



## Mood Medicine for a Moody Gut: Antidepressants in IBS

### CLINICAL QUESTION

**Do antidepressants improve irritable bowel syndrome (IBS) symptoms?**

### BOTTOM LINE

Tricyclic antidepressants (TCAs) improve overall IBS symptoms and abdominal pain in ~55% of patients versus ~35% with placebo at ~2-6 months. Mirtazapine shows similar, based on 1 small randomized, controlled trial (RCT). About 25-55% experience adverse effects (examples: drowsiness, dry mouth) with TCAs or mirtazapine compared to 5-35% with placebo. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) achieve similar pain relief but without consistent overall improvement. Limited evidence to suggest differing efficacy based on IBS subtype.

### EVIDENCE

- Focusing on the largest systematic review. Doses generally on lower end; half of RCTs specified IBS subtype. At 1.5-6 months:<sup>1</sup>

- TCAs (14 RCTs, 1290 patients): Including largest, primary care only RCT of amitriptyline 10-30mg.<sup>2</sup>
  - Proportion with global IBS improvement (pain, bloating, quality of life): 56% versus 37% (placebo); number needed to treat (NNT)=6.
  - Proportion with abdominal pain improvement: 54% versus 33% (placebo); NNT=5.
  - Adverse event withdrawals: 10% versus 6% (placebo); number needed to harm (NNH)=25.
    - Adverse events in largest RCT (drowsiness, dry mouth): 54% versus 35% (placebo); NNH=5 for each.<sup>2</sup>
- SSRIs (8 RCTs, 385 patients) and SNRIs (3 RCTs, 134 patients):
  - Global improvement: No difference.
  - Abdominal pain improvement: 45-93% versus 25-66% (placebo); NNT=4-5.
  - Adverse events: No difference.
- Mirtazapine (1 RCT, 67 patients):
  - Global improvement: 62% versus 30% (placebo); NNT=4.
  - Abdominal pain improvement: 65% versus 27% (placebo); NNT=3.
  - Adverse events (drowsiness, dry mouth, fatigue, weight gain): 25-35% versus 3-9% (placebo); NNH=4-5 for each.<sup>3</sup>
- Other systematic reviews similar.<sup>4-6</sup>
- Majority of TCAs, SSRIs, and SNRIs studied: No clear within-class differences.
- Limitations: Most RCTs small and short duration (4-12 weeks), high dropout rates, publication bias, inconsistent definitions of meaningful improvement.

## CONTEXT

- Guidelines<sup>7</sup> and pathways<sup>8</sup> recommend TCAs or SSRIs regardless of comorbid depression or anxiety.
- Largest TCA RCT suggests possible preferential benefit for diarrhea-predominant IBS,<sup>2</sup> but overall support for this theoretical benefit is weak.<sup>9</sup>
- Indirectly, dietary interventions (examples: FODMAP, Mediterranean diet) may have comparable efficacy to antidepressants.<sup>10-12</sup>
  - Evidence for antidepressants appears stronger than for antispasmodics, probiotics, or opioid receptor modulators.<sup>13-15</sup>

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*Authors have no conflicts of interest to declare.*

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