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EDITORIALS

Adverse effects of statins

The BMJ and authors withdraw statements suggesting that adverse events occur in 18-20% of patients

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In October last year we published an article by John Abramson and colleagues that questioned the evidence behind new proposals to extend the routine use of statins to people at low risk of cardiovascular disease.[1] Abramson and colleagues set out to reanalyse data from the Cholesterol Treatment Trialists' (CTT) Collaboration. Their contention was that the benefits of statins in low risk people were less than has been claimed and the risks greater.

In their conclusion and in a summary box they said that side effects of statins occur in 18-20% of people. This figure was repeated in another article published in the same week in *The BMJ* by Aseem Malhotra.[2] *The BMJ* and the authors of both these articles have now been made aware that this figure is incorrect, and corrections have been published withdrawing these statements. The corrections explain that although the 18-20% figure was based on statements in the referenced observational study by Zhang and colleagues—which said that "the rate of reported statin-related events to statins was nearly 18%,"[3] *The BMJ* articles did not reflect necessary caveats and did not take sufficient account of the uncontrolled nature of Zhang and colleagues' data.

This editorial aims to alert readers, the media, and the public to the withdrawal of these statements so that patients who could benefit from statins are not wrongly deterred from starting or continuing treatment because of exaggerated concerns over side effects.

The true incidence of adverse events from use of statins in people at low risk continues to be disputed. Data compiled by the CTT Collaboration show that rates of adverse effects are similar in the active and the placebo arms in trials of statins. However, generalising from clinical trials to wider populations may be problematic because of patient selection; for example, exclusion of older patients, patients with co-morbid conditions or potential drug-drug interactions, and women. In addition, when compared with the full clinical study reports, published accounts of clinical trials in medical journals report only a minority of adverse events.[4] Access to the full data from trials of statins would help determine the rates of serious adverse events in statin and control groups; although in their correction Abramson and colleagues say that this probably won't help to determine the frequency of statin related events that are less than serious.

Readers may like to know how the erroneous statements came to be published, why it has taken us seven months since publication to correct them, and what other action we are considering.

Abramson and colleagues' article was submitted and peer reviewed. The peer reviewers' comments are posted as a web extra, with the reviewers' permission. The initial submission reported that Zhang and colleagues found that "18% of statin treated patients had discontinued therapy because of statin related events." This was a misreading of Zhang and colleagues' data that was not picked up by the peer reviewers or editors. During the revision process the authors placed more certainty on the 18% figure in their conclusions, and this was rounded up to "nearly 20%" in a summary box. The revised article with these changes was not subject to further external review. This is part of our process that we are now revisiting.

Writing, peer reviewing, and editing are human processes subject to error, which is why we must be, and are, ready to correct things when they are found to be wrong. We were alerted to the error by Rory Collins, professor of medicine and epidemiology at Oxford University and head of the CTT Collaboration whose data were reanalysed by Abramson and colleagues. Collins visited me at *The BMJ* in early December, then took the matter up in the UK media towards the end of March,[5] and finally put his concerns in a letter to me, marked not for publication, on 31 March. He declined several requests to send a rapid response or letter for publication. Others did send rapid responses questioning the 18-20% figure,[6 7] and both sets of authors responded.[8 9] Meanwhile *The BMJ*'s editors sought to unpick the evidence as presented in the paper by Zhang and colleagues and to agree the wording of a correction with the authors, who have cooperated throughout this process. The text of the correction, which includes a further interpretation of Zhang and colleagues' data, has been peer reviewed.

Is a correction enough in this case? Collins thinks not. He has requested retraction of both articles. Guidelines of the international Committee on Publication Ethics state that journals should consider retracting a publication if there is clear evidence

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that the findings are unreliable, either as a result of misconduct or honest error.[10] The question in the case of these two articles is whether the error is sufficient for retraction, given that the incorrect statements were in each case secondary to the article's primary focus. In the case of Abramson and colleagues, this was that the CTT data failed to show that statins reduced the overall risk of death in people with a <20% 10 year risk of cardiovascular disease; for Malhotra it was that saturated fats are not the main dietary cause of heart disease.

However, as the editor responsible for publishing the articles, I have a vested interest in not retracting them unless the case for doing so is completely clear. So I have decided that the right thing to do is to pass this decision to an independent panel. Iona Heath, former chairwoman of the Royal College of General Practitioners and of *The BMJ*'s ethics committee, has agreed to chair the panel, whose members will include people with no "dog in this fight," but with expertise in clinical trial and observational study methodology and in designing and implementing editorial policies on retraction. Full details of the panel and processes will be published shortly. I have asked that all submissions to the panel be placed in the public domain on bmj.com, and I have committed to implementing the panel's recommendations in full.

Meanwhile *The BMJ* will continue to debate the important questions raised in both these articles: whether the use of statins should be extended to a vastly wider population of people at low risk of cardiovascular disease; and the role of saturated fat in heart disease.

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