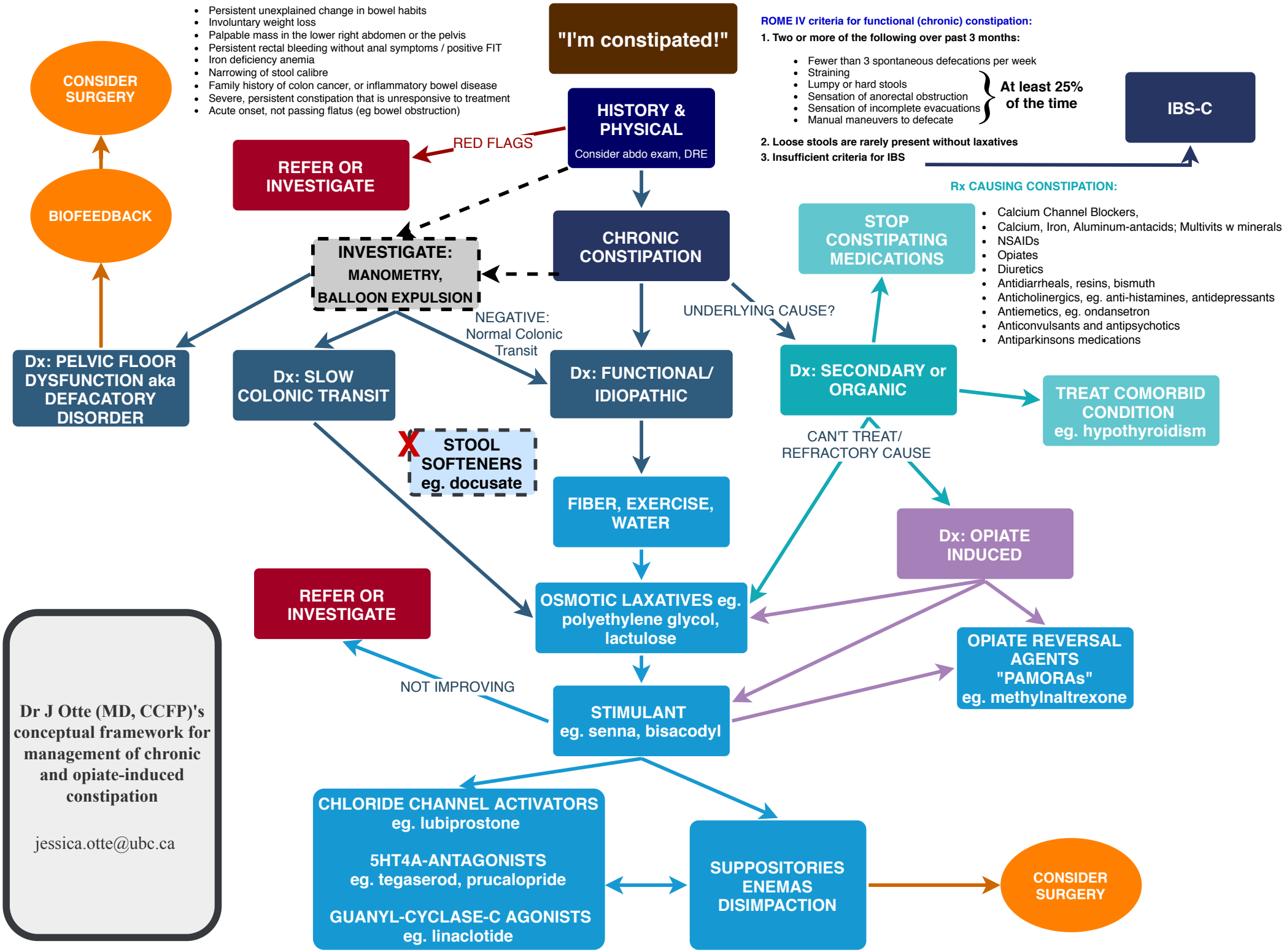
"I'm constipated!"
HISTORY & PHYSICAL
Consider abdo exam, DRE
RED FLAGS
REFER OR INVESTIGATE
Persistent unexplained change in bowel habits
Involuntary weight loss
Palpable mass in the lower right abdomen or the pelvis
Persistent rectal bleeding without anal symptoms / positive FIT
Iron deficiency anemia
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)
CONSIDER SURGERY
BIOFEEDBACK
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
At least 25% of the time
2. Loose stools are rarely present without laxatives
3. Insufficient criteria for IBS
IBS-C
CHRONIC CONSTIPATION
INVESTIGATE: MANOMETRY, BALLOON EXPULSION
NEGATIVE: Normal Colonic Transit
UNDERLYING CAUSE?
Rx CAUSING CONSTIPATION:
STOP CONSTIPATING MEDICATIONS
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
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
CAN'T TREAT/ REFRACTORY CAUSE
FIBER, EXERCISE, WATER
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 DISIMPACTION
CONSIDER SURGERY
Dr J Otte (MD, CCFP)'s conceptual framework for management of chronic and opiate-induced constipation
jessica.otte@ubc.ca

Dr J Otte (MD, CCFP)'s ***Summary of Therapeutics for Management of Chronic Constipation*** *– Jessica.Otte@ubc.ca – May 2021*

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
Water – H_2O	?			**LIMITED:** unless dehydration is present (in elders in LTC)	III[1 2]
Biofeedback (relax anus while pushing intraabd. to extrude balloon w sensors)	Retraining control of anorectum	Invasive, requires diagnostics, not readily available	MSP vs private $$$	**MAYBE:** Might improve psych/clinical outcome measures in pelvic floor dysfunction; wide diversity in protocols. Insufficient evidence: low quality, biased, short term studies	II[3] I[4]
Positioning – feet up (eg. Squatty Potty™)	Allows structurally easier transit of stool		$	**MAYBE:** increased bowel emptiness, reduced straining patterns, but ?funding, small N, short time (2wks), cross-over study	III[5]
Exercise	?Magic; ^ peristalsis by increasing HR/RR			**LIMITED:** 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	II[3] II[6]
Soluble Dietary Fiber, Bulk-forming Agents (psyllium [Metamucil], inulin [Benefibre] calcium polycarbophil, methycellulose, prunes, etc.)	Expand with water, increase bulk of the stool, thereby increasing frequency * **NOT** for slow colonic transit (eg elders) or OIC	Require adequate fluid to act. Dose-dependent bloating, gas. Risk of bowel obstruction.	$	**PROBABLY, IF LOW FIBRE DIET**: 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	II[3] III[7] II[8]
Stool Softeners (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	$	**PROBABLY NOT:** 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.	I[9] II[10] I[3]
Osmotic Agents (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]	**YES,** 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	I[11] III[12] I[13] I[14]

Stimulants (senna [Sennakot], Bisacodyl [Dulcolax, Ex-Lax, sodium picosulphate, cascara])	Stimulate myenteric plexus → increases peristalsis; decreased transit time means decreased water absorption	Cramping, rare elyte imbalance. NO link between senna & colon Ca or damage to myenteric plexus	$	**YES, senna effective as adjuvant; Bisacodyl works but poorly tolerated.** In network meta-analysis, bisacodyl and sodium picosulfate ranked best at 4 wks BUT Bisacodyl most likely to cause adverse events. No known high-quality study comparing senna vs placebo; 3+ RCTs compared senna with another laxative: groups receiving senna fared better than comparison. 1 large RCT of Bisacodyl vs placebo : increase of 4.3 BMs/wk, btter QoL	I[15] I[3] II[16]
Chloride Channel Activator (lubiprostone [Amitiza])	^GI fluid by stim Type 2 Cl^- channels in GI epithelium apical membrane	Nausea, diarrhea, headache, may "reduce pain/ bloating"	$$$ [not on *BC Form*]	**YES:** 3 RCTs: increased spontaneous bowel movements and improved self-reported symptoms of chronic constipation. In opiate-induced constipation, NNT = 15 (95% CI, 9–51)	I[3] I[17]
Guanylate Cyclase-c Receptor Agonist (linaclotide [Constella])	^GI fluid via cystic fibrosis transmbr conductance channel & desensitizes pain fibers via guanylate cyclase C	Diarrhea, abdo pain, flatulence, headache. **BLACK BOX:** Death due to dehydration in neonatal mice.	$$$$ [no coverage, not on Plan P]	**YES:** Compared with placebo (*n* = 1582) showed a smaller risk for therapy failure Insufficient evidence to support use in OIC	I[3] II[18]
5-Hydroxy-Tryptamine Receptor 4 Agonists (tegaserod [Zelnorm], prucalopride [Resotran] more selective for gut)	Binds to 5-HT4 receptors, stimulating GI peristalsis and increasing motility	Headache, nausea, diarrhea. FDA removed tegaserod in 2008 (re: CV risks) but restored 2019 for low risk women	$$$$ prucalopride [no coverage, not on Plan P]	**YES:** Stool frequency was increased with prucalopride vs placebo 6 short RCTs +ve, 1 RCT at 24wks -ve. In IBS, modest improvements in stool frequency with tegaserod; clinical significance unclear. Tegaserod may alter visceral sensitivity (part of pathophysiology of IBS) - Prucalopride ranked 1st in network meta-analysis for 3 SBMs/wk • at 24 weeks prucalopride = placebo… Insufficient evidence to support use in OIC	I[3] I[13] I[19] I[15]
Peripherally Acting μ-Opioid Receptor Antagonists ("PAMORAs") - Naloxogel [Movantik] PO - Methylnaltrexone (SQ) [Relistor]	Release bound opioids from μ-Opioid receptors in GI tract	Diarrhea, abdo pain, flatulence. No opiate reversal. More flatulence, dizziness with methylnaltrexone in pall patients vs other laxatives.[20] + risk of bowel perf. No incr in rates of serious ADEs[21]	$$$$ $$$$$ methylnaltrexone [no coverage, not on Plan P]	**YES:** In opiate-induced constipation (OIC) Network Metanalysis, 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 & safest BUT not only peripheral acting (so reverses analgesia!). 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. *Best reserved for patients for whom other laxatives haven't worked → naldemedine: N/A yet but 52wk efficacy data (not for other PAMORAs)	I[22] I[23,24,17] II[18]

Enemas eg. micro-lax, sodium phosphate [Fleet], et cetera	Mechanically expand colon. Some contain electrolytes/oncotic agents to prevent absorption of water; Hyperosmotic variants draw water.	Invasive, diarrhea, anal leakage. Risk of bowel perforation.	$$ (+ system costs)	**MAYBE:** Patients who received osmotic laxative + rectal stimulant + weekly enema vs osmotic laxative: more complete rectal emptying. Enemas: One RCT,1 three non-randomized studies, all paeds popl[n]: Enema vs PEG: significantly improved symptoms relative to PEG in days 1-3, but no diff day 5. Children who received an enema were significantly more likely to revisit the ED than those who did not. NICE: option for cases in which all oral medications have failed	II[25] V[26]

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