

CLINICAL CARE GUIDELINES

CONSTIPATION GUIDELINES

Author and position	Dr Jane Grundy, F	Dr Jane Grundy, FY1 and Dr Emma Husbands SpR St Richard's Hospice				
Approved by	St Richard's Hospi	St Richard's Hospice, Worcester, Clinical Guidelines Committee				
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Introduction: Why Do We Need New Guidelines?

In 2007, a local audit was carried out at St Richard's Hospice, assessing documentation of constipation. 10 in-patient admissions were assessed. The average age of the patient group was 64 years (range 40-79) and all had metastatic cancer. The standards of the audit were based upon guidelines from the Solihull Marie Curie Hospice Constipation Pathway (2007) and Lothian Palliative Care Guidelines (2002). The standards were as follows:

- 1. All patients should have a detailed assessment of bowel function on admission
- 2. Bowel function should be documented daily
- 3. All patients on opioids should be prescribed regular laxatives unless there is documentation that this is not necessary

Recommendations for practice from the audit led to the current St Richard's Hospice constipation guidelines (Appendix 1). Those recommendations were:

- All patients to have a detailed assessment of bowel function on admission including: normal bowel pattern, frequency of stool, stool consistency, stool size/volume, ease of passage, presence of blood/mucous, continence
- Stool charts for all patients to be completed daily to include stool consistency, stool size/volume and ease of passage
- Routine prescription of laxatives for patients on opioids

The West Midlands Palliative Care Physicians (2007) have produced guidance on the management of constipation in palliative care, but these are not evidence-based, rather a summary of current specialist practice in the West Midlands region. Furthermore, they offer guidance and general principles rather than specific, chronological guidelines.

Interestingly, there are no guidelines for the management of constipation within Worcestershire Acute Hospitals NHS Trust, the British Society of Gastroenterology or the National Institute of Clinical Excellence (NICE).

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Definitions and Principles:

Constipation is defined as the passage of small hard faeces infrequently and with difficulty (Fallon and O'Neill (1997), Larkin *et.al.*(2008)).

More specifically, the World Gastroenterology Organisation (WGO) Practice Guidelines define constipation as 2 or more of the following in any 12 week period during the previous 12 months (Rome Criteria)(WGO (2007)):

- Fewer than 3 bowel movements per week
- Hard stool in more than 25% bowel motions
- Sense of incomplete evacuation in more than 25% of bowel motions
- Excessive straining in more than 25% bowel motions
- A need for digital manipulation to facilitate evacuation

In practice, the patient's perception and comparison of their current bowel habit and ease of passage with what they consider to be normal is a large determinant of whether or not doctors consider the patient to be constipated. ((Larkin *et al.*(2008), Miles *et al*(2006)). Thus both objective and subjective elements are important in diagnosing constipation.

Background To Constipation In Palliative Care: Why Is It Important?

About 50% of patients admitted to specialist palliative care units report constipation, but about 80% will ultimately require laxatives (Fallon and O'Neill (1997)). The majority of palliative care patients have cancer and constipation is often particularly a problem in colon and ovarian cancers. Furthermore, opioid analgesia is very often necessary in all advanced malignancies to control pain adequately (Miles *et al.*(2006)). Constipation is one of the most common side effects of opioid usage. It can be difficult to manage, particularly as tolerance does not tend to develop with regards to constipation (Benyamin *et.al.* (2008)). In some cases when it is particularly severe, opioid-related constipation can contribute to under-dosing and inadequate analgesia, and in some cases requiring an opioid-switch. (Benyamin *et.al.* (2008)).

Constipation can cause multiple unpleasant symptoms such as abdominal and rectal pain, abdominal distension, anorexia, nausea and vomiting, urinary retention, confusion and other negative effects on the patient's sense of wellbeing (Larkin *et al.* (2008), West Midlands Palliative Care Physicians (2007)). As well as physical suffering, constipation is a significant cause of psychological distress, preoccupation and agitation in terminally ill patients (Miles *et al.* (2006), (Larkin *et al.* (2008)). In some cases, treatment of constipation can provide complete relief of agitation and obviate the need for anxiolytics or sedation (Fallon and O'Neill (1997)).

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Causes of Constipation

There are many reasons why palliative care patients may develop constipation. Common causes are listed in table 1.

Table 1: Common causes of constipation in palliative care patients (Fallon and O'Neill (1997))

Associated with malignancy	Associated with debility	Drugs
Hypercalcaemia	Immobility	Opioids
Abdominal/pelvic tumour	Poor food intake	Antiemetics with anticholinergic properties
Spinal cord compression	Poor fluid intake	Anticholinergic drugs
Cauda equina syndrome		Vinca chemotherapy agents (WGO)
Depression		

Choi et. al. (2002) postulate that opioids account for a quarter of cases of constipation in terminally ill patients. Opioids cause constipation by acting upon peripheral opioid receptors (particularly mu₂ and kappa₁₋₄) to reduce bowel peristalsis and increase sphincter tone at the ileocaecal valve and the anal sphincter, thereby slowing transit and allowing increased absorption of fluid. They also decrease intestinal fluid secretions and reduce rectal sensitivity to distension. All of these actions contribute to infrequent, passage of hard stool that is difficult to pass (Choi et.al.(2002), Fallon and O'Neill (1997), palliativedrugs.com(2003)).

Existing Guidelines and Evidence For Clinical Management of Constipation In Palliative Care

There is little good quality evidence in the literature to guide management of constipation in palliative care patients.

In a recent meta-analysis by Miles *et. al.* (2006), of 212 studies identified, only 3 were of adequate methodological quality and sufficiently statistically and clinically homogeneous to be included. Between the 3 included studies, the laxatives compared lactulose, senna, co-danthromer, misrakasneham (an ayurvedic remedy) and magnesium hydroxide combined with liquid paraffin. They all demonstrated a limited level of efficacy, but a significant number of participants required "rescue laxatives". Of interest, senna plus lactulose was significantly more effective than co-danthromer, and this was the only significant difference demonstrated between the laxatives compared across the studies (Miles *et.al.*(2006)). Despite their comprehensive literature search and meta-analysis of the 3 included studies, the authors concluded that there remains insufficient randomised controlled trial data to determine the best management of constipation in palliative care (Miles *et.al.*(2006)).

A pan-European working group of physicians and nurses has recently evaluated the published evidence and produced clinical practice recommendations for the treatment of constipation in palliative care patients (Larkin *et.al.*(2008)). Due to the limited evidence in the literature, highlighted above, their key recommendations are based on expert clinical opinion, relevant research findings from other settings and best practice from the countries represented. Please see box 1.

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Box 1: Key Recommendations From the Pan-European Working Group For Management of Constipation In Palliative Care (Larkin *et.al.* (2008))

- Constipation in palliative care is fundamentally defined by the patient
- If the patient complains of constipation or defecates less than 3 times/week assessment is warranted
- A thorough patient history and physical examination are essential
- A checklist of key facts should be used to assess causative factors and impact of constipation – this assessment should be continuous throughout the patient's care
- If malignant intestinal obstruction is suspected this should be investigated by radiology
- Preventative measures such as ensuring privacy and comfort, encouraging activity and increasing fluid intake should be ongoing during the patient's care
- Generally a combination of a softener and a stimulant laxative is recommended.
- Rectal intervention should be avoided where possible, but may be necessary
 where oral medication has been unsuccessful in re-establishing a regular bowel
 pattern

The working group advocate support for the patient in determining how problematic their constipation is, and wherever possible to take a more pro-active role in the prevention and management of their constipation (Larkin *et.al.*(2008)).

They report that an accurate history should include pattern of normal bowel movement, frequency and consistency of stools, ease of passage and associated symptoms, for example nausea, vomiting, abdominal pain and distension. A history of diarrhoea should prompt investigation to rule out overflow as the cause (Larkin *et.al.*(2008), palliativedrugs.com(2003)). Furthermore, they suggest a checklist of key facts that should be established by the healthcare professional when constipation is suspected:

- Frequency and consistency of bowel movements: Is the patient continent or incontinent? When were the bowels last opened? What was the consistency of the last stool? Is there blood in the stool? Is there mucus in the stool?
- Changes in the patient's bowel pattern: Does the patient feel more constipated than normal? How characteristic of recent bowel habits was the last defecation? Is the level of straining greater than usual during defecation? Is the urge to defecate largely absent?
- Discomfort and pain: Is defecation painful? Is there discomfort during defecation? Does the patient feel a need to defecate but is unable to do so because of rectal pain or movement induced pain?
- Sensation of complete evacuation: Does the patient feel satisfied after defecation?
- How important is regular bowel movement to the patient? Does the patient have feelings of anxiety about their bowel pattern? Does constipation cause concern or worry?
- Environmental factors affecting bowel movement: Does the patient have sufficient privacy to defecate? Does the patient require assistance to get to a toilet? Does the patient feel sufficiently comfortable to defecate (Use of bedpans can cause abnormally high strain pressures, the patient can also feel

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physically unstable on a bed pan which can affect confidence and ability to defecate)?

Constipation assessment scales such as the Bristol Stool Form scale, currently in use at St Richard's Hospice and Worcestershire Royal Hospital, are considered by the working group to be useful validated tools (Larkin *et. al.*(2008)).

Possible causes for the constipation, as well as exacerbating factors should also be enquired about including drugs (particularly,but not solely opioids (please see table 1)), mobility, diet, fluids and access to a toilet (Larkin *et.al*(2008)).

Fallon and O'Neill (1997) and palliativedrugs.com emphasise the importance of the physical examination including general observation, abdominal examination and digital rectal or stomal examination.

With a presentation of constipation it is also vital to rule out the clinical emergencies of bowel obstruction and spinal cord compression. Bowel obstruction may be suspected if the history is suggestive, or from clinical signs such as abdominal distension, visible peristalsis and high-pitched or absent bowel sounds. A plain abdominal x-ray would be an appropriate next step if bowel obstruction is suspected (Fallon and O'Neill (1997)).

Spinal cord compression may be suspected if the history is suggestive, or from clinical signs such as neurological deficit, including anal tone and/or urinary problems. If spinal cord compression is suspected an urgent MRI is required (West Midlands Palliative Care Physicians (2007)).

Larkin et.al. (2008) report that a common-sense approach, encouraging patients where feasible, to take practical steps to prevent or reduce the risk of constipation through dietary measures, maintaining adequate fluid intake and encouraging appropriate exercise is part of the healthcare professional's duty of care. However, research suggests that there is a limit to the influence of these lifestyle factors upon constipation, and these factors should not be solely relied upon. Furthermore, due to the considerable intake of fluid required, reliance on dietary fibre for the relief of constipation palliative care is inappropriate (Larkin in et.al.(2008), palliativedrugs.com(2003), West Midlands Palliative Care Physicians (2007)).

The West Midlands Palliative Care Physicians (2007) recommend the prescription of regular, oral laxatives as soon as patients are commenced on opioid medications. More specifically, palliativedrugs.com(2003) recommend the commencement of codanthromer upon prescription of opioids. Although, there is very little good quality evidence and consequent uncertainty regarding which laxatives to prescribe for constipation in palliative care patients, the key recommendations, based on expert clinical opinion, relevant research findings from other settings and best practice, are to use a combination of softener and stimulant, which is also in line with the World Gastroenterology Organisation Practice Guidelines for constipation in palliative care (WGO(2007)). The ultimate choice of laxatives is made on an individual basis (CKS(2008), Larkin *et al*(2008)). If no bowel action occurs within 3 days the working group (Larkin *et al*(2008)) and palliativedrugs.com(2003) suggest that the doses of oral laxatives be titrated upward daily or on alternate days, and that adequate

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oral laxative dose titration can halve the need for rectal interventions. However, a rectal examination is still essential for determining future management at this stage. (Larkin *et.al.*(2008)).

Of interest, both the World Gastroenterology Organisation and the pan-European working party recommend increasing softener dose if colic is present (Larkin *et.al.*(2008), WGO(2007)). Furthermore, Larkin *et.al.*(2008) recommend reducing the softener and increasing the stimulant dose if faecal leakage becomes a problem. Also of clinical interest is the advice not to use danthron-containing preparations in incontinent patients because of the risk of skin irritation (Larkin *et.al.*(2008), Palliative Drugs.Com(2003)).

The final recommendation from the pan-European working group is that oral laxatives should, where possible, be used in preference to rectal measures. Rectal treatments are advised where oral measures are unsuccessful, for instance in patients who cannot tolerate or swallow oral laxatives, when there is faecal impaction or in patients with spinal cord lesions and disrupted innervation to the lower bowel (Larkin *et.al.*(2008)). The World Gastroenterology Organisation recommends glycerine or docusate suppositories for hard faeces on rectal examination and bisocodyl suppositories for soft faeces (WGO(2007)).

If oral and rectal measures prove unsuccessful in treating drug-induced constipation, it may be worth considering whether alternative, less constipating medication is appropriate, for instance an opioid-switch in opioid-induced constipation (Benyamin *et.al.*(2008)).

For the purposes of this guideline a flow-chart summary/Bristol stool chart has been produced which can be found in appendix 1 of this document and is present in each patient folder. Bowel movements for inpatients should be clearly documented on the patient stool record, appendix 2.

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Overview of Laxatives:

Oral laxatives may be divided into 3 main groups based on their main mode of action (please also see tables 2 and 3):

- 1. Softening
- 2. Stimulating peristalsis
- 3. Combination of softening and stimulating peristalsis

Table 2: Oral Laxatives (Palliative Drugs.Com(2003), Larkin et.al.(2008), West Midlands Palliative Care Physicians (2007))

Predom	inantly	Predom	inantly	Combination	
Softe	ning	Stimulating	Peristalsis		
Surfactants	Sodium	Anthracenes	Senna	Surfactant	Co-danthrusate,
	docusate			&	
			Danthron	Anthracene	Co-danthromer
	Poloxamer				
Osmotic	Lactulose	Polyphenolics	Bisacodyl		
	Macrogols		Sodium		
			picosulphate		
	Magnesium				
	salts				
Lubricants*	Liquid	Bulking	Ispaghula		
	paraffin				
			Methyl-		
			cellulose		

^{*} Rarely used due to danger of aspiration pneumonia (Fallon and O'Neill (1997))

Table 3: Rectal Interventions (Palliative Drugs.Com(2003), Larkin et.al.(2008), West Midlands Palliative Care Physicians (2007))

Softening	Stimulant	Combination (osmotic)
Glycerine	Bisacodyl	Phosphate enema
Docusate sodium		Sodium citrate
Arachis oil		

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The Future

In 2003 a protocol for a Cochrane systematic review exploring the role of acupuncture in the treatment of chronic constipation was developed, however, there are no published results as yet. (Zhao *et al* (2003)).

Several new pharmacotheraputic approaches are under investigation for the treatment of constipation from any cause, including prucalopride and tegaserod (WGO (2007)). These drugs are selective 5-hydroxytryptamine type 4 receptor agonists, that stimulate giant migrating contractions of the bowel (WGO(2007)).

More specifically there is increasing evidence for the treatment of opioid-induced constipation with peripherally-acting mu-opioid receptor antagonists such as alvimopan and methylnaltrexone (Choi *et al* (2002), Kharasch (2008), Larkin *et.al.*(2008), McNicol *et al* (2008), Portenoy *et.al.*(2008), Thomas *et.al.*(2008)). The N-methylation of naltrexone prevents the molecule crossing the blood-brain-barrier, therefore preserving the analgesia action within the central nervous system (Kharesch *et.al.*(2008), Larkin *et.al.*(2008)).

In a recent double-blind randomised controlled trial, in 133 palliative care patients who had received opioids for 2 or more weeks and who had received stable doses of opioids and laxatives for 3 or more days without relief of opioid-induced constipation, methylnaltrexone was significantly superior to placebo in stimulating laxation. 48% had laxation within 4 hours with methylnaltrexone compared to 15% receiving placebo (p<0.001), after one dose and 52% had laxation within 4 hours after 2 or more doses of methylnaltrexone compared to 8% receiving placebo (p<0.001)) without evidence of exacerbation of pain or precipitation of opioid withdrawal. Reported side-effects of methylnaktrexone in this trial were abdominal pain and flatulence (Thomas *et al* 2008).

A smaller multicentred, randomised, parallel-group trial of 33 patients with a double-blind phase during the first week, found similar benefits of methylnaltrexone when compared to placebo, with no reduction in analgesia or precipitation of opioid withdrawal. Although, of interest, 11 of the 33 patients did not complete the trial due to patient request (details not provided, 1 due to adverse effects) (Portenoy *et al* (2008)).

In the United States subcutaneous methylnaltrexone has been approved for use in the treatment of opioid-induced constipation in palliative care patients with advanced illness including cancer and acquired immuno-deficiency syndrome with laxative-resistant opioid-induced constipation (Kharesch (2008)). In April 2008 the European Medicines Agency approved the use of methylnaltrexone by subcutaneous injection for the relief of opioid-induced constipation; although its expense currently prohibits its routine, widespread use (Larkin $et\ al(2008)$).

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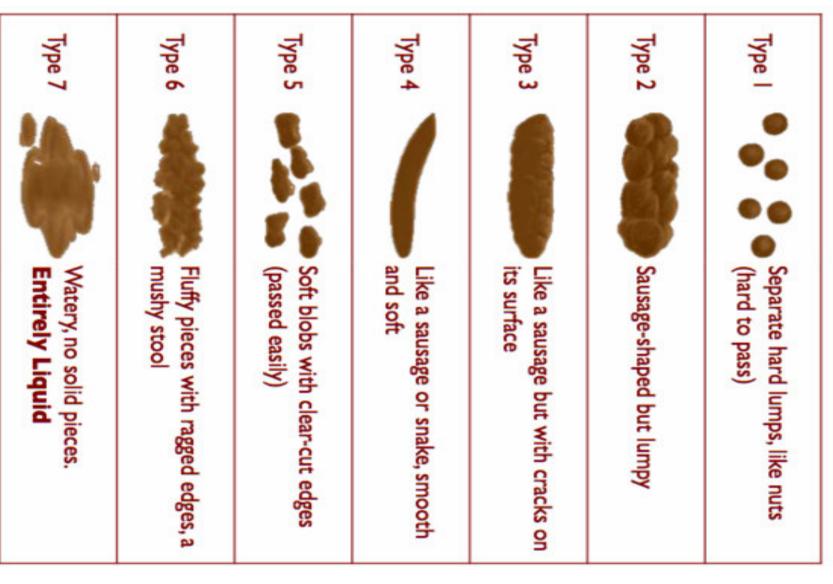
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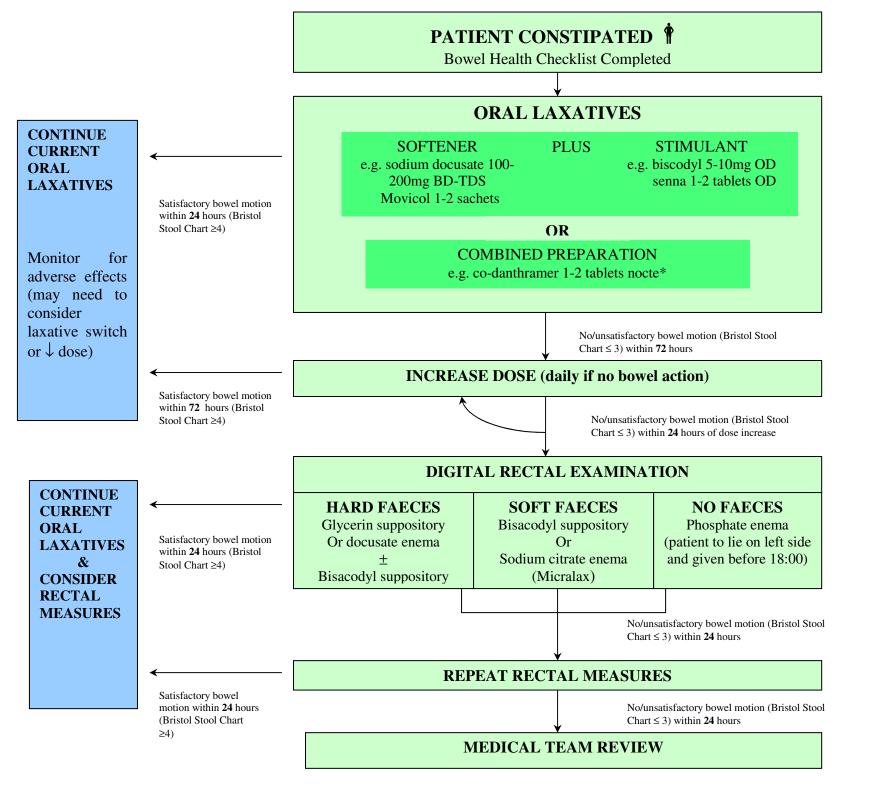
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Bristol Stool Chart





Consider alternative, less constipating medication

*

Encourage patient's choice of fluids, all day

*

Optimise patient's mobility with input from physiotherapist and occupational therapist

*

Optimise toilet privacy

*

Ensure pain relief is adequate

^{*} Do not use if patient incontinent

Appendix 2

ST RICHARDS HOSPICE BOWEL ASSESSMENT CHART

<u> </u>	
Patient name	DoB

•		•			
^	100 10	ssio	~ I7~	.+~	
M ()	11111	^	71 I X	116	
, ,,		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			

NURSING ASSESSMENT:

Date last opened bowels _____ Bristol Stool type_____

[1-3 = constipated, 4-5 = normal, 6-7 = loose motions]

Do you feel that your bowel habits are currently normal for you?	y or N
If No:	
Is the patient on medication that will put them at risk of constipation?	y or N
Does the patient have reduced mobility/activity?	y or N
Does the patient have a history of constipation?	y or N
Doe the patients' medical history (disease/surgical etc) put them at risk of	
constipation?	y or N
Does the patient think they are drinking less than normal?	y or N
Does the patient think they are eating less than normal	y or N

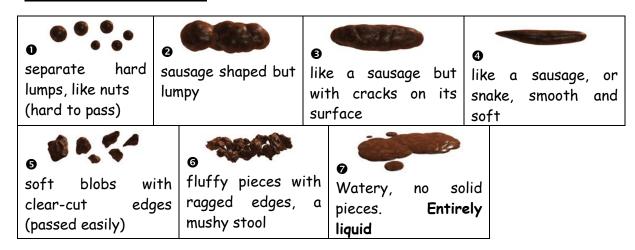
Ιf	yes	to	any	of	the	above	the	patient	is	at	risk	of	constipation
					N	Jurses	siano	ature					Date

Medical Examination:

PR -

Doctor's signature......Date.......

BRISTOL STOOL CHART



Bowel chart

Record all bowel activity including

- 1. Stool type see Bristol stool chart below
- 2. Quantity S=Small, M=Moderate, L=Large
- 3. Any other comments e.g. presence of blood, melaena, mucous etc

DATE	BOWEL ACTIVITY	DATE	BOWEL ACTIVITY