

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Depressive symptoms in people with a vision impairment: A cross-sectional study to identify who is most at risk
AUTHORS	Nollett, Claire; Ryan, Barbara; Bray, Nathan; Bunce, Catey; Casten, Robin; Edwards, Rhiannon Tudor; Gillespie, David; Smith, Daniel J; Stanford, Miles; Margrain, Tom

VERSION 1 – REVIEW

REVIEWER	Dr Keziah Latham Anglia Ruskin University Cambirdge, UK
REVIEW RETURNED	08-Sep-2018

GENERAL COMMENTS	<p>This is a well written manuscript that makes a significant contribution to the literature on depression and visual impairment. I have some minor comments regarding description of the methods, and factors considered in the discussion.</p> <p>Methods</p> <p>Page 6 line 39: were the physical illnesses and ocular diagnoses collected by open-ended self-report or by selection from a specified list of conditions? Table 2 suggests it may have been a list?</p> <p>Page 6 line 56: was corrected acuity based on habitual / presenting or best correction?</p> <p>Page 7 line 31: specification of *primary* ocular diagnosis doesn't quite match with the description of 'number of ocular diagnoses' specified on the page 6 line 39 or the presentation in Table 3.</p> <p>Results</p> <p>Table 3: It would be worth specifying that ocular diagnosis refers to any diagnosis, rather than primary diagnosis (at least it is assumed this is the case since $n > 990$).</p> <p>Table 4: It would be helpful for the interpretation of the NEI VFQ 7 data for the methods to clarify the directionality of the person measures. It is presumed that a more positive person measure reflects greater perceived difficulty with visual functioning.</p> <p>Page 13 line 7-10: couple of typos. Unneeded full stop after 5, rations rather than ratios, 'are' needed between 'and presented'.</p> <p>Page 16 line 22: Physical health has a significance of $p = .051$ in the final model. Is it appropriate to consider this as 'remaining associated'?</p> <p>Discussion</p> <p>An increased number of eye conditions is associated with a lower odds of depression (page 16 line 33), but this surprising finding is</p>
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	<p>not considered in the discussion, beyond noting it on page 17 line 18.</p> <p>Page 17 line 19: gender is not associated with depression in this study, but has been associated in previous studies as outlined in the introduction. Further comment in the discussion would be relevant.</p> <p>Page 18 line 38: There is little specific comparison to the results of similar studies from the Netherlands, Belgium and Australia (Page 5 line 15). To what extent are the findings from these studies generalizable, and to what extent is the UK cohort different?</p> <p>Page 18 line 26: It has previously been shown that depressive symptoms explain a significant proportion of self-reported difficulty in visual functioning (Tabrett & Latham, IOVS 2011, 52, 5293), and this reference would be worth considering for inclusion to support the statement that 'those with worse self-reported visual function are at more risk of depressive symptoms'.</p>
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REVIEWER	Hilde van der Aa Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Ophthalmology, Amsterdam Public Health research institute, De Boelelaan 1117, Amsterdam, the Netherlands
REVIEW RETURNED	14-Oct-2018

GENERAL COMMENTS	<p>This cross-sectional study investigates factors that are related to clinically significant depressive symptoms in a large sample of adults with visual impairment from England and Wales. The article is well written. I only have some minor comments:</p> <ul style="list-style-type: none"> - A fairly simple method was chosen to deal with missing data. This should be addressed as a limitation in the Discussion section. - Is data of the non-responders available? A non-response analysis would be informative. If not, this should be addressed as a limitation in the Discussion section. - Table 1-4 are described in much detail. I would suggest combining these tables and mentioning the outcomes of the univariable regression analysis here. So it is clear if the differences that are described are statistically significant. - Some of the factors that were found related to depression in this sample, may not be specific for people with visual impairment (i.e. age, ethnicity, physical health). This should be discussed in the Discussion section.
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VERSION 1 – AUTHOR RESPONSE

Response to reviewer 1

Methods

1. Page 6 line 39: were the physical illnesses and ocular diagnoses collected by open-ended self-report or by selection from a specified list of conditions? Table 2 suggests it may have been a list?

They were indeed collected by selection from a list, with an 'other' category in which the participant was asked to specify what illness/diagnosis. We have clarified this by adding "from a list of seven, plus 'other' category" to the physical illnesses, and "from a list of five, plus 'other' category" to the ocular diagnoses.

2. Page 6 line 56: was corrected acuity based on habitual / presenting or best correction?

Corrected acuity was based on presenting corrected binocular visual acuity and we have clarified this in the Measures section.

3. Page 7 line 31: specification of *primary* ocular diagnosis doesn't quite match with the description of 'number of ocular diagnoses' specified on the page 6 line 39 or the presentation in Table 3.

We thank the reviewer for drawing this to our attention. Indeed, we meant total number of ocular diagnoses and the word primary should not be included. This has been removed from where it was mentioned in the Procedures section.

Results

4. Table 3: It would be worth specifying that ocular diagnosis refers to any diagnosis, rather than primary diagnosis (at least it is assumed this is the case since $n > 990$).

We have moved the asterisk indicating the footnote to Table 3 and reworded the footnote with the intention of making it clearer that we are referring to all diagnoses, not just the primary diagnosis.

5. Table 4: It would be helpful for the interpretation of the NEI VFQ 7 data for the methods to clarify the directionality of the person measures. It is presumed that a more positive person measure reflects greater perceived difficulty with visual functioning.

This is an important point and we have clarified this by adding a sentence to the Measures section and a footnote to Table 4 explaining that a higher score indicates a greater perceived difficulty with visual functioning.

6. Page 13 line 7-10: couple of typos. Unneeded full stop after 5, rations rather than ratios, 'are' needed between 'and presented'.

We have corrected the three typos listed.

7. Page 16 line 22: Physical health has a significance of $p = .051$ in the final model. Is it appropriate to consider this as 'remaining associated'?

We thank the reviewer for spotting this error and have corrected the paragraph on physical health in the results section to 'This association remained when controlling for demographics and eye health but was no longer associated when controlling for subjective health and visual functioning.' We have made changes to the Abstract and Discussion to reflect the changes made to the Results section.

Discussion

8. An increased number of eye conditions is associated with a lower odds of depression (page 16 line 33), but this surprising finding is not considered in the discussion, beyond noting it on page 17 line 18.

After returning to the data to understand this finding, we have amended the paragraph on vision related factors in the Discussion to acknowledge this surprising finding, and to suggest it may be due to the relationship between number of eye conditions and physical illnesses which might cause eye problems (eg. Diabetes).

9. Page 17 line 19: gender is not associated with depression in this study, but has been associated in previous studies as outlined in the introduction. Further comment in the discussion would be relevant.

We have added to the demographics section of the Discussion to include a consideration of the findings on gender and depression across studies and why the findings might vary from ours.

10. Page 18 line 38: There is little specific comparison to the results of similar studies from the Netherlands, Belgium and Australia (Page 5 line 15). To what extent are the findings from these studies generalizable, and to what extent is the UK cohort different?

In the Discussion, we do compare our findings to those from the Netherlands, Belgium and Australia: where they are similar and where they differ. However, we note this was not explicit and have made this clearer by adding the country names into the Discussion when referencing the studies.

11. Page 18 line 26: It has previously been shown that depressive symptoms explain a significant proportion of self-reported difficulty in visual functioning (Tabrett & Latham, IOVS 2011, 52, 5293), and this reference would be worth considering for inclusion to support the statement that ‘those with worse self-reported visual function are at more risk of depressive symptoms’.

We have taken the reviewer’s advice and inserted the recommended reference to support this statement (reference 26).

Response to reviewer 2

12. A fairly simple method was chosen to deal with missing data. This should be addressed as a limitation in the Discussion section.

Please see response in point 13 below.

13. Is data of the non-responders available? A non-response analysis would be informative. If not, this should be addressed as a limitation in the Discussion section.

In response to point 12 & 13: We thank the reviewer for noting the oversight of these limitations in the discussion. We do not have data on the non-responders, so are unable to perform a non-response analysis. Therefore, we have amended the final paragraph of the limitation section in the Discussion to acknowledge that the fact there are non-completers, plus the simple method of excluding missing cases from the analysis, may have introduced a risk of bias.

14. Table 1-4 are described in much detail. I would suggest combining these tables and mentioning the outcomes of the univariable regression analysis here. So it is clear if the differences that are described are statistically significant.

We thank the reviewer for this suggestion. After much consideration, we chose to keep the tables in their current format for the following reasons: We feel the modelling results should remain together in Table 5 as this aids with understanding the flow from univariable to multivariable model and the steps in between. We also feel that combining Tables 1-4 would create a very large table which may be cumbersome to read and difficult to format for print.

15. Some of the factors that were found related to depression in this sample, may not be specific for people with visual impairment (i.e. age, ethnicity, physical health). This should be discussed in the Discussion section.

We agree this is a useful point to make and have it added it to the section which considers the findings in the Discussion section.

VERSION 2 – REVIEW

REVIEWER	Dr Keziah Latham Anglia Ruskin University Cambridge, UK
REVIEW RETURNED	09-Nov-2018
GENERAL COMMENTS	The authors have addressed all the queries raised in my original review. My only remaining comment is with regard to the finding that a greater number of eye conditions is associated with a lower risk of

	depression in the final model. The authors discuss this point in terms of those with multiple eye conditions also more likely to have other physical health conditions. However, would one not expect those with poorer physical health to have a greater risk of depression, rather than a lower one? So this still seems a surprising finding - has similar been reported elsewhere in the literature?
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REVIEWER	Hilde van der Aa Amsterdam UMC, VUmc, the Netherlands
REVIEW RETURNED	08-Nov-2018

GENERAL COMMENTS	Overall, I'm satisfied with the response that the authors provided. However, I still believe that the univariable regression outcomes are best mentioned in table 1-4, where they can be related to the differences that are shown there. If the univariable outcomes would have been used to choose variables that are used in the multivariable regression analysis, this would have 'aided understanding the flow from univariable to multivariable model and the steps in between', however this is not the case.
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VERSION 2 – AUTHOR RESPONSE

Response to reviewer 1

My only remaining comment is with regard to the finding that a greater number of eye conditions is associated with a lower risk of depression in the final model. The authors discuss this point in terms of those with multiple eye conditions also more likely to have other physical health conditions. However, would one not expect those with poorer physical health to have a greater risk of depression, rather than a lower one? So this still seems a surprising finding - has similar been reported elsewhere in the literature?

On further reflection, we agree with the reviewer this is not an adequate explanation and have gone back to the literature to investigate this finding further. After consulting previous studies and much discussion between the authors, we believe this finding could be due to differing levels of acceptance around vision loss between people with one eye condition and those with three or more. We have provided our proposed explanation for this based on previous literature but also note that the work in this area is sparse and further research is needed to investigate this finding and possible explanation. Please see manuscript for our full explanation.

Response to reviewer 2

I still believe that the univariable regression outcomes are best mentioned in table 1-4, where they can be related to the differences that are shown there. If the univariable outcomes would have been used to choose variables that are used in the multivariable regression analysis, this would have 'aided understanding the flow from univariable to multivariable model and the steps in between', however this is not the case.

We thank the reviewer for this further comment and accept their view on this. Therefore we have changed Tables 1-4 accordingly to incorporate the univariable logistic regression analysis, and thus removed it from Table 5 which now contains just the multivariable regression.