

# Research

## The reliability of single-field fundus photography in screening for diabetic retinopathy: the Central Australian Ocular Health Study

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**D**iabetic retinopathy (DR) is one of the leading causes of preventable vision loss in Australia.<sup>1,2</sup> The global prevalence of diabetes mellitus (DM) is on the rise, with 366 million (4.4% of the estimated world population) expected to be affected by the year 2030.<sup>3</sup> In Australia, a nationwide cross-sectional survey in 2002 showed that the prevalence of diabetes in Australia had more than doubled since 1981. At the time of the survey, 8.0% of adult men and 6.8% of adult women living in Australia had diabetes, and 15.3% of people with diabetes had DR.<sup>4</sup>

DR is detected at similar rates in both Indigenous and non-Indigenous Australians with DM.<sup>5,6</sup> However, the burden of DR is much higher among the Indigenous Australian population because of the higher prevalence of DM within this group. A recent eye health survey in Indigenous Australians showed the prevalence of self-reported diabetes to be more than eight times higher (37%) than in non-Indigenous Australians. This is a striking figure, as 30 years ago, only 0.03% of Indigenous people had diabetes.<sup>5</sup>

DR has little or no symptoms until vision loss develops, so regular DR screening is critical for early diagnosis and treatment.<sup>2,3</sup> Vision loss can be prevented in up to 70% of people who are at risk through timely intervention.<sup>2,7</sup> However, the rates of adherence to regular eye examinations in those with DR consistently fall below the recommended rate, and are as low as 50% in some studies.<sup>8,9</sup> In particular, there is a significant shortfall in the delivery of DR screening to remote regions of Australia. This may have resulted from a shortage of service providers, obstacles in accessing centrally located specialist services and under-utilisation of visiting services. Improv-

### Abstract

**Objective:** To assess the accuracy of grading diabetic retinopathy (DR) using single-field digital fundus photography compared with clinical grading from a dilated slit-lamp fundus examination in Indigenous Australians living in Central Australia.

**Design, setting and participants:** Cross-sectional study comparing DR grades in participants with diabetes mellitus presenting for examination at remote community clinics from 1 July 2005 to 30 June 2008.

**Main outcome measures:** Sensitivity and specificity of grading using digital photography compared with the clinical gold standard of slit-lamp fundus examination.

**Results:** Of the 1884 participants recruited for the study, 1040 had self-reported diabetes mellitus and, of those, 360 had fundus photographs available (706 eyes) that were able to be graded. On clinical grading, 163 eyes had any DR and 51 eyes had vision-threatening DR (VTDR). The sensitivity and specificity for detecting any DR were 74% (95% CI, 67%–80%) and 92% (95% CI, 90%–94%), respectively. The sensitivity and specificity for detecting VTDR were 86% (95% CI, 77%–96%) and 95% (95% CI, 93%–97%), respectively.

**Conclusion:** Single-field digital fundus photography is a valid screening tool for DR in remote communities of central Australia and may be used to provide eye care services to this region with acceptable accuracy.

ing the availability of fundus cameras and training local staff in their use may help overcome some of the barriers to DR screening.

An ideal screening method requires acceptable sensitivity and specificity, and cost-effectiveness. A recent meta-analysis confirmed the use of retinal photography as a valid screening tool for DR in resource-poor settings.<sup>10</sup> Our study was designed to evaluate the validity of single-field fundus photography as a screening tool for DR in remote Central Australian communities.

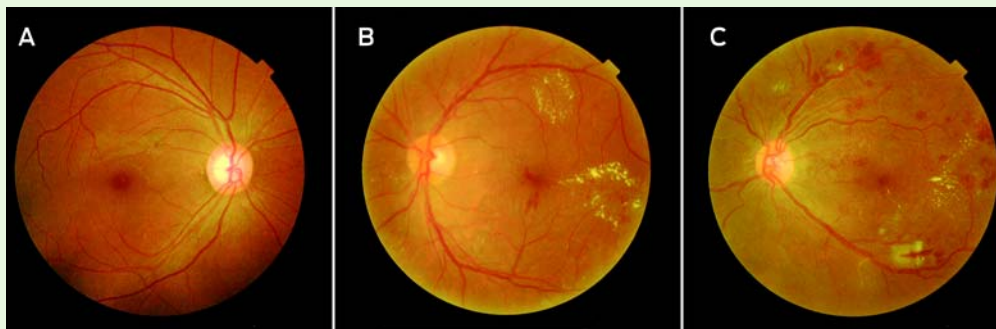
### Methods

The design, recruitment process and baseline characteristics of the Central Australian Ocular Health Study (CAOHS) have previously been described in detail.<sup>11</sup> The CAOHS took place in remote communities of Central Australia, excluding the relatively urbanised area of Alice Springs. The participants were recruited during

once-weekly remote clinic visits over 36 months from 1 July 2005 to 30 June 2008. Ethics approval for the study was obtained from the Central Australian Human Research Ethics Committee according to the tenets of the Declaration of Helsinki. The aims of the study were explained to participants with the help of an interpreter when needed, and written informed consent was obtained.

All participants underwent detailed ocular examination. Baseline acuity was measured using a tumbling E acuity chart at 3 metres in a well lit room. An optometrist performed subjective refraction and determined refracted visual acuity. The optometrist performed a slit lamp examination of the anterior segment, followed by pupil examination using a hand torch. After an assessment of anterior chamber depth, the pupils were dilated using tropicamide 1.0% and phenylephrine 2.5% solution. The visiting ophthalmologist (TH) performed stereoscopic slit-lamp funduscopy using a 90-

**1 Fundus photographs (examples from study cohort) showing a normal fundus (A), clinically significant macular oedema (B) and proliferative diabetic retinopathy (C)**



diopetre fundoscopy lens. The presence and degree of DR was graded using the Early Treatment of Diabetic Retinopathy Study (ETDRS) adaptation of the modified Airle House classification of DR<sup>12</sup> by clinical comparison with standardised photographs (Box 1). The DR was graded as either no DR (level 10–13), minimal non-proliferative DR (NPDR) (level 14–19), mild NPDR (level 20–39), moderate NPDR (level 40–49), severe NPDR (level 50–59) and proliferative DR (PDR) (level 60–85). Clinically significant macular oedema (CSMO) was defined as any retinal thickening within 500 µm of the fovea associated with retinal thickening that is at least one disc area in size within one disc diameter of the fovea.

For the purposes of data analysis, the NPDR and PDR groups were collapsed into “any DR”. CSMO and PDR groups were also collapsed into one category, named “vision-threatening DR” (VTDR).

Where possible, each participant with DM underwent single-field 45-degree fundus photography after pupillary dilation. An ophthalmologist or trainee ophthalmologist took the photographs using a Topcon TRC-NW100 digital fundus camera (Topcon Corporation). The photos were centred on the fovea with a 45 degree field of view.

In line with many other papers reporting accuracy of screening photographs for DR, our paper has included data from both eyes to allow comparative assessment of accuracy of our study alongside others.<sup>10</sup> The photos from individual patients were not assessed in pairs, but in a random order to minimise bias.

Various screening modalities for DR have been studied to meet the

increased demand for screening, with variable rates of success. These include screening using mydriatic and non-mydriatic photography, and examination by different health professionals, including physicians, general practitioners and optometrists. To date, the ETDRS 7-field fundus photographs and ETDRS protocol are the only validated reference standard for detecting and staging of DR. Others have evaluated the validity of single-field fundus photography by comparing the accuracy of diagnosis against either a clinical gold standard of slit-lamp fundus examination<sup>13–16</sup> or an imaging gold standard of 7-field fundus photographs.<sup>17–19</sup> Although dilated stereoscopic fundoscopy has an inherent weakness in that it cannot be validated or verified as there is no permanent record, it is by far the most commonly used method of DR evaluation in clinical practice. It allows clinicians to determine the presence of DR or VTDR. Thus, in our study, we set out to assess the validity of a screening method compared with standard clinical practice.

A single clinician (JL) graded the fundus photographs in a masked fashion using ETDRS criteria. Photos were graded as having either “any DR” or “VTDR” (ie, CSMO and/or PDR). The photo grades were compared with clinical grades from the dilated slit-lamp fundus examination, which was used as the gold standard for comparison. A subset of the fundus photos were selected at random using a pseudorandom number generator, and regraded by the original grader in a masked fashion to establish the intra-grader reliability for photo grading.

The statistical analysis was performed using SAS 9.1 (SAS Institute).

Test statistics, 95% CI, kappa coefficients as a measure of intra-examiner assessment and *P* values are presented.

## Results

From the 1884 individuals recruited across 30 remote communities, 1040 had self-reported DM. Fundus photos were available for 396 of those patients (792 eyes). The remaining participants were not photographed because of space limitations of the light plane used to access the remote communities, the camera being needed at other locations, or intermittent maintenance of the camera. Of the available images, 86 photographs were ungradable because of media opacity or defocus, leaving 706 fundus photographs that were used for analysis. Of the 360 patients included for analysis, 131 were male (36%) and 229 were female (64%). The mean age of patients was 48 years (range, 20–83 years; SD, 13 years). This was similar to the whole sample of 1040 patients with diabetes, where the mean age was 50 years (range, 20–93; SD, 14 years; *t* = 1.90; *P* = 0.06), and 66% of patients were female ( $\chi^2$  = 0.88; *P* = 0.38).

Any DR was detected in 163 eyes (23%) by clinical examination and in 162 eyes (23%) using fundus photography (Box 2, A). Of those with any DR detected by clinical examination, 52 (32%) had minimal NPDR, 63 (39%) had mild NPDR, 38 (23%) had moderate NPDR, one (1%) had severe NPDR, nine (6%) had PDR and 42 (26%) had CSMO.

VTDR was detected in 51 eyes (7%) on clinical examination and in 78 eyes (11%) using photo grading. Seven eyes with VTDR diagnosed clinically were not detected on photo screening, and 34 eyes were incorrectly diagnosed by photo grading as having VTDR (Box 2, B), leaving 44 eyes with VTDR (6%).

The sensitivity, specificity and kappa values for detecting any DR were 74% (95% CI, 67%–80%), 92% (95% CI, 90%–94%) and 0.67 (95% CI, 0.60–0.74; *P* < 0.0001), respectively (Box 3). The sensitivity and specificity for detecting VTDR were 86% (95% CI, 77%–96%), 95% (95% CI, 93%–97%) and 0.65 (95% CI, 0.55–0.76; *P* < 0.0001), respectively (Box 3).

The kappa values for intragrader reliability for detecting any DR and

## 2 Accuracy of single-field 45-degree fundus photography in detecting any diabetic retinopathy (DR)\* and vision-threatening diabetic retinopathy (VTDR) in 360 patients (706 eyes) using clinical slit-lamp fundoscopy as the gold standard

A: Any DR				B: VTDR			
		Clinical slit-lamp fundoscopy (gold standard) grading				Clinical slit-lamp fundoscopy (gold standard) grading	
Single-field fundus photography grading	No. of eyes with any DR	No. of eyes with any DR	No. of eyes with no DR	Single-field fundus photography grading	No. of eyes with VTDR	No. of eyes with VTDR	No. of eyes with no VTDR
	No. of eyes with no DR	42	502		No. of eyes with no VTDR	7	621

\* Both of the categories "any DR" and "VTDR" include eyes with proliferative DR.

VTDR were 0.83 (95% CI, 0.72–0.94;  $P < 0.0001$ ) and 0.88 (95% CI, 0.77–0.99;  $P < 0.0001$ ), respectively.

## Discussion

The current National Health and Medical Research Council (NHMRC) *Guidelines for the management of diabetic retinopathy* recommend annual retinal examinations for Indigenous Australians, in contrast to every 2 years for the non-Indigenous population.<sup>20</sup> Access to ophthalmology services is one major limitation to achieving screening goals in remote regions of Australia. A recent national population-based survey of eye health in the Indigenous Australian population redefined the gap in eye health between this group and other Australians. It is reported that 44% of Indigenous Australians had not had a diabetic eye screening in the past year.<sup>5</sup>

A systematic review of DR screening techniques supported retinal photography with mydriasis as the preferred method.<sup>21</sup> Research comparing the accuracy of detecting DR using mydriatic and non-mydriatic fundus photographs showed an improvement in specificity with mydriasis.<sup>22</sup> Other studies have shown that photos without mydriasis were often of poor quality and unable to be graded, especially in older patients and in the presence of media opacities.<sup>18,19</sup> The higher failure rate of fundus photography in our study (11%; 86/792) compared with the reported failure rate of dilated fundus photography (4%–8%)<sup>14–16,18</sup> may have resulted from a higher prevalence of media opacities, such as corneal scarring and cataract, among Indig-

nous Australians.<sup>23</sup> Media opacity or small pupils would increase the likelihood of a false negative result, reducing the sensitivity of the screening photography. Thus we would argue that mydriasis is essential to improve diagnostic accuracy in this population group.

In our study, of the seven false-negative gradings for VTDR, two had PDR outside the limits of the single-field photograph; the remainder had CSMO that was identifiable as retinal thickening only without lipid exudation. An important feature of fundus photos as a test for DR is the probability of missing a diagnosis of DR. However, with the low rate of false-negative results, as in our study, there is a higher probability of a correct diagnosis with regular repeat testing, even if an initial test is incorrectly negative.

Most of the studies of fundus photographs to date are based largely on white populations.<sup>14,16,18,19</sup> Previous studies evaluating fundus photography as a screening tool in Indigenous Australians were based on non-mydriatic fundus photographs with smaller sample sizes.<sup>24,25</sup> To our knowledge, this is the first study that assesses the accuracy of detecting DR and VTDR in a

large sample of Indigenous Australians using single-field dilated fundus photography compared with clinical examination. Our patient recruitment was somewhat limited by factors such as availability of instruments, and space and weight restrictions on light planes. However, this is unlikely to have introduced a systematic bias and we were able to obtain photographs of a representative sample of 706 eyes.

CSMO is the most common cause of VTDR. However, in the absence of stereoscopic views, as with single-field digital photos, assessment for VTDR is limited to detecting associated features, such as lipid exudates or haemorrhages, rather than retinal thickening. Our results show that the false-positive grades on fundus photographs were largely attributable to pigment hyperplasia or depigmentations that mimicked the appearance of lipid and haemorrhages. This problem can be overcome in the clinical setting by using stereo-photos and red-free filters, which were not available for the model of camera used in this study. However, a false-positive diagnosis of VTDR is preferable as it will not lead to vision loss compared with a false-negative diagnosis.

Cost analysis studies have demonstrated the potential cost-effectiveness of photo-screening in remote settings in maintaining both a high level of sight-years as well as being cheaper than visiting specialist programs.<sup>26,27</sup>

The NHMRC recommends that DR screening modalities need to be cost-effective and easy to administer, and to have a sensitivity of at least 60% and specificity levels of 90%–95%.<sup>20</sup> The accuracy of the photo-screening in our study exceeds this minimum requirement, with sensitivities of 74% and 86% for detecting any DR and VTDR, respectively. Likewise, the specificities for detecting any DR and VTDR meet

## 3 Diagnostic characteristics and interrater reliability for detecting any diabetic retinopathy (DR) and vision-threatening diabetic retinopathy (VTDR)

Diagnostic characteristics	Any DR (95% CI)	VTDR (95% CI)
Sensitivity	74% (67%–80%)	86% (77%–96%)
Specificity	92% (90%–94%)	95% (93%–97%)
Positive predictive value	75% (68%–81%)	56% (45%–67%)
Negative predictive value	92% (90%–94%)	99% (98%–100%)
Positive likelihood ratio	9.8 (7.2–13.4)	16.6 (11.8–23.5)
Negative likelihood ratio	0.3 (0.2–0.4)	0.1 (0.1–0.3)
Kappa	0.67 (0.60–0.74)	0.65 (0.55–0.76)



the NHMRC guideline of greater than 90%, at 92% and 95%, respectively. These values are comparable to the reported sensitivities and specificities of studies that compared diagnostic accuracy of single-field fundus photography with that of clinical examination. The sensitivities of detecting any DR have been reported from 38% to 96%, and specificities from 79% to 98%.<sup>13-16</sup> Although definitions of VTDR vary in different studies, the sensitivities and specificities were higher for detecting VTDR, with ranges of 82%–100% and 70%–100%, respectively.<sup>13-16</sup> In addition, the measure of reliability of inter-examiner and intra-examiner assessment (kappa coefficient  $\kappa$ ) showed a moderate level of agreement ( $\kappa = 0.67$  and  $0.65$  for any DR and VTDR, respectively).

Our study highlights the strength and simplicity of single-field fundus photography for DR screening; however, there is still room for improvement. Future research could investigate the adjunctive use of optical coherence tomography (OCT) to improve screening for CSMO within this population. The development of conveniently portable OCT would reduce the risk of false-negative gradings, confirm tentative diagnoses of retinal thickening, and the images generated could enhance patient comprehension of what is happening in DR. In addition, while single-field fundus photography may be feasible for screening for DR in a remote setting, if this approach is to be considered, future research must also establish whether there is likely to be sufficient uptake of this modality by the workforce currently in place in remote communities. Thus, measures such as this should be undertaken after consultation with current health providers to ensure that the desired outcome is achieved.

## Conclusion

Our results show that single-field dilated fundus photography in Indigenous Australians meets the minimum screening requirements recommended by the NHMRC. It also has adequate sensitivities, specificities and repeatability for detecting DR to determine need for referral or repeat screening frequencies. It is therefore a

valid screening tool for DR in remote communities within Central Australia. This technique may be used to complement visiting specialist eye care services to this region with acceptable accuracy. Providing optometrists or other trained technicians who visit the communities with fundus cameras or installing fundus cameras in the medical clinics of remote communities and training local staff to recognise signs of DR may help identify patients who require referral in a timely manner. Alternatively, remote clinics can be linked via high-speed internet connection to reading centres and/or ophthalmologists who can give their opinion and make recommendations on further action.

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