Management of Constipation in Patients with Cancer

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While certainly not the most glamorous of symptoms, constipation can have a devastating impact on a patient's quality of life. In fact, constipation can rival, or exceed, pain as a source of distress for patients and families (Sykes, 2005). If not treated appropriately, constipation can lead to such serious complications as bowel obstruction.

Constipation is defined as "the infrequent and difficult passing of hard stools" (Dalal, Fabbro, & Bruera, 2006). Patients, however, may have other ways to describe this problem, including flatulence, bloating, sensation of incomplete evacuation of stool, excessive straining, nausea, decreased appetite, and generalized abdominal discomfort (Dalal et al., 2006; Sykes, 2005).

Constipation affects the vast majority (> 95%) of cancer patients using opioids (Mancini & Bruera, 1998), and it often is considered to be the most troublesome side effect of pain management (Goodman, Low, & Wilkinson, 2005). It also is a time-intensive symptom management problem for nurses. One study found that 80% of community nurses can spend up to half a day each week simply managing constipation (Poulton & Thomas, 1999).

Constipation is associated with complications that include pain, intestinal obstruction, urinary retention or frequency, overflow diarrhea, and fecal incontinence (Watson, Lucas, Hoy, & Back, 2006). An advanced practitioner (AP) needs to be aware of the risk factors and pathophysiology of constipation, to perform an assessment, and to recommend appropriate treatments.

Pathophysiology and Risk Factors

Constipation is categorized as being either primary or secondary in nature. Primary constipation includes normal transit constipation, constipation-predominant irritable bowel syndrome, slow transit constipation, and pelvic floor dysfunction (Bharucha, 2007; Doughty, 2002). Secondary constipation is caused by neurologic disorders, metabolic problems, use of medications, presence of obstructive lesions, and lifestyle factors such as not exercising, consuming a low-fiber diet, and not drinking adequate amounts of fluids (Doughty, 2002).

The gut and small intestines facilitate enzymatic and bacterial breakdown of food and absorption of nutrients and water. Unusable waste byproducts are consolidated and expelled from the body in the form of stool through the process of peristalsis (rhythmic contractions of intestinal smooth muscle).

Table 1. Potential causes of constipation in the cancer patient

Primary or extrinsic factors
Advanced age
Poorly nutrition status
Inadequate fluid intake
Decreased mobility
Inadequate privacy

Secondary causes
Structural abnormalities
Bowel obstruction
Pelvic tumor
Radiation fibrosis
Painful anorectal conditions
Surgical complications (e.g., adhesions)

Metabolic effects
Hypercalcemia
Hyperglycemia
Hypothyroidism
Dehydration
Hypokalemia

Neurologic disorders
Spinal cord compression
Sacral nerve infiltration
Cerebral tumors

Iatrogenic causes (pharmacologic therapies)
Cytotoxic agents (e.g., vinca alkaloids, oxaliplatin, thalidomide)
Antiemetics (5-hydroxytryptamine antagonists)
Opioid therapy
Angiotensin converting enzyme inhibitors
Aluminum antacids
Antiarrythmics
Anticholinergics
Antihistamines
Antihypertensives
Antiparkinson agents
Antispasmodics
Barbiturates
Calcium channel blockers
Diuretics
Iron
Tricyclic antidepressants

Note: Adapted from Woolery et al. (2008).

Constipation results from the presence of inadequate water in the stool or gut lumen and/or slowed or impaired peristalsis in moving the stool toward expulsion. The longer that the stool remains in the large intestine, the more water is reabsorbed from waste products, and the stool becomes harder and more difficult to pass. The effort to evacuate stool is inversely proportional to its size, explaining why straining patients may pass a small, hard stool (Sykes, 2005).

Table 1 summarizes potential etiologies of constipation in the cancer patient (Woolery et al., 2008). The causes of this medical condition in this patient population typically are multifac-torial, and a hospitalized patient with advanced cancer can have multiple reasons to be consti-pated. Five common causes of constipation in the cancer patient include the malignancy (e.g., tumor burden), complications of the disease (e.g., dehydration, spinal cord compression, immobil-ity), previous laxative abuse, use of cancer thera-pies, and interventions for symptom management (e.g., opioids; Woolery et al., 2008).

In addition, constipation can be mechanical in nature. It may be caused by the tumor itself (i.e., a lesion growing into and blocking the bowel lumen or external compression of the gut lumen by an abdominal or pelvic tumor) or by neuro-logic impairment, such as damage to the lumbo-sacral spinal cord, caudal equina, or pelvic plexus (Sykes, 2005). Multiple other factors can cause or exacerbate constipation in the cancer patient, including electrolyte imbalances (e.g., hypercal-cemia), decreased oral intake, dehydration, low intake of fiber, weakness, inactivity and immobil-ity, confusion, depression, lack of privacy, unfa-miliar surroundings, emotional stress, disruption of routine, and concurrent diseases (e.g., diabetes, diverticular disease) and medication use (Dalal et al., 2006; Sykes, 2005).

Unfortunately, constipation is a primary side effect of many medications used by cancer pa-tients. For example, drugs with anticholinergic properties (e.g., haloperidol, phenothiazines), antacids (e.g., calcium, aluminum compounds), diuretics, iron supplements, anticonvulsants, anti-hypertensives, and chemotherapeutic drugs (e.g., vincristine, oxaliplatin, taxanes, thalidomide) all can cause significant constipation (Wool-ery et al., 2008). However, the greatest cause of medication-induced constipation for cancer pa-tients undoubtedly is opioids. Constipation, the one side effect of opioids to which patients do not develop tolerance, can be a serious barrier to the use of this analgesic class for cancer-related pain.

Opioids act on opioid receptors in the smooth muscle of the gut to inhibit and slow peristalsis and to increase rectal sphincter tone. Opioid receptors in the gut are affected by both paren-teral and oral administration of opioids (Sykes, 2005). However, opioids administered transder-mally (e.g., via the transdermal fentanyl patch) may cause somewhat less constipation than does morphine (Miaskowski et al., 2005; Radbruch et al., 2000).

Assessment

A thorough history of the patient's bowel transit pattern and fluid and dietary intake, a medication review, and a physical examination are essential. Inquiring about a patient's bowel habits may be awkward, as many people do not feel comfortable when answering personal and intimate questions about bodily functions. Ensuring privacy during the patient interview, asking specific questions that avoid ambiguity and confusion, using appropriate medical terminology (i.e., "stool" versus a similar slang word or phrase), and being sensitive to the patient's discomfort often is the best approach.

Certain questions provide specific information with the fewest possible inquiries. What is the patient's normal bowel pattern (frequency, time of day)? What are the usual characteristics (color, consistency, odor) of the stool? What was the date of last bowel movement? What was the degree of straining or pain involved? Was there any associated abdominal pain, cramping, nausea/vomiting, excessive gas, bleeding, or feelings of rectal pressure? Did the patient have any urge to defecate? Did it feel as though the stool had been completely evacuated? (Dalal et al., 2006). Specifically, health professionals should inquire about any laxative use and measures that relieved constipation for the patient in the past. It is important that all of these points are addressed and that frequency of stool passage is not the sole focus (Goodman et al., 2005). Table 2 describes the National Cancer Institute's (NCI's) grades to quantify constipation (NCI, 2006).

A bowel record completed by the patient provides information on the frequency and type of stool passed, exercise, nutrition, treatment of constipation, and a description of any other symptoms. It is important to understand changes in the individual's bowel habits from their normal pattern. The Bristol Stool Form Scale may be used to assist patients in recording their stool patterns (Palma & Halpert, 2008). The "Rome Criteria" defined by Thompson et al. (1999) and described by Sykes (2005) often is used to assess and define constipation for research purposes. It diagnoses constipation as the presence of two or more of the following symptoms for at least 3 months: straining at least 25% of the time, hard stools at least 25% of the time, incomplete evacuation at least 25% of the time, and two or fewer bowel movements per week.

Various visual analog scales and questionnaires can be used to assess constipation. The Constipation Assessment Scale (CAS), an eight-item scale developed by McMillan and Williams (1989) that has been validated for use by cancer patients, takes only a couple minutes to complete, making it very useful in the clinical setting. Additional assessment tools to measure constipation have been used, but not all have been validated in the oncology population; in addition, not all consider quality of life. An excellent resource for further study of symptom assessment tools is www.chcr.brown.edu/pcoc/toolkit.htm.

The physical exam should include assessment of the abdomen for distension, firmness, tenderness, and the presence/absence of bowel sounds and, possibly, a digital rectal examination to search for hard stool in the rectal vault and to rule out impaction. Rectal exams generally should be avoided in patients who are neutropenic or thrombocytopenic (Dalal et al., 2006). A vaginal examination may be performed on females to rule out a rectocele or cystocele (Doughty, 2002).

Table 2. National Cancer Institute's (NCI's) different grades of constipation

Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Life-threatening or disabling	Grade 5
Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms; regular use of laxatives or enemas	Symptoms interfering with activities of daily living; obstipation with manual evacuation	Life-threatening consequences (e.g., obstruction, toxic megacolon)	Death

Note: Adapted from NCI (2006).

Patients who pass small amounts of loose stool actually may be significantly constipated. Impacted fecal material can be broken down by bacteria into a liquid form that squeezes around the impacted mass. A thorough assessment and rectal exam can help to avoid this diagnostic error (Sykes, 2005).

The nurse should be alert for signs of bowel obstruction, which may include alternating constipation and diarrhea, gut colic, severe abdominal pain, and unexplained nausea and vomiting, especially after oral intake is attempted. Patients at risk for bowel obstruction include those with a past history of this complication, abdominal or pelvic tumors, surgical adhesions, previous intestinal surgery, and untreated, severe constipation (obstipation; Sykes, 2005).

Plain abdominal radiographs can be helpful in assessing bowel gas patterns, indicating the amount of stool in the gut, and evaluating the patient for bowel obstruction (Dalal et al., 2006). Depending upon the results of the roentgenogram, additional imaging with a computed tomography scan or specialized bowel transit studies may be needed. Stool analysis also may be helpful. Small, hard pellets suggest slow colonic transit, ribbon-like stools suggest stenosis or hemorrhoids, and blood or mucus suggest the presence of a tumor, hemorrhoids, or colitis (Dalal et al., 2006; Sykes, 2005).

Management

The goal of managing constipation is to promote frequency of bowel movements and easy passage of stool that maintains an individual's comfort (Goodman et al., 2005). A key point in deciding on a management strategy for patients with constipation is to rule out intestinal obstruction and to clarify the reasons that stool passage is blocked. The management approach will differ depending on whether the gut is blocked by feces or if a mechanical blockage (e.g., due to tumor) is present. Attempts to treat constipation with aggressive stimulant laxatives in the setting of a mechanical intestinal obstruction may cause serious complications and pain. If there is any doubt, only use laxatives that have a predominantly softening action to avoid causing complications (Sykes, 2005). A discussion of the management of malignant bowel obstructions is beyond the scope of this article.

The patient's bowel regimen, which ideally includes a combination of pharmacologic and non-pharmacologic interventions, should be started when opioids are first prescribed and continued while these drugs are used. Contrary to popular belief, use of "weaker" opioids (e.g., codeine) or lower doses of opioids are likely to cause constipation (Dalal et al., 2006). Despite the knowledge that opioids cause significant symptoms, many patients begin using these drugs without beginning an adequate bowel regimen. This is particularly unfortunate, since this side effect of opioids is completely preventable, and poorly managed constipation can be a main reason why cancer patients refuse to take opioids for pain. In fact, Wee et al. (2010) revealed that 43% of patients who were taking opioids and were admitted to a palliative care unit had not been on prophylactic laxatives.

The prevention of constipation is paramount in managing this medical problem. Constipation truly is a symptom in which "an ounce of prevention is worth a pound of cure."

PHARMACOLOGIC THERAPY

Laxatives, the mainstay of constipation therapy, may be given orally or rectally. They include bulk-forming agents, osmotic agents, contact cathartics, agents for colonic lavage (i.e., enemas), lubricants, prokinetic drugs, and opioid antagonists (Dalal et al., 2006). There is no evidence to suggest that one laxative is superior to another (Goodman et al., 2005), and there is no single correct approach in managing constipation in cancer patients (Dalal et al., 2006). The small number of randomized studies done on constipation have not produced a definitive management strategy (Dalal et al., 2006). Most importantly, bowel regimens must be individualized and titrated to response.

The majority of patients with advanced cancer require laxatives (Sykes, 2005). These agents can generally be divided into two types: those that soften the stool ("mushers"), and those that stimulate gut peristalsis ("pushers"). A combination of both types of laxatives often is most effective (Sykes, 2005).

Laxative therapy should be given regularly on a daily basis. It often begins with an oral laxative taken every night. Higher doses should be divided into two to three daily doses. If stools become too soft or liquid, holding laxatives for 24 hours and resuming at a lower dose usually solves the prob-

lem (Sykes, 2005). Preventative measures to take during opioid therapy include administration of a stimulant laxative plus a stool softener (e.g., two senna/docusate sodium tablets every morning, up to 8–12 tablets/day; National Comprehensive Cancer Network, 2009). Most cancer patients require laxatives to prevent constipation, including those on "around-the-clock" opioid therapy.

Adherence to laxative medications improves if healthcare providers do not unnecessarily alter a regimen that has been working for a patient and if they heed patients' preferences for selection of a laxative (i.e., pill or liquid, sweet or less flavor; Sykes, 2005).

A summary of oral laxatives appears in Table 3 (Lembo & Camilleri, 2003). Use of bulk-forming laxatives (e.g., methylcellulose, psyllium) generally is contraindicated for oncology patients. If bulk-forming agents are not taken with adequate water, a viscous fecal mass may result that can cause intestinal obstruction and serious complications. The effectiveness of these agents in severe constipation also is questionable (Sykes, 2005).

Enemas and suppositories may be culturally or personally unacceptable to a patient. However, they offer a fast onset of action, and they may be a helpful alternative for patients who cannot swallow. Use of enemas and suppositories generally should be avoided by cancer patients who are neutropenic or thrombocytopenic. For patients with refractory constipation despite oral laxatives, initial use of a suppository followed by administration of enemas containing sodium phosphates or mineral oil may be helpful.

Rectal lavage, or instillation of large-volume enemas containing normal saline, should be performed cautiously and as a last resort. Enemas containing tap water or soap and water should be avoided due to risk of circulatory overload and irritation to the rectal mucosa (Sykes, 2005).

New pharmacologic treatments for constipation include chloride channel activators, selective 5-hydroxytryptamine type 3 (5-HT_3) and type 4 (5-HT_4) agonists, investigational drugs, and probiotics. Lubiprostone acts as a selective chloride channel activator that increases intestinal chloride secretion, resulting in availability of fluid that eases passage of the stool. Tegaserod, a 5-HT_4 agonist, recently was taken off the market, because increased cardiac events occurred during therapy. Other 5-HT_4 agonists currently are being

investigated; these include renzapride, which is both a 5-HT_4 receptor agonist and a 5-HT_3 receptor agonist (Woolery et al., 2008).

The Oncology Nursing Society's Putting Evidence into Practice (PEP) guidelines state that methylnaltrexone is used for opioid-induced constipation (Woolery et al., 2008). This selective opioid antagonist binds at the μ-opioid receptor. However, because it is unable to cross the blood-brain barrier, it functions peripherally in tissues such as those of the gastrointestinal tract. Thus, the constipating effects of opioids are diminished without impacting the analgesic effects on the central nervous system. Methylnaltrexone is given subcutaneously and can be used daily, if needed (Thomas et al., 2008). A bowel movement should occur within 1 to 4 hours after methylnaltrexone is given. Adverse events include abdominal cramping, flatulence, nausea, and dizziness. However, methylnaltrexone is expensive, and some hospitals do not carry the medication.

Another pharmacologic treatment for constipation currently under study is probiotics. These agents may supply the gut with healthy bacteria that normalize intestinal function to increase motility and relieve constipation. Patients using probiotics have reported having an increased number of bowel movements and less straining (Pohl, Tutuian, & Fried, 2008).

NONPHARMACOLOGIC TREATMENT

A key stimulus to peristalsis and defecation is activity, and patients should be encouraged to be as mobile as possible. Adequate fluid and fiber intake also is helpful. For most patients with cancer, it is preferable to enhance oral intake by using gentle encouragement and by providing foods and drinks that the patient likes (Sykes, 2005). Warm, caffeinated products, such as coffee, also may have a gentle stimulant effect and promote defecation.

In one study of geriatric patients (Beverley & Travis, 1992), individuals who consumed a natural laxative mixture (i.e., raisins, currants, prunes, dates, and prune concentrate) experienced more natural and regular bowel movements and were more satisfied with the bowel regimen overall than were those given stool softeners, lactulose, and other laxatives (Dalal et al., 2006).

Adequate fluids are essential for preventing and treating constipation. Adults should drink at least 2 L of fluid each day.

Table 3. Medications commonly used for constipation

Medication	Maximal recommended dose	Comments
Osmotic laxative		
Magnesium hydroxide	15–30 mL 1–2 times/day	A small percentage of magnesium is actively absorbed in the small intestines; hypermagnesemia can occur in patients with renal failure and in children
Magnesium citrate	150–300 mL, as needed	
Sodium phosphate	10–25 mL with 12 oz. (360 mL) of water, as needed	Hyperphosphatemia can occur in patients with renal insufficiency; commonly used for bowel preparation before colonoscopy
Poorly absorbed sugar		
Lactulose	15–30 mL 1–2 times/day	Synthetic disaccharide consisting of galactose and fructose linked by bond resistant to disaccharidases; not absorbed by the small intestine; undergoes bacterial fermentation in the colon with formation of short-chain fatty acids; gas and bloating are common side effects

Sugar alcohols
  Sorbitol
  Mannitol
	15–30 mL 1–2 times/day	Poorly absorbed by intestine; undergoes bacterial fermentation

Polyethylene glycol and electrolytes	17–36 g 1–2 times/day	Organic polymers that are poorly absorbed and not metabolized by colonic bacteria; may cause less bloating and cramping than other poorly absorbed sugars; can be mixed with noncarbonated beverages
Polyethylene glycol 3350	17–36 g 1–2 times/day	Does not include electrolytes; packaged for more regular use
Stimulant laxative		Stimulates intestinal motility or secretion

Anthraquinones
  Cascara sagrada
  Senna
	325 mg (or 5 mL)/day
	187 mg/day
		Converted by colonic bacteria to their form; may cause melanosis coli, a benign condition that usually is reversible within 12 months after the cessation of laxative use; no definitive association between anthraquinones and colon cancer or myenteric nerve damage has been established

Diphenylmethane derivatives
  Bisacodyl
  Sodium picosulfate
	
	5–10 mg every night
	5–15 mg every night
		Hydrolyzed by endogenous esterases; stimulates secretion and motility of small intestine and colon
		Hydrolyzed to its active form by colonic bacterial enzymes; affects only the colon

Stool softener Docusate sodium	100 mg 2 times/day	Ionic detergents soften stool by allowing water to interact more effectively with solid stool; results in modest fluid secretion; efficacy for treatment is not well established
Mineral Oil	5–15 ml orally every night	An emollient providing lubrication for the passage of stool; long-term use can cause malabsorption of fat-soluble vitamins and anal seepage; lipoid pneumonia can occur in patients predisposed to aspiration of liquids
Bulk-forming laxative[a]		Increases colonic residue, stimulating peristalsis
Psyllium	Titrate up to 20 g	Natural fiber that undergoes bacterial degradation, which may contribute to bloating and flatus; should be taken with plenty of water to avoid intestinal obstruction; allergic reactions (e.g., anaphylaxis and asthma) are rare
Methylcellulose	Titrate up to 20 g	Semisynthetic cellulose fiber that is relatively resistant to colonic bacterial degradation
Polycarbophil	Titrate up to 20 g	Synthetic fiber of polymer of acrylic acid; resistant to bacterial degradation

Note: [a]Not recommended if unable to take large amounts of liquids and/or on opioids that slow peristalsis. Source: Lembo & Camilleri (2008).

Bedpans provide an additional anatomic challenge by increasing the pressure required to expel stool and should be avoided, when possible. Toileting patients by walking them to the bathroom or by using a bedside commode and assistive devices such as walkers, extended toilet seats, and lifts is important. APs should urge patients to use a commode or bathroom whenever feasible and should optimize patient privacy and uninterrupted time for bathroom use (Sykes, 2005). Greater activity may increase peristalsis and decrease constipation. An exercise program that is tolerated and appropriate for the patient should be included in the management plan.

APs have an instrumental role in educating oncology patients about constipation. They must help patients and caregivers understand the link between using opioids and other medications and developing constipation, and they must assist patients in preventing constipation and minimizing unnecessary discomfort and possibly serious complications. APs also can ensure that every cancer patient on opioids has an effective and acceptable bowel regimen in place.

In 2008, the American Gastroenterological Association developed a Chronic Constipation Guidelines Pocketcard, a practical tool that provides the most current evidence to manage constipation optimally (Palma & Halpert, 2008). The pocketcard can be obtained at www.myguidelinescenter.com. The Oncology Nursing Society also has a PEP card for constipation (Woolery et al., 2008).

Conclusion

Constipation is an extremely common, often overlooked symptom in the oncology population. Prevention is the key to minimizing the distress of constipation. Advanced practitioners can be powerful advocates in helping patients and caregivers to ensure that bowel function remains comfortable.

REFERENCES

Beverley, L., & Travis, K. (1992). Constipation: proposed natural laxative mixtures. *Journal of Gerontology Nursing, 18,* 5–12.
Bharucha, A. E. (2007). Constipation. Best Practice & Research *Clinical Gastroenterology, 21,* 709–731. doi:10.1016/j.bpg.2007.07.001
Dalal, S., Fabbro, E., & Bruera, E. (2006). Symptom control in palliative care—part I.: oncology as a paradigmatic example. *Journal of Palliative Medicine, 9,* 391–407. doi:10.1089/jpm.2006.9.391

Doughty, D. B. (2002). When fiber is not enough: current thinking on constipation management. *Ostomy Wound Management, 48,* 30–41.
Goodman, M., Low, J., & Wilkinson, S. (2005). Constipation management in palliative care: a survey of practices in the United Kingdom. *Journal of Pain and Symptom Management, 29,* 238–244. doi:10.1016/j.jpainsymman.2004.06.013
Lembo, A., & Camilleri, M. (2003). Chronic constipation. *New England Journal of Medicine, 349,* 1360–1368.
Mancini, I., & Bruera, E. (1998). Constipation in advanced cancer patients. *Supportive Care Cancer, 6,* 356–364.
McMillan, S. C., & Williams, F. A. (1989). Validity and reliability of the Constipation Assessment Scale. *Cancer Nursing, 12,* 183–188.
Miaskowski, C., Cleary, J., Burney, R., Coyne, P., Finley, R., Foster, R., ...Zahrbrock, C. (2005). Guidelines for the management of cancer pain in adults and children. Glenview, IL: American Pain Society.
National Cancer Institute. (2006). Common terminology criteria for adverse events v.3.0. Retrieved from ctep.cancer.gov/forms/CTCAEv3.pdf.
National Comprehensive Cancer Network. (2009). NCCN clinical practice guidelines in oncology: adult cancer pain V1. Retrieved from www.nccn.org.
Palma, J. A., & Halpert, A. (2008). Guidelines Pocketcard: managing chronic constipation. Baltimore, MD: International Guideline Center.
Pohl, D., Tutuian, R., & Fried, M. (2008). Pharmacologic treatment of constipation: what is new? Current Opinion in Pharmacology, 8, 724–728. doi:10.1016/j.coph.2008.07.008
Poulton, B., & Thomas, S. (1999). The nursing cost of constipation. *Primary Health Care, 9,* 17–22.
Radbruch, L., Sabatowski, R., Loick, G., Kulbe, C., Kasper, M., Grond, S., ...Lehmann, K. A. (2000). Constipation and the use of laxatives: a comparison between transdermal fentanyl and oral morphine. *Palliative Medicine, 14,* 111–119.
Sykes, N. (2005). Constipation and diarrhoea. In Doyle, D., Hanks, G., MacDonald, N. (Eds.), Oxford textbook of palliative medicine (pp. 483–506). Oxford, UK: Oxford Medical Publications.
Thomas, J, Karver, S., Cooney, G. A., Chamberlain, B. H., Watt, C. K., Slatkin, ...Israel, R. J. (2008). Methylnaltrexone for opioid-induced constipation in advanced illness. *New England Journal of Medicine, 358,* 2332–2343.
Thompson, W. G., Longstreth G. F., Drossman, D. A., Heaton, K. W., Irvine, J., & Müller-Lissner, S. A. (1999). Functional bowel disorders and functional abdominal pain. *Gut, 45,* 1143–1147.
Watson, M. S., Lucas, C. L., Hoy, A. M., & Back, I. N. (2006). Constipation. In Oxford handbook of palliative care (pp. 254–257). New York, NY: Oxford University Press.
Wee, B., Adams, A., Thompson, K., Percival, F., Burslem, K., & Jobanputra, M. (2010). How much does it cost a specialist palliative care unit to manage constipation in patients receiving opioid therapy? *Journal of Pain and Symptom Management, 39,* 644–653. doi:10.1016/j.jpainsymman.2009.09.007
Woolery, M., Bisanz, A., Lyons, H. F., Gaido, L., Yenulevich, M., Fulton, S., ...McMillan, S. C. (2008). Putting evidence into practice: evidence-based interventions for the prevention and management of constipation in patients with cancer. *Clinical Journal of Oncology Nursing, 12,* 317–337. doi:10.1188/08