

Editor's request	Response	Changes
<p>1. However, it is not very well written or presented, and at present is not in a state to be published in an academic journal. There is almost no attempt to contextualise the data within the relevant literature, and the Results section could be written and presented more clearly and with more detail. The paper gives the impression of something that was written for other purposes, maybe a report.</p>	<p>Accepted</p>	<p>Have made several changes to give more context, and have extensively restructured. Changes are not tracked where the only change is to change the position of text in the document, as it would be too confusing, but all changes of content are tracked.</p>
Reviewer: 1		
<p>2. Given the fact that this report comes from the US and that the authors seek for publication in a European/Scandinavian journal, there should be a clear statement about the cultural background of the trial and the report. This should start with the title (The Citalopram CIT-MD-18 Pediatric Depression Trial in the United States</p>	<p>We agree with making it clear that it is a US trial, but felt it too cumbersome to change the title (but see below for other changes)</p>	
<p>3. should continue with the abstract (rephrase objective),</p>	<p>Done</p>	<p>Added 'conducted in the United States'</p>
<p>4. and should be made clear also in the first paragraph of the introduction.</p>	<p>Done</p>	
<p>5. Furthermore, it should be indicated by the ®symbol both in the abstract and in the first paragraph that Celexa and Lexapro are US brand names for Citalopram and Escitalopram, respectively,</p>	<p>Done, except the Celexa and Lexapro Marketing and Sales Practices Litigation is the official name of the litigation, therefore the ® symbol is not used here</p>	<p>Have italicized <i>Celexa and Lexapro Marketing and Sales Practices Litigation</i></p>

<p>6. and that Forest stands for Forest Research Institute (describe function of the institute).</p>	<p>In all the litigation, 'Forest' means "Forest Laboratories", but to be more specific Forest Research Institute is a wholly-owned subsidiary of Forest Laboratories, Inc. Forest Research Institute provides the research, development, and clinical evaluation of pharmaceutical products.</p>	<p>Have used the full name when first mentioning Forest</p>
<p>7. From reading the results, it does not become sufficiently clear how the primary outcome measures were substituted by post hoc outcome measures (page 8).</p>	<p>We missed inaccuracies that arose out of earlier edits and are grateful to the reviewer for drawing our attention to this potentially misleading segment. We have extensively rewritten it.</p>	<p>See track changes for rewriting for clarity.</p>
<p>8. It is a common procedure to regard a difference at <math>p=0.052</math> as a trend for significance (page 9). This could be admitted in the manuscript to avoid further discussion.</p>	<p>Done</p>	<p>Altered to 'statistically <u>marginally</u> insignificant'</p>
<p>9. Does the typo in the cited sentence " Any patient...." on top of page 10 stem from the protocol or from the authors of this manuscript?</p>	<p>Our typo</p>	<p>corrected</p>

<p>10. Both in the introduction and the discussion a comment on the broader frame of reference of drug trials in children might add to the value of the paper. For instance, there could be a reference to the higher vulnerability of the developing brain and the lower efficacy of most psychotropic medications including the higher risk of adverse events in this young population.</p>	<p>Have added a paragraph to the introduction</p>	<p>Now reads: The use of antidepressant medication in children and adolescents has been controversial because of concerns about efficacy ( ), the greater vulnerability of the developing brain to psychotropic medications and higher risk of adverse events and suicide ( ), in this young population. Nevertheless pediatric antidepressant consumption is high and increasing ( ), led by prescribing trends in the United States. Thus well-conducted and reported research in evidence-based practice is required. The medical literature, however, is replete with publication bias ( ) and misrepresentation of outcomes ( ) facilitated by endemic ghostwriting ( ). The extent to which the pharmaceutical industry controls the content of journal articles with marketing ‘spin’ has led some to charge that “journals have devolved into information laundering operations for the pharmaceutical industry.” ( ) In order to exemplify this pervasive practice, the following article is a deconstruction of a report of Forest Laboratories’ study CIT-MD-18...</p>
	<p>And this to the conclusion</p>	<p>See track changes for expansion and contextualization of our work.</p>
<p>11. In addition, the concern about a worldwide trend of prescribing more drugs to children could be mentioned (as evidenced also in this journal recently).</p>	<p>agreed</p>	<p>See 10</p>
<p>12. Similarly, it could be addressed that the US absorbs the vast majority of worldwide drug prescriptions for children.</p>	<p>agreed</p>	<p>See 10</p>
<p>Reviewer: 2</p>		
<p>13. While the first two authors acknowledge that they have had legal support in giving evidence</p>	<p>Everything reported here is ‘public’ information.</p>	<p>Several minor changes, eg, replacing ‘misrepresentation’ with ‘mischaracterisation’; making some statements more neutral.</p>

<p>to the legal challenge mounted by a group of plaintiffs, if the article were to be published it would need to be over-viewed carefully by a lawyer to ensure that the journal was not compromised legally. This may be relatively straightforward if the lawyer were to judge that everything reported here had been considered in court and therefore was 'public' information. However, that may not be so.</p>	<p>Michael Baum, Esq., senior partner of Baum, Hedlund, Aristei, &amp; Goldman, who litigated this case and was responsible for the release of the documents cited into the public domain, had already scrutinized for potential libel. We arranged a second legal review of the manuscript by Mr Ron Goldman Esq another senior partner. We adapted the paper to meet the requirements of legal review. We acknowledge both for legal review.</p>	
<p>Reviewer: 3</p>		
<p>14. This manuscript provides extensive primary source documentation of corporate intent to mislead the anticipated professional readership of Am J Psychiat regarding the effectiveness of citalopram in treatment of major depressive episodes in youth. Because of the importance of documentation that no selective reporting by he authors of this submitted manuscript occurred, it is reasonable that they be asked to</p>	<p>Noted</p>	<p>Have added to acknowledgments: The authors warrant that findings have been reported fairly and non-selectively.</p>

make such a statement.		
15. Similarly, the corporations and other agents engaged in the planning, funding, and preparation of the citalopram study manuscript, as well as those individuals engaged in the writing or review of such writing of the citalopram manuscript, should be provided opportunity to comment on the actions described in the manuscript submitted to Acta that involve putative distortion of facts and recommendations. However, a professional journal generally has little or no staff or budget to utilize in investigative inquiry. If any court system or regulatory system evidence has been brought regarding the citalopram study and preparation of the original manuscript, some of such may be germane to what might be published in Acta. For several reasons, the judicial/regulatory system is best suited to address many of the actions asserted in this manuscript. That said, there is still a useful societal and professional value of publication of such a manuscript in a respected, widely read journal such as Acta.	No changes required.	
Reviewer: 4		
16. Introduction: Reference to some more general data on rates of use of antidepressants in children would be useful,	agreed	Added to opening para of introduction
17. along with a description of existing literature on ghost-writing (e.g. David Healy's work)	agreed	Added to opening para of introduction

18. and previous findings of publication bias in antidepressant research, including the meta-analysis by Whittington et al which included unpublished data and found few effects.	agreed	Added to opening para of introduction
19. Methods: Note it is 'materials and methods'	typo	corrected
20. Some more description of the process of analysis would be useful, such as comparison between published report and study data revealed in the confidential documents, including the study protocol, scrutiny of e mails and other correspondence relating to authorship and manuscript production.	Good idea	Added to methodology: All authors examined the CIT-MD-18 study protocol, the final study report, and drafts of the ghostwritten manuscript to evaluate the accuracy of the reporting of the methodology and data in the article published in the names of Wagner et al. Forest's publication plans, related documents from Prescott Medical Communications, and email correspondence between Forest and Prescott employees and Dr. Wagner were reviewed to analyse manuscript production and determine the extent of ghost writing and unearned authorship.
21. In the description of the power calculation, is it specified what effect size they were aiming to detect?	In the original power statement in the study protocol, no effect size was described (confirmed by searching cit-18 study protocol and study report)	Have added: There is no reference to effect size in the study protocol.
22. Results: Overall this section could be more clearly presented and more data would be useful.	Have included more data and reworded parts. See also #7 above	
23. I would suggest the section is divided into a subsection on 'authorship' and one on 'results' or 'data', and to incorporate the first paragraph in the second section.	Good advice, divided into authorship and data	RESULTS OF DECONSTRUCTION  <i>1. Authorship</i>  <i>2. Data</i>
24. I would not describe the e mail about	We think that most	Now reads: 'Fulfilling requirements for the manuscript's authorship

<p>authorship that is quoted on P 7 as ‘banter’. I agree this is a very important quote, but to my mind it simply states the bold fact that the writer and author are not the same under this system of authorship, and might not have been meant light-heartedly.</p>	<p>people would agree that this was light hearted, but have altered as requested.</p>	<p>did not appear to be treated with gravity.’</p>
<p>25. The statement that there is no evidence the manuscript was circulated to the other authors is potentially libellous, so the authors need to be very sure that they have grounds to make this suggestion, and provide more evidence to back it up. Are they sure they have seen all the correspondence about the trial? Are there e mails suggesting these authors agree to be authors without evidence that they have seen the manuscript?</p>	<p>Agree this claim is too strong</p>	<p>Altered to read: ‘Although she advised Forest about journal placement and marketing strategy ( ), we could find no evidence in the extensive documents that we reviewed that Dr. Wagner contributed to the study design, analysis of data, or preparation of the first draft of the manuscript. Nor could we find evidence that her Forest-designated co-authors, Drs. Adelaide Robb and Robert Findling, contributed to the production of the manuscript’s initial drafts, or that they were ever circulated to or reviewed by them.’</p>
<p>26. The data on the results of the study is difficult to follow. The authors seem to be making two substantive points: first that the original, per-protocol primary outcome was not statistically significant (although it was very nearly so, which should be acknowledged), and was inflated by adding the unblinded participants; second – an interaction effect was not reported.</p>	<p>Have clarified this by altering confusing heading <b>interaction</b></p>	<p>Now 2 separate headings:  <i>Mischaracterisation of primary outcome</i>  <i>Failure to publish negative secondary outcomes, and undeclared inclusion of Post Hoc Outcomes</i></p>
<p>27. It is difficult to judge the situation with the effect size, so I wouldn’t make this a big point, but just it is worth mentioning.</p>	<p>We think that our discussion of ES is suitably brief.</p>	
<p>28. I wanted to know if any other outcomes were misreported. Was the response criterion used in the published paper the same as the one in the</p>	<p>The outcome ‘response’ was not mentioned in the study protocol, nor</p>	<p>Have made it clear that response was a post hoc variable</p>

protocol?	its amendments.	
29. Were the other secondary outcomes like the CGI reported accurately in the published paper?	Those that were reported were reported accurately	Have made this clear
30. Were the reasons for the dropout of the five citalopram subjects reported?	No	
31. Was there any other discrepancy in how adverse events were reported?	Yes, so have expanded this section	See extensively reworked <i>Mischaracterisation of adverse events</i>
32. On the subject of the Lundbeck trial, why should the company have been expected to know the results if it had not been published? I agree it seems likely, but not certain that they should have known.	We cite an email that demonstrates this.	
33. Discussion: This section should relate the findings back to the literature covered in the introduction, and should mention the similar analysis of study 329.	Done	See extensive rewrite of discussion
34. It needs to stress why this sort of analysis is important.	Done	See extensive rewrite of discussion