Effective Health Care

Choosing Antidepressants for Adults

Clinician's Guide

This guide summarizes clinical research comparing the effectiveness and safety of commonly used antidepressants for adults with major depression. The medications included in this guide are the selective serotonin reuptake inhibitors (SSRIs) and other agents approved for depression in the United States over the past 20 years. The reviewed drugs are listed on the back page.

This guide does not cover depression in children or adolescents, postpartum depression, or depression in people with coexisting psychiatric disorders. It also does not include tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), St. John's Wort, psychotherapy, light therapy, or exercise. It does not cover any combination of therapies.

Clinical Issue

More than 16 percent of Americans will be affected by major depression at least once during their lifetime.

Pharmacotherapy is a primary treatment strategy for depression, but almost 40 percent of people will not respond to the first antidepressant they take. Medication side effects are common. More than 60 percent of people on antidepressants will experience at least one.

Owing to the substantial nonresponse rate and the high incidence of side effects, many people need to try several different antidepressants before finding one that works for them and that they can tolerate. The success of any antidepressant choice will ultimately depend on a balance of depression relief, side effects, and cost.

Clinical Bottom Line

- All the antidepressants in this guide are effective for treating the acute phase of major depression in adults, including those 60 and older.

  LEVEL OF CONFIDENCE: ●●○

- Response rates vary initially but are similar after 4 weeks of treatment with citalopram, fluoxetine, mirtazapine, paroxetine, and sertraline.

  LEVEL OF CONFIDENCE: ●●○

- Although the reasons vary (side effects versus inadequate response), overall discontinuation rates are similar for the antidepressants in this guide.

  LEVEL OF CONFIDENCE: ●●●

CONFIDENCE SCALE

The confidence ratings in this guide are derived from a systematic review of the literature. The level of confidence is based on the overall quantity and quality of clinical evidence.

HIGH ●●● There are consistent results from high quality studies. Further research is very unlikely to change the conclusions.

MEDIUM ●●○ The findings are supported but further research could change conclusions.

LOW ●○○ Further research is very likely to change the conclusions.

SOURCE: The source material for this guide is a systematic review of 293 research publications representing 187 studies. The review, *Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression* (2007), was prepared by the RTI International-University of North Carolina Evidence-based Practice Center. Of the 187 studies included in the review, pharmaceutical companies financially supported 126. The Agency for Healthcare Research and Quality (AHRQ) funded the systematic review and this guide. The guide was developed using feedback from clinicians who reviewed preliminary drafts.

Phases of Treatment

Treatment of depression is generally broken down into three phases: the acute phase (usually 6–12 weeks), during which treatment is directed at obtaining remission of symptoms; the continuation phase (4–9 months), during which treatment is directed at preventing relapse; and the maintenance phase (6 months to years), during which the treatment goal is preventing the recurrence of a new distinct episode of major depression.

Acute Phase

- All the medications in this guide work equally well to treat the acute phase of depression.

  LEVEL OF CONFIDENCE: ●●○
- All these antidepressants are limited by substantial nonresponse rates. Four of every 10 people will not respond to the first medication prescribed.
- There is no evidence to guide selection of the best initial drug for an individual.

Subsequent Phases

- All the antidepressants in this guide can prevent relapse or recurrence of depression, with the exception of duloxetine, which has not been studied.

  LEVEL OF CONFIDENCE: ●●○
- Because most clinical trials have examined only the acute phase of major depression, there is little evidence comparing these medications for the continuation or maintenance phases of depression treatment.

Selecting an Antidepressant

Although the antidepressants included in this guide have similar effectiveness and side effect profiles, individual response will vary. The success of an antidepressant choice depends on finding a medication that works and that a particular individual can tolerate.

Onset of Action

It takes about 6–8 weeks for most people to begin to get the full therapeutic effect of antidepressants.

- Response rates vary initially but are similar after 4 weeks of treatment with citalopram, fluoxetine, mirtazapine, paroxetine, and sertraline.

  LEVEL OF CONFIDENCE: ●●○
- If faster onset is important, consider mirtazapine. It brings greater relief of depression within the first month but is similar to other antidepressants beyond 30 days. The faster onset of action should be balanced with the higher likelihood of weight gain.

Second-Line Agent

Consider switching drugs if the initial antidepressant does not relieve symptoms.

- Usually 1 of every 4 people who do not respond to the first antidepressant tried will respond after switching drugs, according to a recent clinical trial known as the STAR-D trial.
- Evidence is insufficient to determine which drug to choose as a second agent.

Accompanying Symptoms

- For people with symptoms of anxiety that accompany their depression, the antidepressants in this guide work equally well in relieving their anxiety.

  LEVEL OF CONFIDENCE: ●●○
- The antidepressants in this guide can relieve symptoms that accompany depression, such as insomnia, pain, somatization, melancholia, and psychomotor symptoms. However, the evidence is insufficient to determine if any particular antidepressant works best for any particular symptoms.

Tolerability

Monitoring an individual's ability to tolerate an antidepressant is important because up to 15 percent of people discontinue their drugs due to side effects.

- People taking venlafaxine are more likely to discontinue due to side effects than people taking any of the SSRIs (11.5 percent versus 8.5 percent).

  LEVEL OF CONFIDENCE: ●●●

Side Effect Profiles

- If sexual dysfunction is a concern, consider bupropion.
- If weight gain is a concern, avoid mirtazapine and paroxetine.
- If diarrhea is a concern, avoid sertraline.

Dose and Cost

Dosing regimens and cost may also influence adherence for some individuals. Drugs and prices are listed on the back page.

Side Effects

The most common side effects of the antidepressants in this guide are constipation, diarrhea, dizziness, dry mouth, fatigue, headache, insomnia, nausea, sexual dysfunction, sweating, tremor, and weight gain. More than 60 percent of people taking antidepressants experience at least one side effect. The medications in this guide have not all been compared with each other for each individual side effect. Here is what the research can tell us:

Weight Change

- Mirtazapine causes higher weight gain than comparator drugs (citalopram, fluoxetine, paroxetine, and sertraline). The mean range of weight gain with mirtazapine at 6–8 weeks of treatment is about 2–7 lbs. However, the variation in weight gain is large, and some people may gain substantially more weight.

  LEVEL OF CONFIDENCE: ● ● ○

- Paroxetine causes higher average weight gains (about 3.6 percent of body weight, or 5 lbs for someone weighing 150 lbs) than does fluoxetine or sertraline. About 25 percent of people on paroxetine gain more than 7 percent of their body weight.

  LEVEL OF CONFIDENCE: ● ● ○

- Bupropion causes modest weight loss (about 2.5 lbs from baseline) compared with placebo.

  LEVEL OF CONFIDENCE: ● ● ○

Nausea and Vomiting

- Nausea and vomiting are the most common clinical reasons people discontinue an antidepressant during the first 30 days of treatment.

  LEVEL OF CONFIDENCE: ● ● ○

- Nausea and vomiting are 10 percent more common for people taking venlafaxine than for people taking SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline).

  LEVEL OF CONFIDENCE: ● ● ●

Sexual Dysfunction

- Fewer people taking bupropion have sexual problems than do people taking fluoxetine or sertraline.

  LEVEL OF CONFIDENCE: ● ● ○

- More people taking paroxetine have sexual problems than do people taking fluoxetine, fluvoxamine, nefazodone, or sertraline (16 percent for paroxetine versus 6 percent for the others).

  LEVEL OF CONFIDENCE: ● ● ○

Diarrhea

- More people taking sertraline (8 percent more) have diarrhea than do people taking bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, or venlafaxine.

  LEVEL OF CONFIDENCE: ● ● ○

Discontinuation Syndrome

- Discontinuation syndrome (acute headache, dizziness, and nausea) is most common for people who abruptly discontinue paroxetine or venlafaxine.

  LEVEL OF CONFIDENCE: ● ● ○

- Discontinuation syndrome is least common with fluoxetine.

  LEVEL OF CONFIDENCE: ● ● ○

Risks of Serious Harm

Serotonin Syndrome

These antidepressants carry a risk of serotonin syndrome, a potentially life-threatening condition caused by toxic levels of serotonin. Common symptoms include confusion, shivering, sweating, fever, hypertension, tachycardia, tremor, nausea, and diarrhea. Evidence is insufficient to tell us how these antidepressants compare for the risk of serotonin syndrome.

Adult Suicide

The suicide risk for antidepressants has received considerable attention. The evidence is insufficient to draw conclusions about comparative risks of suicide among adults taking the antidepressants in this guide.

In May 2007, the Food and Drug Administration updated the warning that these antidepressants increase the risk of suicide for young adults. The warning, previously for age 18 and younger, was expanded to include those up to age 24.

DOSE & PRICE OF SELECTED ANTIDEPRESSANTS

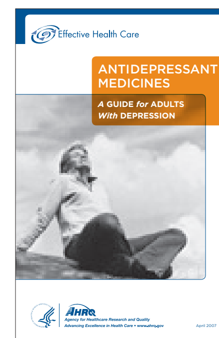
Drug Name[1]	Brand Name	Dose[2]	Price for 1-Month Supply[3]	
			Generic	*Brand*
Bupropion	Wellbutrin®	75 mg tid 150 mg tid	$ 65 $ 175	$ 160 $ 210
	Wellbutrin SR®	150 mg daily 150 mg bid 200 mg bid	$ 60 $ 115 $ 230	$ 85 $ 175 $ 320
	Wellbutrin XL®	150 mg daily 300 mg daily 450 mg daily	NA	$ 125 $ 165 $ 290
Citalopram[4]	Celexa®	10 mg daily 20 mg daily 40 mg daily 60 mg daily	$ 75 $ 75 $ 80 $ 155	$ 90 $ 95 $ 100 $ 195
Duloxetine	Cymbalta®	20 mg bid 30 mg bid 60 mg bid	NA	$ 215 $ 240 $ 240
Escitalopram[4]	Lexapro®	10 mg daily 20 mg daily	NA	$ 80 $ 85
Fluoxetine[4]	Prozac®	10 mg daily 20 mg daily 40 mg daily 40 mg bid	$ 80 $ 80 $ 160 $ 320	$ 145 $ 150 $ 295 $ 595
	Prozac Weekly®	90 mg once wkly	NA	$ 110
Fluvoxamine[4]	Only available as generic	50 mg daily 100 mg daily 150 mg daily	$ 75 $ 80 $ 160	NA
Mirtazapine	Remeron®	15 mg daily 30 mg daily 45 mg daily	$ 80 $ 85 $ 85	$ 105 $ 110 $ 110
Nefazodone	Only available as generic	50 mg bid 100 mg bid 300 mg bid	$ 90 $ 90 $ 200	NA
Paroxetine[4]	Paxil®	10 mg daily 20 mg daily 40 mg daily 60 mg daily	$ 80 $ 80 $ 85 $ 165	$ 95 $ 100 $ 110 $ 210
Sertraline[4]	Zoloft®	50 mg daily 100 mg daily 200 mg daily	$ 85 $ 85 $ 170	$ 90 $ 90 $ 180
Trazodone	Desyrel®	50 mg daily 100 mg tid 150 mg tid	$ 15 $ 65 $ 130	$ 70 $ 355 $ 305
Venlafaxine	Effexor®	37.5 mg bid 50 mg bid 75 mg tid	NA	$ 135 $ 140 $ 220
	Effexor XR®	75 mg daily 150 mg daily 225 mg daily	NA	$ 110 $ 120 $ 230

[1] These drugs were evaluated in the systematic review.
[2] Doses are representative of those used in the research studies.
[3] Average Wholesale Price from *Drug Topics Redbook*, 2007.
[4] Selective serotonin reuptake inhibitor (SSRI).
SR = sustained release, XL/XR = extended release, bid = twice a day, tid = three times a day, NA = not available.

Still Unknown

- There is insufficient evidence to guide selection of the best initial drug for an individual or choice of a second line agent.
- We do not have enough data to determine if any antidepressant works best for men versus women or in people of different races or ethnicities.
- Evidence is insufficient to determine whether people age 60 and older experience different side effects than younger people when they take these drugs.

Resource for Consumers



Antidepressant Medicines: A Guide for Adults With Depression is a companion to this Clinician's Guide. It can help people talk to their health care professional about medications for major depression. It provides information about:

- Benefits, side effects, and price of antidepressants.
- Seeking advice from a health care professional about depression treatment options.

For More Information

For electronic copies of the consumer's guide, this clinician's guide, and the full systematic review, visit this Web site: **www.effectivehealthcare.ahrq.gov**

For free print copies call:

The AHRQ Publications Clearinghouse
(800) 358-9295

Consumer's Guide, AHRQ Pub. No. 07-EHC007-2A
Clinician's Guide, AHRQ Pub. No. 07-EHC007-3

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The photos in this guide are of models and are used for illustrative purposes only.

AHRQ Pub. No. 07-EHC007-3
August 2007