

Documents relating to a complaint about *The BMJ* made to COPE by Jane Armitage, Rory Collins et al, October 2014 - April 2016

Introduction

In October 2014, a letter of complaint was sent to the Committee on Publication Ethics (COPE) about *The BMJ*'s handling of two papers that were critical of plans to extend the use of statins to people at low risk of cardiovascular disease.[1] [2]

The complaint took 18 months to resolve, with COPE concluding in April 2016 that *The BMJ* had acted appropriately.

It was always our aim to ensure that the complaint and associated documentation would be made public, whatever the outcome.[3] We initially asked COPE to publish the documents but have now understood that this is not their policy. Prompted by misreporting of the outcome of the complaint in the *Lancet* [4] we now make available the documents below, in chronological order.

1. Abramson JD, Rosenberg HG, Jewell N, Wright JM. Should people at low risk of cardiovascular disease take a statin? *BMJ* 2013;347:f6123.
2. Malhotra A. Saturated fat is not the major issue. *BMJ* 2013;347:f6340.
3. Parish E, Bloom T, Godlee F. Statins for people at low risk. *BMJ* 2015;351:h3908.
4. Horton R. Offline: Lessons from the controversy over statins. *Lancet* 2016;388 (No 10049):1040, 10 September 2016.

1. Letter of complaint from Armitage et al, October 2014

A letter dated 23 October 2014 (not published here as we do not have the authors' permission) asked COPE to consider whether the Editor in Chief of *The BMJ* had breached its code of conduct for editors of medical journals. The letter sought to draw COPE's attention to editorial actions at *The BMJ* relating to its handling of two articles published in 2013. The letter pointed to the fact that *The BMJ*'s editor is running a Too Much Medicine campaign, which may have led these papers to be published in *The BMJ*. It expressed concern that misrepresentation of the benefits and harms of statins in *The BMJ* will have led people to stop, or not to start, taking statins.

The letter then itemised issues of specific concern. First, that *The BMJ* had been advised that the results presented for myopathy were "misleading" and that the journal should fact check information relating to important public health issues before publication. It also expressed concern that the editor continues to dispute that this matter is an error. Secondly, that *The BMJ*'s editor failed to address a peer reviewer's concerns about a correction to one of the articles, and that the author of the referenced study had confirmed that *The BMJ* correction was misleading. Thirdly, that the Editor made an incorrect statement in an editorial, about the peer review of the Abramson paper, which she took 11 days to correct. Fourthly, that it took three months for the editor to act on requests for the peer reviewers' comments and that these showed that the article by

Malhotra had been reviewed by Abramson. Fifthly, that the panel set up by *The BMJ* to consider the concerns raised by Rory Collins in 2013 was not and should not be called “independent.” Sixthly, that the timeline of events created by *The BMJ* highlights a letter calling for the statins panel not to retract the articles, which was coordinated by a journalist who contributes to *The BMJ*. Seventhly, that some material that was submitted to the statins panel was not published, specifically: a submission relating to a letter sent to NICE by Aseem Malhotra and others. The letter also questioned legal advice which led *The BMJ* to redact a statement from a submission to the statins panel, in which Eugene Braunwald of Harvard Medical School said that the right to free speech does not include the right to falsely shout “Fire” in a crowded room. [*Editor’s note:* this statement was retracted from the published submission because of legal advice that it was defamatory of John Abramson and colleagues and Aseem Malhotra. The implication is that these authors knew there was no “fire” but claimed there was, whereas the facts of the matter remain in dispute.] We include it in this précis for clarification.

The letter was signed by: Jane Armitage, Professor of Clinical Trials and Epidemiology, University of Oxford; Colin Baigent, Professor of Epidemiology, University of Oxford; Emily Banks, Professor of Epidemiology and Public Health, Australian National University, Canberra; Valerie Beral, Professor of Epidemiology, University of Oxford; Rory Collins, BHF Professor of Medicine and Epidemiology, University of Oxford; Professor John Danesh, Professor of Epidemiology and Medicine, University of Cambridge; Stephen MacMahon, Professor of Medicine, University of Oxford; Sir Mark Pepys, Director, Wolfson Drug Discovery Unit, University College London; Richard Peto, Professor of Medical Statistics and Epidemiology, University of Oxford; Neil Poulter, Professor of Preventive Cardiovascular Medicine, Imperial College, London; Peter Sandercock, Professor of Medical Neurology, University of Edinburgh; Robert Souhami, Emeritus Professor of Medicine, University College London; Nicholas Wald, Professor of Environmental and Preventive Medicine, Queen Mary University of London

2. COPE report on complaint on BMJ Statin papers, dated 12 January 2015

Process and timeline

August 2014: phone conversation with Virginia Barbour (VB) and Professors Collins and Baigent

October 2014: Letter from Professor Armitage and colleagues received at COPE

November 2014: Discussed at Officers’ t-conference November and agreed VB would review and report back to Officers

VB investigated and prepared report

December 2014: Report discussed at Officers’ t-conference

January 2015: Report sent to Professor Armitage and colleagues with copy to Dr Fiona Godlee.

VB review

Review of correspondence received at COPE

Review of BMJ enquiry – published report <http://www.bmj.com/about-bmj/independent-statin-review-panel>

Review of Papers and correspondence published in BMJ – last reviewed 1 December 2014 <http://www.bmj.com/content/349/bmj.g5688/rapid-responses>
Review of other recent related articles published in academic journals and lay press, eg Armitage, Collins and Baigent [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(14\)61765-7/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61765-7/fulltext)

Background

Professor Armitage and colleagues have asked us to consider the actions of the BMJ in relation to the peer review of these papers, the process and the outcome of the review commissioned by the journal. In addition we were contacted by Dr Simpson of the British Cardiovascular Society.

Specifically (from Professor Armitage and colleagues' letter)

“Consequently, given the public health implications, we are seeking advice from COPE as to whether the BMJ's handling of this matter, as described below (with embedded links to supporting materials), has been consistent with COPE's Code of Conduct and Best Practice Guidelines for Journal Editors.”

It is important to note, as I have done to Professor Collins earlier, that we are not a statutory or regulatory body but a voluntary membership organization. These are the [terms](#) under which we can consider complaints about our members. Specifically, we cannot get involved in individual editorial decisions. In addition, we do not investigate individual cases but aim to facilitate a dialogue between the parties. Finally, it is not appropriate for COPE to make a specific recommendation on the specific medical issues raised here, regardless of any public health implications.

The approach that we take therefore and the way in which we have considered this case and others, is what would have been our advice had this case been brought to a COPE forum. Specifically, we encourage an open debate (in our terms we say that “To facilitate an open dialogue, we believe that correspondence relating to concerns should be open, and we will copy all parties on correspondence from COPE (unless there are legal or other compelling reasons for confidentiality) and expect that all parties will do the same.”) and therefore we will also send this report to Dr Fiona Godlee, Editor of the BMJ.

Summary of issues

It appears that there are three issues here.

1. Was the review process pre publication appropriate for the papers?
2. Was the post publication process appropriate, including the handling by the panel and its recommendations?
3. Has the literature been corrected: is there anything further that could or should be done in this debate now?

For the first two issues, when I spoke with Professors Collins I advised him if he had not already done so and/or remained unhappy about the handling of these papers he should to contact the journal's publisher directly. It appears that this has not happened

directly but we note that Baroness Ilora Finlay, President of the British Medical Association was cc'ed in letters to us.

Review of the above questions:

1. *Was the review process pre publication appropriate for the papers?*

Professor Armitage and colleagues lay out a number of issues that occurred during the review of the paper. These have been extensively documented and discussed, including in the report from the review panel. Consideration of this is therefore folded into the discussion below.

2. *Was the post publication process appropriate, including the handling by the panel and its recommendations?*

Was the review panel completely independent? It is worth pointing out that it is highly unusual for a journal to even consider setting up a panel to review its processes. Generally speaking journals consider these issues internally only. Notwithstanding that, the panel's composition, its deliberations, and conclusions were apparently all made public. If there are documents or other relevant information that have not been made public as Professor Armitage and colleagues claim we would agree that they should be. **We recommend the journal review the allegations by Professor Armitage and colleagues and add any missing material.**

The panel had the following terms of reference:

- a) ToR1. To consider whether either or both articles should be retracted

The panel found that neither paper met the COPE criteria for retraction.

We understand that there are differences of opinion in these matters, but in the end the decision to retract papers does lie with the Editor. The Editor did seek advice from a separate review panel and this panel agreed with the Editor's decision on retraction. The panel made separate recommendations about the corrections (see ToR3)

- b) ToR 2 To review and comment on the process by which the articles were published.

The panel said: "The panel has made a number of suggestions aimed at improving the editorial process and was concerned about the late inclusion of an unscrutinised reference on a short timescale. However, the panel concedes that the peer review and editorial processes must rely on goodwill to a very considerable extent and can never be completely foolproof – especially in view of the time pressures under which authors, peer reviewers and editors are working."

Our understanding from notes published in the journal that the Editor has accepted the recommendations of the panel. However, it would appear that it would be appropriate for the journal to now explain how these recommendations have been acted on. **We suggest that the journal and the publisher should work jointly to do this and make public the results of this, and specifically address the alleged breaches of the COPE Code of Conduct and what has been done to address these.**

- c) ToR 3 To review and comment on how criticisms and complaints against the articles were raised, and how the journal responded.

The panel concluded “The BMJ editorial staff should implement a significant event audit in relation to the need for the correction. The aim of the audit would be to try and identify what would need to have been in place to ensure that the correction was made in a more timely fashion.”

We suggest that the journal and the publisher should work jointly to do this if not already undertaken and make public the results of this.

3. *Has the literature been corrected: is there anything further that could or should be done in this debate now?*

Without having an opinion on one or other side of the debate on the use of statins and their side effects, it is clear that this is a topic on which there is a considerable range of opinion and no purpose is served by censoring either side of the debate. There has been much discussion in previous COPE forums of the need for post publication criticisms to be aired in the journal that it was originally published in and we note that the BMJ repeatedly offered Professor Collins and colleagues the opportunity to respond, but they declined. We think that it is unfortunate that the most important issue here, ie having a full response in in the BMJ of the specific issues of concern to Professor Collins and colleagues in the Abrahamson and Malhotra papers has not yet happened and we feel this needs to be rectified as soon as possible, notwithstanding other comments published in newspapers and other journals. **We therefore strongly recommend that a response by Professor Collins and colleagues on the substantive scientific issues they dispute is submitted and published in the BMJ itself as soon as possible.**

Finally, we note that Professor Armitage and colleagues allege that in a number of instances authors of comments and other material post publication did not have competing interests fully declared. **The journal should review these comments and ensure that all competing interests are declared appropriately.**

In conclusion and in order for the debate on this important issue to be as clear as possible and hopefully to allow the discussion about these particular papers to finalized, **we urge the BMJ, its publisher and Professors Collins, Armitage and colleagues to work together to make public a follow on from this debate which addresses the various unresolved issues:**

- the outcome of the review of the peer review process that the BMJ has undertaken,
- the publishing of any further submissions to the review panel;
- a response to alleged breaches of the COPE Code of Conducts and the journal’s response to these;
- the publication of a response by Prof Collins and colleagues in the BMJ itself on the substantive issues of the incidence of side effects statins.

3. BMJ response to points raised in the complaint to COPE, sent 11 May 2015

In this document, we aim to respond point-by-point to the concerns raised by Professors Armitage, Collins and colleagues in their complaint to COPE dated 23 October 2014.

In each response, we use the section heading used in the letter of 23 October, then attempt to disambiguate the various complaints being made. We note the section(s) of the [COPE code of conduct](#) to which the section refers and provide our response to each alleged breach of the relevant section.

1. "Publishing incorrect side-effect claims despite being advised they were misleading":

We understand this complaint to be that an editor said in an editorial meeting, in the light of reviewer Smeeth's comments, that it didn't matter if the numbers (complaining of muscle pain in statin vs control groups) were wrong as this could be highlighted in the Rapid Responses to the article online, as follows

- A. that there are low editorial standards at The BMJ, with the editors failing to protect the academic record, as detailed in point C.
- B. that this error persists and has not been corrected.

Response: the issue has been raised in rapid responses, making the distinction between myopathy, myalgia and myositis, all of which appear under a heading "Myopathy". Abramson responded on 20 December saying the argument is 'semantic'. In our view, the complaint in part concerns the use of a short heading (Myopathy) to cover multiple conditions that are then enumerated individually in the text (myopathy, muscle pain, musculoskeletal disorders overall and injuries). The Heath panel also commented on this issue, saying "The panel thought that including three different definitions of muscle problems, widely ranging in severity, all under a heading of the more serious myopathy, might lead to the reader to conflate these. However, as Abramson et al point out in their submission to the panel (SP23), myopathy and myalgia can be conflated in the opposite direction by referring to severe problems as if they included milder ones and this can also lead to misinterpretation."

The Editor has again discussed this issue with Abramson, a copy of whose response can be read (attached).

- C. This section refers to items in the [COPE Code of Conduct](#) as follows:

1.1. Editors should be accountable for everything published in their journals.

Response: The Editor in Chief and her staff do indeed hold themselves accountable for all the content published in the journal

- D. **1.6. [This means the editors should] maintain the integrity of the academic record;**

Response: In areas of disagreement between one reviewer and an author, or indeed between one reviewer and another, we believe an editor can reasonably decide to let the point be debated post-publication. In this case, there seems to be

continuing debate on precisely how best to represent this issue.

E. **1.8. [This means the editors should] always be willing to publish corrections, clarifications, retractions and apologies when needed.**

Response: We believe *The BMJ* has shown itself very willing to correct and clarify all the issues raised around the publication of these articles. It seems from our detailed analysis (below) that one point may have been missed from the private concerns that were sent to the journal by Professor Collins in letters to the editor marked “not for publication” or mentioned in conversation or via third parties. We apologise wholeheartedly for all such omissions. We would once again urge Professor Collins and colleagues, as COPE has urged, to make any remaining criticisms or concerns public in the pages of the journal. We do not feel a retraction was required on this occasion, and this conclusion was supported by the Heath panel.

F. **8.1. Editors should take all reasonable steps to ensure the quality of the material they publish, recognising that journals and sections within journals will have different aims and standards.**

Response: The Heath panel concluded that the journal’s processes were broadly appropriate, as did our internal review [published alongside this response]. We did however note a number of areas where we could improve our processes to make them even more robust and rigorous, and we have put this into practice. We will continue to review our processes and improve them where we can.

G. **12.1. Errors, inaccurate or misleading statements must be corrected promptly and with due prominence.**

Response: We believe errors and inaccuracies have indeed been corrected with due prominence. Although there was an interval of several months between publication of the Abramson article and its correction, discussion around the article was ongoing on the journal’s website during this period. In general the pace of corrections and retractions is regrettably slow (see [Steen RG: J Med Ethics 2011;37:249-253 doi:10.1136/jme.2010.040923](#))

2. “Publishing a misleading “correction” of other incorrect side-effect claims”

In essence, we read this complaint as follows. That in drafting a correction, the editor chose not to listen adequately to reviewer Smeeth on the subject of how to present the number of people complaining of side effects and also did not take adequate account of the views of Zhang *et al.* who felt moved thereafter to submit a further Rapid Response in clarification.

- A. In complaining about this process of reviewing the correction and deciding what it should say, the complaint refers to items in the COPE Code of Conduct as follows:

1.6. [This means the editors should] maintain the integrity of the academic record;

7.1 Editors should strive to ensure that peer review at their journal is fair, unbiased and timely.

Response: Once again we had a disagreement between parties and had to decide

how to proceed. On this occasion, the authors of the Zhang *et al.* study said the correction was fine as drafted but reviewer Smeeth felt it was not. The Editor made a decision to publish in a timely way with minor amendments to address Smeeths concern but without final resolution on this point; and to encourage further public discussion of this issue. The correspondence about the correction, between Fiona Godlee and the authors of Zhang *et al.* [included below], and Fiona Godlee and Liam Smeeth [also included below], is provided with this document.

B. 8.1. Editors should take all reasonable steps to ensure the quality of the material they publish, recognising that journals and sections within journals will have different aims and standards.

Response: Every effort was indeed made to ensure the quality of the articles and the correction, and where our critical event audit identified how processes could be improved we have amended them.

C. 17.1 Editors should have systems for managing their own conflicts of interest as well as those of their staff, authors, reviewers and editorial board members

Response: We are unsure of the relevance of this section of the code to the issue of the handling of the correction. In relation to the correction we believe we consulted the appropriate parties and asked the panel to consider its suitability. In terms of the editor's own conflicts of interest, she highlighted in [the editorial announcing the convening of the Heath panel](#) "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." We therefore feel that the issues of conflict of interest have been adequately handled with regard to the correction and the question of retraction.

3. "Publication of inaccurate editorial and media statements accompanying the published "correction"

We read this complaint as being that the [Editorial](#) said that a statement about side effects was missed by peer reviewers when in fact this statement was inserted by the authors after review, in a version of the article that was not re-reviewed. Specifically, we interpret the complaint as being that the editor knew this but that she published an editorial saying something she knew to be untrue, repeated this statement to the media, and took 11 days to correct it, in breach of the following COPE guidelines:

A. 8.1. Editors should take all reasonable steps to ensure the quality of the material they publish, recognising that journals and sections within journals will have different aims and standards.

12.1. Errors, inaccurate or misleading statements must be corrected promptly and with due prominence.

Response: Professors Armitage, Collins and colleagues [highlight notes on the manuscript tracking system from the Analysis editor](#) noting that the error was introduced in the revised article that was not peer reviewed. Although this note was made before publication of the Editorial, unfortunately the Editor-in-Chief did not appreciate this point in time to amend the editorial before publication, nor at the point at which she issued the press release and discussed the matter

with Professor Collins on the Today programme. This issue was corrected subsequently in less than two weeks, as soon as it was clear that it needed to be.

4. “Inappropriate use of Abramson to review the accompanying paper by Malhotra

This complaint concerns the delay in making the review of Malhotra paper available, when the reviews of the Abramson paper were made available much earlier.

- A. There is an implication that this was a deliberate delay due to reluctance on the part of the journal, and a disbelief in the description of a ‘technical problem’.

Response: When presenting peer review reports for articles, it is the journal’s preference to present the comments separate from the article. However, the peer review of the Malhotra article was provided as comments within a PDF, which could not be easily displayed. It was therefore necessary to prepare a version of his comments that could be seen in the context in which they were provided but read easily and reliably by users of The BMJ’s website. This is what is now provided as a Data Supplement to the article at http://www.bmj.com/content/bmj/suppl/2014/07/07/bmj.f6340.DC1/See_peer_review_for_this_article.pdf. As this is a non-standard presentation it took us some time. We reject the suggestion that we were deliberately delaying posting of the reports.

- B. The complaint is that use of Abramson to review Malhotra’s article is in breach of the following COPE guidelines:

7.1 Editors should strive to ensure that peer review at their journal is fair, unbiased and timely.

Response: While it is not ideal with hindsight to have had Abramson review the article by Malhotra, it is not unusual to have two authors of related articles review each others work. In the light of our critical event audit we are making every effort to ensure that in future in such cases we seek a wider range of opinions; [see the document detailing our audit.](#)

Best practice for editors {Described by COPE as “more aspirational and [were] developed in response to requests from editors for guidance} **would include: ensuring that appropriate reviewers are selected for submissions (i.e. individuals who are able to judge the work and are free from disqualifying competing interests)**

Response: As above, we would agree that best practice would include avoiding such reviewer-author pairs.

5. “Questionable independence of The BMJ’s review of published errors

- A. We see the essence of this complaint as being that the Heath panel wasn’t in fact independent of the journal, and that its Terms of Reference come from the Editor. **Response:** We appreciate the concern that the panel was not entirely independent of all connections with the journal. We would note, however, that there is no guidance or best practice on appointing such a panel, as it is an unprecedented move. Our aim in appointing the panel was to have it act in lieu of an ombudsman. The panel was given access to all information and asked to evaluate all issues. It acted completely independent of input from the editorial team, and reached its own conclusions.

- B. That the panel was not sufficiently rigorous in considering the harm caused.
Response: In our view the panel was extremely rigorous. In fact, the independent retractionwatch website noted [“This is the most detailed justification for a journal’s decision not to retract a paper that we’ve seen in a long time, perhaps ever.”](#) But the panel was not tasked with considering whether or not statins should be prescribed and for whom.
- C. That the panel members are biased on the issues at hand and members did not declare all relevant papers and COIs, related to litigation and to collaboration with Abramson.
- a. an undeclared paper by the chair (Heath) claiming statins cause cancer in the elderly. **Response:** We read this paper differently, as saying people on statins don’t die of cardiovascular events but do die of cancers, suggesting that there is little life-saving effect of statins, but not that the statins are a cause of cancer. It says ““The most likely reason [for the observed phenomenon] is substitution of cause of death.”
 - b. A paper by panel member Hippisley-Cox on statins and their side-effects (about cataracts, inter alia) is not specifically declared.
Response: This article is, we believe, declared in the [panel’s materials](#), thus: “In 2010 we published an observational study in the BMJ to quantify unintended effects of statins which is referenced in the Abramson paper⁸” - 8. Hippisley-Cox J, Coupland C. Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database. BMJ 2010;340:c2197.
 - c. Two other undeclared papers by a panel member that made similar claims about the efficacy of statins to those made in the Abramson paper.
Response: This concerns articles by panel member Furberg, who conflicts of interest declaration states “Publication of a large number of studies of statin and other lipid studies” but does not enumerate them.
 - d. Undeclared litigation work by panel member Furberg.
Response: *Professor Furberg declares that he has done no litigation work in the past decade related to the safety statins. Professor Furberg also asked the journal to note that he has been a co-author and collaborator with the Oxford group on multiple articles in the past 7 years, and might therefore be expected to be biased in their favour, but he aims for balance.*
 - e. This is in breach of COPE guidelines:
17.1 Editors should have systems for managing their own conflicts of interest as well as those of their staff, authors, reviewers and editorial board members
Response: *The BMJ* does indeed have such systems, and declares conflicts of interest for staff (listed for [editors](#) on their profile pages), authors (on each paper), reviewers (on each review) and editorial board members (listed for [board members](#) on their profile pages) .
17.2. Journals should have a declared process for handling submissions from the editors, employees or members of the editorial board to ensure unbiased review
Response: *The BMJ* does indeed have such systems, and if we have missed any we will correct them (please see below). But we are unsure of the relevance of this guideline in the context of the panel.

6. “BMJ links to public statements in support of its own position”

- A. The timeline published with the panel’s report links to a [supporting letter with 500 signatories](#) without pointing out that journalist Jeanne Lenzer coordinated it and we pay her for some work.

Response: The Editor was not aware of Lenzer’s role in coordinating the letter and certainly did not commission or pay her to do so. Lenzer was at the time a freelance journalist known to do some work for the BMJ and declares that she helped coordinate the open letter after she was approached by a group of concerned physicians.

- B. That Lenzer had attempted to publish this letter elsewhere without declaring that she sometimes works for The BMJ.

Response: As noted above, Lenzer was not acting for the journal in this regard.

- C. That Lenzer published a 2013 paper listing Abramson as a collaborator and with a member of the panel as a co-author.

Response: As Lenzer was not involved in the work of the panel, her work with a panel member and with Abramson does not appear to be relevant. Her co-author was panel member Furberg. As noted above (point 5Cc) his conflicts of interest declaration states “Publication of a large number of studies of statin and other lipid studies” but does not enumerate them in detail. However, our understanding is that in fact Furberg had no interaction with Abramson in his role as an external reviewer of this paper.

- D. This is in breach of COPE guidelines:

17.1 Editors should have systems for managing their own conflicts of interest as well as those of their staff, authors, reviewers and editorial board members

Response: This issue is primarily addressed above (point 5Cd). We note that as panel member Furberg is a member of The BMJ’s editorial advisory board, he has a [generic conflicts of interest statement](#) in addition to the one prepared specifically for the Heath panel.

17.2. Journals should have a declared process for handling submissions from the editors, employees or members of the editorial board to ensure unbiased review

Response: As noted above we do have such systems but are unsure of the relevance here, as the Lenzer submission reported by Professors Armitage, Collins and colleagues was not submitted to *The BMJ*.

7. “Inaccurate statements about materials posted with the review panel report

Both the panel report and the accompanying editorial say that all relevant material is published, but it is not.

- A. A submission to the panel about a letter by Malhotra and others to NICE was not posted.

Response: As we understand it, Professor Collins wrote privately to the panel to ask about this issue and the panel declined to respond in private, preferring to discuss all these issues openly. Now that this matter is being made public, the panel have advised the journal that they did not consider the letter to NICE and Professor Collins complaint about it relevant to their work.

- B. The claim to have redacted things for legal reasons is untenable - and one piece of redacted claim is reiterated.

Response: The journal takes legal advice when it believes content might be

defamatory or otherwise in breach of good practice. It did so on this occasion, and redacted those parts of statements that were highlighted by counsel as problematic. We continue to decline to publish this statement on legal advice.

C. This is in breach of COPE guidelines:

14.1. Editors should encourage and be willing to consider cogent criticisms of work published in their journal.

Response: We believe we have shown the journal to be very willing to consider and respond to cogent criticisms. We do, however, also have to take legal advice and respond to it.

15.1 Editors should respond promptly to complaints and should ensure there is a way for dissatisfied complainants to take complaints further. This mechanism should be made clear in the journal and should include information on how to refer unresolved matters to COPE.

Response: The journal has responded promptly and on numerous occasions to these complaints. We also make plain how to take matters further, and note that this complaint is via COPE.

17.1 Editors should have systems for managing their own conflicts of interest as well as those of their staff, authors, reviewers and editorial board members.

Response: We believe we have responded on this point, above, and are unsure how it applies to this specific concern.

4. Letter from John Abramson and colleagues, in response to the letter of complaint from Armitage *et al*, sent to *The BMJ* 20 March 2015 and included with the response to COPE, 11 May 2015

We would like to thank Prof. Collins *et al* for the opportunity to respond to their ethics complaint regarding our BMJ article of October 2014.¹ First Prof. Collins *et al* state that in the section of our paper titled "Myopathy," we "misleadingly compared" the rates of myopathy (as defined by CTT) to the rates of musculoskeletal symptoms reported in the NHANES observational study, "which did not assess myopathy" and which "had no 'blinded' comparator group." Second, Prof. Collins *et al* raise concern about our having failed to respond to an "error" in our original manuscript that had been pointed out by a peer reviewer: that the frequency of musculoskeletal symptoms reported in the manuscript was "misleading" because only musculoskeletal symptoms among statin users were ascertained, without taking into account the fact that "muscle pain is incredibly common in the general population." And finally, Prof. Collins *et al* state that in response to Cochrane Collaboration statin trial reviewers' Rapid Response, which expressed concern about our use of the term "myopathy," the BMJ allowed us "to repeat our misleading claim."

None of these statements about the article as published in the BMJ or our response to the Cochrane Collaboration statin trial reviewers is correct.

¹ Abramson J, Rosenberg H, Jewell N, Wright JM, Should people at low risk of cardiovascular disease take a statin? *BMJ* 2013;347:f6123 doi: 10.1136/bmj.f6123 (Published 22 October 2013, Correction May 15, 2014)

Addressing the first issue, Prof Collins et al wrote in their complaint that, under the heading of “Myopathy,” we had “misleadingly compared” the rate of statin-associated myopathy reported in the CTT meta-analyses “(i.e. a severe muscle problem with a specific definition)” to the rate of more common statin-associated musculoskeletal symptoms based on the NHANES survey as reported by Buettner et al² “(which did not assess myopathy)”.

Notwithstanding the opinion of Prof. Collins et al about what the definition of myopathy should be, there is not one universally accepted definition. We relied upon the approach taken by Fernandez et al in the *Cleveland Clinic Journal of Medicine*, titled “Statin myopathy: A common dilemma not reflected in clinical trials,”³ cited as footnote 11 in our Rapid Response of 20 December 2013. This article acknowledges that “little consensus exists on how to define the adverse muscle effects of statins, which may contribute to the under-diagnosis of this complication.” The authors define three categories of statin-induced myopathy: myalgia (muscle symptoms without elevation of CK enzyme), myositis (elevated CK with or without muscle symptoms), and rhabdomyolysis (muscle symptoms with CK level ≥ 10 times the upper limit of normal). These authors’ broad definition of myopathy is clear in the following excerpt:

Another reason [statin-induced myopathy is so uncommon in clinical trials] is that these trials were designed to assess the efficacy of statins and were not sensitive to adverse effects like muscle pain. When they looked at myopathy, they focused on rhabdomyolysis—the most severe form—rather than on myalgia, fatigue, or other minor muscle complaints.

This broader definition of “myopathy” is consistent with that presented in the 2002 American College of Cardiology/American Heart Association/National Heart, Lung, and Blood’s “Clinical Advisory on the Use and Safety of Statins.”⁴ Focusing specifically on the use of the term “myopathy,” this document states that because the terminology describing muscle toxicity was inconsistent, it would provide more specific definitions. “Myopathy” was then defined as “a general term referring to any disease of muscles.” Under the general heading of myopathy, the document identified three subcategories of muscle problems:

- Myalgia—muscle ache or weakness without creatine kinase (CK) elevation.
- Myositis—muscle symptoms with increased CK levels.
- Rhabdomyolysis—muscle symptoms with marked CK elevation (typically substantially greater than 10 times the upper limit of normal [ULN]) and with creatinine elevation (usually with brown urine and urinary myoglobin).

The Canadian Working Group on statin adverse events and intolerance also chose to adopt the broad definition of myopathy as a collective term encompassing all forms muscle disease:⁵

² Buettner C, Davis RB, Leveille SB, et al, Prevalence of Musculoskeletal Pain and Statin Use, *J Gen Intern Med*, 2008; 23:1182–6

³ Fernandez G, Spatz ES, Jablecki C, Phillips PS, Statin myopathy: A common dilemma not reflected in clinical trials, *Cleveland Clinic Journal of Medicine*, 2011;78:393-403

⁴ Pasternak RC, Smith SC, Bairey-Merz CN, et al., ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins, *Circulation* 2002;106:1024-1028.

⁵ Mancini GBJM, Baker S, Bergeron J, et al., Diagnosis, Prevention, and Management of Statin Adverse Effects and Intolerance: Proceedings of a Canadian Working Group Consensus Conference, *Canadian Journal of Cardiology*, 2011; 27: 635–662.

The term does not necessarily connote symptoms or any degree of CK elevation. For example, several myopathies may present with normal CK levels, including steroid myopathy, critical-illness myopathy, pediatric dermatomyositis, myotonic dystrophy type 2, and the periodic paralyses. Indeed, biopsy evidence suggests that even some statin induced myopathic changes may be present in the context of normal CK levels.

On the other hand, the CTT as well as the National Lipid Association and the FDA, have chosen to define myopathy as having muscle symptoms *and* CK levels > 10 times the upper limit of normal. This measure of a statin-induced muscle problem is limited to significant muscle inflammation, a small subset of the broader category of statin-related muscle problems. Which of the two definitions is most relevant is a matter of opinion, but use of one definition or the other is neither factually wrong nor misleading.

The external panel appointed by The BMJ to determine whether retraction of our article was warranted, wrote this about our use of term “myopathy”:

The panel thought that including three different definitions of muscle problems, widely ranging in severity, all under a heading of the more serious myopathy, might lead to the reader to conflate these. However, as Abramson et al point out in their submission to the panel (SP23), myopathy and myalgia can be conflated in the opposite direction by referring to severe problems as if they included milder ones and this can also lead to misinterpretation.

The frivolous nature of the ethics complaint by Prof. Collins et al about our reporting multiple types of statin-related muscle symptoms under the single heading of “Myopathy” is made clear in Prof. Collins’ citation of a 2014 article in his request for retraction of our BMJ article.⁶

These carefully conducted randomised trials and meta-analyses of trials (along with meta-analyses of relevant observational studies; for example, Macedo et al; BMC Medicine 2014)...

Four out of five of the authors of the article by Macedo et al are members of the Cochrane Heart Group.⁷ Under the heading titled “Myopathy,” this article includes multiple definitions of muscle problems associated with statin use: an increased odds ratio of myopathy with no definition, a significant decrease in grip strength associated with statin therapy in both men and women,⁸ CTT’s finding of increased risk of myopathy (without definition), and the results of an observational study showing that the prevalence rate of any myopathic event (which used the ACC/AHA/NHLBI definition described above⁹) associated with statin initiation is approximately 250 such events per 10,000 person years. Although

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<http://journals.bmj.com/site/bmj/statins/SP15%20Note%20from%20Rory%20Collins%20for%20the%20panel%20considering%20the%20retraction%20of%20Abramson%20and%20Malhotra%20papers.pdf> Accessed April 12, 2015

⁷ Unintended effects of statins from observational studies in the general population: systematic review and meta-analysis, *BMC Medicine*, 2014;12:51. <http://www.biomedcentral.com/1741-7015/12/51> Accessed April 12, 2015.

⁸ Ashfield TA, Syddall HE, Martin HJ, et al, Grip strength and cardiovascular drug use in older people: findings from the Hertfordshire Cohort Study. *Age Ageing* 2010, 39:185–191.

⁹ Nichols GA, Koro CE: Does statin therapy initiation increase the risk for myopathy? An observational study of 32,225 diabetic and nondiabetic patients. *Clin Ther*, 2007, 29:1761–1770.

not stated in the article by Macedo et al, 95% of the myopathic events reported in this last study were either myalgia or myositis,¹⁰ not meeting the CTT's criteria for myopathy.

In retrospect, had we stated explicitly that we were using the broader definition in the "Myopathy" section of our paper, this confusion would have been avoided. But our comparison of the rates of myopathy as defined by CTT (symptoms plus CK levels > 10 times normal) to the absolute increase in the number of statin-users vs. non-users experiencing musculoskeletal symptoms would not have changed. However, it should be noted that neither the 2012 nor 2015 CTT meta-analyses state that their definition of "myopathy" is limited to people with muscle symptoms plus enzyme elevations (this definition is relegated to a footnote). Although we think the CTT's approach minimizes the frequency with which people treated with statins experience muscle symptoms, we do not feel that this warrants a letter of complaint about the Lancet's CTT publications to the Committee on Publication Ethics.

Addressing the second issue, Prof Collins et al state that we failed to respond to a peer reviewer's comment that the results from the NHANES study in our manuscript were misleading because (in essence) we presented uncontrolled data on the rate of musculoskeletal symptoms reported by statin users in the NHANES survey. Had this data been uncontrolled, Prof. Collins et al would have been correct that it was meaningless because musculoskeletal symptoms are so common in the general population. However, in order to determine the "muscle effects" of statins, Buettner et al¹¹ used the NHANES database to compare the prevalence of any musculoskeletal pain in statin users and non-users among a sample of 3,580 adults ≥ 40 years of age.

In response to the peer reviewer's comment, we wrote to BMJ editors:

The NHANES data [were] not simply the incidence of muscle pain in statin-takers, but the difference in prevalence of muscle pain between statin takers and non-statin takers, so this should be an accurate reflection of the effect [of] statins on the prevalence of muscle pain. This was clarified in the updated manuscript.

Based on the reviewer's comment, we revised the language in the published article to clarify that the NHANES data did not simply reflect the background incidence of muscle pain in statin users, but rather the authors compared the prevalence of muscle symptoms in statin users and non-users.

Finally, the ethics complaint by Prof. Collins' et al states that when Cochrane Collaboration statin trial reviewers pointed out our "error" conflating myopathy (per the definition adopted by CTT) with the broader category of statin-related muscle problems (described above) in Rapid Response letters, "the BMJ allowed Abramson et al to repeat their misleading claim instead of correcting it."

The Cochrane reviewers letter stated:¹²

They also conflate muscle pain (myalgias), an important side effect of statins, with myopathy, a rare and more serious problem, both of which warrant ongoing study.

¹⁰ *Ibid.*

¹¹ Buettner et al, *op.cit.*

¹² *BMJ* 2014;348:g1520

We responded:¹³

This is a semantic criticism, with which we disagree. From a practical point of view, statin induced myopathy includes: myalgia (muscle symptoms without raised creatine kinase), myositis (raised creatine kinase, with or without muscle symptoms), and rhabdomyolysis (creatinine kinase >10 times the upper limit of normal).¹⁴ Furthermore, histopathological findings of myopathy occur in patients with or without muscle symptoms and normal creatine kinase levels.^{15 16 17}

Ironically, two of the three Cochrane reviewers who submitted the Rapid Response in question were co-authors on the paper by Macedo et al, whose section titled “Myopathy” didn’t only conflate myalgias with myopathy, but also failed to inform readers which definition pertained to which findings.

The external panel appointed to adjudicate Prof. Collins’ request for retraction of our BMJ article did not find fault with either the editors’ selection of Rapid Responses sent to us, or with our replies:

Rapid responses

Assessment

The journal received several rapid responses that raised substantive criticisms and discussion of the Analysis article. The editors’ selections of rapid response letters that were directed to John Abramson for further response and discussion were appropriate. Editors’ decision-making about those selections and their follow-up was executed in a timely manner. John Abramson and colleagues responded to the selected letters promptly.

In conclusion, we do believe there is an important ethical issue raised by our article and The BMJ’s editorial decisions related to our article. The unrelenting harassment we have been subjected to by Prof. Collins—in the media, in the demand for retraction of our paper that was unanimously rejected by the external panel (with Prof. Collins having been unwilling to make public the concerns he expressed to The BMJ about our paper prior to the panel’s decision), and now through a letter of complaint to the Committee on Publication Ethics about The BMJ’s handling of our article—is creating an atmosphere in which responsible scientific discourse is being strongly discouraged. Specifically, these ongoing tactics are inimical to improving our understanding of the benefits and risks of statins. If this process is allowed to continue or be repeated, a great disservice will be done to the public.

John Abramson, Harriet Rosenberg, Nicholas Jewell, J M Wright

(John Abramson and Nicholas Jewell serve as experts in litigation, including cases involving statins)

¹³ *BMJ* 2014;348:g1523

¹⁴ Fernandez G, Spatz ES, Jablecki C, Phillips PS, Statin myopathy: A common dilemma not reflected in clinical trials, *Cleveland Clinic Journal of Medicine*, 2011;78:393403

¹⁵ Draeger A, Monastyrskaya K, Mohaupt M, et al, Statin therapy induces ultrastructural damage in skeletal muscle in patients without myalgia, *Journal of Pathology*, 2006; 210: 94–102.

¹⁶ Association between statin-associated myopathy and skeletal muscle damage, *Canadian Medical Association Journal*, 2009;181(12):E11E18.

¹⁷ Phillips PS, Haas RH, Bannykh S, et al, Statin Associated Myopathy with Normal Creatinine Kinase Levels, *Annals of Internal Medicine*, 2002;137:581585

5. Response to COPE from Tim Brooks, CEO of BMJ sent to The BMJ 4 May 2015 and included with the response to COPE, 11 May 2015

In its response to a complaint from Professor Sir Rory Collins, the Committee on Publication Ethics (COPE) invited both *The BMJ's* editor Dr Fiona Godlee and 'the publisher' to respond. After discussion we determined that the 'publisher' response was probably best coming from me. Dr Godlee reports to me, and as CEO I have a fiduciary responsibility to the board of BMJ, as well as to our owner, the British Medical Association (BMA).

(It should be noted that – as stated every week in *The BMJ* - the BMA cedes complete editorial independence to the Editor-in-Chief. The Association's assurance of quality control stems from BMA Council's sole authority to appoint and remove the Editor-in-Chief).

The issue is whether taking statins is on balance a good thing or a bad thing for people who are at lower risk of heart disease. (There is little if any dispute that statins are good for people at elevated risk). Prof Collins believes they are a good thing. Others – including John Abramson, the author of the original piece that triggered Prof Collins's complaint – don't agree. The issue is important, because the work of Prof Collins's unit, the Clinical Trial Service Unit at Oxford University, and others has directly informed new UK and US guidelines that greatly extend the universe of adults for whom statins are recommended as routine medication.

Professor Collins's original complaint to *The BMJ*, in October 2013, has proliferated and ramified through correspondence and investigation such that the files are centimeters thick. It would take the kind of obsessive who read the entire report of the Warren Commission into Kennedy's assassination, to plough through it all.

Also published here – and slightly more digestible – are the journal's responses to the points raised by Professor Collins in his complaint to COPE and by COPE in its response to Collins. As 'publisher', I am going to stand back from the detail and make some fairly basic observations.

The BMJ made some mistakes in the editing process as a result of which author errors, relating to statistics about reported side effects from statins were not picked up. *The BMJ* and the authors of the two articles concerned have corrected them. As with all organisations committed to self-improvement, *The BMJ* has sought to learn from those mistakes and tighten or create procedures to avert their recurrence. I am satisfied it has done so, and thus has benefited from this episode. This does not mean the journal will not make mistakes in the future. It is edited by humans. What is important is how you deal with the mistakes you make. To be clear: The BMJ has done nothing wrong in publishing these papers as part of a scientific debate. The panel found that the error did not compromise the principal arguments made in either of them.

From the outset, Dr Godlee has invited Prof Collins to state his views in writing in *The BMJ*. He has yet to do so: despite stating it at great length, in a series of letters marked 'not for publication'. Rather than take up this invitation, in fact, he had recourse to *The Guardian*, in March last year, to attack *The BMJ* for publishing the original pieces.

As a result of the article in *The Guardian*, the BBC's Today programme followed up the story, on March 22nd last year, with a live interview of both parties. In this interview, Prof Collins said that when he first complained to Dr Godlee, she 'fobbed me off'. I reproduce here that first email exchange, so that you can judge for yourself whether this is right. Note that Dr Godlee's reply was made on the very same day that she received the initial complaint:

On 30 Oct 2013, at 05:34 pm, Rory Collins wrote: Dear Fiona It seems that you and the BMJ have decided to take a stand against the widespread use of statins to protect people from suffering heart attacks and strokes. I can guess at some of the reasons, but I would very much welcome an opportunity to discuss this with you since I do think that there is a danger that mis-representation of the evidence in the BMJ could cause a lot of harm, which I know is not your intention. Might it be possible for me to drop by your offices sometime soon when I am in London to discuss my concerns — as well as, of course, yours? Best wishes,

On 30 Oct 2013, at 18:27, Fiona Godlee wrote: Dear Rory. Very happy to meet. Julia will be able to suggest some dates. As for the BMJ's position on statins, I don't think we have one. The article by Abrahams [*sic*] and co was submitted and peer reviewed and published in the usual way. I guess they might have chosen the journal because of our too much medicine campaign. If there is anything factually incorrect or misleading in it, I would urge you to send a rapid response which we would almost certainly want to publish as a letter. In fact I do hope you will do this anyway as readers will want to know what members of the CTT collaboration make of these authors' analysis. If you have any difficulties submitting a rapid response, our letters editor Sharon Davies can help and is copied in. All best wishes, Fiona

Prof Collins insisted that correction of editing errors was insufficient, and that the only remedy was for *The BMJ* to retract the offending articles. Retraction of papers in a scientific journal, as many readers will understand, is a very rare event. Normally it occurs only if the underlying research is shown to be entirely unreliable, either as a result of fraud or profound error, or if the research reported is unethical or plagiarised. . Otherwise scientific publishing relies upon the process of publication and counter-publication to drive thinking forward in the area under inquiry.

Dr Godlee – determined throughout this process to ensure that right was done to all concerned, including of course the original, complained-of authors – took the unprecedented step of establishing an independent panel of experts to assess Prof Collins's complaint and to judge whether indeed the original articles should be retracted. She undertook in advance to abide by their decisions. – and has done so.

In his own submission to that panel, [Prof Collins wrote](#) that Abramson and the other authors concerned seemed to have a 'deliberate intent to mislead the medical profession and the public despite the potential for harm to patients': an astonishing allegation. The panel concluded that there was nothing in the articles to suggest the authors acted malevolently or fraudulently.

Prof Collins's response to the establishment of this panel was to speak to *The Guardian* again. He dismissed the idea that the panel was independent, and called for the General Medical Council or the Department of Health to investigate instead. The panel, for the

record, included, among others, the Senior Deputy Editor of the *Annals of Internal Medicine*, (one of *The BMJ*'s main competitors), a professor of cardiology and of public health at Yale; and a professor of pharmacoepidemiology at the London School of Hygiene and Tropical Medicine. By accusing *The BMJ* of investigating itself, Prof Collins appeared to characterise the panel members as Dr Godlee's poodles. I don't know what they made of that.

The panel reported that it had no contact with *The BMJ* about its deliberations. The panel's findings were published in full by *The BMJ*, along with all the accompanying documentation, and all of that can be found [online](#). The panel made a number of recommendations to the journal for improving procedures, but *unanimously* rejected Collins's view that the articles should be retracted, and noted with concern that he did not use the pages of the journal, as repeatedly offered, to make his counter-arguments.

RetractionWatch – an independent website/pressure group which works to keep scientific publishing honest – [commented](#) on the publication of the panel's work: 'This is the most detailed justification for a journal's decision not to retract a paper that we've seen in a long time, perhaps ever'.

Two further things I would like to note. In his submission to the panel, Collins detailed the grants received by his unit to fund research over the past 20 years (until one year ago) [*Editor's note: this refers to the time of writing, May 2015*]. Merck (which makes many hundreds of millions of dollars every year from cholesterol-lowering drugs) has funded the Unit's work to the tune of £179,700,000 over the past 20 years. The next biggest funder has been Schering-Plough – which was acquired by Merck in 2009 – at £40m. That combined total is equivalent to a run rate of £900,000 per month every month for 20 years; in today's money that amount is almost certainly more than £1m per month, on average. After Merck/Schering, the next biggest funder in Collins's declaration was the Medical Research Council at £13,700,000 over the 20-year period. That money does not of course go into Prof Collins's pocket: it is to fund the research; but he is right to declare such funding as a potential conflict of interest.

Trials included in the Cholesterol Treatment Trialist's Collaboration (CTTC) were, as Abramson noted, funded by statin manufacturers (a fact acknowledged by Prof Collins and the CTTC). Abramson for his part correctly declared as conflict of interest that he and one of his co-authors serve as experts for plaintiff's lawyers in drug industry litigation (including statins).

Abramson, author of the original article that triggered the complaint, is a lecturer in health policy at Harvard Medical School; somebody whose views on mass medication in principle merit respect just as Prof Collins views do. The possibility for differing views on this, as on every scientific subject, was exemplified by a [letter to *The BMJ*](#) from Klim McPherson, Visiting Professor of Public Health Epidemiology at Oxford University – in other words a colleague of Prof Collins. He described the NICE guidance on statins, which is based directly on Prof Collins's work, as 'foolhardy'. He subsequently told a *BMJ* journalist 'It is quite obvious to me that muscular myopathy is much more common than Rory [Collins] believes and that it's quite disabling'. [[BMJ 2014;349:g5007](#)].

I have no idea whether Collins or McPherson is closer to the truth on this point. The truth in science – as in every field of human enquiry - is generally speaking beyond our

grasp. We advance towards it haltingly, through debate and discussion, through trial and – yes – error, enduring reverses and encountering blind alleys, as we ascend towards this summit of righteous knowledge; only to discover that the ascent is of a convex slope, and what we thought of as the peak, is merely a foothill on the journey. As Voltaire said: ‘Doubt is not a pleasant state; but certainty is a ridiculous one’.

The BMJ, through this process of patiently and openly dealing with Prof Collins’s complaints, has opened up its internal workings to a degree that is possibly unmatched, and certainly not exceeded, by any other scientific journal. This has made it a better journal. I am proud of the work of Dr Godlee and her team, and I stand by that work, and by them. I trust that this is the end of this matter – although not, of course, the end of the debate on the role of statins in prescribing habits.

6. Email correspondence between Fiona Godlee and Liam Smeeth, May 2014

On 11 May 2014, at 18:18, Fiona Godlee <fgodlee@bmj.com> wrote:

Many thanks Liam. I will strengthen the comment about the uncontrolled nature of the data and the equal rates in active and placebo arms in the RCTs. I sent the text of the correction to Zhang et al, and they have come back saying they are happy with the interpretation placed on their data in the correction, so I propose to leave the 9% figure as it stands. Many thanks again for your help. Best wishes, Fi

On 9 May 2014, at 17:05, Liam Smeeth <Liam.Smeeth@lshtm.ac.uk> wrote:

Dear Fiona

two comments.

1. While they have apologised, they have also undertaken a new misleading calculation to come up with a figure of 9%.

As I said in my referee's report:

In the randomised Heart Protection Study, almost one third of people in both arms (i.e. including the placebo arm) complained of muscle pain and the effect estimate was 0.99 (95% CI 0.95 to 1.03). Serious rhabdomyolysis was rare: 5 cases in the 10,269 allocated to simvastatin and 3 cases in the 10,267 allocated to placebo.

This means that in any observational study of statin use, a large number of people (likely to be something like one third) will get muscle pain that they would have got without statins. A varying proportion of this muscle pain (that is nothing to do with statins) will be blamed on statins, and a varying proportion of people will then stop their statins because of wrongly blaming them for muscle pain. Even if the 9% is the correct number, interpreting this as being the people who had side effects caused by statins is plainly wrong.

7. Email correspondence between Fiona Godlee and Alexander Turchin, co-author of Zhang et al , May 2014

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.

8. Second letter from Armitage, Collins et al to COPE, 10 June 2015

In a letter dated 10 June 2015 (not published here as we do not have the authors' permission) the complainants expressed the view that The BMJ's response to COPE was inadequate. They set out again the specific examples of "inappropriate editorial behaviour" and their view of the inadequacy of The BMJ's response in each case. They conclude by asking COPE to decide whether the BMJ had contravened its Code of Conduct and if so to rectify the situation, and they express the view that it should be up to COPE and not The BMJ to make its conclusion public along with any relevant material. The letter is signed by the same 12 people as the previous letter of complaint.

Nuffield Department of Population Health
Richard Doll Building
Old Road Campus
Headington
Oxford OX3 7LF

15 April 2016

Dear Professors Armitage, Baigent and Collins

We are writing in response to the concerns raised to the attention of COPE regarding the publications in the BMJ by Abramson and Malhotra. The concerns and the journal's response have been reviewed by three of the COPE Trustees. Trustees with a potential conflict of interest were not included in the decision-making process.

We would like to first of all reiterate COPE's remit and the scope of our review of this case (<http://publicationethics.org/contact-us#complaints>). COPE is a membership organization and not a regulatory authority; COPE membership by journals and publishers is voluntary.

COPE's goals are the education of our members and the promotion of a better understanding of publication ethics overall. We provide a number of resources to our members, one of these is the COPE Code of Conduct which also includes best practices as an aspirational guide on steps journals can take to enhance their workflows. COPE guidelines are just that and not mandates, failure to implement all of the goals outlined under the best practice guidelines does not in itself imply deviation from ethical publishing practices.

COPE does not complete regular audits of member journals to verify compliance with the Code of Conduct, however we do consider complaints against members and follow up on those as necessary. We encourage self-audit at journal level and have developed a self-audit tool which we make available to our members. This is intended to assist them in identifying aspects of their practices that may require improvement and to promote transparency in their processes.

In situations where concerns are identified about a journal's process, either through an internal audit or a complaint, the key consideration is to ensure the journal is able to address the original issue in a reasonable manner and implement any necessary procedural changes to prevent the situation arising again. The fact that an error or a procedural gap is identified does not demand sanctions, and as noted above COPE does not have regulatory powers.

Upon review of the information available, we understand that the BMJ completed a self-audit of their processes related to the peer review of the articles and the handling of the concerns raised upon publication. The journal took steps to correct the articles and implemented procedural changes to address issues identified through their internal audit.

We believe that the journal took extraordinary steps to follow up on the concerns raised by convening an independent panel, whose findings they have since reported publicly at <http://www.bmj.com/about-bmj/independent-statins-review-panel>.

We recognize that different journals will have different processes in place and differing resources available to follow up on concerns raised to their attention, and thus that some level of flexibility is necessary on how journals develop and implement practices to address ethical challenges they face. In light of this, the main principle for addressing such challenges is to be as transparent as possible; we consider that the BMJ acted as per this principle by posting information on their internal audit publicly.

COPE also has a Code of Conduct for publishers which indicates that publishers should foster editorial independence. The documentation supplied by the publisher supports that they acted in line with this expectation.

In consideration of the above and upon review of the information available, we believe that the BMJ acted appropriately by completing an internal investigation and audit to a high standard, and promoted transparency by making information on the process publicly available.

While we appreciate that our response will not fully satisfy your original request, we believe that the journal acted with due diligence and in line with the expectations under the COPE Code of Conduct. We appreciate that differences in opinion may remain that COPE is unable to resolve in the context of this review. It is clear there are differing opinions on the science, however, those differences are best resolved by open dialogue in the scientific literature.

Thank you for raising this matter to the attention of COPE and we apologize for the time it has taken to conclude this case.

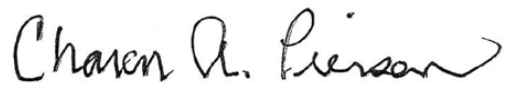
With best wishes,



Chris Graf, co-Vice-chair



Geri Pearson, co-Vice-chair



Charon Pierson, COPE Secretary