

Please see page 13 and 14 for the relevant highlighted text

## SP14 Statins: Timeline

Produced by Jane Smith 31 May 2014

*This has been produced by looking at records of the Abramson paper on the BMJ's manuscript tracking system; by examining email exchanges; and by asking questions of some BMJ editors*

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The date format is: DD.MM.YY

The timeline of the Abramson paper is in black, as is most of the post-publication timeline

The timeline of the Malhotra paper is in green

Correspondence with Rory Collins in blue

Comments by JS are in italics

{Statements in curly brackets are statements given by the people mentioned in response to questions about what happened}

Redactions (■■■■■■) are to remove the names of individuals who played no part in this story

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### 11 June 2013 BMJ.2013.013300

John Abramson et al submit article to BMJ (<http://www.bmj.com/content/347/bmj.f6123/related>). Triggered by the updated Cochrane review on the use of statins in people at low risk, which was updated in light of the Cholesterol Treatment Trialists' (CTT) meta-analysis (Collins et al). The updated review reverses the conclusion of previous Cochrane review, which said that statins were not warranted in people at low risk of cardiovascular disease (<5%).

Abramson et al argue that CTT's own data don't show benefit in low risk people and under estimate side effects – for which Abramson et al draw on other studies, including observational ones

Their conclusion is that doctors and patients should enter therapeutic partnership to decide what is best for them.

Authors request fast track

**13.6.13** BMJ Analysis editor reads and summarises the Abramson et al paper –raises queries and favours sending for external review but not fast track

**14.6.13** Associate editor 1 working on Analysis articles (former BMJ deputy editor) reads, agrees about external review, agrees not fast track though suggests handling swiftly, suspects any change in guidelines will be contentious

**27 June 2013** [NB. This isn't strictly speaking part of the story and I stumbled upon it by accident]

Aseem Malhotra, who is a regular columnist for BMJ, writes a BMJ article entitled "It's time to ban junk food on hospital premises." Almost as an aside he writes:

"How many clinicians are aware that adopting a Mediterranean diet after a heart attack is almost three times more powerful a lifesaving tool than taking a statin for life[ref] and far more acceptable to patients than taking a drug that can cause significant side effects in a fifth[ref to Zhang article]"

This statement prompted no comment in the journal's rapid responses]

*Abramson et al article sent for external peer review*

**27.6.13** Opinion from Liam Smeeth, professor of clinical epidemiology. Says it's interesting and well argued. Major concerns are:

1. Estimates from CTT data – not clear whether they had access to data – or how they estimated their figures

2. Results for myopathy are misleading – muscle pain is very common and trials show no difference between arms. Rhabdomyolysis is v rare
3. 10 fold difference in risk ratio for diabetes comparing CTT and JUPITER and observational studies – needs discussion

**1.8.13** Opinion from Wouter de Ruijter, senior researcher and epidemiologist.

Says it's an important and relevant issue.

The change by Cochrane reviewers is of pivotal importance – will impact guidelines – effects on health and costs

“Although obviously a one sided view they make a v reasonable case”

Get table reviewed by stat [This was not followed up]

He finds their conclusion appealing

**1.8.13** Editorial meeting considers Abramson et al paper.

Present: Analysis editor, Associate editor 1, Associate editor 2 (former neurologist and epidemiologist)

Associate editor 2 says: Important and authors make good case. But impossible for person not familiar with this to judge whether they have been fair in their assessment- Smeeth's review hints they may have overstated harms. “Still it probably doesn't matter too much. If they have got it wrong people can say so in the RRs”

Analysis editor: Wants things spelt out more. Say more about CTT and its rationale

No notes from Associate editor 1

Committee conclusion – initial vote- Y, Y, possibly. Decision Rej and Offer

Nearly a provisional accept – but want them to work harder – clarify facts

- Clarify topical peg
- Clarify who low risk people are
- Be confident of your claims and don't over claim
- Acknowledge your own weaknesses
- Why CTT needed- how do findings relate to the trials
- Suggested adding a timeline and a fact box for patients
- And take on board ref's comments

### **13 Sept 2013 REVISION BMJ.2013.015247**

Abramson et al's covering letter says they have done most things that they were asked to do in revising the article. They do not provide as requested a letter detailing how they have responded to all points

*Revision shows nearly all points covered – notably*

*-explains what CTT is/did*

*-clarified exact origin of table – derived from CTT (they also added statistician as an author)*

*-made more precise the numbers around hard CV endpoints – 140 NNT for 5 years (rather than 91-152)*

*-discussed difference between JUPITER and CTT in incidence of diabetes*

*-amended section on myopathy, clarifying what NHANES said and another randomised study.*

*Ignored point about Heart Protection study*

*-added fact box for patients*

*-added box on what guidelines recommend*

{Analysis editor said that she would have gone through the article to see how authors had responded to points – *that is usual practice*}

### 27.9.13

Aseem Malhotra emails BMJ's Features editor, offering "potentially game changing and much needed piece busting the myth of saturated fat and heart disease. He says there is a "strong evidence base for why all calories are not the same and I also briefly query statins in primary prevention and provide an explanation for why evidence is weak for benefit here."

It is nearly 1600 words – Features editor wonders could it be a feature?

### 27.9.13

Features editor emails BMJ deputy editor/Head of News and Views and says she thinks it is more like an Analysis article than a feature – or if shortened an Observations article

### 30.9.13

Aseem Malhotra emails Head of News and Views and tells him about the article and asks whether it could be published for 12 October issue –ahead of WHO announcement on sugar and because he'll be off work at that time in case press are interested

Head of News and Views speaks to Aseem Malhotra and tells him the article would probably be an Observations and asks him to cut the number of words

**3.10.13** Aseem Malhotra sends revised article – which he has cut to 1300 words. His email says he's confident it will be picked up widely by the press. The article includes "A recent "real world" study of 150,000 patients prescribed statins published in *Annals of Internal Medicine* revealed "unacceptable" side effects including myalgia, gastrointestinal upset, sleep and memory disturbance, and erectile dysfunction in 20% resulting in discontinuation of the drug.[Ref Zhang et al] [As subsequently recognised, the total population in Zhang et al was only 134,000-odd before exclusions, and the word unacceptable doesn't appear in the article]

**4.10.13** Head of News and Views emails Aseem Malhotra saying that he likes the article but hasn't yet done detailed work on it.

Head of News and Views had shown it to BMJ deputy editor/ Head of Research, to see whether she thought it was OK and liked it; she thought it OK and liked it, so he decided to have it peer reviewed. {Most Observations don't get peer reviewed but they do if they are heavily scientific or clinical}

**8.10.13** Head of News and Views sends Aseem Malhotra a shortened version of his article and says he wants to show it to Fiona Godlee, BMJ editor in chief, and get it peer reviewed.

**8.10.13** Head of News and Views asks ■■■■■ to review the Malhotra article. He explains that it is meant to be provocative but BMJ wants to check that it is sound

**9.10.13** Aseem Malhotra emails Head of News and Views giving a reference for a statement in the article about CHD trends and suggests rewording "there are an extra 3 million statin users but it is difficult to prove whether this has had any demonstrable impact." Or he wonders if it is better to remove the sentence altogether

Head of News and Views has difficulty finding other reviewers for the Malhotra article. He learns from Analysis editor about the Analysis article by Abramson et al. Analysis editor suggests asking John Abramson to look at the Malhotra article. They also decide to publish the two articles together – because they are on similar subjects

### 11.10.13

Head of News and Reviews asks John Abramson to look at the Malhotra article and asks for a quick review

■■■■■ says he's not the right person to review the paper, recommends ■■■■■

Head of News and Views asks ■■■■■ to review the Malhotra article

■■■■■ says of the Malhotra article: "This is important" but he can't review it until mid November.

John Abramson agrees to review the Malhotra article.

Analysis editor reads Abramson et al's revision and concludes that it is better though still has some overstatement.

She accepts it and passes it straight to Technical editor for technical editing because there are no accepted Analysis articles; she plans to tweak essentials later.

*[This is almost a month after the revised paper was sent back by the author]*

Analysis editor writes to John Abramson: "There are some minor revisions that need to be made, specifically a few areas where I think the message is a little too strong for the data presented." She adds questions to the manuscript for technical editor, to pass on to the authors at proof stage

### 15.10.13

Proof and queries sent to John Abramson

*Nearly all the questions are about getting more precision for a vague statement or asking for justification/evidence for a statement (<http://www.bmj.com/content/347/bmj.f6123/related>)*

### 16.10.13

John Abramson returns the proof with track changes

\*\*The editor's question on the proof, next to the claim that the net benefit-harm equation has zero overall benefit, is: "This claim seems a bit extreme from the evidence presented. What is the figure for harm". This prompts Abramson to add: "A retrospective cohort study found 18% of statin treated patients had discontinued treatment at least temporarily because of statin related adverse effects. Forty percent of the adverse events were related to musculoskeletal symptoms [Zhang et al]"

The box at the end is changed a lot and the statement "The side effects of statins are under-reported in clinical trials..." gets changed by the author to "The side effects of statins...occur in approximately 20% of people treated with statins."

Abramson leaves decision on what to say about CTT conflicts of interest to editors

Also Abramson asks for sentence about new anti-lipid agents to be reinstated.

Technical editor responds and says the changes are fine.

{Technical editor doesn't remember going back to the Analysis editor about any of the answers to the questions. The Analysis editor thinks she was consulted about one thing – she can't remember what but thinks it wasn't the Zhang statement. The Analysis editor said that if she had seen the returned manuscript she almost certainly would not have queried the Zhang statement: the author

had answered the question, quoted from a paper and given the reference; she would assume that the author had got it right.}

**16.10.13** Head of News and Views emails John Abramson to chase his review of the Malhotra article. He is targeting the 26 October issue of the journal

**17.10.13**

Aseem Malhotra (who has sent three emails since 8 October enquiring about the article) emails to say BBC Breakfast have asked him to appear to discuss myth busting of saturated fats on Wed 23 Oct – wanted press release of his article

BMJ's press officer asks for the current version of the Malhotra article so she can start work on press release

John Abramson sends his review of the Malhotra article in the form of comments in the Word document. He says there are important issues that can quickly be addressed. He makes eight comments – to which Aseem Malhotra responds on the same day as follows:

1. JA says that ref 5 says something different about saturated fat.

AM disputes that is the main conclusion of this reference and makes no change

2. JA asks for comment on National Dairy Council sponsorship of publications on beneficial effects of dairy products.

AM says mentioning this detracts from his message and makes no change

3. JA queries statement about no demonstrable effect of statins on heart disease trends – says that CHD rates have declined dramatically and that this should be acknowledged.

AM accepts comment and amends

4. JA suggests clarifying which group the NNT applies to.

AM amends to low risk group aged 60-70 is 345

6. JA says that treatment based on a pleiotropic effect is just one theory

AM makes no change

7. JA comments that a statement about NNT is more complicated.

AM says he's talking about mortality not recurrent heart attacks so adds "prognostic" to "82 will receive no prognostic benefit"

8. JA comments on sentence "The fact that no other cholesterol lowering drug has demonstrated mortality benefit supports ...that the benefits of statins are independent of its effects on cholesterol" that "This is a stretch" – weak and tangential argument

AM says he thinks this is just JA's opinion and makes no change

**18.10.13** Aseem Malhotra asks to see a proof of his article. He does so. The article is signed off.

**22.10.13 MALHOTRA ARTICLE PUBLISHED ONLINE (appears in print in 26 Oct issue)**

**22.10.13** ABRAMSON ARTICLE PUBLISHED (appears in print in 26 Oct issue)

**23.10.13** First rapid response (RR) to the Malhotra article corrects him about vitamin D (very little in UK milk)

Other RRs pursue their own views about fat, diet, etc

**24.10.14**

RR to Malhotra from Chris Lawson, GP lecturer, Queensland:

"The Zhang 2013 paper does not say what it is represented as saying in this article. There was not a 20% discontinuation rate. There was a 17% rate of statin-related events but only a 10%

discontinuation rate...for all causes, including "no longer necessary", "too expensive" and other non-ADR reasons. Only 12% of discontinuations explicitly for adverse reaction (the authors do note that reporting may have underestimated the ADR rate by a large factor, but they did not have positive evidence of this). Of those patients who discontinued statins, more than 90% were rechallenged and most went on to tolerate statin therapy long-term.

Even more dubiously, the author states that these figures are "massively at odds with the major statin trials that report significant side effects of myopathy or muscle pain in only one in 10 000." Since no reference was provided, I looked into it myself. The Astra-Zeneca product information for Crestor (rosuvastatin) reports that myalgia is common (i.e. 10% or more) and myopathy and rhabdomyolysis are rare, but occur at rates of 0.2-0.4%, much higher than the ~0.01% reported in this article. I haven't gone through every statin study, but I think it's clear that the article has massively misrepresented the evidence on this point.

The saturated fat hypothesis needs challenging, the effectiveness of statins as a large-population intervention needs challenging, and pharmaceutical company data needs challenging, but not like this." (<http://www.bmj.com/content/347/bmj.f6340/rr/668444>)

**25.10.13** The first few RRs to Abramson et al, mainly from GPs, are largely supportive of the position of Abramson et al in being sceptical of benefits from statins in low risk people – but most do not engage with the specifics of the article

**26.10.13** RR to Abramson et al by Amrit Takhar: "The authors quote Zhang's retrospective cohort study finding that 18% of statin treated patients had discontinued therapy (at least temporarily) because of statin related adverse events. However the results of the study also showed that 35% of those who discontinued due to statin adverse effects were rechallenged and the majority of these (92%) were still taking statins 12 months. This would imply the true figure for statin related adverse events is much lower than the 20% quoted in the key message."(<http://www.bmj.com/content/347/bmj.f6123/rr/668850>)

Several RRs to Malhotra, some critical, some supportive

**25.10.13** A critical detailed RR from Nathaniel Thompson-Moore  
(<http://www.bmj.com/content/347/bmj.f6340/rr/668782>)

**31.10.13** Letter from Public Health England reminding of official advice on saturated fats  
(<http://www.bmj.com/content/347/bmj.f6340/rr/669645>)

**31.10.13** A detailed critical RR from Jim Mann  
(<http://www.bmj.com/content/347/bmj.f6340/rr/669477>)

### **30.10.13**

Short email from Rory Collins to Fiona Godlee: saying BMJ seems to have taken a stand against statins – worries that there is a danger that misrepresentation of evidence could do harm and wanting to drop by to discuss.

**30.10.13** Fiona Godlee replies: says yes to chat and asks her PA to fix. Says there is no BMJ policy against statins but BMJ is concerned about overtreatment in general. Suggests RC writes RR

**7.11.13** BMJ letters editor emails John Abramson asking him whether a correction is necessary given Takhar's RR. She suggests he should clarify and reply in an RR to Takhar.

**8.11.13** **Letters editor** emails Aseem Malhotra, asking for a reply to some of the rapid responses to his article (those by Lichtenstein, Lim, Clifton, Tedstone, Mann) so that BMJ can publish his reply with them in the print journal letters section

**8.11.13** Aseem Malhotra replies and says he will respond to the RRs. He asks: “any reason that you've chosen 4 critical articles versus 1 supportive?”

**8.11.3** Letters editor justifies the selection of critical letters as “we like to hear both sides of a debate, of which you had put one side very eloquently”.

**8.11.13** Letters editor writes again to Aseem Malhotra asking him to respond to four other RRs that require clarification: Pearce, O’Sullivan, Goggins, and Lawson.

**12.11.13** Abramson replies to Letters editor “We have reviewed his concerns, our paper, and the paper by Zhang et al, and propose the response” attached {Letters editor posts the rapid response for him}

RR from John Abramson replies to Takhar: “First, as stated in the article by Zhang et al “The rate of reported statin-related events to statins was nearly 18%” in this retrospective cohort study. Second, the incidence of statin-related adverse events reported in the study is far more likely to be a floor rather than a ceiling. As noted in our article, spontaneous reporting of side effects is likely to underestimate the true incidence compared to rates determined prospectively by structured interview. Also, Zhang et al note, the incidence of side effects may have been under-reported because only the first reported statin-related event for each patient was included their analysis. From a clinician’s perspective, the most important response to Dr. Takhar’s concern is that the incidence of statin-related side effects reported by Zhang et al was, in fact, “approximately one fifth.” For low risk patients who do not derive an overall benefit from statin therapy, the finding that many of the patients who experienced statin-related side effects could tolerate statin therapy on rechallenge does not negate the fact they experienced a drug-related side effect while taking a drug that provides them with no net health benefit.”

**14.11.13** Aseem Malhotra sends an RR. He makes a series of assertions to back up his original claims, rather than engaging with the specific points made by critics (<http://www.bmj.com/content/347/bmj.f6340/rr/671980>)

**23.11.14** BMJ prints letters critical of Malhotra and his reply

**27.11.13**

RR to Abramson et al from the Cochrane reviewers, who dispute some of Abramson et al’s analyses (in particular the effect on all cause mortality), and point out that the US guidelines based on the Cochrane 2013 review – which came out three weeks after the Abramson et al article – also emphasise lifestyle choices (<http://www.bmj.com/content/347/bmj.f6123/rr/674751>)

**2.12.13** Rory Collins visits FG

FG follows up with email – explains BMJ has already commissioned a Clinical Review article [full review article] on statins, benefits and harms and invites RC to write an analysis countering Abramson’s article

She will discuss with colleagues how to respond to his concerns

**5.12.14** Aseem Malhotra asks Letters editor to remind him which RRs he needs to respond to. She sends him the list.

**6.12.13** Letters editor emails John Abramson asking him to respond to RR from the Cochrane authors’ (Huffman et al).

**9.12.13** John Abramson replies: to Letters editor and to Analysis editor “ We agree that the Cochrane authors have made substantial comments about our paper, to which readers deserve a response ASAP. We have two thoughts:

- We have asked Rita Redberg to join us in our response
- We believe that the issues of disagreement are becoming clarified, and propose that we work on an article in conjunction with the Cochrane authors to make a point/counterpoint table that will define the points of disagreement and allow readers to make independent evaluations of the arguments.”

**12.12.13** Letters editor emails Aseem Malhotra to chase his replies  
He replies to say he will do them as soon as possible.

{ Head of News and Views said that he chased Malhotra between December and March and then escalated to Fiona Godlee , whose intervention did produce a result- see March 2014}

**19.12.13** John Abramson sends his response to the Cochrane reviewers. He says it may deserve more than a letter.

**20.12.13** Analysis editor replies to John Abramson, thanking him for active engagement with criticisms of his paper. She will get back to him that day.

**20.12.13** Analysis editor writes to John Abramson explaining she has discussed the issue of something more substantial than a rapid response with Fiona Godlee. They think he should post a RR as soon as possible, but they agree it is worth highlighting to a wider readership. Analysis editor suggests that he consider a blog in the new year “ reflecting on your article and the response to it in a less formal way (for example what you made of how the article was received, timing and reaction to it etc). From this blog you could link back to your article, the criticisms of it and your detailed, academic reply. We are planning more coverage of statins and will have a think about how this might fit in.”

{The blog idea was dropped but the correspondence did end up in the print BMJ in the issue of 8 March – as letters but in the Observations slot because the letters were much longer than usual}

**20.12.13**

RR from Abramson et al responds in detail to Cochrane reviewers  
(<http://www.bmj.com/content/347/bmj.f6123/rr/678736>)

**8.1.14**

Another critical RR to Abramson et al from two US pharmacists  
(<http://www.bmj.com/content/347/bmj.f6123/rr/680686>)

**22.1.14 – 30.1.14**

Correspondence between Fiona Godlee and Rory Collins about another paper Collins had offered when he met Godlee in December – on Big Data – which BMJ turned down. Godlee explains why, offers to consider again, and also encourages him to send the article they had discussed on statins - “to present to readers the information you presented to me.” “Although your article would be a



response to the two articles....it would be helpful if you could. ..set your piece in the wider context of the evidence on the benefits and harms of statins.”

Rory Collins says he is working on the statins article.

**16.2.14** Letters editor asks John Abramson to reply to recent RR from Davies and Dietrich

**25.2.14**

Abramson et al respond in detail to Davies and Dietrich in an RR (<http://www.bmj.com/content/347/bmj.f6123/rr/687997>)

**8.3.14** Print BMJ contains the correspondence between Huffman et al and Abramson et al – but published in the Observations slot, not in Letters because they are too long for letters

**21.3.14** Fiona Godlee emails Aseem Malhotra, following a conversation on the phone. She thanks him for agreeing to respond to the four remaining critical RRs. She gives him until the end of the week to do so before the BMJ posts an editor’s note saying he was invited to respond and didn’t

**21.3.14** *Guardian* newspaper carries article on statins:

<http://www.theguardian.com/society/2014/mar/21/-sp-doctors-fears-over-statins-may-cost-lives-says-top-medical-researcher>

This quotes Rory Collins as saying that doctors who worry about the safety of statins are creating uncertainty that could cost lives and criticises BMJ over the Abramson et al and Malhotra articles – which are flawed and misleading.

John Abramson is quoted as saying that statins do not save lives in low risk groups and counters by saying that Collins is scaremongering and that he should release the patient level data. Malhotra similarly queries statins for low risk groups. Fiona Godlee is quoted as saying that the issues raised by the paper deserved public debate. She says that Collins’ comparison with the Wakefield paper and MMR is not correct: ““This is a debate that has been ongoing – the BMJ did not start it. Extending statins to healthy people at low risk is an enormously important decision which should be subject to debate and question.” Godlee is quoted as saying that she had already invited Collins to write an article for the BMJ.

**22.3.14** The *Today* programme [BBC Radio4 morning news and current affairs programme – one of BBC’s most popular radio shows and influential in setting political and other agendas] picks the story up and interviews Collins and Godlee. <http://www.bbc.co.uk/programmes/p01w27zp>

Collins says that the study referenced in the BMJ articles doesn’t say what the BMJ articles say it says. The study doesn’t mention that people who don’t take statins also have the side effects. He wants people to have an informed choice not misinformation.

Godlee says that she has invited Collins several times to write in the journal and engage with the articles. She agrees that the data were quoted from observational studies not RCTs – but often data on adverse effects comes from observational studies. RCTs are bad at reporting harms. For low risk people the balance of benefits and harms is different from that for high risk people.

Collins is asked why he hasn’t written something for publication. He says that he wrote to the editor and visited her and proposed that he write an article – “and that is what we are doing”. But [BMJ is] misleading the public. If people at elevated risk stop taking their statins or don’t take them they are at risk. He says that Dr Godlee doesn’t refer to the people who have side effects when not taking statins. Godlee then says that only Collins’ group has seen these data. Data should be shared.

**29.3.14** RR from Aseem Malhotra responds to critical RRs, citing more studies in support of his original arguments. He corrects the Zhang et al citation and concedes the point about low vitamin D in UK milk (<http://www.bmj.com/content/347/bmj.f6340/rr/692280>)

#### **31.3.14**

Rory Collins emails Fiona Godlee attaching a long letter marked not for publication (SP17). In it he complains that nothing has happened since he visited her and she said she would discuss with colleagues.

He refers to Godlee having had recent opportunity to retract the misleading claims publicly [*not sure what that refers to- perhaps the Today programme*]. And demands retraction of both articles

#### **1.4.14**

FG email Rory Collins– says sorry it has become polarised and personalised.

Points out that RR by Takhur makes similar points and that Abramson has responded. Says Malhotra has also posted a response to his article.

Says that 31 March letter was first time BMJ had received written details of Rory's complaint despite several invitations to send RR or article since first request 5 months ago.

Says that she's satisfied with the replies by Abramson et al for now – sees no need to retract the article, and asks permission to send Collins' letter to Abramson for him to respond to

#### **14.4.14**

Rory Collins emails Fiona Godlee, with a second attached letter marked not for publication (SP18): Says Abramson et al's response to the RR from Takhar doesn't settle the issue, it just repeats the error. Wants a retraction, makes comparison with Wakefield's Lancet article on MMR, wants to see peer reviewers' opinions, wants to know John Abramson and co-authors' Cols

**22.4.14** Fiona Godlee writes to John Abramson enclosing Rory Collins' letter [*presumably RC letter of 14.4.14*]. Says she will again ask Collins to send a letter for publication to which Abramson should respond. Asks if a correction is needed about the Zhang et al study. If not can he explain why not?

**22.4.14** Second email from Godlee to Abramson. Says , having looked more closely at Collins's complaint and the Zhang et al paper, she thinks Abramson's article is incorrect in that not all those 18% who reported statin related adverse events discontinued therapy as a result.

She wants to publish a correction to this effect. She notes that she thinks Collins is wrong in his letter about the definition of statin related events in Zhang et al's paper.

**23.4.14** Fiona Godlee emails Aseem Malhotra telling him that in response to complaint from Rory Collins BMJ proposes to publish a correction – enclosed.

**23.4.14** Aseem Malhotra to Fiona Godlee. Says the correction makes sense and he says he believes he has responded in greater detail already (links to his RR of 29.3.14)

**23.4.14** Fiona Godlee sends revised correction to Aseem Malhotra. She has looked again at Zhang et al and believes her first interpretation was wrong

#### **23.4.14 to 6.5.14**

Between 23.4.14 and 6.5.14 there are multiple email exchanges between Fiona Godlee and John Abramson over the correction, and also some between Godlee and Malhotra. Although the first draft of the correction was straightforward:-

"A retrospective cohort study found that nearly 18% of statin treated patients had a statin related event. The authors concluded that as many as 87% of these patients discontinued treatment at least temporarily as a result." -

the text of the correction becomes more complex as Godlee examines the Zhang paper ever more closely and teases out what it says. In response Abramson suggests some additions to make the correction more accurate/complete

During the interchanges Abramson makes the following points:

- His group is still keen to write on transparency in statin trials (23.4)
- Apologises for having bungled the Zhang text in his article (23.4)
- Says he respects RC's efforts to make sure Zhang et al is interpreted correctly but notes that RC doesn't challenge the primary point of the article – "our recalculation of CTT mortality rates to show there is no mortality benefit of statins for people with <20% 10 yr risk." He wants to add that the mortality calculations have not been challenged (24.4)

#### **23.4.14**

Fiona Godlee replies to Rory Collins' letter of 14.4.14– apologises for the delay, has been on holiday. "The authors of the two articles have defended their overall conclusions in relation to the rates of statin related adverse events. However I agree that their representations of the Zhang et al paper were not entirely accurate and I propose to publish corrections to both papers, the text of which is below. Please could you let me have any comments by close of play on Friday 25 April."

Says CoIs of Abramson and co-authors are given in the original paper – if RC wants more he should post a rapid response. In response to his earlier request to see the peer reviewers' comments, she will ask the peer reviewers' permission to post their reports on bmj.com.

She says there remains debate about benefits and harms of statins. Refers to Ben Goldacre's RR <http://www.bmj.com/content/348/bmj.g2151/rr/695338> and repeats request to RC to write something for publication

Asks for comments on corrections by 25 April

#### **25.4.14**

Rory Collins emails with a third attached letter marked not for publication (SP19)

#### **25.4.14**

Fiona Godlee replies by email, *clearly slight exasperated*, asks Collins again to send a RR. Says she'll get authors to respond, do a correction, write an editorial, press release it. Points out she asked him to do that back in October; if he won't says she'll write the RR based on what she thinks he's saying, ask authors to respond, write editorial, and press release it.

Requests that Collins either sends a RR or a note saying he won't by 1 May

#### **28.4.14**

Rory Collins emails a fourth attached letter to FG, marked not for publication (SP20). Says he didn't mean to exasperate her. Doesn't want to do RR because the side effects issue isn't for debate – it's an error of fact – still not correct. Offers to work with Godlee on correction but still wants article retracted.

#### 28.4.14

Fiona Godlee asks BMJ press officer, for press releases of the two original articles (Abramson and Malhotra). Press officer says that Abramson was not press released, only Malhotra. Press release of Malhotra didn't mention statins.

#### 1.5.14

Fiona Godlee replies to Rory Collins. Apologises for contributing to misunderstandings – she should have made it clearer she wanted something in writing to respond to. Understands why he doesn't want to put things in print. She has asked authors to withdraw their statement about the 18%. Says there is a dispute about the meaning of "statin-related event" – will ask Zhang et al to peer review the correction, and also get comments from the original peer reviewers of the Abramson et al article and others RC has suggested [in fact she only asks the two original reviewers and Zhang et al]. If that fails she offers to convene an independent panel to do the correction.

She proffers some advice to him too – that RC's position that statins have no side effects is extreme. She also will support calls for revealing of the clinical study reports – it would be good if he could support them too.

She also confirms that the two peer reviewers to Abramson have agreed to the posting of their signed reviews on [bmj.com](http://bmj.com); that there will be a correction to Malhotra too. "As an opinion piece this was read before publication by Abramson I think. I will check what record we have of this."

#### 8.5.14 Rory Collins visits Fiona Godlee

9.5.14 Fiona Godlee emails John Abramson and suggests that she and he talk. She wants him to withdraw the statement that side effects occur in 18% of people – which comes from Zhang but is stated as a fact without caveats about the uncontrolled nature of the study.

[No phone conversation took place]

9.5.14 Fiona Godlee sends proposed correction to Liam Smeeth and Wouter de Ruijter, the original reviewers of the Abramson et al article, and to Zhang and co-authors. She tells John Abramson that she has done so. She also tells Abramson that Rory Collins has renewed his calls for retraction on the grounds that people will continue to cite the article unless it is retracted, and that she intends to convene a panel to consider the matter.

9.5.14 John Abramson emails back, suggests replacing his original article with an amended one. He thinks it a gross restriction of academic debate to withdraw the re-analysis of the CTT data on mortality

#### 9.5.14

Liam Smeeth (peer reviewer) responds:

"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.

2. Their last lines:

"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."

are not needed. They are not part of the apology, and the figures themselves and the interpretation are at best debatable."

#### 9.5.14

John Abramson agrees with Fiona Godlee's latest version of the correction but asks for an additional paragraph:

"On the other hand, (notwithstanding the unresolved issue of potential lack of external validity of adverse event rates recorded in clinical trials discussed below), when compared to Clinical Study Reports, journal publications report only 21% of adverse events. [Wieseler B, Wolfram N, McGauran N, Kerekes MF, Vervolgyi V, et al. (2013) Completeness of Reporting of Patient-Relevant Clinical Trial Outcomes: Comparison of Unpublished Clinical Study Reports with Publicly Available Data. PLoS Med 10(10): e1001526. doi:10.1371/journal.pmed.1001526]"

He reiterates that the main point of the article – about the lack of benefit in terms of all cause mortality – has not been challenged.

**9.5.14** Fiona Godlee replies to John Abramson. Says that she has decided to convene a panel because she as editor has vested interest in not retracting the article. The panel "will include someone experienced in distinguishing between the need for correction and the need for retraction. And you, as well as Rory Collins, will be able to put your case. I will also ask that the panel's deliberations are transparent, which will mean that Rory's submission will be published along with yours"

#### 10.5.14

The Zhang et al authors respond, saying that they agree that the correction appropriately characterises their study

#### 10.5.14

Wouter de Ruijter responds and says the correction seems to be scientifically sound. He makes some minor (mainly) language suggestions, plus asks "18-20% [why 18-20% and not 18%, as is written in the Abramson article? I couldn't retrieve the 20% in this article?] of patients."

#### 11.5.14

Fiona Godlee thanks Liam Smeeth. "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.”

#### 11.5.14

Fiona Godlee emails John Abramson to say she has heard back from the peer reviewers and from Zhang et al, and she attaches the final version of the correction and the accompanying editor's note. She says she has incorporated his third caveat further down. Other minor changes are in response to peer reviewers' comments. Zhang et al said they were happy with the interpretation of their data.

#### 12.5.14

Fiona Godlee writes to Rory Collins

Thanks him for coming to see her last week. Sends him the proposed correction

Says she will also correct Malhotra article and link both corrections to other BMJ articles that have mentioned the two articles: Editor's choice and the Huffman-Abramson correspondence in Observations

Says she will write an editorial to highlight the corrections and issue a press release

Says she is setting up a panel to decide on retraction. "Iona Heath, former chair of our ethics committee, has agreed to chair the panel, which will comprise Harlan Krumholz (agreed), Julia Hippisley-Cox (agreed), ■■■■■■ (awaiting reply), Paul Wicks (agreed), and ■■■■■■ (awaiting reply)....Iona will be writing to you shortly to ask for your submission to the panel. All submissions will be placed in the public domain on [bmj.com](http://bmj.com).

#### 12.5.14 Email from Rory Collins to Fiona Godlee

Suggests trialists for the panel - ■■■■■■, ■■■■■■, ■■■■■■. Says final paragraph of online version of correction should be removed as "it was not the specific issue that was being raised about misrepresentation of evidence by them" [*The final paragraph was not removed*]

#### 12.5.14

Email from Fiona Godlee to Rory Collins. Says she is seeking methodologist and CVD expert.

■■■■■■ has declined as he believes he is too close to Collins.

#### 14.5.14

Rory Collins suggests ■■■■■■ for the panel

#### 14.5.14 BMJ press officer sends draft press release to John Abramson and Aseem Malhotra.

John Abramson comes back to suggest amending a sentence that implies that Abramson et al had generated the 18-20% figure from their own work rather than citing Zhang.

This is corrected.

#### 15.5.14 CORRECTIONS TO MALHOTRA AND ABRAMSON PUBLISHED

(<http://www.bmj.com/content/348/bmj.g3329>

<http://www.bmj.com/content/348/bmj.g3332>)

with accompanying

EDITORIAL from Fiona Godlee (<http://www.bmj.com/content/348/bmj.g3306>). Editorial says authors have withdrawn that statement but that Rory Collins is still seeking retraction. She as editor

has vested interest in not retracting so she has set up a panel of independent people who don't have a dog in the fight but are knowledgeable.

#### **15.5.14**

Rory Collins emails Fiona Godlee. Thanks her for meeting. Encloses his four letters plus a note explaining the error for the panel. Says he would welcome chance to comment on the panel's terms of reference (TOR). "The TOR should be clear that the specific reason for considering the retraction of these papers is the repeated misrepresentation of the magnitude of the rate of side effects caused by statins based on the cited paper by Zhang et al." It has nothing to do with whether or not statins should be given to people at lower risk.."

He alleges that the authors are deliberately misconstruing the evidence and BMJ should consider not publishing anything from them again

He queries Iona Heath's independence (because of ethics committee) and her stated views on statins in the elderly

#### **19.5.14**

Rory Collins writes to Iona Heath providing his four letters, the power point slides shown to Godlee on his first visit to her office, the note explaining the error, a supplementary note, and annotated versions of both BMJ articles.

**19.5.14** Press officer sends an advance copy of the press release about the setting up of the panel to Rory Collins, John Abramson, Aseem Malhotra, and Iona Heath

**19.5.14** Membership of panel and terms of reference published  
<http://www.bmj.com/about-bmj/independent-statins-review-panel>