

- Persistent unexplained change in bowel habits
- Involuntary weight loss
- Palpable mass in the lower right abdomen or the pelvis
- Persistent rectal bleeding without anal symptoms / positive FIT
- Iron deficiency anemia
- Narrowing of stool calibre
- Family history of colon cancer, or inflammatory bowel disease
- Severe, persistent constipation that is unresponsive to treatment
- Acute onset, not passing flatus (eg bowel obstruction)

**"I'm constipated!"**

**HISTORY & PHYSICAL**  
Consider abdo exam, DRE

**ROME IV criteria for functional (chronic) constipation:**

1. Two or more of the following over past 3 months:
    - Fewer than 3 spontaneous defecations per week
    - Straining
    - Lumpy or hard stools
    - Sensation of anorectal obstruction
    - Sensation of incomplete evacuations
    - Manual maneuvers to defecate
  2. Loose stools are rarely present without laxatives
  3. Insufficient criteria for IBS
- At least 25% of the time**

**IBS-C**

**REFER OR INVESTIGATE**

RED FLAGS

**INVESTIGATE: MANOMETRY, BALLOON EXPULSION**

**CHRONIC CONSTIPATION**

**STOP CONSTIPATING MEDICATIONS**

**Rx CAUSING CONSTIPATION:**

- Calcium Channel Blockers,
- Calcium, Iron, Aluminum-antacids; Multivits w minerals
- NSAIDs
- Opiates
- Diuretics
- Antidiarrheals, resins, bismuth
- Anticholinergics, eg. anti-histamines, antidepressants
- Antiemetics, eg. ondansetron
- Anticonvulsants and antipsychotics
- Antiparkinsons medications

NEGATIVE: Normal Colonic Transit

UNDERLYING CAUSE?

**Dx: PELVIC FLOOR DYSFUNCTION aka DEFACATORY DISORDER**

**Dx: SLOW COLONIC TRANSIT**

**Dx: FUNCTIONAL/ IDIOPATHIC**

**Dx: SECONDARY or ORGANIC**

**TREAT COMORBID CONDITION eg. hypothyroidism**

**X STOOL SOFTENERS eg. docusate**

**FIBER, EXERCISE, WATER**

CAN'T TREAT/ REFRACTORY CAUSE

**Dx: OPIATE INDUCED**

**REFER OR INVESTIGATE**

**OSMOTIC LAXATIVES eg. polyethylene glycol, lactulose**

**OPIATE REVERSAL AGENTS "PAMORAs" eg. methylnaltrexone**

NOT IMPROVING

**STIMULANT eg. senna, bisacodyl**

**CHLORIDE CHANNEL ACTIVATORS eg. lubiprostone**

**5HT4A-ANTAGONISTS eg. tegaserod, prucalopride**

**GUANYL-CYCLASE-C AGONISTS eg. linaclotide**

**SUPPOSITORIES ENEMAS DISIMPACTIION**

**CONSIDER SURGERY**

**Dr J Otte (MD, CCFP)'s conceptual framework for management of chronic and opiate-induced constipation**  
jessica.otte@ti.ubc.ca

Therapy - examples	Mechanism	Usual/Severe Side Effects	Cost	Efficacy (increasing number of patients who have ≥ 3 complete spontaneous bowel movements/wk; other measures described)	LOE
<b>Water</b> – H <sub>2</sub> O	?			<b>LIMITED:</b> unless dehydration is present (in elders in LTC)	III <sup>1 2</sup>
<b>Biofeedback</b> (relax anus while pushing intraabd. to extrude balloon w sensors)	Retraining control of anorectum	Invasive, requires diagnostics, not readily available	MSP vs private \$\$\$	<b>MAYBE:</b> Might improve psych/clinical outcome measures in pelvic floor dysfunction; wide diversity in protocols.  Insufficient evidence: low quality, biased, short term studies	IB <sup>3</sup>  IA <sup>4</sup>
<b>Positioning</b> – feet up (eg. Squatty Potty™)	Allows structurally easier transit of stool		\$	<b>MAYBE:</b> increased bowel emptiness, reduced straining patterns, but ?funding, small N, short time (2wks), cross-over study	IIB <sup>5</sup>
<b>Exercise</b>	?Magic; ^ peristalsis by increasing HR/RR			<b>LIMITED:</b> One small RCT & some case-control studies: decreased constipation (self-report or Rome criteria); other studies: no effect. Review of 9 RCTs in China: may improve “symptoms” but LOW quality	IIA <sup>3</sup>  IA <sup>6</sup>
<b>Soluble Dietary Fiber, Bulk-forming Agents</b> (psyllium [Metamucil], inulin [Benefibre] calcium polycarbophil, methylcellulose, prunes, etc.)	Expand with water, increase bulk of the stool, thereby increasing frequency  * <b>NOT</b> for slow colonic transit (eg elders) or OIC	Require adequate fluid to act. Dose-dependent bloating, gas. Risk of bowel obstruction.	\$	<b>PROBABLY, IF LOW FIBRE DIET:</b> 3RCTs psyllium > placebo; 1 RCT methylcellulose > placebo; 2 RCT prunes ~ = psyllium in ‘validated questionnaires’; mixed data on straining, # spont BMs/wk, consistency  Prospective cohort of women: higher fiber (20 g/d vs 7 g/d) reduced self-reported constipation, but other studies did not show this. Fiber may help if diet is deficient. One RCT: psyllium more effective than docusate	IB <sup>3</sup>  IB <sup>7</sup>  IB <sup>8</sup>
<b>Stool Softeners</b> (docusate [Colace], mineral oil)	Detergent effect, lowers surface tension at interface, allows water to soften the stool	Bitter taste, nausea. Aspiration of mineral oil → lipid pneumonia	\$	<b>PROBABLY NOT:</b> No study comparing docusate efficacy against placebo. No effect on stool weight, transit time. Inferior to psyllium.  1 Sys review: small effect on stool frequency in chronically ill, but overall quality of evidence was poor.	IA <sup>9</sup> IB <sup>10</sup>  IA <sup>3</sup>
<b>Osmotic Agents</b> (PEG [Lax-a-Day, RestoraLax], lactulose, sorbitol, Mg-OH, glycerin PR)	Hyperosmolar, non-absorbable molecule so adsorb, retain water thereby facilitating stool passage	Diarrhea, nausea, flatulence, dehydration. Rare: electrolyte disturbances.	\$\$ [* PEG not on Plan P]	<b>YES,</b> of osmotic agents, PEG best combo of effective/tolerated: PEG increased frequency of stools relative to placebo (high-quality studies: additional 2.34 stools/week) Retrospective data suggests enduring efficacy of PEG to at least 24mos  PEG better tolerated (no taste). ?Less cramping with milk of magnesia but lower efficacy; PEG more effective than lactulose in terms of need for additional products, stool frequency & form, and relief of abdo pain; mostly peds data but adult subgroup analysis consistent	IA <sup>11</sup>  IB <sup>12</sup>  IA <sup>13</sup> IA <sup>14</sup>

Dr J Otte (MD, CCFP)'s **Summary of Therapeutics for Management of Chronic Constipation** – [Jessica.Otte@ti.ubc.ca](mailto:Jessica.Otte@ti.ubc.ca) – March 2020

<b>Stimulants</b> (senna [Sennakot], Bisacodyl [Dulcolax, Ex-Lax, sodium picosulphate, cascara])	Stimulate myenteric plexus → increases peristalsis; decreased transit time means decreased water absorption	Cramping, rare electrolyte imbalance. NO link between senna & colon Ca or damage to myenteric plexus	\$	<p><b>YES, senna effective as adjuvant; Bisacodyl works but poorly tolerated.</b> In network meta-analysis, bisacodyl and sodium picosulfate ranked best at 4 wks BUT Bisacodyl most likely to cause adverse events.</p> <p>No known high-quality study comparing senna vs placebo; 3+ RCTs compared senna with another laxative: groups receiving senna fared better than comparison.</p> <p>1 large RCT of Bisacodyl vs placebo : increase of 4.3 BMs/wk, better QoL</p>	IA <sup>15</sup>   IA <sup>3</sup>  IB <sup>16</sup>
<b>Chloride Channel Activator</b> (lubiprostone [Amitiza])	↑GI fluid by stim Type 2 Cl <sup>-</sup> channels in GI epithelium apical membrane	Nausea, diarrhea, headache, may “reduce pain/bloating”	\$\$\$ [not on BC Form]	<p><b>YES:</b> 3 RCTs: increased spontaneous bowel movements and improved self-reported symptoms of chronic constipation.</p> <p>In opiate-induced constipation, NNT = 15 (95% CI, 9–51)</p>	IA <sup>3</sup> I  IA <sup>17</sup>
<b>Guanylate Cyclase-c Receptor Agonist</b> (linaclotide [Constella])	↑GI fluid via cystic fibrosis transmembrane conductance channel & desensitizes pain fibers via guanylate cyclase C	Diarrhea, abdominal pain, flatulence, headache. <b>BLACK BOX:</b> Death due to dehydration in neonatal mice.	\$\$\$\$ [no coverage, not on Plan P]	<p><b>YES:</b> Compared with placebo (n = 1582) showed a smaller risk for therapy failure</p> <p>Insufficient evidence to support use in OIC</p>	IA <sup>3</sup>  IIB <sup>18</sup>
<b>5-Hydroxy-Tryptamine Receptor 4 Agonists</b> (tegaserod [Zelnorm], prucalopride [Resotran] more selective for gut)	Binds to 5-HT <sub>4</sub> receptors, stimulating GI peristalsis and increasing motility	Headache, nausea, diarrhea. FDA removed tegaserod in 2008 (re: CV risks) but restored 2019 for low risk women	\$\$\$\$ prucalopride [no coverage, not on Plan P]	<p><b>YES:</b> Stool frequency was increased with prucalopride vs placebo 6 short RCTs +ve, 1 RCT at 24wks -ve. In IBS, modest improvements in stool frequency with tegaserod; clinical significance unclear. Tegaserod may alter visceral sensitivity (part of pathophysiology of IBS)</p> <ul style="list-style-type: none"> <li>- Prucalopride ranked 1<sup>st</sup> in network meta-analysis for 3 SBMs/wk                             <ul style="list-style-type: none"> <li>• at 24 weeks prucalopride = placebo...</li> </ul> </li> </ul> <p>Insufficient evidence to support use in OIC</p>	IA <sup>3</sup> IA <sup>13</sup>  IA <sup>19</sup>  IA <sup>15</sup>
<b>Peripherally Acting μ-Opioid Receptor Antagonists (“PAMORAs”)</b> - Naloxegol [Movantik] PO - Methylnaltrexone (SQ) [Relistor]	Release bound opioids from μ-Opioid receptors in GI tract	Diarrhea, abdominal pain, flatulence. No opiate reversal. More flatulence, dizziness with methylnaltrexone in palliative patients vs other laxatives. <sup>20</sup> + risk of bowel perforation. No increase in rates of serious ADEs <sup>21</sup>	\$\$\$\$  \$\$\$\$ methylnaltrexone  [no coverage, not on Plan P]	<p><b>YES:</b> In opiate-induced constipation (OIC) Network Meta-analysis, significant heterogeneity: Naloxegol NNT=7, methylnaltrexone, NNT=3.4, naloxone NNT=4 to achieve ≥ 3SBMs/wk or increase of ≥1BM/wk vs baseline; *Naloxone most effective &amp; safest BUT not only peripherally acting (so reverses analgesia!).</p> <p>All laxatives [even non-PAMORAs] have similar effectiveness; limited due to insufficient data from few, small RCTs. No studies on PEG in OIC, no RCTs comparing traditional laxatives vs PAMORAs.</p> <p>*Best reserved for patients for whom other laxatives haven't worked → naldemedine: N/A yet but 52wk efficacy data (not for other PAMORAs)</p>	IA <sup>22</sup>      IA <sup>23</sup> , 24,17  IIB <sup>18</sup>

