populations, with variable doses and durations, which creates further difficulty in interpreting such data. We therefore conclude that it is not possible to state with certainty which of the seven most commonly prescribed non-steroidal anti-inflammatory drugs is the safest; six of these seven have similar profiles of adverse events.

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Antidepressants and suicide

Study analyses were flawed

EDITOR,—Two recent articles look at use of antidepressants and death from suicide. John A Henry and colleagues have continued previous work and assessed the relation between death and defined daily dose.[1] Unfortunately, the defined daily dose for dothiepin used in the paper (75 mg) should be 150 mg (references quoted by Henry and colleagues). The correct figure is then 3·08 deaths per million defined daily doses of dothiepin instead of 1·54—the second highest figure, after that for amoxapine. This agrees with a clinical study that showed that dothiepin has greater toxicity in overdose than other tricyclic antidepressants.[2] We are also concerned about the statistical methods used by Henry and colleagues. It is unclear how valid confidence limits are in this context without a clear definition of x and how the standard error (not deviation) was calculated. It is inappropriate to use one tailed tests of significance without a prior hypothesis, and it is incorrect to use Fisher's exact test to compare rates.

In the study by Susan S Jick and colleagues we question the inclusion of flupenthixol, which is more likely to be used for schizophrenia than depression and is usually used as a depot preparation.[3] Also, the overall suicide rate of 8·3 per 10 000 person years of antidepressant use seems remarkably low and is much lower than rates in affective disorder cited in the literature.[4] The data from Henry and colleagues' paper give a death rate for poisoning with dothiepin alone of 11·25 per 10 000 person years of use.[1] These discrepancies raise three possibilities. One is that prescribers were using antidepressants mainly for conditions other than affective disorder. Another is that suicide was considerably underestimated in the cohort. In Henry and colleagues' study only 56% of the deaths due to poisoning were suicides, the remainder being undetermined. To ignore these deaths when comparing outcome may obscure differences in toxicity between antidepressants in overdose. Thirdly, there was systematic underdosing of the antidepressants in the study compared with the defined daily dose. Obviously, combinations of all three factors may have occurred.

Finally, Jick and colleagues comment that their data are consistent with the proposition that those who are determined to commit suicide will find a way that produces the intended outcome. This comment would be supported only if they could show that patients on their database who survived self poisoning went on to commit suicide by other means. This is not supported by the literature, which indicates that most patients who survive after taking an overdose do not subsequently kill themselves by other means.[5]

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Study is based on unproved assumptions

EDITOR,—John A Henry and colleagues draw several familiar conclusions from their study of suicide and antidepressants.[1] They argue that their data "provide a useful guide to the relative toxicities of drugs and an indication of the needs for prescribing policy" and suggest that a considerable number of suicides could be prevented by a switch to routine prescribing of selective serotonin reuptake inhibitors. This opinion is not always expressed in such restrained terms—as the accompanying editorial reminds us[2]—and yet it is based on two unproved assumptions. The first is that relative mortality due to overdose is the same as relative toxicity in overdose. The second is that suicidal patients prescribed a non-toxic drug will not seek an alternative means of killing themselves.

Since the data on relative mortality due to an overdose of antidepressants do not come from randomised trials they could reflect differences between patients prescribed different antidepressants rather than differences between the drugs themselves. There is evidence to support this interpretation. For example, when Farmer and Pinder derived a similar "toxicity" index using data from Intercontinental Medical Statistics they found that for each antidepressant the index was lower in those aged over 65 than in younger people[3]; this cannot be reconciled with the suggestion that the index reflects cardiotoxicity in overdose. If the index measures drug toxicity then it should be stable over time; in fact, the index for amitriptyline calculated for the years 1975-84 is 46·5 (95% confidence interval 43·9 to 49·1)[4] and for the years 1987-92 is 38·9 (35·6 to 42·4).[2]

If antidepressants do differ in toxicity in overdose it does not follow that routine prescribing of drugs with lower toxicity will reduce the suicide rate. Such a conclusion would be justified only if there was no substitution of method—in other words, if the prescription of a more toxic drug offered an opportunity for suicide that the depressed person would not find elsewhere. The study by Susan S Jick and colleagues substantially undermines this "loaded gun" argument against the tricyclic drugs since its main finding is that prescription of an older tricyclic antidepressant (rather than a new drug) does not constitute a risk factor for suicide.[5]

Contrary to the conclusions of this paper, there is uncertainty about the true difference in toxicity of different antidepressants in overdose and about the effect of substitution of method in a suicide prevention strategy based on prescribing policy. The small number of lives that might potentially be saved by prescribing the selective serotonin reuptake inhibitors must be set against the costs. Our cost effectiveness study showed how expensive such a prescribing policy might be when compared with other public health policies,[6] even when the calculations were based on assumptions compatible with the data presented by Henry and colleagues. These latest studies do nothing to challenge our conclusion that a widespread move to prescribing specific serotonin reuptake inhibitors as first line treatment for depression cannot be justified on the evidence available.

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Study did not consider treatment efficacy

EDITOR,—The papers on suicide and antidepressants in the issue of 28 January develop our understanding of this problem further. John A Henry and colleagues point out the differences in the rate of death by overdose for different antidepressants[1] but fail to relate this to efficacy and the fact that only 4-5% of all suicides are due to an overdose of antidepressant.[2] Susan S Jick and colleagues show that many people taking antidepressants commit suicide but do not give data on the number of suicides that occur in untreated depressed patients.[3] Interestingly, they found a distinct difference in crude rates of suicide between people taking tricyclic antidepressants (7·4 (range 4·7-8·7) suicides/10 000 person years) and people taking non-tricyclic antidepressants (flupenthixol, mianserin, fluoxetine, or trazodone; 14·9 (12·0-19·0) suicides/10 000 person years). The further analyses of fluoxetine, the antidepressant with the highest crude rate of suicide (19·0/10 000 person years), suggested that this rate could partly be explained by selection bias, in particular related to "history of suicidal behaviour." There seemed, however, to be "residual factors which reflected a higher risk of suicide for subjects taking fluoxetine."

Evidence suggests that the selective serotonin reuptake inhibitors (such as fluoxetine) are less effective than the tricyclic antidepressants, particularly in the more severe melancholic type of depression.[4] If patients with this type of depression constitute an appreciable proportion of those at risk of committing suicide then the earlier recommendations, based on data on the toxicity of drugs in overdose, that the tricyclic antidepressants should be abandoned may have contributed to an increase in the overall rate of suicide. As was pointed out in a similar debate a year ago, the