From: **Turchin, Alexander,M.D.,M.S.** <ATURCHIN@partners.org>
Date: 10 May 2014 at 22:13
Subject: RE: Request from The BMJ relating to your paper on discontinuation of statins
To: Fiona Godlee <fgodlee@bmj.com>
Cc: Helen Macdonald <HMacdonald@bmj.com>, Huabing Zhang <huabingzhang@yahoo.com>, "Plutzky, Jorge,M.D." <jplutzky@rics.bwh.harvard.edu>

Dear Dr. Godlee,

We have reviewed the original BMJ paper by Abramson et al. and the proposed correction. We agree that the correction appropriately characterizes our study's findings with respect to the statin-related events.

Thank you for the opportunity to provide our input,

Alex

From: Fiona Godlee [fgodlee@bmj.com]
Sent: Friday, May 09, 2014 8:35 AM
To: Turchin, Alexander,M.D.,M.S.; Plutzky, Jorge,M.D.
Cc: Helen Macdonald
Subject: Request from The BMJ relating to your paper on discontinuation of statins

Dear Dr Plutzky, Dr Turchin, Dr Zhang (with apologies, as I don't seem to be able to find Dr Zhang's email address)

I am editor in chief of The BMJ and I am writing to ask for your help in responding to a complaint we have received about an article we published last year.

http://www.bmj.com/content/347/bmj.f6123

The BMJ paper, by Abramson et al, references the study you published in April last year in Annals of Internal Medicine on the discontinuation of statins

http://annals.org/article.aspx?articleid=1671715

The complaint, from Rory Collins in Oxford, is that the paper misrepresents your findings and in so doing, overstates the evidence on the rates of adverse events from statins.

We are working on a correction that we hope will do full justice to the issues involved.

I would be very grateful if you could look at the Abramson et al paper and give me your views on the way it characterises your findings in relation to statin related events.

The draft correction is included below, on which I would welcome your comments

I very much appreciate your help with this matter and would be especially grateful if you could get back to me early next week if at all possible.

All best wishes, Fiona Godlee

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Correction to Abramson et al (Draft - FG - May 9)

In our article, we stated that side effects of statins occur in about 18-20% of patients. We withdraw this statement. Although it was based on statements in the referenced paper by Zhang et al that "the rate of reported statin-related events to statins was nearly 18%," our article did not reflect necessary caveats and did not take sufficient account of the uncontrolled nature of the study. Zhang et al observed that the rate of statin-related events found in their study (18%) was "substantially higher than the 5% to 10% usually described in randomized, placebo-controlled, clinical trials." Two caveats must be considered: As Zhang et al point out, the rate of statin-related events reported in their observational study was uncontrolled, and therefore may be inflated because events attributed to statins might have occurred in a placebo group as well. In addition, although Zhang et al do not make this point, the 5-10% rate quoted by Zhang et al as having been observed in randomised trials was, in many cases, similar in both active and placebo groups.

The exact rate of statin related adverse events in people at low risk of cardiovascular disease remains uncertain. As discussed by Zhang et al, observational studies report rates of [add rates]. Meanwhile, clinical trials may underestimate the frequency of statin-related adverse events due to patient selection, exclusion of older patients and those with comorbid conditions, underrepresentation of women, and selection bias created by willingness to participate in a clinical trial. Access to the full data from the trials of statins would help to determine the

comparative rates of serious adverse events in statin and control groups, but probably would not help to determine the frequency of less-than-serious statin-related adverse events.

Also in our article, we mistakenly said that Zhang et al found that "18% of statin treated patients had discontinued therapy (at least temporarily) because of statin-related events." Based on review of structured EMR categories and automated review of unstructured narratives from follow-up visits of 107 835 patients over 8 years, Zhang et al found that “Of all study patients, 18 778 (17.4%) had a statin-related event documented during the study.” Further, among those who experienced a statin-related event, 59.2% had statin therapy discontinued at least temporarily. However, because of possible mis-categorization due to the limited options in the EMR listed as reasons for discontinuation of statin therapy, the authors of the study concluded that "as many as 87%" of these discontinuations could have been due to statin-related events. This equates to up to 9% of the study population having possibly discontinued statin therapy as a consequence of drug-related adverse events, rather than the 18% we cited.

We note that the primary finding in our article—that CTT data fail to show reduction in overall risk of mortality by statin therapy for people with <20% risk of CVD over the next 10 years—was not challenged in the process of communication about this correction.