

# The prevalence of glaucoma among 45-year-old New Zealanders

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## ABSTRACT

**AIM:** We aimed to estimate the prevalence of glaucoma in New Zealand using a population-based birth cohort of 45-year-olds.

**METHODS:** Study members of the Dunedin Multidisciplinary Health & Development Study participated (n=938 out of 1037 births (91%). The data collected included visual acuity, visual field (VF), refraction, central corneal thickness, intraocular pressure (IOP), axial length, spectral domain optical coherence tomography (OCT), and non-mydratric fundus photographs. Two ophthalmologists reviewed data independently to generate a consensus glaucoma status: "Normal" if no suspicion of glaucoma; "Ocular hypertension" if IOP >21 mmHg; "Glaucoma suspect" if optic disc photograph was suspicious for glaucoma with no more than borderline or non-corresponding VF or OCT abnormalities; and "Glaucoma" if optic disc photograph was suspicious for glaucoma and there were corresponding abnormalities of the OCT or VF.

**RESULTS:** Of 891 participants with sufficient data to assign a glaucoma status, 804 were "Normal" (90.2% [CI 88.3–92.2]), 15 were "Ocular hypertension" (1.68% [95% confidence interval (CI) 0.84–2.5]), 65 were "Glaucoma suspect" (7.30% [95% CI 5.6–9.0]), and 7 were classified as "Glaucoma" (0.79% [95% CI 0.21–1.4]). An additional 73 participants (8.2%, [95% CI 6.3%–10%]) had abnormalities on the OCT scan but were not deemed to be glaucoma suspects.

**CONCLUSION:** The prevalence of glaucoma in New Zealand is between 0.2% and 1.4%, consistent with other population-based studies in the same age group. The study highlights the sensitivity of OCT and the potential for misinterpretation and over-investigation.

The epidemiology of glaucoma has been defined by several large population-based studies, measuring the prevalence in different contexts (Table 1).<sup>1–10</sup> As the incidence of glaucoma increases with age, an increase in the number of affected people is predicted from an ageing global population.<sup>11</sup> Another source of increasing glaucoma prevalence is the wide dissemination of imaging technology, most notably optical coherence tomography (OCT), which is both specific and sensitive in detecting early glaucoma and is widely available as an opportunistic screening method in developed countries.<sup>12</sup>

In New Zealand, no glaucoma prevalence data has been collected, and it has been assumed that the New Zealand prevalence is comparable to surveys from Australia.<sup>7,8</sup> Establishing the prevalence in New Zealand is important to help estimate the burden of this disease.

In the present study, we measured the prevalence of glaucoma in the well-characterised population-based birth cohort of 45-year-old participants of the Dunedin Multidisciplinary Health & Development Study (Dunedin Study).<sup>13</sup> Using

OCT allowed us to consider how this new, more sensitive technology affected the prevalence estimate, in comparison to older studies which only used optic disc photography and visual field tests.

## Methods

### Study design and approvals

This was an observational cross-sectional study. Participants gave written informed consent, and all study protocols were approved by the NZ Health and Disability Ethics Committee.

### Study population

Participants are members of the Dunedin Study, a longitudinal investigation of health and behaviour in a population-representative birth cohort of 1,037 individuals (91% of eligible births; 52% male) born between 1 April 1972 and 31 March 1973 in Dunedin, New Zealand. The longitudinal study was established at age 3-years based on residence in the province.<sup>13</sup> Assessments were conducted at birth and at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and most recently at age 45,

when 94% of the 997 participants still alive took part. Each study member was brought to the research unit for a day of interviews and examinations. Ninety-three percent of eligible age 45 participants also completed MRI scanning. The cohort represents the full range of socio-economic status in New Zealand's South Island, and as adults match the NZ National Health and Nutrition

Survey on adult health indicators, eg BMI, smoking, GP visits.<sup>14</sup> Study participants are primarily of New Zealand European ethnicity (approximately 93%). Written informed consent was obtained from participants, and the study was approved by the New Zealand Health and Disability Ethics Committee.

**Table 1:** Summary of population-based studies measuring the prevalence of glaucoma in middle-aged predominantly Caucasian populations.<sup>1-10</sup>

Study Location, year	Age group	Prevalence	Total no. participants (response rate %)
Sweden, 1981	55–69	0.93%	1511 (77%)
Baltimore Eye Survey, MD, USA, 1991	40–49	0.92% (definite glaucoma, nil probable)	5308 (79.2%)
Beaver Dam Eye Study, WI, USA, 1992	43–54	0.9% (definite glaucoma)	4926 (83.1%)
County Roscommon, Ireland, 1993	50–59	0.72%	2186 (99.5%)
Rotterdam Study, Netherlands, 1994	55–59	0.2%	3062 (80.0%)
Casteldaccia Eye Study, Italy, 1994	40–49	0.4%	1062 (67.3%)
Blue Mountains Eye Study, NSW, Australia, 1996	<60	0.3% (definite glaucoma)	3241 (87.9%)
		0.4% (definite and probable glaucoma)	
Visual Impairment Project, VIC, Australia, 1998	40–49	0.1% (definite glaucoma)	3271 (83.0%)
		0.5% (definite and possible glaucoma)	
National Eye Health Survey, Australia, 2018	50–59	0.2% (definite glaucoma)	4792 (99.1%)
		1.8% (definite or probable)	
Northern Finland Birth Cohort Eye Study, Finland, 2019	45–49	1.1% (definite glaucoma)	3039 (58.9%)
		2.7% (definite and possible glaucoma)	

## Data collection

At age 45-years, the following was assessed: first degree relative with glaucoma; best corrected visual acuity; visual field (VF) on Matrix perimeter (Carl Zeiss Meditec, Dublin, CA, USA); non-cycloplegic autorefractometry; central corneal thickness (CCT) and intraocular pressure (IOP) using the Tonoref III (Nidek, Japan); axial length using IOL Master (Carl Zeiss Meditec, Dublin, CA, USA); spectral domain OCT (Cirrus HD-OCT, model 5000; Carl Zeiss Meditec, Dublin, California, USA) retinal nerve fibre layer (RNFL) by optic disc cube 200x200, macular ganglion cell layer by macular cube 512x128, vertical cup-disc-ratio (CDR), and disc area; un-dilated digital fundus photographs of each eye were taken after five minutes of dark adaptation, using an NMR-45 fundus camera (Canon, Japan).

## Assessment of glaucoma

The diagnosis of glaucoma can be challenging, particularly in the early stages, and disagreement between methods of diagnosis is common.<sup>15</sup> Two masked independent ophthalmologists (GW, JG) viewed the fundus photographs, and subjective comments and diagnostic impressions were recorded, as well as disc damage likelihood scale (DDLS), and vertical CDR (inter-rater agreement was measured).<sup>16–19</sup> The DDLS was calculated for medium sized optic discs, as size could not be measured from the photographs. Discs with DDLS >5, CDR >0.5 or comments suspecting glaucoma or asymmetry of CDR  $\geq 0.2$  were noted to require further review. These suspect discs were reviewed with IOP, CCT, OCT and VF data to generate a consensus glaucoma status:

“Normal” if no suspicion of glaucoma (other non-glaucoma pathology may be present).

“Ocular hypertension” if IOP >21 mmHg and no optic disc abnormality.

“Glaucoma suspect” if optic disc photograph was suspicious for glaucoma with no more than borderline VF or OCT abnormalities (that is, no corresponding abnormalities, or abnormalities not explained by other disease or pathology).

“Glaucoma” if optic disc photograph was suspicious for glaucoma and there were corresponding abnormalities of the OCT or VF.

Each participant was assigned the glaucoma status of their worse eye.

## Data analysis

All data was collated and analysed using Excel (Microsoft, Albuquerque, NM, US). To assess the intra-rater agreement for CDR and DDLS, Bland–Altman plots were constructed, and the mean bias and limits of agreement (mean difference  $\pm$  1.96 standard deviation of differences) were calculated.<sup>20, 21</sup> Standard errors of the prevalence estimates were calculated for a binomial distribution to generate 95% confidence intervals (CI).

## Results

Of the 938 participants, 891 (95%) were assigned a glaucoma status. The 47 who were not assigned had technical difficulties with eye data collection.

### Glaucoma status

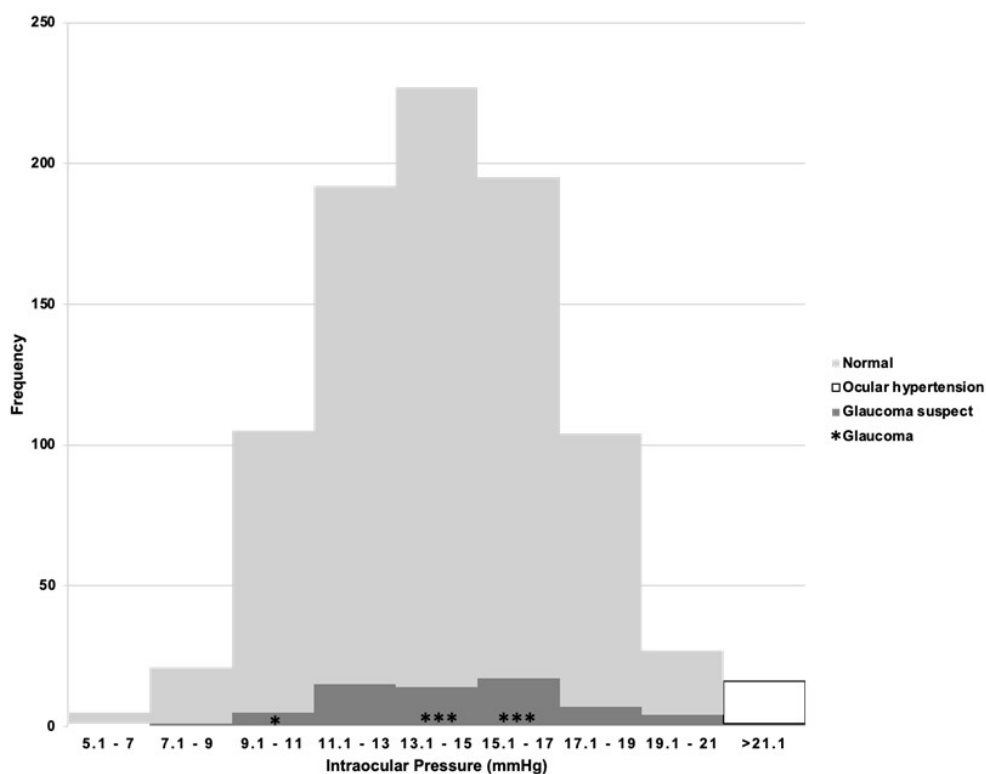
The prevalence of each glaucoma status and the 95% confidence intervals are shown in Table 2.

Among the more suspicious eyes of the 65 participants with glaucoma suspect status: 29 had suspicious discs, of which 22 had borderline abnormalities in OCT; four had borderline abnormalities in VF; one had non-corresponding abnormalities in both OCT and VF; and two had suspicious discs and other risk factors only. The remaining 36 glaucoma suspects had abnormalities in OCT alone, but low suspicion optic disc photographs in both eyes.

**Table 2:** A summary of the prevalence of each glaucoma status.

Glaucoma status	Number of participants	Prevalence (95% confidence interval)
Normal	804	90.2% (88.3–92.2)
Ocular hypertension	15	1.68% (0.84–2.5)
Glaucoma suspect	65	7.30% (5.6–9.0)
Glaucoma	7	0.79% (0.21–1.4)

**Figure 1:** Histogram of intraocular pressures (the higher of the two eyes), with glaucoma status labelled. The higher intraocular pressure in participants with glaucoma are indicated as asterisks.



Among those with glaucoma status, six had abnormalities in OCT corresponding to the glaucomatous optic disc appearance, and one had abnormalities in both OCT and VF (mild) in their more affected eyes.

There were an additional 73 participants (8.2%, CI 6.3%–10%) with abnormalities on the OCT scan who were not deemed to be glaucoma suspects in either eye (non-pathological abnormalities or artefacts) and hence classified as normal.

### Inter-rater agreement of optic disc photographs

Inter-rater reliability was a little greater for CDR (mean difference 0.01, limits of agreement -0.13 to +0.15), as compared with DDLS (mean difference -0.55, limits of agreement -1.9 to +0.8, see Supplemental Figure 1). This indicated that GW rated DDLS scores lower than JG on average.

### Clinical parameters

Both eyes were pooled to calculate average disc metrics (mean  $\pm$  standard deviation and CI). The mean DDLS was  $2.5 \pm 0.88$  (2.4–2.6) and mean CDR was  $0.32 \pm 0.14$  (0.31–0.33). The IOP, CCT, and

RNFL had a normal symmetrical distribution in keeping with previous cohorts. Figure 1 depicts the distribution of glaucoma statuses across the complete range of IOPs.

## Discussion

In this observational, cross-sectional study of predominantly white (Pākehā) 45-year-old New Zealanders, we found the prevalence of glaucoma to be 0.79% (CI 0.2–1.4), based on fundus photographs, OCT, and VF results. The prevalence of ocular hypertension was 1.68% (CI 0.8–2.5), and glaucoma suspect status was 7.30% (CI 5.6–9.0). The prevalence aligns with other population-based studies with Caucasian/white participants of the 40–50-year age group (Table 1).

An additional 73 participants (8.2%, CI 6.3%–10%) had at least one abnormal eye on OCT imaging that was deemed to be non-pathological or artefactual. From a total of 139 participants with abnormal OCT, seven were assigned glaucoma status, and 59 were glaucoma suspects including just 23 who would be suspected of glaucoma by disc photography, IOP and visual fields. Clearly,

OCT technology is highly sensitive, but this comes with a risk of detecting false positives (artefacts).

In this younger 45-year-old cohort with a low prevalence, all of the participants with glaucoma had normal IOP in both eyes, as did all but one eye of one of the 65 glaucoma suspect (21.3 mmHg). This is a greater proportion with normal IOP than would be expected in a Caucasian cohort, and does not fit easily with the idea that ocular hypertension is presumed to be the pathogenic precursor to glaucoma in many cases.<sup>7-10</sup> Possible explanations include that naïve optic disc imaging with OCT detects a broader group of glaucoma cases than previous studies, or that this younger cohort may have a greater prevalence of myopia and thus more similarity to East Asian cohorts (with a very high proportion of normal tension glaucoma). Additionally, no disc haemorrhages were seen in any of the disc photos.

Limitations of this study include the lack of specialist assessment in clinic, gonioscopy or slit

lamp examination in the diagnosis, or adhering to protocols for glaucoma diagnosis from other population-based studies. There was potential for non-contact tonometry and non-stereo disc imaging to reduce the diagnostic accuracy, but data collection was standardised and robust, and diagnostic classifications were made by consensus with the best available information. Due to low numbers, the findings should not be generalised to Māori, Pasifika and Asian ethnic groups, who have different prevalence of glaucoma types.<sup>22</sup>

The prevalence of glaucoma in 45-year-old New Zealanders appears to lie between 0.2% and 1.4%, consistent with other population-based surveys. Future examinations in the same cohort will detect incident cases over time. This is one of the first population-based studies to include OCT in the diagnosis of glaucoma, highlighting the sensitivity of these devices but also the potential for misinterpretation and over-investigation.<sup>23</sup>

**COMPETING INTERESTS**

Nil

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**Supplemental Figure 1:** Bland–Altman plots for cup-to-disc ratio (CDR), and disc damage likelihood scale (DDLS). LOA: limit of agreement.

