Author's response to reviews

Title: Meta-analyses of the association of residential dampness and mold with respiratory tract infections and bronchitis

Authors:

William J Fisk (WJFisk@lbl.gov)
Ekaterina A Eliseeva (EAEliseeva@lbl.gov)
Mark J Mendell (jmendell@lbl.gov)

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Author's response to reviews: see over
Cover Letter for resubmission:

Re: revision per reviewer comments of MS: 1473633104415344 Version 1 - Meta-analyses of the association of residential dampness and mold with respiratory tract infections and bronchitis

Dear Editor:

We are submitting a revised version of our manuscript, reflecting comments from the two reviewers, in “tracked changes” format. Below we list the specific comments and our responses, along with the locations in the manuscript of any revisions.

We hope you find these revisions satisfactory. We confirm again that all the authors of the manuscript have read and agreed to its content. We also confirm that the manuscript is original, has not already been published in a journal, and is not currently under consideration by another journal.

Sincerely,

William J. Fisk
Ekaterina A. Eliseeva
Mark J. Mendell

Reviewer 1: Michal Krzyzanowski
Reviewer's report:
This is useful and well written paper.

Minor essential revisions:
 a) The results presented in table 3 should include the estimate of heterogeneity of the individual study results. If such heterogeneity is detected, its reasons should be explored.

    Response: We have added assessment of heterogeneity of the individual study findings in Table 3, and conducted numerous additional analyses to explore heterogeneity (Table 3; lines 216-221 and 240-244; lines 250-266; lines 378-423.

    b) The list of references of the reviewed studies should be provided in Annex 1 (supplementary material)
Response: We have added links for the bibliographic software back to the reviewed studies in Table 2, so that the studies are included in the References.

c) The last sentence of the “Methods” section (“If asymmetry of the plot…”) is not clear and should be edited.

Response: We have revised this sentence to clarify (lines 223-228).

d) The reference 3 should be checked and updated (the link is http://www.euro.who.int/__data/assets/pdf_file/0017/43325/E92645.pdf , no editor is listed)

Response: We have made this correction.

e) Table 2: explain B,B as a health outcome of Diez et al, 2003.

Response: We have corrected the error (Table 2).
Reviewer 2  
Version: 1 Date: 21 July 2010  
Reviewer: Kathleen Kreiss  
Reviewer's report:  
Major Compulsory Revisions  
1. A major concern is whether the respiratory outcomes examined in this paper associated with dampness are in fact infections. For some, such as pneumonia, the noninfectious causes of pneumonia (such as hypersensitivity pneumonitis) are rare enough that misclassification of the infectious nature of the outcome would be insignificant. In contrast, upper respiratory tract infections overlap in symptoms with allergy and irritation, which also occur in association with damp indoor spaces. It is clinically challenging to differentiate between mechanisms of upper respiratory tract illness in the absence of fever, which would be rare in noninfectious causes. Factors that physicians may use to differentiate infectious from noninfectious causes are time course (abrupt onset and self-limited illness, the latter not apparent to the physician being consulted), persistence apart from a particular environment, and fever. Parents and adult respondents likely use the same cues. We all know of colleagues who come to work snuffling and say that it is just their allergies, even though they don't snuffle most of the time; often we steer clear of such snuffling colleagues in case they have a respiratory infection. With respect to this concern about misclassification of building-associated symptoms with infection, I wonder if the authors should include the supplemental table that appears in Appendix 3, which gives odds ratios for specific health outcomes, so that readers can judge for themselves how compelling the primary reports are. In lumping all respiratory conditions, including colds, are the authors in fact overinterpreting their metaanalyses as supporting increased clinical infection with dampness? Perhaps the authors can acknowledge this possibility or discuss why they think that their findings stand up to such concern for misclassification of allergic or irritative symptoms as infection.  

Response: We think this is an excellent point, and we have now considered this in the analyses and write-up. For our exploration of this issue, see lines 180-186; lines 252-258; Table 3; and lines 383-397. In a new set of models, we excluded, from the larger category of respiratory infections, findings for common cold, nonspecific upper respiratory infection outcomes, and unspecified respiratory infections, considering these to be the outcomes most susceptible to inclusion of allergic or irritant responses misdiagnosed as infections. This resulted in a more homogeneous set of inputs for this restricted respiratory infection outcome, and a slightly higher summary OR.  

Minor Essential Revisions  
2. Results, second paragraph, final sentence: Appendix 2 should be Table 2.  

Response: We have made this correction ( line 271).  

3. Discussion, second paragraph: The sentence starting "Building dampness itself
is unlikely..." is a run-on sentence and would benefit from being separated by a period or semi-colon from the clause "...if these associations are confirmed as causal..."

Response: We have corrected (lines 291-294).

4. Mechanisms of biologic plausibility, second paragraph, second sentence: Tracheobronchitis is a lower respiratory condition, occurring mainly in the chest rather than in the extrathoracic airways. Perhaps the authors included it in the list of upper respiratory tract infections because of the agents? Elsewhere, bronchitis is considered a lower respiratory tract condition and tracheobronchitis is a subset of bronchitis.

Response: We have removed tracheobronchitis from the list of upper respiratory tract infections (line 328).

5. Conclusions, last sentence: "causal" is misspelled as "casual".

Response: We have corrected (line 531).


Response: We have fixed all these errors (highlighted). Note that Periodontology 2000 2009 indicates a 2009 issue of a journal named Periodontology 2000.

7. Table 1, Outcomes line 5: “bronchiolitis” is misspelled.

Response: We have corrected (Table 1).

Discretionary Revisions

8. Mechanisms and biologic plausibility, fourth paragraph: The authors might consider that host defense impairment in children living in damp residences may make infections more clinically apparent or serious. In the environmental tobacco smoke literature, there is some evidence that infectious organisms are not more common in children living with smokers compared to children living in smoke-free households, but children with environmental tobacco smoke have more frequent clinical presentations/diagnoses than children in smoke-free households.

Response: We have added this point, on lines 345-347.
9. Implications, second paragraph, second sentence: The reference 20 given for smoking effects on respiratory infections is much less robust than the following: The health consequences of involuntary exposure to tobacco smoke: a report of The Surgeon General. – [Atlanta, Ga.]: U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, [2006]. Other references for low ventilation effects on infection transmission rates would be those of Don Milton.

Response: We have substituted the recommended reference for passive smoking, and added a reference from Milton for low ventilation rates.

Format Changes Requested by Journal

- Page numbers should be removed.
- Please leave out the subheadings in the Discussion.
- The List of Abbreviations should be in sentence format separating the terms with semi-colons e.g. ARP: attributable risk proportion; CI, etc.
- In the references section, please remove all issue numbers.
- In the tables, all the horizontal lines should be visible.

Response:
We have made all these changes.