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REFLECTIONS

# More Fuel For Debate On Prozac

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How good are Prozac and its relatives at treating depression?

If the claims made by some researchers over the last few years are given any credence, the drugs, despite their popularity, are little better than dummy pills in driving away despair.

The critics insist that as much as 75 percent of the improvement shown by depressed patients taking antidepressants can be attributed to the "placebo effect," the healing power of taking a pill, and the support patients find in clinical trials. They say clinical trials of antidepressant drugs have been tainted by the pro-medication bias of the investigators conducting them.

But a recent report in *The American Journal of Psychiatry* offers a different view. In it, a group of Columbia University scientists review the critics' evidence and find it far from convincing.

The studies cited by the critics "fail upon closer examination" to support their assertions, wrote the scientists, led by Dr. Fredric M. Quitkin, a psychiatrist at Columbia's College of Physicians and Surgeons. And Dr. Donald F. Klein, a co-author of the report, called claims that antidepressants were only slightly better than a placebo "a clear distortion."

The debate is hardly academic.

"We are concerned that these conclusions may discourage depressed people

## Trying to measure drugs' effects on an unmeasurable illness.

from seeking effective treatment," Dr. Quitkin and his colleagues wrote.

It is true that teasing out the healing effects offered by a drug from the benefits bestowed by a dummy pill is a difficult task, particularly when the drug in question is intended to treat chronic illnesses like depression, arthritis or hypertension, whose symptoms worsen at some times and improve at others.

Complicating matters, depression, like most psychiatric illnesses, cannot be detected with blood tests and produces no changes in body tissue or other measurable physiological markers. Studies set up to test the efficacy of treatments for depression must rely upon more subjective measures: doctors' ratings or patients' own assessments.

The wiggle room left by such methods offers a perfect battleground for competing ideologies: those who believe, for example, that drugs are overused and see psychotherapy as the treatment of choice for depression, versus those who view antidepressants as a lifesaving and underused resource.

The skeptics argue that even in the best studies, antidepressants are only minimally effective, and that doctors and patients often can tell, by the presence or absence of side effects, who is taking a drug, and who a placebo.

"Maybe 2 out of 10 people benefit," from taking antidepressants, said Dr. Robert Greenberg, a psychologist at the State University of New York Upstate Medical University at Syracuse, who has been among the most vocal critics.

In their review, however, Dr. Quitkin and his colleagues could find no evidence that bias explained the drug effects shown in clinical trials.

Clinical trial investigators themselves are quick to concede that the measures used to assess subjects' progress are far from perfect.

"Emotions are not linear, and trying to measure something as complex as emotions on an arithmetic scale just becomes very difficult," said Dr. Arif Khan, the director of the Northwest Clinical Research Center in Bellevue, Wash.

In a paper appearing this month in *Archives of General Psychiatry*, Dr. Khan and two colleagues analyzed drug effects in clinical trial data from 8,731 patients participating in 45 studies of seven antidepressants.

The researchers, who obtained the data from the Food and Drug Administration through a request under the Freedom of Information Act, found that 40.7 percent of patients in the trials who received the drugs showed a reduction in symptoms, compared with 30.9 percent of patients who received placebos.

Most studies have found larger differences. In a 1999 review by the federal Agency for Health Care Policy and Research of more than 80 antidepressant studies, for example, 50 percent of patients improved on the drugs, compared with 32 percent on placebos.

Dr. Khan described the effects of drugs in the studies he reviewed as "modest," but he said he had no doubt the drugs worked, particularly for severely ill patients, normally excluded from trials. "When you go out in the real world and look at treated patients and untreated patients, believe me, the difference is very large," Dr. Khan said.

Still, most experts agree that while drugs for depression are effective they are still not effective enough, for enough patients that remains for the future.