

fáith SEEKING UNDERSTANDING

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Antidepressants: Their Ineffectiveness and Risks

Increasingly, the ineffectiveness and risks from antidepressants are being reported in the media and scientific literature. Yet in 2007, antidepressants were the most prescribed class of drugs in the US with 232.7 million prescriptions; and fourth in revenue with \$11.9 billion (IMS Health, 2007 U.S. Sales and Prescription Information). Read the following article and look up the given links before making a decision to use antidepressants. Also be cautious in stopping their use once you've started. Abrupt termination can be dangerous as well.

Ineffectiveness of Antidepressants

In 1998, Irving Kirsch and Guy Sapirstein did a meta-analysis of antidepressant medication and found that 75% of the response to active medications was duplicated by placebos. The correlation between the placebo effect and the drug effect was .90. "These data indicate that virtually all of the variation in drug effect size was due to the placebo." (Kirsch and Sapirstein 1998). Kirsch (2002) wrote that they were surprised at the results; and had not questioned the pharmacological effectiveness of antidepressants before the research. They were attempting to evaluate the placebo effect and while they expected a substantial placebo effect, they did not expect such a small medication effect. The published data provoked considerable debate and led to a further meta-analysis by Kirsch and others of antidepressant medication, using the data submitted to the FDA by the pharmaceutical companies in the process of seeking approval for their medications.

Analysis of data submitted to the FDA for the approval of the six most widely prescribed antidepressants approved between 1987 and 1999 (Prozac, Paxil, Zoloft, Effexor, Serzone and Celexa) found a small but significant difference between the antidepressant drugs and an inert placebo. This relatively small difference was of "questionable clinical significance," according to Kirsch and his fellow researchers (Kirsch et al. 2002).

Walter Brown noted that Kirsch et al.'s (2002) article reminded us that "antidepressants are not as good as their hype would have us believe;" and that simply receiving some help—even with a placebo—can be a powerful balm for depression. He suggested that the meager results could be more from their use with unsuitable patients than from the essential ineffectiveness of antidepressants (Brown 2002). A reasonable critique of the Kirsch et al. (2002) study, but remember that the studies used for the meta-analysis were the very same ones submitted to the FDA by the drug companies for approval of their drugs! If the negligible effects were the result of the medications being given to unsuitable patients, how did they get included in the clinical trials designed to demonstrate the efficacy of the medication? Either the diagnostic screening procedures were unreliable,

or worse, they weren't consistently followed.¹ At the very least, we have the drug companies submitting some very shoddy research to the FDA.

Joanna Moncrieff and Irving Kirsch (2005) reviewed data from The National Institute for Health and Clinical Excellence (NICE) in Great Britain and found that "selective serotonin reuptake inhibitors do not have a clinically meaningful advantage over placebo." Further, evidence that antidepressants were more effective with more severe conditions was not strong; and data on the long term outcome of depression and suicide did not provide very convincing evidence of the benefits of antidepressants. "Given doubt about about their benefits and concern about their risks, current recommendations for prescribing antidepressants should be reconsidered." They indicated there was a need for a thorough re-evaluation of existing approaches to depression and further development of alternatives to drug treatment.

Another meta-analysis by Kirsch et al. (2008) once again demonstrated the ineffectiveness of antidepressants:

These findings suggest that, compared with placebo, the new-generation antidepressants do not produce clinically significant improvements in depression in patients who initially have moderate or even very severe depression, but show significant effects only in the most severely depressed patients. The findings also show that the effect for these patients seems to be due to decreased responsiveness to placebo, rather than increased responsiveness to medication. Given these results, the researchers conclude that there is little reason to prescribe new-generation antidepressant medications to any but the most severely depressed patients unless alternative treatments have been ineffective. In addition, the finding that extremely depressed patients are less responsive to placebo than less severely depressed patients but have similar responses to antidepressants is a potentially important insight into how patients with depression respond to antidepressants and placebos that should be investigated further. (Kirsch et al. 2008, 0268)

Joanna Moncrieff, a British psychiatrist suggested that the term 'antidepressant' was a misnomer. "The small advantage that antidepressants have over placebo in RCTs [randomized controlled trials] is easily accounted for by nonspecific psychological and pharmacological effects. . . . We have no reason to suppose that any drugs can reverse the diverse problems that are labeled as depression." (Moncrieff 2007, 97) Rather than targeting and redressing abnormal biochemical states, she suggested that all psychiatric drugs, including antidepressants, work by producing abnormal drug-induced states.

Psychiatrist and long-time critic of antidepressants, Peter Breggin, commented that it was impossible to prove that antidepressants actually relieved depression, but it seems to be relatively easy to show how they can worsen depression. "If my colleagues wanted to be scientific about it, they would call them 'depressants' rather than antidepressants, and take them off the market." (Breggin 2008b, 53-54)

¹ Diagnostic screening for the studies would have utilized the Diagnostic and Statistical Manual. See "The Illusion of Diagnosis" on the Anselm Ministries web site for an examination of the reliability of psychiatric diagnosis.

Risks with Antidepressants

Suicidal Thinking and Behavior

Within a review and analysis of the violence and suicidality caused by SSRIs, Breggin (2003/2004) noted that soon after the introduction of Prozac (fluoxetine) into the U. S. market, reports began to appear describing fluoxetine-induced violence against self and others. Since that time, there have been many scientific reports and studies confirming that SSRI antidepressants can cause violence, suicide, mania and other forms of psychotic and bizarre behavior.

The FDA has now added black box warnings to all antidepressant medications about the increased risks of suicidal thinking and behavior for children, adolescents and young adults between the ages of 18 and 24, but hedges on the same warnings for adults over the age of 24:

The proposed labeling changes also include language stating that scientific data did not show this increased risk in adults older than 24, and that adults ages 65 and older taking antidepressants have a decreased risk of suicidality. The proposed warning statements emphasize that depression and certain other serious psychiatric disorders are themselves the most important causes of suicide. ([FDA News May 2, 2007](#))

Breggin (2008b, 49) noted that the ‘parsing’ of a warning into age brackets was unusual (he actually said unprecedented), and seemed to be done in order to “obscure the reality that antidepressants cause suicide in children and adults.” A rather serious claim, but let’s look closer at the reanalysis done by GlaxoSmithKline (GSK) for Paxil.

In response to an FDA request of the drug companies to do reanalyses of the data from their clinical trials, GSK had an experienced team of researchers at Columbia University do a reanalysis of their data for Paxil.² Based upon the findings of the reanalysis, GSK stated that young adults, especially those with Major Depressive Disorder (MDD), “may be at increased risk for suicidal behavior during treatment with paroxetine [Paxil].” In adults with MDD of all ages, “there was a statistically significant increase in the frequency of suicidal behaviour in patients treated with paroxetine compared with placebo.” However, because the absolute number (11) and incidence of events was small (.32%), “these data should be interpreted with caution.” The majority of those who attempted suicide while using Paxil during the clinical trials (8 of 11) were between the ages of 18 and 30; and most of the paroxetine patients (9 of 11) reported a social stressor at the time of the suicide attempt. “This observation suggests that the increased risk of suicidal behavior seen with the overall MDD population was driven primarily by events occurring in the younger adult population.” So far, a reasonable extension, it would seem, of the findings. But here’s where it seems the adult age restriction of black box warnings to just young adults may draw upon some questionable data interpretation.

² See the [Briefing Document](#) on the “2006 analysis” of paroxetine on the GSK web site for more information. Also go to Peter Breggin’s site ([breggin.com](#)) to read a report of his documenting how the makers of Paxil minimized the side effects “to make Paxil look safer than it is, and safer than other antidepressant medications.”

First, GSK wants you to think that the incidence is a small percentage (.32%). But look at their data. The study participants taking Paxil were six times more likely to show suicidal behavior (.32% versus .05%), than participants taking a placebo! Also note that the FDA black box warning seems to follow the GSK discussion on its reanalysis of the Paxil data. But if the data suggesting that a statistically significant increase in suicidal behavior should be interpreted with caution because of the small number of absolute cases and the low incidence rate overall, isn't caution equally called for in basing an age restriction on the same data? It is just as reasonable to assume that the noted age range of between 18 and 30 was as much a product of the small number of absolute cases attempting suicide while on Paxil, as it is to have caution in attributing cause for a statistical relationship on the same data. Further study, with a larger population base, would be the proper response before basing an age-restricted warning on the limited data.

The age-restricted warning is consistent with CDC data on suicide rates,³ which reported that suicide was the third-ranked cause of death among 10 to 24 year olds in 2005. But it seems to disregard the CDC data that noted suicide was the second leading cause of death among 25 to 34 year olds. If an "at risk" population of 10 to 24 year olds should be cautioned in their use of antidepressants, why not a population (25 to 34 year olds) who appear to be at an even greater risk of suicide?

GSK noted in their summary and conclusions that the MDD data suggested the higher frequency of suicidal behavior in young adults "may extend beyond the age of 24." And while it was difficult to conclude a causal relationship between Paxil and suicidality, the recent data revealed evidence of a possible increased risk for suicidal behavior in adults along with an increased risk of suicidal behavior and ideation in young adults. But the researchers believed "that the overall risk-benefit assessment for the young adult and the adult patient population remains positive." Breggin (2008b, 49) stated that: "An objective panel of experts—one not riddled with drug-company indebtedness—would have recommended the black-box warnings for all ages."

Just a short rabbit trail here. Recall the above FDA warning stating that: "adults ages 65 and older taking antidepressants have a decreased risk of suicidality." Breggin (2008a) noted a Canadian study by Juurlink et al. that found "nearly a fivefold higher risk of completed suicide" during the first month of SSRI therapy among Ontario residents 66 years and older. The risk was independent of (not influenced by) depression or receiving psychiatric care, "and suicides of a violent nature were distinctly more common during SSRI therapy." (Juurlink et al. 2006, 813) Nevertheless, there was some minimization of this finding in the discussion section, where the authors pointed out that the vast majority of patients treated with SSRI antidepressants do not attempt suicide, but in rare instances these drugs may incite suicidal ideation during the first weeks of drug therapy.

The [Medication Guide for Antidepressant Drugs](#) approved by the FDA for distribution with all antidepressant medication states that "Antidepressant medication may increase suicidal thoughts or actions in some children, teenagers, and young adults when medication is first started."⁴ It later warns that: "Stopping an antidepressant medicine

³ See the data table for the "10 Leading Causes of Death, United States" for 2005 on the [CDC web site](#). Do an advanced search for "top 10."

⁴ Interestingly, Canadian warnings weren't limited to individuals under the age of 24, as in the U.S. Rather, they stated that: "these new warnings indicate that patients of all ages taking these drugs may experience

suddenly can cause other symptoms,” a vaguely worded warning about withdrawal.⁵ Oh, and there can be “other side effects” with each medication, so you need to talk to a healthcare provider about the side effects of the prescribed medication. If any of the following symptoms occur, you should call a healthcare provider right away:

- thoughts about suicide or dying,
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

Breggin pointed out that while the medication guideline did not specify a causal link between the listed reactions and medications, it did imply they were associated with medication. It seems that language admitting that: “A causal role for antidepressants in inducing suicidality has been established in pediatric patients”, was deleted from the warnings section of the medical guidelines through FDA negotiations with the pharmaceutical industry (Lenzer 2005). Within an editorial in *The American Journal of Psychiatry*, Cynthia Pfeffer admitted that an FDA advisory committee “concluded that a causal link exists between antidepressant treatment and pediatric suicidality,” but noted the eventual warnings may have had “the unintended effect of discouraging the prescription of antidepressants for pediatric patients. . . . The black box warning should not discourage practitioners from prescribing, and pediatric patients from using, clinically indicated antidepressants.” Rather it should lead to closer monitoring, and informing pediatric patients and their parents of possible beneficial and adverse effects of antidepressants (Pfeffer 2007, 844; and 845). The argument seems to be that too strong of a warning that antidepressants cause suicidality (in pediatric patients) will lead to a rise in actual suicides among depressed children who need antidepressants, but whose parents or physicians were too afraid to utilize them. While the direction of Pfeffer’s discussion seems to suggest that black box warnings should not discourage the use of antidepressants, black-box warnings are given to emphasize the risks of using a particular medication.

I would hope that the increased risks from antidepressant use would result in a decrease of their use. Unfortunately, there seems to have been little effect on the number of prescriptions dispensed for antidepressants, which have steadily increased since 2003. However, there was a recent dip in sales, as antidepressants dropped \$1.7 billion from

behavioural and/or emotional changes that may put them at increased risk of self-harm or harm of others.” (Breggin 2006b, 59)

⁵ See another article on this web site entitled: “Antidepressant Withdrawal or Discontinuation Syndrome?”

their 2006 totals. See Table 1 below for the comparisons.⁶ Several popular antidepressants: Prozac (2000), Celexa (2003), Wellbutrin (2006) and Zoloft (2008) have lost exclusive patent rights since 2000, allowing the sale of generic forms of the drugs. This has been a likely contributing factor to the steady rise in dispensed prescriptions concurrent with up-and-down sales figures.

Table 1
Sales and Prescriptions Dispensed for Antidepressants

	2007	2006	2005	2004	2003
Antidepressant sales in billions of dollars	11.9	13.6	12.9	13.9	13.8
Antidepressant prescriptions in millions dispensed	232.7	227.4	216	215.8	207.6

Activation and Medication Madness

Breggin (2006b) also noted that the above list of symptoms experienced with antidepressants closely mimics the adverse reaction profile seen with stimulants like amphetamine and methamphetamine. This so-called ‘activation syndrome,’ can exist on a continuum of effects from mild (eg, minimal insomnia, anxiety or irritability) to more severe (violence and mania).

In *Brain Disabling Treatments in Psychiatry*, Breggin (2008a) noted that on 11/8/88, Charles Beasley of Eli Lilly and Company’s⁷ Division of Clinical Neurosciences said: “Floxetine [Prozac] may produce both activation (nervousness, anxiety, agitation, insomnia) and sedation (somnolence, asthenia). Approximately 19% of patients might be expected to report activation during acute therapy with fluoxetine.” So within a year of Prozac being approved by the FDA, officials within Eli Lilly were discussing the potential of ‘activation’ with the first widely used SSRI in the U.S. It took almost 20 years for the public to become aware of the same concern. Breggin cautioned physicians and patients to be alert for the emergence of activation symptoms with the newer antidepressants, as they are a far more common risk than antidepressant-induced suicidality:

Activation has the potential for equally disastrous outcomes and should be the first consideration whenever a patient’s condition begins to worsen while taking antidepressants. If the physician mistakenly identifies these adverse effects as a part of the original psychiatric disorder, he or she may continue or even increase the

⁶ Originally reported in: [IMS Health, 2007 U.S. Sales and Prescription Information.](#)

⁷ The manufacturers of Prozac. See breggin.com for a pdf document of the internal company memo (The Eli Lilly documents: Part IV”) from which the following was quoted.

antidepressant does in the hope of controlling the activation. This can lead to severe cases of mania and psychosis. (Breggin 2006b, 58)

His thinking has coalesced recently into describing the brain-disabling concept of biopsychiatric treatment, which states that all psychiatric treatments—drugs, electroshock, and lobotomy—work by disrupting the brain and mind. Their effects are then misinterpreted as improvements. All psychiatric drugs, including antidepressants, work by causing “a generalized impairment of brain function that reduces overall mental and emotional function; that this disabling effect occurs, as well, in normal volunteers; and that the effect has no specificity for any psychiatric disorder.” (Breggin 2008a, 4) As a consequence of the brain-disabling effect of medications, individuals will often become spellbound—unable to perceive the extent to which they are impaired by the drug. They do not attribute any of the mental or emotional changes in themselves to an adverse drug effect; and often believe they are doing better than ever, when actually they are doing worse. In the extreme, it drives them into suicidal and homicidal behavior. In technical language, this medication spellbinding is intoxication anosognosia: “The inability when intoxicated by drugs to recognize the mental and emotional impairment caused by the intoxication. Medication madness is an extreme expression of medication spellbinding, leading people to behave in ways that they would otherwise reject as hazardous or wrong.” (Breggin 2008b, 19)

How to Identify Antidepressant-Induced Medication Madness

On the basis of a life-long literature review and his own clinical experience, Dr. Breggin (2008a, 154-155) said the syndrome of SSRI-induced suicidality and violence included many, if not all, of the following:

A relatively sudden onset and rapid escalation of the compulsive aggression against self and/or others. A recent (typically within a few months or less) initial exposure to the medication, a recent change in the dose of the medication, a recent change in the dose of the medication, or a recent addition or removal of another psychoactive substance to the regimen.

The presence of other adverse drug reactions, often involving akathisia [a feeling of inner restlessness, coupled with an inability to sit still] or stimulation along a continuum from irritability and agitation to agitated depression and mania, as well as indifference and apathy.

Resolution of the syndrome after termination of the causative medication, often with a marked overall improvement in the individual’s mental status.

An extremely violent and/or bizarre quality to thoughts and actions.

An obsessive, compelling, unrelenting quality to thoughts and actions.

An out-of-character quality for the individual, as determined by the individual’s history.

An alien or ego-dystonic quality [thoughts, impulses, and behavior that repugnant, distressing, unacceptable], as determined by the individual’s subjective report.

Conclusion

If what brought you to read this essay on the ineffectiveness and risks of antidepressants is personal; if you or someone you care about uses antidepressants or has been recommended to try one, don't stop here. I have intentionally added several web links for your ongoing reading and research. If your concern is about some other type of psychiatric medication, turn to the information available through Peter Breggin. His web site (breggin.com) itself has a wealth of information available for starters; many of the sources used here are available there. In addition, he has written several helpful books, again, noted on his web site. Here is very brief overview of two of his more recent works.

In *Medication Madness*, Dr. Breggin described dozens of cases that he has personally evaluated. They were told without embellishment; their truth was dramatic enough. The stories "are about children and adults who have been emotionally injured and sometimes driven mad by psychiatric medications, many committing horrific crimes." (Breggin 2008b, 1) Antidepressants, anti-anxiety medications, antipsychotics and ADHD stimulants are all, at various times, villains in the stories. There is also a chapter on how to make drug withdrawal as safe as possible. Within the second edition of *Brain-Disabling Treatments in Psychiatry*, Breggin relentlessly reviewed the brain-disabling effects of various classes of psychiatric drugs: neuroleptics (antipsychotics); antidepressants; anti-anxiety medications; ADHD stimulants; Lithium and other so-called mood stabilizers used to treat bipolar disorder. He then went on to describe the ravages of Electroconvulsive Therapy (ECT) for depression; drug company deceptions; and even how to more safely stop taking psychiatric drugs. *Medication Madness* was written for the public, while *Brain-Disabling Treatments in Psychiatry* was aimed at professional audiences. Each book can be read with understanding and value regardless of your background.

What should you decide about taking psychiatric drugs? I agree with Peter Breggin that: "It is wisest to avoid any exposure to these toxic chemicals. . . . [I]f you decide to take them, then take as few as possible at the smallest possible dose, and stop taking them as soon as you can." The best decision is to not start taking them, as it seems that they do more harm than good. "If you are already taking them, remember that stopping psychiatric drugs can also be dangerous and needs to be done carefully and with as much experienced clinical supervision as possible." (Breggin 2008b, 321)

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