

# Review: Antidepressive agents improve symptoms and reduce pain in patients with functional gastrointestinal disorders

Jackson JL, O'Malley PG, Tomkins G, et al. Treatment of functional gastrointestinal disorders with antidepressant medications: a meta-analysis. *Am J Med.* 2000 Jan;108:65-72.

## QUESTION

Are antidepressive agents efficacious for treating patients with functional gastrointestinal (GI) disorders?

## DATA SOURCES

Studies were identified by searching MEDLINE (1966 to 1998), PsycLIT (1974 to 1998), EMBASE/Excerpta Medica (1974 to 1998), the Cochrane Library, and the Federal Research in Progress database using the terms antidepressive agents, serotonin reuptake inhibitors, monoamine oxidase inhibitors, amoxapine, clomipramine, tramipramine, desipramine, doxepin, imipramine, amitriptyline, maprotiline, nortriptyline, protriptyline, trazodone, nefazodone, fluoxetine, fluvoxamine, paroxetine, sertraline, femoxetine, venlafaxine, bupropion, citalopram, mianserin, pizotyline, pizotifen, functional colonic diseases, dyspepsia, and abdominal pain. Bibliographies of relevant reviews and studies were scanned.

## STUDY SELECTION

Randomized controlled trials were selected if they compared an antidepressive agent with placebo in an adult population and outcome data were provided.

## DATA EXTRACTION

Data were extracted on study quality, setting, country, dose, study duration, follow-up, patient numbers and characteristics, comorbid psychiatric disease, adverse effects, outcomes (pain or symptom improvement), and quality indicators.

## MAIN RESULTS

90 citations were reviewed, and 11 met the inclusion criteria. Quality scores were moderate with a mean score of 4 on a 9-point scale. 9 studies evaluated tricyclic antidepressants: amitriptyline and tramipramine in 3 studies, desipramine in 2 studies, and doxepin and clomipramine in 1 study each. 8 studies evaluated the irritable bowel syndrome (IBS), 2 evaluated nonulcer dyspepsia, and 1 evaluated both disorders.

Treatment with antidepressants improved GI symptoms (Table) and reduced pain scores (weighted mean difference 0.9, 95% CI 0.06 to 1.2) more than did placebo treatment.

## CONCLUSION

Antidepressant agents improve symptoms and reduce pain in patients with functional gastrointestinal disorders (the irritable bowel syndrome and nonulcer dyspepsia).

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## Symptom improvement with antidepressants vs placebo for gastrointestinal disorders with 4 to 12 wk of treatment\*

Number of studies	Weighted event rates		RBI (95% CI)	NNT (CI)
	Antidepressants	Placebo		
11	69%	36%	192% (120 to 300)	4 (3 to 7)

\*Abbreviations defined in Glossary; weighted event rates and RBI supplied by authors.

## COMMENTARY

Medical treatment of functional GI disorders has often been unsatisfactory. This meta-analysis by Jackson and colleagues presents evidence for the use of antidepressants, but several issues still must be addressed. Meta-analyses may miss unpublished studies that showed no effect; the sensitivity analysis provided suggests that 37 to 157 negative studies would have had to be missed to change the results of the review. In addition, the data found were somewhat limited: Only 8 studies investigated IBS. The others studied nonulcer dyspepsia, which also seems to respond to antidepressants.

The meta-analysis does not establish whether antidepressants in general are effective. 9 trials used tricyclic antidepressants, and their anticholinergic and analgesic effects might have been more important than their antidepressant effects. The 5HT blocker, mianserin, was effective when given alone (1 study), but trials of serotonin-reuptake inhibitors are lacking in patients with IBS.

The role of psychiatric diseases in IBS is complex. A high proportion of patients with IBS are reported to have psychiatric disease, and IBS may be more prevalent in patients with depression (1). Patients with IBS and psychological disorders are also more likely to consult their physicians than are patients who have IBS alone (2, 3).

Patients with IBS often require medication, which may include

tricyclic antidepressants. Placebo responses are high (16% to 59% in this analysis), and many mild-to-moderate cases respond to medical attention, including explanation and reassurance (4). Despite the high placebo response, however, a trial of antidepressants, especially of a tricyclic antidepressant, in patients with functional GI disorders is justified by the evidence provided by Jackson and colleagues.

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