Correspondence

EDITED BY KIRIAKOS XENITIDIS and COLIN CAMPBELL

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Suicide trends and antidepressants

The suicide rate in Sweden decreased by 25% during the 1990s. After analysing trends for the years 1978–96, I proposed that the cause might be the concurrent increased use of antidepressants, and data from Norway, Denmark, Finland, Hungary and the USA supported this hypothesis (Isacsson, 2000). However, naturalistic studies do not allow definite conclusions, which is why the importance of testing this hypothesis in other studies was stressed. Reseland *et al* (2006) recently published an 'extended' (1961–2001) analysis of suicide and the use of antidepressants in the four Nordic countries. They interpreted two non-significant findings as 'contrasting' with my data: in Sweden and Denmark, the decrease in suicide started before the introduction of selective serotonin reuptake inhibitors (SSRIs); the suicide rate in Norway later stabilised despite increased use of SSRIs.

However, the classification of deaths was changed in 1969 with the introduction of the category of uncertain cause of death in ICD–8. Statistics before 1969 are therefore not comparable with later data. Furthermore, forensic pathologists only gradually became accustomed to the new classification and the proportions of suicides to uncertain cases appear to have stabilised first in 1979 (Fig. 1). Thus, the decrease found by Reseland *et al* in 'certain suicides' in 1969–79 may be an artefact. A better way of handling the uncertain cases might be to add them to the certain suicides (Linsley *et al*, 2001). This would mean that the Swedish suicide rates increased in 1969–79, decreased in 1979–89 and decreased rapidly in 1989–99. The 'pre-SSRI' decrease in 1979–89 may be a result of the increased use of tricyclic antidepressants.

Stabilisation in suicide rates is to be expected. Antidepressants cannot save people who avoid doctors, who have treatment-refractory depression, schizophrenia or substance misuse from dying by suicide.

I conclude that the data of Reseland *et al* do not challenge the hypothesis that the increased use of antidepressants is the cause of the prominent decrease in suicide rate since 1990. Moreover, some ten studies provide strong evidence to support the hypothesis (Isacsson & Rich, 2005; Ludwig & Marcotte, 2005).

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Ludwig, J. & Marcotte, D. E. (2005) Anti-depressants, suicide, and drug regulation. *Journal of Policy Analysis and Management*, **24**, 249–272.

Reseland, S., Bray, I. & Gunnell, D. (2006) Relationship between antidepressant sales and secular trends in suicide in the Nordic countries. *British Journal of Psychiatry*, **188**, 354–358.

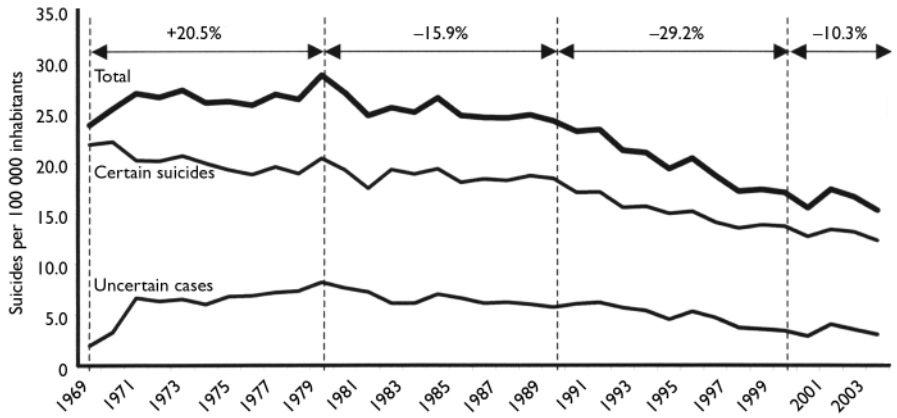

Fig. 1 Suicide rates in Sweden 1969–2003. Percentages refer to the total (suicides + uncertain cases).

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Author's reply: Professor Isacsson raises an important issue concerning the interpretation of national suicide data before and after the introduction (in 1969) of a new classification of deaths, 'injury undetermined whether accidentally or purposely inflicted' (ICD–8). The points he raises do not, however, invalidate our conclusions.

The exclusion of pre-1969 or even pre-1979 (the period when the use of suicide and undetermined categories had stabilised in Sweden) data from our analyses does not alter our main finding that suicide reductions in three of the four Nordic countries preceded the widespread use of SSRIs in the early 1990s. With the exception of Sweden, suicide rates continued to increase, rather than decrease, in the period 1969–79 in the Nordic countries, indicating that the changed classification had a minor impact on apparent trends in these countries.

There are well-recognised problems with interpreting ecological data to infer causal effects. Isacsson cites data from a number of countries where declines in suicide rates have coincided with increased antidepressant prescribing. However, data from other countries, such as England and Wales, Ireland and Italy, demonstrate the opposite pattern (Gunnell & Ashby, 2004). Professor Isacsson suggests that the reduction in suicide rate in Sweden in 1979–89, prior to the use of SSRIs, may be a result of the increased use of tricyclic antidepressants. This is possible, but data from Norway suggest that increased use of non-SSRI antidepressants in the 1970s and 1980s was associated with increases in suicide rates.

Isacsson suggests that the stabilisation in the decline in suicide rates is expected because not all people with depression consult doctors and conditions other than depression contribute to overall suicide numbers.

We agree with this analysis. Nevertheless, the continued year-on-year rise in antidepressant use in the study period does indicate a wider population of individuals, presumably some of whom are at risk of suicide, being treated by these drugs.

Our assessment of suicide and antidepressant prescribing in the Nordic countries was more comprehensive than Isacsson's original analysis and in our view provides weaker evidence than that originally presented (Isacsson, 2000). Nevertheless the most comprehensive assessment of the ecological data to date (Ludwig & Marcotte, 2005) does support Isacsson's view. In an area where the influence of the pharmaceutical industry is widespread we favour a more cautious interpretation of the ecological data.

Declaration of interest

D.G. was an independent advisor to the Medicines and Healthcare Products Regulatory Agency Expert Working Group on the Safety of SSRIs, receiving expenses and an attendance fee.

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Cognitive–behavioural therapy for avoidant personality disorder

Emmelkamp *et al* (2006) reported that cognitive–behavioural therapy (CBT) was more effective than brief dynamic therapy (BDT) for the treatment of avoidant personality disorder. However, the study has several methodological shortcomings.

In the BDT group it is not clear whether and to what extent a manualised treatment was realised. The article includes non-specific references to several psychodynamic manuals and it is not clear what therapeutic procedures were actually carried out. Furthermore, no disorder-specific treatment manual was used. In contrast, in the CBT group the manual of Beck & Freeman (1990) for avoidant personality disorder was applied. No data with regard to adherence and competence were reported and thus it is not clear whether both treatments were carried out with equal competence.

Besides the presence or absence of the diagnosis according to the Structural Clinical Interview for DSM–IV Axis II Disorders (SCID–II) several self-report measures were applied as 'primary outcome measures'. However, the authors focus on a specific measure that they regarded as primary. In addition to other outcome measures, Emmelkamp *et al* used the Personality Disorder Belief Questionnaire (PDBQ; Arntz *et al*, 2004). Arntz *et al* (2004) explicitly included items from Beck & Freeman (1990) and hence the PDBQ is specifically tailored to the effects of CBT. Possibly the most convincing difference between CBT and BDT was found with regard to the number of patients still fulfilling the SCID–II criteria at follow-up (9 *v.* 36%). However, it is not clear whether the 'independent assessor' was masked to the treatment group.

In two outcome measures that refer more specifically to the features of avoidant personality disorder, the Social Phobia Anxiety Inventory (SPAI) and the Avoidance Scale, another measure developed by the authors (Emmelkamp, 1982), both CBT and BDT achieved large and nearly identical pre-/post-treatment effect sizes: 0.92 *v.* 0.82 (SPAI) and 1.88 *v.* 1.75 (Avoidance Scale). Emmelkamp *et al* reported that 'CBT was significantly superior on all primary outcome measures.' However, for the difference between the CBT and BDT groups in SPAI score the P was 0.09, which is not significant at the level of $\alpha=0.01$ set by the authors. Furthermore, at follow-up, there were no differences between CBT and BDT groups in SPAI and Avoidance Scale scores. Differences were only reported for the PDBQ and for two scales that refer to other personality disorders. For BDT, 'no significant difference was found between BDT and control' but no data are reported. Compared with the waiting list control, CBT was only superior in two of six measures but the sample size of the waiting list control was small ($n=15$ *v.* 26 for CBT and 28 for BDT post-treatment). The fact that almost no differences were found between the waiting-list control and both BDT and CBT is (at least in part) a result of the insufficient sample size. Furthermore, at least in some measures, the waiting-list group achieved medium or even large effect sizes.

The results reported by Emmelkamp *et al* (2006) are at variance with those reported by Svartberg *et al* (2004), who found BDT and CBT to be equally effective for cluster C personality disorders.

Overall, the design, statistical analyses and reporting of the results raise serious concerns about an investigator allegiance effect (Luborsky *et al*, 1999).

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Author's reply: Our study was designed in close cooperation with full-time clinicians and in both groups (CBT and BDT) application of manuals was highly flexible to be representative of the respective therapies as they are carried out in clinical practice and to enhance the external validity of the study. Sessions were audiotaped and scored using the Coding System of Therapeutic Focus on Action and Insight (CFAI; Samoilov *et al*, 2000) by two independent raters who were masked to the treatment group (interrater reliability (Kendall's W) ranged from 0.86 to 0.91). In general, results revealed that therapists adhered to the respective therapies (Emmelkamp *et al*, 2004).

To the best of our knowledge there are no measures of 'psychodynamic origin' specifically related to avoidant personality disorder and hence we used the PDBQ. Furthermore, it was not feasible to keep the independent assessors who completed the SCID–II unaware of the treatment group in a number of instances.

Post-treatment CBT was significantly superior to BDT on all 'primary' outcome measures. A significance level of $\alpha=0.1$ set rather than 0.01 as claimed by Leichsenring & Leibing. Even if we exclude the SPAI scores ($P=0.09$), this still leaves superior outcome for CBT on three out of four outcome variables. The lack of power to detect differences between the waiting-list control group and the active treatments is acknowledged as a limitation.

There are important differences between our study and that of Svartberg *et al* (2004). Svartberg *et al* included all types of cluster C and self-defeating personality disorders, rather than limiting their study to avoidant personality disorder. Two-fifths of their sample did not fulfil criteria for avoidant personality disorder treatment and treatment consisted of 40 rather than of 20 sessions. Furthermore, outcome with respect to personality disorders (sic) was only assessed with the Millon Clinical Multiaxial Inventory (Millon, 1994), rather than with the gold standard SCID–II. Finally, the lack of a control group in the study of Svartberg *et al* renders the results difficult to interpret.

In contrast to most other psychotherapy studies, we did our utmost to prevent an effect of investigator allegiance. The study was designed in close cooperation with two psychodynamic therapists (G.F. and H.K.) and two cognitive–behavioural therapists (A.B. and A.K.), who all fully participated in the design of the study, selection of measures, treatment manuals (including degree of flexibility) and therapists.

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Anti-phospholipid antibodies, neuroleptic treatment and cardiovascular morbidity

Joukamaa *et al* (2006) reported a clear relationship between the number of neuroleptic drugs prescribed and mortality of people with schizophrenia. The more important causes of death were cardiovascular disease and unspecified respiratory disease. Moreover, the authors postulated that overlooked venous thrombosis or pulmonary embolism accounted for some respiratory deaths.

Oomen *et al* (1995) documented increased vascular morbidity at 2-year follow-up in patients with anti-phospholipid antibodies who were newly admitted for psychiatric treatment. These patients showed a range of cardiovascular accidents (arterial or venous thrombosis, pulmonary embolism and myocardial infarction). The negative control group without anti-phospholipid antibodies had no vascular complications during follow-up.

Vascular events associated with such autoantibodies range from superficial to life-threatening multiple organ thrombosis developing over a short period ('catastrophic' anti-phospholipid syndrome). Thrombosis in anti-phospholipid syndrome appears to be a 'two-hit' phenomenon. Autoantibodies (the first 'hit') are continually present in the circulation, yet a local trigger (the second 'hit') is required to induce thrombus formation. Erkan & Lockshin (2006) recently suggested the elimination of reversible thrombosis risk factors and heparin prophylaxis during high-risk periods in people with persistent anti-phospholipid antibodies. Chengappa *et al* (1991) and Schwartz *et al* (1998) demonstrated a high prevalence of anti-phospholipid antibodies (about 30%) in patients. A prospective study is ongoing in our departments to confirm the prevalence of anti-phospholipid antibodies with a first episode of acute psychosis before and after neuroleptic treatment. If historical data are confirmed, more attention should be paid to the fact that up to one-third of patients presenting with psychosis have anti-phospholipid antibodies and are at risk of cardiovascular or respiratory morbidity/mortality when neuroleptic treatment or physical restraint are used.

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Letters to the Editor

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