

Prevalence and associations of non-retinopathy ocular conditions among older Australians with self-reported diabetes: The National Eye Health Survey

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Abstract

• **AIM:** To determine the prevalence and associations of non-retinopathy ocular conditions among older Australian adults with diabetes.

• **METHODS:** Multistage random-cluster sampling was used to select 3098 non-indigenous Australians aged 50y or older (46.4% male) and 1738 indigenous Australians aged 40y or older (41.1% male) from all levels of geographic remoteness in Australia. Participants underwent a standardised questionnaire to ascertain diabetes history, and a clinical examination to identify eye disease. We determined the prevalence of uncorrected refractive error, visually significant cataract, cataract surgery, age-related macular degeneration, glaucoma, ocular hypertension, retinal vein occlusion and epiretinal membrane among those with and without self-reported diabetes.

• **RESULTS:** Participants with self-reported diabetes had a higher prevalence of cataract surgery than those without diabetes (28.8% vs 16.9%, OR 1.78, 95%CI: 1.35-2.34 among non-indigenous Australians, and 11.3% vs 5.2%, OR 1.62, 95%CI: 1.22-2.14 among indigenous Australians). Diabetic retinopathy (DR) increased the odds of cataract surgery among self-reported diabetic indigenous and non-

indigenous Australians (OR 1.89, $P=0.004$ and OR 2.33, $P<0.001$ respectively). Having diabetes for ≥ 20 y and having vision-threatening DR increased the odds of cataract surgery among indigenous Australians with diabetes (OR 3.73, $P=0.001$ and 7.58, $P<0.001$, respectively).

• **CONCLUSION:** Most non-retinopathy ocular conditions are not associated with self-reported diabetes. However, to account for Australia's worsening diabetes epidemic, interventions to reduce the impact of diabetes-related blindness should include increased cataract surgery services.

• **KEYWORDS:** retinopathy; diabetes; prevalence; public health; national survey; cataract

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INTRODUCTION

The diabetes epidemic currently affects more than 400 million people worldwide and accounts for 12% of global health expenditure^[1-2]. As the burden of diabetes continues to increase, so too does the burden of its complications, including vision loss^[3]. Most diabetes-related vision loss results from diabetic retinopathy (DR)^[4], which has become the leading cause of blindness in working-age adults worldwide^[3]. However, other ophthalmological complications including cataract^[5-6], glaucoma^[7], ocular hypertension (OHT)^[8] and epiretinal membrane (ERM)^[8] have also been found to be associated with diabetes in some populations. In contrast to the well-established epidemiology of DR^[3], population-based data on other eye conditions, hereafter referred to as 'non-retinopathy ocular conditions', in populations with diabetes, are comparatively sparse, fragmentary and often inconsistent, warranting further investigation.

Research into the associations between non-retinopathy ocular conditions and diabetes in Australia have yielded conflicting results. For example, the Blue Mountains Eye Study (BMES)

in the early 1990s reported that diabetes was significantly associated with cataract, cataract surgery^[9], geographic atrophy [but not other age-related macular degeneration (AMD) subtypes]^[10], ERM^[11], glaucoma and OHT^[12]. In contrast, the Melbourne Visual Impairment Project (VIP) found no associations between diabetes and ERM or AMD^[13], although an association was found with cataract^[14]. Inconsistencies are not isolated to Australia, as the VIP and BMES findings have differed from, but in some cases agreed with, surveys in Singapore^[8], Korea^[8], Barbados^[15] and the United States^[16]. This suggests that the extent to which diabetes is a risk factor for each non-retinopathy ocular condition may vary between populations according to additional modulating factors that have not been adequately examined. Further, while the abovementioned studies explored statistical associations between diabetes and non-retinopathy ocular conditions, they did not report the prevalence of each condition in those with diabetes, limiting the ability of policy-makers to quantify the population-level burden and develop policy accordingly.

Diabetes and its complications are among the leading causes of morbidity in Indigenous Australians^[17]. From the recent National Eye Health Survey (NEHS, 2015-2016), we reported that the prevalence of vision loss among Indigenous Australians with self-reported diabetes was more than double that of those without self-reported diabetes^[18]. While we quantified the prevalence of DR in those with diabetes^[18], the contribution of non-retinopathy ocular conditions to the excess disease burden among diabetic Indigenous Australians was not investigated. Scant evidence has suggested that some non-retinopathy ocular conditions, including cataract^[19] and OHT^[20], are more prevalent in Indigenous Australians with diabetes than those without diabetes, however, no nationally-representative prevalence data for non-retinopathy ocular conditions are available for Indigenous populations with diabetes. Consequently, there is an imperative to investigate the epidemiology of non-retinopathy ocular conditions in Australia's diabetic Indigenous population.

The NEHS was the first nationwide eye health survey of both non-Indigenous and Indigenous Australians. This paper reports and compares the prevalence of a range of non-retinopathy ocular conditions among participants in the NEHS with and without diabetes and examines risk factors for those conditions that were more prevalent among those with self-reported diabetes.

SUBJECTS AND METHODS

Ethical Approval Ethics approval was obtained from the Royal Victorian Eye and Ear Hospital Human Research Ethics Committee (HREC-14/1199H) and additional approvals and endorsements were granted by Indigenous Australian organisations in each State and Territory. The study protocol

adhered to the tenets of the Declaration of Helsinki and all participants provided written informed consent.

Study Population The study design and sampling methodology of the NEHS have been described in detail previously^[21-22]. In brief, a nationwide cross-sectional population-based survey of Indigenous Australians aged 40y or older and non-Indigenous Australians aged 50y or older was conducted from the 11st of March 2015 until the 18th of April 2016. The younger age criterion selected for Indigenous Australians reflects the earlier onset and more rapid progression of vision loss and eye disease in that population^[23]. Multistage random-cluster sampling was used to select 30 population clusters of 150 participants (100 non-Indigenous and 50 Indigenous) per sampling site, drawing from 2011 Australian Census data^[24]. Cluster selection was stratified by geographic remoteness to select participants from major city, inner regional, outer regional, remote and very remote locations. Response rates of 77.6% (1738/2240) in the Indigenous population and 68.5% (3098/4520) in the non-Indigenous populations were achieved.

Examination Procedures All participants underwent a standardised interviewer-administered questionnaire and a series of eye examinations. The protocol has been published^[22]. Briefly, the questionnaire collected sociodemographic data, past ocular and diabetes histories and information about previous engagement with eye healthcare services. To collect diabetes-related data, interviewers asked participants if they had been told by a doctor or nurse that they have diabetes (self-reported diabetes), and if so, at what age the diagnosis had occurred. Participants were asked if they had ever undergone a diabetes eye check by an ophthalmologist or optometrist, and if so, how long ago.

Presenting distance visual acuity (PVA) was assessed in each eye separately using a logMAR chart (Brien Holden Vision Institute, Sydney, Australia). Participants with PVA worse than 6/12 in either or both eyes underwent pinhole testing of the affected eye(s). Autorefractometry (Nidek ARK-30 Type-R handheld autorefractor/keratometer; Nidek Co., Ltd., Hiroishi, Japan) was performed on those who improved to 6/12 or better with pinhole testing, and best-corrected visual acuity was measured.

The anterior segment was examined using a hand-held slit lamp (Keeler Ophthalmic Instruments, Berkshire, UK). Photographs were taken of the anterior segment of eyes that had PVA worse than 6/12 using a digital retinography system (DRS) non-mydratic fundus camera (CenterVue, SpA, Padova, Italy). For all participants, the DRS camera was used to take two-field, 45° colour fundus photographs, centred on the macula and optic disc, respectively. A frequency doubling technology (FDT) perimeter (Zeiss Humphrey Systems &

Welch Allyn, Dublin, CA, USA) was used to identify visual field defects. Intraocular pressure (IOP) was measured in both eyes using an iCare tonometer (iCare, Finland). All tests were conducted by orthoptists, optometrists, ophthalmologists, or research assistants who were thoroughly trained under a standardised protocol under the supervision of an optometrist.

Case Definitions and Classification of Ocular Conditions

Trained retinal graders masked to the identity and clinical characteristics of participants graded fundus photographs for pathology according to standardised protocols. Grading data and/or clinical test results were used to identify and classify the following conditions.

Uncorrected refractive error: Participants were considered to have uncorrected refractive error if they had PVA worse than 6/12 in either or both eyes that improved to 6/12 or better with pinhole or autorefraction.

Visually significant cataract (VSC): To ensure an accurate diagnosis of cataract, a two-step protocol was utilised. First, two experienced optometrists from the Centre for Eye Research Australia independently assessed anterior segment photographs and fundus photographs of participants to categorise them into one of three groups: 1) no cataract, 2) probable cataract, or 3) definite cataract. High inter-rater reliability (85%) and intra-rater reliability (94% and 96%) were achieved, and discrepancies were adjudicated by an ophthalmologist. A high sensitivity and specificity for detecting visually significant cataract has been demonstrated using this method^[25]. Second, in this study, prevalent VSC was defined as cataract that was the main cause of vision loss (<6/12) as determined by two independent ophthalmologists who reviewed relevant questionnaire, grading (cataract and fundus) and clinical data. Any disagreements were adjudicated by a third senior ophthalmologist.

History of cataract surgery: Participants were considered to have undergone cataract surgery if they responded affirmatively when asked if they had previously undergone cataract surgery.

Any AMD: The protocol for classifying prevalent AMD in the NEHS has been published^[26]. AMD was graded according to the Beckman system^[27]. Any AMD included early, intermediate and late AMD.

Late AMD: Based on the above-mentioned protocol for AMD diagnosis, the prevalence of those with late AMD was investigated independently.

Glaucoma: The protocol for diagnosing glaucoma in the NEHS has been published previously^[28]. Participants were graded as having no glaucoma, possible, probable or definite glaucoma by glaucoma specialists. Participants with probable and definite glaucoma were considered to have glaucoma for this analysis.

Ocular hypertension: Participants with IOP readings >21 mm Hg in either eye without glaucoma were considered to have OHT.

Retinal vein occlusion (RVO): Participants with central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) in either or both eyes, as categorised previously^[29], were considered to have RVO for this report.

ERM: ERMs were graded as either cellophane macular reflex (CMR) without retinal folds or the more severe preretinal macular fibrosis (PMF) with retinal folds according to a published protocol^[30]. Both CMR and PMF situated within 3000 µm of the macula were included in this analysis.

Any DR: Because the presence of DR and vision-threatening DR (VTDR) were investigated as potential risk factors for the co-occurrence of non-retinopathy conditions, their levels of classification (published previously)^[18] are provided. DR was categorised according to the modified Airlie House classification method^[31] as minimal non-proliferative DR (NPDR), mild NPDR, moderate NPDR, severe NPDR, or proliferative DR (PDR).

VTDR: VTDR was defined as severe NPDR, PDR or clinically significant macular edema (CSME).

Statistical Analysis Participant characteristics were tabulated for those without self-reported diabetes and those with self-reported diabetes and statistically compared using Pearson's Chi-squared test. The 95% confidence interval (CI) for crude prevalence was estimated using robust standard errors to account for clustering within study site. Population proportions were estimated using post-stratification for age in addition to the survey weights which were derived separately for Indigenous and non-Indigenous participants according to study site.

Age- and sex-adjusted logistic regression was performed separately for Indigenous and non-Indigenous participants to investigate the association between the following ocular conditions and self-reported diabetes: uncorrected refractive error, VSC, history of cataract surgery, any AMD, late AMD, glaucoma, OHT, RVO and ERM. Logistic regression was then performed separately for Indigenous and non-Indigenous participants to investigate the association between conditions more prevalent among the participants with diabetes and the following characteristics among diabetic participants: sex, age, educational attainment, language, location of birth (for non-Indigenous participants only), remoteness of area of residence, time since last eye examination, self-reported stroke, any DR and VTDR. All analyses were performed using Stata/SE version 15.1 (StataCorp LP, College Station, TX, USA).

RESULTS

Participant Characteristics A total of 3098 non-Indigenous Australians aged 50-98y [median age (interquartile range);

Table 1 Characteristics of non-Indigenous and Indigenous participants with and without self-reported diabetes in the National Eye Health Survey (n=4836) n (%)

Characteristics	Non-Indigenous (n=3098)		P ^a	Indigenous (n=1738)		P ^a
	No self-reported (n=2667)	Self-reported (n=431)		No self-reported (n=1093)	Self-reported (n=645)	
Age (y)			<0.001			<0.001
40 to 49	0	0		455 (41.6)	126 (19.5)	
50 to 59	741 (27.8)	72 (16.7)		396 (36.2)	239 (37.1)	
60 to 69	995 (37.3)	173 (40.1)		167 (15.3)	196 (30.4)	
70 to 79	641 (24.0)	123 (28.5)		64 (5.9)	70 (10.9)	
80 to 99	290 (10.9)	63 (14.6)		11 (1.0)	14 (2.2)	
Sex			<0.001			0.020
Female	1472 (55.2)	189 (43.9)		621 (56.8)	403 (62.5)	
Male	1195 (44.8)	242 (56.1)		472 (43.2)	242 (37.5)	
Geographic remoteness			0.360			0.003
Major city	1075 (40.3)	178 (41.3)		478 (43.7)	268 (41.6)	
Inner regional	543 (20.4)	93 (21.6)		213 (19.5)	97 (15.0)	
Outer regional	532 (19.9)	93 (21.6)		236 (21.6)	169 (26.2)	
Remote	328 (12.3)	39 (9.0)		118 (10.8)	63 (9.8)	
Very remote	189 (7.1)	28 (6.5)		48 (4.4)	48 (7.4)	
Educational attainment			0.010			0.022
Less than high school	1129 (42.3)	213 (49.4)		651 (59.6)	427 (66.2)	
Completed high school	413 (15.5)	68 (15.8)		97 (8.9)	47 (7.3)	
Completed trade/university course	1125 (42.2)	150 (34.8)		345 (31.6)	171 (26.5)	
Main language spoken at home			<0.001			<0.001
English	2540 (95.2)	383 (88.9)		1065 (97.4)	606 (94.0)	
Other than English	127 (4.8)	48 (11.1)		28 (2.6)	39 (6.0)	
Place of birth			0.004			
Oceania	1929 (72.3)	287 (66.6)				
Europe	558 (20.9)	97 (22.5)				
Other	180 (6.7)	47 (10.9)				

^aPearson's Chi-squared test.

IQR): 66.2 (59.6-73.6)y], of whom 46.4% were male, participated in the NEHS (Table 1). Of these, 431 (crude prevalence 13.9%, 95%CI: 12.4-15.5) self-reported having diabetes. The weighted prevalence of self-reported diabetes among non-Indigenous Australians was 13.5% (95%CI: 11.8-14.4).

In total, 1738 Indigenous Australians aged 40-92y [median age (IQR): 54.2 (47.6-61.9)y], of whom 41.1% were male, were examined. Of these, 645 had self-reported diabetes, resulting in a crude prevalence of 37.1% (95%CI: 33.8-40.5) and a weighted prevalence of 36.2% (95%CI: 31.6-41.0). The age- and sex-adjusted odds of self-reported diabetes were over six times higher among Indigenous participants compared to non-Indigenous participants [odds ratio (OR): 6.34, 95%CI: 4.85-8.29].

Prevalence of Non-retinopathy Ocular Conditions Among Participants with Self-reported Diabetes Non-Indigenous Australians with self-reported diabetes were significantly more likely than those without self-reported diabetes to have

undergone cataract surgery (adjusted OR 1.78, 95%CI: 1.35-2.34), with a weighted prevalence of cataract surgery of 28.8% compared to 16.9%, respectively (Table 2). Although the weighted prevalence of RVO among non-Indigenous Australians was over 3 times higher for those with self-reported diabetes compared to those without (2.2% vs 0.7%) this difference was not found to be statistically significant (age and sex adjusted OR 1.97, 95%CI: 0.87-4.45). The prevalence of all other non-retinopathy ocular conditions did not differ notably between non-Indigenous Australians with and without self-reported diabetes.

Reflecting the findings amongst non-Indigenous participants, Indigenous Australians with self-reported diabetes had higher odds of having had cataract surgery than those without self-reported diabetes (weighted prevalence 11.3% vs 5.2%, OR 1.62, 95%CI: 1.22-2.14; Table 3). Among Indigenous participants, there was moderate evidence of a higher prevalence of VSC among those with self-reported diabetes

Table 2 The prevalence of non-retinopathy ocular conditions among non-Indigenous participants with and without self-reported diabetes (n=3098)

Parameters	Without self-reported diabetes (n=2667)			With self-reported diabetes (n=431)			Multivariable logistic regression OR (95%CI)
	Cases ^a	Crude prevalence % (95%CI)	Weighed prevalence ^b % (95%CI)	Cases ^a	Crude prevalence % (95%CI)	Weighed prevalence ^b % (95%CI)	
Uncorrected refractive error	364/2667	13.6 (12.0, 15.3)	13.6 (11.5, 15.7)	55/431	12.8 (9.7, 15.8)	12.1 (8.5, 15.8)	0.88 (0.64, 1.19)
Visually significant cataract ^c	84/2653	3.2 (2.4, 3.9)	2.7 (1.9, 3.4)	20/426	4.7 (2.3, 7.1)	2.6 (1.3, 3.9)	1.31 (0.77, 2.23)
History of cataract surgery	501/2667	18.8 (16.8, 20.8)	16.9 (15.4, 18.4)	130/431	30.2 (25.8, 34.6)	28.8 (24.8, 32.7)	1.78 (1.35, 2.34)
Any AMD ^c	704/2279	30.9 (25.5, 36.3)	28.1 (22.7, 33.5)	122/350	34.9 (28.1, 41.6)	33.1 (26.0, 40.3)	1.04 (0.83, 1.28)
Late AMD ^c	26/2206	1.2 (0.7, 1.7)	1.2 (0.5, 1.8)	7/335	2.1 (0.7, 3.5)	1.9 (0.2, 3.7)	1.41 (0.64, 3.09)
Glaucoma	129/2667	4.8 (3.9, 5.8)	4.4 (3.4, 5.4)	23/431	5.3 (3.5, 7.2)	4.4 (2.8, 5.9)	1.00 (0.68, 1.45)
Ocular hypertension	111/2667	4.2 (3.3, 5.0)	4.3 (3.4, 5.1)	16/431	3.7 (1.9, 5.5)	3.9 (1.2, 6.5)	0.95 (0.57, 1.58)
Retinal vein occlusion ^c	20/2495	0.8 (0.4, 1.2)	0.7 (0.3, 1.1)	7/395	1.8 (0.4, 3.1)	2.2 (0.4, 4.1)	1.97 (0.87, 4.45)
Epiretinal membrane ^c	315/2503	12.6 (11.1, 14)	11.1 (9.7, 12.4)	52/395	13.2 (9.5, 16.8)	12.4 (8.6, 16.1)	0.94 (0.69, 1.29)

AMD: Age-related macular degeneration; CI: Confidence interval; OR: Age and sex adjusted odds ratio comparing those with and without self-reported diabetes. ^aNumber of cases/number gradable for each condition; ^bPost-stratified by population age and weighted according to sampling protocol; ^cMissing values: visually significant cataract (n=19), any AMD (n=469), late AMD (n=557), retinal vein occlusion (n=208), epiretinal membrane (n=200).

Table 3 The prevalence of non-retinopathy ocular conditions in Indigenous participants with and without self-reported diabetes (n=1738)

Parameters	Without self-reported diabetes (n=1093)			With self-reported diabetes (n=645)			Multivariable logistic regression OR (95%CI)
	Cases ^a	Crude prevalence % (95%CI)	Weighed prevalence ^b % (95%CI)	Cases ^a	Crude prevalence % (95%CI)	Weighed prevalence ^b % (95%CI)	
Uncorrected refractive error	180/1093	16.5 (13.8, 19.1)	16.2 (14.1, 18.3)	120/645	18.6 (14.7, 22.5)	18.8 (15.2, 22.3)	0.97 (0.76, 1.25)
Visually significant cataract ^c	29/1086	2.7 (1.4, 3.9)	2.3 (1.0, 3.6)	43/632	6.8 (4.7, 8.9)	7.8 (5.1, 10.4)	1.78 (0.99, 3.22)
History of cataract surgery	61/1093	5.6 (4.3, 6.8)	5.2 (4.0, 6.5)	81/645	12.6 (9.3, 15.8)	11.3 (7.5, 15.1)	1.62 (1.22, 2.14)
Any AMD ^c	185/940	19.7 (16.2, 23.1)	19.6 (15.5, 23.6)	130/474	27.4 (22, 32.8)	29.4 (22.2, 36.7)	1.22 (0.94, 1.58)
Late AMD ^c	3/931	0.3 (0.0, 0.7)	0.3 (0.0, 0.7)	0/460	0	0	NA
Glaucoma	29/1093	2.7 (1.7, 3.6)	2.8 (1.7, 4.0)	23/645	3.6 (2.4, 4.7)	3.5 (1.9, 5.2)	1.20 (0.74, 1.94)
Ocular hypertension	35/1093	3.2 (1.9, 4.5)	3.4 (2.0, 4.7)	20/645	3.1 (1.8, 4.4)	3.0 (1.4, 4.7)	1.20 (0.66, 2.18)
Retinal vein occlusion ^c	8/1030	0.8 (0.2, 1.3)	0.9 (0.2, 1.5)	6/575	1.0 (0.3, 1.8)	0.9 (0.1, 1.7)	1.01 (0.36, 2.81)
Epiretinal membrane ^c	64/1031	6.2 (4.7, 7.7)	6.2 (4.3, 8.1)	59/577	10.2 (7.7, 12.7)	8.7 (5.5, 11.9)	1.19 (0.88, 1.61)

AMD: Age-related macular degeneration; CI: Confidence interval; NA: Not applicable; OR: Age and sex adjusted odds ratio comparing those with and without self-reported diabetes. ^aNumber of cases/number gradable for each condition; ^bPost-stratified by population age and weighted according to sampling within each study site; ^cMissing values: visually significant cataract (n=20), any AMD (n=324), late AMD (n=347), retinal vein occlusion (n=133), epiretinal membrane (n=130).

compared with those without (OR 1.78, 95%CI: 0.99-3.22). The weighted prevalence of any AMD among Indigenous Australians with diabetes was also higher (29.4%) compared to those without self-reported diabetes (19.6%), although there was a lack of statistical power to provide conclusive evidence of this association (OR 1.22, 95%CI: 0.94-1.58).

Risk Factors for Non-retinopathy Ocular Conditions Among Participants with Self-reported Diabetes Because a history of cataract surgery was found to be significantly more common among participants with self-reported diabetes than those without diabetes, we identified modulating factors that were associated with having undergone cataract surgery in those with diabetes. For non-Indigenous Australians, older

age was associated with higher odds of having had cataract surgery (OR 3.31, 95%CI: 1.33-8.20 in those aged 60-69y to OR 25.43, 95%CI: 9.83-68.93 in those aged ≥80y compared to those less than 60 years of age, Table 4). The presence of any DR was also associated with a higher likelihood of having undergone cataract surgery in the non-Indigenous group (OR 2.33, 95%CI: 1.36-3.99). Non-Indigenous participants with self-reported diabetes who had undergone their last diabetic eye examination 2-20y prior (OR 0.45, 95%CI: 0.21-0.94) or any eye examination 1-2y (OR 0.49, 95%CI: 0.29-0.83) prior to participating in the survey were less likely to have had cataract surgery than those whose last examinations were less than one year previously.

Table 4 Associations between potential risk factors and non-retinopathy conditions among participants with self-reported diabetes (n=1076)

Parameters	Non-Indigenous (n=431)		Indigenous (n=645)			
	History of cataract surgery		History of cataract surgery		Visually significant cataract	
	Cases	OR (95%CI)	Cases	OR (95%CI)	Cases	OR (95%CI)
Sex						
Female	61/189	Reference	46/403	Reference	31/395	Reference
Male	69/242	0.99 (0.63, 1.56)	35/242	1.33 (0.81, 2.19)	12/237	0.61 (0.29, 1.30)
Age (y)						
40 to 49		NA	4/126	Reference	2/124	Reference
50 to 59	6/72	Reference	16/239	2.16 (0.71, 6.61)	8/235	2.2 (0.42, 11.36)
60 to 69	40/173	3.31 (1.33, 8.20)	31/196	5.74 (1.97, 16.70)	15/192	5.17 (1.27, 21.09)
70 to 79	40/123	5.30 (2.12, 13.26)	24/70	15.65 (5.14, 47.60)	12/68	13.53 (2.80, 65.47)
80+	44/63	25.43 (9.38, 68.93)	6/14	23.47 (5.47, 100.71)	6/13	52.25 (8.98, 304.04)
Geographic remoteness						
Major city	47/178	Reference	28/268	Reference	13/262	Reference
Inner regional	32/93	1.30 (0.72, 2.35)	14/97	1.36 (0.65, 2.81)	5/96	0.94 (0.56, 1.57)
Outer regional	33/93	1.45 (0.80, 2.63)	28/169	1.62 (0.89, 2.95)	15/166	1.84 (0.79, 4.31)
Remote	12/39	0.79 (0.34, 1.86)	9/63	1.36 (0.57, 3.24)	6/63	1.8 (0.77, 4.25)
Very remote	6/28	0.46 (0.16, 1.33)	2/48	0.29 (0.06, 1.35)	4/45	1.84 (0.58, 5.87)
Educational attainment						
Less than high school	71/213	Reference	57/427	Reference	31/419	Reference
Completed high school	20/68	1.00 (0.52, 1.91)	5/47	0.76 (0.27, 2.12)	6/46	1.81 (0.58, 5.66)
Completed trade/university course	39/150	1.05 (0.62, 1.77)	19/171	1.08 (0.60, 1.94)	6/167	0.56 (0.21, 1.51)
Main language spoken at home						
English	113/383	Reference	77/606	Reference	39/595	Reference
Other than English	17/48	2.00 (0.98, 4.10)	4/39	0.74 (0.25, 2.23)	4/37	1.68 (0.69, 4.08)
Place of birth						
Oceania	85/287	Reference		NA		NA
Europe	32/97	1.10 (0.65, 1.89)				
Other	13/47	1.26 (0.59, 2.72)				
Self-reported stroke^a						
No	116/391	Reference	64/555	Reference	36/544	Reference
Yes	13/37	1.09 (0.49, 2.41)	17/88	1.44 (0.77, 2.71)	7/86	0.84 (0.29, 2.45)
Duration of diabetes (y)^a						
<5	28/103	Reference	9/152	Reference	7/150	Reference
5 to <10	20/101	0.68 (0.33, 1.39)	11/122	1.36 (0.52, 3.51)	9/119	1.48 (0.63, 3.47)
10 to <20	44/139	1.15 (0.62, 2.12)	18/203	1.17 (0.49, 2.79)	10/201	0.8 (0.25, 2.63)
20+	36/86	1.73 (0.89, 3.36)	42/160	3.73 (1.68, 8.30)	16/155	1.35 (0.54, 3.42)
Time since last diabetic eye check (y)^a						
<1	72/208	Reference	41/224	Reference	12/218	Reference
1 to <2	23/84	0.70 (0.38, 1.30)	19/134	0.78 (0.41, 1.46)	9/132	1.35 (0.50, 3.62)
2 to 20	12/65	0.45 (0.21, 0.94)	10/110	0.46 (0.22, 1.00)	6/108	1.02 (0.35, 3.02)
Never	20/66	0.68 (0.35, 1.33)	10/167	0.27 (0.13, 0.58)	13/165	1.63 (0.68, 3.90)
Time since last eye check (y)						
<1	89/245	Reference	53/262	Reference	16/255	Reference
1 to 2	30/147	0.49 (0.29, 0.83)	22/251	0.41 (0.23, 0.71)	15/246	1.13 (0.54, 2.37)
>2	11/38	0.87 (0.39, 1.95)	6/109	0.21 (0.09, 0.53)	8/108	1.31 (0.59, 2.90)
Never					4/65	5.85 (1.94, 17.69)
Any diabetic retinopathy^a						
No	69/263	Reference	29/311	Reference	19/308	Reference
Yes	43/115	2.33 (1.36, 3.99)	35/261	1.89 (1.06, 3.36)	13/258	0.89 (0.37, 2.10)
Vision threatening diabetic retinopathy^a						
No	102/352	Reference	38/481	Reference	26/478	
Yes	6/18	1.70 (0.54, 5.36)	21/65	7.58 (3.66, 15.71)	0/62	NA

^aMissing values: Self-reported stroke (n=5), duration of diabetes (n=10), time since last diabetic eye check (n=18), any diabetic retinopathy (n=126), vision threatening diabetic retinopathy (n=160). Cases: Number with history of cataract surgery or visually significant cataract/number with self-reported diabetes and non-missing value for the characteristic. CI: Confidence interval; OR: Age and sex adjusted odds ratio for history of cataract surgery.

As with non-Indigenous Australians, older age was associated with a large increase in the odds of having undergone cataract surgery among Indigenous Australians with diabetes (Table 4). Indigenous Australians who reported that they had diabetes for 20 or more years had 3.73 (95%CI: 1.68-8.30) times higher odds of having have undergone cataract surgery than those who had been diagnosed within the past 5y. Having DR increased the odds of having had cataract surgery among Indigenous Australians with diabetes by 89% (OR 1.89, 95%CI: 1.06-3.36), while the odds of having a history of cataract surgery were 7.58-fold for those diagnosed with VTDR compared to those without VTDR (95%CI: 3.66-15.71). Indigenous participants with diabetes who were less likely to have had a history of cataract surgery included those who had never had a diabetic eye examination (OR 0.27, 95%CI: 0.13-0.58) and those who had not had any type of eye examination within the past year (OR 0.21 to OR 0.41).

A significant age-related increase in the odds of VSC was observed among Indigenous participants with self-reported diabetes. The odds of VSC increasing from 5.17 (95%CI: 1.27-21.09) for those aged 60-69y to 52.25 (95%CI: 8.98-304.04) for those aged ≥ 80 y compared to those aged 40-49y. Indigenous Australians with self-reported diabetes who had never undergone an eye examination were almost six times more likely to have had VSC compared to those who had their eyes examined within the past year (OR 5.85, 95%CI: 1.94-17.69).

DISCUSSION

This paper has reported the prevalence of non-retinopathy ocular conditions among non-Indigenous and Indigenous Australians with self-reported diabetes. Epidemiological risk factors for conditions found to be more prevalent among those with diabetes were also identified. These findings were based on the first nationally-representative survey of both Indigenous and non-Indigenous populations in Australia, and the data presented herein may consequently provide significant value to national diabetes and eye healthcare programmes.

The finding that the prevalence of cataract surgery among non-Indigenous Australians with diabetes was double that of non-Indigenous Australians without diabetes reflects previous findings from the BMES, which reported a prevalence of 12% in diabetic and 5.9% in non-diabetic participants^[9]. Notably however, the prevalence of cataract surgery among non-Indigenous Australians with diabetes in the NEHS was substantially higher than in the BMES, suggesting that the uptake to cataract surgery services by non-Indigenous Australians with diabetes may have improved significantly in recent years. Greater uptake to cataract services may be partly attributable to a significant increase in adherence rates to national diabetic eye examination guidelines since

the BMES^[32]. The prevalence of cataract surgery among diabetic Indigenous Australians, while higher than that of non-diabetic Indigenous Australians, was considerably lower than diabetic non-Indigenous Australians, illustrating that further improvements in diabetic eye examination adherence rates are required to attenuate the potential excess burden of blindness that may result from a high prevalence of diabetes-related cataract. DR was associated with a considerable increase in the odds of having undergone cataract surgery, and VTDR further exacerbated this risk four-fold amongst Indigenous Australians. Because this was a cross-sectional study, the causal relationship between cataract surgery and DR cannot be ascertained. One possibility is that, because both cataract and DR tend to develop with a longer duration of diabetes, participants with DR were likely to have had more advanced disease and might have already undergone vision-restoring cataract surgery. This is further supported by the 3.7-fold higher odds of having had cataract surgery among those with a duration of diabetes of more than 20y. A second possibility is that the reason cataract surgery, but not VSC, was associated with VTDR in Indigenous Australians, was that having had cataract surgery may have worsened the progression of DR in at-risk participants. The capacity for cataract surgery to worsen DR and accelerate the development of CSME has been described^[33].

Strong inferences about the 3.4-fold higher prevalence of VSC among Indigenous Australians with diabetes compared to those without diabetes cannot be made from the findings of this study, owing to the lack of a statistical association. Although the lack of a strong association reflects previous research in Indigenous populations^[19], other studies in Australia^[10] and elsewhere^[8,15] have reported significantly higher rates of cataract in diabetic populations, and corroborating clinical and molecular research has substantiated this link by revealing likely pathogenic mechanisms underpinning the development of diabetic cataracts^[34-35]. Two key factors may have attenuated the association in the present study. First, research amongst Indigenous Australians has suggested that the relationship between diabetes and cataract depends on the cataract subtype, with posterior subcapsular cataract, but not other subtypes, being more prevalent in those with diabetes^[19]. Because we did not differentiate between cataract subtypes, we may have lacked the specificity to detect a significant association. Second, the prevalence of cataract surgery among Indigenous Australians has increased in recent years^[36]. Considering that a history of cataract surgery was significantly associated with diabetes in this analysis, had the cataract surgery coverage rate been lower, the prevalence of VSC would have been correspondingly higher, which would likely have revealed a significant association between VSC and diabetes.

We found some evidence of an association between self-reported diabetes and RVO among non-Indigenous Australians. Although the BMES found no association between diabetes and RVO^[37], the Beaver Dam Eye Study in the United States reported that diabetes more than doubled the odds of RVO^[38]. Owing to a small sample of diabetic participants with RVO in the NEHS ($n=7$) it is unclear if the association might have been stronger with a larger sample size. A similarly weak association was found between AMD and diabetes in Indigenous Australians. A Meta-analysis has shown diabetes to be a risk factor for AMD^[39]. Detailed studies that consider additional factors such as diabetes subtype should therefore be conducted to determine whether there is any relationship between diabetes and AMD in the Indigenous population.

The lack of any salient link between self-reported diabetes and the other non-retinopathy conditions in this study should be considered in the context of the largely inconsistent literature. For example, the Singapore Malay Eye Study (SiMES) reported that OHT and ERM were significantly more prevalent among those with diabetes than those without diabetes^[8]. Perhaps more representative of the ethnic composition of Australia, diabetic populations in Europe^[40] and the United States^[41] have similarly reported associations between diabetes and high IOP, and indeed, the BMES in Australia reported that ERM^[11], OHT and glaucoma^[12] were associated with diabetes. However, reflecting the NEHS, the VIP found no significant relationships between self-reported diabetes and either ERM^[42] or AMD^[13]. This may be due, in part, to the use of self-report in the VIP in contrast to glycaemic testing in the BMES to identify diabetes. Other reasons for disagreement between the NEHS and previous research are difficult to identify with confidence because inter-study comparability is limited by differences in sampling and examination methods, geographic coverage, disease classification, and the fact that the epidemiology of diabetes has changed significantly since previous surveys. It may be inferred from disagreement between studies, that whether non-retinopathy ocular conditions are more prevalent among diabetic populations depends on several modulating factors, and further research is required to identify genetic, lifestyle and healthcare utilisation risk factors in each population. Nevertheless, the finding that most ocular conditions were not significantly more prevalent among those with self-reported diabetes may provide some relief to concerned stakeholders in the health workforce who are already facing the increasing challenges of developing programmes and providing treatment for the multitudinous complications arising from diabetes^[43].

The major limitation of this study was the use of self-report to identify participants with diabetes which may have led to underreporting of diabetes^[44]. Nevertheless, while some

ascertainment bias may have affected our estimates, self-report is frequently used for population-based surveillance of diabetes and several studies have reported adequate reliability, at least for previously diagnosed diabetes^[45-46]. The absence of glycemic testing in the study protocol is likely to have resulted in an underestimation of the true prevalence of diabetes due to missed cases of undiagnosed disease. An additional limitation was that our risk factor analysis did not include a number of important risk factors for ocular conditions including family, smoking and medication history, biochemical data and type of diabetes, which may have influenced our results and limit the applicability of these findings to clinical decisions about which diabetic patients require regular monitoring.

In conclusion, we have reported that both Indigenous and non-Indigenous Australians with self-reported diabetes were significantly more likely to have a history of cataract surgery than those without self-reported diabetes. In conjunction with a high prevalence of VSC among Indigenous Australians, these findings suggest that Australians with diabetes have an elevated risk of developing cataracts. Approximately 1.5 million Australian adults are diabetic, and if current incidence rates persist, one-third of Australians will be diabetic by the year 2025^[47]. The prevalence and risk factor data presented in this report will optimise the deployment of resources, including specialist eye healthcare personnel and early detection and treatment modalities, to ameliorate the burden of blindness among the growing diabetic population in Australia.

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