Author’s response to reviews

Title: Factors associated with impaired colour vision without retinopathy amongst people with type 2 diabetes mellitus: A cross-sectional study

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Author’s response to reviews:

Dear Dr Shipley,

Re: Manuscript No BEND-D-16-00188

Title: Factors associated with impaired colour vision without retinopathy amongst people with type 2 diabetes mellitus: A cross-sectional study

We would like to thank the reviewers for their feedbacks to the above manuscript. We have revised the manuscript according to the comments raised by the reviewers.

Reviewer’s comments and authors’ responses:

1. Methods

When abbreviating the Lanthony D15 test the authors should use the designation D15d, so that the test used in the study is not confused with the Farnsworth D15 test.

We thank the Reviewer for highlighting the error. We had used the Farnsworth D15 test, instead of the desaturated Lanthony D15. We apologise for this error.

Under “Abstract” section, paragraph 2 line 25, page 3, we have amended following sentences:
Their diagnosis were affirmed from oral glucose tolerance test results and they were screened for impaired colour vision using the Farnsworth D-15 instrument.

Under “Methods” section, paragraph 3 line 44, page 7, the following sentence was amended:

The Farnsworth D-15 was selected for this study.

Under “Methods” section, paragraph 1 line 16, page 10, we have revised the following sentence:

A pilot study of 15 people with T2DM was carried out at the study site, which showed that 47% of them had ICV, as detected by the Farnsworth D-15 test.

2. Methods

The illumination used at the testing set should be described. The recommendation that the test should be done under daylight illumination or an illuminant that reproduces this condition is of essence for the color testing situation of this type of test. This information must be added to the methods.

We appreciate the Reviewer’s valuable input.

Under “Methods” section, paragraph 2 line 1, page 9, the following sentence was amended:

Colour vision testing for all participants was done in the same room, beside the window with natural daylight illumination.

3. Methods

Treatment of the results of the Lanthony color vision in the paper is not satisfactory. The Lanthony color vision test has been the object of quantification procedures that are available in the literature (Bowman, K. J. (1982) A method for quantitative scoring of the Farnsworth panel D-15. Acta Ophthalmol. 60, 907-916.; Vingrys, A. J. and King-Smith, P. E. (1988) A quantitative scoring technique for panel tests of color vision. Invest. Ophthalmol. Vis. Sci. 29, 50-63.) . The authors must consider the quantification of the data obtained. The binary classification used is very poor, since it ignores the degree of color vision loss. The classification of the test outcome for each subject was done by visual inspection, a procedure that may be
useful in clinical practice, but is not acceptable for research purposes as long as an objective, quantifiable procedure is available. If the quantification is applied, the statistical analysis will have to reformulated.

The Lanthony desaturated D15 test should not be referred to as a screening test. The Farnsworth D15 is a screening test, used to detect severe defect, as in congenital color blindness, but the D15d or Lanthony is a test developed to detect more subtle color vision losses characteristic of acquired dyschromatopsia.

We appreciate the Reviewer’s valuable input and apologise for the error.

The Farnsworth D15 was the instrument used in this study. We agree with the Reviewer that the Farnsworth D15 test is a screening test and cannot be used to quantify the defect. Since the intent of our study was to identify the presence or absence of impaired colour vision in patients with type 2 diabetes, we felt that its screening using the Farnsworth D15 test was sufficient.

Further, the heavy patient loads in public primary care clinics in Singapore (polyclinics) only allow the screening of impaired colour vision among the target patients. It was not feasible to perform a more rigorous and preferred colour vision test (example: Farnsworth-Munsell 100 hue test). We have acknowledged this as a limitation of our study design and have included this in our discussion section. In addition, we have also acknowledged the limitations of the Farnsworth D15 test as a screening tool in our “Methods” section, paragraph 1, page 9.

Under “Methods” section, paragraph 1, line 18, page 9, following sentence was amended:

As Farnsworth D15 is a screening test, individuals with mild colour vision impairment may be misclassified as no colour vision impairment. The screening test would separate them into two groups (1) strong/medium ICV (“ICV+”) or (2) mild ICV or normal color vision (“ICV-“).

Under “Discussion” section, paragraph 2 line 18, page 16, following sentence was amended:

The study has its limitations. Farnsworth D15 test was used to screen and identify those with ICV. Patients with mild ICV or diffuse losses in colour vision might potentially be misclassified as individuals with normal colour vision due to the lack of discrimination power of the Farnsworth D15 instrument.
4. Results

Results from 31 patients were excluded due to "ambiguous result from the D-15 test". The authors should explain what they meant by this. What have they considered ambiguous in the results of these patients? May the so called ambiguous results point to a diffuse result, rather than a result that is consistent with one of the axes? If so, the outcome of a predominant tritan defect may be challenged. Again, the point taken above about the need for quantification applies to the question of why these results were excluded.

We would like to clarify the statement regarding the ambiguous results.

A total of 31 (3.7%) participants were excluded as the results from the Farnsworth D15 test did not follow any specific pattern on second examination (performed on the same day), even after further instructions were given. This could be due to subjects’ lapse of understanding of the instructions, thereby affecting the execution of the Farnsworth D-15 test. The inclusion of these 31 dubious results might potentially skew the results. We have thus deliberately omitted these “ambiguous” results from the data analysis. The authors believed that the exclusion of these participants were unlikely to result in a selection bias, as only 3.7% of the total recruited participants were excluded.

General comments

5. One of the main points is that the findings of the study should be better discussed in the context of the literature and it would be relevant to have hypotheses formulated to try to explain them.

Whilst there has been extensive research relating to diabetic retinopathy and its associated risk factors, studies pertaining to ICV are relatively sparse based on our literature review. Nonetheless we have added in our postulations based on findings from five related studies (References 1 to 5).

6. Findings that deserve further treatment in the discussion are the type of color vision defect that was found and the association of color vision loss in this population with age and level of education.

Again, we found a paucity of literature on the association between tritanomaly, the predominant ICV and type 2 diabetes mellitus. We have cited older studies by Fong DS et al and Ayed S et al, as well as more recent literature from Cho NC et al and Zhang X et al (References 11 to 14). In fact even the latest study in 2013 only revealed secondary findings. There is a need for further
studies to understand the association between ICV and underlying pathological process relating to type 2 diabetes mellitus.

7. The type of color vision defect should be discussed with relation to the type of test used. It should be taken into account that other researchers using other instruments found non selective (diffuse) losses rather than impairment restricted to the tritan axis.

We thank the author for the comment. As the colour vision test used in our study was a screening tool rather than a diagnostic tool, we recognise the potential limitation of the instrument in detecting diffuse losses. Thus we only report major colour vision deficiency such as tritanomaly.

Under “Discussion” section, paragraph 2 line 18, page 16, following sentence was amended:

“The study has its limitations. Farnsworth D15 test was used to screen and identify those with ICV. Patients with mild ICV or diffuse losses in colour vision might potentially be misclassified as individuals with normal colour vision due to the lack of discrimination power of the Farnsworth D15 instrument.”

8. In view of the fact that the study found better results of blood pressure, glycemia and lipid status in patients with color vision defect, the authors present in the discussion the idea that those patients become more careful and better observant of control of the diabetes. This interpretation strikes me as excessively speculative. In order to make such a statement it would be necessary to show that the subjects are conscious of their color vision losses. It is very likely that they are not conscious that they have impairment in color discrimination, first because the losses are not always very severe and second because their development is very gradual, leading to an adaptation to the condition. It is not uncommon to find subjects with severe dyschromatopsia that are surprised by their color vision test results and were not at all aware that they had any color vision impairment. In the present study, the color vision losses range from light to severe, so they may be in great part not realized by the patient. In any case, there should be clear evidence that the patient is cognizant of his color vision shortcomings to be able to point dyschromatopsia as a factor that may contribute to his diabetes care.

We apologise for any perceived deviant interpretation and have amended the relevant segment. Indeed we could only assess the relationship between the factors which were found to be significantly associated with ICV. We agree with the reviewer that it is inappropriate to indicate any cause and effect, and have suggested alternative study design to determine the cause and effect of the observed factors.
We hope that we have adequately addressed the queries and comments raised by the Reviewer. We welcome further clarifications if deemed necessary and look forward to hearing from the editorial team again soon.

Yours truly

Dr Ngiap Chuan Tan

Lead author

The authors' response letter has been included as a supplementary file.