

**Clinical Inquiries**

FROM THE FAMILY PRACTICE INQUIRIES NETWORK

**Which Antidepressant Is Best to Avoid Sexual Dysfunction?**

**Searchable Question**

In patients being treated for depression, which antidepressants have a low risk of sexual side effects?

**Evidence-Based Answer**

Bupropion (Wellbutrin), nefazodone (Serzone), amitriptyline (Elavil), and moclobemide (Manerix, a reversible inhibitor of monoamine oxidase type A not available in the United States) have been shown to cause less sexual dysfunction than selective serotonin reuptake inhibitors (SSRIs). [Strength of recommendation: B, based on individual randomized controlled trials (RCTs)] Among SSRIs, fluvoxamine (Luvox) may cause less sexual dysfunction than sertraline (Zoloft). [Strength of recommendation: B, single RCT] No other differences between or within classes of antidepressants have been demonstrated in RCTs.

**Evidence Summary**

The incidence of sexual side effects between different antidepressants in adults with depressive or anxiety disorders has been reported by 25 RCTs, most of which were included in two recent descriptive systematic reviews.<sup>1,2</sup> [References 1 and 2--Evidence level 1A] Bupropion led to less sexual dysfunction (or to more sexual satisfaction) than sertraline or fluoxetine in four trials. The number needed to harm (NNH), that is, the number of patients who have to take the drug for one patient to experience sexual dysfunction, ranged from two to 17, depending on the type of dysfunction.<sup>1,2</sup> Nefazodone led to less sexual dysfunction (or to more sexual satisfaction) than sertraline in two trials (NNH: two to seven).<sup>1-3</sup> [Reference 3--Evidence level 1B] Moclobemide led to less sexual dysfunction than four SSRIs in one trial (NNH: five) and to greater sexual desire than doxepin (Adapin) in one trial (number needed to treat: eight).<sup>2-4</sup> [Reference 4--Evidence level 1B] The *accompanying table*<sup>1-4</sup> summarizes the different adverse sexual effects and the agents that cause them.

---

**Significantly Different Adverse Sexual Effects Caused by Various Antidepressants**

---

<i>Outcome</i>	<i>Agents</i>
Increased sexual desire	Moclobemide* (Manerix) >doxepin (Adapin)
Diminished sexual desire	Fluoxetine (Prozac) >bupropion (Wellbutrin); sertraline (Zoloft) >nefazodone (Serzone)
Sexual arousal disorder	Sertraline, fluoxetine >bupropion; sertraline >nefazodone
Ejaculatory abnormality	Sertraline >nefazodone
Orgasm dysfunction, male	Sertraline >bupropion
Orgasm dysfunction, female	Sertraline >bupropion
Orgasm dysfunction, total	Sertraline, fluoxetine >bupropion
Sexual dysfunction, male	Sertraline >amitriptyline (Elavil)
Sexual dysfunction, female	Sertraline >nefazodone
Sexual dysfunction, total	Sertraline >fluvoxamine (Luvox), nefazodone; SSRI >moclobemide
Sexual satisfaction	Bupropion, nefazodone >sertraline

> = "is associated with a greater incidence of the measured outcome than"; SSRI = selective serotonin reuptake inhibitor.

\*--Not available in the United States.

note: No significant difference was found for the following: sertraline vs. citalopram (Celexa); paroxetine (Paxil) vs. fluvoxamine or fluoxetine; amitriptyline vs. amoxapine (Asendin) or mirtazapine (Remeron); clomipramine (Anafranil) vs. fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram; phenelzine (Nardil) vs. imipramine (Tofranil).

Information from references 1 through 4

There were no other consistent differences between classes of antidepressants. One trial reported less sexual dysfunction resulting from amitriptyline than from sertraline (NNH: seven), but numerous trials have not shown differences between clomipramine (Anafranil) and other SSRIs.<sup>1,2</sup> One trial showed less sexual dysfunction resulting from fluvoxamine than from sertraline (NNH: six), but no differences between other SSRIs have been demonstrated.<sup>1,2</sup> Limitations to many of the published studies include small sample sizes, failure to control for baseline differences in sexual function between groups of patients, and lack of uniform means of inquiring into sexual adverse effects.

### Recommendations from Others

Guidelines issued by the American Psychiatric Association<sup>5</sup> (APA) and the American College of Physicians/American Society of Internal Medicine<sup>6</sup> (ACPASIM) do not provide specific

recommendations regarding which antidepressant to prescribe to minimize sexual dysfunction. [References 5 and 6--Evidence level 1A] The APA notes that SSRIs can carry a risk of sexual side effects, whereas the ACPASIM states that the data are insufficient to estimate incidence rates, thus making quantitative comparisons among antidepressants impossible.

### **Clinical Commentary**

Bupropion appears to be the best antidepressant for use in patients who are concerned about drug-related sexual dysfunction. Amitriptyline may be a less expensive and suitable alternative, but it has other worrisome adverse effects. Nefazodone may have a low incidence of sexual dysfunction, but it has been associated with hepatotoxicity and was withdrawn from the Canadian and European markets. Moclobemide is not available in the United States.

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group ([http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)).

This series of Clinical Inquiries is coordinated for *American Family Physician* by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN.

JOHN SMUCNY, M.D., and MICHAEL S. PARK

Department of Family Medicine

State University of New York Upstate Medical University Syracuse, N.Y.

### **REFERENCES**

1. Gregorian RS, Golden KA, Bahce A, Goodman C, Kwong WJ, Khan ZM. Antidepressant-induced sexual dysfunction. *Ann Pharmacother* 2002;36: 1577-89.
2. Montgomery SA, Baldwin DS, Riley A. Antidepressant medications: a review of the evidence for drug-induced sexual dysfunction. *J Affect Disord* 2002;69:119-40.
3. Ferguson JM, Shrivastava RK, Stahl SM, Hartford JT, Borian F, Ieni J, et al. Reemergence of sexual dysfunction in patients with major depressive disorder: double-blind comparison of nefazodone and sertraline. *J Clin Psychiatry* 2001;62:24-9.
4. Philipp M, Tiller JW, Baier D, Kohnen R. Comparison of moclobemide with selective serotonin reuptake inhibitors (SSRIs) on sexual function in depressed adults. The Australian and German Study Groups. *Eur Neuropsychopharmacol* 2000; 10:305-14.
5. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry* 2000;157 (4 suppl):1-45.

6. Snow V, Lascher S, Mottur-Pilson C. Pharmacologic treatment of acute major depression and dysthymia. American College of Physicians-American Society of Internal Medicine. Ann Intern Med 2000;132:738-42.

*Address correspondence by e-mail to John Smucny, M.D., [smucnyj@upstate.edu](mailto:smucnyj@upstate.edu). Reprints are not available from the authors.*

*Copyright Family Practice Inquiries Network. Used with permission.*

---

Copyright © 2004 by the American Academy of Family Physicians.

This content is owned by the AAFP. A person viewing it online may make one printout of the material and may use that printout only for his or her personal, non-commercial reference. This material may not otherwise be downloaded, copied, printed, stored, transmitted or reproduced in any medium, whether now known or later invented, except as authorized in writing by the AAFP. Contact [afpserv@aafp.org](mailto:afpserv@aafp.org) for copyright questions and/or permission requests.