

## Evidence-based treatment recommendations for OTC management of chronic constipation

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### ABSTRACT

Chronic constipation is a common gastrointestinal condition, and most individuals self-treat with multiple over-the-counter (OTC) laxatives prior to consulting a health care provider. This brief report is a synopsis of an updated systematic review the authors conducted of published data on the efficacy and safety of OTC treatments to provide evidence-based recommendations. After applying the selection criteria, 41 randomized controlled clinical trials of  $\geq 4$ -week duration were identified and analyzed. Standardized definitions of constipation were applied across these studies; however, definitions for stool frequency and consistency varied. Overall, the short- and long-term efficacy of polyethylene glycol-based preparations and senna were supported by good (grade A) evidence suggesting their use as first-line laxatives. Modest evidence (grade B) supported the use of other agents including the stimulants bisacodyl and sodium picosulfate, fiber, fruit-based laxatives, and magnesium oxide. Additional evidence from rigorously designed studies is needed to support the use of other options for chronic constipation. The OTC products studied were generally well tolerated with common adverse effects being abdominal pain, cramping, bloating, diarrhea, and nausea.

**Keywords:** Constipation; systematic review; osmotic laxatives; over the counter; stimulant laxatives.

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Constipation is the most common functional gastrointestinal disorder in the world, with a prevalence of 7%–12% when using ROME IV criteria (Palsson et al., 2020; Sperber et al., 2021). Given this high prevalence, constipation imparts a significant quality-of-life burden that is comparable to that of other common chronic conditions (Belsey et al., 2010). Despite these impacts, there are important gaps in knowledge and the implementation of effective treatment. Further complicating this is that almost two-thirds of individuals with chronic constipation never discuss their condition with a health care provider (HCP; Oh et al., 2020) and 40%–50% self-treat with OTC laxatives (Oh et al., 2020; Pinto Sanchez & Bercik, 2011). However, more than half of patients with chronic

constipation are unsatisfied with their OTC laxative, and they typically use multiple OTC products prior to consulting an HCP (Harris et al., 2017). Frustration with OTC treatment options for constipation may be related to an inadequate knowledge of the relative efficacy of various agents. Thus, it is important for HCPs to have a good understanding of the relative efficacy of treatment choices based on available evidence to help promote patient care. This report provides a synopsis of findings from a recently published review of the literature on OTC products for constipation (Rao & Brenner, 2021).

Selection of an OTC laxative is complicated by the availability of many classes of agents with differing mechanisms of action. Furthermore, the quality and quantity of evidence between agents varies considerably. In an effort to clarify the literature, the authors conducted an updated systematic review of data published over the past 15 years to allow an evidence-based approach to the selection of OTC laxatives (Rao & Brenner, 2021). From searches of PubMed and Embase databases, the authors identified 41 randomized controlled trials that used an established definition of constipation (preferably ROME criteria to distinguish functional chronic constipation from defecation disorders) and evaluated treatment over at least four weeks. The authors found that the overall quality of studies had improved compared with a previous review (Ramkumar & Rao, 2005) with a greater use of standardized definitions of constipation. However,

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there was still substantial variability in the study design and in the quantity and quality of data between the various classes of agents (Rao & Brenner, 2021). There were also few studies that assessed long-term therapy. Notably, there was a lack of standard outcome parameters between studies. Although stool frequency (eg, bowel

movement [BM], complete spontaneous BM), and consistency were commonly used, the definition of these outcomes varied considerably.

Increasing fiber is commonly recommended as a first-line approach to treating constipation, and soluble fiber laxatives (eg, psyllium) are the most

**Table 1. Comparative evidence-based recommendations for OTC products in the management of constipation**

OTC Products for Constipation	Level of Evidence <sup>a</sup>	Adverse Events
Best evidence (recommendation grade A) <sup>b</sup>		
Osmotic		
PEG	I	Mild-to-moderate abdominal distension, diarrhea, loose stools, flatulence, and nausea
Stimulant		
Senna	I	Diarrhea, abdominal pain
Moderate evidence (recommendation grade B) <sup>b</sup>		
Fruits		
Kiwi	I	Mild flatulence, bloating
Mango	II	
Prunes	II	
Ficus	II	
Fiber		
Psyllium	II	Abdominal distension/pain, flatulence
SupraFiber (mixed fiber)	II	
Stimulant		
Bisacodyl	I	Diarrhea, flatulence, abdominal pain
Sodium picosulfate	I	
Magnesium containing		
Magnesium oxide	I	Diarrhea, abdominal pain
Magnesium-rich water	I	
Insufficient/no evidence for recommendation		
Fiber		
Bran/methylcellulose	NA	Mild to moderate abdominal distension/pain, flatulence
Polydextrose	I	
Inulin	I	
Surfactant		
Docusate	NA	Mild diarrhea, cramping

<sup>a</sup>The level of evidence was graded as good (Level I), fair (Level II), or poor (Level III).

<sup>b</sup>The recommendation was graded as A (good evidence in support), B (moderate evidence in support), C (poor evidence in support), D (moderate evidence against), or insufficient (insufficient evidence).

Note: NA = not assessed; OTC = over the counter; PEG = polyethylene glycol.

commonly recommended first-line agents by gastroenterologists (Menees et al., 2015). Despite this, the authors found that evidence supporting the use of fiber laxatives is relatively modest. Psyllium was no more efficacious than placebo for improving global constipation symptom scores in two trials, and it was less effective than lactulose, mangos, and prunes for treating constipation in direct comparative trials. Other fiber laxatives (ie, polydextrose, inulin) also demonstrated inconsistent benefits over placebo.

The surfactant docusate is another commonly prescribed agent because it is considered benign and thought to soften the stool and facilitate passage (Fakheri & Volpicelli, 2019). The previous systematic review (Ramkumar & Rao, 2005) found little evidence to support the use of docusate, and in this updated review, there were no clinical trials that established the efficacy of docusate. Furthermore, there is little scientific rationale for the use of docusate because it does not affect either of the underlying biologic mechanisms of constipation (ie, slowed colonic transit, pelvic floor dysfunction).

In contrast to fibers and docusate, there was robust evidence establishing both the short- and long-term efficacy of PEG-based preparations. Polyethylene glycol was superior to placebo over up to six months of treatment in three well-designed trials. In addition, PEG demonstrated significantly greater efficacy compared with several prescription-only agents (ie, tegaserod, prucalopride, and lactulose), and PEG was similarly effective to naloxegol for treating opioid-induced constipation. Overall, there was sufficient evidence to assign PEG a grade A recommendation (**Table 1**) (Rao & Brenner, 2021). Senna was also given a grade A recommendation, based on the positive results of two shorter trials in which senna demonstrated improved BM frequency versus placebo. However, one of the studies used higher doses of senna than those normally used in clinical practice.

The data supporting other agents was much more modest, with none having the required two placebo-controlled trials for the highest recommendation. This includes the stimulants bisacodyl and sodium picosulfate (similar agents with the same active metabolite), fruit-based laxatives (ie, kiwifruit, mango, ficus, prunes), and magnesium oxide, with each demonstrating superiority to placebo in single clinical trials.

As expected, the review found that the OTC products studied were generally safe and well tolerated. Gastrointestinal symptoms, such as abdominal pain, cramping, bloating, diarrhea, and nausea, were the most common treatment-emergent adverse events observed, although there were some differences between agents. In particular, the stimulants bisacodyl and sodium picosulfate were associated with an increased risk of gastrointestinal adverse events.

In summary, it is important to base constipation OTC recommendations on well-controlled clinical trials. Our updated systematic review found that there is good evidence to recommend PEG or senna as first-line agents for the treatment of constipation, although there is moderate evidence supporting fiber supplements, fruits, stimulants, and magnesium-based products. There is poor evidence to support the use of docusate in clinical practice.

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## References

- Belsey, J., Greenfield, S., Candy, D., & Geraint, M. (2010). Systematic review: Impact of constipation on quality of life in adults and children. *Alimentary Pharmacology and Therapeutics*, 31(9), 938–949. <https://doi.org/10.1111/j.1365-2036.2010.04273.x>
- Fakheri, R. J., & Volpicelli, F. M. (2019). Things we do for no reason: Prescribing docusate for constipation in hospitalized adults. *Journal of Hospital Medicine*, 14(2), 110–113. <https://doi.org/10.12788/jhm.3124>
- Harris, L. A., Horn, J., Kissous-Hunt, M., Magnus, L., & Quigley, E. M. M. (2017). The better understanding and recognition of the disconnects, experiences, and needs of patients with chronic idiopathic constipation (BURDEN-CIC) study: Results of an online questionnaire. *Advances in Therapy*, 34, 2661–2673. <https://doi.org/10.1007/s12325-017-0633-5>
- Menees, S. B., Guentner, A., Chey, S. W., Saad, R., & Chey, W. D. (2015). How do US gastroenterologists use over-the-counter and prescription medications in patients with gastroesophageal reflux and chronic constipation? *American Journal of Gastroenterology*, 110(11), 1516–1525. <https://doi.org/10.1038/ajg.2015.156>
- Oh, S. J., Fuller, G., Patel, D., Khalil, C., Spalding, W., Nag, A., Spiegel, B. M. R., & Almario, C. V. (2020). Chronic constipation in the United States: Results from a population-based survey assessing healthcare seeking the use of pharmacotherapy. *American Journal of Gastroenterology*, 115(6), 895–905. <https://doi.org/10.14309/ajg.0000000000000614>
- Palsson, O. S., Whitehead, W., Törnblom, H., Sperber, A. D., & Simren, M. (2020). Prevalence of Rome IV functional bowel disorders among adults in the United States, Canada, and the United Kingdom. *Gastroenterology*, 158(5), 1262–1273.e3. <https://doi.org/10.1053/j.gastro.2019.12.021>

- Pinto Sanchez, M. I., & Bercik, P. (2011). Epidemiology and burden of chronic constipation. *Canadian Journal of Gastroenterology*, 25(Suppl.B), 11b-15b. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3206560/>
- Ramkumar, D., & Rao, S. S. C. (2005). Efficacy and safety of traditional medical therapies for chronic constipation: Systematic review. *American Journal of Gastroenterology*, 100(4), 936-971. [https://journals.lww.com/ajg/Abstract/2005/04000/Efficacy\\_and\\_Safety\\_of\\_Traditional\\_Medical.34.aspx](https://journals.lww.com/ajg/Abstract/2005/04000/Efficacy_and_Safety_of_Traditional_Medical.34.aspx)
- Rao, S. S. C., & Brenner, D. M. (2021). Efficacy and safety of over-the-counter therapies for chronic constipation: An updated systematic review. *American Journal of Gastroenterology*, 116(6), 1156-1181. <https://doi.org/10.14309/ajg.0000000000001222>
- Sperber, A. D., Bangdiwala, S. I., Drossman, D. A., Ghoshal, U. C., Simren, M., Tack, J., Whitehead, W. E., Dumitrascu, D. L., Fang, X., Fukudo, S., Kellow, J., Okeke, E., Quigley, E. M. M., Schmulson, M., Whorwell, P., Archampong, T., Adibi, P., Andresen, V., Benninga, M. A., Bonaz, B., Bor, S., Bustos Fernandez, L., Chei Choi, S., Corazziari, E. S., Francisci, C., Hani, A., Lazebnik, L., Yeh Lee, Y., Mulak, A., Masudur Rahman, M., Santos, J., Setshedi, M., Fahrial Syam, A., Vanner, S., Wong, R. K., Lopez-Colombo, A., Costa, V., Dickman, R., Kanazawa, M., Hassanzadeh Keshteli, A., Khatun, R., Maleki, I., Poitras, P., Pratap, N., Stefanyuk, O., Thomson, S., Zeevenhooven, J., & Palsson, O. S. (2021). Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation global study. *Gastroenterology*, 160(1), 99-114. <https://doi.org/10.1053/j.gastro.2020.04.014>