Prevalence of diabetic retinopathy at first presentation to the retinal screening service in the greater Wellington region of New Zealand 2006–2015, and implications for models of retinal screening

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ABSTRACT

AIM: To describe the prevalence of diabetic retinopathy (DR) in patients at first presentation for diabetic retinal screening in the greater Wellington region with the intent of service evaluation.

METHODS: This is a retrospective study using data collected from patients newly referred for diabetic retinal screening between 2006–2015 (prevalence analysis, n=12667). The prevalence of DR was calculated by gender, ethnicity, age, type of diabetes and glycaemic control (HbA1c). Chi-square test and multiple logistic regression was used for data analysis.

RESULTS: The prevalence of any DR was 22.5% (n=2852) (non-sight-threatening (NST-DR) n=2562, 20.2%, sight-threatening (ST-DR) n=290, 2.3%). Type 1 diabetes and poor HbA1c control were strongly associated with any degree of DR. Old-age (>65 years), and Asian and Pacific Island (PI) ethnicity had moderately greater odds compared with European. Male gender had marginally increased odds for any DR.

CONCLUSION: This study identified a large proportion (97.7%) of patients (no DR n=9815, 77.5%, NST-DR n=2562, 20.2%) who can be managed in the community by appropriately supported primary care providers, and do not require referral to secondary care ophthalmology. In addition to early detection of ST-DR (2.3%), retinal screening is an early opportunity for education of patients with no DR or NST-DR.

The prevalence of diabetes by district health board (DHB) area in New Zealand is estimated to range from 4.17% to 8.35%.[1] The Ministry of Health estimated 260,458 diagnosed cases of New Zealanders with diabetes as at December 2015,[2] and projects an average annual growth rate of new diabetes diagnoses of 5% according to Diabetes Surveillance: population-based estimates and projections for New Zealand.[3]

Blindness due to diabetic retinopathy (DR) is the most common cause of newly reported cases of visual loss in working-age adults (20–74 years of age),[4,5] which has debilitating implications to daily living, as well as the ability to remain in the workforce. In New Zealand, approximately 20–25% of people with diabetes have DR, with an estimated 12% requiring care from ophthalmology.[6,7]

The benefits of retinal screening in reducing the burden to society of sight-threatening (ST) diabetic eye disease and incidental non-diabetic eye disease are long established.[8] However, there is ongoing discussion surrounding how to best carry out screening, and particularly, the point of

referral from primary care (collaborative teams including technicians, nurses, general practitioners (GPs) and optometrists) to secondary care (ophthalmology).[9]

The three DHBs that make up the greater Wellington region are Wairarapa DHB (Masterton District, Carterton District, South Wairarapa District), Hutt Valley DHB (Upper Hutt City, Lower Hutt City), and Capital & Coast DHB (Kapiti Coast District, Porirua City, Wellington City). The greater Wellington region was estimated by New Zealand Ministry of Health to have 24,499 diagnosed cases of diabetes as at December 2015.[2] Retinal screening was a component of the national Diabetes Get Checked Programme introduced in June 2000 that provides a free annual review for all patients with diabetes. However, prior to 2002, screening was only available from a single site at Wellington Hospital, and was limited to approximately 400 screens per annum. This meant it was not possible for regional GPs to refer all the population diagnosed with diabetes to the public health system for retinal screening.

The solution in the greater Wellington region was initiated by Wellington Independent Practitioner's Association to make use of a single visit to contracted community optometrists for screening and primary care management of DR. Since its implementation, the service has been continued by Compass Health Primary Health Organisation (PHO) (for Capital & Coast and Wairarapa DHBs) and Te Awakairangi Health Network and Ropata Medical PHO (for Hutt Valley DHB). Diagnosis and management rather than detect and refer is the clinical competence standard for New Zealand optometrist registration, and diabetic retinal screening and monitoring has been part of the optometry scope of practice since the introduction of the Health Practitioners Competence Assurance Act 2003.[10,11]

Retinal screening in the greater Wellington region is funded by the three DHBs, and is free to eligible patients enrolled with their local GP. Screening and reporting is completed within 90 days of referral. The greater Wellington region currently has nine community optometry sites, 24 optometrists, of whom 23 have therapeutic pharmaceutical agent (TPA) endorsement, 11 retinal cameras and five optical coherence tomographers (OCT). Designated ophthalmologists provide support to contracted optometrists by reviewing retinal images and overseeing peer review events. Approximately 11,000 screens were performed in 2015—3.2% were referred to ophthalmology secondary care at Wellington Hospital Eye Clinic for diabetic eye disease, and 96.8% remained in the community with primary care optometry.[12] This model of care resonates with many aspects of the New Zealand health strategy 2016,[13] as the overall goal is to provide more accessible, timely and quality health care to New Zealanders.

The aim of this study is to provide New Zealand-specific epidemiology data on DR in the greater Wellington region, and to assess the effectiveness of this model in health care delivery. Coverage and did-not-attend (DNA) rates will be used to evaluate completeness and equity of care between population groups.

Methods

Research design

This is a retrospective evaluation study. Anonymised patient data from 1st January 2006 to 31st December 2015 was obtained from Compass Health PHO. A scope of review was submitted to The Health and Disability Ethics Committees (HDEC), and this study is exempt from full ethics review. An out-of-scope letter was issued by HDEC in February 2016. The letter stated this study is consistent with an audit and related activity to evaluate how the optometrist screening delivery model may support regional service design.

Data inclusion criteria

Eligible patient were those diagnosed with diabetes and referred by their GPs or nurses for diabetic retinal screening with a contracted community optometrist for the first time. Referrals are posted, faxed or emailed by GPs or practice nurses to the community optometrist. The GP practices use in-house systems to check that referral has been made and outcome screening report is received from the optometrist. GP practices checks off retinal screening as a component that must be completed for the DHB-funded "Get Checked" diabetic health review (replaced in 2012 by Diabetes Care

Improvement Package), which is also a PHO performance Programme indicator.[14] Patient data was included for analysis if all reporting fields described in the screening report were complete. Patients with null values in the age, gender, HbA1c, type of diabetes or DR grading fields were excluded for analysis. DR grading of a patient was defined based on the most advanced DR grading of the two eyes.

Screening process

The screening procedure was in accordance with the standards for retinal screening methods in the National Diabetes Retinal Screening Grading System and Referral Guidance,[12] which included measurement of the patient's habitual and pinhole visual acuities, retinal photography, grading the severity of DR,[12] immediate discussion of results and patient education by the screening optometrist, and scheduling for rescreening/monitoring or referral. Habitual and pinhole visual acuities were functional measures of the patient's vision and estimation of best corrected vision respectively. Reduced visual acuity may be indicative of cataract, diabetic macula oedema or other non-diabetes-related eye diseases. Mydriatics were indicated when ocular media opacity and/or pupil miosis inhibit the view of the retina. Clinical examination with binocular indirect ophthalmoscopy or slit lamp biomicroscopy was performed when photos were inadequate or views outside of the photographable area were required, eg patients diagnosed with type 1 diabetes for longer than 15 years are at higher risk for chronic hypoxia-induced neovascularisation in the retinal periphery.[12] The use of dilated retinal photography and clinical examination by trained clinicians have been described as sensitive screening and monitoring tests.[15] In cases of suspected macula oedema, OCT was used to aid the diagnosis, and informed screening optometrists of referral urgency for ophthalmology care. The screening report was sent to the referrer and Compass Health, or a referral was sent to the hospital as required.

Screening report

The report included patient details such as ethnicity, age, latest HbA1c, type of diabetes, year of diagnosis for diabetes, co-existing health problems and medications. Screening details in the report specified whether mydriatics was used, whether digital retinal photography or clinical examination was conducted, VA, grading of DR and any relevant notes from the screening optometrist. If ophthalmology referral was actioned, the referral reasons and ophthalmology clinic were specified on the report.

Study parameters

1. Prevalence of non-sight-threatening DR (NST-DR) * at first presentation from a cohort of patients with type 1 or type 2 diabetes.
2. Prevalence of sight-threatening DR (ST-DR) ** at first presentation from a cohort of patients with type 1 or type 2 diabetes.
3. Odds ratio of DR (adjusted by age, gender, and ethnicity and disease characteristics (diabetes type and glycaemic control as indicated by HbA1c) using logistic regression).
4. The DNA rate to diabetic screening at first presentation, and for all referrals (including first referrals and returning patients).
5. Coverage rate calculated as the number of screenings done by optometrists at the last quarter in 2015 divided by the number of enrolled diabetic patients in the region.

* NST-DR in the Wellington model is defined as disease grading R1-R3 (minimal-moderate) for retinopathy, and M1-M3 (minimal-moderate) for maculopathy.

** ST-DR in the Wellington model is defined as disease grading R4 (severe non-proliferative DR) or R5 (proliferative DR) for retinopathy, and M4 (moderate) or M5 (severe) for maculopathy.

Statistical analysis was performed by Chi-square test and multiple logistic regression, using SAS® software version 9.4 (SAS Institute Inc., Cary, NC, USA).

The definitions of NST-DR and ST-DR used in this study are consistent with the New Zealand Diabetic Retinal Screening, Grading, Monitoring and Referral Guidance 2016.[12] ST-DR is DR where additional medical management and/or surgical treatment may be required to prevent permanent functional vision loss.[12] In the Wellington model this is the clinical referral point from

primary care (community optometrist) to secondary care (ophthalmology clinic in hospital setting). Such clinical referral point evolved over the years through frequent communication, peer review and support from ophthalmologists.[7]

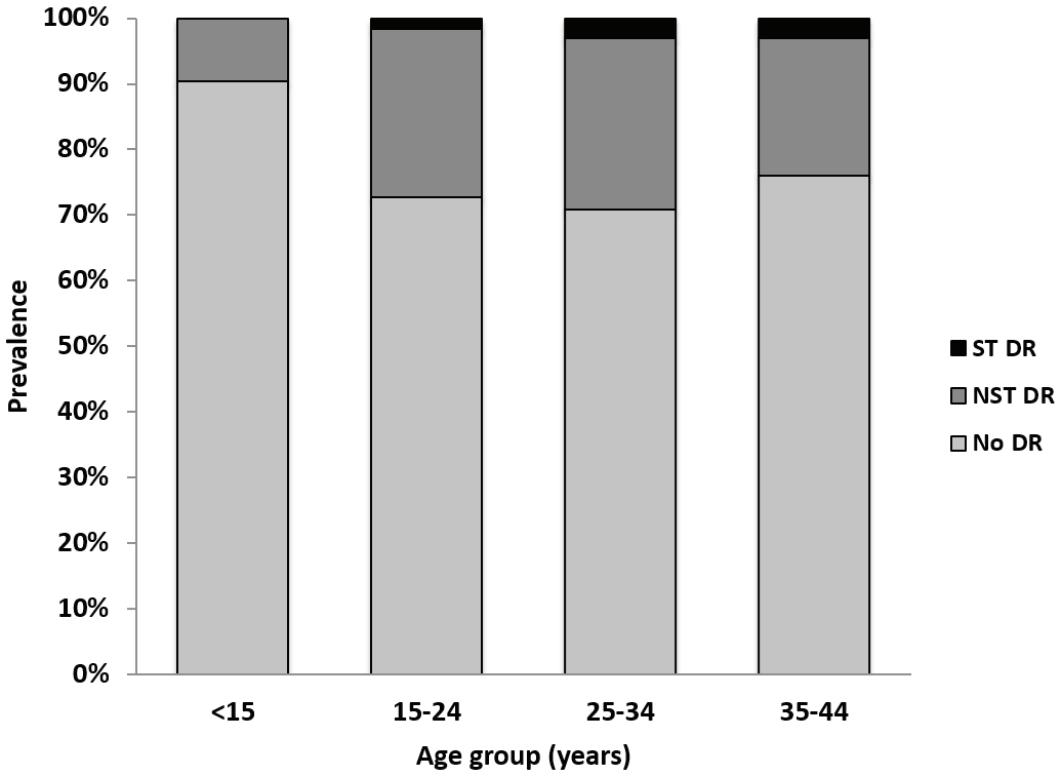
Results

Seventeen thousand five hundred and eight patients attended their first diabetic retinal screening from 2006–2015, and those with incomplete data for age, gender, HbA1c, type of diabetes or DR grading (n=4,841) were excluded for DR prevalence analysis. This led to a total of 12,667 patients being included in DR prevalence calculation. The overall prevalence of any form of DR is 22.5% (n=2,852), with 20.2% (n=2,562) being NST-DR (R1, 2, 3, and M1, 2, 3), and 2.3% (n=290) being ST-DR (R4, R5, M4, M5). Table 1 shows patient demographics and prevalence of DR by gender, ethnicity and age. Fifty-five percent of the study cohort were male (n=6,968), and 45% were female (n=5,699). Most of first-time retinal screening patients were European (n=7,165, 56.6%). The majority of patients fell into the middle-aged category (45–64 years old, n=6,156, 48.6% of cohort), followed by the old-age category (>65 years, n=3,876, 30.6% of cohort). Univariate analysis by chi-square test showed a statistically significant different in the prevalence of DR when compared by gender (DF = 2, $p<0.001$), ethnicity (DF=8, $p<0.001$) and age groups (DF=4, $p<0.001$).

Table 1: Prevalence of DR by gender, ethnicity and age groups.

						Chi-square test	
	Total (n)	Total %	No DR	NST-DR	ST-DR	Degree of freedom (DF)	*p*-value
Total							
	12,667	100.0%	9,815 (77.5%)	2,562 (20.2%)	290 (2.3%)		
Gender							
Male	6,968	55.0%	5,307 (76.1%)	1,482 (21.3%)	179 (2.6%)	2	0.0002
Female	5,699	45.0%	4,508 (79.1%)	1,080 (19.0%)	111 (1.9%)		
Ethnicity							
European	7,165	56. 6%	5,619 (78.4%)	1,418 (19.8%)	128 (1.8%)	8	<0.0001
Māori	1,641	13.0%	1,294 (78.9%)	307 (18.7%)	40 (2.4%)		
PI	1,335	10.5%	994 (74.4%)	296 (22.2%)	45 (3.4%)		
Asian	1,486	11.7%	1,106 (74.4%)	340 (22.9%)	40 (2.7%)		
Other/ Unknown	1,040	8.2%	802 (77.1%)	201 (19.3%)	37 (3.6%)		
Age							
Young (≤44)	2,635	20.8%	1,981 (75.2%)	583 (22.1%)	71 (2.7%)	4	0.0003
Mid (45–64)	6,156	48.6%	4,851 (78.8%)	1,158 (18.8%)	147 (2.4%)		
Old (≥65)	3,876	30.6%	2,983 (77.0%)	821 (21.2%)	72 (1.9%)		

Figure 1: Prevalence of DR in the young-age category (≤44 years) in 10-year age bands.



It is interesting to note that although the young-age category (≤44 years, n=2,635, 20.8%) had the smallest proportion of the entire cohort, DR was the most prevalent for both the NST-DR and ST-DR categories (Table 1). Following this observation, all patients ≤44 year old were further stratified into 10-year age bands. In the <15 years old age group, 9.6% of the patients had NST-DR, and there was no ST-DR. In the 15–24 year-old age group, there was a marked >2.5x increase in the prevalence of NST-DR (25.7%) (Figure 1). As for ST-DR, the most significant increase in prevalence was from none in the <15 group to 1.6% in the 15–24 year-old group, which then nearly doubled to 3.0% in the 25–34 year-old age group.

Table 2 shows prevalence of DR in different diabetes disease types and levels of HbA1c control. 7.2% (n=918) of the patients in this cohort had type 1 diabetes, and 92.8% (n=11749) had type 2 diabetes. There was significantly greater prevalence for both NST-DR and ST-DR in type 1 diabetes (DF=2, p<0.0001) using univariate analysis by chi-square test. HbA1c provided information on the level of glycaemic control, and patients were grouped into three categories, (1) HbA1c ≤ 64 mmol/mol (good control), (2) HbA1c = 65–75 mmol/mol (moderate control), and (3) HbA1c>75 mmol/mol (poor control), with reference to The Diabetic Retinal Screening, Grading, Monitoring and Referral Guidance.[12] Poor HbA1c control associated with a significantly higher prevalence of both NST-DR and ST-DR, using chi-square test (DF=4, p<0.0001).

The association of DR with gender, ethnicity, age group, diabetes type and HbA1c control was assessed using logistic regression (Table 3). Having type 1 diabetes and poor HbA1c control is strongly associated with any degree of DR in this patient cohort. The odds of people with type 1 diabetes having any DR is 3.17 (95% CI 2.70–3.72) times the odds of people with type 2 diabetes, and the odds of people with poor HbA1c control having any DR is 2.22 (95% CI 1.98–2.49) times the odds of people with good control. The old-age category (OR = 1.72, 95% CI 1.50–1.98), Asian ethnicity (OR = 1.51, 95% CI 1.32–1.73), and PI ethnicity (OR = 1.33, 95% CI 1.15–1.54) also have moderately greater odds when compared to the reference levels of young-age and European ethnicity respectively, for having any degree

Table 2: Prevalence of DR in different diabetes disease types and glycaemic control categories.

						Chi-square test	
	Total (n)	Total %	No DR	NST-DR	ST-DR	Degree of freedom (DF)	*p*-value
Diabetes type							
Type 1	918	7.2%	530 (57.7%)	330 (36.0%)	58 (6.3%)	2	<0.0001
Type 2	11,749	92.8%	9,285 (79.0%)	2,232 (19.0%)	232 (2.0%)		
Glycaemic control (HbA1c in mmol/mol)							
Good (≤64)	9,419	74.3%	7,606 (80.8%)	1,679 (17.8%)	134 (1.4%)	4	<0.0001
Moderate (65–75)	1,353	10.7%	962 (71.1%)	352 (26.0%)	39 (2.9%)		
Poor (>75)	1,895	15.0%	1247 (65.8%)	531 (28.0%)	117 (6.2%)		

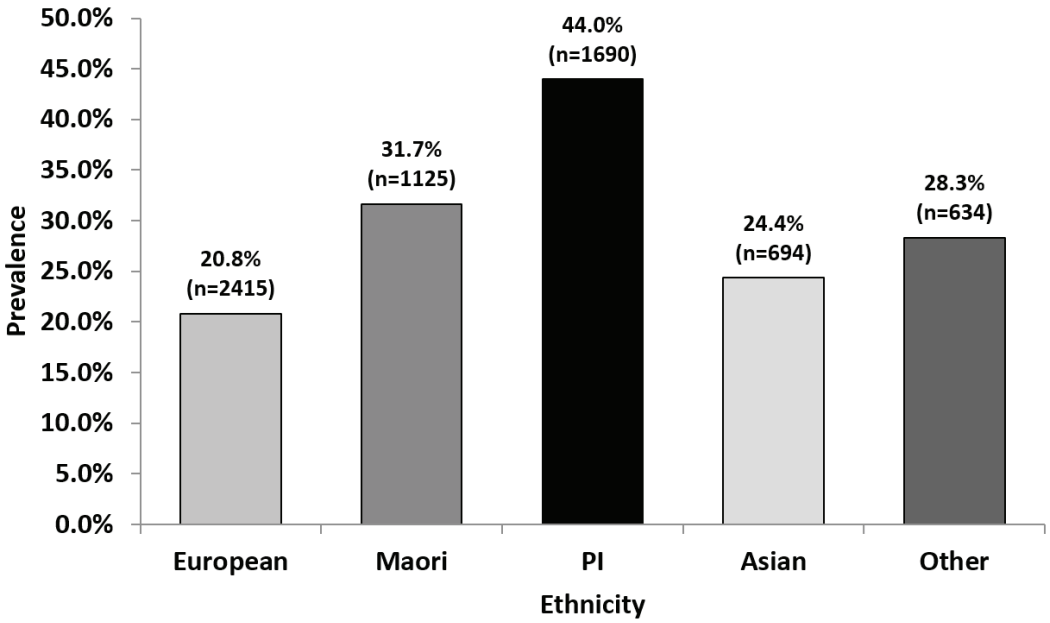
of DR. Male patients have approximately 20% increase in the odds of having any DR (OR=1.21, 95% CI 1.11–1.32) compared to female patients.

The mean DNA rate (DNA n=6,558, divided by the total number of referrals n=24,066) of first-time referrals between 2006–2015 was 27.3% (Figure 2). Patients identified with PI ethnicity had the highest DNA rate (DNA n=1,690, attendance n=2,153, 44.0%), followed by Māori ethnicity (DNA n=1,125, attendance n=2,427, 31.7%). The mean DNA rate of all referrals between 2006–2015

Table 3: Odds ratio estimates for any DR, adjusted by age, gender, ethnicity, diabetes type and HbA1c control using multiple logistic regression.

Categories	**Effect**	**Point estimate**	**95% Wald confidence limits**	
Age category	Middle-age vs young	1.29	1.14	1.45
	Old-age vs young	1.72	1.50	1.98
Gender	Male vs female	1.21	1.11	1.32
Ethnicity	Māori vs European	1.06	0.92	1.21
	PI vs European	1.33	1.15	1.54
	Asian vs European	1.51	1.32	1.73
	Other/unknown vs European	1.14	0.97	1.34
Diabetes Type	Type 1 vs 2	3.17	2.70	3.72
HbA1c Control	Moderate control vs good control	1.64	1.44	1.88
	Poor control vs good control	2.22	1.98	2.49

Figure 2: DNA rate of first-time referrals between 2006–2015.



(including first presentation and returning patients) was 12.9% (DNA n=13,191, attendance n=89,017).

The estimated mean coverage rate (Q4 2015) of diabetic retinal screening for the three DHBs in the greater Wellington region is 88.9% (numerator is the number of patients diagnosed with diabetes and enrolled in a CCH, Wairarapa and Hutt Valley GP practice who have received a valid retinal screening in the last two years to the end of the reporting quarter on 31st December 2015 (n=17,237), and the denominator is the number of patients diagnosed with diabetes and enrolled in a CCH, Wairarapa or Hutt Valley GP practice on the 31st December 2015 (n=19,397)—data provided by Compass Health PHO and Hutt Valley DHB and Te Awakairangi Health Network).

Discussion

We report in this study that 77.5% of those referred for the first time for diabetic retinal screening between 2006–2015 in the Wellington region had no DR, which was comparable with that reported in Waikato (78.0%),[16] and lower than Northland (81%).[6] ST-DR was 2.3% in this study for the Wellington region, which was lower than Waikato (3.1%), and higher than Northland (1.8%). However, it should be noted that the definition of ST-DR is different by region, as the Wellington model regarded grade 4–5 retinopathy/maculopathy as sight-threatening, while the Waikato and Northland study considered grade 3–5 retinopathy/maculopathy as sight-threatening.[6,12,16] With an appropriate primary care workforce and supporting systems in place, the Wellington model referral threshold for ST-DR is safe and an efficient use of limited public hospital secondary care resources.[7]

The findings from this study also identified the characteristics associated with having any degree of DR. Those with type 1 diabetes had the greatest odds, followed by poor and moderate HbA1c control, when compared within their respective variable group. Old-age and Asian ethnicity were also found to have moderately increased odds. The reasons to increased risks for DR may be due to a combination of genetic and environmental factors such as lifestyle and increased co-morbidities, especially in old-age.[17] Our finding was in agreement with evidence from the literature that the prevalence of DR and the prevalence of blindness due to DR is greater in type 1 than type 2 diabetes.[4,18] It is also well established in the literature that the mean HbA1c was the dominant predictor for DR, and that a 10% reduction in HbA1c is associated with 43–45% lower risk in DR progression.[19] Similarly, an increased prevalence of DR in old age (>65 years of age) and Asian ethnicity have been described in the literature.[20,21] Patients with the aforementioned demographic and disease characteristics require the most attention from primary care providers to optimise referral and attendance to screening appointments.

It is also interesting to note that the data presented in Figure 1 showed no ST-DR, 9.6% NST-DR in the <15-years age group, while 90.4% had no DR. The prevalence of NST-DR then increased dramatically in the 15–24-years age group to 25.7%. This data suggests that it may be beneficial to screen those <15 years of age, and by educating these young patients and their parents at an early stage, this dramatic increase in the prevalence of DR may be preventable. The American Diabetes Association recommends annual screening for young-onset diabetes patients beginning 3–5 years after diagnosis of diabetes once the patient is 10 years or older.[22] This reiterated the value of diabetic retinal screening in the adolescent population, which provides us the opportunity for patient education, with the end-goal of minimising DR progression.

The coverage rate (Q4 2015) of diabetic retinal screening for the three DHBs in the greater Wellington region is 88.9%. This compared with 77% in Northland, New Zealand,[6] and 78.7% in the national DR service in Scotland, UK.[23] The high screening rate in the greater Wellington region compares with the study by Frederikson and Jacobs (2008), in which retinal screening was accessed by 92% of diabetic patients. Such sustained high coverage rate is likely due to the differences in the patient journey offered in Wellington compared with Northland and national retinal screening service in Scotland, UK. There are close links between GPs, community optometrists, lead ophthalmologist and Compass Health in Wellington, with a common goal of developing and maintaining accessible retinal screening service. Convenient appointment times and locations are also available in Wellington. Long-established community optometry sites provide continuity of care and make use of existing optometry practice infrastructure. A large amount of time and effort is put into the process between GP referral and retinal screening attendance. There are up to five contact interactions (optometrist to patient up to three times, and GP/nurse to patient up to two times) used as opportunities to find out why DNA is happening, and then provide a solution for that patient (standard operating procedures provided by contracted community optometrists and Compass Health PHO). Upon referral from GP, the optometrist (receptionist) phones the patient directly to book an appointment; a reminder (text or phone message) is given the day before the appointment. At the first and second DNA occurrence, the optometrist (receptionist) repeats the booking process. At third DNA the patient is returned to the referring GP/nurse, who then contacts patient, and if appropriate, another referral to the optometrist for retinal screening to start the process again. In the Wellington model, patients have the opportunity to view the photographs, have it explained by a clinician, be advised of the outcome, and the opportunity to ask questions during the appointment, rather than having to wait up to four weeks for the results.[24] A retinal screening patient in Northland or Scotland may require multiple appointments to achieve the same outcome as one appointment in Wellington, with a clinical optometrist working within their scope of practice. Northland model is primarily technician-based in mobile clinics, with grading of retinopathy undertaken offsite after the appointment. National retinal screening in Scotland, UK operates with computer-generated referral letters and communications to patients, GPs, optometrists, ophthalmologists and diabetologists,[25] and a specialist software for DR photography. Grading of retinal photographs undergo three levels of grading—Level 1 uses auto-grading by a computer programme that detects microaneurysms, Level 2 graders are optometrists or nurse practitioners and Level 3 graders are medical retina trained ophthalmologists.[24]

The mean DNA rate was 27% for first time referrals, compared to 12.9% in all referrals (this study) and 7% in all referrals reported by Frederikson and Jacobs.[26] This suggests that new referrals may be more likely to miss their screening appointments than those who have had screening services, and warrants further investigation. This indicates the importance of promoting diabetic retinal screening services, especially to newly diagnosed diabetic patients. Māori and PI ethnicity had the highest DNA rate, and therefore, were likely to be under-represented in this study cohort. This is consistent with findings from analysis of the national diabetes annual review that Māori and ethnic minorities

are often under-represented.[27] Such barrier to health care may be attributed to lack of motivation, social, family and transport difficulties.[27] We propose that liaison with GPs and community health care providers may improve patients' understanding of long-term consequences of diabetes, such as preventable blindness due to DR. This could in turn raise patient awareness and the value of diabetic retinal screening, despite the barriers. The main benefit of retinal screening for most participants at first presentation is the opportunity for face-to-face education about their health condition. Diabetes self-management education programmes have been shown to assist behavioural changes,[28] which are significant in limiting the long-term health consequences and economic impact of diabetes. A technician-only retinal screening programme where grading might be performed offsite and after the patient has gone is a lost opportunity for concurrent patient education. In the Wellington model, patients are shown the photos of their own eyes at the time of the screening appointment, and have the opportunity for immediate discussion with an optometrist who can answer their questions about their health condition.

Importantly, this study suggests 97.7% (those with no DR and NST-DR) of first presentation population can be managed in the community by primary care. This is possible because the scopes of practice for health practitioner have changed since the introduction of Health Practitioners Competence Assurance Act 2003,[11] and because of the increased availability of digital imaging technology such as retinal photography and OCT. There are 472 optometrists with TPA endorsement of 704 optometrists in practice nationwide, and 71% of optometrists in practice are under the age of 50 (data provided by New Zealand Optometrists and Dispensing Opticians Board). There is one ophthalmology clinical nurse specialist (data provided by Nursing Council of New Zealand), of 145 nurse practitioners in practice,[29] and 45% of registered nurses in practice are aged 50 or over.[13] As the New Zealand health workforce is ageing, the challenge is to continually invest time and funds in training new health professionals. The Wellington model makes use of an existing trained primary care ophthalmic workforce and existing fully equipped community optometry sites supported by local general practice and hospital ophthalmology. Thus, the current New Zealand optometric workforce provides a feasible solution to alleviate the volume of diabetic retinal screening that currently strains ophthalmology services in public hospitals.[30]

Conclusion

The prevalence of ST-DR is low in those referred for diabetic retinal screening for the first time. This reflects a large proportion of patients at first presentation having no DR or NST-DR, who do not require ophthalmology care and are safe to remain in community screening. The optometrist-based diabetic retinal screening service in the greater Wellington region has a high coverage rate and comparable attendance rate with other models, and is well accepted by local clinicians and patients. Patient education and optimisation of attendance, especially those with greater risk profiles will benefit patient outcome.

Competing interests:
Lily YL Chang was awarded the New Zealand Association of Optometrists (NZAO) postdoctoral scholarship for manuscript preparation (funded by NZAO and Ministry of Health (MOH)).
Arier C Lee's service of statistical analysis was funded by the NZAO and MOH.

Acknowledgements:
We would like to acknowledge Dr Keith Maslin (consultant ophthalmologist) and Dr Lesley Frederikson (national director for NZAO) for their support and advice during manuscript preparation, the New Zealand Optometrists and Dispensing Opticians Board and Nursing Council of New Zealand for providing additional information on New Zealand optometrists and nurses. We are also grateful for Chris Gellen (Compass Health PHO), for assisting with preparation of raw data, calculation of coverage rate and DNA rate, and acknowledge assistance of Chris Kerr and Liz Dutton (Compass Health PHO), Jodi Caughley (Hutt Valley Health), and Diane Taylor (Te Awakairangi Health Network).

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URL:
http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2017/vol-130-no-1450-17-february-2017/7161

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