

## Key Points

1. Depression and anxiety are common among Chiari sufferers
2. A much hyped report found that recently approved anti-depressants may not be as effective as first thought
3. Researchers compared studies in the published medical literature to studies in the FDA registry, which contains the complete data available for a drug
4. For 12 anti-depressants found that nearly one third of the studies submitted to the FDA were never published in the medical literature
5. Studies with positive results were 12 times more likely to be published than ones that did not find anything
6. Also found that 11% of the studies had conflicting conclusions between the version in the medical literature and the FDA's opinion on the study results
7. Overall, the published medical literature overstated the effectiveness of the drugs by an average of 32% compared to the complete FDA data set
8. Still each drug was found to be more effective in treating depression than a placebo

## Definitions

**double blind** - type of clinical trial design in which neither the investigators nor the subjects are aware of whether people are receiving the treatment under study or a placebo

**FDA** - Food and Drug Administration, government agency responsible for approving the sale and marketing of prescription drugs

**neurotransmitter** - a chemical messenger in the brain

**placebo** - an inactive substance which is used as a basis of

## Review Shows Anti-Depressants May Not Be Effective

**May 31, 2008** -- In a report which received national media attention, a group of researchers (Turner et al.) has found that recently approved anti-depressants may not be as effective in treating depression as first thought. This news is especially disturbing for the Chiari community where depression and anxiety rates are much higher than average.

Although it has not been studied extensively, there is evidence that depression and anxiety may affect upwards of 50% of Chiari patients. It is not clear whether Chiari causes these mood problems directly, meaning that the compression or lack of spinal fluid flow alters the neurochemistry of the brain, if it is a secondary effect, or most likely a combination of both. Research has shown that chronic pain can fundamentally reduce levels of serotonin - a key neurotransmitter in regulating mood - and depression is very common among chronic pain sufferers. Similarly, research has also found that people dealing with chronic diseases in general, especially ones which involve functional limitations, are very prone to developing depression and other mood disorders.

As expressed so eloquently in the book, *Contents Under Pressure*, the effects of dealing with Chiari related depression can be profound and include work, family relationships, and in some cases can even lead to thoughts of suicide. Suicide is a topic not generally discussed in the Chiari literature, but if depression rates are truly near 50% then odds are the suicide rate among Chiari patients is much higher than average (Ray D'Alonzo deserves credit for pointing this out). Indeed, while this has not been established scientifically, Conquer Chiari has received many anecdotal stories along these lines.

For the patient, depression can become overwhelming, however to date most cases have been considered to be treatable through anti-depressant medication, various types of therapy, or a combination of both. Research across the board has shown that anti-depressant medications in particular are very effective in treating many cases of mild to moderate depression. That is why the study by Turner et al. created quite a stir when it was released in the January 17th, 2008 issue of the *New England Journal of Medicine* (one of the premiere and most widely read medical journals).

In their research, the scientists focused on 12 anti-depressant drugs which were approved by the FDA between 1987 - 2004, including well known ones such as Zoloft, Prozac, and Paxil. When a drug manufacturer begins working on a drug, they must register with the FDA all the clinical trials they will run to support their application. This is done in advance of the actual trials and the results are turned over to the FDA whether they show a positive effect for the drug or not. For this study, the researchers compared the studies that were in the FDA registry for the 12 identified drugs to what had been published in the medical literature. In other words, they were looking to see if all the studies associated with these drugs had been published for dissemination to the medical community, and also if the conclusions drawn in the published articles matched the view of the FDA.

Specifically, the team found 74 FDA registered studies involving 12,564 patients for the 12 anti-depressants. For each study, the scientists looked to see if it could be found in the general medical literature. If it was found, they looked to see if the conclusion drawn in the published study matched the FDA conclusion on whether the study found a positive result for the effectiveness of the drug versus a placebo. All the studies were randomized, double blind, placebo controlled in design, which is considered scientifically rigorous.

Of the 74 FDA registered studies, almost a third (23), were never published in the medical literature (Figure 1). Of the studies which were not published, the vast majority were deemed to be a negative or questionable outcome by the FDA. In fact, the researchers found that studies with positive results were 12 times more likely to be published than ones with negative or ambiguous results. The lack of publication of these studies dramatically changed the apparent overall effectiveness of the drugs. In the published medical literature, 94% of the studies showed positive results for the anti-depressants, whereas the FDA registry revealed a much lower 51% success rate. In addition to the studies which weren't published, they also found that the conclusions of 11 studies (15%) in the medical literature conflicted with the conclusions of the FDA. In other words, the FDA may have found a negative result for a specific study, but the published report presented the same data as a positive result.

Finally, the researchers used statistical techniques to quantify the difference in the drugs' effectiveness in the medical literature versus the FDA registry. They found that for each of the 12 drugs, the effectiveness was overstated by 11%-69% (Figure 2). Overall, the average effectiveness was reported to be 32% higher in the published literature versus the complete FDA database.

The authors go to great lengths to point out that why certain studies were not published is not clear and they are not accusing anyone in particular. They also stress that each and every one of the 12 drugs was found to be more effective than a placebo by the FDA. However, given how frequently these drugs are prescribed and how

comparison for a drug

**randomized** - type of study design in which participants are randomly assigned to receive either the treatment under study or a placebo

**serotonin** - a neurotransmitter important for regulating mood

### Common Chiari Terms

**cerebellar tonsils** - portion of the cerebellum located at the bottom, so named because of their shape

**cerebellum** - part of the brain located at the bottom of the skull, near the opening to the spinal area; important for muscle control, movement, and balance

**cerebrospinal fluid (CSF)** - clear liquid in the brain and spinal cord, acts as a shock absorber

**Chiari malformation I** - condition where the cerebellar tonsils are displaced out of the skull area into the spinal area, causing compression of brain tissue and disruption of CSF flow

**decompression surgery** - general term used for any of several surgical techniques employed to create more space around a Chiari malformation and to relieve compression

**syringomyelia** - condition where a fluid filled cyst forms in the spinal cord

### Source

Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. [Selective publication of antidepressant trials and its influence on apparent efficacy](#). N Engl J Med. 2008 Jan 17;358(3):252-60

important the timely treatment of depression is, one has to wonder whether this report will alter patient care. After all, the complete FDA data set found that only slightly more than half the research studies showed a positive effect. On the other hand, that means that 50% of the research found that the medications have provide a clear, statistically significant benefit. **[Note:** It is important to understand for anyone currently taking anti-depressant medication, this does not mean you should stop taking it. Always discuss medication use and dosage with a qualified medical professional.]

One also has to wonder whether a similar bias can be found in other commonly prescribed medications and if the medical community will find a way to address this issue.

**Figure 1: Published Results vs FDA Opinion (74 Studies, 12,564 Subjects)**

Publication Status	Number of Studies (%)	Number of Subjects (%)
Agrees with FDA Decision	40 (54%)	7,272 (58%)
Conflicts with FDA Decision	11 (15%)	1,843 (15%)
Results Not Published	23 (31%)	3,449 (27%)

**Note:** Results were categorized as either positive, negative, or questionable

**Figure 2: Difference In Effect Size Between FDA and Published Studies For Selected Drugs**

Drug - Brand Name	% Change In Effect
Wellbutrin	+55%
Prozac	+14%
Paxil	+40%
Overall Weighted Mean	+32%

**Note:** Change represents how much more effective the drugs were found to be in the published literature versus the complete FDA database

### Related C&S News Articles:

[Exercise As Good As Medication For Treating Major Depressive Disorder](#)

[More Than Half Of Patients With Chronic, Disabling Spinal Problems Suffer From Major Depression](#)

[Tips For Fighting Chiari Related Depression](#)

[Let's Think About Thinking - The Cognitive Effects Of Chiari](#)

[Home](#) | [About Us](#) | [Email](#) | [Donate](#) | [Get Involved](#) | [Privacy Policy](#)

**Disclaimer:** This publication is intended for informational purposes only and may or may not apply to you. The editor and publisher are not doctors and are not engaged in providing medical advice. Always consult a qualified professional for medical care. This publication does not endorse any doctors, procedures, or products.