

# BMJ Open Evaluation of the prevalence of non-diabetic eye disease detected at first screen from a single region diabetic retinopathy screening program: a cross-sectional cohort study in Auckland, New Zealand

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## ABSTRACT

**Objectives** To evaluate the prevalence of incidental non-diabetic ocular comorbidities detected at first screen in a large diabetic retinopathy (DR) screening programme.

**Design** Cross-sectional cohort study.

**Setting** Single large metropolitan diabetic eye screening programme in Auckland, New Zealand.

**Participants** Twenty-two thousand seven hundred and seventy-one participants who attended screening from September 2008 to August 2018.

**Results** Hypertensive retinopathy (HTR) was observed in 14.2% (3236/22771) participants. Drusen were present in 14.0% participants under the age of 55 years, increasing to 20.5% in those 55 years and older. The prevalence of neovascular age-related macular degeneration (AMD) was 0.5% in participants aged <55 years, 2.4% in participants aged 55–75 years and 16% in participants aged >75 years. Retinal vein occlusion and retinal arterial embolus were prevalent in 0.7% and 0.02%, respectively, in participants aged <55 years, increasing to 2.2% and 0.4%, respectively, in those >75 years. Cataracts were common being present in 37.1% of participants over the age of 75 years. Only 386 individuals (1.7%) were labelled as glaucoma suspects. Geographic atrophy, epiretinal membrane, choroidal nevi and posterior capsular opacification had an increased prevalence in older individuals.

**Conclusions** Our data suggest that AMD, HTR and cataracts are routinely detected during DR screening. The incorporation of the detection of these ocular comorbidities during DR screening provide opportunities for patients to modify risk factors (smoking cessation and diet for AMD, blood pressure for HTR) and allow access to cataract surgery.

## INTRODUCTION

Diabetes mellitus (DM) is a major health issue in New Zealand (NZ) and currently it is estimated that 260 000 (7.7%) adults are living with diabetes.<sup>1</sup> In individuals living with diabetes, the reported prevalence of

## Strengths and limitations of this study

- This is a large, cross-sectional study involving data collected in a regional diabetic retinopathy (DR) screening programme over a 10-year period.
- Our study has high generalisability as participants have a diverse range of ethnicities.
- The methodology provides for the robust identification of drusen, age-related macular degeneration (AMD), hypertensive retinopathy, glaucoma suspect, retinal vein occlusion and retinal arterial embolus.
- Our observations were based on a participant's first presentation for routine DR screening, so our cohort will be younger than the general population attending for routine DR screening, with reported incidence of age-related diseases therefore lower.
- The undifferentiated classification of all drusen sizes into one entity meant that we could not differentiate between normal age-related changes, early AMD and intermediate AMD.

diabetic retinopathy (DR) is around 35% and it is unanimously accepted that the early detection and treatment of DR significantly reduces preventable blindness.<sup>1</sup>

Due to the high prevalence of diabetes and the well-described association of diabetes with other ocular diseases,<sup>2</sup> there is likely to be a significant prevalence of non-DR ocular disease present in those individuals attending for routine screening. Currently, there is a paucity of data relating to non-DR pathology that is detected during routine screening, with the current literature limited to small datasets of between 1000 and 4000 individuals.<sup>3–9</sup> The aim of this study is to examine the prevalence of common non-diabetic ocular comorbidities in people living with diabetes

attending for their first retinal screen in a large, single region DR screening programme in NZ and reviewing the utility of including the detection of these pathologies in the screening process.

## METHODS

Auckland is the largest city in NZ with a population of 1.6 million.<sup>10</sup> A retrospective audit was conducted on the centralised DR screening database from September 2008 to August 2018, looking at the incidental detection of important ocular comorbidities at the first screening visit.

Auckland District Health Board's (ADHB) DR screening programme uses a three-tier grading system, with ophthalmic technicians acquiring the retinal photographs and performing a primary grade. The grading is recorded on a standardised pro forma, which in addition to DR and maculopathy, also includes non-diabetic related pathologies. Non-diabetic pathology was defined as ocular disease other than DR. These included hypertensive retinopathy (HTR), drusen, age-related macular degeneration (AMD) and glaucoma suspect. If the retinal images are normal, they are signed off, with the images from 1 in 10 being audited by the secondary grading team. If the photographer was unable to acquire an image of sufficient quality, the individual is examined at the slit lamp by an experienced optometrist and graded accordingly. All individuals in whom an abnormality is identified (both diabetic and non-diabetic) are passed to the secondary grading team. If the participant has referable DR or other significant ocular disease, the images are passed up to the programme's lead ophthalmologist who is the final arbitrator as to the nature of the pathology identified. Details on demographics and health conditions such as known glaucoma, systemic hypertension and smoking status are recorded at the time of screening. Advanced AMD was classified as either neovascular AMD or geographic atrophy.<sup>11</sup> The presence of epiretinal membrane (ERM) was determined on cellophane reflex at the macula with or without retinal folds.<sup>12</sup>

The prevalence of the following incidental findings was analysed: drusen, AMD, ERM, HTR, retinal vein occlusion (RVO), retinal arterial embolus, glaucoma suspect, choroidal nevus, congenital hypertrophy of retinal pigment epithelium (CHRPE), cataracts and posterior capsular opacification (PCO). As RVO was not subcategorised at source, we were unable to identify the proportion of RVOs that could be subclassified as either branch RVO, hemi-RVO or central RVO.

Graders reported the presence of HTR when signs consistent with grade 2 or greater (Keith, Wagener and Barker classification)<sup>13</sup> were observed. Vein occlusion was characterised by occluded and sheathed retinal veins in the case of old vein occlusions and retinal oedema, optic disc hyperaemia, scattered superficial and deep flame haemorrhages and venous dilation in the case of a more recent event.<sup>14</sup> Retinal arterial embolus was detected as a

dull or reflective round, rhomboidal or rectangular lesion lodged in retinal arterioles.<sup>15</sup>

Glaucoma suspects were classified based on cup-to-disc ratio (CDR) of  $\geq 0.7$ , CDR asymmetry of 0.2 between eyes, neuroretinal rim width  $\leq 0.1$  between 11:00 and 13:00 or 17:00 and 19:00 or if there was a disc margin haemorrhage.<sup>16</sup> Choroidal nevus was defined as flat unequivocally pigmented choroidal lesions at least 500  $\mu\text{m}$  in diameter.<sup>17</sup> CHRPE was defined as a round, flat, hyperpigmented, well-demarcated lesion with punched-out hypopigmented or depigmented lacunae, surrounded by a narrow hypopigmented halo, with normal overlying retina and vasculature.<sup>18</sup>

If the participant had lens opacities or PCO that was compromising the participant's vision, they were referred for slit lamp review and either cataract or PCO recorded on the reporting pro forma as appropriate.

For the purposes of investigating the associations of disease with ethnicity, the ethnicities were compressed according to the NZ level 1 classification with the exception that we replaced Middle Eastern with Indian reflecting the large Indian and Fijian Indian community.<sup>19</sup> For statistical purposes, people who self-identify with more than one ethnicity were routinely classified to only one ethnicity in a defined prioritised order. NZ ethnicity classifications only enable identification of the Indian South Asian population, who represent around 90% of South Asians in NZ.

## RESULTS

The database comprised 22 771 participants with type 1 and type 2 DM aged 12–98 years (mean 56.0 (SD 15.7)). Overall, 9764 (43%) participants were younger than 55 years, 10 850 (48%) participants were aged 55–75 years and 2157 (9%) participants were older than 75 years. Ethnicity data were available for 69.2% of the cohort; 34.5% were identified as European, 12.1% as Māori, 20.2% as Pasifika, 15.6% as Indian, 15.3% as other Asian and 2.5% as other ethnicities. At the baseline screening assessment, 1284 (5.6%) participants had referable DR and 818 (3.6%) participants had sight-threatening DR. Overall, 1587 (7.0%) individuals had referable maculopathy and 1182 (5.2%) had sight-threatening maculopathy. The prevalence rates from our study mirror other published data on the prevalence of DR in NZ.<sup>20 21</sup> The mean visual acuity of our cohort was 6/7.5 Snellen letters.

Most individuals enrolled in screening had type 2 diabetes (91.3%), 7.4% had type 1 diabetes, 0.1% had gestational diabetes and 1.2% had other types of DM. Overall, 54.1% of individuals were male. The mean duration of diabetes and mean HbA1c at first presentation was 6.4 years (SD 6.7 years, range 0–65 years) and 63.5 mmol/mol (SD 16.9 mmol/mol, range 38–169 mmol/mol), respectively. Overall, 12.3% self-identified as smokers. Thirteen thousand six hundred and seventy eight (60.1%) of all individuals were recorded as being hypertensive or on blood pressure lowering medications. The

**Table 1** The prevalence of ocular comorbidities in screened participants with diabetes

	Number/prevalence at each age category (n/%)							
	<55 years		55–75 years		>75 years		Overall	
Total number of participants	9764		10850		2157		22771	
Prevalence of ocular comorbidity	n	%	n	%	n	%	n	%
Drusen	1369	14.0	2232	20.6	440	20.4	4041	17.7
Neovascular AMD	45	0.5	259	2.4	349	16.2	653	2.9
Geographic atrophy	9	0.1	22	0.2	7	0.3	38	0.2
Glaucoma suspect	92	0.9	207	1.9	87	4.0	386	1.7
ERM	196	2.0	869	8.0	244	11.3	1309	5.7
Arterial embolus	2	0.0	24	0.2	9	0.4	35	0.2
Vein occlusion	67	0.7	176	1.6	48	2.2	291	1.3
Hypertensive retinopathy	1286	13.2	1702	15.7	248	11.5	3236	14.2
Choroidal nevus	168	1.7	287	2.7	96	4.5	551	2.4
CHRPE	9	0.1	7	0.1	0	0.0	16	0.1
Cataracts	332	3.4	1992	18.4	801	37.1	3125	13.7
PCO	4	0.0	26	0.2	30	1.4	60	0.3

AMD, age-related macular degeneration; CHRPE, congenital hypertrophy of retinal pigment epithelium; ERM, epiretinal membrane; PCO, posterior capsular opacification.

prevalence increased with age: 42.5% individuals aged <55 years, 72.2% individuals aged 55–75 years and 78.5% individuals aged >75 years. The prevalence of hypertension among different ethnic groups was similar: European 64.1%, Māori 67.5%, Pasifika 65.5%, Indian 60.1% and other Asian 57.5%.

The prevalence of participants with non-DR ocular comorbidities categorised by age is shown in table 1. There were 10 181 (45%) individuals with at least one ocular comorbidity. Three thousand two hundred and eighty eight (14%) had a diagnosis of multiple ocular comorbidities. The most common ocular comorbidities detected were Drusen (4041), HTR of grade 2 or above (3236) and cataract (3125). Overall, 653 individuals had neovascular AMD, of which 503 were known to be hypertensive. Participants with hypertension were more likely to have neovascular AMD than participants without hypertension, 3.7% versus 1.6% (OR=2.3, 95% CI: 1.9 to 2.7). Of the 3236 individuals with HTR only, 70% (2260) were either currently taking blood pressure medications or known to have hypertension. There was a marked ethnic disparity in HTR with greater prevalence being observed in Māori (17.0%) and Pasifika (17.4%) compared with Europeans (10.9%), Indians (13.1%) and other Asians (14.3%). There was a slightly higher prevalence of drusen among Asians, 20.4% compared with other ethnic groups Europeans (17.3%), Māori (15.5%), Pasifika (18.0%) and Indians (17.3%).

## DISCUSSION

ADHB has provided funding for a systematic, DR screening programme since 2008. In addition to recording and

grading DR, the programme also systematically collected data on selected non-DR ocular pathology. The most common non-DR ocular findings observed were drusen, cataract and HTR. Although uncommon, ERM, RVO, glaucoma suspect, retinal arterial embolus, neovascular AMD, geographic atrophy and PCO were increasingly prevalent with older age.

### Drusen and AMD

The prevalence and age predilection for drusen and AMD in our cohort (table 1) is similar to those previously reported.<sup>3–5,9</sup> The prevalence of both intermediate and late AMD increases with age,<sup>22</sup> and as expected, neovascular AMD was rare (0.5%) in participants aged <55 years, but increased significantly with age, being observed in 16.2% of those aged >75 years. In line with other published data, we found that there was a positive correlation between hypertension and neovascular AMD, OR=2.3, 95% CI: 1.9 to 2.7.<sup>23 24</sup>

Neovascular AMD requires urgent treatment if vision loss is to be prevented. Our data highlight both the importance of grading teams being alert to this pathology and the need for a pathway to rapidly triage these patients into treatment services. Although we cannot report on the prevalence of intermediate AMD in our cohort as we did not differentiate between the types of drusen, arguably intermediate AMD is also an important condition to identify. Vision loss in participants with intermediate AMD is mild and often goes unnoticed,<sup>25</sup> and identifying these asymptomatic participants with intermediate AMD therefore provides an opportunity to counsel individuals on both appropriate dietary modifications and smoking cessation strategies.<sup>25</sup>

## Hypertension and HTR

As expected,<sup>2</sup> there was a high prevalence of systemic hypertension, 60.1% (13678) in our cohort. HTR was also relatively common being observed in 3236 individuals (14.2%), was largely independent of age and was predominantly a bilateral disease, consistent with it being a sign of target organ damage from systemic hypertension.<sup>26</sup> While there are few studies which report the rates of HTR in a cohort of participants undergoing DR screening, our data are broadly in line with other published data.<sup>3 9</sup> HTR is known to be both more prevalent and severe in participants with poorly controlled hypertension and is associated with an increased risk of stroke, renal impairment and cardiovascular disease.<sup>26</sup> Hypertension is also an independent risk factor for both the development and progression of DR.<sup>26</sup> Good blood pressure control reduces both the macrovascular and microvascular complications from diabetes.<sup>1</sup> While we found that the prevalence of hypertension was similar across all ethnicities, HTR was more prevalent in Māori and Pacific peoples. The New Zealand Diabetes, Heart and Health Survey 2002/2003 revealed that Māori and Pacific people had higher average systolic and diastolic blood pressure levels compared with individuals of other ethnicities and this could explain the higher rates of HTR we observed in these groups.<sup>27</sup> The same study also revealed that just 65% of those known to have hypertension were on treatment and approximately 3%–6% of the cohort had hypertension that had not been diagnosed.<sup>27</sup> In our cohort, HTR was observed in 2260 (16%) of individuals known to have hypertension and 976 (4.3%) who were not diagnosed with hypertension. This suggests that hypertension is not only undertreated but is also underdiagnosed in people living with diabetes in NZ. Retinal screening therefore offers a valuable opportunity to provide feedback to patients and their treating physicians prompting them to review, and if need be, optimise blood pressure control and cardiovascular health. This may be particularly valuable for Māori and Pasifika, who have a significantly higher rate of cardiovascular mortality compared with other New Zealanders.<sup>28</sup>

## RVO and retinal arterial embolus

RVO and retinal arterial embolus, which are associated with systemic hypertension,<sup>26</sup> were mainly unilateral diseases and showed greater prevalence with increasing age. These findings are in line with data derived with large population studies.<sup>15 29</sup> Retinal arterial embolus was much less common being observed in 0.02% of individuals aged <55 years and 0.4% in >75 years. These data on both RVO and arterial emboli prevalence are consistent with the low prevalence rates found in other screening studies (RVO 0.2%–0.5% and arterial emboli 0.1%).<sup>3 4</sup>

While a proportion of retinal arterial emboli presents acutely, it is clear that many are asymptomatic as demonstrated by the 1.3%–1.4% prevalence of asymptomatic retinal arterial embolus in other population based studies.<sup>2</sup> The detection of a retinal emboli should alert the clinician to a full cardiovascular and cerebrovascular

risk assessment to identify the source of the emboli and modify any cardiovascular risk factors.<sup>2</sup>

## Glaucoma suspect

After excluding patients known to have glaucoma, 386 (1.7%) individuals were labelled as 'glaucoma suspects'. As expected, the prevalence increased with age, being four times higher in participants over age 75 years compared with those under 55 years. Due to the anonymised nature of our data, we were unable to evaluate how many of these individuals identified as glaucoma suspects were eventually diagnosed with glaucoma. It is recognised that individuals with diabetes are at an increased risk of glaucoma<sup>2</sup> and published data from other screening programmes, although with older cohorts, indicate a prevalence of 'glaucoma suspects' of between 2.5% and 3.7%.<sup>6 7</sup>

It is noteworthy that only a minority of participants identified as being glaucoma suspects in these studies were subsequently diagnosed with glaucoma after further evaluation. The diagnosis of glaucoma is multifactorial requiring an optic neuropathy with corresponding visual field changes, interpreted in the context of the intraocular pressure, family history and corneal thickness.<sup>30 31</sup> Even with these data, the proportion of false positives for suspected glaucoma referred from community optometry remains high.<sup>32</sup> The utility of a colour fundal photograph at a single point in time to diagnose glaucoma is therefore questionable and thus periodic untargeted screening for open-angle glaucoma is currently not recommended, except in specific high-risk groups.<sup>33–35</sup> As the prevalence of undiagnosed glaucoma in the population undergoing routine DR screening is low, these data suggest that referral to ophthalmology services of those identified as glaucoma suspects in the process of routine DR screening is not justified.

## Other ocular disease

The prevalence for the other ocular conditions was low: ERM 5.7%, choroidal nevus 2.4% and CHRPE 0.1%. We believe that these findings have little importance and they can therefore be considered incidental findings with minimal clinical significance.<sup>12 17 18</sup> Three thousand one hundred and eighty-five individuals had a media opacity, either cataract or PCO, which impacted the quality of the retinal photograph. As expected, the prevalence of these media opacity increased significantly with age. The presence of cataract, particularly in those individuals with poorly dilating pupils, will significantly impair the detection of diabetic maculopathy and early retinopathy. While not all media opacity detected during routine diabetic retinal screening requires surgery, these data reveal the importance of providing a mechanism whereby those individuals in whom high quality images are not obtainable to be examined at the slit lamp. It also demonstrates the need to have a clear, accessible pathway to cataract surgery for those individuals with visually significant cataract.

## Study strengths

This is a large, cross-sectional study involving data collected in a regional DR screening programme over a 10-year period. Our study has high generalisability as participants have a diverse range of ethnicities. The methodology provides for the robust identification of drusen, AMD, HTR, glaucoma suspect, RVO and retinal arterial embolus and was overseen by a single senior ophthalmologist over a 10-year period. The prevalence rates of those conditions which we believe are important to identify during routine DR screening, neovascular AMD and HTR were similar to those that have previously been reported elsewhere.<sup>3–5,9</sup>

## Study limitations

The usual limitation of retrospective cohort studies applies to this study. Our observations were based on a participant's first presentation for routine DR screening, so our cohort will be younger than the general population attending for routine DR screening. The reported incidence of age-related diseases will therefore be lower when compared with the general population of people who are undergoing routine screening. As the presence of media opacity can significantly impair the ability of the grading team to read both diabetic and non-diabetic pathology, it is possible that the true incidence of disease is higher than what we report. Finally, the undifferentiated classification of all drusen sizes into one entity meant that we could not differentiate between normal age-related changes, early AMD and intermediate AMD.

## Implications for screening program design

While it is incontrovertible that DR fulfils Wilson and Jungner's criteria for screening,<sup>36</sup> our data suggest that there are other important conditions observed during screening that will impact health outcomes and should be routinely reported. Based on our data we recommend that screening for neovascular AMD and intermediate AMD be incorporated into existing DR screening programmes. Although a cost analysis of this proposal is beyond the scope of this paper, the simultaneous screening of AMD and DR has previously been shown to be cost effective.<sup>37</sup> Our data also suggest that systemic hypertension is both under-recognised and undertreated in people living with diabetes. Incorporating blood pressure screening into and accurately identifying HTR into the DR screening pathway will not only provide health benefits for all<sup>9</sup> but may also help address the acknowledged inequity in cardiovascular health outcomes for Māori and Pacific populations.<sup>28</sup> Our data confirm the need for DR screening programmes to provide both a facility for patients to be examined at the slit lamp and for easy access to cataract surgery if required. We believe that our data on the non-diabetic ocular conditions, observed at the time of retinal screening, will help inform healthcare providers about the expected demands that will be placed on ophthalmology services as a result of DR screening above and beyond DR alone.

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**Data availability statement** All data extracted from the screening database were deidentified at source. Data are available upon reasonable request.

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