Author’s response to reviews

Title: Cholinesterase Research Outreach Project (CROP): Point of care cholinesterase measurement in an Australian agricultural community

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Author’s response to reviews:

Reviewer #1: The authors investigate the integration of AchE monitoring into routine health checks, and examine for association between AchE activity and agrichemical use for farmers in South West Victoria. The authors measure AchE activity at baseline and follow up for both farmers and non-farmers. I have gone through the manuscript critically, and in my opinion the following issues are needed to be addressed for the improvement of the paper.

1. The authors measure baseline AchE activity. However, it is not clear whether the farmers have been pesticide-free before measuring this baseline AchE activity and for how long. This information may be added to clarify to what extend the farmers have been pesticide-free before measuring baseline and to discuss the influence of this on the results. -This is now noted in both methods and limitations sections.

2. The authors use AchE activity as a measure of pesticide exposure. However, only 14.6% of the farmers and non of the non-farmers use anticholinestase inhibiting compounds. Therefore, a discussion about the influence of this on the results would be of interest. - Complete, Extra comment added within discussion – this is also noted later as a limitation of the study in the limitations section.

3. The authors find a significant reduction in AchE activity from baseline to follow up for both farmers and non-farmers. A discussion about potential explanations for the lack of difference between the two groups would be of interest. - This has been address as above

4. Line 30-31: It says that "Acetylcholinesterase can be measured in red blood cells (AchE) and plasma (PchE)". However, acetylcholinesterase can not be measured in plasma -
cholinesterase can be as plasma cholinesterase. Therefore, the sentence may be changed appropriately.

Complete

5. The "methods" section in the abstract may be revised to include study design and an overall idea of the set up for data collection (as in line 151-153). - Complete

6. Line 202-205: The authors mention that fasting blood glucose, respiratory functions and eyesight were measured. However, the results of these tests are not to be found in the result section, neither in table 1. For the reader to gain knowledge about these results, they may be added to the result section or in table 1.- Completed – Glucose and Respiratory results added to Table 1

7. Line 245-250: The authors have recorded PPE used by farmers and non-farmers. For the reader to gain knowledge about all PPE used for respectively farmers and non-farmers, all percentages for all PPE recorded for respectively farmers and non-farmers may be added to the text or in table 1. - Complete – separate table – Table 2

8. Table 1: Information about use of agrichemicals and PPE status of farmers can not be found in the table as stated in the table text. Therefore, the table may be changed appropriately to include this information. - This is complete and included in manuscript.

Furthermore, for easier comparison of the two groups, statistical comparison with p-value for difference between farmers and non-farmers may be added for each variable as a separate column in the table.

Reviewer #2: Comments for the Author:

This manuscript reports the findings of Cholinesterase Research Outreach Project (CROP): Point of care cholinesterase measurement in an Australian agricultural community. This study demonstrates that integration of AChE monitoring into routine health checks for those at risk and to also examine any association between AChE activity and agrichemical use.

The study is relatively small scale but contains important data that highlight the ongoing concern over the exposure of farmers to agrichemicals particularly OP pesticides in Australia. However, there are a considerable number of areas where the manuscript requires clarity or improvement. The major points are listed below.
Abstract;

Line 31. PChE is not analysed in this study, why mention of this in abstract and other places. - Addressed as per reviewer 1

Line 32. Sentence starting with Subclinical effects… not relevant in abstract. - Removed

Line 38. Sample size mentioned in Abstract are not matching with numbers tables. Ex non-forming 15 in abstract but in table it was 14. - Completed

Methodology section includes information of many parameters like behavioural data, psychological status, physical assessment etc., which are not reflected in discussion, abstract or any other place.

First time mention of PChE should be elaborated as Plasma Cholinesterase (PChE).

Background; information given in background section is very vast, it can be focused only towards objectives of the manuscript.

There is no rationale given for why liver, kidney and gut contents were examined rather than just one organ. Explain in the text why was this done as a central component of the study? - This statement is unclear as these parameters are not measured specifically.

Methods;

Line 152 Ache levels were monitored at four time points from baseline to 9th weeks. It is contradictory to the sentence given in line no.210.

Study participants; selection of control subjects should be elaborated. There residential locations, nature of job etc., Give reason why sample size of control is less. - This control group were a conveniance sample

Line 171. Sample size should be corrected. - Complete

Line 210. What is need of mentioning "within a 12 week period? - This has been removed for clarity

Line 217. Change the word "Kolmogorov Smirnoff test' in to Kolmogorov Smirnov test - Complete
Results;

Line 229. Refer the sample size mentioned in the abstract and correct it according. - Complete

Line 246. Details of usage of PPE is not at all mentioned in Tables or graphs. - Rectified Table now included as Table 2

Why should non farming participants use PPE, need explanation on selection of control and the information of PPE usage data. - Non farming participants where asked the same questions for consitency and to determine use of PPE in the event of household/garden chemical use.

Line 267-269, 270. While mentioning p value of ANOVA, F values should be mentioned. Similarly all the place wherever p values are mentioned. - Complete

Discussion;

In general the data obtained from the study results should be discussed continuously. The given much importance for review of information on usage of AChE data and other cholinesterase literature. Authors need to give much attention in discussion the existing data and its importance when compared with earlier study and his own observation from the study.

Text in many paragraphs are overlapping, it has to be reduced and rewritten.

Many paragraphs largely describes about how much AChE data is useful. There is link between what is current data point and related observation.

Line 379-382, Repetition of sentence check line no.83-84. - Reworded – the authors believe this is an important point to emphasise

Line 387-390. Is just a review, not a discussion - Reworded.

Line 445. The work "also" nor appropriate here. - Removed

Reference;

References:

In general it is used excessive amount of references (36 Nos). The bibliographic search looks not sufficiently updated: 6 of 36 (16,6 %) cites are before 1999. 20 of 36 (55,5%) are of the period 2000-2010. The remaining 10 cites of between 2011-2017 and other 2 cites.
Authors should try to maintain at least 50% reference in recent one. Although pertinent, the old citations need a refinement. The manuscript lacks of more attention about what happened in literature in the last ten years about this topic worldwide. Refs 28-33 are part of the methodology section- many of which are outlining the various techniques used during collection of anthropometric and behavioural data. - A number of referenced have been updated to reflect more recent and global research in this topic area. Some older references have been removed as per recommendation.

Total participants in Farmers 41 the percentage should be (100%), similar in Non-formers it has be modified - Done

The sample size 41 is not matching for the details on health status, bodily pain, risk level, alcohol intake, alcohol use etc., also verify in non-farmers (short term risky alcohol use data). This may be due to questions not being answered by participants. - This is now amended and outlined in Table 1.

Table 2 data is not clear. Author has to explain the importance this data, % of total individual chemical sue is irrelevant. I would suggest to remove this table. Information on this aspects are resulted in text and discussion too. - Complete

Check unit mentioned in graphs Figure 1 b. and Figure 2 b. Whether is distribution try to give suitable caption - Clarification added to figure captions included lines 571 – 577 in manuscript.