Author's response to reviews

Title: Comparability of HbA1c and lipids measured with dried blood spot versus venous samples: A systematic review and meta-analysis

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Author's response to reviews: see over
March 24, 2014

Dr Magdalena Morawska
Executive Editor
BMC Clinical Pathology

Dear Dr Morawska,

We were pleased to know that our submission to *BMC Clinical Pathology* was seen as potentially acceptable for publication subject to sufficient revision and response to the reviewers’ comments.

Based on the instructions provided, we have uploaded the revised manuscript and associated documents. You will find we have modified the manuscript according to the comments made by the reviewers. Appended to this letter is our point-by-point response. We would like to take this opportunity to express our sincere thanks to the reviewers for identifying areas of our manuscript that required corrections and modification. We would also like to thank you for allowing us to resubmit a revised copy of the manuscript.

I hope that the revised manuscript is accepted for publication in *BMC Clinical Pathology*.

Sincerely yours,

Eshan T. Affan
*MPhil(Medicine) candidate, Sydney Medical School, The University of Sydney*
Reviewer 1

1- In method section, please define the duration of the searches; last date of the searches; was July 2012 or another date?
This has been revised.

2- In result section of the main manuscript, please refer to number of references; from ....to....after address tables1 and 2.
This has been addressed.

3- In result section; line 3 of this section and the next sentence are confusing. You said "15 studies included", then you said ref.19 and 20 excluded. But the data of ref.20 are shown in the table-1 and table-2. Please recheck tables and clear the final number of eligible studies. according to Fig-1 it is expected 15 articles not 16. You can describe at first excluded ref. and then show the final included studies.
This reference has been removed from the table.

4- In result section; in the first line of the second paragraph, please recheck the total number of the participants; the correct number is 1160. please correct.
The number in the results section is for the number of individual participants in the studies. 1160 was the total number of samples in the studies. Some participants gave multiple blood samples. This is clarified in the table legend.

5- In result section; table 1, please recheck "regression equation data". Randomly I checked the second formula of the ref.28; but was shown errors. The correct formula was:
DBS=1.25V-1.09 (not 1.o1).
So, it's better to recheck all of data.
I have amended this error. I have also checked all the others and found no other mistakes.

6- In result section, tables 1 and 2 please consider regular pattern to describe the details in the first column. According to date, or Alphabetical of the authors of ref.
The tables have been reordered alphabetically by the authors’ names.

7- In result section, table 1 and table 2, based on previous mention the data of ref.20 should omit.
Has been omitted.

8- In result section; table 2, please describe the "Col.II". If you omit ref.20, it will omit.
This has been amended.

9- In result section; fig. 2A-2F please clear the number of the studies in the title of each Fig.
We chose to minimize the information on the figures to preserve clarity, the number of studies in each figure can be inferred from the tables.

10- In result section; fig 2E, if included ref.20 in the analysis, should be omit and re-analysis them.  
**That reference was not included in this figure or the pooled regression line.**

11- In result section, fig 3 and 4 are optional. You can omit or not. Your description in the manuscript is enough.  
**We prefer to retain the figures but leave the decision to the discretion of the journal editor.**

12- In result section; Suppl. fig 1 is correct but suppl. fig.2 is wrong. in the first fig. you have considered 15 studies, but in the second fig. they are 16 studies. You said ref. 20 excluded due to unclear its sample size.  
**The first figure also has 16, it is difficult to see but two of the data points are almost overlapping.** That reference which has now been excluded was for the triglycerides section. These supplemental figures apply only to the HbA1c analysis where there were 16 samples. Now there are 17 due to the addition of a new study brought to our attention by reviewer 3.

13- in ref. section, please check for abb. of the j names of the ref.27, and 35. In addition, the abb. name of the j of ref. 38 is similar to j of the ref.32. please, correct.  
**These have been amended.**
Reviewer 2

A. Major revisions:
1. The paper wishes to assess suitability of using DBS method for community based estimation of HbA1c and lipids by comparing various studies, but does not include in its analysis parameters which influence results of each study. As a result the conclusions are not supported by analysis. Authors must analyse those parameters also.

   This is a rather vague comment and it is not clear to us what additional parameters the reviewer wishes us to include in the analyses. We would note that we are necessarily limited in the breadth of the analyses we can complete because we are dealing with published data rather than the original data sets. We acknowledge that the analyses are imperfect, and have noted this in the discussion. But we strongly dispute the suggestion that the conclusions we have drawn are not substantiated by the study findings. The body of the data are in fact strikingly consistent in many regards and much of the observed variability is explained by the subsidiary analyses we have undertaken.

2. How do the authors account for differences in regressions due to method of analysing HbA1c eg. HLPC etc. Is it important or not needs to be answered.

   We believe the differences are due to the different reliability of the various analytic methods employed. We believe this is an important consideration in future studies that use this approach.

B. Minor revisions
1. Under Introduction section, para 1 line 10: clarify the meaning of of the statement “compared to venous samples, DBS.....” is it just comparison of sample collection or includes its analysis also.

   It is referring to only the sample collection here. This has been clarified in the revision.
Reviewer 3

Major Essential Revisions:
1. Review article missing key CDC publication- Lacher et. al., Clin Chem Acta, 2013, 422, 54-58. **This article has now been included.**
2. Results from above reference provide results for HbA1c, TC, and HDL that may alter overall findings. **All of the above have now been included in the analysis and interpretation. The data did not substantively change the conclusions**
3. Authors should do a final literature review to make sure other key publications are not missed. **This has been done and no further studies were identified.**

Minor Essential Revisions:
1. Many typos and inconsistent punctuation.  
   Adjusted according to Microsoft Word spelling and grammar check
2. Page 2, Line 1, add (HbA1c) after haemoglobin  
   Amended
3. Page 2, Line 7, change haemoglobin to (HbA1c)  
   Amended
4. Many places period needs to be placed after reference instead of before reference  
   Amended
5. Page 6, Last line, "no studies reporting HDL" needs to be updated (see missing reference above).  
   Amended
6. Page 8, Line 13, dried blood spot already defined, use "DBS"  
   Amended