PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effect of different financial competing interest statements on readers' perceptions of clinical educational articles: a randomised controlled trial
AUTHORS	Schroter, Sara; Pakpoor, Julia; Morris, Julie; Chew, Mabel; Godlee, Fiona

VERSION 1 – REVIEW

REVIEWER	Tee L Guidotti Occupational + Environmental Health & Medicine
REVIEW RETURNED	13-Jul-2018

GENERAL COMMENTS	This paper describes a well-designed, largely "negative" study (yes, of course we do nor favor that word but it summarizes the findings), addressing and probably answering a key question with a possibly unexpected answer: that readers probably do not pay much attention to conflict of interest. However, the response rate was very low, although typical of mass invitations to participate. The study was basically done on a residual (or even "survivor" population) that had the interest, time, and motivation to participate in contrast to the vast majority of their peers. It may have been difficult to do otherwise but the authors should have discussed this issue and the implications for generalizability.

REVIEWER	Mark H. Ebell MD, MS University of Georgia, USA
REVIEW RETURNED	07-Aug-2018

GENERAL COMMENTS	General comments: Isn't there also work that shows that authors disclosing COI were MORE likely to be biased in their presentation? Sorry, don't have reference but I recall that. I also think the magnitude of the intervention (only affecting a single of three authors, and that one listed third in order) may have been at least partially responsible for the lack of effect seen. Specific comments: Introduction Page 4, line 5: It is a bit odd to see "Competing interests" abbreviated as "COI". Perhaps insert an "also known as conflict of interest" Page 4, line 33: what was the direction fo the influence on reader perceptions?

	Page 4, line 48: American Family Physician has had this “zero tolerance” policy in place for many years, was I believe first to do that. Would be worth mentioning, especially as the text makes it seem that this is unusual or unique. Page 5, line 19-20: Were doctors in training included? Or is that what you mean by “junior doctors” in line 31? Why oversample junior doctors? Page 5, lines 29-32: Did the invitation explain the purpose of the study? Please clarify, could obviously bias results. Page 5, line 47-50: Was there any way to verify whether physicians actually went to the site? For example, through a unique link in their email that would generate a log? Page 7, line 29-30: I see now that the invitation did not explain purpose, might want to move this information earlier, i.e. page 5 lines 29-32. Page 7, lines 36-46: For future reference, Roland Grad and Pierre Pluye at Magill have developed validated tool for evaluating impact of literature on practice (Information Assessment Method or IAM). BTW, I am not one of those two! Page 8, lines 19-28: This is surprising. Every survey requires IRB approval in US. Page 8, lines 36-39: What is the justification for choosing a 1 point difference as “clinically significant? Page 11, lines 19-21: Were there more new or potentially conflicted drugs discussed in the gout trial compared with dyspepsia? Page 11, para 33-50: Please add a better justification for your sampling strategy of 1/3 GP, 1/3 specialist, and 1/3 trainee. Why not just choose GPs in practice and then choose a condition they ALL treat like pneumonia or diabetes or hypertension?

REVIEWER	Quinn Grundy The University of Sydney, Charles Perkins Centre and Faculty of Pharmacy
REVIEW RETURNED	14-Aug-2018

GENERAL COMMENTS	The authors have performed a parallel group randomised controlled trial to investigate whether disclosed conflict of interest influences UK doctors’ confidence, interest, assessment of importance, and likelihood to change practice in the context of educational articles. The authors found that doctors’ confidence (the primary outcome) was not affected by the presence of a disclosed conflict of interest, which was presented in three variations. This experiment is the first to my knowledge, to examine the impact of conflict of interest disclosures in the context of articles that do not report primary research. Of interest, the negative findings sharply contrast with previous similar experiments in the context of primary research articles. The trial is rigorously conducted and the methods are of low risk of bias in terms of random allocation, blinding of participants and the statistician, and reporting of all outcomes per protocol. I have some specific comments in relation to the reporting and interpretation of the findings: Abstract: - Following my comment below (under Discussion), I suggest the Conclusions section could call for more meaningful disclosure practices.

	Article summary: - The final bullet referring to “non-financial” interests seems to me to be beyond the scope of this study. “Non-financial” interests are not well-defined and disclosure requirements are highly variable. I would suggest that the final bullet reflect the limitation that outcome measures remain based on self-report rather than assessing objective changes in practice. Introduction: - The authors cite a common definition of conflict of interest, however, they also propose a mechanism for risk of bias, namely, that “professional views held by an individual . . .may be influenced or compromised” (p 4, lines 8-9). This suggests that conflict of interest is a cognitive bias. However, I feel the IOM and Thomson’s definition suggest more so that conflict of interest is situational. This better accounts for the fact that conflicts of interest arise in specific contexts and may also explain why readers did not perceive the disclosed conflict of interest to be relevant. I would suggest amending the definition of conflict of interest and exploring in the Discussion ways that conflict of interest statements could better communicate relevance or risk of bias. - In the second paragraph of the Introduction, the authors allude to several mechanisms by which bias might be introduced into educational articles. However, to justify the research question and communicate the importance of the study, it would be helpful if the authors explicitly outlined the evidence demonstrating why financial relationships between authors and specifically, the pharmaceutical industry, pose a risk of bias and warrant policy attention. Methods - As the intervention, the authors selected two clinical reviews previously published by The BMJ. What is the likelihood that participants had read these articles previously? For example, when were they published? Were they widely viewed? How closely do they reflect current evidence-based practice? I wonder if confidence or level of interest, for example, could be affected by perception of standard practice or whether the piece is ‘cutting edge’. - I am interested to understand the reason that the authors presented multiple authors (3) and the choice to include authors both with and without conflicts of interest. Did this differ from the authors’ previous trials in the context of primary research articles? Qualitative research on conflict of interest suggests that people believe conflicts of interest can be “balanced” or canceled out, for example, by having ties to multiple companies, or including people with and without conflicts of interest. Perhaps this could also account for the negative findings? - In the Introduction, the authors state that “there is a lack of research exploring the actual, rather than perceived, effect of competing interests on reader perceptions” and this study fills that gap. However, the outcome measures still rely on author self-evaluation and self-report and assess a hypothetical change in practice. While this still advances our understanding of the impact of conflict of interest statements on readers, this is an important limitation to note.

	- If space allows, I would suggest including a small table with the four survey questions that were used to measure the primary and secondary outcomes to help readers understand exactly what was measured. Results - In comparison to the authors' previous trials employing a similar methodology, were these educational articles rated more, less or similarly "interesting" or "important" to primary research? i.e. are average scores of 6s and 7s indicative of interest/importance? - For the secondary outcome "likelihood to change practice", Table 4 presents the findings for respondents who replied "extremely likely." This strikes me as a conservative measure and I wonder if findings are consistent if respondents replying "likely" and "extremely likely" are grouped for analysis? Discussion - On page 13, line 44, the authors state that COIs were "subtler" in the context of clinical review articles -- in what way? Please explain what these are contrasted with. - The authors explain that a limitation of the study is that participants were asked to read an article that they might not have selected themselves, which I agree is an important limitation. Perhaps in calling for future research there is some way to conduct a natural experiment where participants evaluate conflict of interest disclosures in the context of articles that are highly relevant to their practice. Similarly, I wonder if another limitation is that the relationship was with a fictional pharmaceutical company? Did the authors receive any feedback to that effect? In judging relevance, it could be that readers did not perceive a conflict given that the company does not manufacture drugs for these conditions. - I feel this Discussion has the opportunity to call for more meaningful disclosure practices within the context of biomedical research. The authors posit that lower awareness or inattention may be responsible for the negative findings. However, as the authors state, these types of disclosure are typical in biomedical research and sometimes perceived to be 'business as usual.' In addition to suggestions regarding the role of conflict of interest in critical appraisal, I suggest that journal editors could invite a more reflexive stance in relation to disclosures, especially in the context of educational articles. For example, in addition to reporting conflicts of interest, the authors, or the editors, could position the authors in relation to the work and the external relationships and call readers' attention to risks of bias. - The authors call for the evaluation of the effect of "non-financial COIs" on readers perceptions in future work (pg 15, line 7). Currently, "non-financial COI" is being used to label highly diverse "interests" ranging from religious beliefs to diet to involvement in previous related research. In this context, the authors call attention to relationships with commercial entities where no money is involved, but transfers of value, furthering commercial ends are present. I would suggest not using this term

	but instead referring to these as indirect financial COIs or something to that effect

REVIEWER	Prof Jane Blazeby University of Bristol, UK
REVIEW RETURNED	21-Aug-2018

GENERAL COMMENTS	This paper probably addresses a novel question. 1. It is unclear whether the literature has been searched systematically to look for similar studies since the review which is cited published in 2005 – it is possible that literature has been missed on this subject. Whilst it is stated that this is the 'first study ' to look at COIs in clinical educational material – this needs supporting evidence. 2. Choice of article to examine how the COIs influenced readers' opinions. As stated clinical educational articles tend to be subject to bias. They are informed by non-systematic evidence – yet they are highly regarded. Because of this it is possible that COIs are considered to be less influential and readers are impressed by the educational nature of the articles (often written by well known clinicians) and therefore one may hypothesise that such articles are not influenced by COIs. Could the discussion consider these issues? 3. It would be interesting to know if specialists in the fields of dyspepsia and gout are differently influenced by the COI statements (as they may be aware that the educational article is not based on evidence). Is an exploratory subgroup analysis possible or worth commenting on in the discussion? 4. Primary outcome. The choice is very inclusive and likely influenced by many things – I have concerns that it is not a sensitive indicator relating to COIs. I also have concerns about the assumptions made about the sensitivity of the measure to detect a clinically relevant 'confidence in the article' level – which may all mean that the study is underpowered 5. I appreciate why patients were not included in the work – however, gaining public involvement about the study would have been possible and a missed opportunity - or even widening the team to include more clinicians from the different categories of doctors may have improve the study design 6. Despite these concerns about I think its an important RCT that warrants publication

VERSION 1 – AUTHOR RESPONSE

	Comment	Response	Description of the location and wording of all revisions that have been made (clean version)
	Editor's comments		

1	- Please revise the ‘Strengths and limitations’ section of your manuscript (after the abstract). This section should contain five short bullet points, no longer than one sentence each, that relate specifically to the methods.	We have revised these statements.	Strengths and limitations section, p4.
2	- Kindly re-upload each figure under ‘Image’ file designation with at least 300 dpi resolution and at least 90mm x 90mm of width in either TIFF or JPG format.	We have revised Figure 1.	Figure 1
3	- Kindly re-upload Appendix in PDF format.	We have uploaded PDFs.	Appendices
	Reviewer 1		
1	This paper describes a well-designed, largely "negative" study (yes, of course we do nor favor that word but it summarizes the findings), addressing and probably answering a key question with a possibly unexpected answer: that readers probably do not pay much attention to conflict of interest. However, the response rate was very low, although typical of mass invitations to participate. The study was basically done on a residual (or even "survivor" population) that had the interest, time, and motivation to participate in contrast to the vast majority of their peers. It may have been difficult to do otherwise but the authors should have discussed this issue and the implications for generalizability.	We have added additional detail to the study limitations section of the Discussion.	We added this to the Discussion on p15: “The extent to which we can generalise the findings from the small sample of volunteers who had the time, interest and motivation to take part to all readers is unknown; those who volunteered may differ from their peers in ways we did not capture.”
	Reviewer 2		
1	Isn’t there also work that shows that authors disclosing COI were MORE likely to be biased in their presentation?	Work indicating that authors disclosing COI are more likely to be biased has	We added this to the Introduction on p6:

	Sorry, don't have reference but I recall that.	now been incorporated into the Introduction.	"Of concern too is evidence from the social sciences suggesting that disclosure of COIs may even enhance bias: conflicted authors may feel a 'moral release' from having simply declared they are conflicted, or may even exaggerate to counteract any expected discounting of their opinion.[11-12]"
2	I also think the magnitude of the intervention (only affecting a single of three authors, and that one listed third in order) may have been at least partially responsible for the lack of effect seen.	This is an important point that we have added to the Discussion.	P16: "We only included a COI for the last of the three listed authors and this may have influenced the magnitude of any effect, but our earlier trial only reported a COI for one of three authors and did find a significant effect.[7]"
3	Page 4, line 5: It is a bit odd to see "Competing interests" abbreviated as "COI". Perhaps insert an "also known as conflict of interest"	We have added this.	P5: "Researchers, clinicians and academic institutions often have competing interests, also known as conflicts of interest (COIs), and collaborations with industry are often considered necessary to facilitate progress and innovation in medical research.[1]"
4	Page 4, line 33: what was the direction fo the influence on reader perceptions?	We have indicated that the trials showed a negative effect.	P5: "We have previously reported the results of two randomised controlled trials comparing the effect of COI statements related to financial interests against no competing interests and demonstrated a significantly negative influence of COIs on readers' perceptions of the credibility of medical research.[6, 7]"
5	Page 4, line 48: American Family Physician has had this "zero tolerance" policy in place for many years, was I believe first to do that. Would be worth mentioning, especially as the text makes it seem that this is unusual or unique.	We have now indicated this in the Introduction.	We have added this to P6: "Many years ago the *American Family Physician* became the first journal to introduce a 'zero tolerance' policy for COIs in clinical educational articles.[13] In the 1990s *The New England Journal of Medicine* implemented a stringent policy whereby editorialists had to be free from financial ties to drugs or devices discussed in the editorial,[14, 15] but this policy was relaxed in 2002 to exclude only those with significant ($10,000) financial interest due to difficulties in recruiting authors.[16] In 2015 *The BMJ* implemented a 'zero

			tolerance' policy on the presence of any relevant financial COI related to industry for authors of its clinical editorials and some education articles.[17]"
6	Page 5, line 19-20: Were doctors in training included? Or is that what you mean by "junior doctors" in line 31? Why oversample junior doctors?	In the UK junior doctors are qualified doctors practising at any stage between graduation and completion of specialist postgraduate training. We did not oversample junior doctors. On 9 we say: "Accordingly, in Sample 1, for each of the eight groups, 255 readers (85 GPs, 85 consultants and 85 junior doctors) were invited to take part." On page 11 we further describe the sample – "A third of respondents were consultants, a third GPs, and a third junior doctors;"	No changes made.
7	Page 5, lines 29-32: Did the invitation explain the purpose of the study? Please clarify, could obviously bias results.	Participants were not told the purpose of the study as this would bias the results. Participants were told we were seeking	We have added the following to p7: "Participants were not told the purpose of the study to avoid biasing responses."

		volunteers to take part in a short online research project for The BMJ and once they had agreed, they were simply invited to do the task needed.	
8	Page 5, line 47-50: Was there any way to verify whether physicians actually went to the site? For example, through a unique link in their email that would generate a log?	We did not check whether the participants actually opened the files in the way described. Even if we had, visiting the pages does not equate to reading them. However, an analysis of the responses to the free text questions indicates a high level of engagement with the task.	No changes made.
9	Page 7, line 29-30: I see now that the invitation did not explain purpose, might want to move this information earlier, i.e. page 5 lines 29-32.	See response to point 7.	We have added the following to p7: “Participants were not told the purpose of the study to avoid biasing responses.”
10	Page 7, lines 36-46: For future reference, Roland Grad and Pierre Pluye at Magill have developed validated tool for evaluating impact of literature on practice (Information Assessment Method or IAM). BTW, I am not one of those two!	Thank you for this useful reference.	No changes made.
11	Page 8, lines 19-28: This is surprising. Every survey	We have revised the Ethics and	Ethics and trial registration p9: “We did not submit the study for ethical approval as this is not required for this

	requires IRB approval in US.	trial registration section.	type of survey with doctors in the UK. However, the study proposal and study materials were reviewed by *The BMJ's* Ethics Committee and they did not have substantive ethical concerns."
12	Page 8, lines 36-39: What is the justification for choosing a 1 point difference as "clinically significant?	In the sample size justification section on p9 we state "We assumed that a one-unit difference on the 10-point scale was important on the basis that a 0.5-unit difference was important in our previous studies using a 5-point scale.[6, 7]" A 1 point difference on the 1 to 10 scale indicates a 10% shift in value, which we thought to be a reasonable change.	No changes made.
13	Page 11, lines 19-21: Were there more new or potentially conflicted drugs discussed in the gout trial compared with dyspepsia?	Whether or not the drugs in the gout compared to dyspepsia educational article are more conflicted is a difficult judgement to make, particularly as the articles discussed several therapeutic options.	No changes made.
14	Page 11, para 33-50: Please add a better justification for your sampling strategy of 1/3 GP, 1/3 specialist, and 1/3 trainee. Why not just choose GPs in practice and then	We sampled a broad range of doctors so that our findings would be generalisable to the clinical	We added the following to the Methods on p7:

	choose a condition they ALL treat like pneumonia or diabetes or hypertension?	workforce. We appreciate that we could have sampled in a different way. Of note, given that dyspepsia and gout are common conditions, we would expect the majority of practicing clinicians to have an understanding of their treatment and some clinical experience of managing these conditions. Further, we are not aware of any evidence suggesting that the influence of COIs would have a greater effect on clinicians used to treating the relevant condition. For example, it could be hypothesized that clinicians less accustomed to managing these conditions would gain more from reading an educational article, and would pay more attention to COIs as they may have fewer preconceptions about different treatments. In addition, analysis of the subgroups who were currently treating the conditions showed no significant difference in the primary outcome (Table 5).	"A range of clinical specialties and stages of training were included to facilitate generalisability of study findings to the clinical workforce, and the clinical conditions of the educational articles were accordingly selected to reflect conditions which the vast majority of clinicians would be expected to have had experience in managing."

	Reviewer 3		
1	The authors have performed a parallel group randomised controlled trial to investigate whether disclosed conflict of interest influences UK doctors' confidence, interest, assessment of importance, and likelihood to change practice in the context of educational articles. The authors found that doctors' confidence (the primary outcome) was not affected by the presence of a disclosed conflict of interest, which was presented in three variations. This experiment is the first to my knowledge, to examine the impact of conflict of interest disclosures in the context of articles that do not report primary research. Of interest, the negative findings sharply contrast with previous similar experiments in the context of primary research articles. The trial is rigorously conducted and the methods are of low risk of bias in terms of random allocation, blinding of participants and the statistician, and reporting of all outcomes per protocol.	No changes requested.	No changes made.
2	Abstract: - Following my comment below (under Discussion), I suggest the Conclusions section could call for more meaningful disclosure practices.	The abstract has been amended accordingly.	The following has been added to the abstract p2: "More meaningful COI disclosure practices may be needed, which highlight context-specific potential sources of bias to readers."
3	Article summary: - The final bullet referring to "non-financial" interests seems to me to be beyond the scope of this study. "Non-financial" interests are not well-defined and disclosure requirements are highly	We have made this change to the Article Summary.	We added this to the Article Summary on p4: "Our outcome measures were all self-reported and we did not assess objective changes to practice."

	variable. I would suggest that the final bullet reflect the limitation that outcome measures remain based on self-report rather than assessing objective changes in practice.		
4	Introduction: - The authors cite a common definition of conflict of interest, however, they also propose a mechanism for risk of bias, namely, that "professional views held by an individual . . .may be influenced or compromised" (p 4, lines 8-9). This suggests that conflict of interest is a cognitive bias. However, I feel the IOM and Thomson's definition suggest more so that conflict of interest is situational. This better accounts for the fact that conflicts of interest arise in specific contexts and may also explain why readers did not perceive the disclosed conflict of interest to be relevant. I would suggest amending the definition of conflict of interest and exploring in the Discussion ways that conflict of interest statements could better communicate relevance or risk of bias.	We have changed the definition of COI in the manuscript to that of the Institute of Medicine and have added discussion around conflict of interest statements as suggested by the reviewer.	We have made the following changes to the Introduction and Discussion: P5: "COIs are defined as 'circumstances that create a risk that professional judgements or actions regarding a primary interest will be unduly influenced by a secondary interest'.[1][2]" p16: "It is also possible that readers did not consider the COIs to be directly relevant to the topics of the educational articles, and the perceived role of COIs may be context-dependent. COI statements may therefore be more meaningful if they were to specify the relevance of a COI to the subject topic, rather than, as an example, simply stating the existence of a tie with a pharmaceutical company."
5	- In the second paragraph of the Introduction, the authors allude to several mechanisms by which bias might be introduced into educational articles. However, to justify the research question and communicate the importance of the study, it would be helpful if the authors explicitly outlined the evidence demonstrating why financial relationships between authors and specifically, the pharmaceutical industry, pose a risk of bias and warrant policy attention.	Discussion of this has now been added to the Introduction.	We added this to the Introduction on p5: "The possibility that COIs may bias the medical literature and potentially affect patient care has been highlighted in many studies. For example, a 2017 Cochrane review found that drug and device studies sponsored by the manufacturer demonstrated more favorable efficacy and conclusions than studies sponsored by other sources.[3] Whether bias is conscious or unconscious, COIs may therefore compromise the medical evidence

			which drives development of recommendations for clinical care.[3]"
6	Methods - As the intervention, the authors selected two clinical reviews previously published by The BMJ. What is the likelihood that participants had read these articles previously? For example, when were they published? Were they widely viewed? How closely do they reflect current evidence-based practice? I wonder if confidence or level of interest, for example, could be affected by perception of standard practice or whether the piece is 'cutting edge'.	We do not know the likelihood that participants had read the prior publications previously. The full version of the articles were published in 2013 and they have been widely viewed online. The survey was conducted in 2016 and so it is unlikely that major changes to practice were recommended for these common conditions in that period. However, our initial sampling served a purpose here as some of those who received the dyspepsia article in sample 1 indicated that the use of prokinetic drugs is no longer recommended. As such we revised the article to exclude this section for the main study. We did not receive comments about the practice described in the gout article not being curent. We have now added publication dates in the Methods section and discuss the point that	Methods p8: We added the publication date of the articles. "We selected two clinical reviews previously published by *The BMJ in 2013 describing* two conditions commonly seen by doctors, requiring treatment by drugs, and familiar to all clinical specialties."

		confidence and interest could have been influenced by the perceived standard practice to the Discussion. The reviewer raises a good point, but this is in the subgroup analysis reported on page 12: "Analysis of the subgroups who were currently treating the conditions showed no significant differences between the groups for the level of confidence (primary outcome) in the article (gout: *P*=.18; dyspepsia: *P*=.64), (Table 5)." And on page 14: "Many readers in this study may also have been familiar with the medical conditions under discussion, and their own clinical practice already in alignment with the review conclusions."	
7	- I am interested to understand the reason that the authors presented multiple authors (3) and the choice to include authors both with and	This is an interesting point.	We have made this clearer in the Discussion on p16:

	without conflicts of interest. Did this differ from the authors' previous trials in the context of primary research articles? Qualitative research on conflict of interest suggests that people believe conflicts of interest can be "balanced" or canceled out, for example, by having ties to multiple companies, or including people with and without conflicts of interest. Perhaps this could also account for the negative findings?	In our first study about herpes all 3 authors had a financial COI (employees potentially owning stock and/ or holding stock options in the company) or all 3 had "none declared". In our second study we added another arm to the first study where just 1 of the 3 authors was a recipient of funding for studentships and research grants from the company for the paper on herpes. In our second study we also added a new paper about problem lists. For the financial COI group just one of the authors had a financial COI (employee potentially owning stock and/ or holding stock options in the company) and for the grant group one of the authors was a recipient of funding for studentships and research grants from the company. Overall, importance, relevance,	"We only included a COI for the last of the three listed authors and this may have influenced the magnitude of any effect, but our earlier trial only reported a COI for one of three authors and did find a significant effect.[7]"

		validity, and believability ratings were significantly lower in the “financial statement” group than in the “none declared” group. Validity ratings for the “financial statement” group were also significantly lower than for the “grants statement” group. We found significant differences in the ratings between papers for all five measures (P<0.001), with the problem lists paper scoring significantly higher than herpes paper. In the current study where just one of the authors had a COI we did not find a significant difference.	
8	- In the Introduction, the authors state that “there is a lack of research exploring the actual, rather than perceived, effect of competing interests on reader perceptions” and this study fills that gap. However, the outcome measures still rely on author self-evaluation and self-report and assess a hypothetical change in practice. While this still advances our understanding of the impact of conflict of interest statements on readers, this is an important limitation to note.	We have revised this statement in the Introduction as we agree this may have been confusing for readers. We have added the use of self-reported outcome measures as a study limitation in the Discussion and in the Article Summary.	We have revised p5 to say: “However, there has been little research exploring the effect of competing interests on reader perceptions. “ And the Discussion p15 to say: “Sixthly, we only looked at the effect on self-reported outcome measures not on actual changes to practice.” Article Summary p4:

			"Our outcome measures were all self-reported and we did not assess objective changes to practice."
9	- If space allows, I would suggest including a small table with the four survey questions that were used to measure the primary and secondary outcomes to help readers understand exactly what was measured.	The questionnaire is included as supplementary data with the published protocol in BMJ Open and this is already indicated on p 7: "(see protocol supplementary materials for the questionnaire)."	No changes made.
10	Results - In comparison to the authors' previous trials employing a similar methodology, were these educational articles rated more, less or similarly "interesting" or "important" to primary research? i.e. are average scores of 6s and 7s indicative of interest/importance?	We used a different scale in the earlier studies (0 to 5, rather than 0 to 10). However, standardising the scores from the previous trials (simply multiplying by 2), it would seem that the importance and interest scores in this trial were slightly higher. However, it is important to acknowledge that there may be a 'period' effect (15 years difference) as well as a 'content' effect.	No changes made.
11	- For the secondary outcome "likelihood to change practice", Table 4 presents the findings for respondents who replied "extremely likely." This strikes me as a conservative measure and I wonder if findings are consistent if respondents replying "likely" and "extremely likely" are grouped for analysis?	Respondents only used the extremes of the 0 to 10 scale (that is, extremely unlikely / unlikely or extremely likely) and no one scored between 2 and 9 inclusive. Hence, the findings would be exactly the same if the 'likely' and 'extremely likely'	No changes made.

		categories were combined.	
12	Discussion - On page 13, line 44, the authors state that COIs were "subtler" in the context of clinical review articles -- in what way? Please explain what these are contrasted with.	To clarify, we did not mean that COIs are always 'subtler' in educational articles but meant specifically in the COIs we wrote in these educational articles, in contrast to our earlier trials. We have now specified that this was in contrast to prior similar trials, and that the subtler COIs were in contrast to these trials (now cited).	We have amended to read as follows p14: "In contrast to previous trials evaluating the influence of COIs on readers' perceptions, our study used a clinical review article (where possible biases may be less visible) and subtler financial COIs (although these were still typical of those seen in medical practice).[6-7]"
13	- The authors explain that a limitation of the study is that participants were asked to read an article that they might not have selected themselves, which I agree is an important limitation. Perhaps in calling for future research there is some way to conduct a natural experiment where participants evaluate conflict of interest disclosures in the context of articles that are highly relevant to their practice. Similarly, I wonder if another limitation is that the relationship was with a fictional pharmaceutical company? Did the authors receive any feedback to that effect? In judging relevance, it could be that readers did not perceive a conflict given that the company does not manufacture drugs for these conditions.	We have added this idea for future research. We also appreciate the reviewers' comments about the use of a a fictional company but did not receive any comments from participants about this, despite them making lots of free text comments. Whilst a handful of readers did comment that they didn't know if the company Jenka Pharmaceuticals produced drugs for gout/dyspepsia this was in the	We have added this to p15: "Further research could study the effects of COI statements in the context of articles that are highly relevant to readers' own clinical practice."

		context of trying to assess the magnitude of the reported COI.	
14	- I feel this Discussion has the opportunity to call for more meaningful disclosure practices within the context of biomedical research. The authors posit that lower awareness or inattention may be responsible for the negative findings. However, as the authors state, these types of disclosure are typical in biomedical research and sometimes perceived to be 'business as usual.' In addition to suggestions regarding the role of conflict of interest in critical appraisal, I suggest that journal editors could invite a more reflexive stance in relation to disclosures, especially in the context of educational articles. For example, in addition to reporting conflicts of interest, the authors, or the editors, could position the authors in relation to the work and the external relationships and call readers' attention to risks of bias.	The discussion has been amended to incorporate this.	We have added the following to the Discussion p16: "In addition, given that some form of COI among leadership figures in clinical research is now very common, it is possible that the simple presence of a COI is not sufficient to attract attention. Rather, in addition to reporting COIs, authors or journal editors should consider positioning the COI in relation to the topic of the article so that any context-specific risk of bias is clearer to the reader."
15	- The authors call for the evaluation of the effect of "non-financial COIs" on readers perceptions in future work (pg 15, line 7). Currently, "non-financial COI" is being used to label highly diverse "interests" ranging from religious beliefs to diet to involvement in previous related research. In this context, the authors call attention to relationships with commercial entities where no money is involved, but transfers of value, furthering commercial ends are present. I would suggest not using this term but instead referring to these as indirect financial COIs or something to that effect	We have added the word indirect to account for these diverse interests.	P16: "Further, our research has focused only on financial COIs but it would also be important to evaluate the effect of non-financial or indirect COIs on readers' perceptions, such as unpaid consultancies which may include reimbursements for travel expenses, meals and drinks.[22]"

	Reviewer 4		
1	This paper probably addresses a novel question. It is unclear whether the literature has been searched systematically to look for similar studies since the review which is cited published in 2005 – it is possible that literature has been missed on this subject. Whilst it is stated that this is the 'first study ' to look at COIs in clinical educational material – this needs supporting evidence.	A literature review was undertaken of articles published in MEDLINE via PubMed. We searched for trials published up to the 1st of January 2016, with no date or language restrictions, using the following search terms in either the title or abstract of an article: "conflict of interest" OR "competing interest" OR "conflicts of interest" OR "competing interests" AND "trial". The search generated 922 articles, of which we reviewed any controlled trials which evaluated the influence of COIs in medical articles (original research, reviews, or educational articles) on readers' perceptions.	No changes made.
2	Choice of article to examine how the COIs influenced readers' opinions. As stated clinical educational articles tend to be subject to bias. They are informed by non-systematic evidence – yet they are highly regarded. Because of this it is possible that COIs are considered to be less influential and readers are impressed by the educational nature of the articles (often written by well known clinicians) and therefore one may hypothesise that such	We have added this to the Discussion section.	We have added the following to the Discussion p15: "Further, educational articles are typically written by highly regarded clinicians who are well known or 'trusted' experts in their field, which may mean that COIs are considered by readers to be less influential or less important in this context."

	articles are not influenced by COIs. Could the discussion consider these issues?		
3	It would be interesting to know if specialists in the fields of dyspepsia and gout are differently influenced by the COI statements (as they may be aware that the educational article is not based on evidence). Is an exploratory subgroup analysis possible or worth commenting on in the discussion?	As it states on p10, we did some subgroup analysis: “Separate analyses of covariance (ANCOVA) were performed for each of the two clinical reviews, and, in addition, for the subgroups who were currently treating the conditions.” And in the results on p12 we say: “Analysis of the subgroups who were currently treating the conditions showed no significant differences between the groups for the level of confidence (primary outcome) in the article (gout: P=.18; dyspepsia: P=.64), (Table 5).” We have now added this to the Discussion.	We have added the following to the first paragraph of the Discussion on p14: “Subgroup analysis of those who were currently treating the conditions found no significant difference in the level of confidence in the article.”
4	Primary outcome. The choice is very inclusive and likely influenced by many things – I have concerns that it is not a sensitive indicator relating to	We feel that confidence, as measured on a 10-point Likert scale, is a	No changes made.

	COIs. I also have concerns about the assumptions made about the sensitivity of the measure to detect a clinically relevant ‘confidence in the article’ level – which may all mean that the study is underpowered	relevant measure of the impact of trust in an article (which can be affected by COIs). In terms of sensitivity, the 1 to 10 scale was fully used by the respondents (ie. the confidence ratings varied between 1 and 10) showing that this scale differentiated well between respondents.	
5	I appreciate why patients were not included in the work – however, gaining public involvement about the study would have been possible and a missed opportunity - or even widening the team to include more clinicians from the different categories of doctors may have improve the study design	Regarding widening the team to include more clinicians from different categories of doctors: We set about answering a very editorial question and sought the views of all our editors and asked for examples of COIs they regularly see in educational material at The BMJ. As editors of a general medical journal, these editors receive submissions from many areas of medicine. As such the COI statements used in the study reflect those commonly seen across medicine. We agree that initiating patient and public involvement early in the work might have broadened	We have revised our PPI statement on p10 to: “We did not include patients as study participants. Patients were not involved in setting the research question, designing the study, the conduct of the study, or the interpretation of the results. Our patient editor, recently invited patients and members of the public attending a workshop at the Cochrane Colloquium 2018 on "*Meeting the challenge of research empowerment through co-production and expert patient review*" how patients and the public could have been involved in this research and they reported that they did not see relevant opportunities to do so. However, a patient and public reviewer for The BMJ did make an interesting suggestion for a further study with the general public as the participants as it is important to know how people value and consider COIs when reading articles.” We have revised our acknowledgements on p17 to: “We thank the editors in *The BMJ* education team (Cath Brizzell, Tony Delamothe, Giselle Jones, Navjoyt Ladher, Emma Parish, Alison Tonks, Sophie Cook), and Theo Bloom for their

		the scope and usefulness of the study. However, as the study design was based on previous research there was little scope for change other than the COI statements themselves, but these needed to reflect real life examples of COIs regularly seen by editors. As such potential for involvement from patients and the public was limited. Our patient editor, Amy Price, recently invited patients and members of the public attending a workshop at the Cochrane Colloquium 2018 on "*Meeting the challenge of research empowerment through co-production and expert patient review*" how patients and the public could have been involved in this research and they reported that they did not see relevant opportunities to do so. However, a patient and public reviewer for The BMJ did make an interesting suggestion for a further study with the general public as the participants as it is important	help in designing the study; the authors of the original clinical reviews for giving us permission to use their work and Emma Parish for editing these articles for use in the study; Keith Bates, Data Analyst at the British Medical Association, for providing data about BMA members and help with sampling; and our patient editor Amy Price, Julie Sprakel (BMJ patient and public reviewer) and participants at the workshop at the Cochrane Colloquium 2018 for their thoughts on how patients might have been involved in this study and ideas for further research.”

		to know how people value and consider COIs when reading articles. This feedback has stimulated us to consider some further work on how patients and the public interpret COI statements. We have revised our PPI statement within our manuscript and thanked the workshop participants, the BMJ patient reviewer, and our patient editor in the acknowledgements section.	
6	Despite these concerns about I think its an important RCT that warrants publication	NA.	No change needed

VERSION 2 – REVIEW

REVIEWER	Quinn Grundy The University of Sydney, Australia
REVIEW RETURNED	04-Oct-2018

GENERAL COMMENTS	The authors have comprehensively addressed all of my comments and I have no further comments.

REVIEWER	Jane M Blazeby University of Bristol, UK
REVIEW RETURNED	13-Oct-2018

GENERAL COMMENTS	The authors have responded very well to my concerns and the others raised by the referrees with an expanded discussion