

# Monocular and binocular visual impairment in the UK Biobank study: prevalence, associations and diagnoses

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## ABSTRACT

**Objective** To determine the prevalence of, associations with and diagnoses leading to mild visual impairment or worse (logMAR >0.3) in middle-aged adults in the UK Biobank study.

**Methods and analysis** Prevalence estimates for monocular and binocular visual impairment were determined for the UK Biobank participants with fundus photographs and spectral domain optical coherence tomography images. Associations with socioeconomic, biometric, lifestyle and medical variables were investigated for cases with visual impairment and matched controls, using multinomial logistic regression models. Self-reported eye history and image grading results were used to identify the primary diagnoses leading to visual impairment for a sample of 25% of cases.

**Results** For the 65 033 UK Biobank participants, aged 40–69 years and with fundus images, 6682 (10.3%) and 1677 (2.6%) had mild visual impairment or worse in one or both eyes, respectively. Increasing deprivation, age and ethnicity were independently associated with both monocular and binocular visual impairment. No primary diagnosis for the recorded level of visual impairment could be identified for 49.8% of eyes. The most common identifiable diagnoses leading to visual impairment were cataract, amblyopia, uncorrected refractive error and vitreoretinal interface abnormalities.

**Conclusions** The prevalence of visual impairment in the UK Biobank study cohort is lower than for population-based studies from other industrialised countries. Monocular and binocular visual impairment are associated with increasing deprivation, age and ethnicity. The UK Biobank dataset does not allow confident identification of the causes of visual impairment, and the results may not be applicable to the wider UK population.

## INTRODUCTION

At present, data on the prevalence, associations with and diagnoses leading to visual impairment among middle-aged adults in the UK, especially those of working age, are lacking. Reliable prevalence data do exist but mainly for children and the elderly or for those with certifiable visual impairment. For middle-aged adults, the most widely used data come from a number of international, population-based studies, many of

## Key messages

### What is already known about this subject?

Current and reliable data on the prevalence of, associations with and diagnoses leading to monocular and binocular impairment is lacking, particularly for middle-aged adults.

### What are the new findings?

In this study with UK Biobank participants, the prevalence of monocular and binocular visual impairments was 10.3% and 2.6%, respectively. Increasing Townsend deprivation score, age and ethnicity were independently associated with both monocular and binocular visual impairments. Uncorrected refractive error, cataract, amblyopia and vitreoretinal interface abnormalities were the common identifiable causes of visual impairment. Despite the use of self-reported eye history, fundus photographs and spectral domain optical coherence tomography images, no identifiable cause for the recorded level of visual impairment was found in almost half the eyes.

### How might these results change the focus of research or clinical practice?

The UK Biobank dataset does not allow confident identification of the primary causes of visual impairment. However, most of the visual impairment in middle-age with an identifiable cause would be amenable to treatment. Despite the large number of participants, results from the dataset may still not be applicable to the wider UK population. Future research should explore the reasons behind the association of visual impairment with deprivation and ethnicity.

which concluded almost 20 years ago.<sup>1</sup> Given the recent increases in obesity and diabetes mellitus and national differences in ethnicity, smoking history and socioeconomic status, the findings of these studies may not be relevant to the current UK population.

UK Biobank is a voluntary, cross-sectional study of UK residents that aims to investigate how lifestyle, environment and genes influence the health of adults, aged 40–69 years, in the UK.<sup>2</sup> The size and breadth of the UK Biobank dataset provides a unique



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opportunity to collect accurate data on the prevalence and causes of visual impairment among participants. The aims of this project were to determine the prevalence of monocular and binocular visual impairment among UK Biobank participants, to investigate associations with known and potential socioeconomic, biometric, lifestyle and medical variables and to determine the causes of visual impairment among UK Biobank participants using self-reported eye history and image grading.

## MATERIALS AND METHODS

### Study population

Over the course of 2006–2010, UK Biobank recruited 503 325 participants at 22 centres by postal invitation (5.47% response rate).<sup>2</sup> Data collection during the baseline and enhanced assessments has been reported elsewhere.<sup>3–5</sup> Deprivation was assessed using the Townsend score: a measure of deprivation for each post-code area, derived from census data on employment, household overcrowding, car and home ownership.

Additional enhancements to the baseline assessment visit were included for the collection of eye data from 2009. This included visual acuity with habitual correction, using a semiautomated system using logMAR optotypes, autorefractometry and self-reported eye history for 133 668 participants, of whom 65 033 also underwent colour fundus photography and spectral domain optical coherence tomography (OCT) imaging. From these 65 033 UK Biobank participants with imaging, 8359 cases had mild visual impairment or worse (logMAR >0.3 or Snellen >6/12) in at least one eye and were matched with controls, without visual impairment, by age (5 year bands), sex and ethnic group at a ratio of 1:4.

In a nested pilot study, the ability to identify both the primary cause of and associations with visual impairment, using self-reported eye history and image grading, was investigated in a subset of 25% of those with visual impairment and fundus imaging. Cases for the nested pilot study were selected in order to be representative of all participants with visual impairment in terms of visual acuity, age, sex and ethnicity.

The UK Biobank project received approval from the North-West Multicentre Research Ethics Committee. Approval was also obtained for access to anonymised UK Biobank data by researchers, without the need for additional approvals.

### Baseline and enhanced assessments

Data collection during the baseline and enhanced assessments has been reported elsewhere.<sup>3–5</sup> In brief and of relevance to the eye, this comprised a history of spectacle or contact lens wear, eye surgery and disease, logMAR acuity, refractive error and fundus imaging. Using the Topcon 3D-OCT 1000 Mark 2 (Topcon Corporation, Tokyo, Japan), a single non-mydratic, 45° digital, colour image, centred on the fovea, and a spectral domain OCT cube scan of the macula, covering a 6mm\*6mm retinal

area (128 horizontal line scans comprised of 512 A-scans) were captured for both eyes.

### Analysis of fundus photographs and OCT images

Images were analysed using the Topcon OCT viewer software (V.4.21, Topcon Corporation) by experienced clinicians or by non-medical graders, certified for the detection and classification of diabetic retinopathy by the National Health Service (NHS) Diabetes Eye Screening Programme. Fundus photographs were assessed for image quality, media opacity, optic disc or retinal vascular or other abnormalities and the presence of signs of age-related maculopathy. OCT images were assessed for image quality, vitreoretinal interface abnormalities (VRIA) and intraretinal abnormalities. The presence or absence of ocular abnormalities and disease was confirmed using standard definitions.<sup>6–10</sup> Image quality grades are defined in online supplementary table 1. The main reason for adequate or inadequate images was assessed as being either technical or the result of media opacity.

### Assigning the primary diagnosis leading to visual impairment

Using the results of image grading and the level of visual impairment, together with self-reported eye history, graders assigned the primary diagnosis leading to visual impairment for each eye in a sample of 25% of the cases. (These cases were selected in order to be representative of the larger group of all participants with visual impairment in terms of the degree of visual impairment, age, sex and ethnicity.) For eyes in which no cause was identified, the presence or absence of habitual correction at the time visual acuity was recorded, and the refractive errors were noted. For the eyes with unaided visual impairment, uncorrected refractive error was considered to be the cause of visual impairment when no other pathology was identified and there was a spherical equivalent of  $\geq -1$ DS or  $\geq +2$ DS for mild visual impairment (logMAR >0.3 to <0.45),  $\geq -1.5$ DS or  $\geq +3$ DS for moderate visual impairment (logMAR 0.45 to <1.0),  $\geq -3$ DS or  $\geq +6$ DS for severe visual impairment (logMAR 1.0 to <1.3) and  $\geq -4$ DS or  $\geq +8$ DS for blindness (logMAR  $\geq 1.3$ ). As the best-corrected visual acuity was not recorded for participants, it was not possible to identify if participants with visual impairment despite habitual correction were also uncorrected. Visual acuity data was incomplete for one eye of 36 cases, and only the visual acuity data for the fellow eye was included.

### Statistical analysis

Descriptive statistics were used to report the prevalence and primary diagnoses leading to visual impairment in the UK Biobank participants. The characteristics of the cases were initially compared with the controls using descriptive statistics, both for all cases and then according to monocular or binocular visual impairment status. Univariate multinomial logistic regression models were used to investigate the association between known risk factors and other predetermined socioeconomic,

biometric, lifestyle and medical variables and both binocular and monocular visual impairment compared with the matched controls. Those factors found to be associated with visual impairment at a 10% level (to account for potential correlation between factors) were then included in a multivariable multinomial logistic regression model. Only those that were significantly associated ( $P < 0.05$ ) with visual impairment remained in the final multivariable model. Although the cases and controls were matched by age, sex and ethnic group, it is recommended also to adjust for these variables to account for any remaining differences; therefore, the final multivariable models included these variables irrespective of their association with visual impairment.<sup>11</sup> The final multivariable model was checked for collinearity ( $r > 0.7$  and  $P < 0.05$ ) between variables included in the model, and no evidence was found.

## RESULTS

From the 65 033 UK Biobank participants with imaging and self-reported eye history, 8359 had mild visual impairment or worse in at least one eye. The majority (6682; 80%) had monocular visual impairment, and the degree of visual impairment was typically mild or moderate (online supplementary table 2). As a proportion of all the eligible UK Biobank participants with baseline and extended eye assessments (65 033), the prevalence of monocular and binocular visual impairment was 10.3% (95% CI 10.0% to 10.5%) and 2.6% (95% CI 2.5% to 2.7%), respectively. The prevalence of mild, moderate, severe visual impairment and blindness in the better-seeing eye of those with binocular visual impairment was 1.63% (95% CI 1.53% to 1.73%), 0.92% (95% CI 0.85% to 0.99%), 0.03% (95% CI 0.02% to 0.04%) and 0%, respectively. The estimated prevalence of the same categories in the worse-seeing eye of those with monocular visual impairment was 5.7% (95% CI 5.5% to 5.9%), 4.0% (95% CI 3.8% to 4.2%), 0.57% (95% CI 0.51% to 0.63%) and 0.06% (95% CI 0.04% to 0.08%), respectively.

There were differences in the baseline descriptive statistics in relation to ethnicity, deprivation, employment status, smoking status, medications and self-reported health conditions between the 8359 cases and the 24 438 matched controls (online supplementary table 3). For example, 25.5% of cases lived in the most deprived quintile compared with 21.4% of the controls. There would also appear to be proportionally more cases with binocular visual impairment living in deprived areas, compared with those with monocular visual impairment. Of those with binocular visual impairment (1677), 30.9% lived in the most deprived quintile compared with only 24.1% of those with monocular visual impairment (6682).

The following factors were found to be significantly (at 5% level) associated with monocular or binocular visual impairment, compared with controls: age, ethnicity, deprivation, employment, systolic blood pressure, waist hip ratio, current smoking status, the presence of a smoker in household, medication for hypertension or

hypercholesterolaemia and a history of diabetes mellitus, cardiovascular or cerebrovascular disease (online supplementary table 4). These factors were included in a multivariable model to identify independent factors associated with visual impairment. Sex (as a matching variable) and estimated total retinol daily intake (as associated with the outcome at the 10% level) were also included in the multivariable model. Only age, ethnicity and deprivation remained significantly (at 5% level) associated with monocular and binocular visual impairments (online supplementary table 4). Those living in the most deprived quintile were 25% more likely than those in the least deprived quintile to have monocular visual impairment rather than no impairment, and 84% more likely to have binocular visual impairment, on adjustment for differences in age, sex and ethnic group. With each increasing decade of age, the risk of monocular visual impairment increases by 13%, and the risk of binocular visual impairment increases by 24%, adjusting for ethnic group, sex and deprivation differences. Black and other ethnic participants were 29% and 53%, respectively, more likely to have binocular visual impairment rather than none, compared with white participants, accounting for age, sex and deprivation differences. However, no significant association was found between ethnicity and monocular visual impairment compared with none, with or without adjustment for age, sex and deprivation differences, indicating that the association between ethnicity and visual impairment may only apply to binocular visual impairment.

For the sample of 25% of the cases with visual impairment, the primary diagnoses leading to monocular and binocular visual impairments are shown in online supplementary table 5. In both the better-seeing and worse-seeing eyes of those with binocular visual impairment, the most common identifiable causes were uncorrected refractive error, cataract and vitreoretinal interface disease. For the cases with monocular visual impairment, the most common identifiable causes were cataract, self-reported amblyopia and uncorrected refractive error. No primary cause for the level of visual impairment could be identified for up to 49.8% of eyes with visual impairment.

The majority of OCT images were of high quality, with the quality of 1836 (73.5%) images rated as good and 550 (22.0%) rated as adequate. The quality of the colour fundus photographs was lower with 1157 (46.3%) images rated as good, 811 (32.5%) rated as adequate, due to either technical issues (649) or media opacity (162), and 528 (21.2%) images were felt to be of inadequate quality, due to either technical issues (429) or media opacity (99).

## DISCUSSION

For the UK Biobank population with baseline and extended eye data, the prevalence of monocular and binocular visual impairment was 10.3% and 2.6%, respectively. Visual impairment was associated with increasing age and deprivation and ethnic minority status. Cataract,

amblyopia and uncorrected refractive error were the most common identifiable causes of visual impairment. However, despite access to self-reported eye history, autorefractometry, colour fundus photography and spectral domain OCT imaging, it was not possible to identify the primary cause of visual impairment for almost 50% of participants.

The prevalence of both binocular and monocular visual impairment in the UK Biobank cohort is lower than for many studies from other industrialised countries.<sup>5</sup> For an urban Canadian population aged 40 years and over, Robinson *et al* reported a binocular visual impairment prevalence of 2.7%.<sup>12</sup> Among residents of Victoria, Australia, VanNewkirk *et al*<sup>13</sup> recorded that the prevalence of any visual impairment was 4.2%, although both visual acuity and visual field were included in the definition of visual impairment. Similarly, Rahi *et al*<sup>14</sup> identified binocular visual impairment with habitual correction in 4.5% of British adults aged 44 or 45 years. However, for the NHANES study population, Vitale *et al* reported visual impairment prevalence figures of 4.3% and 8.8% among adults aged 40–59 years and aged 60 years and over, respectively, and in a systematic review, Bourne *et al* estimated the prevalence of moderate visual impairment of worse to be 3.9% for Western European adults aged over 50 years.<sup>15</sup> For monocular visual impairment, the British Birth Cohort reported a prevalence of 11.9% with habitual correction among a comparable group of adults aged 44 or 45 years.<sup>14</sup> Much higher figures were reported for other studies. The Blue Mountains Eye Study reported prevalence figures of 3.6% and 8.2% among adults aged 49–59 years and 60–69 years, respectively.<sup>16</sup> Nowak *et al* reported a prevalence of monocular visual impairment of 27.5% among adults aged 35–97 in Poland.<sup>17</sup> Much of the difference in the reported prevalence may be explained by differences in the age and sex of the participants in each study, the definitions of visual impairment and by the nature of the studies themselves.<sup>18</sup>

The UK Biobank study used the Townsend score to record deprivation. This index is determined by combining four census variables and can be calculated for any geographical area including postcodes. Increasing deprivation was associated with both monocular and binocular visual impairment among UK Biobank participants. This association has been reported before, both for UK Biobank and other populations.<sup>4 5 19</sup> However, it is unclear whether increasing deprivation adds to the risk of visual impairment by, for example, delaying access to eye care services, even though such services are often free within the UK NHS or is a consequence of visual impairment and downward social drift. In this study, employment status was associated with both monocular and binocular visual impairments on univariate analysis only. However, Cumberland *et al* identified an association between visual impairment and a range of economic variables, including employment, income and household structure, in a larger study involving UK Biobank participants.<sup>5</sup> Given the association between visual impairment

and socioeconomic status, initiatives to tackle preventable visual impairment may help to address health inequality.

Black or black British and other (non-white, or Asian or black) ethnicity were also positively associated with binocular visual impairment. Although the number of cases with these ethnicities was small, associations between visual impairment and ethnicity have been described before for both UK and US populations.<sup>20 21</sup> While glaucoma and diabetic retinopathy are common diagnoses leading to severe visual impairment and blindness in people of black ethnicity, cataract is the more common diagnoses of milder visual impairment in the same population.<sup>22</sup> Increasing age was also associated with categories of visual impairment, even those cases and controls were matched in 5-year age bands. No significant, independent association was found with the other, predetermined biometric, lifestyle and medical variables. This may reflect the low prevalence of visual impairment due to retinal vascular diseases, such as age-related macular degeneration, diabetic retinopathy and retinal vascular occlusion, in the study population.

For the UK Biobank participants with binocular visual impairment, uncorrected refractive error and cataract were the two most common identifiable diagnoses leading to visual impairment in the better-seeing eye. These two conditions were the largest causes of both mild and moderate visual impairment, but inherited retinal disease and myopic degeneration were the largest causes of severe visual impairment. In contrast to the sight impairment certification data, age-related macular degeneration, glaucoma and diabetic retinopathy were uncommon diagnoses leading to visual impairment.<sup>23</sup> Shweikh *et al* reported a 1.7% prevalence of self-reported glaucoma among UK Biobank participants, but mean visual acuity was good at better than logMAR 0.1 in each eye, so that the contribution of glaucoma to visual impairment based on an acuity definition alone may be smaller than expected.<sup>4</sup> In a systematic review, Bourne *et al* estimated that uncorrected refractive error and cataract were the most common causes of moderate and severe visual impairment in adults in Western Europe, with refractive error accounting for almost 50% of the visual impairment burden.<sup>1</sup> Many other studies have also reported that uncorrected refractive error accounts for the majority of visual impairment in adults from developed nations.<sup>12–15</sup>

For monocular visual impairment, cataract, amblyopia and uncorrected refractive error were the most common identifiable diagnoses leading to visual impairment. For moderate or worse visual impairment, self-reported amblyopia was the single most common diagnosis. In the Blue Mountains Eye Study, amblyopia was the most frequent diagnosis leading to mild or worse unilateral visual impairment in persons aged 49–59 years, but cataract was the most common cause of mild unilateral visual impairment in older people.<sup>9 16</sup> Similarly, Nowak *et al* reported that uncorrected refractive error, amblyopia, cataract and ARMD were the most common causes

of monocular visual impairment among adults, aged 35–97 years, and data from the British Birth Cohort suggest that refractive error accounted for 43% of monocular visual impairment.<sup>14 17</sup> By contrast, in the Salisbury Eye Evaluation Study, involving American adults aged 65–84 years, ARMD, other retinal diseases, trauma and amblyopia were the most common causes of monocular blindness.<sup>24</sup>

No primary cause for the recorded level of visual impairment could be identified in almost half of the eyes in the nested study. Visual acuity in the UK Biobank study was recorded using a semiautomated computerised test, based on the EDTRS logMAR chart. Although this test system has not yet been validated within a similar study population, it seems unlikely that there are significant errors in the recording of visual acuity as LogMAR vision charts are considered to be the reference standard for assessing visual function. Self-reported use of either spectacles or contact lenses was over 80%, both for participants with and without visual impairment.<sup>18</sup> Habitual correction worn at the time of the visual acuity test was assumed to be correct, and uncorrected refractive error was only considered to be a potential cause of visual impairment when either there was no habitual correction or the correction was reported as forgotten. The absence of a best-corrected or pin-hole acuity measure makes it likely that the contribution of uncorrected refractive error may have been underestimated.<sup>25 26</sup> The absence of lens or anterior segment images and slit-lamp examination also means that underdiagnosis may also apply to cataract, especially as a cause of mild and moderate visual impairment. The inclusion of spectral domain OCT images may have contributed to a higher prevalence of visual impairment due to vitreoretinal interface disease was then expected.

Image quality was generally good, particularly for the OCT images. The inclusion of the OCT images is likely to have aided in the diagnosis of macular oedema and VRIA.<sup>27</sup> Even when the quality of either image was graded as inadequate, it was often possible to derive some information that could be used for grading, either from the inadequate image itself or the other image. This was most often the case when the fundus photograph was graded as inadequate, but the OCT image was graded as good or adequate. MacGillivray *et al* also identified problems with the quality of the colour fundus images among UK Biobank participants.<sup>28</sup>

This study has a number of strengths and potential weaknesses. The UK Biobank project was large and had good geographical coverage. It was one of the first to collect spectral domain OCT images and over 65 000 participants had baseline and extended eye data, meeting the criteria for inclusion in this study. Many of the key findings in relation to the causes of and associations with visual impairment are consistent with other studies. However, the UK Biobank study is not a population-based study, and the response rate to the invitation to participate was very low. Participants were generally healthier, older,

more affluent and more likely to be urban than the full UK population and so may not be representative.<sup>3 5 18 26</sup> This study also involved only those participants with baseline and enhanced eye assessments. As a result, the visual impairment prevalence figures reported here may not be applicable to the wider UK population and are likely to be minimum prevalence estimates. Furthermore, for the cases with both monocular and binocular visual impairments, no cause was identified in almost 50% of cases. Habitual correction was assumed to be correct, and this may have underestimated the contribution of refractive error. Similarly, many eyes may have more than one diagnosis leading to visual impairment. Without a single pathology to explain all of the impairment, no diagnosis would be recorded for these eyes, potentially reducing the overall contribution of both refractive error and ocular pathology. Finally, the diagnosis of monocular and binocular amblyopia was also based on the self-reported eye history and normal imaging but did not take account of refractive error.<sup>29</sup> Limiting the analysis to UK Biobank participants with both baseline and extended eye data may also have caused the study to be underpowered.<sup>5</sup>

The prevalence of visual impairment of any level in the UK Biobank cohort is lower than for population-based studies from other industrialised countries. Although visual impairment was typically mild or moderate, monocular and binocular visual impairment were associated with increasing age and deprivation and ethnic minority status. Cataract and uncorrected refractive error were the most common identifiable causes of both monocular and binocular visual impairments. Despite access to self-reported eye history and both fundus photographs and spectral domain OCT images, no cause was identified for the level of visual impairment recorded in almost half the cases. Therefore, the methodology used in the UK Biobank study may be inadequate to identify the primary causes of visual impairment with confidence. Results from analysis of the UK Biobank dataset may also not be applicable to the wider UK population.

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**Contributors** MM planned the study, secured funding, led the image grading and data analysis and was responsible for the initial draft of the manuscript. DS and TMF have been involved in the study design, data analysis and review of the manuscript. The other members of the UK Biobank Eye and Vision Consortium are listed as collaborators and have had the opportunity to review the data and comment of the data before the manuscript was submitted for publication.

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