Flaws in the NIMH-Funded Study "Evaluation of Outcomes with Citalopram [Celexa] for Depression Using Measurement-Based Care… Implications for Clinical Practice"

A report by
Citizens Commission on Human Rights

This is a study that has been recently touted in the media as "new," showing that SSRI antidepressants can be effective in the treatment of depression. However, the findings of this study show a remarkably low percentage of people actually had a remission (lessening) of symptoms. In fact, the authors used measurement-based care in actual practice, something unusual, but the results were no better than that found in 8-week or 12-week clinical drug trials for treatment of depression. Approximately 70% of the study's participants did not have a remission of symptoms and over 50% did not even have a response to the drug.

1. The study, by Trivedi, *et al.*, attempts to compare the rates, timing and predictors of remission of symptoms of depression in the "real world" versus those found in clinical drug trials. The authors used measurement-based care in actual practice, which included routine measurement of symptoms and side effects of drugs given at each treatment visit and modification of medication doses based on what was found. The authors attempted to single out responses to one drug, the SSRI antidepressant citalopram (Celexa), despite patients taking other medications.

- "The overall remission rate was 27.5% [using one particular self-test] and 32.9% [using another similar test]. The overall…response rate was 47%.… Remission rates from research-based, 8-week, randomized, placebo-controlled efficacy trials with depressed, symptomatic volunteers range from 25% to 40%, and 12-week efficacy trials with subjects suffering from chronic depression reveal even more modest remission rates of 22%-30%." ("Remission" was defined in the study as "a virtual absence of symptoms" of depression symptoms. "Response" was defined as "a meaningful reduction of symptoms"– at least 50% according to depression surveys used in the study to measure a person's symptoms. "Placebo" is defined as an inactive substance used in clinical trials as a comparator.)

- Robert Whitaker, author of *Mad in America*: *Bad Science, Bad Medicine, and the Enduring Mistreatment of the Mentally Ill*, stated after reviewing this study, "If only 30 percent achieve remission, what do we say about the other 70%? They are all harmed somewhat by the side effects of the drugs, and some of course had serious side effects, including serious psychiatric events. And so what this study shows is this: No benefit on the target symptom against what is the commonly acknowledged placebo response rate, and thus, in the aggregate, no rationale for using the drugs, since we know that many patients will suffer side effects. The net in this risk-benefit analysis is, once again, a negative to the health of the treated group."[1]

2. The study excluded participants whom researchers knew would not respond to antidepressants.

- "Patients…were excluded from the study…[those with] a clear history of nonresponse or intolerance (in the current major depressive episode) to any…antidepressant in the first two treatment steps." [2]

3. The study lacks a placebo "control group" and therefore has no comparison to patients given a sugar pill or other sham treatment. Yet studies have repeatedly shown placebo to be as effective as drugs in some people.

- "Study limitations includes open treatment design, the use of a single antidepressant agent (citalopram), and the lack of placebo control."

- According to Robert Whitaker, "It [the study] shows, once again, that these drugs don't work even on the target symptom of depression. Again, you need a comparison group. What is the natural rate of remission? What is the rate of remission with a placebo? There is a huge body of evidence showing that you would expect at least 30 percent to remit, and another 15 to 20 percent—at least—to improve somewhat. And of course when the NIMH (National Institute of Mental Health) compared an SSRI to St. John's Wort to placebo, placebo was the most efficacious, and an SSRI no more effective than St. John's Wort. That's what we see, once again, with this study. There is no comparator, but the improvement rate is roughly in line with placebo improvement rates over 50 years of studies (actually the placebo response rate in the 1950s and 1960s was around 46%, and so we've gone down since then)." [3]

4. Some study participants could have experienced improvements from other medical treatments and drugs that patients were also taking during the study.

- "Concomitant [occurring or existing concurrently] treatments for current general medical conditions [as part of ongoing clinical care], for associated symptoms of depression [e.g., sleep, anxiety, and agitation], and for citalopram side effects [e.g., sexual dysfunction] were permitted on the basis of clinical judgment." In other words, the researchers didn't know that the benefits the patients received during the study were the results of citalopram or some other medication. [4]

5. The authors also clearly state that life conditions have considerable bearing on one's outlook toward life and can contribute to or take away from any treatment "result." This itself casts more doubt on whether the stated remission rates of the study were even due to the antidepressant.

- "Several…features were associated with higher remission rates, including lower…severity [of depression]; being…better educated, and more highly paid; and having private insurance, fewer concurrent general medical and psychiatric disorders, better pretreatment physical and mental function…[and] greater life satisfaction…."

- Lower remission rates were associated with being unemployed; having a lower income; being non-Caucasian, male, and less educated; and having poorer function and lower quality of life…."

References:

[1] Robert Whitaker, comments on file with CCHR International.

[2] Madhukar H. Trivedi, M.D., *et al*., "Evaluation of Outcomes with Citalopram for Depression Using Measurement-Based Care in STAR*D: Implications for Clinical Practice," *American Journal of Psychiatry*, 163:1, Jan. 2006, p. 29.

[3] Robert Whitaker, comments on file with CCHR International.

[4] Madhukar H. Trivedi, M.D., *et al*., "Evaluation of Outcomes with Citalopram for Depression Using Measurement-Based Care in STAR*D: Implications for Clinical Practice," *American Journal of Psychiatry*, 163:1, Jan. 2006, p. 31.

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