Author's response to reviews

Title: Use of traditional cooking fuels and the risk of young adult cataract in rural Bangladesh: a hospital-based case-control study

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Manuscript: Use of traditional cooking fuels and the risk of young adult cataract in rural Bangladesh: a hospital-based case-control study

Responses to Reviewers’ Comments

Reviewer #1 Version 1

Major compulsory revisions

1. The abstract should be rewritten since the results and conclusions suggest that the study provides evidence that certain types of biomass fuels are a risk factor for cataract and support the results of other studies. Since there is no comparison with clean fuels this is misleading.

The abstract has been rewritten accordingly.

2. More information is required on the data collection, in particular possible bias from the author who both carried out the eye examinations, conducted the interviews and carried out the statistical analysis. Why was a semi-structured questionnaire used? There is a concern that using a semi structured questionnaire might be particularly subject to interviewer bias, or to errors resulting from variation in the way of asking questions. This and the fact that the author both examined and interviewed people must be included in the Discussion under limitations.

The author did not carry out the eye examinations, although the first author did conduct the interviews and jointly with the second author did the data analysis. The questionnaire consisted of closed-ended questions, except for the filling in of the year-fuel table, which required start times and end times of exposures to be indicated. Whether this should be considered semi-structured or structured is debatable. The authors do not think such a questionnaire is subject to interviewer bias or errors resulting from the way in which questions are asked. Knowledge of the status of the interviewee could, theoretically, introduce interviewer bias, but the largely structured content of the questionnaire should have minimized this. The discussion of limitations has been revised accordingly. (Discussion, para 13)

3. Results. No information is provided on response rates. The authors stated earlier in the Methods that people who refused to participate were excluded. It is a drawback of the study that information is not available on either non response or characteristics of non responders as this could be a source of selection bias. This limitation must be addressed in the Discussion.

Details of response rate are now included in the Results section. Non-response was minimal. (Results, para 1)

4. In the Introduction the authors speculate that the higher rates of cataract in women might reflect exposure to biomass cooking fuels but they do not present
any results by sex. The authors should give the results by sex in the present study. It was surprising that that such a high proportion of people stated they cooked regularly as this must include men.

The patterns of exposure to the main biomass fuels are now included in the paper (Table 4 and Results, para 11)). The patterns were quite different for males and females.

5. Table 3 and the analyses shown in Tables 4 and 5 are based on “ever” versus “never” for various types of cooking fuels. As the “never” group includes other types of fuel and as “clean” cooking fuels (kerosene or gas) use was very rare (only 7 controls and no cases), the analysis is contrasting different types of cooking fuels all of which are “unclean fuels”. This analysis may be the reason why cow dung appears to be “protective” because it is being compared to other types of biomass fuels i.e. to rice and wood crops but not to clean fuels. The authors should show for each case/control group the numbers using each of the different types of fuels both alone and in various combinations. The analysis should use this measure to calculate the Odds ratios for different combinations of biomass fuels. It is not at all clear what would be the reference group. Ideally it would be clean fuels but the numbers are too small. The authors must consider that a major limitation of their study is that homogeneity in the use of biomass fuels in their study population makes it difficult to examine biomass fuels as a risk factor.

The inclusion of the details of patterns of use (Table 4) should clear up some of the problems concerning the nature of the reference groups. The model of lifetime exposure (Table 6) should reflect the independent effect of each fuel type, adjusted for the magnitude of exposure to each other fuel type, and therefore the inverse association of cow dung use with case status should not be the result of cow-dung users using less wood/ dry leaves and rice straw.

6. The discussion is well written but the literature review must include the comment that previous studies have used either clean fuels as the comparison group or other indicators of exposure such as type of stove or the analysis has been carried out only in women.

This information has now been included in the Discussion. (Discussion, paras 3 & 5)

**Minor Essential Revisions**

1. **Case control recruitment**

   A key problem in case control studies is possible biases in case and control selection. It is important therefore that the authors give more information on how cases and controls were selected or selected themselves to the clinics. How was information on the floating hospital advertised in the target population? Was proximity to the hospital a factor in attendance? Were people referred from village health centres or other sources? Why did the authors choose 2 different types of controls per case and why did they use hospital rather than population
based controls?

The (new) location of the floating hospital is advertised in the local media before and during its mooring at each location. As there are relatively poor healthcare facilities offering healthcare provision above primary level throughout most of rural Bangladesh, the arrival of the floating hospital is regarded as a rare opportunity to obtain specialized care at minimal cost. The potential catchment area is thus likely to be wide, although almost certainly proximity to the hospital must play a part in the decision of villagers to visit the hospital. We do not have hard data on whether patients were referred from village health centres, but it would seem likely that some of the patients were so referred. A note has been added to the subsection of Study Population to indicate the situation. (Methods, Study population, para 1)

Our decision to use two control groups was based on the following. We believed we would get a fuller and more consistent level of response from using hospitalized controls. They would also be likely to be similarly distributed across the catchment area as the cases. Using similarly distributed controls recruited in the community would have been a near impossible task for the investigators. However, provision of eye disease healthcare is a major component of the overall healthcare provision of the hospital, so that a large proportion of patients have eye problems. A control sample directly representative of non-case patients at the hospital would therefore be over-represented by eye-problem patients. Since it is possible that the exposure histories of these patients would be more similar than those of patients in general to those of the cases, such a situation would lead to an underestimation of any true association. On the other hand, using only non-eye disease controls would mean that any associations found might not be specifically related to cataract but more generally to other eye diseases. Our solution (?) was to use the two types of control group. This explanation is now given. (Methods,, Sample selection, para 4)

2. Case definition. Is the cataract definition of lens opacification and VA <6/18 based on either eye, or the worst eye or both eyes? Why was cataract surgery not based on an aphakic/pseudophakic lens rather than a definition of a report by a qualified ophthalmologist.

The definition of case has been described more clearly in the Methods section. (Methods, Sample selection, para 1)

3. Please give the exposure on which the sample sizes were calculated. What was the basis for the 30% prevalence of exposure assumption? Why were cases of myopia excluded?

A report (Local Government Engineering Department. Country report no EP/RAS/106/GEF, 2006) indicated that the proportion of household in rural Bangladesh using traditional fuel (including all types) was over 90%. Given that we were concerned with individual types of traditional fuel (3 types expected), that there would be some overlap in the use of these fuels, and that our exposure was defined for people who did
the cooking, we anticipated that somewhere around 30 to 50% would probably be exposed to each type. The basis of sample size calculation given in the earlier draft of the manuscript was too vague. This has now been revised. (Methods, Study population, para 2)

4. History of exposure to cooking fuels. This is the primary exposure and more information is required. How was history of exposure defined? Is it based on household use of cooking fuels, or the exposure based on cooking fuel use by people who cook? Why was the age of exposure taken from 11 years?

The definition of exposure to the cooking fuel was defined as the use of the fuel by the person doing the cooking. Recall of exposures during childhood (younger than about 11 years) were expected to be unreliable. This information is now included. (Methods, Data collection, para 2)

5. More details are also required on collection of other data which are presented in the results, for example a diagnosis of hypertension or diabetes. How many people understood these terms and/or could be expected to know if they have these problems. Were other measures used e.g. measured blood pressure or glucose? More information needs to be given on how a family history of cataract was obtained, sunlight exposure and tobacco smoking

Information of these exposures was obtained by interview only. This has now been stated. (Methods, Data collection, para 3)

6. Table 1 indicates that there is a higher proportion of people with secondary education in both control groups compared to cases, and more cases and eye controls with low incomes compared to non eye controls. The possibility that this be a bias in the control selection rather than a true difference in risk factors should be considered in the Discussion

This issue has now been included among the limitations in the Discussion section. (Discussion, para 11)

**Discretionary Revisions**

1. The Introduction could be shortened as it includes information which is not directly relevant to the paper or is repetitious. The first two paragraphs could be removed as this is general information and well known to the readers (also cataract is not the leading cause of blindness in developed countries).

The first two paragraphs of the previous draft have been replaced with a short introductory paragraph (Background, para 1) and the previous third paragraph shortened. (Background, para 2)

2. The description of the previous survey in Bangladesh (third paragraph) has repetition of information and needs to be shorter.
The repetition has been removed. (Background, para 2)

3. Page 4, 3rd and 4th sentence. Either drop or amend because it does not follow that because the proportion of young people in the population is higher in Bangladesh than other countries, there a difference in the age specific rates of cataract in Bangladesh. If this is the case, a supporting reference should be given.

This part has been explained in greater detail. (Background, para 2)

4. English also needs attention on Page 5 second sentence.

Done. (Background, para 3, 2nd sentence)

5. Table 1, age groups should be given in the usual way i.e. 20-29, 20-39 etc.

Done. (Table 1)
**Reviewer #2  Version 1**

*This is an interesting manuscript about risk factors for young adult cataract in Bangladesh.*

**Major compulsory revisions**

1. *Given the difference in distribution of years of sunlight exposure between the case and control groups, this variable should be included in the multivariate models.*

   Sunlight exposure was considered in the prototype multivariate model, but, following the principle of retaining only those variables that were of significance to the fit of the model or of interest to the objectives of the study, it was removed during model refinement. (indicated in Results, para 6)

2. *The authors should consider other potential confounders to their observed association between cooking fuel and young adults cataract, specifically dehydrational crises. There is a fairly large body of literature on the relationship between dehydrational crises and cataract. It is possible that cooking fuel use is associated with access to clean water, which could bias the results.*

   Unfortunately, we did not obtain any data that could be used to identify experience of dehydrational episodes. However, acknowledgement of the possibility that such a condition could be relevant is included in the Discussion (para 11). As, in our study population, there was no evident association with our indicators of socioeconomic status and educational attainment was controlled for in the multivariate models, it would seem somewhat inappropriate to discuss this issue at any length.

3. *The authors need to add information in the methods section about the protocol for determining that reduced visual acuity was due to cataract as opposed to some other ocular condition.*

   The description of the method for diagnosing cataract has been revised. Opacity of the lens or its capsule needed to be indicated on both clinical on slit-lamp examination, together with a VA poorer then 6/18 on the Log Mar VA Chart, in either eye. Case definition also included patients having a pseudophakic lens as a result of cataract surgery within the previous 5 years. This definition has been revised in the Sample selection subsection. (Methods, Sample selection, para 1)

**Minor essential revisions**

1. *English language editing*

   Done.

**Discretionary revisions**

1.
This is an interesting paper demonstrating an association between cooking fuels and cataract.

**Major Compulsory Revisions**

1. The paper would benefit from editing to make it substantially shorter. In particular, the results and discussion sections are both too long, and both need to be reduced by at least one quarter in length.

The Results section has been slightly reduced (but not to 75%) by combining the two controls (at the final stage only). Discussion has similarly been reduced somewhat.

2. Methods. Detail is required on how the diagnosis of lens opacity was made (who by, what equipment, which criteria), and whether the controls were also examined in a similar manner to exclude the diagnosis.

Please see the response to a similar comment by the previous reviewer. The controls were indeed examined in the same manner as the cases. The information is now given. (Methods, Sample selection, para 4)

3. Selection bias. The possibility of selection bias due to selection of controls and the possible implications of this question needs to be considered in more detail in the discussion. Please also state the level of non-response among cases and controls in order to allow assessment of the extent of selection bias.

The question of selection bias has now been discussed. The level of non-response has been given. (Results, para 1)

4. Although it is useful to demonstrate differences between the two types of controls in table 1, in the subsequent tables these control groups should be combined as they show similar patterns. This would greatly simplify the paper. The authors can then state in the text any large differences between the two control groups in comparison with the cases, but avoid being too speculative.

The authors consider that the separation of the results in ever-use regression model remains important, and the logic for combining them for the lifetime use model is detailed in the Results section. (Results, para 9)

5. The reader needs to understand more about the characteristics of the users of these different types of fuel in order to identify alternative reasons for the positive association between wood or dry leaves or use of rice straw with cataract, but a protective effect of cow dung. Could the authors include a table comparing (for cases and controls) the socio-demographic characteristics of different fuel users?
With the exception of educational attainment and sex, socio-demographic characteristics were found to be unrelated with fuel use per se, but related with sex of the subject. The authors felt that a table showing these relationships explicitly would unduly lengthen an already long paper.

**Minor Essential Revisions**

1. Throughout the authors refer to the identification of “risk” of cataract, whereas they are identifying the “odds”.

It is the view of the authors that “risk” may be used in a general way to indicate how likely an event is to occur or a characteristic to be present. In this view, “risk” can be measured on a number of scales, which include both probability and odds.

2. Abstract. Please clarify in the methods that case status was dependent on lens opacity plus visual impairment.

This has been revised in the Abstract as well as in the Methods section. (Sample selection, para 2).

3. Introduction. Paragraph 3 (describing results of the national survey) is much too long. There is no need to give both the crude and age-standardised results. The final sentence about neighbouring countries is not necessarily relevant as it relates to different age ranges.

The paragraph (now para 2) has been shortened.

4. Introduction, final paragraph, 3rd line from bottom. Even in your age group this is still probably age-related cataract so please rephrase this sentence.

Done. (Background, para 4)

5. Methods. “Case recruitment” section, line 5. This should be “Visual Acuity Chart or” not “and or”.

The definition for case has been revised to give a clearer description. (Methods, Sample selection, para 1)

6. Methods. “Non-cataract eye-disease controls” The sentence “controls of either type who were not willing to participate... were excluded” is obvious and does not need to be stated.

It has been removed.

7. Methods. “Non-cataract eye-disease controls” 4 lines from bottom. Please correct this to read: “Matching was done to allow control for the potential confounders”
The Methods section now includes this information. (Methods, Sample selection, para 4)

8. Methods. “Data collection” section. The final section on informed consent needs to be included under the ethics section.

Done. (Methods, Ethical considerations, para 1)


It is not possible to shorten this section without omitting important information, necessary for the reader to understand in detail how the analysis was carried out.

10. Results. As specified above, the results section is much too long.

The Results section has been slightly reduced.

11. Results, paragraph 3 needs to be merged with paragraph 1 as both relate to table 1.

Done. (Results, para 1)

12. Results, paragraph 5. Unclear what is meant by case status was #3.

The file has printed incorrectly, It should be “< 0.2”. (Results, para 6)

13. Results, paragraph 9. Section on how the model was fitted needs to be moved to the methods section.

Done. (Methods, Statistical analysis, paras 1 & 2)

14. Discussion. As specified above, the discussion section is much too long. This section also needs to be restructured so that the authors specify upfront that a positive association was identified between wood or dry leaves or use of rice straw with cataract, but a protective effect of cow dung.

The opening paragraph of the Discussion has been revised to provide the main findings more explicitly. (Discussion, para 1)

15. Discussion. The authors devote more than a page to the discussion of other risk factors for cataract in relation to the existing evidence from the literature. Since this is not the key message of the paper I suggest that the authors reduce this to one paragraph only.

This part has been reduced. (Discussion, parass 10, 11 & 12)
16. Discussion, limitation section. Inaccuracy of recall would likely lead to bias, albeit it non-differential misclassification bias, which as the authors point out would underestimate the results towards the null. Please correct this section which says that it is unlikely that recall misinformation was biased (I think they mean differential).

The word “biased” has been changed to “differential”. (Discussion, para 13)

17. Discussion, page 18, paragraph 2. I suggest that the authors combine the two control groups for the analyses and so this paragraph would be redundant.

The new analysis shows the comparison with the combined controls (in addition to separate comparisons for the ever-use model and alone for the lifetime use model). The text of the Discussion has been revised to follow the results of this revised analysis strategy.

18. Discussion, final sentence. Given the unexpected findings and lack of biological support, I believe that their recommendation is premature.

The recommendation has been toned down to “may be a useful approach…” (Discussion, para 19)

19. Tables. The authors need to cite p-values to 2 decimal places only, throughout. OR with 95% CI are more informative than p-values and should replace the p-values.

The authors do not quite understand the reason for quoting p-values to only 2 decimal places. If the p-value turns out to be 0.003, should it be shown as “0.00” or as “<0.01”? It is noted that in many journals p-values of less than 0.001 are to be shown as “<0.001”. If the journal editorial policy it is give the p-values to 2 decimal places, the authors can do so, but the above uncertainty need to be resolved.

The authors agree with the concept of showing 95% CI rather than p-values for odds ratios, and we have given the 95% CI throughout. However, the p-values that we have given are not strictly speaking referring to the same information. The p-values from the multivariate model (from likelihood ratio test) show the overall statistical significance of the contribution to the fit of the model of inclusion of the corresponding variable. This information is not the same as that indicated by the Wald test p-value (that is, testing the null hypothesis that the OR is equal to 1), and in the case of a variable with more than 2 categories it cannot be judged from the 95% CI’s of each level.

20. Table 1. This table is very busy and needs to be reduced. For instance, the sections on BMI, hypertension, diabetes and myopia are not critical to the analyses and can be removed from the tables and merely mentioned in the text.

BMI, HT, DM and myopia have been removed from the table. (Table 1)
21. **Table 2.** The authors should combine the two control groups for the purpose of this table, and cite in the text that the associations were similar when using the two control groups. Gas and kerosene use was so low that it can be merely cited in the text rather than included in the table.

The authors suppose the comment actually refers to Table 3, but wish to maintain the separation between the 2 control groups. Underlying the study was the concept that NC controls might be more similar to cases than NE controls, but because of the large number of NC patients at the hospital as well as an interest in distinguishing risk factors for young adult cataract from those of other eye diseases in young adults, the NC controls were included in the study. Gas and kerosene have been removed from the table. (Table 3)

22. **Tables 4 and 5.** Please combine the two control groups.

The combined control comparison has been added to the ever-use model (now in Table 5) and presented alone in the lifetime-use model (now Table 6).

23. **Figure 1 is not needed and can be discarded.**

Removed.