

**Studies have found that antidepressants have no clinically significant benefit over placebo pills (inert pills) in the treatment of mild to moderate depression, while they provide some benefit for severe depression, at least in the short term. Recent research also suggests that antidepressants may be associated with a risk of increased mortality, at least among the elderly.**

For the majority of people taking antidepressants (around 85%) they work, on average, no better than placebo pills (inert pills). This conclusion has been demonstrated by numerous 'meta-analyses' – these are studies that have gathered together all of the clinical trials that have, in this case, attempted to assess whether antidepressants work better than placebo pills.

Professor Irving Kirsch (Harvard Medical School) conducted the most noted and perhaps definitive of such analyses. Kirsch's meta-analysis included all the major clinical trials of SSRI antidepressants – both those that were published and the nearly 40% that were withheld from publication by the pharmaceutical companies who sponsored or conducted them (the withheld trials largely showed negative results). After pooling all the data, Kirsch's analysis revealed that the vast majority of people who took the antidepressant experienced, on average, no clinically significant improvement over those who took the placebo.<sup>1</sup>

Kirsch's findings have been consistently replicated. Walter Brown, professor of psychiatry at Brown University, co-authored two studies that independently analysed the same set of clinical trials surveyed by Kirsch. His results confirmed that for a small minority of patients (the most severely depressed – 10-15%), antidepressants were shown to have some minor benefits over sugar pills. But for mildly/moderately depressed patients (85-90% patients) antidepressants offered no advantage over placebos, alternative therapies, or even moderate exercise.<sup>2</sup>

A further, major meta-analysis commissioned by the NHS, and published this time in *The Lancet*, again showed the difference between placebos and antidepressants is so modest, that for mild to moderate depression antidepressants they were not worth having at all.<sup>3</sup> As the lead author of the study stated: 'Our widespread comparative meta-analysis of antidepressants showed pretty clearly, that the difference between the published and unpublished studies of antidepressants in children, was that for the published trials, all the drugs worked, while for the unpublished trials none of the drugs worked.'<sup>4</sup>

In addition to working no better than placebos for most patients, antidepressants are now coming under serious scrutiny for their potentially damaging effects, such as increasing the likelihood that a person who takes them will become chronically ill. As Giovanna Fava, an Italian psychiatrist, writes, 'The time has come for debating and initiating research into the likelihood that psychotropic drugs actually worsen, at least in some cases, the progression of the illness which they are supposed to treat.'<sup>5</sup>

Researchers at the University of Louisville Medical School, who have recently explored this area, have highlighted evidence that 'in some individuals, persistent use of antidepressants may be pro-depressant'. One such researcher, El-Mallakh, suggests that SSRIs may in fact deplete serotonergic function, causing a 'chronic and treatment-resistant depressive state... in individuals who are exposed to potent antagonists of serotonin reuptake pumps [SSRIs] for prolonged periods'.<sup>6</sup> Such concerns are compounded by research that associates antidepressants with a significantly higher risk of relapse following cessation of the drug vs. a placebo. A meta-analysis performed by researchers at McMaster University (Ontario), for instance, shows that the risk of relapse in the three months following

discontinuation was 21.4% for placebo but rose to 43.3% for SSRIs and 55.2% for SNRIs.<sup>7</sup> The authors suggest that this increase in relapse is caused by the brain's 'pushback' against the effects of antidepressants; an effect that renders the person more susceptible to depression following cessation.

Alarming, three recent, large, prospective epidemiological studies have found that, even after controlling for depressive symptoms, antidepressant use is associated with an increased risk of death in the elderly. In one study the number of deaths per year caused by antidepressants was estimated to be 10.8 out of 1000 elderly people taking antidepressants.<sup>8</sup> Another study estimated that antidepressants caused the deaths of roughly 5 in 1000 elderly women per year.<sup>9</sup> It is possible that these higher rates of mortality are specific to the elderly; however current research cannot rule out the possibility that the cumulative effects of antidepressants on the integrity of the brain and peripheral processes could shorten the lifespan considerably.

Furthermore, several UK charities that support patients withdrawing from psychiatric drugs report that many people suffer from severe, long-term withdrawal effects after coming off antidepressants. In some cases these symptoms are reported to last for years and can be very debilitating. There is also evidence of long-term or perhaps permanent sexual dysfunction following discontinuation of SSRIs.<sup>10</sup>

Despite what the evidence tells us, antidepressants are still being prescribed at a remarkable rate. There were over 50 million prescriptions of antidepressants dispensed in England in 2012 alone. Furthermore, while most of the antidepressant effect is now understood to be a 'placebo effect' we also know that between 40% and 70% of people taking them (depending on the study consulted) experience side effects. The NHS's list of side effects include: sickness, dizziness, low sex drive, erectile dysfunction, blurred vision, diarrhoea, dry mouth, feeling agitated or shaky, loss of sleep, excessive sweating, and in some cases increased confusion and suicide ideation.<sup>11</sup>

There are many other negative effects that have also been noted, but which rarely (if ever) are included in official lists of 'side effects'. For example, in 2009 a team of researchers at The University of Oxford assessed over 38 patients who had taken SSRIs antidepressants for periods between 3 and 48 months. Their results were published in the British Journal of Psychiatry, and what follows constitutes a summary:<sup>12</sup>

- Most participants described a general reduction in the intensity of all the emotions that they experienced, using words like 'dulled', 'numbed', 'flattened' or completely 'blocked', to capture how they felt.
- A few participants described feeling no emotions at all, while others reported their emotional experience had become more 'cognitive' or 'intellectual'.
- A few described how the emotions that were at times present seemed 'unreal', 'fake' or 'artificial'. Almost all participants, paradoxically, described a reduction in their positive emotions, including a reduction happiness, enjoyment, excitement, anticipation, passion, love, affection and enthusiasm.
- Most participants also described feeling emotionally detached from their surroundings. Most also described feeling detached from other people. Specifically, they felt reduced sympathy and empathy, and felt detached during social interactions. Many participants also described an emotional detachment from their friends and family, including their partner or children.

- Almost all participants described not caring about things that used to matter to them. They cared less about themselves, about other people and about the consequences of their actions. Not caring could have both helpful and unhelpful consequences: it could reduce the sense of pressure and stress, but it could also increase the likelihood that important tasks were neglected.
- Many participants felt they just did not care as much about the consequences to themselves of their behaviour. A few participants went further, mentioning thoughts of self-harm or suicide that they related to their emotional detachment and numbness. Many participants reported being less sensitive or courteous towards other people, having reduced concern for others' feelings, and reduced concern about other peoples' opinions of them. Some participants described being less concerned or even unable to care about responsibilities in their everyday lives.
- All participants experienced a reduction of intensity or frequency of negative emotions. Most considered that at some stage the reduction in negative emotions was beneficial to them. Although this reduction was usually at some stage a relief, many participants also reported it impaired their quality of life. Participants described the need to be able to feel negative emotions when appropriate, such as grief or concern. Some were unable to respond with negative emotions, such as being unable to cry when it was appropriate to do so.
- Some participants felt their personality had changed in some way. They felt they were not the person that they used to be. Participants also reported that specific aspects of their personality, and, in particular, emotional aspects, had been changed or lost. Some participants believed that at times their antidepressant had made them behave out of character.

A separate study published in 2014, confirms much of the above. It surveyed 1,829 antidepressant consumers, and confirmed these drugs have widespread adverse psychological effects. For instance, and as a result of taking antidepressants, 62% of patients reported suffering from 'sexual difficulties'; 60% from 'feeling emotionally numb'; 52% reported 'feeling not like myself'; 42% experienced a 'reduction in positive feelings'; 39% reported 'caring less about others'; 55% experienced 'withdrawal effects'; while over 50% aged 18 to 25 reported suicidal feelings. On the up side, 82% reported that the drugs had helped alleviate their depression, however, as we also know from meta-analyses, that figure was mostly due to the placebo effect. The authors state: 'While the biological side-effects of antidepressants, such as weight gain and nausea, are well documented, the psychological and interpersonal effects have been largely ignored or denied. [Yet] they appear to be alarmingly common.'<sup>13</sup>

Antidepressants have effects, but mostly they have placebo effects, side effects and negative effects such as those described above. There is no research to date confirming that they have any kind of 'curing' effect, and there has yet to be discovered a clear biological 'disease' that these pills target and treat. Furthermore, various studies suggest that long-term use of antidepressants may in fact increase the chronicity of depression and lead to higher mortality rates, at least among the elderly.

© Council for Evidence-based Psychiatry 2014

You may freely copy, adapt and distribute this work for any purpose. This work is licensed under a Creative Commons Attribution 4.0 International License.

To contact us or for more information please visit [cepuk.org](http://cepuk.org).

<sup>1</sup> For a full account of this study see: Kirsch, I. (2009), *The Emperor's New Drugs: exploding the antidepressant myth*, (London: Bodley Head p.54)

<sup>2</sup> Khan A, Redding N, Brown WA (2008), The persistence of the placebo response in antidepressant clinical trials, *Journal of Psychiatric Research* 42 (10): 791–796

<sup>3</sup> Whittington, C.J & Kendall, T (et al), Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data, *The Lancet*, Volume 363, Issue 9418, Pages 1341-1345, 24 April 2004

<sup>4</sup> Quoted in Davies J. (2013), *Cracked: why psychiatry is doing more harm than good*, (London: Icon)

<sup>5</sup> Fava G. (1994), Do antidepressant and anti-anxiety drugs increase chronicity in affective disorders? *Psychotherapy and Psychosomatics*, 61:125-31.

<sup>6</sup> El-Malakh R.S., Gao Y., Jeannie Roberts R. (2011), Tardive dysphoria: the role of long term antidepressant use in inducing chronic depression, *Medical Hypotheses*, 76 (2011) 769–773

<sup>7</sup> Andrews P., Anderson Thomson Jr J., Amstadter A. & Neale M. (2012), Primum non nocere: an evolutionary analysis of whether antidepressants do more harm than good, *Frontiers in Psychology*, Vol 3; 117

<sup>8</sup> Coupland, C., Dhiman, D., Morriss, R., Arthur, A., Barton, G., and Hippisley-Cox, J. (2011), Antidepressant use and risk of adverse outcomes in older people: population based cohort study, *BMJ*, 343. doi: 10.1136/bmj.d4551

<sup>9</sup> Smoller, J. W., Allison, M., Cochrane, B. B., Curb, J. D., Perlis, R. H., Robinson, J. G., Rosal, M. C., Wenger, N. K., and Wassertheil-Smoller, S. (2009), Antidepressant use and risk of incident cardiovascular morbidity and mortality among postmenopausal women in the Women's Health Initiative Study, *Arch. Intern. Med.*, 169, 2128–2139

<sup>10</sup> Csoka A.B., Shipko S. (2006), Persistent Sexual Side Effects after SSRI Discontinuation, *Psychotherapy and Psychosomatics*, 2006; 75:187–188

<sup>11</sup> Middleton, H. and Moncrieff, J. (2011), They won't do any harm and might do some good: time to think again on the use of antidepressants? *British Journal of General Practice*, (1): 47-9.

<sup>12</sup> Price, J., Cole, V., Goodwin G. M. (2009), The Emotional Side-Effects of Selective Serotonin Reuptake Inhibitors: qualitative study. *The British Journal of Psychiatry*, 195: 211-217

<sup>13</sup> Gibson K, Cartwright C and Read J, 2014, Patient-centred perspectives on antidepressant use: A narrative review, *International Journal of Mental Health Nursing* - in press