Author’s response to reviews

Title: Pesticide use and opportunities of exposure among Palestinian farmers and their families, 1998-2006: Cross-sectional Studies from Beit-U’mmar village in Hebron governorate, Occupied Palestinian Territory

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Author’s response to reviews:

Dear Editor-in-Chief
Environmental Health
Re- MS: 1679305043379589#

We thank the Editor for considering our article and for providing us with the opportunity to resubmit “Pesticide use and opportunities of exposure among Palestinian farmers and their families, 1998-2006: Cross-sectional Studies from Beit-U’mmar village in Hebron #governorate, Occupied Palestinian Territory” for publication as an article in #Environmental Health.#

# Please note we have changed a word "Palestine’ in the title as you suggested in accordance with the official UN designated. The enclosed paper is a revised version of the manuscript #where we have considered the reviewers’ comments and highlighted them in blue colour. #We would like to thank the reviewers for their valuable comments. We have responded #below to all items, which are numbered in order to make the reading easier. Page #specifications of changes made refer to the revised manuscript.#

Pesticides are used intensively in developing countries. Adverse health effects caused by #pesticide exposures have been reported in Palestinian territory and worldwide. #

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To our knowledge, no studies on long-term changes in pesticide use have been reported #from developing countries. In the present study, we aimed to explore possible differences in #farmers’ use of pesticides (compounds, quantities, and handling) and personal protective #equipment in Beit-U’mmar village in 1998 and 2006. All in all, we observed some positive #trends in pesticide practices
between these two periods.

The manuscript is original work and has not been published elsewhere in whole or part. The paper is not under review for publication elsewhere.

Each of the authors has participated sufficiently in the conception and design of the work or the analysis of the data, as well as writing of the manuscript. We believe that the manuscript represents valid work. All authors have read the final version of the manuscript and approve it for publication. The data are available, upon request, for examination.

The present studies were supported by the Norwegian Programme for Development, Research and Education (NUFU) pro X1 50/2002-Norway and Norwegian State Education Loan Funds.

Again we would like to thank the Editor for considering our work and also thanks to the reviewers for their valuable and fruitful comments. We have responded to all reviewers’ comments and have revised our article to be fit to the journal style. Also we have performed language corrections in the revised manuscript. All our responses to the reviewers’ comments as follows:

Reviewer 1: Ewan MacFarlane

Reviewer’s report and author’s responses:

This is a well-prepared and written manuscript concerning an interesting study which appears to have been of high scientific quality. I offer the following comments as constructive criticism to the authors.

The question posed by the authors is novel and well defined. The methods are appropriate and described in sufficient detail for replication. I am limited in my ability to critique the particular analysis method chosen (ordinary least squares linear regression model) since I am not familiar with this particular regression model, however the description provided is clear and would seem to justify its use. The data and study design appear to be sound. The format of the manuscript follows an appropriate format and the results are presented in a clear and conventional format. The discussion and conclusions are balanced and supported by the data. The title and abstract are appropriate and the writing style is generally acceptable, though a few minor imperfections in the English require correction.

Specific points for attention:

1. Abstract

• (Abstract (Conclusions) last sentence) The word “secular” is used correctly according to its original meaning (i.e., over a long period, usually >10 yrs), however this meaning has become nearly obsolete in English over the past couple of decades and I doubt that most English readers would understand it in this way anymore. I suggest an expression such as “long-term” would improve clarity.
Response 1-1: This has been changed to “long-term, page 4”.

# 2. Background section #

• #(1st paragraph, first sentence) It would make more sense to add the term “exposure” in this sentence, for example: “risk of exposure to occupational hazards such as...”. #

Response 1 -2: We added the term "exposure" in the background text in the first sentence (page 5).

• #(1st paragraph, 3rd sentence) The word “have” is unnecessary, ie “...may harm humans...” is fine.#

# Response 1-3: We changed the sentence to “However, pesticides also endanger humans and the environment” (page 5). #

#3. Methods section #

• #(1st paragraph, 3rd sentence) I wonder if the reference [25] should go at the end of this sentence since it appears that both the population/age and occupation data are all from the census. Otherwise, if the occupation data are from another source, add reference. #

Response 1-4: We have changed this paragraph and rearranged all information presented here. Reference 25 had been moved to the end of the paragraph because it is related only to the number of inhabitants and distribution of age. All data about the economic situation of the village are collected from the municipality, as specified in the revised text (page 7). #

• #(2nd paragraph, 1st sentence) The term “farming couples” would make more sense in English than “couples of farming”.#

Response 1-5: We agree. We have replaced it with "farming couples" in the Design sub-section (page 7).

# #

• #(4th paragraph) For the benefit of international readers not familiar with the local farming industry structure, please add something describing the typical employment/business arrangements of these farmers. For example, are they predominantly farm owner/operators, employees, share-croppers etc.#

# #

Response 1-6: The farmers are predominantly farm owners where farming is a family business. We described the economic situation in the village more closely in the revised Methods section under the Study area sub-section (page 7). See also response 1-4. #

• If the data are available, please indicate what proportion of survey respondents were living in houses on the farm property itself and what proportion lived elsewhere. Please also indicate if the 1998 and 2006 survey
samples included any of the same individuals – i.e. were the 1998 #farmers included in the 2006 survey or was the later survey a totally different #group.

Response 1-7: Most farmers are living in the village center, a few kilometers away from their own cultivated lands. This information was added to the paragraph "Interpretation of the results" (page 15). See also response 3-2. Only nine farmers from 1998 were included into the 2006 study. This information has been added in #Methods, Study population sub-section. See also Response 1-8.

* Please mention why were wives not included in the 2006 survey? It was interesting to see that in the 1998 survey wives were highly involved in the family farming tasks and this is an interesting finding in itself and leaves the reader wondering why wives were not included in 2006.

Response 1-8: The two surveys were originally not intended to examine pesticide changes over time. The 1998 survey was part of a study addressing pesticide use and potential effects on reproduction and fecundability. The objective of the 2006 survey was to study farmers’ pesticide use and potential effects on respiratory function. This explains why the inclusion criteria were slightly different, and why the wives were included in 1998 but not in 2006. This issue has been addressed in more detail in #Methods, Design sub-section of the revised manuscript (page 7).

#4. Discussion section #

* Throughout the discussion the authors have compared their results with studies from Palestine and other developing countries. This is good but it would strengthen the international interest in this study if, in addition, the authors also compared the findings with results from developed countries. This would indicate whether the findings are specific to agriculture in developing countries or if they are more generally applicable. For example low PPE use is also seen in farmers in developed countries (Perry MJ et al, Am J Ind Med 2002;41:70.3 and MacFarlane et al, Occup Environ Med 2008;65:141-146). Similar comparisons for each of the main findings would be most illuminating and would contextualise the results more broadly and strengthen the discussion considerably.

Response 1-9: We agree. The two new references have been added in the text [39 and ##40], (page 14).

* It is possible that the apparent general reduction in pesticide use seen between the 1998 and 2006 surveys may have been influenced by the apparent dramatic difference in the number of farmers who were raising animals as part of their farming activities between the two surveys (Table 2). This would be worth mentioning in the discussion since in general animals may be associated with less intensive pesticide use than crops (see also MacFarlane et al, Occup Environ Med 2009;66:497-501).

Response 1-10: We have not discussed this issue because we doubt that the
differences in animal tending have much impact in this population. Farmers in this village keep only a few animals, such as one donkey, a couple of sheep/goats or perhaps five to ten hens. The main activity is crop production for all, and raising animals is not for commercial use in this village. Also because questions were asked differently in 1998 and 2006, we decided to delete information on to animals from the text under the questionnaire sub-section (page 9) and from table (2).

• #(1st paragraph, 4th sentence) “…there are large rooms for further improvements…” is idiomatically incorrect, it should be “…there is room for further improvement…”#

Response 1-11: We have deleted this sentence, page 13.

• #(1st paragraph, 5th sentence) This sentence repeats what is already documented in the results section and does not add to the discussion. Therefore I recommend deletion of this sentence (“Sixteen out of 47…”). #

Response 1-12: We had followed your comment and deleted the sentence, page 13.

# #

• #(“Interpretation of the results”, 1st paragraph, 3rd sentence) This sentence is a bit unclear. I think the authors may be referring to “cumulative exposure”, if so the use of this term would clarify. Otherwise, a clearer explanation of why long agricultural work history with pesticide use implies higher exposure is needed.

Response 1-13: The reviewer is right. We have now specified that a long history in farming implies high cumulative exposure, page 14.

• #(“Interpretation of the results”, 2nd paragraph) The discussion of the reasons reported by the surveyed farmers for not using PPE is good but presumably these are survey results which should be summarised in the Results section prior to this discussion. #

Response 1-14: We agree and have added reasons for not using PPE in the Result part ##(page 14).#

• #(“Interpretation of the results”, 2nd paragraph, last sentence) It is noted that in 1998 many of the surveyed farmers believed they developed immunity from the effects of pesticides. This is very interesting but just as interesting is whether this belief remained prevalent in the 2006 survey. Please mention if this belief was or was not also common in 2006. If this data was not collected in 2006, please explain. #

Response 1-15: During the two periods the farmers had participated in educational programs and workshops aimed to enhance farmers' knowledge on pesticide exposure. So we anticipated that the farmers in Beit-U'mmar village changed their thoughts about immunization. For that reason we omitted this question from 2006 survey. We have made this issue clearer in the Results
section

• #("Interpretation of the results", 3rd paragraph) The first part of this paragraph deals with the important issue of what is often referred to in occupational epidemiology as “take-home exposure”. If the authors were to define this exposure type using this or an equivalent term it would clarify this section. I suggest also using a reference such as Lu et al, 2000 [43] in this context (there are many other references that would also be suitable).

Response 1-16: We agree. We have referred to "take-home" exposure in more detail in the Interpretation of the results section (page 15). Lu et al (reference 45 in the revised manuscript) is one of the references here.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Response 1-17: We have performed language corrections in the revised manuscript.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I have no competing interests

Reviewer 2: Erik Jors

Reviewer's report and author's responses:

A Is the question posed by the authors new and well defined? The aim of the paper is to explore possible differences in farmers' use of pesticides and personal protective equipment in a Palestine village between two points in time – 1998 and 2006. This question is well defined but not a new one although former articles from developing countries mainly have dealt with the evaluation of a change in habits due to an intervention towards a defined group of farmers, whereas this one has no evaluation purpose.
B. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

Ideally the same persons interviewed in 1998 should have been interviewed again in 2008, to be able to say something more accurate about changes in the use of pesticides and protective equipment.

Response 2-1: See Response 1-7. We agree with the Reviewer that this would have been ideal. This issue has been discussed in more detail in the revised Study population part (page 8) and Validity part of the Discussion (page 13).

Comparing two cross-sectional studies as it is done here can be used as well if the sample sizes are appropriate and representative for the population of farmers. But the reasons for selecting the size of the samples and the inclusion criteria are not well described and it is unclear if the samples are representative for the farming population in the area, especially the little sample size from 1998. A judgment of the total number of farmers in the municipality in 1998 would be of value to be able to compare the relevance of the sample size.

Design – the whole paragraph

Response 2-2: We agree with the Reviewer that representativeness of the two study populations is crucial when results should be interpreted. There were several problems (different objectives in 1998 and 2006, see Response 1-8; somewhat different inclusion criteria in 1998 and 2006; low response in 1998, and a lack of official registration of farmers in 1998). These problems have been outlined in more detail in a rewritten Validity part of the Discussion and have also been mentioned in Methods and considered in the Abstract, Interpretations and Conclusions.

Major compulsory revision:

#1. To be able to replicate the procedure for selecting the farmers should be described in more details and explained if calculations of sample size were used to know if the sample size is representative. Moreover the reasons for using the different inclusion criteria in 1998 and 2008 should be explained more in detail.

Response 2-3: In principle, we agree. We did not perform sample size estimation in 1998. The explanation for our choices is given in Responses 1-8 and 2-2.

Discretionary revision:

#2# The analysis could be improved if the authors could identify the same farmers interviewed in 1998 in the 2006 group and make an additional analysis of this cohort of farmers to be able to minimize the risk that the differences reported are found by chance.

Response 2-4: We agree, but we found that only nine farmers of the 1998 study participated in 2006. See also Responses 1-7, 1-8, and 2-1.
In ‘Study area and population’ it is stated that the main crops were grapes and plums, in results second paragraph vegetables are added and the last paragraph in Results apples are added. This is a little confusing and could be avoided by only mentioning the types of crops grown in ‘Study area and population’ unless data analysis about pesticide handling in the different crops is undertaken.

Response 2-5: The crop distributions are provided in Table 2. We agree that the differences could be confusing, and have specified grapes, plums, vegetables and apples in Methods (page 7) and deleted this from the Results section.

C. Are the data sound and well controlled? #
The procedure for controlling the data is not clear and the authors reports that the questionnaires used differed between 1998 and 2006, which can be problematic.

Questionnaires – the whole paragraph #

Minor essential revision: #

4. It should be explained what was the differences in the questions posed between 1998 and 2006 and how these differences were handled in the data interpretation.

Response 2-6: The specific questionnaire items reported in all tables were identical in 1998 and 2006. There were slight differences on other items, such as questions relating to reproductive history and respiratory function, see Response 1-8. One question relating to types of pesticides used differed in 1998 and 2006: In 1998 the question was more general (“what kind of pesticides do you use?”), in 2006 the question specified month (“what kind of pesticides were used for each month from February till September?”). In the revised manuscript (Questionnaire part of Methods), we have stated that the 1998 and 2006 questionnaires were slightly different, and we have specified the identical questions (pages 8 &9)

Discretionary revision: #

2. It would improve the understanding of the procedure of controlling the data if the description were more detailed. Now it is stated that all the variables presented in table 1 and 2 were controlled for, but not how they were controlled for, and if variables that showed no significance between the two groups were excluded. It might be better to control for fewer but relevant variables like age, years of farming, education, social class and main crops grown to avoid diluting the analysis undertaken.

Response 2-7: The multivariate analyses in the original submission were hampered by some problems. First, we tried out binominal regression with estimation of prevalence differences. We had to abandon this because of lack of convergence in several of the analyses. We used ordinary linear (OLS)
regression in the first version, adjusting for #all variables in Tables 1 and 2. The Reviewer is entirely correct in assuming that the #large number of variables in the models diluted the results and yielded a considerable #inflation of the variances and confidence intervals. This is partly the explanation of #some of the non-significant results. We believe that the Reviewer’s suggestion is #excellent, and have followed this in the revised version. Accordingly, we have adjusted #for age, years of farming, education, social class and main crops (plums, apples, #vegetables; grapes were not included because only one farmer of all 311 did not grow #grapes). We have used generalized linear models (GLM) analysis, which provide #results that from a practical point of view is similar to OLS results.#

D. Does the manuscript adhere to the relevant standards for reporting and data #deposition? #

Data about the use of different pesticides that are not obtained from the same #source (farmers and dealers in 1998 and only farmers in 2006) are compared; #this might lead to a false picture on the situation at the two points in time. #

The data are presented in table 1-5. Table 5 might be too large and data could be #presented in another way to increase the overview of the reader. #

Major Compulsory Revision: #

#6. Instead of comparing the information from farmers and distributors in 1998 #with the information from farmers in 2006 as done in the ‘Results’ last paragraph, #the comparison should be made only with information from farmers in 1998 and ##2006. The difference in the amount and types of pesticides reported to be declining #by the authors, might be due to the information from the distributors included in the ##1998 data, and this possibility for mistake must be avoided. The authors are aware #of the problem as seen from ‘Validity of the study’, were they mention it. #

Response 2-8: The prevalence differences in revised Tables 4 and 5 are based on data #from the farmers only. The specification of pesticides used (revised Table 3) is, in #addition based on distributor information. This is more clearly stated in the revised #Validity part of the Discussion (page 13). #

Discretionary revision: #

#2# Table 5 could be changed and instead of reporting all the changes in the use #of the 46 pesticides it could be summarized in e.g. % of farmers using #

insecticides, fungicides, herbicides etc., % of farmers using class Ia, Ib, II etc. #and % of farmers using banned pesticides

Response 2-9: This table (revised Table 3) is rather detailed. The summary requested #from the Reviewer is to some extent provided in the text. We believe that Table 3 is an #important source for the reader when reading the text. We have therefore kept the #table. However, if the Editor agree with the Reviewer, we have no objections of keeping #this as an Appendix to the paper rather than as a table.#
E. Are the discussion and conclusions well balanced and adequately supported by the data?

The data might not be sufficient to conclude that an improvement in the situation from 1998 to 2006 has taken place, because the interviews are not repeated with the same persons and it is not clear whether the samples were representative, especially the sample from 1998.

Response 2-10: We agree that there are potential validity problems, see Response 2-2.

In the 'Discussion' first paragraph an improvement in the handling of pesticides is mentioned including the use of mask and googles, which as seen from table 4 was not significant, whereas the significant change in the use of boots is not mentioned.

Response 2-11: In the new analyses there were no significant changes in PPE use. This information has therefore been changed in Abstract, Results, and Discussion.

Later in ‘Inferences’ and in the ‘Conclusion’ the positive changes it is said that they might be due to different training programs for farmers undertaken by the state and NGO’s. E.g. the change in amount and number of different pesticides used might as well be due to climatic variations with a different pest pressure in 1998 compared to 2006, or it might be due to instability in delivery of pesticides due to conflict with Israel etc.

Response 2-12: We thank the Reviewer for these suggestions and have added the issues relating to climatic variation and the conflict with Israel in the revised interpretation part of the Discussion (page 15) “Improvement” has been changed to “positive changes”.

Major compulsory revision:

8. It must be avoided to include training in the conclusion for the reasons for the changes seen from 1998 to 2006 as this has not been investigated. But if the authors have data on training of the interviewed farmers it would be very good to include them in ‘Results’.

Response 2-13: We have no data on training on individual farmers; consequently, we deleted this sentence from the Conclusion.

Discretionary revision:

9 Instead of stating that the situation has ‘improved’ between 1998 and 2006, which the data are not strong enough to allow the authors to conclude, the word ‘improved’ could modified or be replaced by another phrase like e.g. ‘a difference is seen regarding’, or ‘it seems that an improvement might have taken place’ etc. This will make the conclusions more balanced.

Response 2-14: We agree that more balance is needed. See Response 2-2.
In the discussion part, it could be included some reflections on the influence of climatic variations in the use of pesticides amounts and variety the two years and if relevant the conflict with Israel, that might have hampered the import of pesticides and thus be due to the lesser use in 2006.

Response 2-15: Again we agree with the Reviewer that reduction of pesticide use could be to climate change or to conflict and we add a sentence in the Discussion part.

See also response 2-12.

F. Do the title and abstract accurately convey what has been found?

In the Abstract ‘Results’ the use of a respiratory mask is mentioned as an improvement, although this result is not significant. And later in ‘Conclusion’ the changes found are connected to the training which we as mentioned above should not be included in the conclusion, but only discussed as a possibility in the ‘Discussion’ part.

Response 2-16: See Response 2-11 concerning respiratory mask. We have rephrased the conclusion part and followed the reviewer’s suggestion concerning the training issue.

Major compulsory revision:

The conclusion should be made more balanced.

Response 2-17: We agree, see Responses 2-2 and 2-14.

Minor essential revision:

The use of a mask should not be mentioned as a positive change, as the result is not significant.

Response 2-18: There was a slight but non-significant change. See also responses 2-11 and 2-16.

G. Is the writing acceptable? Yes.

Level of interest: An article whose findings are important to those with closely related research interests.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.
Reviewer 3: Elihu Richter #

Reviewer’s report and author’s responses: #
The investigators have done a nice job of analyzing their findings on an important topic. There is a good fit between objectives, methods, results and discussion on an important and painful problem: massive community wide occupational and familial exposures in the Palestinian agricultural environment. Methods, stats, Results, #analysis of results, lit review solid and straightforward. Table 5 should go before #tables 3 and 4, for obvious reasons.#
Response 3-1: Former Table 5 has now been moved (now, Table 3).#

Given the circumstances and context, some statements would be needed on child exposure, either in the house, or the field, given the fact that the house is right next to the field, and a lot of the mixing, etc, is done there. #
Response 3-2: We agree, see Response 1-16. #

The paper should also give some strong statements as to the potential for health risks from the agents, uses, modes and circumstances of exposures based on prior knowledge from elsewhere, coupled with strong statements about recommendations.#
Response 3-3: We have added health risk as an important rationale for sound pesticide practices in the Conclusion. #

Also, the Richter-Gasteyer paper, cited by the authors, makes the point that the strongest predictor of reduction in health risk comes from substitution and reduction in use, and other papers from elsewhere cast doubt on the efficacy of whole day use of PPE in the presence of continued sloppy conditions of exposure. #The authors should examine and develop this point in the context of their own circumstances. #
Response 3-4: This interesting and important information is added to the reference to #Richter et al. 1997 (Interpretations) (page 14). As we did not include any data on adverse health effects, we are not able to develop this point based on the present study. #

The paper by Richter et al. in Israel Journal of Med Sciences 1992, has detailed findings on reduction in use of organophosphates applied to cotton crops followed by increase in cotton yield. This paper, which came out of the WHO-Euro OP #Study, should be cited. #
Response 3-5: We thank the Reviewer for the suggestion and have added this
Pesticide Sources: In the Palestinian Authority, and elsewhere there has been a fair amount of under the counter buying and selling of illegal pesticides, both within the PA and from Israel and Jordan. This point should be addressed.

Response 3-6: Illegal buying and selling has been addressed on page 6 (Background) and in the Discussion (Inferences, page 17).

There is a need for stronger government region-wide policies to promote an emphasis on Substitution, based on models elsewhere, involving the PA, Israel and Jordan. Without such regional cooperation and regulation, the situation will remain bad.

Response 3-7: We agree. The need for international cooperation has been added in the second paragraph of the Inferences sub-section (pages 16 and 17).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests