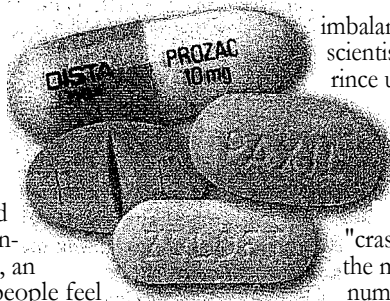


# The case against antidepressants

*A growing chorus of critics is challenging the widespread use of antidepressants. Why?*

## How do antidepressants work?

No one knows for sure. The most commonly prescribed antidepressants in the U.S. alter levels of a neurotransmitter called serotonin, which has been linked to feelings of well-being. These drugs, grouped together as selective serotonin reuptake inhibitors (SSRIs) and marketed under such names as Prozac, Celexa, Zoloft, and Paxil, essentially keep serotonin in the brain's synapses for an instant longer than usual; in theory, an increase in the level of serotonin is what makes people feel less depressed or anxious. About three quarters of people who take antidepressants say that the drugs improve their lives. Antidepressants are now the most commonly prescribed medication for adults up to age 59. One in 10 Americans, or 30 million people, takes them every day, generating \$10 billion in annual sales. But a spate of critics have recently stepped forward with books and studies that challenge the efficacy of antidepressants, and the theory behind how they work. These critics even charge that the profligate use of SSRIs and other psychiatric medications is unpredictably altering the brain chemistry of millions of people, and contributing to the epidemic of mental illness in the U.S.



imbalance of neurotransmitters, some psychiatrists and scientists say. This is one reason SSRI users can experience unpleasant side effects, ranging from agitation to reduced sex drive to an increase in suicidal thoughts. In his book, *Anatomy of an Epidemic*, science writer Robert Whitaker argues that long-term use of SSRIs makes people dependent on an artificially elevated level of serotonin, so they "crash" back into depression when they try to go off the medication. It's no coincidence, he says, that "the numbers of adults and children disabled by mental illness has risen at a mind-boggling rate" since the use of antidepressants and other psychoactive drugs became widespread.

## Don't people say the drugs help them?

Yes; many do. That can be explained, says Kirsch, by the well-documented "placebo effect": People often recover from a physical or mental illness if they believe a pill or other treatment will help them. "These drugs work because people hope and expect they will," Kirsch says. The drug companies disagree; they say different people respond to the drugs in different ways, which is why studies of a single drug across a large group can show negligible effects when measured against a placebo. It's all a matter of matching the right SSRI to the right patient, the drug companies likened psychiatrists, Peter D. Kramer, author of *Listening to Prozac*, says that SSRIs help many of his depressed, anxious, or highly neurotic patients get "unstuck" from negative patterns of thinking and behavior. Antidepressants "make the brain more flexible," he recently wrote in *The New York Times*. "They've earned their place in the doctor's satchel."

## What evidence do critics have?

They point to numerous studies—including many done by Big Pharma itself—that have found that SSRIs are little more effective at relieving depression and anxiety than placebos, or "dummy pills." In the book *The Emperor's New Drugs*, psychologist Irwin Kirsch revealed that more than half of the clinical trials sponsored by drug companies for the Food and Drug Administration between 1987 and 1999 found that SSRIs alleviated depression no better than placebos. (See box.) A more recent study published in *JAMA*, the journal of the American Medical Association in January 2010 found that for mild to moderate depression, the difference between placebos and antidepressants was "nonexistent to negligible." The medications proved significantly more effective in only the most severe cases, about 13 percent of patients.

## What's the lure for SSRIs?

The critics are hoping to persuade psychiatrists and society as a whole to stop viewing drugs as a go-to cure for depression. Studies show that in cases of mild or moderate depression, psychotherapy—talk therapy—relieves symptoms at the same rate as drugs or placebos; even regular, vigorous exercise has been shown to alleviate symptoms of depression as well as pills do. But insurance companies now resist paying for more than a few sessions of talk therapy. In addition, most of the doctors prescribing antidepressants are primary-care doctors, not psychiatrists, and they can't offer talk therapy. So SSRIs will probably remain widely prescribed for the foreseeable future—especially since many people say they can't live without them. "I believe antidepressants have saved my life on several occasions," says the author John Crace, who has written about his struggles with severe depression. "The professionally well might say I am deluded, that I am the victim of a medical conspiracy. Possibly I am. But rather deluded than dead."

## How SSRIs were approved

If Prozac and its chemical cousins are barely more effective than placebos, how did the drug companies get the government to approve them? To approve a drug, the Food and Drug Administration requires pharmaceutical companies to provide just two positive trials showing that it's more effective than a placebo. But the FDA does not set a limit on the number of negative trials a company can carry out before coming up with two positives. Theoretically, a drug company could carry out hundreds of failed trials before finally ending up with two successful ones. Not only that, but the company doesn't even have to tell the public about the unsuccessful trials. For his book on antidepressants, psychologist Irwin Kirsch used Freedom of Information Act laws to uncover dozens of unpublished scientific trials by Big Pharma in which antidepressants failed to perform better than placebos. When drug companies submit studies of medications to the FDA, Kirsch says, "Adverse data are suppressed. It's as if the fox has been hired to guard the hen house."

## Is depression caused by chemical imbalance?

There's actually little evidence supporting this widespread belief, which was heavily promoted by the drug companies. In fact, studies have found that the levels of serotonin in depressed people's brains are the same as they are in those of nondepressed people. If neurotransmitters play some role in depression, critics say, it's clearly not a simple matter of cause and effect. "The serotonin theory of depression," says Irish psychiatrist and author David Healy, "is comparable to the masturbatory theory of insanity."

## So what do these drugs do?

They actually create an unnatural