

# A Review of Irritable Bowel Syndrome

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**Conflict of Interest Disclosures:** Mr Romm reports being cofounder and CEO of Cityblock Health with equity and salary compensation. No other disclosures were reported.

1. Gee RE, Shulkin D, Romm I. A blueprint for comprehensive Medicaid reform. *JAMA*. 2021;325(7):619-620. doi:10.1001/jama.2021.0013

## A Review of Irritable Bowel Syndrome

**To the Editor** In the recent Review on diagnosis and treatment of irritable bowel syndrome (IBS),<sup>1</sup> Dr Camilleri stated: “Overall, evidence so far does not show psychological therapies to be effective in relieving symptoms of IBS.” Camilleri also suggested that psychological treatments may be beneficial only in patients with comorbid psychological symptoms. We believe neither statement is supported by the available evidence.

First, systematic reviews and meta-analyses have demonstrated that psychological treatments, primarily cognitive behavior therapy (CBT) and gut-directed hypnotherapy (GDH), yield significant, long-lasting improvements across several patient-reported outcomes, including core IBS symptoms. In these studies,<sup>2</sup> which included more than 4000 patients in 40 randomized clinical trials (RCTs), many of which were blinded, 60% to 70% of patients responded to psychological treatments for IBS. The number needed to treat was 4 (95% CI, 3-9), which is lower than the numbers needed to treat for rifaximin, 10.5 (95% CI, 8-16), and for eluxadoline, 12.5 (95% CI, 8-33),<sup>2</sup> which are other novel pharmacological agents for IBS. In addition, GDH has demonstrated comparable efficacy with the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet but is advantageous because it lacks the challenges of implementing a dietary treatment.<sup>3</sup> Moreover, treatment effects of behavioral therapies have been shown to be maintained up to 18 months,<sup>4</sup> which is longer than has been demonstrated for pharmacological or dietary intervention studies.

Second, contrary to psychological treatments for psychiatric disorders, behavioral treatments for IBS focus on symptom-specific mechanisms and outcomes. Although the evidence about psychological comorbidities as predictors of response to behavioral treatments in IBS is limited, a large trial demonstrated that patients with IBS who had lower anxiety levels at baseline showed better response to CBT than those with higher anxiety.<sup>5</sup> Moreover, other CBT trials have shown that changes in fears specific to gut symptoms, cognitions, and behaviors, rather than psychological comorbidity per se, drive symptom improvement.<sup>4</sup>

Based on the evidence to date, we believe that in addition to dietary and/or pharmacological therapies, behavioral therapies should not only be offered to patients with IBS but also may serve as first-line treatments for IBS and should not be limited to patients with psychological comorbidities. The main issue with behavioral therapies for IBS is not their lack of efficacy but their availability to most patients due to a dearth of qualified behavioral health professionals. With the inception of the Rome Foundation Psychogastroenterology Group in 2018 and advances in telehealth, these barriers to care will presumably begin to decline.

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**Conflict of Interest Disclosures:** Dr Taft reported being a founder and owner of Oak Park Behavioral Medicine LLC. Dr Keszthelyi reported receiving grants from Allergan, Will Pharma, Grunenthal, ZonMw, Horizon 2020, United European Gastroenterology, Rome Foundation, and Maag-Lever-Darmstichting. Dr Van Oudenhove reported receiving grants from Nestlé and serving as a consultant for Danone.

1. Camilleri M. Diagnosis and treatment of irritable bowel syndrome: a review. *JAMA*. 2021;325(9):865-877. doi:10.1001/jama.2020.22532
2. Ford AC, Moayyedi P, Chey WD, et al; ACG Task Force on Management of Irritable Bowel Syndrome. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Am J Gastroenterol*. 2018;113(suppl 2):1-18. doi:10.1038/s41395-018-0084-x
3. Peters SL, Yao CK, Philpott H, Yelland GW, Muir JG, Gibson PR. Randomised clinical trial: the efficacy of gut-directed hypnotherapy is similar to that of the low FODMAP diet for the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016;44(5):447-459. doi:10.1111/apt.13706
4. Ljótsson B, Hedman E, Lindfors P, et al. Long-term follow-up of internet-delivered exposure and mindfulness based treatment for irritable bowel syndrome. *Behav Res Ther*. 2011;49(1):58-61. doi:10.1016/j.brat.2010.10.006
5. Lackner JM, Jaccard J; IBS Outcome Study Research Group. Factors associated with efficacy of cognitive behavior therapy vs education for patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2019;17(8):1500-1508.e3. doi:10.1016/j.cgh.2018.10.033

**In Reply** In their letter about my Review of the diagnosis and treatment of IBS,<sup>1</sup> the citation by Dr Taft and colleagues of the systematic review endorsed by the American College of Gastroenterology (ACG) omits the summary statement: “Various psychological therapies appear to be effective in IBS, but the interpretation of many studies is hampered by the absence of a true sham control which is, admittedly, difficult to construct for these particular interventions.” Their letter also did not mention that the ACG recommendation’s evidence for “some psychological therapies for overall symptom improvement in IBS patients” was weak and the quality of evidence was very low.<sup>2</sup> In a subsequent, more comprehensive systematic review and meta-analysis,<sup>3</sup> the updated recommendation stated that CBT, relaxation therapy, multicomponent psychological therapy, hypnotherapy, and dynamic psychotherapy were all beneficial when data from 2 or more RCTs were pooled. However, there was heterogeneity between studies; issues regarding trial design, including lack of blinding; and funnel plot asymmetry, suggesting publication bias or other kinds of reporting bias.

My review’s recommendation to select patients with IBS for psychological therapies based on psychological comorbidity is consistent with the goals of precision medicine, especially in light of the dearth of qualified behavioral health professionals, as noted by Taft and colleagues. Selection of patients for behavioral therapy based on psychological comorbidity is also supported by evidence from the IBS Outcome Study (IBSOS) of 436 patients with IBS (average age, 41 years; 80% female) who were

randomly assigned to groups that received 4 or 10 sessions of CBT or education over 10 weeks. This study<sup>4</sup> showed that baseline levels of anxiety and anxiety sensitivity (fear of arousal symptoms) were associated with improved gastrointestinal symptoms following CBT compared with IBS education. Moreover, a recent study,<sup>5</sup> based on latent class analysis of 1375 adults in the community self-identifying as having IBS, demonstrated that 53% had a high psychological burden with diverse gastrointestinal symptom profiles. This finding supports the notion that patients with psychological comorbidity can be identified and treated with psychotherapy, rather than using the resource for all patients with IBS. It is also worth noting that there was higher IBS severity (based on the Irritable Bowel Syndrome Symptom Severity Scale [IBS-SSS]) in those with high psychological burden.<sup>5</sup>

The numbers needed to treat between pharmacological and behavioral therapies cited by Taft and colleagues are not strictly comparable, given the absence of a true sham control group with behavioral therapies. In addition, although the Clinical Global Impressions-Improvement Scale for IBS symptoms with behavioral therapy was superior to education alone during 1 year of follow-up in the IBSOS study,<sup>4</sup> it is noteworthy that there were no significant differences throughout the 12 months in the severity of IBS based on the IBS-SSS.<sup>6</sup>

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1. Camilleri M. Diagnosis and treatment of irritable bowel syndrome: a review. *JAMA*. 2021;325(9):865-877. doi:10.1001/jama.2020.22532
2. Ford AC, Moayyedi P, Chey WD, et al; ACG Task Force on Management of Irritable Bowel Syndrome. American College of Gastroenterology monograph on management of irritable bowel syndrome. *Am J Gastroenterol*. 2018;113(suppl 2):1-18. doi:10.1038/s41395-018-0084-x
3. Ford AC, Lacy BE, Harris LA, Quigley EMM, Moayyedi P. Effect of antidepressants and psychological therapies in irritable bowel syndrome: an updated systematic review and meta-analysis. *Am J Gastroenterol*. 2019;114(1):21-39. doi:10.1038/s41395-018-0222-5
4. Lackner JM, Jaccard J, IBS Outcome Study Research Group. Factors associated with efficacy of cognitive behavior therapy vs education for patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2019;17(8):1500-1508. doi:10.1016/j.cgh.2018.10.033
5. Black CJ, Yiannakou Y, Guthrie EA, West R, Houghton LA, Ford AC. A novel method to classify and subgroup patients with IBS based on gastrointestinal

symptoms and psychological profiles. *Am J Gastroenterol*. 2021;116(2):372-381. doi:10.14309/ajg.0000000000000975

6. Lackner JM, Jaccard J, Radziwon CD, et al. Durability and decay of treatment benefit of cognitive behavioral therapy for irritable bowel syndrome: 12-month follow-up. *Am J Gastroenterol*. 2019;114(2):330-338. doi:10.1038/s41395-018-0396-x

#### CORRECTION

**Content Error:** In the Review article titled "Oral Antiplatelet Therapy After Acute Coronary Syndrome: A Review," published in the April 20, 2021,<sup>1</sup> issue of *JAMA*, aspirin's role in inhibiting platelet activation should have been reported as "irreversible." The reference supporting this statement has been updated. This article was corrected online.

1. Kamran H, Jneid H, Kayani WT, et al. Oral antiplatelet therapy after acute coronary syndrome: a review. *JAMA*. 2021;325(15):1545-1555. doi:10.1001/jama.2021.0716

**Data Errors in Table:** In the Research Letter titled "Reasons for Admissions to US Children's Hospitals During the COVID-19 Pandemic," published in the April 27, 2021, issue of *JAMA*,<sup>1</sup> there were 2 data errors in Table 2. For the pneumonia and bronchiolitis rows, the minus signs indicating negative values were omitted from the upper bounds of the 95% CIs for the adjusted change in values for spring (March 15 to May 31). The upper CI bound for the pneumonia row should have read -53.5 and the upper CI bound for the bronchiolitis row should have read -83.9. This article has been corrected online.

1. Gill PJ, Mahant S, Hall M, Berry JG. Reasons for admissions to US children's hospitals during the COVID-19 pandemic. *JAMA*. 2021;325(16):1676-1679. doi:10.1001/jama.2021.4382

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