

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	How Well are National Guidelines Relating to the General Sales of Aspirin and Paracetamol, Adhered to By Retail Stores: A Mystery Shopper Study
<b>AUTHORS</b>	Molloy, Phillip; Chambers, Ruth; Cork, Tania

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Stephen Waring York Teaching Hospitals NHS Foundation Trust
<b>REVIEW RETURNED</b>	15-Oct-2015

<b>GENERAL COMMENTS</b>	<p>I enjoyed reading this fascinating and novel research paper, which presents an alarming failure of UK retailers to adequately observe guidance concerning the limits for supply of aspirin and paracetamol. There are a couple of points that the authors should consider:</p> <ol style="list-style-type: none"> <li>1. Readers may expect the findings to have been referred to the MHRA for further investigation and enforcement, and it would be helpful to insert a comment to reassure readers that MHRA has been notified.</li> <li>2. Was there any feedback to the specific retailers to highlight their failure to comply with current legislation? This should be included in the Discussion section.</li> <li>3. The authors should include mention of the increasing hazard posed by internet sales, which may not be subject to the same legislative restrictions and difficult to monitor. A reference to a recent UK case of paracetamol poisoning arising from internet purchase could be included: Hewitt D et al. <i>Curr Drug Saf.</i> 2013;8:203-6.</li> <li>4. I like the authors call for clearer labelling but perhaps their proposals could go further. Perhaps a large and distinct warning could be applied to all paracetamol containing products, similar to warning labels applied to tobacco products or hazardous chemicals. Perhaps difficult to achieve but this might actually lessen the tendency to treat these analgesics as an everyday consumer item.</li> </ol>
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<b>REVIEWER</b>	Hank Chang-Tse Du Current: United Lincolnshire Hospitals NHS Trust Previously: School of Pharmacy and Pharmaceutical Sciences, Cardiff University
<b>REVIEW RETURNED</b>	28-Nov-2015

<p><b>GENERAL COMMENTS</b></p>	<p>Formatted comments are also attached as a PDF document for improved readability.</p> <p>Page 1  * Line 33: Stated “22% of stores sold more than 96 tablets of paracetamol”. However, a different figure of 23% was reported in the Results section (Page 3, line 45).</p> <p>Page 2  * Line 5: No definition of non-pharmacy retail outlet  * Line 6: missing close bracket follow OTC  * Line 13: No mention of the difference between General Sales List (GSL) and Pharmacy (P) only medicines, which together are commonly referred to as OTC medicines. The differences between the two legal categories need to be clarified as the maximum pack size for paracetamol and aspirin sold OTC is different for a P and a GSL medicine. P medicines are also subject to more rigorous checks as they can only be sold from a registered retail pharmacy business under the supervision of a pharmacist as well as being unavailable for self-selection.  * Line 14: Law not defined/referenced  * Line 14: Statement needs clarifying as law does not restrict the sale quantity of effervescent tablet of paracetamol/aspirin (reference: RPS Medicines, Ethics and Practice 2015)  * Line 15: Incorrect unit used, should be mg not Gm. Incorrect strength, should be 500mg and 75mg -300mg.  * Line 20: In the introduction section, what were the preliminary investigations that lead to the observation of non-compliance of sale in non-pharmacy retail outlets?  * Line 23: the unit of measure ‘tablets’ not stated (e.g. 3x16 ‘tablets’)  * Line 32: Superdrug and Boots - do these contain an in-store pharmacy? If contain in-store pharmacy, are they similar to supermarkets?  * Line 39: (Methodology) Rationale for the ‘Two-Phase’ design not stated  * Line 39: (Methodology) Target number of stores to be included in the study not stated  * Line 39: (Methodology) No clear inclusion or exclusion criteria described for the selection of retail stores  * Line 39: (Methodology) No clear statement on what outcome measure will be reported  * Line 39: (Methodology) Number of repeated visit by the shopper, if any? Maximum number of repeated visits?  * Line 39: Season in which the study was carried out not stated.  * Line 43: “to span many different bargain and other retail shops” Sentence unclear, do the authors mean ‘include’?  * Line 48: It is unclear whether effervescent tablets were included in the study, which has no legal limit on quantity that could be sold OTC. Products in sachet form was mentioned in the ‘Limitations’ section (page 6, line 37) but is not mentioned here. Similarly, there is no legal restriction on the quantity of powder formula that could be sold OTC.  * Line 52: (Methodology) The £50 incentive for shopper who purchased the most OTC paracetamol/aspirin could have introduced bias and this was not discussed in the ‘Limitations’ section. As an example, each shopper could have been motivated to a different degree, which has led to a difference in their performance (i.e. number of packs purchased) especially when challenged by a member of store staff at the checkout.</p>
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	<p>Page 3</p> <ul style="list-style-type: none"> <li>* Line 29: A description of preliminary research not stated. This preliminary work appears to have enabled the researchers identify stores that are suitable for data collection (i.e. had sufficient stock)</li> <li>* Line 29: Require clarification on whether effervescent preparations are included in the study</li> </ul> <p>Page 4</p> <ul style="list-style-type: none"> <li>* Line 5: 12/36 should be 33%.</li> <li>* Line 20: Unclear what is meant by paracetamol content: is this referring to the combined total quantity of paracetamol in one unit pack of 'flu remedy' or is it per dose unit?</li> <li>* Line 31: Unit of measure is not stated 96 'tablets' (300mg)</li> </ul> <p>Page 5</p> <ul style="list-style-type: none"> <li>* Line 13: Number of retail stores containing warning signs not stated. Please define 'most'.</li> <li>* Line 28: The authors need to report how many of the retailers visited had an in-store pharmacy. If a high proportion of them had an in-store pharmacy then this potentially suggests an under utilisation of pharmacists' skills.</li> <li>* Line: 37: It appears that sachets of paracetamol and/or aspirin had been purchased. These are presumably in powder form. According to the information in RPS Medicines, Ethics and Practice (2015), there is no legal limit on the sales of powder formulations of paracetamol and aspirin. Authors need to clarify how much of products purchased OTC were in powder formulation and amend the results where necessary.</li> </ul> <p>Page 6</p> <ul style="list-style-type: none"> <li>* Line 6: Define 'extremely' poor</li> <li>* Line 7: The statement 'legal quantity by selling more than 96 tablets' is unclear/incorrect as the legal limit for non-effervescent aspirin/paracetamol sold OTC is 100 tablets not 96.</li> <li>* Line 12: 'Bargain stores were more likely to breach national guidelines' is probably not a fair statement, as no statistical analysis had been performed to test the statistical significance in the differences found between the two 'types' of retail stores</li> <li>* Line 24: Hypothesis relating to the 'education level of lay-cashiers' not stated anywhere in the text</li> <li>* Line 31: "were breaching MHRA guidelines and the law" Which piece of legislation is this referring to?</li> <li>* Line 34: The study did not set out to investigate commercial greed and its findings can not substantiate such claim. This statement also contradicts what was mentioned earlier in the same paragraph (line 31), that cashier may not have been aware of MHRA guidance.</li> <li>* Line 39: Suggest changing from 'so easy' to 'potentially more likely'</li> <li>* Line 42: Unit of measure missing; 112 tablets</li> <li>* Line 53: Suggest to use 'may' instead of 'should' recognise</li> </ul> <p>Page 7</p> <ul style="list-style-type: none"> <li>* Line 4: It is unclear what kind of initiate '#paracetamolchallenge' is to the reader</li> <li>* Line 5: Spelling error - wide scale</li> <li>* Line 11: Clarify what is meant by 'adequate warning', such as?</li> <li>* Line 34: Most (if not all) paracetamol-containing products already carry a warning label on the maximum quantity that could taken during any 24-hour period</li> <li>* Line 41: "uneducated lay advice at the check out in stores" - Please provide a reference to support this statement if possible</li> </ul>
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	<p>* Line 43: The suggestion that paracetamol-related harm is more likely to be avoided through staff education can not be substantiated by the results of this study. No reference is provided to support this statement. The relationship between staff education and paracetamol-related harm is likely to be indirect.</p> <p>* Line 44: "This strengthens the need for cashier education and the potential dangers of selling more paracetamol in one transaction, than the guidelines permit on their customers' health" - Sentence is unclear</p> <p>* Line 45: In what ways are alcohol and tobacco more highly regulated than OTC medicines? Please provide a reference.</p> <p>* Line 47: The present study did not investigate whether training programme had been implemented by the retailer, nor did the authors provide a reference that suggests the absence of training is the cause of inappropriate sale.</p> <p>* Line 51: Choice of word 'trigger' not most appropriate. Spelling error 'breach' not 'brech'</p> <p>* Line 53: punitive measures, such as? Reference?</p> <p>* Line 55: Reference 18 (Greene et al. 2006) investigated the OTC sale of paracetamol only. Its results, therefore, share no similarity to the present study as far as the inappropriate sale of aspirin is concerned. The generalisability of the results on the inappropriate sale of aspirin may needs to be reconsidered.</p> <p>Page 8</p> <p>* Line 7: Spelling error - breaching</p> <p>* Line 13: The authors suggested that nothing has changed in terms of the level of paracetamol-related overdose and cited reference 18 (published in 2006) to support this. However, in the introduction section, a more recent study (reference 12) published in 2013 found that there had been a 43% fall in death rate following pack size and sales restriction. Contradictory statements.</p> <p>* Line 15: Unclear by the term 'OTC medication state'</p> <p>* Line 16: There is no reference and the present study provides no evidence to support the claim that:</p> <ul style="list-style-type: none"> <li>a) pharmacists are adhering to MHRA guidance or</li> <li>b) individuals are purchasing paracetamol from non-pharmacy outlets because of refused sale by pharmacists</li> </ul> <p>* Line 25: "widespread non-adherence to national best practice guidelines" would be an assumption without an appropriate evidence to support this claim.</p> <p>* Line 30: "it is likely that stocks of paracetamol will be far less, in people's homes. Consequently, individuals are likely to take less paracetamol which is easily to hand, in a deliberate overdose in response to a sudden crisis" sentence requires more clarity.</p> <p>* Line 29 to 35: Assumptions have been made here and are not stated, as there are other ways of obtaining paracetamol in large quantities (i.e. through internet).</p> <p>Figure 1: the accompanying text/title is unclear in explaining that each bar represents the average number of tablets/capsules sold per brand per transaction per store.</p> <p>Figure 2: as for figure 1</p> <p>Figure 3: near impossible to distinguish the different shades of blue. Suggest using a bar chart with letter coding.</p> <p>Reference 10: Check format and year of publish is incorrect (published in 2009, not 2015).</p>
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<b>REVIEWER</b>	Emery R Eaves University of Arizona, United States
<b>REVIEW RETURNED</b>	30-Nov-2015

<b>GENERAL COMMENTS</b>	<p>Overall this is an excellent paper and a very well described and interesting study. I recently published a paper on OTC medication use among chronic pain sufferers (Eaves 2015) and will be interested to cite these findings in future research. That said, I recommend some revision of the discussion and conclusion to be better aligned with the results and to avoid overarching claims and recommendations. Many of the recommendations can be kept as suggestions for future research or possible solutions, but it is unlikely that regulations are the sole answer to reducing overdose and many of the claims put forth in the discussion are not in line with the results (e.g. how much would be in consumers homes and how likely it is that this would reduce overdose death). I would like to see this paper published with the following minor revisions:</p> <p>Page 3, line 44 “Sixty two shops were selected to span many different bargain and other retail shops as possible (36 supermarkets and 26 bargain stores). The word “as” is missing between span and many.</p> <p>Page 4, line 16, “of” is missing after 98%</p> <p>In the section on interesting comments from mystery shoppers, I very much appreciate the inclusion of accounts of what shoppers were told. It seems unbalanced, though, to have positive accounts for phase 1 and to use phase 2 to describe the negative accounts (times shoppers were not allowed). Why is the phase 1 divided into specific examples and phase 2 is not? Maybe a little more explanation is needed, or a specific example listed similarly for phase 2. This is a minor suggestion, but the comments from phase 1, although interesting and needed, don’t seem to follow with the rest of the format. Please add a few overarching comments or divide the next section similarly.</p> <p>Page 5, lines 22-27 need editing for clarity. There seem to be a few words missing.</p> <p>“Limitations” Should be reported after discussion rather than at the end of results.</p> <p>Page 6, lines 37-39, although important to note the connection between disregard for regulation and potential overdose, the wording here may be overly inflating such risk. There are many other factors contributing to patient overdose (e.g. patients can go to the same store every day to buy these medications and obtain large amounts regardless of whether cashiers sell it to them). I would suggest more neutral wording here, and possibly a call also for educating consumers about the risks. It takes away from the strength of your findings and argument to overemphasize the connection to overdose. I would suggest deleting this sentence, as it also seems out of place coming before the next paragraph and is not necessary.</p> <p>Page 7, lines 3-5: I’m not familiar with the “paracetamol challenge” and cannot tell from the information provided how it is putting young people at risk. Are they being asked not to take paracetamol as part</p>
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	<p>of the challenge and overdosing because they don't participate, or is participation in the challenge causing the hospitalization? Please clarify this and add a bit more information about what the challenge is for international readers. The next sentence "This once again highlights the widescale public ignoranceto paracetamol dangers" is not well supported by the paragraph. I would recommend deleting sentences like this that broaden the argument away from the findings of this paper. The results are important and make a strong case without adding editorializing comments like this one.</p> <p>Page 7, line 20, endquote is missing</p> <p>Page 7, paragraph starting at line 20: This paragraph is another instance of recommendations that seem outside the scope of the results/arguments put forth in this paper. Maybe these suggestions for regulation should be put forth in the conclusion as a suggestion that future research is needed to determine whether (insert your recommendations) would lead to decreases in overdose....</p> <p>The next paragraph, pg 7, lines 31-39 is also well outside the argument of this paper. Although probably excellent recommendations, this is not supported by the research offered in the paper and would need to be supported with research.</p> <p>Page 7, line 41: the use of "purely uneducated" is unnecessary and problematic unless you provide strong evidence of lack of education among cashiers. Simply saying "reliance on lay advice" is sufficient and comes across as less of a judgment on the part of the authors.</p> <p>As mentioned above, the paragraph starting at line 41, page 7, includes several instances of offering opinions that are not supported by the results. Particularly comments such as "It seems bizarre that alcohol and tobacco are so highly regulated and OTC medications are not" are not supported by data (e.g. comparisons of the health risks associated with these drugs) and are not particularly relevant to the argument presented. All such comments need to be removed.</p> <p>Conclusion, page 8, lines 30-32: The authors have not presented data on how much aspirin or paracetamol is in people's homes so how much the amount in homes is influenced by the sale is unknown. The data presented could make a much stronger case for increased regulation if the discussion and conclusion remain better focused on the findings and data presented and the implications of that, rather than making broad claims about how much would be in people's homes and how much less likely overdose would be if regulations were enforced. Questions such as: Are people ignorant of or resistant to regulation? Would consumers obtain less of these medications if regulated? And others are not addressed by this particular study and are places in need of future research. The results section is very strong and makes a very good case for regulation and future research, but the authors should be careful not to overgeneralize and make overly broad claims, which take away from their overall argument.</p>
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## VERSION 1 – AUTHOR RESPONSE

Stephen Waring  
York Teaching Hospitals NHS Foundation Trust

Please leave your comments for the authors below

I enjoyed reading this fascinating and novel research paper, which presents an alarming failure of UK retailers to adequately observe guidance concerning the limits for supply of aspirin and paracetamol. There are a couple of points that the authors should consider:

1. Readers may expect the findings to have been referred to the MHRA for further investigation and enforcement, and it would be helpful to insert a comment to reassure readers that MHRA has been notified.

We agree and have added “Finally, we want to assure readers that our recommendations have been passed onto the MHRA and we encourage their support to drive change.” In the conclusion.

2. Was there any feedback to the specific retailers to highlight their failure to comply with current legislation? This should be included in the Discussion section.

Included “Furthermore, all retail stores have been informed with detailed descriptions of potential floors that we identified in their normal operating procedures.” In the conclusion.

3. The authors should include mention of the increasing hazard posed by internet sales, which may not be subject to the same legislative restrictions and difficult to monitor. A reference to a recent UK case of paracetamol poisoning arising from internet purchase could be included: Hewitt D et al. *Curr Drug Saf.* 2013;8:203-6.

We have included these concerns.

4. I like the authors call for clearer labelling but perhaps their proposals could go further. Perhaps a large and distinct warning could be applied to all paracetamol containing products, similar to warning labels applied to tobacco products or hazardous chemicals. Perhaps difficult to achieve but this might actually lessen the tendency to treat these analgesics as an everyday consumer item.

We feel that making the packaging similar to tobacco and alcohol would not get our message across since these are to discourage users purchasing the items and the health implications of using the products.

Hank Chang-Tse Du  
Current: United Lincolnshire Hospitals NHS Trust  
Previously: School of Pharmacy and Pharmaceutical Sciences, Cardiff University

Page 1

\* Line 33: Stated “22% of stores sold more than 96 tablets of paracetamol”. However, a different figure of 23% was reported in the Results section (Page 3, line 45).

Amended.

Page 2

\* Line 5: No definition of non-pharmacy retail outlet  
Definition (stores without a pharmacy).

\* Line 6: missing close bracket follow OTC

Amended.

\* Line 13: No mention of the difference between General Sales List (GSL) and Pharmacy (P) only medicines, which together are commonly referred to as OTC medicines. The differences between the two legal categories need to be clarified as the maximum pack size for paracetamol and aspirin sold

OTC is different for a P and a GSL medicine. P medicines are also subject to more rigorous checks as they can only be sold from a registered retail pharmacy business under the supervision of a pharmacist as well as being unavailable for self-selection.

We acknowledge that while it is technically correct to call them GSL, we feel readers will better grasp the term OTC. Since we have not used the term OTC inappropriately we feel that keeping this term would be acceptable.

\* Line 14: Law not defined/referenced

Referenced.

\* Line 14: Statement needs clarifying as law does not restrict the sale quantity of effervescent tablet of paracetamol/aspirin (reference: RPS Medicines, Ethics and Practice 2015)

Added that the use of effervescent medications were not used.

\* Line 15: Incorrect unit used, should be mg not Gm. Incorrect strength, should be 500mg and 75mg - 300mg.

Correction made.

\* Line 20: In the introduction section, what were the preliminary investigations that lead to the observation of non-compliance of sale in non-pharmacy retail outlets?

We feel that we have already answered this question in the paper whereby we noticed some non-pharmacy retail outlets were clearly breaching MHRA guidelines advertising 3 for 2 (3 x 16 500mg) paracetamol.

\* Line 23: the unit of measure 'tablets' not stated (e.g. 3x16 'tablets')

Correction made.

\* Line 32: Superdrug and Boots - do these contain an in-store pharmacy? If contain in-store pharmacy, are they similar to supermarkets?

Added that 8 stores contained pharmacies and that shoppers avoided using the pharmacy checkouts.

\* Line 39: (Methodology) Rationale for the 'Two-Phase' design not stated

Study involved two stages as opposed to phases. Term phase replaced with stage.

\* Line 39: (Methodology) Target number of stores to be included in the study not stated

Included target number in methods.

\* Line 39: (Methodology) No clear inclusion or exclusion criteria described for the selection of retail stores

Stated there is no exclusion criteria. Inclusion criteria stated stores within easy access to town centers for example along bus routes.

\* Line 39: (Methodology) No clear statement on what outcome measure will be reported

Amended in the methodology.

\* Line 39: (Methodology) Number of repeated visit by the shopper, if any? Maximum number of repeated visits?

Amended in methods that no shopper revisited a store.

\* Line 39: Season in which the study was carried out not stated.

Season has been included in the methodology.

\* Line 43: "to span many different bargain and other retail shops" Sentence unclear, do the authors mean 'include'?

Amended.

\* Line 48: It is unclear whether effervescent tablets were included in the study, which has no legal limit on quantity that could be sold OTC. Products in sachet form was mentioned in the 'Limitations' section (page 6, line 37) but is not mentioned here. Similarly, there is no legal restriction on the quantity of powder formula that could be sold OTC.

Stated that no effervescence used.

\* Line 52: (Methodology) The £50 incentive for shopper who purchased the most OTC

paracetamol/aspirin could have introduced bias and this was not discussed in the 'Limitations' section.

As an example, each shopper could have been motivated to a different degree, which has led to a difference in their performance (i.e. number of packs purchased) especially when challenged by a

member of store staff at the checkout.  
This is an important point and has been included into imitations.

#### Page 3

\* Line 29: A description of preliminary research not stated. This preliminary work appears to have enabled the researchers identify stores that are suitable for data collection (i.e. had sufficient stock) We felt we had addressed this in the introduction.

\* Line 29: Require clarification on whether effervescent preparations are included in the study  
Addressed in methods.

#### Page 4

\* Line 5: 12/36 should be 33%.

Correction made.

\* Line 20: Unclear what is meant by paracetamol content: is this referring to the combined total quantity of paracetamol in one unit pack of 'flu remedy' or is it per dose unit?  
Clarity has been improved – refers to entire 'flu remedy pack.

\* Line 31: Unit of measure is not stated 96 'tablets' (300mg)  
Correction made.

#### Page 5

\* Line 13: Number of retail stores containing warning signs not stated. Please define 'most'.  
Added 41/62 stores contained warnings.

\* Line 28: The authors need to report how many of the retailers visited had an in-store pharmacy. If a high proportion of them had an in-store pharmacy then this potentially suggests an under utilisation of pharmacists' skills.

Added 8/62 stores contained pharmacies.

\* Line: 37: It appears that sachets of paracetamol and/or aspirin had been purchased. These are presumably in powder form. According to the information in RPS Medicines, Ethics and Practice (2015), there is no legal limit on the sales of powder formulations of paracetamol and aspirin. Authors need to clarify how much of products purchased OTC were in powder formulation and amend the results where necessary.

No sachets of paracetamol/aspirin were purchase. Only sachets containing 'flu remedies were purchased in 'stage 2'.

#### Page 6

\* Line 6: Define 'extremely' poor  
Deleted extremely.

\* Line 7: The statement 'legal quantity by selling more than 96 tablets' is unclear/incorrect as the legal limit for non-effervescent aspirin/paracetamol sold OTC is 100 tablets not 96.  
Effervescences forms were not purchased .

\* Line 12: 'Bargain stores were more likely to breach national guidelines' is probably not a fair statement, as no statistical analysis had been performed to test the statistical significance in the differences found between the two 'types' of retail stores  
Changed language to 'tended'. No statistical analysis was performed.

\* Line 24: Hypothesis relating to the 'education level of lay-cashiers' not stated anywhere in the text  
Language changed.

\* Line 31: "were breaching MHRA guidelines and the law" Which piece of legislation is this referring to?

Reference added.

\* Line 34: The study did not set out to investigate commercial greed and its findings can not substantiate such claim. This statement also contradicts what was mentioned earlier in the same paragraph (line 31), that cashier may not have been aware of MHRA guidance.

Language changed.

\* Line 39: Suggest changing from 'so easy' to 'potentially more likely'

Language change.

\* Line 42: Unit of measure missing; 112 tablets

Unit amended.

\* Line 53: Suggest to use 'may' instead of 'should' recognise

Language altered.

Page 7

\* Line 4: It is unclear what kind of initiate '#paracetamolchallenge' is to the reader

Further elaboration made to increase clarity.

\* Line 5: Spelling error - wide scale

Corrected.

\* Line 11: Clarify what is meant by 'adequate warning', such as?

Further elaboration made. "for example verbally informing customers that both products contain paracetamol and should not be taken in conjunction with one another".

\* Line 34: Most (if not all) paracetamol-containing products already carry a warning label on the maximum quantity that could be taken during any 24-hour period

We acknowledge this but we are stating the front packaging needs to be more explicit to easily identify to consumers that products contain paracetamol/aspirin.

\* Line 41: "uneducated lay advice at the check out in stores" - Please provide a reference to support this statement if possible

Language changed, no reference needed.

\* Line 43: The suggestion that paracetamol-related harm is more likely to be avoided through staff education can not be substantiated by the results of this study. No reference is provided to support this statement. The relationship between staff education and paracetamol-related harm is likely to be indirect.

Language altered, no reference needed.

\* Line 44: "This strengthens the need for cashier education and the potential dangers of selling more paracetamol in one transaction, than the guidelines permit on their customers' health" - Sentence is unclear

Sentence amended.

\* Line 45: In what ways are alcohol and tobacco more highly regulated than OTC medicines? Please provide a reference.

Reference added.

\* Line 47: The present study did not investigate whether training programme had been implemented by the retailer, nor did the authors provide a reference that suggests the absence of training is the cause of inappropriate sale.

\* Line 51: Choice of word 'trigger' not most appropriate. Spelling error 'breach' not 'breech'

Language modified.

\* Line 53: punitive measures, such as? Reference?

\* Line 55: Reference 18 (Greene et al. 2006) investigated the OTC sale of paracetamol only. Its results, therefore, share no similarity to the present study as far as the inappropriate sale of aspirin is concerned. The generalisability of the results on the inappropriate sale of aspirin may need to be reconsidered.

Language modified.

Page 8

\* Line 7: Spelling error - breaching

Correction made.

\* Line 13: The authors suggested that nothing has changed in terms of the level of paracetamol-related overdose and cited reference 18 (published in 2006) to support this. However, in the

introduction section, a more recent study (reference 12) published in 2013 found that there had been a 43% fall in death rate following pack size and sales restriction. Contradictory statements. Sentence modified. We appreciate there has been change but we feel more can be done since the previous study showing change indicated it was the MHRA guidelines which attributed to them. We feel that these guidelines are not being adhered, thus through enforcing them we would see a further decrease in paracetamol misuse.

\* Line 15: Unclear by the term 'OTC medication state'

Language modified.

\* Line 16: There is no reference and the present study provides no evidence to support the claim that:

a) pharmacists are adhering to MHRA guidance or

b) individuals are purchasing paracetamol from non-pharmacy outlets because of refused sale by pharmacists

We have removed this comment.

\* Line 25: "widespread non-adherence to national best practice guidelines" would be an assumption without an appropriate evidence to support this claim.

Language altered.

\* Line 30: "it is likely that stocks of paracetamol will be far less, in people's homes. Consequently, individuals are likely to take less paracetamol which is easily to hand, in a deliberate overdose in response to a sudden crisis" sentence requires more clarity.

Language altered.

\* Line 29 to 35: Assumptions have been made here and are not stated, as there are other ways of obtaining paracetamol in large quantities (i.e. through internet).

Figure 1: the accompanying text/title is unclear in explaining that each bar represents the average number of tablets/capsules sold per brand per transaction per store.

Title modified.

Figure 2: as for figure 1

Title modified.

Figure 3: near impossible to distinguish the different shades of blue. Suggest using a bar chart with letter coding.

Pie chart modified with lettering and font made larger.

Reference 10: Check format and year of publish is incorrect (published in 2009, not 2015).

Reference amended.

Emery R Eaves

University of Arizona, United States

Please leave your comments for the authors below

Overall this is an excellent paper and a very well described and interesting study. I recently published a paper on OTC medication use among chronic pain sufferers (Eaves 2015) and will be interested to cite these findings in future research. That said, I recommend some revision of the discussion and conclusion to be better aligned with the results and to avoid overarching claims and recommendations. Many of the recommendations can be kept as suggestions for future research or possible solutions, but it is unlikely that regulations are the sole answer to reducing overdose and many of the claims put forth in the discussion are not in line with the results (e.g. how much would be in consumers homes and how likely it is that this would reduce overdose death). I would like to see this paper published with the following minor revisions:

Page 3, line 44 "Sixty two shops were selected to span many different bargain and other retail shops as possible (36 supermarkets and 26 bargain stores).

The word "as" is missing between span and many.

Text modified.

Page 4, line 16, "of" is missing after 98%

Text modified.

In the section on interesting comments from mystery shoppers, I very much appreciate the inclusion of accounts of what shoppers were told. It seems unbalanced, though, to have positive accounts for phase 1 and to use phase 2 to describe the negative accounts (times shoppers were not allowed). Why is the phase 1 divided into specific examples and phase 2 is not? Maybe a little more explanation is needed, or a specific example listed similarly for phase 2. This is a minor suggestion, but the comments from phase 1, although interested and needed, don't seem to follow with the rest of the format. Please add a few overarching comments or divide the next section similarly. We feel that both sections highlight negative accounts in both stages.

Page 5, lines 22-27 need editing for clarity. There seem to be a few words missing.

Text modified.

"Limitations" Should be reported after discussion rather than at the end of results.

Limitations moved to the correct section.

Page 6, lines 37-39, although important to note the connection between disregard for regulation and potential overdose, the wording here may be overly inflating such risk. There are many other factors contributing to patient overdose (e.g. patients can go to the same store every day to buy these medications and obtain large amounts regardless of whether cashiers sell it to them). I would suggest more neutral wording here, and possibly a call also for educating consumers about the risks. It takes away from the strength of your findings and argument to overemphasize the connection to overdose. I would suggest deleting this sentence, as it also seems out of place coming before the next paragraph and is not necessary.

We do not think we have overinflated the risk. We observed that 58% and 57% retailers sold more than the MHRA guidelines recommended for paracetamol and aspirin respectively and that 23% and 28% retailers were willing to sell  $\geq 96$  tablets of paracetamol or aspirin. We stated in our discussion that "around three out of five shops breaching national guidelines and one in four shops encroaching or breaking the legal threshold by selling more than  $\geq 96$  tablets of either paracetamol (500mg) or aspirin (75-300mg) in one transaction". We feel that representing the data in this manner gives readers a better interpretation of our results.

Page 7, lines 3-5: I'm not familiar with the "paracetamol challenge" and cannot tell from the information provided how it is putting young people at risk. Are they being asked not to take paracetamol as part of the challenge and overdosing because they don't participate, or is participation in the challenge causing the hospitalization? Please clarify this and add a bit more information about what the challenge is for international readers. The next sentence "This once again highlights the wide scale public ignorance to paracetamol dangers" is not well supported by the paragraph. I would recommend deleting sentences like this that broaden the argument away from the findings of this paper. The results are important and make a strong case without adding editorializing comments like this one.

We have improved the clarity of the relevance of the paracetamol challenge to our study and how this is further evidence of ignorance by the general public to the dangers of paracetamol.

Page 7, line 20, endquote is missing

We are not sure what endquote is missing? 'Flu is short for influenza.

Page 7, paragraph starting at line 20: This paragraph is another instance of recommendations that

seem outside the scope of the results/arguments put forth in this paper. Maybe these suggestions for regulation should be put forth in the conclusion as a suggestion that future research is needed to determine whether (insert your recommendations) would lead to decreases in overdose....  
 Moved to conclusion.

The next paragraph, pg 7, lines 31-39 is also well outside the argument of this paper. Although probably excellent recommendations, this is not supported by the research offered in the paper and would need to be supported with research.  
 Moved to conclusion.

Page 7, line 41: the use of “purely uneducated” is unnecessary and problematic unless you provide strong evidence of lack of education among cashiers. Simply saying “reliance on lay advice” is sufficient and comes across as less of a judgment on the part of the authors.  
 Language modified.

As mentioned above, the paragraph starting at line 41, page 7, includes several instances of offering opinions that are not supported by the results. Particularly comments such as “It seems bizarre that alcohol and tobacco are so highly regulated and OTC medications are not” are not supported by data (e.g. comparisons of the health risks associated with these drugs) and are not particularly relevant to the argument presented. All such comments need to be removed.  
 Reference added to support tobacco and alcohol regulations.

Conclusion, page 8, lines 30-32: The authors have not presented data on how much aspirin or paracetamol is in people’s homes so how much the amount in homes is influenced by the sale is unknown. The data presented could make a much stronger case for increased regulation if the discussion and conclusion remain better focused on the findings and data presented and the implications of that, rather than making broad claims about how much would be in people’s homes and how much less likely overdose would be if regulations were enforced. Questions such as: Are people ignorant of or resistant to regulation? Would consumers obtain less of these medications if regulated? And others are not addressed by this particular study and are places in need of future research. The results section is very strong and makes a very good case for regulation and future research, but the authors should be careful not to overgeneralize and make overly broad claims, which take away from their overall argument.  
 We have restructured and altered some of the language to ensure the data we found is the epicenter of our argument. We feel that including those other issues found by our shoppers will stimulate discussion and potential further research into those areas.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Dr W. Stephen Waring York Teaching Hospitals NHS Foundation Trust York, United Kingdom
<b>REVIEW RETURNED</b>	15-Dec-2015

<b>GENERAL COMMENTS</b>	This remains a very interesting paper, and I commend the authors for addressing the points raised by reviewers. I have no additional comments.
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<b>REVIEWER</b>	Emery R Eaves Post-doctoral Research Associate, Dept. of Family and Community Medicine, University of Arizona, United States
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<b>REVIEW RETURNED</b>	16-Dec-2015
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<b>GENERAL COMMENTS</b>	My concerns were addressed by the revisions. I think this paper makes an important contribution to understanding the overuse of OTC medication.
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