

# Management of Opioid-Induced and Non-Opioid-Related Constipation in Patients With Cancer: Systematic Review and Meta-Analysis

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**PROBLEM IDENTIFICATION:** A systematic review and meta-analysis was conducted to inform the development of national clinical practice guidelines on the management of cancer constipation.

**LITERATURE SEARCH:** PubMed®, Wiley Cochrane Library, and CINAHL® were searched for studies published from May 2009 to May 2019.

**DATA EVALUATION:** Two investigators independently reviewed and extracted data from eligible studies. The Cochrane Collaboration risk-of-bias tool was used, and the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach was used to assess the certainty of the evidence.

**SYNTHESIS:** For patients with cancer and opioid-induced constipation, moderate benefit was found for osmotic or stimulant laxatives; small benefit was found for methylnaltrexone, naldemedine, and electroacupuncture. For patients with cancer and non-opioid-related constipation, moderate benefit was found for naloxegol, prucalopride, lubiprostone, and linaclotide; trivial benefit was found for acupuncture.

**IMPLICATIONS FOR PRACTICE:** Effective strategies for managing opioid-induced and non-opioid-related constipation in patients with cancer include lifestyle, pharmacologic, and complementary approaches.

**KEYWORDS** constipation; symptom management; opioid-induced constipation; cancer; opioids

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Constipation occurs in about 60% of patients with cancer and can be distressing to patients during treatment, survivorship, and palliative care (McMillan et al., 2013). Constipation is the third most common side effect reported by patients with advanced cancer, following pain and anorexia (Clemens et al., 2013). For terminally ill patients with cancer, constipation and bowel dysfunction occurs in as many as 80% of patients and in as many as 90% of patients who are prescribed opioids (Downing et al., 2007; Rhondali et al., 2013). Constipation is often multicausal—a result of organic, functional, or medication-related factors (Bharucha et al., 2013; Clemens et al., 2013; Costilla & Foxx-Orenstein, 2014)—and it often goes unrecognized and undertreated (McMillan et al., 2013).

Opioids have undesirable side effects, including sedation, respiratory depression, and gastrointestinal symptoms such as opioid-induced constipation (OIC) (Benyamin et al., 2008). OIC is defined as an abnormal change in typical bowel habits or patterns of defecation following opioid therapy and is characterized by a decrease in the frequency of spontaneous bowel movements (SBMs) (less than three per week), the development or worsening of straining to pass a bowel movement, a feeling of incomplete evacuation, stool with a harder consistency, or a patient's perception of distress associated with bowel habits (Gaertner et al., 2015; McMillan, 2004; Reville et al., 2009). OIC is caused when opioids bind to enteric nervous system receptors in the gastrointestinal track and induce delayed gastric emptying, decreased intestinal secretion, slow contractions, decreased motility, increased fluid absorption from stool, and increased