doi:10.1186/1757-4749-2-3



THE ROME IV DIAGNOSTIC CRITERIA FOR IBS* IN CHILDREN/ADOLESCENTS¹

ROME IV CRITERIA

Criteria fulfilled for at least **2 months** prior to diagnosis

Abdominal pain at least 4 days per month over at least 2 months, associated with one or more of the following



In children with abdominal pain and constipation, the pain does not resolve with resolution of the constipation[†]



After appropriate evaluation, the symptoms cannot be fully explained by another medical condition



- ✓ Defecation
- ✓ A change in frequency of stool
- ✓ A change in form (appearance) of stool

*The Rome IV diagnostic criteria do not provide diagnostic criteria for IBS subtypes in children; †Children in whom the pain resolves have functional constipation and not IBS.

1. Rome Foundation. ROME IV diagnostic criteria for disorders of gut-brain interaction (DGBI). Published January 16, 2016. Accessed April 28, 2026. <https://theromefoundation.org/rome-iv/rome-iv-criteria/>



PEDIATRIC IBS-C KEY TAKEAWAYS



PED IBS-C EPIDEMIOLOGY⁸⁻¹⁰

Estimated global prevalence of **8.8%**



Prevalence in the US ranges from **1.6-24%** in children **≥4** years old



PED IBS-C CHARACTERISTICS¹⁻⁷

IBS-C is multifactorial and may involve brain-gut dysfunction, altered motility, visceral hypersensitivity, psychological factors, local inflammation, and altered gut flora.



Ped IBS-C is associated with significant disease burden for patients and caregivers



DIAGNOSIS¹¹

Ped IBS-C can be diagnosed by using the Rome IV criteria. Children in whom the abdominal pain resolves have functional constipation and not IBS.



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