ALGORITHM FOR THE MANAGEMENT OF CHRONIC CONSTIPATION

An internationally recognised algorithm is at the end of this document. Coloured boxes next to text relate to those on the algorithm.

DIAGNOSIS

Symptoms should be present for at least 6 months

Key symptoms:

- Straining
- Lumpy or hard stools (Bristol Stool Form Scale type 1 or 2)
- Sensation of incomplete evacuation
- Sensation of ano-rectal obstruction/blockage
- Manual manoeuvres needed to facilitate defaecation
- Fewer than 3 bowel movements per week

Note: Frequent episodes of diarrhoea need further investigation unless laxative induced.

Alarm Symptoms - Need for colonoscopy

- Rectal bleeding in the absence of documented bleeding haemorrhoids or anal fissures
- Unintentional weight loss (>10% in 3 months)
- Change in bowel habit in patient >40yrs
- Patient > 50yrs and no recent imaging
- Patient 40-50yrs with strong family history of cancer or IBD and no recent imaging

LAXATIVE USE

The belief that long term laxatives may damage the bowel (cathartic colon) is not supported by contemporary evidence. In addition there is no increase in colon cancer from chronic laxative use. Long term laxative use may be necessary and should be regarded as safe.

The evidence base for laxative use is poor, with only a handful of randomised control trials, and very few comparative or long term trials. Efficacy between patients varies in an unpredictable way, and even within a single individual efficacy may vary over time due to changes in colonic bacterial flora. The most appropriate laxative for each patient is best determined through trial and error, taking into consideration response, patient preference, ease of use and cost. Some patients have relatively refractory constipation, and combinations of laxatives may be necessary.

There is RCT evidence for the use of lactulose in chronic constipation. Exacerbation of wind/bloating may limit usefulness.

Polyethylene glycol (macrogol) has been shown to be effective in RCTs, and also superior to lactulose. Long-term data are also available supporting its use.

Short term studies have confirmed efficacy of both bisacodyl and senna.

Sodium Docusate is a stool softener with some evidence of efficacy in chronic constipation. It is most useful in combination with other laxatives in refractory cases.

Enemas should be used if rectum is loaded (following PR exam), but in chronic constipation the impaction is usually proximal and enemas may be of limited use.

MANAGEMENT OF CHRONIC CONSTIPATION - DISPELLING THE MYTHS

Is chronic constipation best treated by increasing dietary fibre? ***Not always***

The evidence for increasing fibre intake in the management of chronic constipation is limited and conflicting. Symptom severity does not depend solely on dietary fibre intake. An adequate fibre intake is considered to be 21-25g / day. Fibre based laxatives can be used where dietary fibre intake is known to be poor. It is important to have an adequate fluid intake (1500 – 2000mls per day) before increasing fibre. *Those patients with severe constipation may experience worsening symptoms, such as increased bloating and flatulence with increased fibre.* Primary dysmotility/disordered defecation may explain the poor outcome.

Will increasing fluid intake improve chronic constipation? ***Not always***

The evidence supporting the benefits of increasing fluids in the management of chronic constipation is conflicting. In one study, a significantly reduced fluid intake (from 2.5 L/day to 0.5 L/day for 1 week) led to decreased stool frequency and stool weight in healthy volunteers. However, increasing fluid intake by 2L per day did not affect stool output in healthy volunteers. It is unclear whether fluid improves the effect of fibre on chronic constipation. *Increasing fluids may be more relevant if patients are dehydrated or drinking less than 0.5 L/day.*

Is increasing physical activity beneficial for alleviating chronic constipation? ***Unlikely***

There is no firm link between exercise and improvements in chronic constipation. Prolonged physical inactivity in healthy individuals was shown to slow colonic transit. In another study, chronic constipation was not improved after an extra hour of physical activity daily for 6 weeks. In elderly patients several factors may co-exist, including reduced physical activity, which can lead to constipation. *Moderate exercise should be encouraged because it promotes physical and mental health and wellbeing, and may help relieve feelings of bloating.*

Does a long residence of stools in the colon lead to autointoxication? ***No***

There is no evidence to substantiate the theory that poisonous substances are absorbed by the colon and give rise to diseases.

DRUGS USED ON SPECIALIST INITIATION OR RECOMMENDATION

Prucalopride (selective 5-HT_4 receptor agonist) 2mg daily

Prucalopride is a prokinetic (not a laxative) which improves whole gut motility. The mode of action is different to laxatives; it causes the release of acetylcholine in the gastro-intestinal (GI) tract and this stimulates GI motility. It affects both stool consistency and frequency by accelerating transit through the stomach, ileum and colon, relieving constipation.

It is licensed for use in adults with chronic constipation for whom treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and invasive treatment is being considered.

Pruclaopride is a **Green+ drug** on the County Durham & Darlington Formulary and can only be recommended by a specialist for initiation in primary care; or be initiated by a specialist and transferred to primary care once the patient stabilised.

Start elderly patients on 1mg initially. See BNF for dosage in altered physiology. Patients who are pregnant, or trying to conceive, should not take prucalopride.

Side effects are common but often mild and transient. Include: headache, nausea, abdominal cramps, and dizziness. If side-effects are troublesome the dose can be reduced to 1mg daily.

Prucalopride is absorbed systemically but metabolised very slowly so the potential to interact with other drugs is very low. Time to onset of action of a single dose (2mg) is approximately 3 hours. It should be taken for approximately 1 week before determining effectiveness.

Within the Durham Constipation Clinic (DCC), prucalopride is used for functional constipation. It is effective in around 50% of patients and in refractory cases concomitant laxative use may also be necessary. It is not uncommon to see a loss of efficacy after an initial improvement, there is rarely benefit in increasing the dose or persevering with treatment if there is no improvement within the first month.

Lubiprostone (chloride channel activator), 24 micrograms twice daily

Lubiprostone is a chloride-channel (ClC-2) activator that acts in the gut. It increases intestinal fluid secretion and this increases gut motility.

It is licensed for chronic idiopathic constipation in adults who fail to respond to lifestyle changes and where treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and invasive treatment is being considered. In the first instance a 2-4 week course is recommended, which may promote bowel emptying and greater responsiveness to laxatives. NICE TA318 recommends review of effectiveness after 2 weeks and discontinuation if response is inadequate. In some patients recurrent courses may be required.

Lubiprostone is a **Green+ drug** on the County Durham & Darlington Formulary and can only be recommended by a specialist for initiation in primary care; or be initiated by a specialist and transferred to primary care once the patient stabilised.

No dosage changes are required for elderly patients. See BNF for dosage in altered physiology. Patients who are pregnant, or trying to conceive, should not take lubiprostone.

Lubiprostone acts locally within the intestinal tract, is rapidly metabolised and has very low systemic bioavailability so the risk of drug interactions and adverse effects are low. Time to onset of action of a single dose (24micrograms) is approximately 1 hour, lasting up to approximately 7 hours.

Most common side-effects are nausea (take with food to reduce this) and diarrhoea and abdominal pain, which occur due to its effect on the colon. These are often mild and transient. If diarrhoea is troublesome the dose can be reduced to once daily or less often.

Within the Durham Constipation Clinic, lubiprostone is used for functional constipation.

Linaclotide (Guanylate cyclase –C receptor agonist), 290 micrograms daily

Linaclotide has a secretory action; it increases intestinal secretions and therefore accelerates gut transit time. Faeces moves more quickly through the colon, producing more spontaneous bowel movements thus relieving constipation and its associated symptoms such as abdominal pain and bloating. There is some evidence that it may reduce visceral pain through neuro-modulation.

It is licensed for moderate to severe irritable bowel syndrome with constipation (IBS-C). Treatment should be reviewed after 4 weeks and discontinued if response is inadequate.

Linaclotide is a **Green+ drug** on the County Durham & Darlington Formulary and can only be recommended by a specialist for initiation in primary care; or be initiated by a specialist and transferred to primary care once the patient stabilised.

See BNF for dosage in altered physiology. Patients who are pregnant, or trying to conceive, should not take linaclotide.

Linaclotide is not systemically absorbed and does not interact with other medication. It should be taken 30 -60 minutes before food.

The most common side-effect is diarrhoea which occurs due to its mode of action on the colon. It is usually mild to moderate in intensity and resolves within 7 days for most patients. If diarrhoea is troublesome, linaclotide can be taken less often.

Within the Durham Constipation Clinic, linaclotide is used for IBS-C and for functional constipation if prucalopride and lubiprostone have failed to produce an adequate response.

Naloxegol (mu-opioid receptor antagonist), 25mg daily

Naloxegol is a PEGylated derivative of naloxone. PEGylation reduces naloxegol's passive permeability so central nervous system (CNS) penetration is minimal. It binds to mu-opioid receptors in the gastro-intestinal (GI) tract targeting the underlying causes of opioid induced

constipation (i.e. reduced GI motility, hypertonicity and increased fluid absorption resulting from long-term opioid treatment). Naloxegol decreases the constipating effects of opioids without impacting on the analgesic effects of opioids on the CNS.

It is licensed for opioid induced constipation in adults whose constipation has not adequately responded to laxatives (opioid-induced constipation symptoms of at least moderate severity in at least 1 of the 4 stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least 1 laxative class for at least 4 days during the prior 2 weeks). It should be taken in the morning (to avoid bowel movements at night), on an empty stomach.

Naloxegol is a **Green+ drug** on the County Durham & Darlington Formulary and can only be recommended by a specialist for initiation in primary care; or be initiated by a specialist and transferred to primary care once the patient stabilised.

See BNF for dosage in altered physiology. Patients who are pregnant, or trying to conceive, should not take Naloxegol.

Naloxegol interacts with CYP3A4 inducers (e.g. carbamazepine, rifampicin, St. John's Wort) and CYP3A4 inhibitors (e.g. grapefruit juice, diltiazem, ketoconazole); see BNF for full list of interactions.

The most common side-effects are abdominal pain, diarrhoea, nausea, headache and flatulence. The majority of side-effects are mild to moderate, occur early in treatment and resolve with continued treatment.

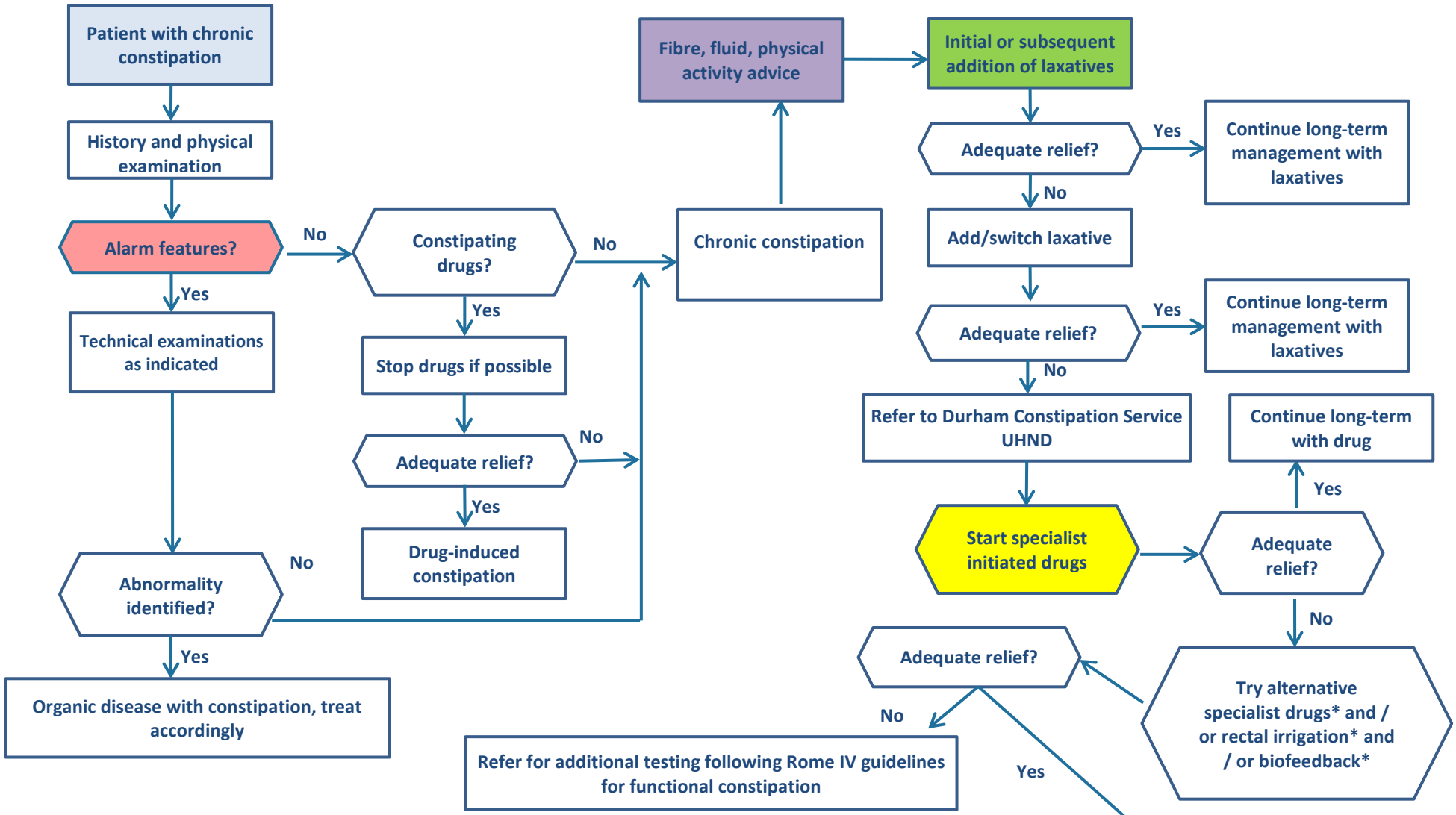
Opioid withdrawal syndrome

At therapeutic doses, there is minimal uptake of Naloxegol across the blood-brain barrier. However, some patients report symptoms of opioid withdrawal (e.g. sweating, shaking, flu like symptoms). These occur shortly after initial administration of Naloxegol and resolve when it is stopped. To avoid this patients can be started on 12.5mg daily and the dose increased to 25mg daily after 2 weeks if no adverse reactions are noted.

OTHER TREATMENTS

Biofeedback and trans-anal irrigation should be considered if the above treatments fail. There are Specialist Nurse led clinics within the Durham Constipation Service which offer these treatments.

Algorithm for chronic constipation



Author	Prof. Yan Yiannakou, Gastroenterology Consultant CDDFT
CDDFT Approval	CS&TC 10 October 2016
CDD PCT Approval	APC 03 November 2016
Date of Review	10 October 2019
Version Number	Algorithm for the management of chronic constipation V1.1

Based on Tack et al. Neurogastroenterol Motil. 2011;