

## **Re: Suicide risk assessment and intervention in people with mental illness**

No psychiatric drugs have been convincingly shown to decrease suicides

The paper by Bolton et al. is called a “state of the art review”, but it is a narrative review with a curious mix of randomised trials, observational studies, cross-sectional studies and retrospective analyses as the basis for the authors’ arguments (1). They say that various drugs can decrease the risk of suicide but their references do not support this. The first reference to this statement is a narrative, unsystematic review by Griffiths et al. (2). For antidepressants, “one trial” said this and “another” trial said that, and there was a “post-hoc analysis” and empty jargon like “There is some evidence.”

Suicides and suicide attempts have been vastly underreported on active drug in the randomised trials, and when this bias is taken into account, it seems that antidepressants increase the risk of suicide (3).

The paper by Griffiths et al. says that clozapine is the only drug approved by the FDA for reducing the risk of suicidal behaviour (2). This is based on a trial that showed a lower hazard ratio of the composite outcome suicide attempt or hospitalizations to prevent suicide attempt on clozapine than on olanzapine (0.76, 95% CI = 0.58, 0.97). However, the trial also found that there were more suicides on clozapine than on olanzapine (five versus three), and Griffiths et al. say that the decrease in suicide attempts might be related to the closer follow-up of clozapine patients given the required biweekly blood counts to monitor for agranulocytosis. I would add that it might also be because clozapine did nothing while olanzapine increased the risk of suicide. This trial proves nothing.

Bolton et al. claim that “There is good evidence for the antisuicidal properties of lithium,” referring to another narrative review that in its abstract says that “Large-scale, retrospective and prospective naturalistic long-term clinical studies, including severely ill, frequently suicidal depressives show that appropriate pharmacotherapy markedly reduces suicide morbidity and mortality” (4). A systematic review in BMJ of randomised trials of lithium is far more cautious (5). In a meta-analysis of four small trials in patients with unipolar or bipolar mood disorders, there were unusually many suicides; six on placebo and none on lithium among only 241 and 244 patients, respectively (5). The authors wrote that the existence of only one or two moderately sized trials with neutral or negative results could materially change this finding. Moreover, the placebo group could have an artificially increased risk of suicide because of withdrawal symptoms. Almost all trials of psychiatric drugs are biased by their cold turkey design: after a short wash-out period, people already on the sort of drug being tested are randomised to another drug or placebo. This design increases suicides in the placebo group artificially (3).

I wonder why the BMJ publishes papers like the one by Bolton et al. No psychiatric drugs have been convincingly shown to decrease suicides while many have been shown to increase the risk of suicide and deaths from other causes (3).

1 Bolton JM, Gunnell D, Turecki G. Suicide risk assessment and intervention in people with mental illness. *BMJ* 2015;351:h4978.

2 Griffiths JJ, Zarate CA Jr, Rasimas JJ. Existing and novel biological therapeutics in suicide prevention. *Am J Prev Med* 2014;47(3 Suppl 2):S195-203.

3 Gøtzsche PC. *Deadly psychiatry and organised denial*. Copenhagen: People's Press; 2015.

4 Rihmer Z, Gonda X. Pharmacological prevention of suicide in patients with major mood disorders. *Neurosci Biobehav Rev* 2013;37(10 Pt 1):2398-403.

5 Cipriani A, Hawton K, Stockton S, et al. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. *BMJ* 2013;346:f3646.

**Competing interests:** No competing interests

**10 December 2015**

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