Author's response to reviews

Title: Visual impairment is associated with physical and mental comorbidities in older adults: a cross-sectional study

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Author's response to reviews: see over
1923835931135123 - Visual impairment and physical and mental health comorbidities in older adults: cross-sectional study of 291,169 patients in primary care

We are grateful for the comments and suggestions of both reviewers and have now addressed these within our revised manuscript as below. We feel that these changes have greatly enhanced this submission.

Please note: changes are easily identified in the revised manuscript with red text.

Reviewer 1

Discretionary revisions

1. The use of the term ‘older’ to describe the sample in the paper is sometimes misleading as it suggests comparison with something. For e.g. in the first sentence of the discussion “we found that older patients with visual impairment….relative to non-Visually impaired controls and that these differences were not accounted for by age...” sounds like you mean older in comparison to younger patients, rather than simply patients in the UK aged >65 years. Consider just describing it exactly, ‘patients aged greater than 65 years with VI...”

RESPONSE: To remove ambiguity, we have replaced the term ‘older’ in the abstract and manuscript with an exact definition of this group. As suggested by the reviewer we have identified the group as ‘patients aged greater than 65 years with visual impairment’ (please see Abstract page 2, line 19; Discussion page 12, line 7).

2. The structure of the Discussion section is unusual. Most scientific papers present a summary of main findings; compare and contrast with other related work; offer plausible reasons for differences in findings; discuss the implications of the findings for researchers/clinicians etc; and then discuss the strengths and limitations. It may facilitate readers if the current discussion was presented in a more usual manner.

RESPONSE: As suggested by the reviewer, the discussion has been restructured in a more conventional manner. Please note that content remains the same apart from any additions which have been identified in other parts of this response letter. We have retained some of the subtitles to help signpost the reader, however we are happy to remove this if the editor feels that they are not required.

3. Indicate in table 3 and 4 that the conditions are ordered by size of odds ratio (largest to smallest).

RESPONSE: As suggested by the reviewer, we have identified in the legend of table 3 and 4 that the conditions are ordered by size of odds ratio (largest to smallest).
Minor Essential Revisions

1. The title should not include the sample size, and could be more specific, e.g. “Vision impairment is associated with physical and mental comorbidities in older adults: a cross-sectional study”.

**RESPONSE:** As suggested by the reviewer we have removed the sample size and modified the title in order to make it more specific. The title now reads “Visual impairment is associated with physical and mental comorbidities in older adults: a cross-sectional study”.

2. The abstract should include the statistical methods used.

**RESPONSE:** We have now included statistical methods into the abstract, it now reads:

> “Prevalence, odds ratios (from prevalence rates standardised by stratifying individuals by age groups (65 to 69 years; 70 to 74; 75 to 79; 80 to 84; and 85 and over), gender and deprivation quintiles) and 95% confidence intervals (95% CI) of 37 individual chronic physical/mental health conditions and total number of conditions were calculated and compared for those with visual impairment compared to those without” (see page 2, line 9-13).

3. The phrase ‘higher levels of multiple comorbidities’ is often used, seemingly to simply mean ‘multiple comorbidities’ or ‘more comorbidities’. The term ‘higher levels’ suggests severity of conditions and that is not what is analysed in this study. The language should be tightened to say exactly what is meant.

**RESPONSE:** We have now clarified what is meant by ‘higher levels of multiple comorbidities’ and adjusted the abstract (see page 2, line 19) and discussion (see page 8, line 4) accordingly.

4. The second sentence in the Principle findings of the discussion, “Indeed…” has not been previously reported and belongs as a main findings in the results. A summary of this finding belongs here (i.e. no data).

**RESPONSE:** The reviewer comments that the following data in the discussion has not been reported in the results: “Indeed, after standardisation the visual impairment group were twice as likely to have five or more physical/mental health comorbidities (OR 2.05 95% CI 1.94-2.18).” In fact this data is reported in the results section (please see table 2). However, we agree that we do not need to report the data a second time in the discussion, and as such the data has been removed from the discussion.

5. The first sentence in the ‘strengths and weaknesses in relation to other studies’ section is unclear. Need to remove ‘which examine multiple rather than singular comorbidities’?

**RESPONSE:** As suggested by the reviewer, we have removed the words ‘which examine multiple rather than singular comorbidities’ from the discussion.

6. Future research could include a need for cohort studies to enable causality to be explored as we are limited by cross-sectional data here.

**RESPONSE:** We have now included the following sentence into the ‘future research’ section of the discussion:

> “The current study is a cross-sectional analysis. Cohort studies are required to enable causality of visual impairment and comorbidities to be explored further.” (see Discussion, page 11, line 18-19)
Major Compulsory Revisions

1. More information should be given in the methods to describe the definition of visual impairment. Looking at the appendix of the read codes, it seems that the cut-off applied was ‘moderate VI in one eye, no VI in the other’. What categories were excluded? What does ‘moderate’ mean in terms of Logmar or Snellen? It would seem that this paper looks at moderate to severe VI, not mild levels. This should be made clear in the title, abstract and main text. It should also be mentioned in the discussion as a limitation.

RESPONSE: We thank the reviewer for this comment and we have now more fully described the definition of visual impairment based upon Read codes. The text inserted into the methods as follows:

“GPs do not routinely record detailed quantitative data about sight such as visual acuity, but will code what they consider to be significant morbidity using Read Codes which are the morbidity coding system used in all UK primary care medical records. The set of Read Codes we used was one created by NHS Scotland Information Services Division to define visual impairment for the purposes of analysing an NHS Scotland general practice morbidity recording national dataset (Practice Team Information) (a full list of the Read Codes used is provided in Appendix 2).” (see methods page 4, lines 11-16).

We have also referenced this webpage to provide information about the NHS Scotland Practice Team Information programme and its approach to defining groups of codes: http://www.isdscotland.org/Health-Topics/General-Practice/GP-Consultations/Grouping-clinical-codes.asp

Based upon the method of coding it is not possible to identify the cut-off’s that were applied in terms of visual acuity, nor the categories that were excluded. We acknowledge that what is being recorded is not true epidemiological measurement of visual function. However, this is balanced against being able to measure in very large representative populations, and having good comorbidity data. As suggested by the reviewer, we have now identified this as a limitation in the discussion. The inserted/revised text is as follows:

“An important limitation is that visual impairment is based on GP recording of one or more Read Codes rather than formal measurement of visual function. The Read Codes used were a broad set which do not always clearly define the exact nature of the visual impairment, and visual impairment is under-recorded compared to epidemiological estimates [1]. However, our expectation is that most people with very severe impairment will have been coded. From this perspective, the finding that 1.8% of the sample were defined as having visual impairment is consistent with 0.5% of Scottish residents being formally registered as visually impaired, which is known to only include about half of those eligible for registration [37]. Registration can only be done by a consultant ophthalmologist with clear visual acuity and visual field criteria defining ‘partially-sighted’ or ‘blind’ registration. The study reported by Van Nispen [17] had clear clinical inclusion criteria for patients with visual impairment, including assessment by an ophthalmologist, but it is important to recognise that this requirement in itself is likely to systematically exclude the very frail, and people who are housebound or resident in care-homes. All studies in this area are therefore likely to be biased in some way, and the limitations of our study are inevitable in all studies relying on routine clinical coding, even in Scottish primary
care where use of electronic medical records is longstanding and coding reasonably reliable. However, these limitations have to be balanced against the ability to analyse data from very large representative samples, and we believe the findings are valid.” (see discussion: page 10, line 2-19)

2. More information on the exact statistical analyses/modelling used should be provided in the methods, for both the univariate and multivariate analyses. It is unclear if age was adjusted for using the categorical grouping or as a continuous variable.

RESPONSE: More information has been given on the statistical analysis used. Age was standardised as a categorical variable for the purpose of standardisation of prevalence rates. We have changed the methods section to make this clearer:

“To control for differences between the two populations in age, gender and deprivation levels we generated standardised prevalence rates by age group (65 to 69 years; 70 to 74; 75 to 79; 80 to 84; and 85 and over), gender and deprivation quintile using the direct method. These age-gender-deprivation standardised rates were then used to calculate odds ratio (ORs) and 95% confidence intervals (95% CI) for those with visual impairment compared to those without visual impairment (controls) for the prevalence of 29 physical conditions (two conditions were excluded: glaucoma since it is a purely ocular condition, and viral hepatitis because only one person with visual impairment had this condition) and eight mental health conditions (depression, alcohol misuse, ‘other psychoactive substance abuse’, learning disability, anorexia/bulimia, ‘anxiety and other neurotic, stress-related and somatoform disorders’, ‘schizophrenia and related conditions’, and dementia), as well as by the number of overall conditions and the number of physical and mental health conditions. We used t tests to analyse differences for mean age and deprivation score and one-way analysis of variance for differences across age groups and deprivation quintiles”. (see page 4, line 24 – page 5, line 12)

3. Findings that are significant at the 0.05 level should be indicated in the tables and p values provided.

RESPONSE: Significance can be taken from the 95% confidence intervals. However to add clarity we have added p values to the tables.

4. The first sentence in the results section ‘comorbidities: visual impairment vs. controls’ adds up data from rows in table 2, but we do not know if this is statistically significant. The same applies for the last sentence in this section.

RESPONSE: These are both significant at p<0.001 and this has been added to the text (see results, page 6, line 11 & 21).

5. Also, it seems from table 2 that people with vision impairment are less likely than controls to have 1 or 2 comorbidities, that there is no difference with 3 comorbidities, and those with vision impairment are more likely to have 4 or 5 or more comorbidities. This should be explained and it maybe does not justify adding them all together to simply say ‘those with VI were more likely to be comorbid than controls’.
RESPONSE: We have now explained more clearly that people with visual impairment are less likely than controls to have 1 or 2 comorbidities and that those with visual impairment are more likely to have 4 or 5 (see Results page 6, line 11-16):

“Whilst controls were more likely to have one (visually impaired 9.9% vs. controls 19.7%; OR 0.55 95% CI (0.50 - 0.60)) or two (visually impaired 14.7% vs. controls 19.9%; OR 0.72 95% CI (0.67 - 0.78)) conditions, the visual impairment group were significantly more likely to have four conditions (visually impaired 15.4% vs. controls 11.7%; OR 1.17 95% CI 1.08-1.26) and five or more conditions (visually impaired 37.4% vs. controls 17.8%; OR 2.05 95% CI 1.94-2.18) (table 2) (even after standardising for age, sex and social deprivation).”

Furthermore, as suggested by the reviewer we have removed the sentence ‘those with VI were more likely to be comorbid than controls’ to increase clarity of results.

6. The second sentence in this section does not make sense: “Differences between...were more pronounced...” More pronounced that what? Tighten this sentence.

RESPONSE: By rephrasing the sentence in point 5 (above), ambiguity has now been removed from this sentence (see Results page 6, line 11-16).

7. Why weren’t more confounding variables controlled for that could impact on prevalence and number of conditions (e.g. marital status, other measures of SES such as income, occupation, education etc.)? This should be discussed as limitation. Why were the 3 assessed variables picked?

RESPONSE: As identified by the reviewer only three confounding variables were controlled for. This is a large routine dataset and we were restricted by what data was available. Clinical records do not reliably record marital status, income, occupation or education, but do reliably record address/postcode. We have therefore used postcode assigned SES because we had near complete data on this, as well as complete data on age and sex (our previous work has shown that these are all powerful predictors of multimorbidity: Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B: Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012, 380(9836):37-43). As suggested by the reviewer we have now identified this within the limitation section of the discussion:

“Additional limitations are that there may be reporting bias, where people who attend frequently are more likely to have all clinical conditions recorded, in which case people with visual impairment recorded will also be more likely to have other conditions recorded, and that we were only able to control for three confounding variables” (page 10, line 21-24).

And

“With regards to other confounders, we were restricted by what data was available. Clinical records do not reliably record marital status, income, occupation or education, but do reliably record address/postcode. We therefore used postcode assigned socioeconomic status, gender and age because we had near complete data on them. However, this represents the trade-off between large and representative routine data analyses and more detailed epidemiological studies which are likely to be smaller and likely less representative (because the sickest and frailest won’t take part). Moreover indicators such as income, occupation or education are likely to be strongly correlated with
each and therefore at least partly accounted for by measures of socioeconomic status such as the Carstairs score used in this study.” (page 11, line 8-16).
Reviewer 2

Major concern:

1) Accuracy of information on the presence/absence of conditions - The prevalence of visual impairment, as detected by Read Code, is quite low. As the authors note, the prevalence of visual impairment among older adults in developed nations is typically found to be substantially higher than the 1.8% rate observed here.

a. Can the authors cite any existing information about the reliability or accuracy of Read Codes to detect vision impairment or any of the other conditions reported here? In any case, it would be helpful (especially for international readers) to define “read codes,” commenting on the process by which they are recorded – e.g., who records them, are there incentives or mandates associated with recording them?

RESPONSE: There is no data about the reliability or accuracy of Read Codes to detect vision impairment/other conditions that the authors are aware of. For many of the comorbidities examined there are financial incentives for GPs to maintain complete and accurate registers, but this is not the case for visual impairment. Having already responded to Reviewer 1 (Major compulsory revisions 1) we have provided more information on Read Codes and the process of recording them. However, we have additionally identified in the discussion the implication of needed better recording of visual impairment in GP records given its important impact on function and quality of life (see discussion page 11, line 25-page 12, line 1):

“Additionally, although there are incentives for GPs to record more accurate and complete registers of some comorbidities, this is not the case for visual impairment.”

b. I am primarily concerned that observed associations represent a reporting bias – i.e., if some people are more likely to have ANY present condition coded (because they utilize healthcare more often or other reasons), then we expect to observe correlation among various conditions, especially in very large datasets with great power to detect relatively small absolute differences (such as 0.2% vs. 0.5% rates). The authors correctly acknowledge that the 1.8% is low and they do comment on the limited reliability of administrative data, but I think they need to more specifically describe the possibility of reporting bias.

RESPONSE: We thank the reviewer for this comment, and have now described the possibility of reporting bias in the discussion (see page 10, line 21 – page 11, line 16):

“Additional limitations are that there may be reporting bias, where people who attend frequently are more likely to have all clinical conditions recorded, in which case people with visual impairment recorded will also be more likely to have other conditions recorded, and that we were only able to control for three confounding variables. Reporting bias is likely to be present to some extent, but we believe the impact of this is likely to be small because patients in the UK are required to register with a single practice to access National Health Service care, and their clinical record is automatically transferred when they change practice. All specialists write to the GP and therefore populate the
primary care record. Reporting bias in cradle-to-grave record is less likely than one where records are created anew every time patients register, although may be present for conditions where patients may significantly self-care (for example constipation) than ones where registers are more complete (for example, ischaemic heart disease). If present, reporting bias would be expected to somewhat inflate the odds ratios of having comorbidity in people with visual impairment compared to those without, but would have less influence on the estimates of comorbidity rates in the visually impaired population.”

c. Even though the comparison of rates between those with and without visual impairment is subject to some bias, I think it is still useful to report on the high prevalence of comorbidity in those being treated for vision impairment. I recommend highlighting the descriptive findings regarding which comorbid conditions appear to be most prevalent in people who were coded as ‘visually impaired’ – and reduce the focus on the comparison between visually impaired and nonvisually impaired, given the inherent problems with defining these two groups.

**RESPONSE:** We thank the reviewer for this comment. Although we had identified the most prevalent physical health (hypertension and CHD) and mental health (depression) conditions in the discussion, we agree with the reviewer that these findings could be further highlighted. Therefore, to increase the focus on the descriptive findings we have 1) also highlighted diabetes as the third most prevalent physical condition (see discussion page 8, line 15) and, 2) moved these paragraphs higher up the discussion.

2) **Minor concerns:**

3) Methods – If I understand the methodology correctly, the authors did not model the data with regression analyses, adjusting for covariables, but rather stratified the population by age/gender/socioeconomic deprivation and directly compared prevalence of each comorbidity. If this is correct, why did authors choose this approach, rather than regression which would have allowed them to control for additional covariables? If they did apply regression analyses, please state that and report what type of regression analysis.

**RESPONSE:** We generated direct standardised prevalence rates to control for differences by age, gender and deprivation. We have changed the methods to make this clearer (see methods, page 4, line 24 – page 5, line 2). We choose this approach as it preserves consistency between the populations being compared and requires fewer assumptions than using regression. Also the dataset was limited in its availability of patient characteristics so no other potential confounders were available limiting the benefits of using a regression model.

4) Table 1 might indicate statistically different proportions. The Methods should then indicate the statistical test used to make such comparisons.

**RESPONSE:** All differences are significant at p<0.001 we have added this to the table and the following to the methods:
“We used t tests to analyse differences for mean age and deprivation and one-way analysis of variance for differences across age groups and deprivation quintiles”. (see page 5, line 11-12)

5) All tables require column headings that more clearly explain what the numbers in the columns represent (i.e., “total number (prevalence)” and “Odds ratio (95% CI)”

**RESPONSE:** To improve clarity, we have provided clearer column headings in all tables.

**Discretionary Revisions**

6) References – These are references that seem relevant to a discussion of the current findings in the context of existing literature. The authors may wish to include these studies in Introduction and/or Discussion.


**RESPONSE:** We thank the reviewer for these references and both have been cited to strengthen our introduction (see Background, page 3, line 10: ref 14&15).