

# Diabetic Retinopathy Screening at the Point of Care (DR SPOC): detecting undiagnosed and vision-threatening retinopathy by integrating portable technologies within existing services

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## ABSTRACT

**Introduction** The aim of this study was to determine the prevalence of diabetic retinopathy (DR) in a low socioeconomic region of a high-income country, as well as determine the diagnostic utility of point-of-care screening for high-risk populations in tertiary care settings.

**Research design and methods** This was a cross-sectional study of patients with diabetes attending foot ulcer or integrated care diabetes clinics at two Western Sydney hospitals (n=273). DR was assessed using portable, two-field, non-mydratric fundus photography and combined electroretinogram/pupillometry (ERG). With mydratric photographs used as the reference standard, sensitivity and specificity of the devices were determined. Prevalence of DR and vision-threatening diabetic retinopathy (VTDR) were reported, with multivariate logistic regression used to identify predictors of DR.

**Results** Among 273 patients, 39.6% had any DR, while 15.8% had VTDR, of whom 59.3% and 62.8% were previously undiagnosed, respectively. Non-mydratric photography demonstrated 20.2% sensitivity and 99.5% specificity for any DR, with a 56.7% screening failure rate. Meanwhile, mydratric photography produced high-quality images with a 7.6% failure rate. ERG demonstrated 72.5% sensitivity and 70.1% specificity, with a 15.0% failure rate. The RETeval ERG was noted to have an optimal DR cut-off score at 22. Multivariate logistic regression identified an eGFR of  $\leq 29$  mL/min/1.73 m<sup>2</sup>, HbA1c of  $\geq 7.0\%$ , pupil size of  $< 4$  mm diameter, diabetes duration of 5–24 years and RETeval score of  $\geq 22$  as strong predictors of DR.

**Conclusion** There is a high prevalence of vision-threatening and undiagnosed DR among patients attending high-risk tertiary clinics in Western Sydney. Point-of-care DR screening using portable, mydratric photography demonstrates potential as a model of care which is easily accessible, targeted for high-risk populations and substantially enhances DR detection.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Diabetic retinopathy (DR) is a leading cause of preventable blindness; however, screening adherence is poor, particularly among those most at risk of disease.

## WHAT THIS STUDY ADDS

⇒ Significant rates of DR were identified in the high-risk diabetes clinics, 39.6% of patients being found to have DR, while 15.8% had vision-threatening diabetic retinopathy (VTDR).  
⇒ Approximately 60% of patients identified to have DR in our high-risk diabetes clinics were previously undiagnosed.  
⇒ Point-of-care screening with a portable fundus camera efficiently improves DR detection in high-risk diabetes clinics; however, mydriasis is necessary for sufficient diagnostic accuracy.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Point-of-care screening in high-risk diabetic clinics is valuable to detect high rates of VTDR and undiagnosed DR. Further research is needed into the cost-effectiveness and diagnostic accuracy of portable devices using mydriasis.

## INTRODUCTION

Diabetic retinopathy (DR) is a common microvascular complication of diabetes mellitus (DM) and with the prevalence of type 2DM exponentially increasing, a concomitant rise in DR prevalence is anticipated.<sup>1</sup> DR is already the leading cause of blindness and visual disability in working-age adults<sup>2</sup> and is among the top five causes of irreversible blindness in Australia.<sup>3</sup> It has devastating impacts on

patients' functional capacity and quality of life, limiting their ability to read, mobilize, socialize, work, and maintain independence.<sup>4</sup>

Digital fundus photography is the most efficient DR screening method.<sup>5</sup> However, animal models suggest that retinal neuronal degeneration may occur before the development of microaneurysms.<sup>6</sup> This supports a role for other methods of assessing retinal function. Full-field electroretinography and pupillometry (ERG) objectively evaluates retinal bioelectrical responses to flashes of light. It enables functional testing of the entire neuroretina surface, detecting signs of DR that can occur prior to microvascular abnormalities.<sup>7</sup>

Up to 90% of cases of DM-associated vision loss are preventable with timely intervention; hence, ophthalmic screening is essential.<sup>8</sup> Australian guidelines recommend biennial visual assessments for all patients with diabetes, while annual assessments are recommended for high-risk patients, including Aboriginal and Torres Strait Islander populations, as well as patients with long DM durations ( $\geq 15$  years).<sup>9</sup> The KeepSight program sends reminders for eye screening to self-registered members.<sup>10</sup> However, a dedicated national DR screening program does not exist in Australia. Currently, the uptake of DR screening is suboptimal, with only 52.7% of Aboriginal and Torres Strait Islander and 77.5% of Non-Indigenous Australians adhering to screening recommendations.<sup>11</sup>

Meanwhile, national DR screening programs have been implemented in several other countries. These use a teleophthalmology model, where retinal images are sent to a centralized location for review by trained graders.<sup>5</sup> The success of these programs has been heralded by the English National Health Service Diabetic Eye Screening Programme, which oversaw a 49% reduction in DR-related blindness in England and Wales (2007–2015), as well as the elimination of DR as the leading cause of blindness, among working-age adults.<sup>12</sup>

Poor engagement with screening programs has been associated with minority ethnicity, lower socioeconomic status, and geographically isolated locations.<sup>13 14</sup> Given the increasing worldwide prevalence of DM, with a disproportionate impact affecting the low-income world and underprivileged groups,<sup>15</sup> the ocular complications expected from this severe disease burden must be addressed with improved DR screening solutions. Developing telescreening programs at easily accessible sites, such as multidisciplinary diabetes clinics, may improve DR screening coverage among high-risk patients.

The Diabetic Retinopathy Screening at the Point of Care (DR SPOC) study is a cross-sectional, interventional, instrument-validation study, conducted across two Western Sydney tertiary hospitals. Our primary aim was to determine whether point-of-care screening using portable devices in high-risk tertiary clinics enhances DR detection by successfully identifying previously undiagnosed DR, as well as vision-threatening diabetic retinopathy (VTDR).

## MATERIALS AND METHODS

This study was performed between February and August 2019 at two tertiary hospitals in Western Sydney. Western Sydney is a diabetes hotspot, with an ethnically diverse, low-socioeconomic population.<sup>15</sup> The treating endocrinologist offered study participation to consecutive patients with diabetes over the age of 18 years, who attended routine appointments at foot ulcer or integrated care diabetes clinics.<sup>16</sup> Informed, written consent was obtained from all participants. Patients with photosensitive epilepsy were excluded from participation, and patients with a family history of angle-closure glaucoma were not offered mydriasis.

Data acquisition and screening investigations were performed by a trained medical student (LSW). Best-corrected visual acuity (VA) was tested with a 3 metre handheld Snellen chart for portability, with pinhole correction tested if 6/6 vision was not initially achieved. The patient was seated in a darkened room for 10 min while a validated questionnaire was conducted regarding ethnicity, spoken languages, type and duration of DM, time and site of previous diabetic eye screening, known DR status, and systemic diseases.<sup>17</sup>

Bilateral two-field 45° non-stereoscopic, color, non-mydratric photographs were taken using a portable, non-mydratric retinal camera (RetinaVue 100; Welch Allyn, Macquarie Park, Australia) (online supplemental file 1). Both macula and optical-disc centered photos were taken of each eye. After 2–3 min, combined pupillometry and electroretinogram (ERG) was performed bilaterally (RETeval, Welch Allyn). Skin-adhesive electrodes were placed beneath both eyes and the Ganzfeld Dome was held over the patient's eye. Flicker ERG flashed light of varying intensity into each eye for approximately 45 seconds, and patterns of pupillary constriction were recorded. A single numerical output was generated, indicating the patient's risk of DR.

Patients were subsequently offered pupillary dilation. This was initially with Minims Tropicamide 1% (Bausch & Lomb, Laval, Canada); however, uptake was poor due to concerns over induced visual disturbance. Subsequently, a less concentrated formulation, Minims Tropicamide 0.5% (Bausch & Lomb), was offered. Following mydriasis, bilateral two-field fundus photographs were retaken with the RetinaVue 100, and these dilated images were used as the clinical reference standard.<sup>18 19</sup> Overall, 53.1% of the study population (n=145) consented to mydriasis.

The patients' most recent (within the last 3 months) HbA1c, estimated glomerular filtration rate (eGFR), and body mass index (BMI) were obtained from their electronic medical record. All results were reviewed by a consultant ophthalmologist (HPD) with access to clinical data, who assessed image quality, graded DR severity, and determined follow-up plans with either an optometrist or an ophthalmologist, within a clinically relevant timeframe. Letters detailing these results were sent to the patient and their nominated general practitioner.

To confer evaluation reliability, a second trained grader (HN), masked to clinical data and previous gradings, reassessed all photographs for DR severity and image quality. Computerized image reordering was used to avoid recall bias. Grading conflicts were arbitrated by a medical retina fellowship-trained ophthalmologist (ATF), masked to clinical data and previous gradings.

DR severity was graded according to the International Classification of Diabetic Retinopathy (ICDR) and Diabetic Macular Oedema (DMO) grading scale.<sup>20</sup> DR was defined as the presence of mild, moderate, or severe non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and/or DMO on ophthalmology evaluation. VTDR was defined, in accordance with the Practice Guidelines for Ocular Telehealth, as an eye having severe NPDR, PDR or DMO.<sup>5</sup> DMO was defined as any hard exudate or obvious retinal thickening within the macula region.<sup>5 20</sup> Image quality was rated using a 5-point Likert scale (1, inadequate for any diagnostic purpose; 2, unable to exclude all emergent findings; 3, only able to exclude emergent findings; 4, not ideal but still able to exclude subtle findings; and 5, ideal quality).<sup>21</sup>

### Statistical analysis

To determine the sensitivity and specificity of the RETeval ERG device, an optimal cut-off score defining DR risk had to first be determined. The receiver operating characteristic (ROC) curve was used to identify the optimal DR cut-off score using Euclidean distances.<sup>22</sup> The score with the lowest Euclidean distance represented the optimal DR cut-off score. Accuracy was measured by the area under the ROC curve, which measures the test's ability to correctly classify those with and without disease. The sensitivity and specificity of the non-mydratric camera and ERG were then determined using point estimates with 95% CI, using the mydratric photographs as the clinical reference standard. Inter-rater grading agreement was assessed using a Kappa test. Patients who declined pupil dilation were excluded from diagnostic accuracy analyses. If no gradable mydratric photographs were obtained, this was recorded as a screening failure, and these patients' results were also excluded from diagnostic accuracy analyses.

Patient characteristics associated with DR were determined using a univariate analysis. Covariate status was determined as of the day of screening, and dark-adapted horizontal pupil size was used.<sup>23</sup> Continuous variables were presented with means and standard deviations (mean±SD). Associations between DR and continuous variables were determined using two-tailed Student's t-tests. Skewed data were presented with medians and interquartile ranges. The associations between DR and skewed data were assessed using Mood's median tests. Changes in discrete variables were analyzed with  $\chi^2$  tests.

Predictors of DR were determined using a logistic regression model. DM duration, eGFR and RETeval score were treated as categorical variables, while HbA1c and

pupil size were treated as dichotomous variables. Appropriate control groups were determined from similar studies. DM duration was grouped into  $\leq 4$ , 5–14, 15–24, and  $\geq 25$  years, with  $\leq 4$  years as the control.<sup>24</sup> eGFR was grouped into  $< 30$ , 30–59, 60–89, and  $\geq 90$  mL/min/1.73 m<sup>2</sup>, with  $\geq 90$  mL/min/1.73 m<sup>2</sup> as the control.<sup>25</sup> Finally, RETeval score was grouped into not measurable,  $< 22$  and  $\geq 22$ , with  $< 22$  as the control. Among the dichotomous variables, HbA1c of  $\geq 7.0\%$ <sup>26</sup> and pupil size of  $< 4$  mm were coded as 1.

Covariates with a p value of  $\leq 0.1$  were entered into a multivariate logistic regression model where variables were then chosen using stepwise, backward elimination. The logistic regression model was validated with c-statistics and Hosmer-Lemeshow statistics. Significance was defined as a p value of  $< 0.05$ . Statistical analyses were conducted with SAS software V.9.4.

## RESULTS

### Basic demographics

Study participation was offered to 327 patients, of whom 273 (83.4%) accepted involvement. Main reasons for study refusal included known DR, time pressure from subsequent appointments, and disinterest (figure 1).

The study population demonstrated a high-risk profile, with patients on average having long DM durations (16.6±11.9 years), an obese metabolic profile (BMI: 31.3±7.0 kg/m<sup>2</sup>), poor glycemic control (HbA1c: 9.1%±2.3%), and a reduced eGFR (67.7±25.4 mL/min/1.73 m<sup>2</sup>). Patients typically demonstrated poor vision, with a median corrected right VA of 6/12 (logMAR 0.3, IQR 0.18–0.48) and left VA of 6/12 (logMAR 0.3, IQR 0.18–0.48).

### DR screening history

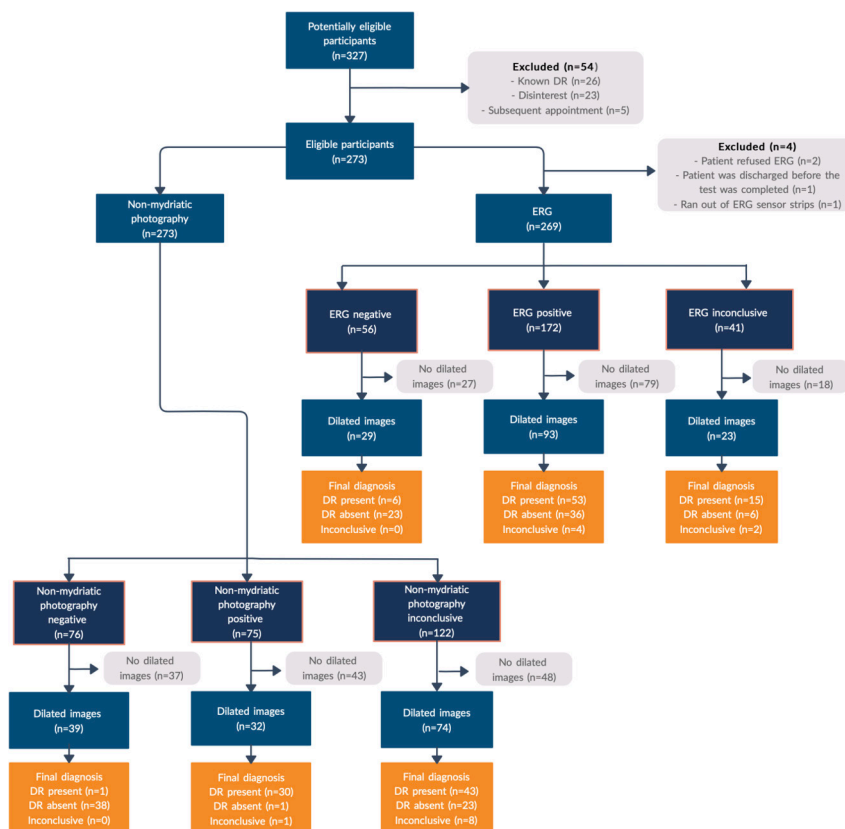
Of the total number of participants, 84.7% reported having a prior dilated fundus examination at least once, while 25.2% reported pre-existing DR. Excluding patients with a pre-existing DR diagnosis, we found that screening rates for the preceding 12 months and 2 years were low at only 47.3% and 67.2%, respectively.

### Inter-rater agreement

Observed inter-rater agreement between the ophthalmologist and trained grader, for individual fundus imaging grading across all diagnostic categories, was 89.8%, (1525/1699) (kappa=0.88, 95% CI 0.86 to 0.90). Arbitration by the medical retina trained specialist was required for the remaining 174 images (10.2%).

### Prevalence of DR and VTDR

DR was diagnosed in 108 patients (39.6%, 95% CI 33.8% to 45.4%), and this was significantly greater than the community rate of 28.5% (95% CI 22.6% to 35.3%) reported by the 2014–2015 National Eye Health Survey (NEHS).<sup>27</sup> Meanwhile, VTDR was identified in 43 patients (15.8%, 95% CI 11.4% to 20.1%), which was more than three times the NEHS community rate of 4.5% (95% CI

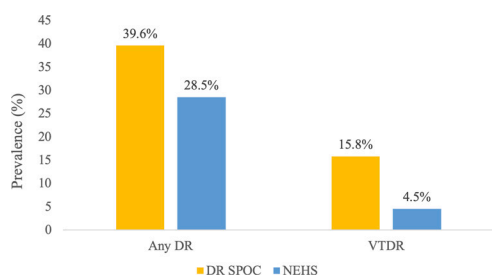


**Figure 1** Standards for Reporting of Diagnostic Accuracy Studies flowchart of the number of patients and image datasets used in the analyses. DR, diabetic retinopathy; ERG, electroretinogram.

2.6% to 7.9%)<sup>27</sup> (figure 2). Of the identified VTDR and NPDR cases, 62.8% and 59.3%, respectively, were previously undiagnosed. Furthermore, among the patients who claimed to have DR screening in the last 12 months and 2 years, 17.4% and 21.8%, respectively, were found to have previously undiagnosed DR.

### Overall findings

No abnormalities were identified in 61 patients (22.3%), while 84 (30.8%) had reduced VA (worse than 6/12 in one eye), without any DR on fundus photographs. These two patient groups were classified as having no DR and served as the comparator for the patients with DR. Twenty patients (7.3%) were found to have an ERG score suggestive of DR, yet had no gradable photographs to provide



**Figure 2** Comparison of DR prevalence in the DR SPOC study versus the 2014–2015 NEHS.<sup>27</sup> DR, diabetic retinopathy; DR SPOC, Diabetic Retinopathy Screening at the Point of Care; NEHS, National Eye Health Survey.

a reference standard. These were classified as screening failures and were referred for ophthalmology review.

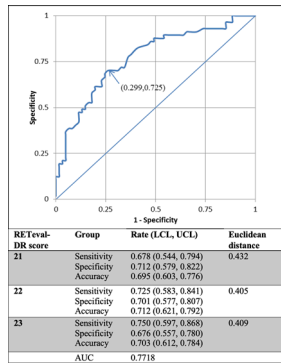
### Diagnostic accuracy of the screening devices

Screening examinations were quick, with mean retinal photography and ERG sessions taking only 4.0 min (SD 1.8) and 3.2 min (SD 1.5), respectively. Participants who did not consent to pupil dilation (n=128) or obtained high RETeval scores without gradable images (n=20), were excluded from sensitivity and specificity analyses. With 16 patients falling under both categories, assessments of diagnostic accuracy were ultimately determined with 141 patients.

Given the high rate of mydriasis refusal, DR status was compared between patients who consented to dilation and those who did not consent to dilation, to assess for selection bias. Assessment of DR status was based on non-mydratric photographs, for equal comparison. No statistical significance in DR status was identified between the two groups (p=0.061), conferring generalizability between the two patient cohorts.

### Non-mydratric photography (RetinaVue 100)

The non-mydratric camera demonstrated 20.2% sensitivity (95% CI 16.1% to 25.0%) and 99.5% specificity (95% CI 98.7% to 99.9%), with an accuracy of 75.9% (95% CI 73.2% to 78.4%) for determining any DR, compared with consensus grading of mydratric photographs. It



**Figure 3** Determination of the optimal RETeval DR cut-off score, with the receiver operating characteristic curve. AUC, area under the curve; DR, diabetic retinopathy; LCL, lower confidence limit; UCL, upper confidence limit.

demonstrated a 13.7% sensitivity and 99.7% specificity for identifying VTDR, as well as a 21.7% sensitivity and 99.9% specificity, for identifying NPDR (online supplemental file 1).

Only 43.3% of non-mydriatic photographs were evaluated by the ophthalmologist as being of adequate or ideal quality for diagnostic purposes (grade 4 or 5), with main artifacts including underexposure and shadowing. Meanwhile, 92.4% of dilated photographs were graded as adequate or ideal (online supplemental file 1).

### ERG (RETeval)

The highest accuracy and lowest Euclidean distance were achieved at a score of 22 (positive predictive value=64.9%, negative predictive value=77.0%) (figure 3). Thus, 22 represents the optimal DR cut-off score, at which the RETeval device demonstrates 72.5% (95% CI 58.3% to 84.1%) sensitivity and 70.1% (95% CI 57.7% to 80.7%) specificity. Area under the ROC was estimated at 0.772, indicating 'fair'<sup>28</sup> diagnostic accuracy of the RETeval.

Furthermore, 20 patients obtained a RETeval score suggesting the presence of DR ( $\bar{x}$ =26.5, SD 4.7) yet had no gradable fundus photographs. RETeval scores were unable to be obtained in 41 (15.0%) patients.

### Bivariate analysis

A bivariate analysis was used to explore associations between the dependent variable (DR) and each patient-characteristic covariate (table 1). The 20 patients whose RETeval score suggested DR, yet had no gradable fundus images, were excluded from the bivariate and multivariate analyses, leaving a sample of 253 patients.

Compared with patients without DR, patients with DR had a significantly longer duration of DM, higher HbA1c, lower eGFR, and smaller pupil size. A RETeval score of  $\geq 22$  demonstrated high statistical significance ( $p < 0.001$ ) as a predictor of DR, compared with a RETeval score of  $< 22$ , demonstrating significant utility of the RETeval device at this optimal cut-off score. Additionally, patients with no measurable RETeval scores had significantly greater likelihoods of having DR, compared with patients with a RETeval score of  $< 22$  ( $p = 0.001$ ).

### Multivariate analysis

A logistic regression model was used to determine the predictors of DR (table 2). The logistic regression model has strong discriminatory properties, with a c-statistic of 0.790. The Hosmer-Lemeshow test fails to reject the null hypothesis that there is a lack of fit for the model.

Overall, patients with a DM duration of 5-14 years (OR=4.18,  $p = 0.007$ ) and 15-24 years (OR=4.37,  $p = 0.005$ ) were significantly more likely to have DR, compared to patients with a DM duration of  $\leq 4$  years. HbA1c was a strong predictor of DR, with patients having an HbA1c of  $\geq 7.0\%$  being 5.7 times more likely to have DR than those with an HbA1c of  $< 7.0\%$  (OR=5.7,  $p = 0.001$ ). eGFR was also a strong predictor of DR, with patients with an eGFR of  $\leq 29$  being 4.7 times more likely to have DR than those with an eGFR of  $\geq 90$  (OR=4.7,  $p = 0.006$ ). Furthermore, RETeval scores of  $\geq 22$  (OR=5.0,  $p < 0.0001$ ), or non-measurable (OR=4.7,  $p = 0.0003$ ), served as very strong predictors of DR, compared to RETeval scores of  $< 22$ . Lastly, patients with a pupil size of  $< 4\text{mm}$  were more likely to have DR, compared with patients with a pupil size of  $\geq 4\text{mm}$  (OR=1.9,  $p = 0.035$ ).

### DISCUSSION

Among our high-risk participants, tertiary point-of-care DR screening services identified a 39.6% and 15.8% prevalence rate of any DR and VTDR, respectively. This was notably greater than reported Australian community rates of any DR at 28.5% and VTDR at 4.5%.<sup>27</sup> These also exceeded the prevalence rates identified by landmark Australian population-based studies, including the Visual Impairment Project,<sup>29</sup> the Blue Mountains Eye Study,<sup>30</sup> the Newcastle Diabetic Retinopathy Study<sup>31</sup> and the Australian Diabetes Obesity and Lifestyle Study,<sup>32</sup> which respectively reported a DR prevalence of 29.1%, 32.4%, 35.0%, and 15.3%, and VTDR prevalence of 2.8%, 11.4%, 11.4%, and 1.2%.

While these population-based studies recruited from the general population, our patients were selected from targeted high-risk clinics; thus, a higher DR disease burden was expected. Concerningly, however, 62.8% of identified VTDR and 59.3% of NPDR cases were previously undiagnosed. This highlights large gaps in screening service utilization, while reinforcing the importance of point-of-care screening.

An Australian national diabetes eye screening reminder program, KeepSight, was launched in October 2018. This system sends reminders to patients, encouraging them to book their next appointment with their eye-care provider. To access this service, patients must both register for KeepSight and book appointments on their own accord.<sup>1</sup> Yet, the poor screening adherence evident in our studied clinics suggests a service dependent on patient motivation should be supplemented by point of care screening in hard-to-reach, high-risk populations.

Lee *et al* found that compared with patients with glaucoma and age-related macular degeneration (ARMD),

**Table 1** Bivariate association of patient characteristics with DR

Patient characteristics	With DR (n=108)		Without DR (n=145)		P value**
	Mean	±SD	Mean	±SD	
Age at screening (years)	62.3	13.0	62.2	16.4	0.950
DM duration (years)	18.4	9.8	14.7	12.9	<b>0.012</b>
HbA1C (%)	9.6	2.3	8.8	2.2	<b>0.005</b>
eGFR (mL/min/1.73 m <sup>2</sup> )	62.2	28.2	72.1	21.8	<b>0.002</b>
BMI (kg/m <sup>2</sup> )	30.8	6.5	32.0	7.3	0.158
Left pupil size (mm)	3.4	1.0	4.0	1.3	<b>0.001</b>
Right pupil size (mm)	3.4	1.1	4.0	1.3	<b>0.001</b>
	Median	IQR	Median	IQR	P value†
Distance (km) from home to GP	4.4	7.8	3.2	4.7	0.110
Eye-care provider	6.7	11.9	5.2	6.0	0.223
Hospital	9.7	11.3	8.8	8.5	0.287
Categorical variables	n	%	n	%	P value‡
Gender: male	73	28.9	89	35.2	0.308
Foot ulcer clinic	48	19.0	47	18.6	0.051
DM type 1 versus type 2	9	3.6	15	6.1	0.545
Other versus type 2	1	0.4	5	2.2	0.183
Ethnicity: Caucasian	38	15.0	64	25.3	0.151
Aboriginal and Torres Strait Islander	4	1.6	7	2.8	0.665
South Asian/Indian	21	8.3	23	9.1	0.457
Pacific Island	12	4.7	8	3.2	0.103
Other	33	13.0	43	17.0	0.877
Home language not English	65	25.7	75	29.6	0.181
Comorbidity: hypertension	89	35.2	111	43.9	0.258
Dyslipidemia	75	29.6	104	41.1	0.693
Ischaemic heart disease	45	17.8	52	20.6	0.348
Peripheral vascular disease	41	16.2	45	17.8	0.250
Transient Ischaemic Attack/ Cerebrovascular Accident	13	5.1	27	10.7	0.156
Chronic kidney disease	73	28.9	80	31.6	<b>0.046</b>
RETeval score not measurable vs <22	23	14.4	22	13.8	<b>0.001</b>
≥22 vs <22	57	27.4	36	17.3	<b>&lt;0.001</b>

Statistically significant values (p <0.05) have been included in bold.

\*Based on t-tests for continuous variables with normal approximation.

†Based on Mood's median tests for two samples for skewed variables.

‡Based on  $\chi^2$  tests for categorical variables.

BMI, body mass index; DM, diabetes mellitus; DR, diabetic retinopathy; eGFR, estimated glomerular filtration rate; GP, general practitioner; TIA, transient ischemic attack.

gaps between eye checks were more likely to occur among individuals with diabetes. While glaucoma and ARMD have solely ocular complications, DM is a costly, chronic disease, hosting a multitude of systemic complications.<sup>33</sup> The Australian Compliance with Annual Diabetic Eye Exams Survey (n=316) revealed transportation and clinic burnout were major barriers to regular eye check-ups.<sup>34</sup> With DR being largely asymptomatic and the majority

of our population having near-normal vision, burnt-out patients may decide to forgo logistically 'out of the way' screening services, with false impressions of security.<sup>35</sup>

### Predictors of DR: patient characteristics

Initiating screening programs in settings accessed by high-risk patients will target the crux of the problem. We found patients with a DM duration of 5–14 years (p=0.007)

**Table 2** Multivariate association with the dependent variable, DR

Independent Variables	Association with DR (n=253)			
	OR	LCL	UCL	P value
DM duration (years)				
≤4	0.229	0.083	0.634	<b>0.005</b>
5–14	0.957	0.454	2.017	0.908
15–24				
≥25	0.508	0.231	1.119	0.093
HbA1c (%)				
≥7	5.690	2.093	15.464	<b>0.001</b>
<7				
eGFR (mL/min/1.73 m <sup>2</sup> )				
≤29	4.703	1.549	14.279	<b>0.006</b>
30–59	1.225	0.541	2.774	0.626
60–89	1.068	0.500	2.228	0.865
≥90				
RETeval–DR score				
Not measurable	4.679	2.021	10.833	<b>0.0003</b>
≥22	5.007	2.579	9.720	<b>&lt;0.0001</b>
<22				
Pupil size (mm)				
<4	1.934	1.047	3.573	<b>0.035</b>
≥4				
–2 Log L				
273.7	Somers' D		0.580	
Likelihood ratio $\chi^2$				
71.6	Gamma		0.586	
R <sup>2</sup>				
0.331	c		0.790	
Hosmer-Lemeshow $\chi^2$				
2.521	Pr > $\chi^2$		0.961	

DM, diabetes mellitus; DR, diabetic retinopathy; eGFR, estimated glomerular filtration rate; LCL, lower confidence limit; UCL, upper confidence limit.

and 15–24 years ( $p=0.005$ ) were significantly more likely to have DR, compared with those with a DM duration of  $\leq 4$  years. Significant associations between DR and longer DM duration have been identified by numerous studies.<sup>29 31 36</sup> Sixty percent of individuals with type 2DM and almost all with type 1DM develop DR within 20 years of diagnosis.<sup>37</sup> Patients attending clinics in our study had a mean DM duration of 16.6 years and a mean HbA1c of 9.1%; hence, routine point-of-care screening should be available for this high-risk cohort, to avoid missed VTDR.

Interestingly, we also found that patients with DR had significantly smaller pupil sizes ( $<4$  mm), compared with those without DR (OR=1.9,  $p=0.035$ ). Pupillary constriction in patients with DR has been identified in other studies, likely secondary to diabetic autonomic neuropathy.<sup>23</sup>

### Diagnostic accuracy of the RetinaVue 100 and RETeval RetinaVue 100

The non-mydratic camera displayed 20.2% sensitivity and 99.5% specificity. Australian guidelines recommend DR screening modalities should have a minimum sensitivity of 60% and specificity of 90%–95%<sup>9</sup>; hence, the poor sensitivity of the non-mydratic camera renders it inappropriate for isolated use in this population.

Portable, non-mydratic photography among our participants had a 56.7% failure rate. A meta-analysis of telemedicine DR screening programs found two-field non-mydratic fundus photography had a failure rate of 19% ( $\pm 10\%$  SD).<sup>38</sup> Underexposure and shadowing complicated poor image quality obtained in the non-mydratic photographs. To take gradable retinal images, the RetinaVue 100 requires a pupil size of at least 3.5 mm

diameter.<sup>39</sup> The presence of lens opacities, coupled with the small mean pupil size in our study population ( $\bar{x}$ =3.7 mm, SD 1.2), may have influenced the high failure rate seen with non-mydratric fundus photography. Thus, the poor 20.2% sensitivity of the non-mydratric camera does not necessarily reflect the camera's overall utility, instead demonstrating its inappropriateness, without mydriasis, for a predominantly elderly,<sup>40</sup> high-risk population, with smaller pupil sizes.

We found portable, mydratric photography produced high-quality retinal images with only a 7.6% failure rate, demonstrating that dilation was generally necessary to assess DR status and identify referable DR. Other prospective studies have similarly found significant reductions in ungradable photos, following mydriasis.<sup>41</sup> Our results support current recommendations for mydriasis in DR screening.<sup>9</sup>

### RETeval

We found a RETeval score of  $\geq 22$  was a strong predictor of DR (OR=5.0,  $p < 0.0001$ ). Using this cut-off, we found that the RETeval demonstrated 72.5% sensitivity and 70.1% specificity. While the sensitivity meets current recommendations, the specificity does not; hence, it should not be used alone as a screening device in this population. ERG scores were unable to be obtained for 41 (15.0%) participants. This screening failure mainly occurred due to patients' inability to keep their eyelids open, or the device's failure to detect small pupils. However, our multivariate analysis identified a non-measurable RETeval as a significant predictor of DR (OR=4.7,  $p = 0.0003$ ). A retrospective study of 279 patients with diabetes found a RETeval score of  $> 23.5$  was associated with an 11-times higher risk of ocular intervention with vitrectomy, intravitreal injections, or laser therapy, compared with those with a score of  $< 23.5$ .<sup>42</sup> Thus, the RETeval may have a role in triaging the urgency of clinical review, when a fundus camera cannot obtain a gradable image.

### Benefits of a tertiary point-of-care screening model

The main advantage of outreach DR screening is improved service accessibility. Cost, transportation, clinic burnout, and poor understanding of the importance of eye screening are the main barriers patients experience to regular eye check-ups.<sup>34 43</sup> Our point-of-care screening model in multidisciplinary clinics may alleviate these barriers. Furthermore, the convenience of point-of-care services can overcome health literacy barriers, providing incentive for patients to have an immediate visual assessment, rather than postponing it.<sup>44</sup> Thus, tertiary point-of-care screening is a targeted and effective way of improving screening coverage for high-risk populations.

We found 17% of patients had undiagnosed DR, despite claiming to have been screened within the last 12 months. While de novo DR development is possible, this result questions the validity of self-reported screening practices or patients' understanding of their diagnosis. Similarly, Fowles *et al* found the rate of self-reported eye

examinations in patients with diabetes was higher than the true rate.<sup>45</sup> This is especially noteworthy for endocrinologists trying to determine appropriate patient management. Therefore, on-site screening is extremely valuable, optimizing the identification of high-risk patients, who would not have otherwise received appropriate screening as recommended.

The portability of hand-held cameras also facilitates greater outreach. There is evidence that fundus image quality and the rate of non-gradable images are better for a fixed than a portable, non-mydratric camera.<sup>46</sup> However, studies using fixed table-top retinal cameras have achieved poor screening uptake, mainly because mobilization was too difficult for ill patients, while others were disinterested.<sup>47 48</sup> Meanwhile, hand-held cameras can physically reach this demographic, those most at risk of developing DR.

Portable cameras also improve the economic feasibility of teleophthalmology services, as they are less expensive than traditional table-top retinal cameras.<sup>49</sup> Furthermore, many elements of our study were facilitated by non-specialists. The devices were operated by a non-specialist with minimal training, while the 89.8% inter-rater agreement between our ophthalmologist and trained grader reinforces how image grading could be performed by trained non-ophthalmologists in the long-run. Long-term operation by non-specialists can substantially improve the financial viability and accessibility of this outreach screening service.

Furthermore, artificial intelligence systems can provide an instant diagnosis once a photograph is taken. This minimizes the need for ophthalmology review, offering significant cost-benefits while improving telescreening outreach.<sup>50</sup>

Future studies could examine the cost-effectiveness of a point-of-care portable screening model's ability to opportunistically identify and prevent disease progression. Many of our participants had unexplained poor vision, indicating the need for a comprehensive eye examination. Horizontal integration with community optometry services could facilitate this.

### Strengths

Our study was strengthened by multiple, masked fundus reviewers with high inter-rater reliability, as well as the use of a pragmatic clinical pathway for patient review.

### Limitations

Our prevalence data may be subject to sampling bias from our 53.1% dilation rate, as no mydratric reference standard was obtained from patients who declined dilation. As DR has a known correlation with miosis,<sup>23</sup> it is possible that our study under-reports the prevalence of DR. We used two-field 45° mydratric digital retinal photography as the reference standard, which performs favorably but slightly less accurately, against biomicroscopic examination and seven-field Early Treatment Diabetic Retinopathy Study (ETDRS) fundus photography.<sup>18 19</sup> Further



studies comparing portable, non-mydratric and mydratric fundus photography with clinical grading or ultrawide-field photography, would help clarify the diagnostic accuracy of this screening methodology in high-risk populations. Additionally, optical coherence tomography is the gold standard for DMO detection. However, our clinical reference used non-stereoscopic images; hence, DMO presenting as retinal thickening without hard exudate would be under-reported.

## CONCLUSION

We identified a concerning high prevalence of DR and VTDR in patients attending high-risk diabetes clinics, with over half of these patients having undiagnosed disease. This reinforces the dire need for improved screening services, tailored for high-risk populations. It also indicates the potential for tertiary point-of-care screening to enhance DR detection. In this population, portable, non-mydratric fundus photography had a high screening failure rate and low sensitivity. Similarly, ERG had a poor screening failure rate, as well as insufficient sensitivity and specificity. However, portable mydratric retinal photography demonstrates promise in teleophthalmology services, with quick examinations and satisfactory diagnostic accuracy, substantially improving screening access for high-risk populations.

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