The Way you Move: A Guide to Pediatric Constipation

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Practical Day of Pediatrics

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Disclosures

None!

Objectives

- Review defecation physiology
- Review existing literature and guidelines for functional constipation
- Learn some clinically helpful information

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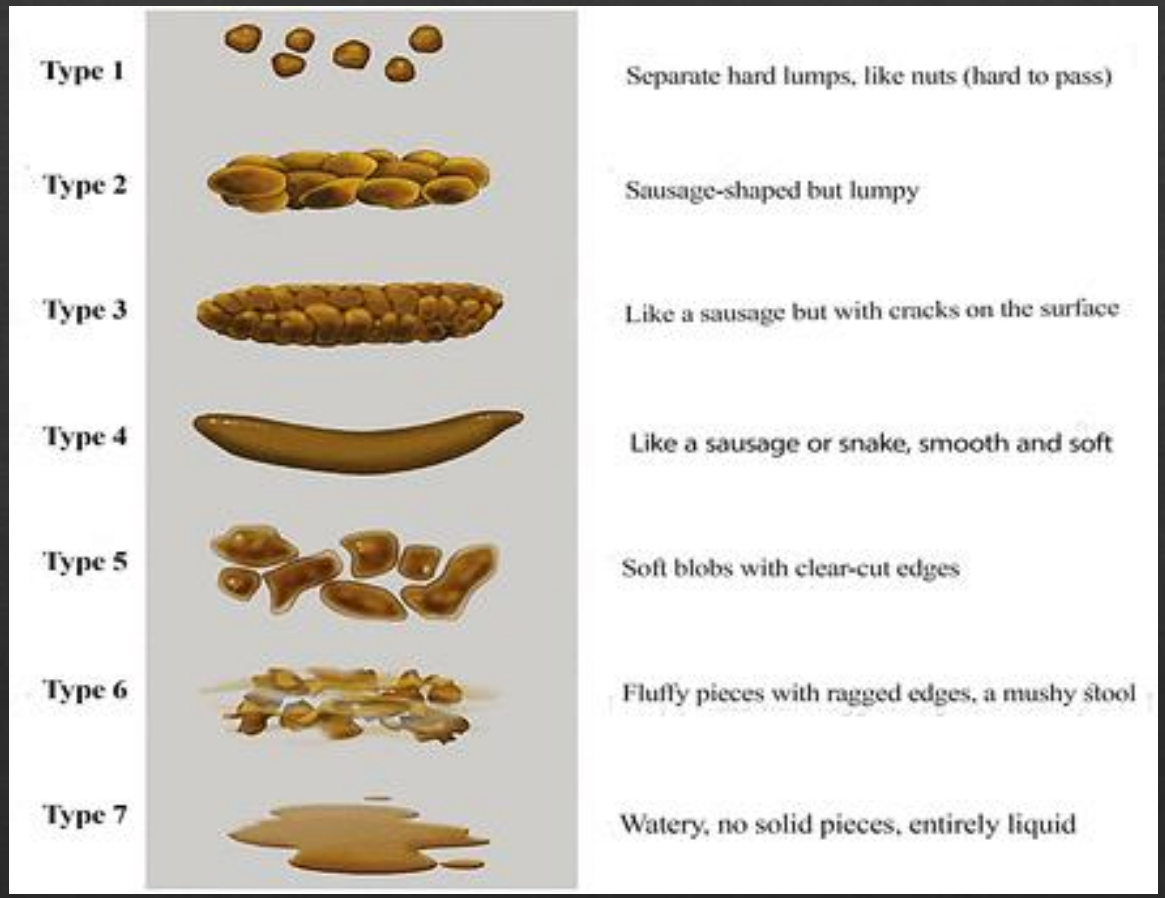
Functional Constipation Definition

Rome IV Criteria

Must include **one month of at least two** of the following in infants up to 4 years of age:
Two or fewer defecations 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, the following additional criteria may be used:
At least one episode/week of incontinence after the acquisition of toileting skills
History of large diameter stools which may obstruct the toilet

Epidemiology



Bristol Stool Chart

- Up to 3% of children worldwide have constipation
- Accounts for ~25% of pediatric GI referrals
- Functional constipation is the most common type of constipation
- Associated with significant affect on quality of life: pain, school absence, bullying, family stress

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Bowel movements: Facts and Physiology

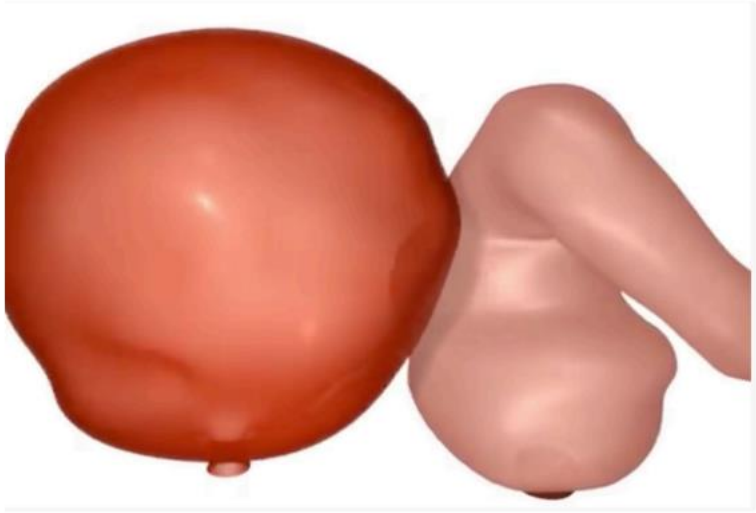
Normal frequency?

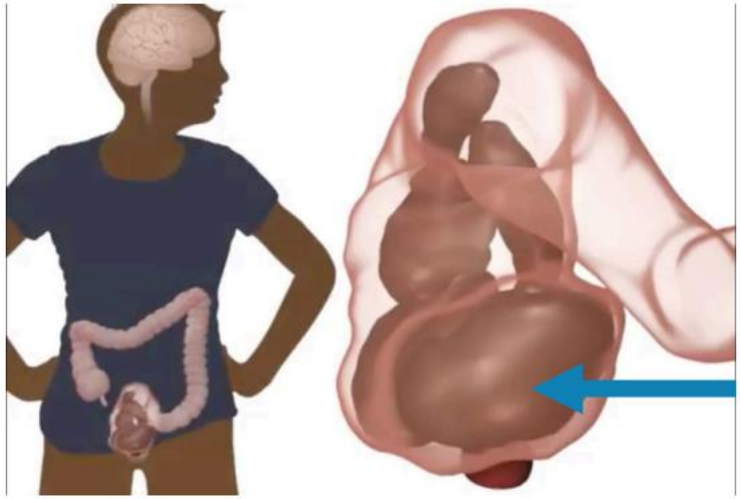
- Adults: 3 x weekly up to 3 x daily
- Children: 4-9 x weekly

Why the difference?

- High amplitude propagating contractions (HAPC)
- Infants and children have more

Pathophysiology of functional constipation



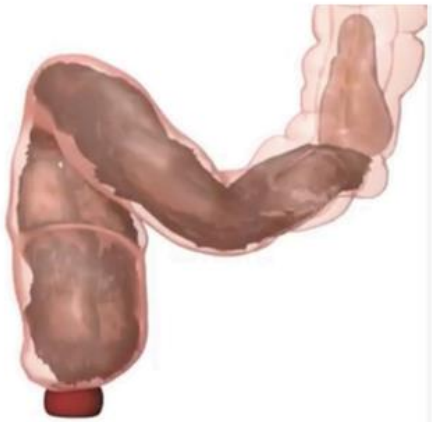


When stool repeatedly sits in the rectum for prolonged periods, the rectum can become dilated like a balloon

The Poo In You – Gikids.org & Colorado Children's Hospital

What causes functional constipation?

Pathophysiology of functional constipation



Dilation of the rectum causes liquid stool to leak out around hard stool and into the underwear (often unknowingly to the child)

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Overflow incontinence

Overflow incontinence covered from 3:02-3:30

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Bowel Movements: Facts and Physiology

Posture: hip flexion increases = creates a more obtuse (open) anorectal angle

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Bowel movements: Facts and Physiology

Gastro-colic reflex

- When the stomach contracts → colon contracts
- Two pressure peaks: 10-50 min, 70-90 min after a meal

Recto-anal inhibitory reflex (RAIR)

- Rectum distends → afferent nerves →spinal cord → efferent nerves → involuntary relaxation of internal anal sphincter

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

M.M. Tabbers, C. DiLorenzo, M.Y. Berger, C. Faure, M.W. Langendam, S. Nurko, A. Staiano, Y. Vandenplas, and M.A. Benninga

- "To assist health care workers in the management of all of the children with constipation in primary, secondary, and tertiary care, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition elected to develop evidence-based guidelines as a joint effort.

The guideline is also not aimed at the management of patients with underlying medical conditions causing constipation, but rather just for functional constipation.

Question 1: What is the definition of functional constipation?

Rome IV Criteria

Must include **one month of at least two** of the following in infants up to 4 years of age:
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History of large diameter stools
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Note: paper based on Rome III. We now have Rome IV

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Reference: theromefoundation.org/rome-iv/rome-iv-criteria

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What questions do you ask parents?

- Hiding when needing to defecate
- Large stools/clogging toilet
- Recurrent UTIs
- Timing/location of bowel movements (ex: only at home, right after school)
- Feeling of incomplete evacuation
- **Can the child differentiate between passage of gas vs stool?**

Families may misinterpret withholding behaviors as straining or pain

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Question 1: What is the definition of functional constipation?

Refractory constipation:

- Constipation not responding to optimal conventional treatment for at least 3 months

Fecal impaction:

- Hard mass in the lower abdomen identified on physical exam
- Dilated rectum filled with large amount of stool on rectal exam
- Excessive stool in the distal colon on abdominal radiography

Question 1: What is the definition of functional constipation?

Diagnosis of functional constipation should be based on history and physical exam

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Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

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Question 2: What are the alarm signs and symptoms that suggest the presence of an underlying disease causing the constipation?

"The major role of history and physical examination in the evaluation of constipation is to exclude other disorders that present with difficulties with defecation and to identify complications."

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

Question 2: What are the alarm signs and symptoms that suggest the presence of an underlying disease causing the constipation?

Alarm signs

If any of these are present, consider a diagnosis other than functional constipation

History	Physical exam
• Onset before 1 month of age • Failure to thrive • Delayed passage of meconium • Bloody stools (in absence of anal fissures) • Bilious emesis • Family history: Hirschsprung's	• Abnormal external anal exam, excluding fissures • Neurologic symptoms (poor anal tone, abnormal reflexes) • Spinal abnormalities (hair tufts, sacral dimple) • Abdominal mass/distention • *always consider abuse*

Tabbers et al., JPGN 2014.

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Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

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Question 3: In the diagnosis of functional constipation in children, what is the diagnostic value of

3.1 Digital rectal examination?

3.2 Abdominal radiography?

Digital Rectal Exam (DRE)

- Evidence does not support use of DRE for diagnosing functional constipation

Abdominal radiography

- Evidence does not support use of abdominal radiography to diagnose functional constipation

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

Question 4: Which of the following diagnostic tests should be performed in children with constipation in order to diagnose an underlying disease?

Labs

- Allergy testing (milk protein)? Evidence inconclusive

- Celiac and thyroid disease screening, calcium levels?

No published evidence

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

So, when do I check labs?

- Typically **not** on the first visit (unless history concerning for celiac, thyroid disease)

- If laxative management does not improve symptoms (good compliance)

- Labs: TTG IgA, serum IgA, TSH/T4, renal panel

Question 5: Which of the following examinations should be performed in children with intractable constipation to evaluate pathophysiology and diagnose an underlying abnormality?

MRI of the Spine

- No evidence to support use of MRI of the spine in patients unless other neurological abnormalities present

Question 6: What is the additional effect of the following nonpharmacologic treatments in children with functional constipation?

Fiber

- No evidence to support use of fiber supplements in treating functional constipation

Fluid

- No evidence to support use of extra fluid intake in treating functional constipation

Probiotics

- No evidence to support the use in the treatment of functional constipation

GUT MICROBIOTA AND THE USE OF PROBIOTICS IN CONSTIPATION IN CHILDREN AND ADOLESCENTS: SYSTEMATIC REVIEW

[Article in English, Portuguese]

Daiane Oliveira Vale San Gomes [1], Mauro Batista de Morais [1]

Affiliations + expand

PMID: 31778407 PMCID: PMC6909257 DOI: 10.1590/1984-0462/2020/38/2018123

Free PMC article

- Systematic review in children
- 2019
- Some benefits: abdominal pain, stool consistency, bowel frequency
- Bottom line: evidence still insufficient to recommend routine use

Effectiveness of Probiotics in Children With Functional Abdominal Pain Disorders and Functional Constipation: A Systematic Review

Carrie A M Wegh [1] [2], Marc A Benninga [2], Merit M Tabbers [2]

Affiliations + expand

PMID: 29782469 DOI: 10.1097/MCG.0000000000001054

- Systematic review in children with functional constipation or functional abdominal pain
- 2018
- *Lactobacillus rhamnosus* GG (Culturelle): reduction in abdominal pain in children with IBS
- Bottom line: insufficient evidence for use in functional constipation

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Reference: Wegh, Benninga, Tabbers. J Clin Gastroenterol. Dec 2018. PMID 29782469

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Fiber – Water Soluble

Start with:

- <5yo 1g BID
- >5yo 2g BID

Pectin (Sure-Jell)

- 1 Tbsp = 2g
- 2 capsules = 1g
- 1 gummy = 2g

Wheat Dextrin (Benefiber)

- 2tsp = 3g
- 1 chew = 1g

Methylcellulose (Citrucel)

- 1 Tbsp = 2g
- 2 caps = 1g

Psyllium (Metamucil)

- 1tsp = 2g
- 5 caps = 2g
- 2 wafers = 6g
- 1 bar = 3g

Nutrisource (expensive but no taste)

- 1tsp = 1 g
- 1 Tbsp = 3g

Question 7: What is the most effective and safest pharmacologic treatment in children with functional constipation?

Best medication for fecal disimpaction (clean out)?

- Polyethylene glycol and enemas equally effective

Best medication for maintenance?

- Polyethylene glycol or lactulose
- Enema use discouraged long term

How long should you treat for?

- Minimum of 2 months (expert opinion only)
- Symptoms resolved for 1 month
- Gradually come off laxatives

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

TABLE 6. Dosages of most frequently used oral and rectal laxatives

Oral laxatives	Dosages
Osmotic laxatives	
Lactulose	1–2 g/kg, once or twice/day
PEG 3350	Maintenance: 0.2–0.8 g · kg^{-1} · day^{-1}
PEG 4000	Fecal disimpaction: 1–1.5 g · kg^{-1} · day^{-1} (with a maximum of 6 consecutive days)
Milk of magnesia (magnesium hydroxide)	2–5 y: 0.4–1.2 g/day, once or divided
	6–11 y: 1.2–2.4 g/day, once or divided
	12–18 y: 2.4–4.8 g/day, once or divided
Fecal softeners	
Mineral oil	1–18 y: 1–3 mL · kg^{-1} · day^{-1}, once or divided, max 90 mL/day
Stimulant laxatives	
Bisacodyl	3–10 y: 5 mg/day
	>10 y: 5–10 mg/day
Senna	2–6 y: 2.5–5 mg once or twice/day
	6–12 y: 7.5–10 mg/day
	>12 y: 15–20 mg /day
Sodium picosulfate	1 mo–4 y: 2.5–10 mg once/day
	4–18 y: 2.5–20 mg once/day
Rectal laxatives/enemas	
Bisacodyl	2–10 y: 5 mg once /day
	>10 y: 5–10 mg once /day
Sodium docusate	<6 y: 60 mL
	>6 y: 120 mL
Sodium phosphate	1–18 y: 2.5 mL/kg, max 133 mL/dose
NaCl	Neonate <1 kg: 5 mL, >1 kg: 10 mL
	>1 y: 6 mL/kg once or twice/day
Mineral oil	2–11 y: 30–60 mL once/day
	>11 y: 60–150 mL once/day

PEG = polyethylene glycol.

Polyethylene Glycol 3350 With Electrolytes Versus Polyethylene Glycol 4000 for Constipation: A Randomized, Controlled Trial

*Noor L.H. Bekkali, *Daniël R. Hoekman, *Olivia Liem, *Marloes E.J. Bongers, *Michiel P. van Wijk, †Bas Zegers, ‡Rolf A. Pelleboer, §Wim Verwijs, *Ba[illegible], ||Maksym Voropaiev, and *Marc A. Benninga

Efficacy and safety of pharmacological therapies for functional constipation in children: a systematic review and meta-analysis

Anna de Geus*, Morris Gordon*, Vassiliki Sinopoulou, Aderonke Ajiboye, Alexander J Thornton, Shiyao Liu, Daniel Arruda Navarro Albuquerque, Marc A Benninga, Merit M Tabbers

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Article

Safety of Polyethylene Glycol 3350 for the Treatment of Chronic Constipation in Children

Dinesh S. Pashankar, MD, MRCP; Vera Loening-Baucke, MD; Warren P. Bishop, MD

» Author Affiliations | Article Information

Utilisation and Safety of Polyethylene Glycol 3350 With Electrolytes in Children Under 2 Years–A Retrospective Cohort

*†Debabrata Roy, ‡Fatma Akriche, §Bharat Amlani, and *†Saad Shakir

Which class do the guidelines recommend?

Try a stool softener or osmotic agent

Try a stimulant laxative

- Some children may require a combination of osmotic agent + stimulant laxative
- Close follow up is recommended to ensure that the regimen is working for the child

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Goals of treatment

- Pass 1-2 soft stools daily

- Allow rectal vault to approach normal size
  - May take months – years to occur
  - Staying on a regular bowel regimen will help the rectum to shrink back down
  - Imaging **NOT** needed to ensure that the rectum has shrunk back down

- **Not a quick fix!**
  - Set the expectation that troubleshooting will be involved
  - Most require treatment for many months before stopping

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Question 7: What is the most effective and safest pharmacologic treatment in children with functional constipation?

- What do you do if you suspect a fecal impaction?

Clean Out Regimen Options *(Goal: transparent liquid stools without sediment)*

Option 1:	*Enemas Only:*	Age < 2 y/o: Peds Fleets enema daily x 3 days; Age > 2 y/o: Adult fleets enema daily x 3 days; may need 1-2 additional days
Option 2:	*Enemas + Miralax*:	Mineral oil enema, Fleets enema followed by Miralax q 30 min to 1 hour for 4 hours
Option 3:	*Oral laxatives only*:	8 am to 8 pm, clear liquid diet (eat BF before 8 am, dinner after 8 pm) 0800 and 2000: dulcolax/senna + miralax; 1000, noon, 1400, 1600, 1800: miralax only (**max of 2 consecutive days)*
Option 4:	*Oral laxatives only*:	Senna + Miralax + Senna (over 2 hours). 1 day only

Question 8: What is the efficacy and safety of novel therapies for children with intractable constipation?

The Use of Linaclotide in Children with Functional Constipation or Irritable Bowel Syndrome: A Retrospective Chart Review

Desiree F. Baaleman[1,2] · Shivani Gupta[1] · Marc A. Benninga[2] · Neetu Bali[1] · Karla H. Vaz[1] · Desale Yacob[1] · Carlo Di Lorenzo[1] · Peter L. Lu[1]

Secretagogues

Linaclotide (guanylate cyclase-C receptor agonist) – FDA approved 6-17yo

- Increases intestinal fluid secretion
- Accelerates intestinal transit
- Decreases visceral pain

Baaleman DF, Gupta S, Benninga MA, Bali N, Vaz KH, Yacob D, Di Lorenzo C, Lu PL. The Use of Linaclotide in Children with Functional Constipation or Irritable Bowel Syndrome: A Retrospective Chart Review. Paediatr Drugs. 2021 May;23(3):307-314. doi: 10.1007/s40272-021-00444-4. Epub 2021 Apr 20. PMID: 33876403; PMCID: PMC8119400.

Table 2 Outcomes of patients with functional constipation (FC)

	Baseline ($N=60$)	Initial follow-up ($N=60$)	Long-term follow-up ($N=15$)
Time after start linaclotide in months, median (IQR)	n/a	2.5 (0.9–3.9)	17 (15–25)
Used medication until follow-up, *n* (%)	n/a	50 (83%)	14 (93%)
Overall improvement of symptoms, *n*/*N* (%)[a]	n/a	27/50 (54%)	13/14 (93%)
Symptoms[b]			
Constipation, *n*/*N* (%)	40/48 (83%)	17/32 (64%)*	2/12 (17%)
BM frequency per week, median (IQR)[c]	4 (2–7)	7 (7–7)*	7 (7–7)
Abdominal pain, *n*/*N* (%)	23/38 (61%)	14/30 (47%)	5/12 (42%)
Fecal incontinence, *n*/*N* (%)	14/38 (37%)	11/30 (22%)	0/10 (0%)
Painful/hard bowel movements, *n*/*N* (%)	13/27 (22%)	7/24 (14%)	0/9 (0%)
Decision at follow-up encounter	n/a		
Continue current dose of linaclotide, *n* (%)		36 (60%)	12 (80%)
Increase linaclotide dose, *n* (%)		7 (12%)	2 (13%)
Decrease linaclotide dose, *n* (%)		1 (1.7%)	0 (0%)
Stop linaclotide, *n* (%)		16 (27%)	n/a
Because of side effects, *n* (%)		11 (69%)	
Because no effect on symptoms, *n* (%)		5 (31%)	
Because of switch to lubiprostone, *n* (%)		1 (1.7%)	

*p Value <0.05 compared with baseline

[a] Includes only patients who used medication until follow-up

[b] Includes only patients who used medication until follow-up and specifically reported details about the given symptom

[c] BM: bowel movement; $n=34$, $n=23$, $n=9$, respectively

Question 9: What is the prognosis and what are prognostic factors in children with functional constipation?

- General
  - ~80% of children treated early will be laxative free by 6 months
  - ~32% (if treatment is delayed)
  - 50-60% recovery rate after 1 year of intensive treatment

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

Question 9: What is the prognosis and what are prognostic factors in children with functional constipation?

- After GI referral
  - 50% will recover (defined as having 3 bowel movements per week without fecal incontinence) and be without laxatives after 6 to 12 months
  - 40% will still be symptomatic despite use of laxatives
  - 10% will do well but remain on laxatives

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

Question 9: What is the prognosis and what are prognostic factors in children with functional constipation?

- Prognostic factors?
  - No real evidence to identify strong prognostic factors (positive or negative)
  - In general, patients with duration of symptoms <3 months before presentation do better long term

Reference: Tabbers et al. J Pediatr Gastroenterol Nutr. 2014. PMID 24345831

When to refer?

- Red flags present
- Initial management attempts have come up short
- Patient with comorbidities (cerebral palsy, poor mobility/motility, genetic syndromes, non verbal, phobias with using the toilet, etc.)
- Family request
- You are just worried

Final Reminders!

- Do not be afraid of stimulant laxatives!
- Polyethylene glycol is safe!
- Do not use abdominal x-rays to diagnose functional constipation!

Thank You!