Author’s response to reviews

Title: Randomised controlled trial of an intervention to improve parental knowledge and management practices of fever

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Author’s response to reviews:

HRB Clinical Research Facility and School of Public Health, University College Cork, Ireland.

Dr Maria Zalm,
Editor, BMC Pediatrics.

15 April 2019

Dear Dr Zalm,
Thank you for sending our study, “Randomised controlled trial of an intervention to improve parental knowledge and management practices of fever” out for review. The reviewers gave thorough consideration to the paper and their comments have improved the paper immensely. We have made major revisions to the paper. We have now responded to the reviewer’s comments and address each of them below, as well as in a tracked changes version of the manuscript. We trust that this answers all queries. If we are required to make further changes, we are happy to do so.

Please note, by agreement with the authors, we have changed the authorship line-up slightly. Laura Sahm will be second author and Frances Shiely will be last and the corresponding author. We have all agreed that this better reflects the level of contribution to the paper. I note the
editorial policy of a change of authorship form. I would be grateful if you would let me know if this is necessary given we are at the revision stage.

If you have any further queries, please do not hesitate to contact me.

Sincerely yours,
Frances Shiely
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Response to Reviewers

Reviewer 1: R. Oostenbrink
The paper addresses an important topic, how to inform parents on fever, and evaluate the effect of developed information material in a trial. I have 3 major comments:

1. The manuscript very much focus on knowledge of fever in terms of definition temperature, and management strategies. Knowledge of alarming signs and risks of fever is not included at all in this paper?

We thank the reviewer for his helpful suggestion. This paper is part of a larger PhD thesis which focused on knowledge, attitudes and beliefs of parents on fever and febrile illness in children. We initiated the study by generating an evidence base exploring what factors influence the knowledge, attitudes and beliefs of parents around fever and febrile illness in children. We generated the information resources for parents arising from this research and this is why this paper is focused as such on temperature definition (which was a key concern for parents) and the management strategies around fever. As pharmacists and physicians, we were keenly interested in antipyretic use, as in our jobs, we are all too aware of the misuse of antipyretics. Hence, the temperature definition for fever is an area that requires education as well as the management of fever, without the use of antipyretics, if possible. Evidence from our previous study, “Parental knowledge, attitudes and beliefs regarding fever in children: an interview study” (Kelly et al. 2016) shows that parents are aware of the risks of fever. They stated there was a need for an education initiative, which prompted the design of the information leaflet and an assessment of its effectiveness. We have revised the introduction of the paper, to give the study context. Changes are too numerous to present here but please see the tracked changes document.

2. The manuscript describes the trial and a qualitative analysis of the developed material. This is confusing, as they include the qualitative analysis in the part describing the comparison of intervention group and control group (although the qualitative analysis comes from the intervention group). Next I wonder what the value is of this qualitative analysis as they also performed such analysis in refs 1,2,6. So, I would expect a more thorough description of the value of these additional results to the previous refs. Anyway, I suggest to include this part of the analysis in a separate paragraph.
We agree with the reviewer. This is confusing. We also agree that it doesn’t add to the paper. We have rewritten the results section having considered the reviewer’s comments, added some tables and excluded the qualitative analysis.

3. The trial compares knowledge of parents on fever at two timepoints after providing information material (intervention) to a control group. There is no T-zero comparison of knowledge between the groups before the intervention. One could argue that if randomised properly, differences between the intervention and control group are related to the intervention. However, the groups seem quite different (nationality, age children, etc). In this sense lacking a Tzero comparison makes that current conclusions on the effect of the intervention are far too strong, and should be more nuanced. Next, please explain why not a Tzero comparison has been performed. Discuss the effects of potential differences in the compared groups.

We thank the reviewer for his helpful comment. We did not seek the parent’s knowledge level prior to receiving the intervention. It would have strengthened the study considerably. We have however still shown knowledge increase post intervention, and knowledge retention after two weeks. This is a small study and one which we intend to repeat on a larger scale, we will take the reviewers advice and attain T-zero knowledge levels for our larger study. We have toned down the effect of the intervention in the results and conclusions section. We have also highlighted the differences in the compared groups in the methodology section under the heading “participants and demographics”.

Further comments:
Study outcomes:
4. Why is the primary outcome knowledge of definition of fever, as even literature applies different definitions (over 38 vs over 38.5 degrees C).

We thank the reviewer for this comment. As practitioners, we know from experience that parents administer antipyretics based on the temperature of the child. As we wish to change the incorrect use and overuse of antipyretics we wish to assess how much parents know about fever and what is the correct definition of fever. We are aware of the different definitions of fever in the literature. We chose ≥38 degrees Celsius as the definition of fever as per NHS guidelines ≥38 degrees Celsius, and this is the definition we have used throughout this study. https://www.nhs.uk/conditions/fever-in-children/ It is also defined as such in Marcy, S. M., Kohl, K. S., Dagan, R., Nalin, D., Blum, M., Jones, M. C., ... &amp; O’Brien, K. (2004). Fever as an adverse event following immunization: case definition and guidelines of data collection, analysis, and presentation. Vaccine, 22(5-6), 551-556.

Sample size:
5. For measurement on second timepoint the power is not achieved, as 50 persons per group are required. This is not discussed at all.

This is correct. There was dropout, and this is to be expected in a follow-up study. We have acknowledged this drop out now in the limitations of the study section.
Datatreatment/analysis
6. See my previous remark to differences in control/intervention group. One could argue that evaluation of the effect of the intervention should be controlled for potential confounders or differences in the two groups. Why not used a repeated measurement approach including the comparison at various timepoints?

We accept the reviewers point above. We consulted a statistician, Dr Darren Dahly, HRB Clinical Research Facility, Cork for advice on the appropriate analysis for this study. There were no associations between the primary outcome and any of the sociodemographic factors so controlling for potential confounders in the two groups was not deemed necessary. We were interested in establishing if the intervention arm or the control arm were more likely to select the correct answer (given the range of possible answers), and if this was the same at the two time points. We were advised by Dr Dahly that logistic regression was the appropriate methodology to show this. Repeated measures methodology would show the difference between the intervention arms at the two time points, or the difference in control arms at the two time points, and we were not interested in this for this paper.

Results
7. These are written very complicated. The main question is what the effect of the intervention is on outcomes. So only oddsratios for the intervention at the timepoints are informative. A table with the percentages for the different outcomes could be provided additionally. Please provide better insight what is the main outcome and the secondary ones

We agree with the reviewer. This was very complicated. We have completely rewritten the results section and added tables as suggested.

8. The results are not coherent with the described secondary outcomes (improvements in knowledge of management practices to use antipyretics and tepid sponging (methods) versus use medication, alternating medication, using medication together, use tepid sponging, satisfaction leaflet (results).

Thank you to the reviewer for pointing this out. We have rewritten the methods section to better describe the primary and secondary outcomes of this study and they are now consistent with respect to the methods and the results sections.

9. I wonder what the value is of including parents with children aged 16-29 years in this analysis, as these parents reflect old knowledge of fever (usually young children are affected by fever most, with highest risks, so they are the main focus of such interventions, education of parents on fever currently may be different from 10-20 years ago).

We thank the reviewer for this comment. Our inclusion criteria for recruiting parents was that they have a child less than 5 years of age. This did not exclude parents who had some older children additionally. We agree with the reviewer that they will have more experience parenting, but the number of children in the family or the ages of the other children should not effect this intervention as we are testing knowledge after reading the leaflet, and retention two weeks later.
Discussion
10. The discussion goes beyond the topic of the trial. I would expect that if the development of the information material is published before (ref 1,2,6) how to provide information etc is not a topic of this paper (paragraph 2 and 3 of disc).

Thank you to the reviewer for this comment. We agree with him on these points. We have now amended the discussion, and also toned it down, to accurately reflect the information presented and the need for further study to validate other claims.

11. Costeffectiveness (paragraph 4 disc) is not a topic of this study?
Thank you to the reviewer. We agree, costeffectiveness is not an outcome in this study. We have deleted any references to costeffectiveness.

12. Discussion of the results given limitations of the study (see above) should be extended
Thank you to the reviewer. We have we have rewritten the limitations of the study and included the attrition between T1 and T2.

Conclusions:
13. Please focus more on the primary outcome and the conclusions should be more nuanced.
Thank you to the reviewer for this helpful comment. We have now rewritten the conclusions with a focus more on the primary outcome (as suggested by reviewer 2) and the conclusions are more nuanced as requested.

Reviewer 2

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
No - there are major issues

STATISTICS - Is the use of statistics in the manuscript appropriate?
No - there are issues with the statistics in the study
INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This study asks an interesting question on a common ED complaint. However, there are some significant methodological limitations that may negatively impact translation of results into practice.

REQUESTED REVISIONS:
1. The hypothesis needs to be stated.
   We thank the reviewer for this comment and note it was also requested by the other reviewer. We have now clearly stated the primary and secondary outcomes in the study both in the methods section and the results section. We have also presented the results section to coincide with the stated outcomes.

2. The sample size seems quite low given the multicentre nature so more information is needed to justify the sample size such as the minimal clinically important difference.
   Thank you for this comment. We based our sample size on a MCID of 27%. This is large and resulted in a small sample size. We have explained this in greater detail now in the methods section.

3. The primary outcome needs to be clearly stated.
   Thank you to the reviewer for this helpful comment. We have rewritten the methods section and the results sections, based on recommendations from you and the other reviewer. The primary and secondary outcomes are now clearly stated and analysed accordingly and results presented.

4. A repeated measures statistic should have been employed rather than logistic regression for each question.
   We accept the reviewers point above. We consulted a statistician, Dr Darren Dahly, HRB Clinical Research Facility, Cork for advice on the appropriate analysis for this study. We were interested in establishing if the intervention arm or the control arm were more likely to select the correct answer (given the range of possible answers), and if this was the same at the two time points. We were advised by Dr Dahly that logistic regression was the appropriate methodology to show this. Repeated measures methodology would show the difference between the intervention arms at the two time points, or the difference in control arms at the two time points, and we were not interested in this for this paper.
ADDITIONAL REQUESTS/SUGGESTIONS:

5. The authors should provide details on how the knowledge survey was developed and should include the actual survey.

Thank you to the reviewer for this helpful suggestion. We have added details in the methods section under the heading “Information Leaflet Design”. We have also included the survey we used in Appendix 2 and the questionnaires we used at T1 and T2 in appendices 3 and 4.

6. Analysis of the primary outcome should be based on intention to treat.

Thank you to the reviewer for this helpful comment. The analysis was conducted on an intention-to-treat basis. In one part of the paper we said that “data were analysed by MK per protocol”. What MK meant was per the previously published protocol. This was a poor description which led to confusion and we have rectified this and said the data were analysed on an intention to treat basis.