

Vitreoretinal interface abnormalities in middle-aged adults with visual impairment in the UK Biobank study: prevalence, impact on visual acuity and associations

Martin McKibbin,¹ Tracey Farragher,² Darren Shickle² UK Biobank Eye and Vision Consortium

To cite: McKibbin M, Farragher T, Shickle D. Vitreoretinal interface abnormalities in middle-aged adults with visual impairment in the UK Biobank study: prevalence, impact on visual acuity and associations. *BMJ Open Ophthalm* 2017;**1**: e000057. doi:10.1136/bmjophth-2016-000057

Received 20 November 2016
Revised 03 April 2017
Accepted 11 April 2017

ABSTRACT

Objective The aim of this study was to determine the prevalence of vitreoretinal interface abnormalities (VRIA), the degree of visual impairment and associations with VRIA among adults, aged 40–69 years, in the UK Biobank study.

Methods and analysis Colour fundus photographs and spectral domain optical coherence tomography images were graded for 25% of the 8359 UK Biobank participants with mild visual impairment or worse (LogMAR >0.3 or Snellen <6/12) in at least one eye. The prevalence and contribution of VRIA to visual impairment was determined and multinomial logistic regression models were used to investigate association with known risk factors and other predetermined socioeconomic, biometric, lifestyle and medical variables for cases and matched controls.

Results The minimum prevalence of any VRIA was 17.6% and 8.1% in the eyes with and without visual impairment, respectively. VRIA were identified as the primary cause of visual impairment in 3.6% of eyes. Although epiretinal membrane and vitreomacular traction were the most common VRIA, the degree of visual impairment was typically milder with these than with other VRIA. Visual impairment with a VRIA was positively associated with increasing age (relative risk ratio (RRR) 1.22 (95% CI 1.07 to 1.40)), female gender (RRR 1.28; 1.08 to 1.52) and Asian or Asian British ethnicity (RRR 1.60; 1.10 to 2.32).

Conclusions VRIA are common in middle-aged adults in the UK Biobank study, especially in eyes with visual impairment. VRIA were considered to be the primary cause of visual impairment in 3.6% of all eyes with visual impairment, although there was variation in the degree of visual impairment for each type of VRIA.

INTRODUCTION

Despite the widespread use of spectral domain optical coherence tomography (OCT) in routine clinical practice, there is limited data on the prevalence and visual consequences of different vitreoretinal

Key messages

What is already known?

- ▶ Several population-based studies have reported the prevalence of posterior vitreous detachment and vitreoretinal interface abnormalities (VRIA) and the association of VRIA with visual impairment.

What are the main findings?

- ▶ In this study with UK Biobank participants, VRIA were common abnormalities, both in eyes with and without visual impairment, and were identified at least four times more often with spectral domain optical coherence tomography (OCT) imaging than with colour fundus photography. Visual impairment due to VRIA was typically mild or moderate and the most common VRIA were epiretinal membrane and vitreomacular traction. Visual impairment in one or both eyes and a VRIA was positively associated with increasing age, female gender and Asian or Asian British ethnicity.

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

- ▶ VRIA are common abnormalities, even when the prevalence of other retinal pathology is low. The size of the UK Biobank project may provide additional opportunities to identify novel associations with VRIA. Spectral domain OCT imaging should be used in any future epidemiological studies documenting the prevalence of VRIA.



CrossMark

¹Department of Ophthalmology, Eye Clinic, Leeds Teaching Hospitals NHS Trust, Leeds, UK

²Academic Unit of Public Health, University of Leeds, Leeds, UK

Correspondence to

Mr Martin McKibbin; martin.mckibbin@nhs.net

interface abnormalities (VRIA). Much of the existing epidemiological data are derived from slit-lamp examination, either alone or in combination with grading of colour fundus photographs, but several VRIA are not readily identifiable using these techniques.

Table 1 Baseline characteristics of the cases and controls

Baseline characteristic	Controls without visual impairment (n=7704)	Cases with visual impairment but without VRIA (n=1671)	Cases with visual impairment and VRIA (n=419)
Age, median (IQR)	61 (54–65)	61 (54–65)	61 (55–66)
Sex			
Female, n (%)	4288 (55.7)	956 (57.2)	206 (49.2)
Male, n (%)	3416 (44.3)	715 (42.8)	213 (50.8)
Ethnicity			
White, n (%)	6881 (89.9)	1503 (90.5)	364 (87.5)
Asian or Asian British, n (%)	257 (3.4)	49 (3.0)	22 (5.3)
Black or Black British, n (%)	374 (4.9)	73 (4.4)	22 (5.3)
Other ethnic group, n (%)	142 (1.9)	36 (2.2)	8 (1.9)
Townsend deprivation index quintiles			
First—least deprived	1304 (16.9)	227 (13.6)	63 (15.1)
Second	1474 (19.2)	280 (16.8)	70 (16.7)
Third	1501 (19.5)	335 (20.1)	87 (20.8)
Fourth	1763 (22.9)	377 (22.6)	103 (24.6)
Fifth—most deprived	1653 (21.5)	448 (26.9)	95 (22.7)
Blood pressure diastolic, median (IQR)	82 (75–89)	82 (75–89)	82 (75–88)
Blood pressure systolic, median (IQR)	141 (128–154)	140 (127–154)	142 (129–155)
Body mass index category			
Normal/Underweight, n (%)	2366 (31.8)	521 (32.3)	132 (32.1)
Overweight, n (%)	3251 (43.7)	678 (42.0)	171 (41.6)
Obese, n (%)	1816 (24.4)	416 (25.8)	108 (26.3)
Whole body impedance, median (IQR)	595 (534–664)	598 (539–667)	583 (527–652)
Waist:hip ratio, median (IQR)	0.88 (0.81–0.94)	0.88 (0.81–0.94)	0.89 (0.82–0.95)
Pulse wave arterial stiffness index, median (IQR)	9.34 (7.26–11.37)	9.28 (7.2–11.24)	9.82 (7.46–11.54)
Current smoking status			
No, n (%)	6989 (91.0)	1485 (88.9)	374 (89.3)
Yes, n (%)	485 (6.3)	143 (8.6)	32 (7.6)
Occasionally, n (%)	203 (2.6)	42 (2.5)	13 (3.1)

Continued

Table 1 Continued

Baseline characteristic	Controls without visual impairment (n=7704)	Cases with visual impairment but without VRIA (n=1671)	Cases with visual impairment and VRIA (n=419)
Medications			
Systemic hypertension, n (%)	1804 (23.6)	405 (24.5)	107 (25.8)
Hypercholesterolaemia, n (%)	1597 (20.9)	367 (22.2)	107 (25.8)
Medical history			
Cancer, n (%)	806 (10.5)	173 (10.4)	42 (10.0)
Diabetes mellitus, n (%)	458 (7.7)	114 (8.6)	42 (11.8)
Cardiovascular and/or cerebrovascular disease, n (%)	2431 (40.8)	544 (40.9)	151 (42.4)
Depression: n (%)	392 (6.6)	79 (5.9)	19 (5.3)

VRIA, vitreoretinal interface abnormalities.

The UK Biobank study aims to investigate the influence of lifestyle, environment and genes on the health of adults, aged 40–69 years, in the UK.¹ The study recruited more than 500 000 UK residents and provides a unique opportunity to collect accurate data on the frequency and causes of visual impairment among participants. We have already identified that VRIA were the fourth most common cause of identifiable visual impairment among UK Biobank participants.² In this paper, we report the prevalence and visual consequences of different types of VRIA, both in eyes with and without visual impairment and investigate associations with VRIA within the UK Biobank cohort.

METHODS

Study design and population

All UK Biobank participants completed a baseline assessment that comprised a questionnaire, with health and disease questions, followed by recording of physical measurements and collection of biological samples. Eye health questions and physical measures were added several years after the start of the study and included visual acuity with habitual correction using a computerised, semiautomated system using LogMAR optotypes, refractive error, intraocular pressure and corneal biomechanics. Digital fundus photography and spectral domain OCT images were taken on both eyes using the Topcon 3D-OCT 1000 Mark 2. A single non-mydratric, 45° digital, colour image, centred on the fovea and a spectral domain OCT cube scan of the macula, covering a 6 mm×6 mm retinal area (128 horizontal line scans comprised of 512 A-scans), were captured for both eyes.

Baseline visual acuity, refraction, corneal biomechanics and intraocular pressure (IOP) data were recorded for 133 668 participants and, from this

cohort, colour fundus photographs and spectral domain OCT images were also captured in 65 033 participants. For these participants with fundus and OCT images, 8359 were identified as having mild visual impairment or worse (LogMAR >0.3 or Snellen <6/12) in at least one eye. In this 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 were selected to be representative of all participants with visual impairment in terms of visual acuity, age (5-year bands), sex and ethnicity (Asian, Black, Mixed, White or other background). Controls did not have visual impairment but were matched for the cases by age, sex and ethnicity at a ratio of approximately 4:1.

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.

Image grading and definitions

Images were analysed using the Topcon OCT viewer software (V.4.21, Topcon, Tokyo, Japan) and graded by clinicians or experienced, non-medical graders. Analysis involved all of the eyes with visual impairment and some of the fellow, non-impaired eyes of consecutive cases with monocular visual impairment. 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. SD OCT images were assessed for image quality, VRIA and intraretinal abnormalities. Fundus photographs

Table 2 Overall prevalence of VRIA on image grading of colour fundus photographs and OCT images

		Monocular visual impairment eyes (n=1684)	Binocular visual impairment eyes (n=812)	No visual impairment eyes (n=472)
Colour fundus images	Gradeable images	1362	645	385
	ERM	64 (4.7%*)	24 (3.72%*)	7 (1.82%*)
	FTMH	2 (0.15%*)	0	0
Spectral domain OCT images	Gradeable images	1615	775	464
	VMT at fovea	14 (0.87%*)	12 (1.55%*)	3 (0.65%*)
	VMT elsewhere	10 (0.62%*)	8 (1.03%*)	3 (0.65%*)
	ERM at fovea	50 (3.1%*)	22 (2.84%*)	5 (1.08%*)
	ERM elsewhere	274 (16.96%*)	125 (16.13%*)	31 (6.68%*)
	FTMH	3 (0.19%*)	2 (0.26%)	0
	PTMH	12 (0.74%*)	3 (0.39%*)	5 (1.08%*)
	Foveoschisis	5 (0.31%)	3 (0.39%*)	0

*Of gradeable images.

ERM, epiretinal membrane; FTMH, full-thickness macular hole; OCT, optical coherence tomography; VMT, vitreomacular traction; VRIA, vitreoretinal interface abnormalities.

were considered to be ungradeable when either the fovea or the optic disc or more than 33% of the total image was not visible. OCT images were considered to be ungradeable when severe artefacts were present or the signal strength was reduced across the image set to the extent that major interfaces could not be clearly identified. The senior clinician supported the other graders whenever there was any uncertainty about the grading outcome and repeated the grading of 2.5% of the images (80% abnormal and 20% normal) for quality assurance purposes. The decision of the senior clinician was adopted in any disputed cases.

For the presence or absence of VRIA, standard definitions were used for the following abnormalities:

vitreomacular traction (VMT), epiretinal membrane (ERM) either alone or in combination with intraretinal cysts and other abnormalities, lamellar or partial-thickness macular hole (PTMH), full-thickness macular hole (FTMH) and foveoschisis.^{3 4}

Using the self-reported eye history and the image grading outcomes, graders were asked to identify the primary cause of visual impairment, taking account of the level of visual impairment. Unless a single pathology was sufficient to explain all or the majority of the recorded level of visual acuity, no primary cause of visual impairment was recorded.

Table 3 Relative contribution of VRIA to each category of visual impairment

Visual impairment category	Monocular visual impairment, n (%*)	Binocular visual impairment-better seeing eye, n (%*)	Binocular visual impairment-worse seeing eye, n (%*)
Mild (LogMAR >0.3–<0.45)	29 (3.2)	10 (3.8)	2 (2.4)
Moderate (LogMAR 0.45–<1.0)	29 (4.2)	2 (1.5)	12 (4.1)
Severe (LogMAR 1.0–<1.3)	2 (2.3)	0	2 (8.0)
Blindness (LogMAR >1.3)	0	0	1 (16.7)
Total	60	12	17

*Of all the eyes with that level of visual impairment.

VRIA, vitreoretinal interface abnormalities.

Statistical analysis

Descriptive statistics were used to report the prevalence of VRIA in the UK Biobank participants and the contribution of both any and each type of VRIA to the visual impairment categories. The characteristics of the cases with visual impairment, both without and with VRIA, were also compared with the controls using descriptive statistics. 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 visual impairment, both without and with VRIA, 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.⁵ 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

In this pilot study, colour fundus photographs and spectral domain OCT images were reviewed for 2090 UK Biobank participants, of whom 1684 had monocular visual impairment and 406 had binocular visual impairment.

Image quality

Image grading for the presence of VRIA in the 2496 eyes with visual impairment was not possible due to image quality for 489 (19.6%) colour fundus photographs and 106 (4.2%) OCT scans.

For the 472 eyes without visual impairment but included in the analysis, image grading was not possible for 87 (18.4%) colour fundus photographs and 8 (1.7%) OCT scans.

Prevalence and types of VRIA

Of the 2090 UK Biobank participants included in this pilot study, VRIA were present in one or both eyes of 419 (20.0%) participants. The baseline characteristics of the cases with and without VRIA and controls are shown in [table 1](#). At least one VRIA was identified in 444 of 2496 eyes (17.6%) with visual impairment of any cause and in 38 of 472 eyes (8.1%) without visual impairment.

For the eyes with gradeable images, at least one VRIA was identified in 88 (4.4%) eyes with visual impairment and 7 (1.8%) eyes without visual impairment using colour fundus photography. With OCT imaging, any VRIA was identified in 444 (22.1%) of eyes with visual impairment and 38 (8.2%) of eyes without visual impairment. All the VRIA identified using colour fundus photography were also identified on OCT imaging and none were identified on colour fundus photography alone. Many eyes had more than one type of VRIA, including 99 of the eyes with visual impairment and 9 of those without. Additional retinal pathology, such as evidence of diabetic retinopathy or age-related maculopathy, was seen in 88 (18.7%) eyes with VRIA and visual impairment and in 97 (20.7%) of the eyes with VRIA but no visual impairment.

ERM was the most common individual VRIA on both colour fundus photography and OCT imaging. Both FTMH and ERM were identified at least three times more often on OCT imaging than on colour fundus photography. Apart from FTMH, all VRIA were identified in both the eyes with visual impairment and in the eyes without visual impairment, according to the definition used in this study. Only PTMH was more common in the eyes without visual impairment. The relative frequency of each VRIA, for all gradeable images but regardless of the cause of visual impairment, is shown in [table 2](#).

Table 4 Level of visual impairment associated with each of the main VRIA in the 89 eyes with VRIA as the primary cause of visual impairment

Visual impairment category	Epiretinal membrane	Foveoschisis	Full-thickness macular hole	Partial-thickness macular hole	Vitreomacular traction
Mild (LogMAR >0.3–<0.45)	26	4	0	3	8
Moderate (LogMAR 0.45–<1.0)	26	2	4	4	7
Severe (LogMAR 1.0–<1.3)	1	1	1	1	0
Blindness (LogMAR >1.3)	0	1	0	0	0
Total	53	8	5	8	15

VRIA, vitreoretinal interface abnormalities.

**Table 5** Associations with VRIA and visual impairment—controls as comparator: multinomial logistic regression

Variable	Relative risk ratio (95% CI) compared with controls: univariate		Relative risk ratio (95% CI) compared with controls: multivariable*	
	Visual impairment but no VRIA (n=1671)	Visual impairment and any VRIA (n=419)	Visual impairment but no VRIA (n=1671)	Visual impairment and any VRIA (n=419)
Age (per decade) [†]	1.02 (0.99 to 1.06)	1.2 (1.05 to 1.37)	1.03 (0.995 to 1.07)	1.22 (1.07 to 1.40)
Sex (compared with male) [†]				
Female	0.94 (0.90 to 0.98)	1.3 (1.09 to 1.54)	0.94 (0.90 to 0.98)	1.28 (1.08 to 1.52)
Ethnicity (compared with White) [†]				
Asian or Asian British	0.87 (0.75 to 1.02)	1.62 (1.12 to 2.34)	0.83 (0.71 to 0.97)	1.60 (1.10 to 2.32)
Black or Black British	0.89 (0.79 to 1.01)	1.11 (0.75 to 1.64)	0.79 (0.69 to 0.90)	1.17 (0.79 to 1.74)
Other ethnic group	1.16 (0.94 to 1.43)	1.07 (0.56 to 2.02)	1.04 (0.83, 1.29)	1.10 (0.58 to 2.09)
Townsend deprivation index quintiles (compared with first quintile—least deprived) [†]				
Second	1.09 (0.90 to 1.32)	0.98 (0.69 to 1.40)	1.09 (0.91 to 1.32)	0.99 (0.69 to 1.41)
Third	1.28 (1.07 to 1.54)	1.20 (0.86 to 1.68)	1.29 (1.07 to 1.55)	1.21 (0.86 to 1.69)
Fourth	1.23 (1.03 to 1.47)	1.21 (0.88 to 1.67)	1.24 (1.04 to 1.49)	1.21 (0.87 to 1.68)
Fifth—most deprived	1.56 (1.31 to 1.85)	1.19 (0.86 to 1.65)	1.59 (1.33 to 1.91)	1.18 (0.85 to 1.64)
BP diastolic (per increase 1)	0.998 (0.993 to 1.003)	0.998 (0.989 to 1.007)	—	—
BP systolic (per increase 1)	0.999 (0.997 to 1.002)	1.001 (0.997 to 1.006)	—	—
BMI category (compared with normal/underweight)				
Overweight	0.95 (0.84 to 1.07)	0.94 (0.75 to 1.19)	—	—
Obese	1.04 (0.90 to 1.2)	1.07 (0.82, 1.38)	—	—
Whole body impedance (per increase 100) [†]	1.04 (0.99 to 1.09)	0.88 (0.79 to 0.98)	—	—
Waist-hip ratio (per increase 0.1) [†]	1.03 (0.99 to 1.08)	1.11 (1.001 to 1.23)	—	—
Pulse wave arterial stiffness index (per increase 1)	0.99 (0.97 to 1.005)	1.00 (0.996 to 1.01)	—	—
Current smoking status (compared with No) [†]				
Yes	1.39 (1.14 to 1.69)	1.23 (0.85 to 1.79)	—	—
Occasionally	0.97 (0.70 to 1.36)	1.20 (0.68 to 2.10)	—	—
Medications (compared with none)				
BP	1.05 (0.93 to 1.19)	1.13 (0.90 to 1.41)	—	—

Continued

Table 5 Continued

Variable	Relative risk ratio (95% CI) compared with controls: univariate		Relative risk ratio (95% CI) compared with controls: multivariable*	
	Visual impairment but no VRIA (n=1671)	Visual impairment and any VRIA (n=419)	Visual impairment but no VRIA (n=1671)	Visual impairment and any VRIA (n=419)
Cholesterol [†]	1.08 (0.96 to 1.22)	1.32 (1.06 to 1.65)	—	—
Medical history (compared with none)				
Cancer	0.99 (0.83 to 1.18)	0.95 (0.69 to 1.32)	—	—
Diabetes mellitus [†]	1.13 (0.91 to 1.39)	1.61 (1.15 to 2.25)	—	—
Cardiovascular and/or cerebrovascular disease	1.00 (0.89 to 1.13)	1.07 (0.86 to 1.33)	—	—
Depression	0.90 (0.70 to 1.15)	0.80 (0.50 to 1.28)	—	—

*Those variables identified as associated univariately (<5% level) were included in a multivariable model and remained in model if significantly associated at 5% level. As cases were matched by age, sex and ethnic group, these variables were included in the multivariable model irrespective of their association.

[†]Univariate association with visual impairment at 5% level—included in initial multivariable model. BP, blood pressure; BMI, body mass index; VRIA, vitreoretinal interface abnormalities.

For the five FTMHs identified on OCT imaging, the mean, minimum width on OCT imaging was 530 µm, with one being small in size (<250 µm) and four being large (more than 400 µm). All cases of VMT causing visual impairment would be classified as focal (maximum width <1500 µm), with a mean VMT width of 367 µm.

Relative contribution of VRIA to visual impairment

VRIA were identified as the most likely, primary cause of visual impairment in 89 eyes (3.6%) of 83 participants (4.0%) participants. This included 60 (3.6%) eyes of participants with monocular visual impairment and 12 (3.0%) and 17 (4.2%) of the better and worse-seeing eyes, respectively, of participants with binocular visual impairment. The relative contribution of VRIA to each category of visual impairment for all 2090 cases is shown in table 3.

Main VRIA causing visual impairment

ERM and VMT were the most common primary diagnoses leading to visual impairment in 53 (58.9%) and 15 (16.7%) of the eyes with VRIA, respectively. The degree of visual impairment was typically milder for both ERM and VMT than for the other VRIA leading to visual impairment. Mean LogMAR acuity in the eyes with visual impairment due to VRIA was 0.53 (range 0.32–1.2) for ERM, 0.46 (0.32–0.64) for VMT, 0.58 (0.34–1.0) for PTMH, 0.7 (0.32–1.3) for foveoschisis and 0.82 (0.64–1.25) for FTMH. The categories of visual impairment for each VRIA diagnosis are given in table 4.

Although the number of eyes without visual impairment but with a VRIA was small, 13 eyes had a central VRIA that had the potential to affect visual acuity. Mean LogMAR acuity was 0.02 (range –0.08 to 0.10) for the three eyes with VMT involving the fovea, 0.10 (range –0.02 to 0.24) for the five eyes with ERM involving the fovea and 0.10 (range –0.06 to 0.22) for the five eyes with PTMH.

Associations with VRIA

Compared with the controls without visual impairment, age, gender, ethnicity, deprivation, whole body impedance, waist:hip ratio, current smoking status, cholesterol medications and those with diabetes were individually significantly associated (at 5% level) with visual impairment, either with or without VRIA. On inclusion in a multivariable model, only age, gender, ethnicity and deprivation remained significantly associated with visual impairment. For the cases with visual impairment, the presence of VRIA was positively associated with increasing age (relative risk ratio (RRR) 1.22; 95% CI 1.07 to 1.40), female sex (RRR 1.28; 1.08 to 1.52) and Asian ethnicity (1.60; 1.10 to 2.32). These associations were not seen in the cases with visual impairment but without VRIA. Compared with controls, visual impairment but without VRIA was

negatively associated with female sex (RRR 0.94; 0.90 to 0.98), Asian ethnicity (RRR 0.83; 0.71 to 0.97) and Black ethnicity (RRR 0.79; 0.69 to 0.90) and positively associated with increasing deprivation (RRR 1.59; 1.33 to 1.91 for the most deprived quintile). Associations between predetermined risk factors or potential, novel associations and VRIA with visual impairment are shown in [table 5](#).

DISCUSSION

Among UK Biobank participants with visual impairment, VRIA were identified as the most likely, primary cause of visual impairment in 3.6% of eyes, and the prevalence of any VRIA was 17.6% in the eyes with visual impairment and 8.1% of the eyes without visual impairment.

The overall prevalence of VRIA in this study, for the eyes with and without visual impairment, is comparable to other studies. In the population-based Beijing Eye Study, the prevalence of ERM was 2.2% per eye, based on grading of fundus photographs alone.⁶ In other population-based studies and using a combination of fundus photographs and slit-lamp examination, Miyazaki *et al*⁷ and McCarty *et al*⁸ reported ERM prevalence figures of 4.0% and 6%, respectively. With time domain OCT and fundus photography, the Handan Eye Study recorded a prevalence of 3.4% for ERM alone.⁹ With the benefit of spectral domain OCT, Fusi-Rubiano *et al*¹⁰ reviewed the OCT images from consecutive patients attending a retina clinic and reported a prevalence of 7.3% for any VRIA. However, almost 40% of the cases in that series had vitreomacular adhesion alone. In an urban Chinese population, Liu *et al*¹¹ reported a prevalence of 16.8% for any VRIA among adults without eye disease, excluding eyes with posterior vitreous detachment alone. Meuer *et al*¹² reported a prevalence of 39.7% for any VRIA, excluding macular and paravascular cysts, among the residents of Beaver Dam.

Differences between the VRIA prevalence reported here and other published series are likely to be the result of differing VRIA definitions, methods of ascertainment of pathology and the population characteristics. In keeping with more recent studies that used spectral domain OCT imaging, this study included a variety of subtypes of VRIA. As reported in the Beaver Dam study, the data presented here illustrates the superiority of spectral domain OCT over fundus photography in identifying both ERM and FTMH.¹² Other VRIA, such as VMT and foveoschisis, would not be expected to be identifiable on colour fundus photography. Several studies have shown that the prevalence of ERM and other VRIA increases with age, the presence of other retinal pathology, prior cataract surgery and myopia.^{7 9 11 12} In this study of UK Biobank participants, the prevalence of VRIA in the eyes with visual impairment was at least twice that in the eyes without. The mean age of the participants

studied here was 61 years, compared with 74 years in the Beaver Dam study, and other retinal disease was identified in over 20% of the eyes with visual impairment and a VRIA.

Among UK Biobank participants, ERM and VMT were the most common VRIA causing visual impairment, but the visual acuity with these abnormalities was typically better than for partial or full-thickness macular holes and foveoschisis. Fusi-Rubiano *et al*¹⁰ reported a decrease in visual acuity as the grade of VRIA changed from VMT to FTMH. The same study also identified that many eyes with VMT did not have visual impairment. The data presented in this article illustrate that VRIA were more common in the eyes with visual impairment but were also present in 8% of the eyes without visual impairment, using the predetermined LogMAR acuity >0.3 to define visual impairment. Mean visual acuity in the eyes in the Beaver Dam study with both epiretinal membrane and partial-thickness macular hole was better than this threshold.¹² Similarly, in the series reported by Fusi-Rubiano *et al*, the majority of eyes with VMT retained good visual acuity and there was a large range of visual acuities recorded for each VRIA, with the possible exception of FTMH.¹⁰ Some of the eyes with VRIA in the UK Biobank also had visual acuity levels better than LogMAR 0.3 but worse than LogMAR 0.0.

Increasing age, female sex and Asian ethnicity were significant associations with visual impairment and VRIA among UK Biobank participants using multivariable analysis, even though cases and controls were matched by age, sex and ethnicity. With each additional decade, the prevalence of VRIA was 22% greater for the cases with a VRIA in one or both eyes than for the controls without visual impairment. For female cases with VRIA, the prevalence of VRIA was 28% greater than for the controls. The associations of VRIA with increasing age and female sex have been reported before and are likely to reflect the trend for detachment of the posterior hyaloid with increasing age and female sex.^{9 11 13} The association with Asian ethnicity, but not other ethnic minority status, may be a consequence of the high prevalence of myopia in this group.^{9 14} No association was seen with other variables, including serum cholesterol, diabetes mellitus and smoking status, that have previously been reported as being positively associated with a range of VRIA.^{7 11} However, medication for cholesterol, diabetes mellitus and smoking status were found to be associated with visual impairment at the 5% level on univariate analysis and were included in the initial multivariable model.

The image quality of the colour fundus photographs reviewed for this study was variable but the quality of the OCT images was much better, with only 3.7% of all the OCT images judged to be ungradeable. By comparison, in the Beaver Dam study, OCT images from 9% of eyes were excluded because the image was either missing or ungradeable.¹² In the Beijing Eye

study, 5.5% of OCT images were felt to be of insufficient quality for grading.¹⁵

This pilot study has a number of strengths and potential weaknesses. The UK Biobank was one of the first to use spectral domain OCT imaging and over 65 000 participants met the criteria for inclusion in this study. Many of the key findings in relation to the prevalence of VRIA and the level of associated visual impairment are consistent with other studies. Images were graded by experienced clinicians and graders. Although there must be some uncertainty about the identification of VRIA as the primary cause of visual impairment, the deformation of the retinal architecture was greater in the eyes with VRIA identified as the primary cause than in the eyes with VRIA as an incidental finding. Furthermore, the degree of visual impairment was typically mild or moderate for most VRIA and especially for VMT and ERM. However, the UK Biobank study is not a population-based study and the response rate to the invitation to participate was low.¹ Participants were generally healthier, older, more affluent and more likely to be urban than the full UK population and so may not be representative.^{14 16} As a result, the prevalence figures reported here may not be applicable to the wider UK population and are likely to be minimum estimates.¹⁷ This pilot study involved image grading for a representative sample of only 25% of the participants with visual impairment and not all of the fellow eyes without visual impairment were included. The lack of association with other previously reported variables on multivariable analysis may also suggest that this study was underpowered. The prevalence of VRIA in the control population without visual impairment is also not known.

VRIA are common findings in middle-aged adults in the UK Biobank study, both in eyes with and without mild visual impairment or worse, and many eyes have more than one interface abnormality. VRIA were identified as the most likely, primary cause of visual impairment in 3.6% of eyes, with ERM and VMT the most common diagnoses leading to visual impairment. Visual impairment with VRIA was positively associated with increasing age, female sex and Asian or Asian British ethnicity.

Acknowledgements The authors would like to thank Nicola Dowd, Richard Cannon, Mike Stockton and Grigorios Tzamos for their advice and help with image grading and the creation of the customised grading database. This research has been conducted using the UK Biobank Resource under Application Number 1100.

Contributors TF and DS have been involved in the study design, data analysis and review of the paper. The other members of the UK Biobank Eye and Vision Consortium have had the opportunity to review and comment on the data before the manuscript was submitted for publication.

Funding This study was supported as an Investigator Initiated Trial by Alcon Research Ltd.

Competing interests None declared.

Patient consent Patient consent is not required, anonymised data only were made available to me by UK Biobank.

Ethics approval North-West Multicentre Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Collaborators Prof Tariq ASLAM (ManchesterUniversity); Prof Sarah BARMAN (KingstonUniversity); Prof Jenny BARRETT (Universityof Leeds); Prof Paul BISHOP (ManchesterUniversity); Mr Peter BLOWS (MoorfieldsEye Hospital, London); Dr Catey BUNCE (King'sCollege London); Dr Roxana CARARE (Universityof Southampton); ProfUsha CHAKRAVARTHY (Queens University, Belfast); Miss Michelle CHAN (Moorfields Eye Hospital, London); Mrs Antonietta CHIANCA (UCL Institute of Ophthalmology);Dr Valentina CIPRIANI (UCL Institute ofOphthalmology); Prof David CRABB (CityUniversity, London); Mrs PhilippaCUMBERLAND (UCL Institute of Child Health); Dr Alexander DAY (Moorfields Eye Hospital, London); Miss Parul DESAI (Moorfields Eye Hospital, London);Prof Bal DHILLON (University of Edinburgh);Prof Andrew DICK (University of Bristol);Dr Cathy EGAN (Moorfields Eye Hospital, London);Prof Sarah ENNIS (University of Southampton);Prof Paul FOSTER (UCL Institute of Ophthalmology);Dr Marcus FRUTTIGER (UCL Institute ofOphthalmology); Dr John GALLACHER (Universityof Oxford); Prof David (Ted) GARWAY-HEATH(UCL Institute of Ophthalmology); Dr JaneGIBSON (University of Southampton); MrDan GORE (Moorfields Eye Hospital, London); Mr Srinu GOVERDHAN (University of Southampton); Prof Jeremy GUGGENHEIM (Cardiff University); Prof Chris HAMMOND (King's College London); Prof Alison HARDCASTLE (UCL Institute of Ophthalmology);Prof Simon HARDING (University of Liverpool);Dr Ruth HOGG (Queen's University, Belfast);Prof Anne HUGHES (Queen's University, Belfast);Dr Pirro HYSI (King's College London); Mr Pearse A KEANE (UCL Institute of Ophthalmology);Prof Sir Peng Tee KHAW (UCL Institute ofOphthalmology); Mr Anthony KHAWAJA (MoorfieldsEye Hospital, London); Mr GerassimosLASCARATOS (Moorfields Eye Hospital, London); Prof Andrew LOTERY- University of Southampton); Prof Phil LUTHERT (UCL Institute of Ophthalmology);Dr Tom MAGGILLIVRAY (University of Edinburgh);Dr Sarah MACKIE (University of Leeds); Prof Keith MARTIN (University of Cambridge); Ms Michelle MCGAUGHEY (Queen's University Belfast);Dr Bernadette MCGUINNESS (Queen's UniversityBelfast); Dr Gareth MCKAY (Queen'sUniversity Belfast); Mr Martin MCKIBBIN (LeedsTeaching Hospitals NHS Trust); Dr DannyMITRY (University of Edinburgh); ProfTony MOORE (UCL Institute of Ophthalmology); Prof James MORGAN (Cardiff University); Ms Zaynah MUTHY (UCL Institute of Ophthalmology); Mr Eoin O'SULLIVAN (King's College Hospital); Dr Chris OWEN (St George's, University of London); Mr Praveen PATEL (Moorfields Eye Hospital,London); Mr Euan PATERSON (QueensUniversity Belfast); Dr Tunde PETO (Queen'sUniversity Belfast); Dr Axel PETZOLD (UCLInstitute of Neurology); Prof Jugnoo RAHI(UCL Institute of Child Health); DrAlicja RUDNICKA (St George's, University of London); Miss Carlota Grossi SAMPEDRO (University of EastAnglia); Mr Jay SELF (University ofSouthampton); Prof Sobha SIVAPRASAD (MoorfieldsEye Hospital, London); Mr David STEEL (NewcastleUniversity); Mrs Irene STRATTON (GloucestershireHospitals NHS Foundation Trust); MrNicholas STROUTHIDIS (Moorfields Eye Hospital, London); Prof Cathie SUDLOW (University of Edinburgh); Dr Caroline THAUNG (UCL Institute of Ophthalmology);Miss Dhanes THOMAS (Moorfields Eye Hospital,London); Prof Emanuele TRUCCO (Universityof Dundee); Mr Adnan TUFAIL (MoorfieldsEye Hospital, London); Dr Marta UGARTE (MoorfieldsEye Hospital, London); Dr VeroniqueVITART (University of Edinburgh); ProfStephen VERNON (University Hospital, Nottingham); Mr Ananth VISWANATHAN (Moorfields Eye Hospital, London);Miss Cathy WILLIAMS (University of Bristol);Dr Katie WILLIAMS (King's College London);Prof Jayne WOODSIDE (Queen's University Belfast);Prof John YATES (University of Cambridge);Dr Max YATES (University of East Anglia);Ms Jennifer YIP (University of Cambridge);Dr Yalin ZHENG (University of Liverpool);Dr Haogang ZHU (City University, London).

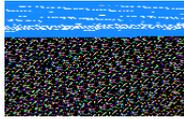
Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>



© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

1. Sudlow C, Gallacher J, Allen N, *et al*. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;12:e1001779.
2. McKibbin M, Farragher T, Shickle D. *Poster 174. The causes of and associations with visual impairment in middle-aged adults in the UK Biobank project*. Birmingham: BMJ Publishing Group, 2016.
3. Duker JS, Kaiser PK, Binder S, *et al*. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology* 2013;120:2611–9.
4. Stalmans P, Duker JS, Kaiser PK, *et al*. Oct-based interpretation of the vitreomacular interface and indications for pharmacologic vitreolysis. *Retina* 2013;33:2003–11.
5. Pearce N. Analysis of matched case-control studies. *BMJ* 2016;352:i969.
6. You Q, Xu L, Jonas JB. Prevalence and associations of epiretinal membranes in adult Chinese: the Beijing eye study. *Eye* 2008;22:874–9.
7. Miyazaki M, Nakamura H, Kubo M, *et al*. Prevalence and risk factors for epiretinal membranes in a Japanese population: the Hisayama study. *Graefes Arch Clin Exp Ophthalmol* 2003;241:642–6.
8. McCarty DJ, Mukesh BN, Chikani V, *et al*. Prevalence and associations of epiretinal membranes in the visual impairment project. *Am J Ophthalmol* 2005;140:288.e1–288.e8.
9. Duan XR, Liang YB, Friedman DS, *et al*. Prevalence and associations of epiretinal membranes in a rural Chinese adult population: the Handan Eye Study. *Invest Ophthalmol Vis Sci* 2009;50:2018–23.
10. Fusi-Rubiano W, Awad M, Manjunath R, *et al*. Spectrum of morphological and visual changes due to vitreomacular interface disorders encountered in a large consecutive cohort of patients. *Eye* 2015;29:397–402.
11. Liu L, Yue S, Wu J, *et al*. The prevalence and distribution of Vitreoretinal Interface abnormalities among Urban Community Population in China. *J Ophthalmol* 2015;2015:1–6.
12. Meuer SM, Myers CE, Klein BE, *et al*. The epidemiology of vitreoretinal interface abnormalities as detected by spectral-domain optical coherence tomography: the Beaver Dam eye study. *Ophthalmology* 2015;122:787–95.
13. Hayreh SS, Jonas JB. Posterior vitreous detachment: clinical correlations. *Ophthalmologica* 2004;218:333–43.
14. Cumberland PM, Bao Y, Hysi PG, *et al*. Frequency and distribution of refractive error in adult life: methodology and findings of the UK Biobank Study. *PLoS One* 2015;10:e0139780.
15. Shao L, Xu L, You QS, *et al*. Prevalence and associations of incomplete posterior vitreous detachment in adult Chinese: the Beijing Eye Study. *PLoS One* 2013;8:e58498.
16. Shweikh Y, Ko F, Chan MP, *et al*. Measures of socioeconomic status and self-reported glaucoma in the UK Biobank cohort. *Eye* 2015;29:1360–7.
17. Dawes P, Dickinson C, Emsley R, *et al*. Vision impairment and dual sensory problems in middle age. *Ophthalmic Physiol Opt* 2014;34:479–88.



Vitreoretinal interface abnormalities in middle-aged adults with visual impairment in the UK Biobank study: prevalence, impact on visual acuity and associations

Martin McKibbin, Tracey Farragher and Darren Shickle

BMJ Open Ophthalmol 2017 1:
doi: 10.1136/bmjophth-2016-000057

Updated information and services can be found at:
<http://bmjophth.bmj.com/content/1/1/e000057>

These include:

References

This article cites 16 articles, 2 of which you can access for free at:
<http://bmjophth.bmj.com/content/1/1/e000057#BIBL>

Open Access

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>