PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A comparison of the causes of blindness certifications in England and Wales in working age adults (16-64 years), 1999-2000 with 2009-2010
AUTHORS	Liew, Gerald; Michaelides, Michael; Bunce, Catey

VERSION 1 - REVIEW

REVIEWER	Tiarnan Keenan, MRCOphth Clinical Research Fellow, University of Manchester and Manchester Royal Eye Hospital, UK Previously consulted for Alimera Sciences Inc
REVIEW RETURNED	08-Oct-2013

GENERAL COMMENTS	This is an important paper presenting novel data. I have some specific points as follows: The title is made slightly confusing by the years. It almost looks as if 10 years of data are being presented, i.e. 1999/2000 to 2009/10. It might be clearer to use 'versus' instead of 'to. The authors concede that incidence of blindness differs from incidence of registered blindness, and discuss this effectively with supporting references (published 1994, 2005, 2006). I presume that there are no more recent papers or data on this? The exact dates of data collection should be given earlier, and certainly in the Methods section and Abstract, as 2009-2010 is ambiguous (e.g. calendar years, NHS years etc). As the authors point out, they have presented the data as numbers and proportions, rather than rates per x population (though it would be possible to present both). This does mean that they can comment on relative contributions to the pool of visual impairment by one disease versus another. However it limits further discussion. Is the change statistically significant? The relative contribution of diabetic retinopathy/maculopathy to registered blindness may have decreased, but has the incidence of registered blindness from diabetes also decreased? Without knowing this, it makes it difficult for the authors to stray into their discussion of the potential effects of screening programmes and glycaemic control. 'Whether increased rates of certification for inherited eye diseases' and 'rates of blindness certification for optic atrophy have also increased' - do the authors mean rates as in numbers per time period? I suspect that most people would read these rates to mean numbers per population per time period.

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	I wonder whether it's possible that some cases of hereditary retinal disorders were labelled as 'degeneration of macula and posterior pole', and that this occurred more commonly in 1999-2000 versus 2009-2010? The manuscript was very well presented, and clearly defined its objectives and methods, with a thorough discussion of relevant points and strengths/limitations.

REVIEWER	Christopher G Owen Reader in Epidemiology, St George's, University of London
REVIEW RETURNED	08-Nov-2013

GENERAL COMMENTS	While the numbers of blind certifications amongst the working age population of England and Wales are useful to know, providing patterns in older adults would be very informative, especially as the number of blind certifications amongst the working age population is low compared to older adults. A paper considering adults of all ages could be considered. If not the paper should make it very clear throughout that the findings refer to working age adults. Given the change in certification over the decade of comparison, greater caution should be used in interpretation. For instance, caution should be exercised in attributing reductions in DR/M blindness to improvements in screening / treatments. Note, population trends in diabetes / treatments are not cited. Real and artefactual explanations for change could be explored more. For instance, apparent increases in hereditable retinal disorders over a ten year period seem unlikely (similarly reductions caused by myopia) – may suggest diagnostic transfer. Geographic variability in certifications may allow the role of immigration to be commented on further. Unclear why comparisons with 2007-8 data were not made (Bunce, Eye, 2010). Meaning of 'Crown Copyright' to non-UK readers should be outlined. Data plural throughout, i.e., these data.

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Tiarnan Keenan, MRCOphth

1.This is an important paper presenting novel data. I have some specific points as follows:

The title is made slightly confusing by the years. It almost looks as if 10 years of data are being presented, i.e. 1999/2000 to 2009/10. It might be clearer to use 'versus' instead of 'to.
We agree with this and have amended the title as suggested. The title now reads "Changes in the Leading Causes of Blind Certifications in Working Age Adults in England and Wales 2009/2010 versus 1999/2000 – With Diabetic Retinopathy Now No Longer the Leading Cause."
2. The authors concede that incidence of blindness differs from incidence of registered blindness, and discuss this effectively with supporting references (published 1994, 2005, 2006). I presume that there are no more recent papers or data on this?
This is correct. To our knowledge there are no more recent references.
3. The exact dates of data collection should be given earlier, and certainly in the Methods section and Abstract, as 2009-2010 is ambiguous (e.g. calendar years, NHS years etc).
We now state clearly in the Methods and Abstract that data were collected from forms with a

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certification date between the 1st April 2009 and the 31st March 2010, and between the 1st April 1999 to 31st March 2000.

4. As the authors point out, they have presented the data as numbers and proportions, rather than rates per x population (though it would be possible to present both). This does mean that they can comment on relative contributions to the pool of visual impairment by one disease versus another. However it limits further discussion. Is the change statistically significant? We are sorry that we were not more explicit with regards our methodology. We looked at the data mainly to answer the question as to whether or not diabetes is still the leading cause of certifiable visual loss in the working age group. This claim is made in virtually every grant application and research paper investigating diabetic retinopathy. Formally assessing whether or not the proportion has changed over time is not the objective of this paper and we are sorry that this was not made more explicit.

We are not able to state the rate per population, as the number of patients with diabetes in England and Wales is not known precisely.

We have now performed a chi square test and the difference in proportions is statistically significant. We now state this in the Results.

"X2 tests were performed to test differences in proportions.…..This difference was statistically significant (P=0.009)."

5. The relative contribution of diabetic retinopathy/maculopathy to registered blindness may have decreased, but has the incidence of registered blindness from diabetes also decreased? Without knowing this, it makes it difficult for the authors to stray into their discussion of the potential effects of screening programmes and glycaemic control.

It is difficult to determine if the incidence of blindness from diabetes has changed as the prevalence of diabetes is not known precisely. Most published papers have only reported estimated prevalence based on general practice surveys, with values ranging from 1-2% of the general population.(Khunti K, British Journal of General Practice 1999; deLusignan BMC Family Practice 2005) We do accept the reviewer's point but in the absence of robust data on the prevalence of diabetes we are unable to answer it directly.

We intentionally avoided commenting on the incidence of blindness from diabetes in the manuscript, as our data alone could not determine this. Nonetheless, regardless of the actual incidence rates of blindness, our data do show that both the absolute numbers as well as proportion of registrable blindness due to diabetes have decreased, making it no longer the leading cause of registrable blindness in working age adults. We would like to highlight again that our aim is not to report on the incidence of blindness, but rather to challenge the often repeated statement that diabetes is the leading cause of blindness is working age adults.

We hope we have made this point more clearly in the revised Discussion.

"This report is not designed to identify the reasons behind these changes or estimate the incidence of blindness from diabetes. The prevalence of diabetes in the UK is not known with certainty, with several limited general practice surveys suggesting a range of between 1-2% of the general population11-14; we are thus not able to estimate the incidence of blindness from diabetes. Nonetheless, available data suggest the prevalence of diabetes in England and Wales has increased over the period in question11;13, which would be expected to lead to increased rates of blindness if other factors remained constant. In this context we speculate that several intervening public health developments may have contributed to the reduction in both absolute and proportional rates of registrable blindness from diabetes amongst working age adults."

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6.'Whether increased rates of certification for inherited eye diseases' and 'rates of blindness certification for optic atrophy have also increased' - do the authors mean rates as in numbers per time period? I suspect that most people would read these rates to mean numbers per population per time period.

We mean rates as in numbers per time period, and have now made this clearer to read “Whether increased numbers of certification for inherited eye diseases” and “numbers of blindness certification for optic atrophy have also increased…”
7. I wonder whether it's possible that some cases of hereditary retinal disorders were labelled as 'degeneration of macula and posterior pole', and that this occurred more commonly in 1999-2000 versus 2009-2010?
We agree that it is possible that mislabeling occurred. We now discuss this further in the Discussion.

“Another possibility is that diagnostic transfer or misclassification may have occurred, for example where some cases of hereditary retinal disorders may have been mislabeled as 'degeneration of macula and posterior pole'. In order to explain the increase in hereditary retinal disorders, this would have had to occur preferentially in 1999-2000 versus 2009-2010. However, misclassification of diabetic retinopathy/maculopathy as hereditary retinal disorders is unlikely to occur given how different the conditions are, and so would not explain the absolute reduction in the number of certifications for blindness due to diabetes.”

8. The manuscript was very well presented, and clearly defined its objectives and methods, with a thorough discussion of relevant points and strengths/limitations.

Reviewer Name Christopher G Owen
1. While the numbers of blind certifications amongst the working age population of England and Wales are useful to know, providing patterns in older adults would be very informative, especially as the number of blind certifications amongst the working age population is low compared to older adults.
We agree that causes of blind certifications amongst the elderly is of interest but this is the focus of a separate paper. Although the number of certifications in the working age population may be lower compared to older adults, their economic impact is likely to be greater.
2. A paper considering adults of all ages could be considered. If not the paper should make it very clear throughout that the findings refer to working age adults.
We have revised the manuscript and are now explicit that any mention of blindness refers only to working age adults, starting with the title - “Changes in the Leading Causes of Blind Certifications in Working Age Adults in England and Wales 2009/2010 versus 1999/2000 – With Diabetic Retinopathy Now No Longer the Leading Cause. “

3. Given the change in certification over the decade of comparison, greater caution should be used in interpretation. For instance, caution should be exercised in attributing reductions in DR/M blindness to improvements in screening / treatments. We agree and now clearly state that our attempt to explain our findings is speculative and should be read with caution.

“In this context we speculate that several intervening public health developments may have contributed to the reduction in both absolute and proportional terms of registrable blindness from diabetes amongst working age adults…… Nonetheless this remains speculative at present, and such explanations should be read with caution.”

4. Note, population trends in diabetes / treatments are not cited. Real and artefactual explanations for

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change could be explored more. For instance, apparent increases in hereditable retinal disorders over a ten year period seem unlikely (similarly reductions caused by myopia) – may suggest diagnostic transfer. We now cite population trends in diabetes and treatment of diabetes.

“Nonetheless, available data suggest the prevalence of diabetes in England and Wales has increased over the period in question11;13…”

“Concurrent with these screening programmes, in 2004 the Quality and Outcomes Framework17 was introduced to incentivise general practitioners in the United Kingdom to improve primary care management of several conditions including diabetes. Several studies have documented an improvement in the quality of care for diabetes since this was introduced,18;19 and the effort may have contributed to the improvement in glycaemic control documented since the late 1990s.17;20”

We thank the reviewer for the suggestion that diagnostic transfer may have occurred and now discuss this further.

“Another possibility is that diagnostic transfer or misclassification may have occurred, for example where some cases of hereditary retinal disorders may have been mislabeled as 'degeneration of macula and posterior pole'. In order to explain the increase in hereditary retinal disorders, this would have had to occur preferentially in 1999-2000 versus 2009-2010. However, misclassification of diabetic retinopathy/maculopathy as hereditary retinal disorders is unlikely to occur given how different the conditions are, and so would not explain the absolute reduction in the number of certifications for blindness due to diabetes.“

5. Geographic variability in certifications may allow the role of immigration to be commented on further. Unfortunately we do not have access to this data and are unable to comment on this. Ethnicity data on a large proportion of CVI forms is missing, and we believe this data is not missing at random and thus would be unreliable.

6. Unclear why comparisons with 2007-8 data were not made (Bunce, Eye, 2010). The Eye 2010 paper does not present data for the working age group which is why we did not make comparison with this publication. We have not reproduced the data from this publication as we do not think it would add to the current manuscript, which focuses on the most up to date data from 2009-2010.

7. Meaning of ‘Crown Copyright’ to non-UK readers should be outlined. We now state :
“…CVI data under Crown copyright, meaning the copyright is owned by the British Government.

8. Data plural throughout, i.e., these data.
We have made the changes.

VERSION 2 – REVIEW

REVIEWER	Christopher G Owen St George's, University of London
REVIEW RETURNED	24-Jan-2014

GENERAL COMMENTS	The paper is well written - I have no further comments. Authors may wish to consider the following more recent references to describe UK trends in diabetes? Diabetes UK. State of the nation 2012 report. Thomas MC, Hardoon SL, Papacosta AO, Morris RW, Wannamethee SG, Sloggett A, Whincup PH. Evidence of an accelerating increase in prevalence of diagnosed Type 2 diabetes in

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	British men, 1978-2005. Diabet Med 2009;26(8):766-772. Gonzalez EL, Johansson S, Wallander MA, Rodriguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. J Epidemiol Community Health 2009;63(4):332-336.

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