Most NCISH recommendations are not specific to suicide or homicide; instead they are about raising the standard of care overall, although benefits to safety can be shown—eg, NCISH noted reduced patient suicide rates in services that adopted recommendations designed to strengthen community care.[10] One of these recommendations was for a multidisciplinary review involving the family after a patient suicide—a marker for the learning culture that the Berwick Review regarded as vital.

NCISH showed that most patients who die by suicide are regarded as low risk at their final service contact, so only limited benefit can be had by focusing exclusively on patients known to be at high risk. A major reduction in suicide deaths depends on what is done for patients at perceived low risk—the so-called low risk paradox. Safety needs to be built into the care of all patients at points of conspicuous weakness (eg, on wards, at discharge, and when patients are taking illicit drugs or losing contact with services).

The research community will have to address similar questions. How are testimonies from patients or families used to inform a study, especially more difficult areas of staff–patient relationships, such as self-harm or personality disorder? Is the balance right between transparency of data and confidentiality for those who provide it? More broadly, is the openness principle compatible with anonymous peer review? Will researchers and funders, including government departments, guarantee candour when results are not what they hoped for? And does the system of assessing the performance of publicly funded universities place enough priority on benefit to the public? Despite changes, research assessment exercises continue to favour the impact factor of the journal where a study is published rather than its impact on health, safety, or quality of life. In doing so, they run the risk of creating the kind of organisational distraction exposed in the Francis Inquiry Report.

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Attacks on antidepressants: signs of deep-seated stigma?

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For the **article in *The Times*** see http://www.thetimes.co.uk/tto/health/news/article4076351.ece

For the **article in *The Guardian*** see http://www.theguardian.com/commentisfree/2014/apr/30/psychiatric-drugs-harm-than-good-ssri-antidepressants-benzodiazepines

Psychiatry is used to being attacked by external parties with antidiagnosis and antitreatment agendas. However, the recent disclosure that a doctor (Professor Peter Gøtzsche) had joined a new group, the Council for Evidence-based Psychiatry, whose launch was accompanied by newspaper headlines such as "Antidepressants do more harm than good, research says" and "Psychiatric drugs are doing us more harm than good" in *The Times* and *The Guardian* plumbs a new nadir in irrational polemic. What is especially worrying is that this doctor is a co-founder of the Nordic Cochrane collaboration, an initiative set up to provide the best evidence for clinical practitioners. What is the truth about antidepressant efficacy and adverse effects, and why would Professor Gøtzsche apparently suspend his training in evidence analysis for popular polemic?

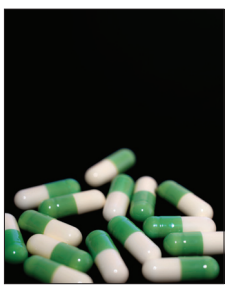
Depression is a serious and recurrent disorder that is currently the largest cause of disability in Europe[1] and is projected to be the leading cause of morbidity in high-income countries by 2030.[2] Antidepressants have an impressive effect size in the treatment of

acute cases of depression, with a number needed to treat of around six.[3] For example, the recently updated Cochrane review of amitriptyline,[4] which involved 18 randomised controlled trials and 1987 participants, shows that it is significantly more effective than placebo in achieving acute response (odds ratio 2·67, 95% CI 2·21–3·23), and that significantly fewer participants allocated to amitriptyline than to placebo withdrew from trials because of treatment inefficacy. How can this finding represent more harm than good? A smaller proportion of treated patients withdrew because of side-effects and the pattern of results was the same in industry-sponsored and independently funded trials.[4] Indeed, in general, effect sizes for psychiatric indications do not differ from those of drugs used in physical medicine.[5] Moreover, antidepressants have an impressive ability to prevent recurrence of depression, with a number needed to treat of around three, which makes them one of the most effective of all drugs.[6]

Suicide kills about 6000 people every year in the UK.[7] Most of these people are depressed and more than 70% are not taking an antidepressant at the time of death.[8] Blanket condemnation of antidepressants by lobby groups and colleagues risks increasing that proportion. In countries where antidepressants are used properly, suicide rates have fallen substantially.[9]

Of course, all active drugs have adverse effects, but for the new antidepressants these are rarely severe or life-threatening, even in overdose situations. Indeed, the new antidepressants, especially the selective serotonin reuptake inhibitors, are some of the safest drugs ever made. In our experience, the vast majority of patients who choose to stay on them do so because they improve their mood and wellbeing rather than because they cannot cope with withdrawal symptoms when they stop. Many of the extreme examples of adverse effects given by the opponents of antidepressants are both rare and sometimes sufficiently bizarre as to warrant the description of an unexplained medical symptom. To attribute extremely unusual or severe experiences to drugs that appear largely innocuous in double-blind clinical trials is to prefer anecdote to evidence. The incentive of litigation might also distort the presentation of some of the claims.

Antipsychiatry groups usually claim that depressed patients should be treated with exercise and psychotherapy instead of drugs. However, little controlled evidence exists to support the use of psychotherapy as an alternative to antidepressants in major depression. Indeed, if psychotherapy had to be tested according to the same rules as drugs, then whether or not it could be licensed for this indication is questionable.[10] Moreover, the implication that, unlike antidepressants, psychotherapy is free of adverse effects is highly misleading. Suicidal ideation[11] and even completed suicide[12] are recognised adverse effects with psychotherapy, and sexual interference with patients by therapists is a matter of concern.[10] Finally, exercise treatment, as the recent Cochrane review concludes, "is moderately more effective than a control intervention for reducing symptoms of depression, but analysis of methodologically robust trials only shows a smaller effect" and exercise is no more acceptable to patients than are psychological or pharmacological treatments.[13]


Robert Brook/Science Photo Library

What motivates doctors with a commitment to evidence-based practice to make such a series of flawed statements about antidepressants? We can only speculate. First, general practitioners (GPs) clearly see a lot of patients with minor somatic and psychiatric problems. We know from our contacts with GP colleagues that such patients might not be who a GP with a conventional internal medicine background yearns to treat. It might be comforting to believe that treatment doesn't really matter. Second, contemporary bien pensant society remains resolutely dualist in its language and its understanding, and doctors are part of that society. The idea of a medicine for something lacking in substance (the mind) might seem a priori implausible, irrational, and undesirable. Third, the anti-psychiatry movement, although now long in the tooth, has revived itself with the recent conspiracy theory that the pharmaceutical industry, in league with psychiatrists, actively plots to create diseases and manufacture drugs no better than placebo. The anti-capitalist flavour of this belief resonates with anti-psychiatry's strong association with extreme or alternative political views.

Whatever the reasons, extreme assertions such as those made by Prof Gøtzsche are insulting to the discipline of psychiatry and at some level express and reinforce stigma against mental illnesses and the people who have them. The medical profession must challenge these poorly

thought-out negative claims by one of its own very vigorously.

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DJN has received grants and personal fees from Lundbeck and GSK; and personal fees from Lilly, BMS, Otsuka, Servier, and Pfizer. GMG has received grants and personal fees from Servier and Lundbeck; personal fees from Teva, Otsuka, Takeda, Eli Lilly, Merck, GSK, and AstraZeneca; and grants from P1vital. DJN and GMG have a small number of stocks in P1vital, a CNS experimental medicine research consultancy company. SL has received research funding from Abbvie, Roche, and Pfizer in connection with genetic, brain imaging, and therapeutic studies of people with schizophrenia. He has also been paid by Janssen and Roche to speak at or chair educational meetings about schizophrenia, as well as to contribute to advisory boards about new antipsychotic treatments. The other authors declare no competing interests.

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Why I think antidepressants cause more harm than good

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]