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Visual impairment and depression: Age-specific prevalence, associations with vision loss, and relation to life satisfaction

Brunes A, Heir T Visual impairment and depression: Age-specific prevalence, associations with vision loss, and relation to life satisfaction

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Institutional review board statement: The Regional Committee for Medical and Health Research Ethics gave permission to carry out the study in accordance with procedures for anonymized data (Reference number: 2016/1615A).

Informed consent statement: All participants gave their informed consent to take part in the study.

Conflict-of-interest statement: No potential conflict of interest was reported by the authors.

Data sharing statement: Data are from the research project European Network for Psychosocial Crisis Management - Assisting Disabled in Case of Disaster (EUNAD). Public availability may comprise privacy of the respondents. According to the informed consent given by each respondent, the data is to be stored properly and in line with the Norwegian Law of Privacy Protection. However, anonymized data is available to researchers who provide a methodological sound proposal in accordance with the informed consent of the respondents. Interested researchers can contact project leader Trond Heir (trond.heir@medisin.uio.no) with request for our study data.

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Professor Rajesh R Tampi
Editor, World Journal of Psychiatry
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Date: 15.04.2020

Dear Rajesh R Tampi, Editor-in-chief,

We are pleased to know that our manuscript '*Visual impairment and depression: Age-specific prevalence, associations with vision loss, and relation to life satisfaction*' has been reviewed for possible publication in *World Journal of Psychiatry*. We appreciate the comments and recommendations by the Editor and from the Reviewer, and think that we have been able to address them in ways that strengthen the manuscript.

This is the fourth article submitted from a study about coping with traumatic events and mental health in individuals with vision impairment. Of the submitted articles, three have been published. An earlier version of this paper is located on the Elsevier's preprint server SSRN (https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3323116). The paper will not be submitted elsewhere until a final decision has been made by this journal. There are no potential conflicts of interest.

We look forward to receive your response.

Sincerely,

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Response to Reviewer

Major comments

1. *My most important concern involves the fact that the analyses that were reported do not seem to have taken into account the stratified nature of the sample, with oversampling of young and middle-aged adults. Stratified samples differ from simple random samples and demand methods that take the sampling strategy into account.*

Response: We agree with the reviewer that stratified random sampling results in differential probabilities of selection. There are two approaches for presenting estimates of equally allocated age-stratified samples. One approach is to obtain data about the age distribution of the target population, and then use weighted procedures in the analysis so that the overall estimate accurately reflects the proportions in the population. The other approach is to calculate stratum-specific estimates for the different age groups. When using the latter approach, it is safe to make comparisons between groups without using weights^[1]. In the present study, we decided to follow the second approach.

To highlight the performance of age-stratified analyses, the following sentence was added to the 'Materials and Methods' section under the heading 'Statistical analysis', on page 9:

To account for the age-stratified sampling method, we tested in all analyses whether the estimates varied across the different age groups (years: 18–35, 36–50, 51–65, ≥ 66) by performing statistical analyses of cross-tabulated data or by including a product term between age and each independent variable in a regression model.

1. **Hibberts M**, Johnson B, Hudson K. Common survey sampling techniques. In: Gideon, L. Handbook of survey methodology for the social sciences (pp. 53-75). New York, NY: Springer, 2012.

2. *I miss an overall prevalence estimate of depression and major depression across all age groups.*

Response: We chose to present age-specific estimates as we do not know the exact age distribution in the visual impairment population, and thus the opportunities for using weights is limited. To highlight the age-stratified nature of our analyses, the following sentences were added to the 'Results' section, on page 11 and 12:

Although this type of categorization resulted in higher rates of depression, the results from the analysis supported our main findings of severe depression being most prevalent among the youngest participants (Table S1).

Furthermore, we observed a somewhat higher percentage of depressed participants with functional limitations in the two youngest age groups (18–35 years: 92%; 36–50 years: 92%) than that found among the oldest participants (≥ 66 years: 70%) ($p = 0.10$).

There were no statistical interactions between age and any of the other independent variables ($p > 0.05$).

None of the interactions involving age and the other independent variables reached statistical significance ($p > 0.05$).

Among the 421 participants that were offered mental health care, 45 (10.7%) participants had a consultation with a psychologist, **with similar rates across the different age groups (p = 0.91).**

3. Page 9, first paragraph. Visual impairment “acquired < 20 years” means VI acquired before one reached 20 years of age or less than 20 years ago at the time of the interview? That variable is sometimes described as “nature of VI” and sometimes it is described as “losing vision late in life”. I think that in this case the inconsistent nomenclature generated some confusion. Moreover, I would like to ask why the 20-years cutoff was used and if those data were collected as a continuous time variable that was later dichotomised.

Response: We thank the Reviewer for the comment. We decided to rename the ‘cause/nature of VI’ variable into ‘age of VI onset’, as this term is more consistent with that used in earlier research, e.g.^[1]. Also, we changed the variable from focusing on the years since onset of visual impairment to when in life the vision loss occurred. A description of how the new variable was created has been added to the ‘Materials and Methods’ section under the heading ‘Independent variables’, on page 9:

Lastly, we created an ‘age of VI onset’ variable by subtracting the participant’s age with the number of years since VI onset. The variable was categorized into the following three categories: ‘congenital’, ‘childhood/adolescence (2–24 years)’, and ‘adulthood (≥ 25 years)’.

The main analyses have been changed accordingly by including the new ‘age of VI onset’ variable into the regression model. The revised results are highlighted in red font in text and in Table 3.

1. **Foxman SG, Heckenlively JR, Bateman JB, Wirtschafter JD.** Classification of congenital and early onset retinitis pigmentosa. *Arch Ophthalmol* 1985; **103**: 1502-1506.

4. I understand that the regression analyses that were presented concern all depressive disorders, however I would like to ask the authors to repeat those analyses using major depression as the outcome. Isn't major depression more important clinically than "any depression"? At a minimum, I think the authors should present the results for both major depression and overall depression separately.

Response: We followed the Reviewer's recommendation and performed supplementary analysis using major depression as the outcome. Unfortunately, the binomial GLM analysis did not converge. We therefore decided to run a robust log-Poisson regression^[1]. The results of the multivariable Poisson regression are shown in the following table:

Covariates	Prevalence ratio (95% CI)
Age (cont. 10-year intervals)	0.70 (0.59–0.82)
Female gender (ref. male)	1.37 (0.83–2.24)
Education (cont.)	0.75 (0.59–0.96)
Severity of VI (ref. moderate)	
Severe	1.19 (0.68–2.08)
Blind	1.14 (0.57–2.28)
Age of VI onset (ref. congenital)	
Childhood/adolescence	1.52 (0.81–2.87)
Adulthood	2.66 (1.40–5.05)
Progressive (ref. stable)	1.21 (0.71–2.05)
Other impairments (ref. none)	1.94 (1.20–3.13)

The table shows that the estimates obtained from the supplementary analysis is quite similar to that presented in Table 3. Nevertheless, if the reviewer wants to, we are happy to include the results from the supplementary analysis using major depression as the outcome.

We agree with the reviewer that major depression is of greater clinical significance due to its high disease burden in Westernized countries. However, there are two main reasons for using any depression as the outcome instead of just using major depression. First, both major depression and other depressive disorder are a part of the DSM-V manual^[2]. Both conditions may require treatment as they can be very distressful to the individual and cause substantial impairment in functioning^[2]. The PHQ-9 allows us to categorize both conditions^[3]. However, no previous studies have examined the prevalence of other depressive disorders in the VI population. Second, we followed the one-in-ten rule when selecting the number of covariates in the regression model^[4]. By having more cases of depression, we are thus able to include a higher number of covariates in the regression model without causing bias or losing meaningful information.

To highlight the novelty of research about other depressive disorder in this population, the following information was added to the 'Discussion' section under the heading 'Strengths and limitations', on page 12:

Our study is the largest study to date to address the prevalence of depression in VI populations across the entire adult age range, **and the first to report estimates of other depressive disorder.**

1. **Petersen MR**, Deddens JA. A comparison of two methods for estimating prevalence ratios.

BMC Med Res Methodol 2008; **8**: 9 [PMID: 18307814 DOI: 10.1186/1471-2288-8-9]

2. **American Psychiatric Association.** Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5). Washington, DC: American Psychiatric Pub, 2013.
3. **Kroenke K, Spitzer RL, Williams JB, Löwe B.** The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: A systematic review. *Gen Hosp Psychiatry* 2010; **32**: 345-359 [PMID: 20633738 DOI: 10.1016/j.genhosppsy.2010.03.006]
4. **Hosmer Jr DW, Lemeshow S, Sturdivant RX.** Applied logistic regression. Hoboken, NJ: John Wiley & Sons, 2013.

5. *Results that were presented in the abstract and in the main text describe young age as a risk factor for depression using the following prevalence ratio 0.85, 95% CI: 0.76, 0.94. I think it would be more accurate to state that older age was protective, because the interpretation of those results is that each year of life decreases by 15% the prevalence of depression when keeping the remaining variables constant. Moreover, that estimate is really remarkable and probably too good to be true because it would imply that people with VI aged 10 years above the mean age of the study population (if that variable was centred) would have 150% decreased risk of depression. I believe that once the sampling method is taken into account, that estimate will change.*

Response: We agree with the Reviewer that the correct interpretation of the results from the analysis is to state that older age was protective. Changes have been made throughout the manuscript in order to obtain a more correct interpretation of the results for age.

We are sorry for not providing a description in the manuscript about how age was treated in the regression models. In this paper, the age variable was rescaled into 10-year intervals to make the estimate more meaningful and easier to understand^[1]. Thus, the correct interpretation of the prevalence ratio for age is as follows: for each 10-year increase in age the prevalence of depression decreased by 15%.

To highlight that the age variable was rescaled into 10-year intervals, the following information was added to the 'Materials and Methods' section under the heading 'Statistical analysis', on page 9:

To reduce the risk of sparse data bias, we decided to model age (10-year intervals) and education as continuous variables.

We also added the following sentence in the footnote of Table 2:

#: rescaled into 10-year age intervals.

We agree with the Reviewer that variables, such as gender, education and severity of impairment, would probably receive different estimates after the application of sampling weights to the analysis. However, in contrast to the Reviewer's opinion, we believe that the unweighted and weighted analysis would result in similar estimates for the age variable. The reason for this is that, in this age-stratified sample, the rates of depression within a specific age category will not be affected by the number of participants in the category. For example, in the age category 36–50 years, a random selection of, let's say, two-hundred or four-hundred participants will most likely produce similar estimates of depression.

1. **Hosmer Jr DW**, Lemeshow S, Sturdivant RX. Applied logistic regression. Hoboken, NJ: John Wiley & Sons, 2013.

6. *What criteria were adopted to decide which patients to refer to psychological counseling?*

Response: The following sentence has been added to the 'Materials and Methods' under the heading 'Referral to psychologist', on page 8, to clarify which participants that were referred to psychological counselling. We hope the Reviewer is satisfied with the added information.

Referral to psychologist. During the study it became apparent that the need for professional help was large and unmet in the sample population. Based on early feedback we received from the participants, we decided to offer referrals for psychological counselling for the subsequent participants (421 of 736 participants). **Patients were referred to psychological counselling for subjectively experienced mental disorder with the desire for professional help.** The psychologist recorded the number of participants who met for counselling and the main themes of the consultations.

7. I think it would be important to present the data on suicidal ideation among people with visual impairment. I would recommend excluding the analyses involving life satisfaction and depression because that comparison sounds really obvious, and I would recommend performing analyses using suicidal ideation as the outcome variable.

Response: We agree with the Reviewer that the relationship between depression and lower levels of life satisfaction seems obvious, but we still think that it is of importance to include these results because it support the argument that untreated depression in people with VI deserves greater public and political awareness.

We chose to exclude our results on scoring of the PHQ items, including suicidal ideation, because the main aim of the paper is about depressive disorders and not its symptoms. However, we agree with the reviewer that suicidal ideation among people with visual

impairment is an important topic, and we will gladly publish our data on suicidal ideation in future papers.

8. The conclusion of the abstract is not completely aligned with the conclusion of the main text. In the abstract the authors “suggest a need for mental health professionals with specific expertise in the challenges faced by those with VI”, which is somewhat outside of the scope of the results that were presented because the study did not address the appropriateness of the level of expertise of mental health professionals treating people with VI and depression. On the other hand, the statement available in the text that depression in people with VI should be addressed by healthcare authorities and user organisations seem more reasonable.

Response: We agree with the reviewer that our abstract conclusion was somewhat outside the scope of the results. We generally followed the Reviewer’s suggestion. The abstract conclusion has been revised to read as follows:

Our findings suggest that depression in adults with VI, and especially among young and middle-aged adults, warrants greater attention by user organisations, clinicians and healthcare authorities.

9. Page 15, last paragraph. It would be great if you could provide a reference supporting the claim that there is a lack of knowledge among health personal about the mental health adversities associated with VI.

Response: We are happy to include a reference. The following reference has been added to the reference list, on page 23:

38. Roche YSB, Chur-Hansen A. Knowledge, skills, and attitudes of psychologists working with persons with vision impairment. *Disabil Rehabil* 2019 ; 11: 1-11 [DOI: 10.1080/09638288.2019.1634155]

The reference has also been added to the text, on page 15.

10. Table 2. I would like to suggest using just one p-value for the overall comparisons across age groups and men and women as was done in table 1.

Response: We thank the Reviewer for the suggestion. However, we would like to emphasize that we chose to perform stratified analysis instead of using weighting procedures to handle the stratified nature of the sample.

Nevertheless, we have discussed the Reviewer's comment and has concluded that the table is somewhat difficult to understand as it includes a high number of p-values. Additionally, since the study aim was to present age-specific estimates of depression, we chose to replace the p-values for the comparisons between women and men with p-values for comparisons across the different age groups.

11. I was not able to understand the content of table S1. Do the numbers represent the overall PHQ-9 score? If they do, please, remove the % symbols and the # and modify the title of the table to make it clearer. Please, add a footnote describing the maximum range possible for that scale.

Response: We agree. Changes have been made to the heading and content of Table S1 to make it more understandable and easier to read. Also, we have added information to the table footnotes describing how the variable was computed and categorized.

Furthermore, we have made some changes to the 'Materials and Methods' under the heading 'Statistical analysis', on page 9, to make it easier to understand the methods of the supplementary analysis.

To explore differences between classification methods, we performed supplementary analysis by using the sum score method of the PHQ-9 dichotomized into no or mild depression (a sum score < 10) and moderate to severe depression (a sum score ≥ 10)^[18]. A sum score of 10 or higher has been recommended as the most optimal cut-off in screening for major depression^[18,19].

We have also made some revisions to the 'Results' section, on page 11, in the paragraph that presents the results from the supplementary analysis:

We then performed a supplementary analysis by estimating the proportion of the study population with moderate to severe levels of depression. Although this type of categorization resulted in higher rates of depression, the results from the analysis supported our main findings of severe depression being most common among the youngest participants (Table S1).

12. Please provide a copy of the document whereby the Regional Committee for Medical and Health Research Ethics confirmed that the study required no formal ethical approval as it was carried out in accordance with principles of anonymized data (Reference number: 2016/1615A).

Response: We are sorry for the confusion. The document 'Institutional Review Board Approval Form or Document' has been renamed into 'Approval from Regional Committee for Medical and Health Research Ethics'. We hope the revised title makes it clearer for the reader that the document contains the formal approval by the ethical committee.

Minor Comments

Page 12, second paragraph, please substitute “having additional impairments” for “having addition impairments”.

Response: We agree with the Reviewer, and have replaced the term ‘having additional impairments’ with the term ‘having addition impairments’.

Response to Editor

1. *Scientific quality : 1C. The article is visual impairment and depression: age-specific prevalence, associations with vision loss, and relation to life satisfaction, within the scope of World Journal of Psychiatry. Summary of peer-review report: This is an interesting and well-written manuscript about an important and often overlooked public health problem. However, the conclusion of the abstract is not completely aligned with the conclusion of the main text.*

Response: We thank the Editor for the comment. Major revisions have been made to the abstract conclusion. We hope the Editor is satisfied with the revised conclusion:

Our findings suggest that depression in adults with VI, and especially among young and middle-aged adults, warrants greater attention by user organisations, clinicians and healthcare authorities.

2. *Author should supplement more data about psychological counseling and major depression vs overall depression.*

Response: We followed the Editor's recommendations. The following information was added to the 'Results' section under the heading 'Referral to a psychologist', on page 12:

Of the 45 referred to counselling, 30 (8.4%) had no depression, 13 (28.9%) had major depression, and 2 (10.0%) had other depression ($p < 0.001$).