Why I think antidepressants cause more harm than good

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I declare no competing interests.

This paper was published in Lancet Psychiatry 9 July 2014. Citation:

Gøtzsche PC. Why I think antidepressants cause more harm than good. Lancet Psychiatry 2014;1:104-6:

http://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)70280-9/fulltext

In The Lancet Psychiatry, David Nutt and colleagues[1] stated that headlines such as "Antidepressants do more harm than good" plumb a "new nadir in irrational polemic." I disagree and describe here the evidence that supports my argument so that readers can judge for themselves what they think about the defence of these drugs by Nutt and colleagues.

With regard to the benefits of antidepressants, in its large meta-analysis of 100 000 patients, half of whom were depressed, the US Food and Drug Administration (FDA) noted that 10% more patients responded on antidepressants than did those on placebo,[2] and the Cochrane review of depressed patients reported similar results[3] (ie, one patient might benefit for every ten patients treated).

I believe those results were exaggerated, however, for several reasons.[4] Most importantly, the trials were not effectively blinded. Antidepressants have conspicuous side-effects and many patients and their doctors will therefore know whether the blinded drug is active or placebo. A systematic review of 21 trials[5] in a variety of diseases that had both masked and non-masked outcome assessors, and which had mostly used subjective outcomes, found that the treatment effect was exaggerated by 36% on average (measured as odds ratio) when non-masked observers rather than masked ones assessed the effect. The effect of antidepressants is assessed on highly subjective scales (eg, the Hamilton scale), and if we assume that the blinding is broken for all patients in the trials and adjust for the bias, we will find that antidepressants have no effect (odds ratio 1.02).[4]

However, I do not believe that the blinding is always broken, only that the reported effect is highly likely to have been exaggerated. Many years ago, adequately blinded trials of tricyclic antidepressants were done, in which the placebo contained atropine, which causes dryness in the mouth like the active drugs do. These trials reported very small, clinically insignificant effects of tricyclic antidepressants compared with placebo (standardised mean difference 0.17, 95% CI 0.00–0.34).[6]

Another worrying finding in randomised trials is that as many patients stop treatment on SSRIs as on placebo for any reason.[7] After only 2 months, half the patients have stopped taking the drug.[8] This finding suggests that, overall, considering benefits and harms together, the patients find the drugs useless. More importantly, no research shows whether these drugs work for the outcomes that really matter, such as saving relationships and getting people back to work.

With respect to the harms of antidepressants, most patients who take these drugs will experience side-effects. The package inserts list many common side-effects, of which one of the most frequent is sexual problems. In a study[9] designed to assess this side-effect, sexual problems developed in 604 (59%) of 1022 patients who all reported no problems with sexual function before they started using an antidepressant. The symptoms include decreased libido (50% of patients on fluoxetine), delayed orgasm or ejaculation (also 50%), no orgasm or ejaculation (39%), and erectile dysfunction or decreased vaginal lubrication (22% for both combined).

Even when tapering off them slowly, half the patients have difficulty stopping the drugs because of withdrawal effects, which can be severe[10] and long-lasting.[4] We noted that withdrawal symptoms were described in similar terms for benzodiazepines and SSRIs and were very similar for 37 of 42 identified symptoms.[11] However, they were not described as dependence for SSRIs.[11] To define similar problems as "dependence" in the case of benzodiazepines and as "withdrawal reactions" in the case of SSRIs is irrational. For patients, the symptoms are just the same; it can be very hard for them to stop either type of drug.

Psychiatrists often argue, as did Nutt and colleagues,[1] that antidepressants protect against suicide. However, I believe that no good evidence in support of this idea exists. Good observational studies have refuted it,[12] and results from randomised trials[13] have shown that antidepressants are associated with increased risk of suicide attempts (5.6 more suicide attempts per 1000 patient-years of SSRI exposure compared with placebo). Antidepressants have not only been associated with suicide but also with homicide.[4,14–16] The FDA's analysis[2] showed that suicidal behaviour is increased with antidepressants until about the age of 40 years—but in fact, the situation is much worse than this. Suicides and suicide attempts were vastly underreported in the FDA's analysis for various reasons.[4] For example, only five deaths by suicide were recorded in 52 960 patients on antidepressants in the 2006 FDA analysis[2] whereas five deaths by suicide were recorded in 2963 patients on paroxetine alone in a meta-analysis from 1993.[17]

SSRIs are particularly harmful for elderly patients. Results from a carefully controlled cohort study[18] of people older than 65 years of age with depression showed that SSRIs led to falls more often than did older antidepressants or if the depression was left untreated. For every 28 elderly people treated for 1 year with an SSRI, there was one additional death, compared with no treatment.[18] SSRIs have also stimulant effects and might precipitate conversion to bipolar disorder in about 10% of children aged 10–14 years under the care of mental health services.[19]

SSRIs are very poor drugs and I doubt they are safe at any age. The first SSRI was fluoxetine, which the German drug regulator deemed "totally unsuitable for the treatment of depression".[14,20] I, and others,[4,21] have written about the controversy surrounding this drug and the process by which it nevertheless came to be approved and widely used.

I have written previously[4] that there has been heavy marketing and widespread crime committed by drug companies, including fraud, illegal promotion, and corruption of psychiatrists. In the USA, psychiatrists receive more money from the drug industry than any other specialty.[4,22] As a result, enough antidepressants are prescribed every year in Denmark to provide treatment for every person in the country for 6 years of their lives.[4] I believe this situation is not sound and that it also partly portrays the fact that many patients cannot stop these drugs because of intolerable withdrawal symptoms.

SSRIs have been shown to have minimal or non-existent benefit in patients with mild or moderate depression[23] and I think they might not even work for severe depression.[4] They should be used very sparingly, if at all, and always with a clear plan for tapering off them. The so-called maintenance studies, in which patients after successful treatment get randomly assigned to continue with the drug or a placebo, cannot be interpreted as showing that the patients still need the drug because withdrawal symptoms, which can include depression, are inflicted on the placebo group.

Nutt and two of his co-authors, Guy M Goodwin and Stephen Lawrie, have between them declared 22 conflicts of interest in relation to drug companies.[1] I wonder whether this declaration explains their dismissal of psychotherapy (although it is effective and recommended by NICE) and their description of my evidence-based views as a somewhat irrational polemic that is insulting to the discipline of psychiatry and is reinforcing stigma against mental illnesses. They also talk about anti-psychiatry, anti-capitalism, and a conspiracy theory. This is the language of people who are short of arguments.

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