

Discussion

In a cohort of studies submitted to the Swedish regulatory agency to secure marketing approval for five selective serotonin reuptake inhibitors for the treatment of major depression we have found evidence of duplicate publication, selective publication, and selective reporting. In our material this selective reporting was the major cause for bias in overall estimates based on published data.

Strengths and limitations of study

To our knowledge, access to full reports and study protocols for all studies, published as well as unpublished, is unique to our investigation. This has enabled us to study the impact of different sources of publication bias. It also allowed us to elucidate the sometimes complex pattern of publications. Our investigation is restricted to one class of antidepressant drugs, but there is no reason to believe that drug manufacturers have different policies for reporting and publishing studies of different drugs. Indeed, in a review of an antiemetic drug a similar pattern of duplicate publication has been reported.⁴ Thus, our results are likely to be valid for other classes of drugs with a similar structure of the efficacy documentation—that is, several studies with small to medium sample size.

Conclusions

The outcome of our investigation should not be used to dispute the value of systematic literature reviews and meta-analyses in general. However, for anyone who relies on published data alone to choose a specific drug, our results should be a cause for concern. Without access to all studies (positive as well as negative, published as well as unpublished) and without access to alternative analyses (intention to treat as well as per protocol), any attempt to recommend a specific drug is likely to be based on biased evidence. The probable choice of a specific selective serotonin reuptake inhibitor based on a pooled analysis of publicly available data is not likely to be supported by an analysis considering the total body of evidence.

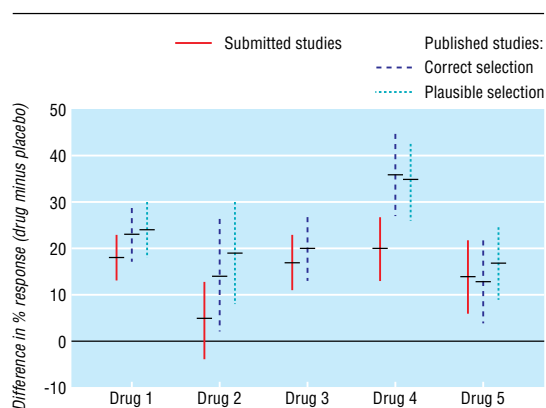


Fig 3 Differences (95% confidence intervals) in response rate (% response to drug minus response to placebo). Results from pooled analyses of all submitted studies, correct selection of published studies (duplicates excluded), and plausible selection of published studies (including probably undetectable duplicates)

What is already known on this topic

Duplicate publication, selective publication, and selective reporting are likely to introduce bias in systematic literature reviews and meta-analyses

Several reports have provided evidence of duplicate publication and selective publication as well as the tendency to publish only studies with significant findings

What this study adds

Access to full documentation of all studies (published and unpublished) made it possible to investigate the relative impact of the different sources of bias

Selective reporting (tendency to publish the more favourable per protocol results only) was a major cause for bias

A sponsor in control of all studies does not seem to improve the situation with respect to duplicate publication, selective publication, and selective reporting

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Corrections and clarifications

London GP cleared of serious professional misconduct
This news article by Clare Dyer (26 April, p 898) reported that the judicial committee of the Privy Council quashed a finding by the General Medical Council of serious professional misconduct against Dr Michael Silver, a general practitioner from Edmonton, north London. We would like to make it clear that the GMC's professional conduct committee had found that the nature of the GP's misconduct had been of a "managerial, organisational and communications" nature and did not relate to the diagnosis or treatment of a patient.

West Nile encephalitis

We always try to spell out abbreviations in the *BMJ*. However, in the "Virus detection" box in figure 3 in this clinical review by Tom Solomon and colleagues (19 April, pp 865-9) some confusion arose with the abbreviation RT PCR. This was spelt out both times as "real time PCR [polymerase chain reaction]." The first time was indeed correct, but the second should read: "Reverse transcriptase PCR."