Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit
Horizon scanning report

The detection of diabetic retinopathy utilising retinal photography in rural and remote areas in Australia

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We acknowledge the contribution of Peter Day, NZHTA, for the data on clinical need and burden of disease in New Zealand.

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Executive Summary

The current "gold standard" for the detection of diabetic retinopathy in Australia is an ophthalmoscopic examination performed by an ophthalmologist. There is a short supply of ophthalmologists in Australia, with the majority servicing well-populated urban centres. Retinal photography has been recognised as a viable alternative to direct, using a hand held ophthalmoscope or lamp, or indirect, using a slit-lamp biomicroscope, ophthalmology. Retinal photography may be performed with or without mydriasis (dilation of the pupil), however it has been suggested that mydriasis may be a barrier to undertaking a screening programme. This report has assessed the safety and effectiveness of screening for diabetic retinopathy utilising a one or two step process. Trained, non-medical, health workers take retinal photographs and may also interpret them. Alternatively they may be posted or emailed to an ophthalmologist for final interpretation.

Results indicate that *non-mydriatic retinal photography* is more efficient at detecting vision threatening diabetic retinopathy, than it is for detecting all forms of diabetic retinopathy, with improved sensitivity (86%), specificity (77%), negative predictive values (98%) but decreased positive predictive values (33%). In the studies assessed for this report the number of inadequate or ungradable retinal photography images ranged from 3.7 to 15%. This is of particular concern to budget holders since patients who cannot be assessed must be referred to an ophthalmologist for further evaluation.

Mydriatic retinal photography is proficient when used to diagnose referable or vision threatening diabetic retinopathy; with high sensitivity (71-88%) and specificity (86-99%), variable positive predictive ability (45-88%) and high negative predictive value (98-99%). However, there was greater variation in these values when *mydriatic retinal photography* was used to detect *all* forms of diabetic retinopathy such as background, maculopathy, pre-proliferative and proliferative retinopathy. As with *non-mydriatic retinal photography,* the number of ungradable images was high, ranging 4 to 22%.

False positive and false negative rates for both *non-mydriatic* and *mydriatic* retinal photography were lower when diagnosing referable retinopathy compared to the detection of *all* types of retinopathy.

It is difficult from these diverse results to determine which form of retinal photography undertaken by trained health workers is the most effective tool for the diagnosis of diabetic retinopathy. In studies that compared *mydriatic* and *non-mydriatic* retinal photography, retinal photography with mydriasis was significantly more effective at detecting diabetic retinopathy than non-mydriatic photography ($p<0.001$). The rate for correctly identifying patients with referable diabetic retinopathy, the positive predictive value, increased from 33 to 45 per cent when mydriasis was utilised. In addition, retinal photographs with mydriasis were more likely to be excellent or adequate for the diagnosis of diabetic retinopathy when compared to non-mydriatic retinal photography ($p<0.0001$).

Providing thorough training for health workers in the technique of taking retinal photographs, with or without mydriasis, is important as results indicate that an excellent or adequate photograph is more likely to be taken by a credentialed photographer than by a non-credentialed photographer (p=0.001).

The cost-effectiveness of any screening programme depends on the disease prevalence, compliance to the programme, the sensitivity and specificity of the screening method and cost. The prevalence of diabetic retinopathy may be particularly relevant for Aboriginal populations, where the prevalence of diabetes and therefore possibly diabetic retinopathy, is higher compared to other Australian populations. Screening with either mydriatic or non-mydriatic retinal photography by a mobile clinic in rural areas was found to be cost-effective.

Introduction

The National Horizon Scanning Unit, Department of Public Health, University of Adelaide, on behalf of the Medical Services Advisory Committee (MSAC), has undertaken an Horizon Scanning Report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play of the introduction of retinal photography by health workers in rural and remote areas and reading by ophthalmologists.

In Australia, there are currently two Medicare Benefits Schedule (MBS) item numbers indicated for retinal photography when conducted by ophthalmologists. However, there is no MBS item number available for the ophthalmologists' *reading* of retinal photographs taken by other health workers. Retinal photography for the detection of diabetic retinopathy amongst people with diabetes may be offered through ophthalmologists in Australia, however ophthalmoscopy would be the preferred modality for detection. More commonly they would be utilised by health workers or General Practitioners in rural or remote communities.

This Horizon Scanning Report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of ophthalmological reading of retinal photographs taken by other health workers in rural and remote areas, as well as its present use, the potential future application of the technology, and its likely impact on the Australian health care system.

This Horizon Scanning Report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with retinal photography undertaken by health workers in rural and remote areas and read by ophthalmologists.

Background

Description of the Technology

The procedure

There are currently two fundus cameras registered on the Australian Register of Therapeutic Goods, the Topcon retinal camera (Topcon Australia Pty Ltd, ARTG number 56998) and the Canon CR6-45NM non-mydriatic retinal camera (Canon Australia Pty Ltd, ARTG number 79250) (Figure 1).

Retinal cameras previously used bright visible light to view the fundus or back of the eye and required the use of mydriatic agents, such as tropicamide, to dilate the pupil. Newer models of retinal cameras utilise infrared sensitive video cameras, which allow viewing of the patient's eye without the need to dilate the pupil, eliminating the use of mydriatic agents (Heaven et al 1992). However, it is believed that, mydriatic eye drops should be used, if possible, as

a better quality photograph is produced with pupil dilation (Mak et al 2003). Photographs should be taken in a darkened room, regardless of whether mydriatic eye drops have been used, to simulate physiological pupil dilation. The illuminating source for photography is a xenon flash, which constricts the pupil immediately. An interval of approximately five minutes should be allowed between photography of the first and second eye to allow pupil recovery from the first flash (Heaven et al 1992). The camera has a small television screen and the operator aligns and focuses the retinal view using this screen prior to taking the retinal photograph. The 45º field is centred on the fovea (the centre of the retina and the region of highest visual acuity) and includes the optic disc and the entire macula (Figure 2). The camera can be operated by a trained technician and produces either film based photographs (polaroid prints or slides) or digital, making it ideal for telemedicine. A photograph of each eye is printed and attached to patient details, which should include identification details as well as the duration of diabetes and the type of diabetic treatment that the patient is undergoing. Photographs can either be interpreted by trained readers or delivered to an ophthalmologist for reading (Williams et al 2004; Heaven et al 1992). As non-mydriatic retinal photographs do not provide a complete view of the retina they cannot be used to grade the severity of retinopathy. Therefore, if any degree of retinopathy is detected, the patient should be referred to an ophthalmologist for a full assessment. Non-mydriatic cameras are portable and easily transported to rural or remote settings and non-medical, trained staff are able to perform retinal examinations (NHMRC 1997a). Many screening projects transport the retinal cameras in purpose-built vans with the camera installed in a robust frame supported by cushioning or airbags in order to avoid excess vibration (Lawrenson 1992; Ellingford 1992).

Figure 1 The Canon CR6-45NM non-mydriatic retinal camera (Canon Inc 2004)

Intended purpose

Non-mydriatic retinal photography (through undilated pupils) is intended to screen people with diabetes for diabetic retinopathy (DR). It is recommended that people with diabetes be screened for DR either yearly or biennially by an ophthalmologist, general practitioner or a suitable trained health worker (NHMRC 1997a).

Diabetic retinopathy results from damage to the microcirculation of the eye, specifically the retina. People with diabetes have elevated blood sugar and blood pressure levels which may result in damage to small blood vessels. Endothelial cells lining retinal vessels rest on a foundation layer of basement

membrane. The major histological change is thickening of the basement membrane, which stops the flow of essential chemicals into and out of the retina. (American Academy of Ophthalmology 2003; MedWeb 2004; NHMRC 1997a). The exact mechanism that causes thickening of the basement membrane is unknown, however hyperglycaemia appears to be a major initiating factor (Evans et al 2000). As a consequence, fluid leaks out of the capillaries causing swelling or thickening of the macula, a small area in the centre of the retina responsible for seeing fine detail clearly, and blurring vision. This is referred to as macular oedema, which is the most common cause of vision loss in people with diabetes. This may result in focal but not peripheral vision loss. Macular ischemia occurs when the small blood vessels become so damaged that they close completely depriving the macula of sufficient nutrients. The early stages of this condition are referred to as non-proliferative or background diabetic retinopathy, which is characterised by retinal vascular microaneurysms[1], blot haemorrhages and "cotton wool" spots. As the disease progresses, damaged cells release vascular endothelial growth factor, which stimulates neovascularisation. These new blood vessels grow on the surface of the retina or optic nerve, in an attempt to supply the retina with sufficient nutrients. However, these new blood vessels are extremely delicate and prone to bleeding, which in turn may leak and cause scarring on the retina, resulting in vitreous haemorrhage[2] or retinal detachment. This condition is described as proliferative diabetic retinopathy. It is characterised by intra-retinal microvascular abnormalities, an increased number of microaneurysms and haemorrhages, and may cause severe loss of both central and peripheral vision (Figures 1 and 2) (American Academy of Ophthalmology 2003; MedWeb 2004; NHMRC 1997a).

Once DR has developed the only proven successful treatment is laser therapy (photocoagulation) combined with continued control of the patient's diabetes. These treatments cannot improve vision but will prevent further damage to the macula and complications from neovascularisation. Retinal damage is irreversible and therefore early screening to detect DR with subsequent treatment is essential. Photocoagulation has been demonstrated to lead to a 2 to 7 fold reduction in further vision loss. The side effects of this laser treatment may be serious however, as a laser burn applied to the macula or fovea, may permanently impair visual acuity and central vision. Some loss of night and colour vision may also occur (NHMRC 1997b). If an excessive amount of bleeding in the fluid of the eye (vitreous humour) has occurred, a vitrectomy may have to be performed. This involves removing the vitreous with the haemorrhage through a scleral incision, often under local anaesthesia, and replacing the fluid with a clear balanced salt solution, which still allows light to pass through the eye to form an image on the retina. Complications of vitrectomy include macular scar formation, cataracts, retinal detachment and neovascular glaucoma (NHMRC 1997a).

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1 Focal dilation of retinal capillaries occurring in diabetes mellitus, retinal vein obstruction, and absolute glaucoma.

2 Haemorrhage into the vitreous, the transparent gel that fills the inner portion of the eyeball between the lens and the retina.

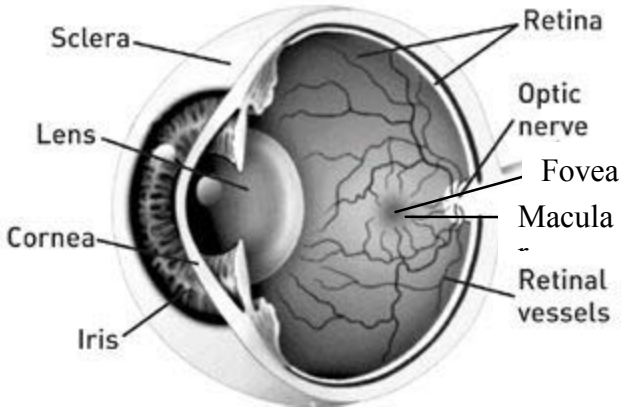

Figure 2 The normal eye (American Academy of Ophthalmology 2003)

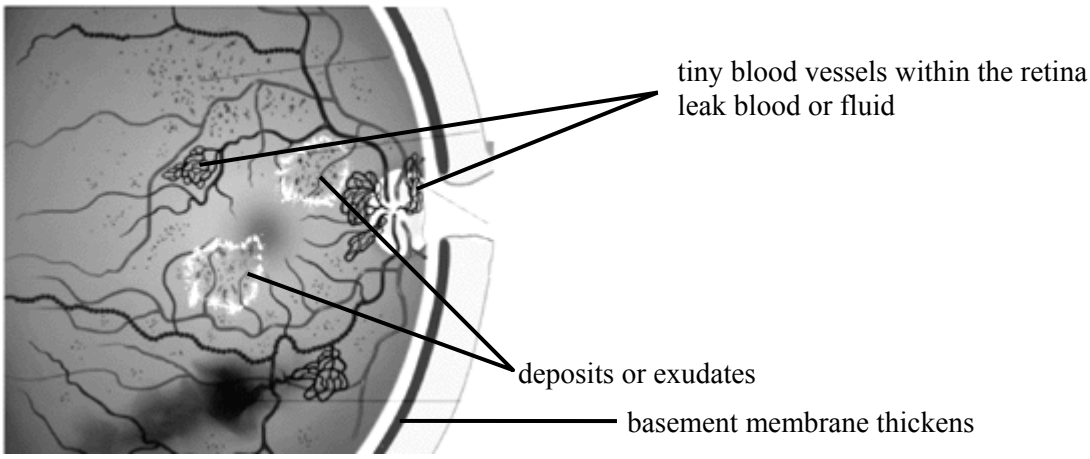

Figure 3 The eye affected by non-proliferative diabetic retinopathy (American Academy of Ophthalmology 2003)

Risk factors for developing DR include the length of duration of diabetes, elevated glycosylated haemoglobin (HbA1C) levels, hyperlipidaemia, elevated blood pressure and nephropathy as indicated by proteinuria or albuminuria (Fong et al 2004; NHMRC 1997a). In addition, at time of clinical diagnosis of non-insulin dependent diabetes mellitus (NIDDM), some individuals already have evidence of DR indicating that their diabetes may have developed several years prior to diagnosis. This may result in serious damage to eyesight (Tapp et al 2003).

Lifestyle factors such as good glycaemic control (6.5-7.0 mmol/L), reducing cholesterol levels (<5.0 mmol/L), reducing alcohol intake, which in turn will reduce blood pressure (<130/80 Hg), smoking cessation (smoking 20 cigarettes per day will triple the rate of DR development) and increasing exercise have been shown to reduce the incidence of DR (Figure 4a and 4b) (MedWeb 2004, NHMRC 1997a).

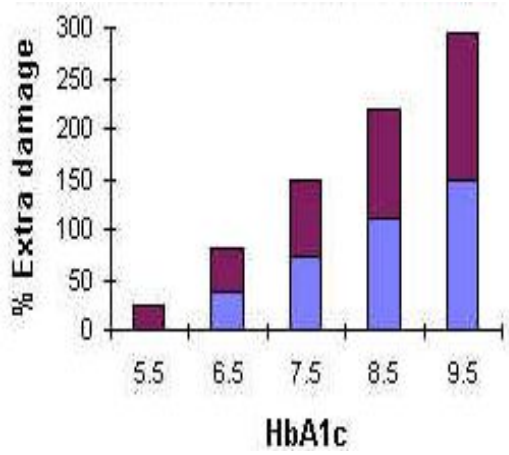

Figure 4a Additional damage from elevated HbA1C levels, with (dark shade) and without (light shade) cigarette smoking (MedWeb 2004)

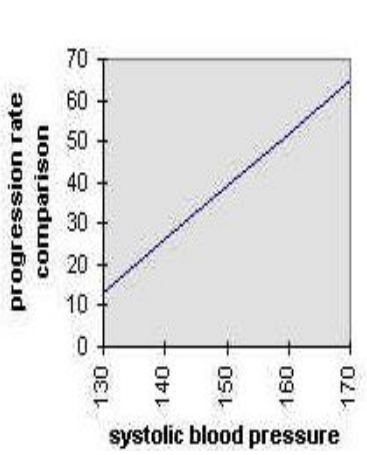

Figure 4b Progression rate of diabetic retinopathy with increasing blood pressure

Clinical need and burden of disease

Type-1 or insulin dependent diabetes mellitus (IDDM) sufferers have a near-total lack of insulin due to the auto-immune destruction of the insulin producing beta cells of the pancreas. IDDM represents approximately 10-15 per cent of all diabetic patients, however 98 per cent of childhood diabetes is IDDM. Type-2 or non-insulin dependent diabetes mellitus (NIDDM) is characterised by reduced levels of insulin or insulin resistance, and represents approximately 85-90 per cent of diabetic sufferers, most of whom are over the age of 40 years. Gestational diabetes is a temporary form of diabetes, which occurs during pregnancy in 3-8 per cent of females not previously diagnosed with diabetes (AIHW 2002).

It is estimated that approximately one million people suffer from one of the three types of diabetes (Type-1, Type-2 and gestational diabetes) in Australia.[3] Gestational diabetes may not be a temporary form of diabetes and may be a significant risk factor for the development of Type II diabetes in later life. In addition, the offspring of women who develop gestational diabetes are at increased risk of developing Type II diabetes in later life. There is currently a lack of reliable incidence and prevalence data for diabetes in Australia. Estimates for the age-standardised prevalence of IDDM for 1999-2000 was 298 per 100,000 or approximately 37,000 individuals over the age of 25 years (AIHW 2002). The National Diabetes Register collects information on the number of new users of insulin since 1999. There were 4,548 new cases of IDDM, aged 0-39 years, for the years 1999-2001, 50 per cent of these cases were children aged 0-14 years (Table 1). The most recent data on the incidence of childhood diabetes in Australia for the years 2000-2001 indicate an

[3] Total population in Australia was 20,122,416 as at June 16, 2004. Source: Australian Bureau of Statistics.

incidence of 20.3 and 18.9 per 100,000 for males and females, respectively (Table 2) (AIHW 2003).

Table 1 New insulin users with Type-1 diabetes, 1999-2001[4]

Age at first use of insulin	Males		Females		Persons	
	Number	Per cent	Number	Per cent	Number	Per cent
0-14	1207	46.7	1092	55.7	2299	50.5
15-24	570	22	389	19.8	959	21.1
25-39	810	31.3	480	24.5	1290	28.4
Total	2587	100	1961	100	4548	100

Source: AIHW 2003

Table 2 New cases of insulin dependent diabetes mellitus amongst 0-14 year olds (rates per 100,000), 2000-2001

Age at first use of insulin	Males	Females
0-4	14.2	11.4
5-9	20.1	21.2
10-14	26.4	23.6
Total	20.3	18.9

Source: AIHW 2003

Of the 21,346 new insulin users on the National Diabetes Register for the years 1999-2001, 12,167 (57%) had Type II diabetes. The majority (90%) of these patients were aged over 35 years (AIHW 2003). The prevalence of Type II diabetes is increasing and has been associated with obesity, poor nutrition and physical inactivity. The Australian population prevalence of Type II diabetes is approximately 7 per cent (Table 3). The prevalence of self-reported Type II diabetes is slightly higher in Indigenous Australians (AIHW 2002), with a tendency towards earlier age of onset, compared to the non-Indigenous Australian population (OATSIH 2001). There is also evidence that substantial undiagnosed disease occurs amongst Indigenous Australians, which may be as high as the number of individuals actually diagnosed (Wakerman & Grundy 2001).

[4] Total population in Australia was 18,972,350 as at August 7, 2001. Source: Australian Bureau of Statistics.

Table 3 Prevalence of persons with non-insulin dependent diabetes mellitus, 1999-2000

Age (years)	Males (%)	Females (%)	Persons (%)
25-34	0.1	0.1	0.1
35-44	2.4	1.9	2.1
45-54	6	5.2	5.6
55-64	16	9.9	13
65-74	21.2	15.5	18.1
75+	20.9	24.4	23
Total	7.6	6.7	7.2

Source: AIHW 2002

The Australian Diabetes, Obesity and Lifestyle study conducted in 1999-2000 found that 15.4 per cent of all people with diabetes (Type I and Type II diabetes) had some degree of DR. The prevalence of DR in this study was 21.9 per cent in those with known Type II diabetes and 6.2 per cent in those people newly diagnosed with diabetes (both types). The prevalence of proliferative DR was 2.1 per cent in people with known Type II diabetes and 1.2 per cent of participants had vision-threatening DR (Tapp et al 2003). Other studies report that approximately 10-15 percent of newly diagnosed Type II diabetes patients have symptoms of DR (NHMRC 1997b). Diabetic retinopathy has become a greater problem in the Type II diabetes population due to the rapidly increasing prevalence of, and delays associated with, diagnosis of Type II diabetes (Taylor 1996). The prevalence of DR was found to increase dramatically with the length of duration of diabetes; a prevalence of 7.4 per cent for people who had diabetes for 0-4 years, 25.6 per cent for those with diabetes for 5-9 years, 33.8 per cent for those with diabetes for 10-19 years and 60.5 per cent for those with diabetes for 20 or more years (AIHW 2002).

There are limited data on the prevalence of diabetic retinopathy in the Aboriginal and Torres Strait Islander population. Jaross et al (2003) conducted a cross-sectional study of the Aboriginal diabetic population in the Katherine region of the Northern Territory in 1993 and again in 1996. The prevalence of DR was 18 per cent in 1993 and 21 per cent in 1996. Of these patients, in 1993 and 1996, 13 and 10 per cent had maculopathy, 8 and 6 per cent had clinically significant macular oedema, 0.9 and 1.3 per cent had proliferative DR and 8.5 and 6.7 per cent had vision-threatening DR, respectively (Jaross et al 2003). Other studies have found that up to 31 per cent of Aboriginal and Torres Strait Islander people have DR. These data are likely to underestimate the magnitude of the DR problem in this community as not all members of these communities are screened. In addition, the Aboriginal and Torres Strait Islander people often have co-morbidities such as elevated blood pressure and diabetic nephropathy, which are both associated with the development and severity of DR (AIHW 2002). In addition, issues such as the diversity and heterogeneous nature of the Aboriginal and Torres Strait Islander people in relation to language, location, perception of health and illness, socioeconomic status and lack of access to appropriate health care may result in delayed diagnosis of Type II diabetes. These delays may result in severe DR being present at the

time of diabetes diagnosis (Wakerman & Grundy 2001). The NHMRC evidence based guidelines for the management of Type II diabetes mellitus (2001) recommends that Aborigines over the age of 35 be tested for type II diabetes. This would involve either a fasting blood plasma glucose level (which may be considered impractical in a rural or remote setting), or a random blood sample. The blood should be analysed in the laboratory not on a glucose meter (NHMRC 2001).

Diabetic retinopathy is the most frequent cause of new cases of blindness amongst the adult population (age 20-74 years) in developed countries. It causes approximately 10 per cent of all blindness in Australia and the majority of these cases are preventable by early detection and treatment with laser therapy (Confos et al 2003). The 1995 National Health Survey in Australia reported that 4.9 per cent of people with diabetes also reported blindness, which was five times the reported rate amongst people without diabetes (AIHW 2002).

The number of public hospital separations in Australia associated with diabetes in 2001-02, was 25,277 (AIHW 2004).[5] In 1999-2000 there were 7,733 hospitalisations for diabetes related eye complications (including retinopathy, glaucoma and cataract), accounting for 2.3 per cent of all diabetes related hospitalisations. Hospitalisation with eye complications tends to increase with age and the average length of stay was 7.5 days (AIHW 2002).

The burden of diabetes in New Zealand is similar to the Australian situation but proportional to the total population.[6] The estimated incidence of Type I diabetes was 25.8 cases per 100,000 persons aged up to 19 years in 2001.[7] The New Zealand National Health Survey estimated the prevalence of known diabetes (including gestational, Type I and Type II diabetes) in persons aged over 15 years in the year 2000 was 111,273. In this survey, the highest prevalence of diabetes occurred amongst Maori (8.3%) and Pacific Island (8.1%) New Zealanders, with Asians and Others (4%) and New Zealanders of European origin (3.1%) having comparatively lower rates. Approximately 60 per cent (or 61, 503) of known diabetics had a free annual diabetes check-up with their general practitioner, in the year 2003. Of these individuals, approximately 60 per cent had been screened for diabetic retinopathy within the past two years, accounting for roughly 36 per cent of all known diabetics in New Zealand.[8] There is currently no information on the number of diabetic persons with DR in New Zealand.

[5] 2,538, 5,418 and 17,321 for the Australian Refined- Diagnosis Related Group numbers K01Z, K60A and K60B, respectively.
[6] Total population in New Zealand was 4,058,921 as at June 16, 2004. Source: Statistics New Zealand.
[7] Lipid and Diabetes Research Group, Christchurch Hospital, New Zealand.
[8] Provided by Sandy Dawson, Chief Clinical Advisor, Health Services, Clinical Services Directorate, Ministry of Health, New Zealand

Stage of development

Fundus photography with mydriatic and non-mydriatic retinal cameras is an established technique in Australia and New Zealand. An advantage of retinal cameras compared to the gold standard of ophthalmoscopy is that a hard copy of the retina is produced for future reference, allowing accurate documentation of disease progression (Taylor 1996). The use of mydriatic retinal cameras does not lend itself to opportunistic screening, as it requires a dedicated room with a camera installed for patients (with dilated pupils) to sit in for 20-30 minutes. In a screening clinic approximately four to five photographs per hour could be taken providing there is one technician dedicated to conducting visual acuity tests and dilating patient pupils, with another technician dedicated to taking photographs (personal communication Dr Mak[9]).

Non-mydriatic cameras however, are portable, easily transportable and are ideal for use in rural or remote settings where trained, non-medical staff are able to perform retinal examinations. Taking retinal photographs is a technical procedure, which is best performed by trained enrolled or registered nurses, Aboriginal health workers or dedicated retinal photographic technicians (personal communication Dr Mak). Photographs produced from these sessions can be sent to a central location to be read by an ophthalmologist (NHMRC 1997a).

Treatment Alternatives

Existing Comparators

The gold standard for the detection and classification of DR is either direct, using a hand held ophthalmoscope or lamp, or indirect, using a slit-lamp biomicroscope. With these techniques, a bright light is shined onto the back of the eye allowing visualisation of the retina and is ideally conducted by an ophthalmologist. Patient's eyes must be dilated when using this technique. Direct ophthalmoscopy has been shown to have poor sensitivity (50%) if conducted by non-ophthalmologists (Williams et al 2004). A meta-analysis conducted by the United Kingdom's National Health Service reported that direct ophthalmoscopy does not usually meet required sensitivity standards (>80%) for retinopathy screening. However, there is limited evidence that professionals using indirect slit-lamp ophthalmoscopy can achieve the required standards. In screening for sight threatening retinopathy, the specificities achieved were higher than 91% (review standard 95%), but there was a much greater spread for sensitivity with only one study reaching the 80% sensitivity standard (NHS 2002). A systematic review by Williams et al (2004) reported that single-field fundus photography, when compared to the gold standard of dilated ophthalmology by an ophthalmologist, has a sensitivity ranging from 38 to 100 per cent and a specificity ranging from 75 to 100 per cent (Williams

[9] Dr Mak is a public health physician, Communicable Disease Control, Health Department of Western Australia and Associate Professor and Head of Population and Preventative Health, University of Notre Dame, Western Australia

et al 2004). Ophthalmoscopy is time consuming, requiring a specialist and as such is not suitable for use as a DR screening tool (Al Sabti et al 2003).

In Australia there is a mal-distribution of qualified ophthalmologists across States and between rural and urban areas. In 1996, 77.5 per cent of ophthalmologists had their primary practice located in a capital city, 9.6 per cent in urban areas and 12.9 per cent in rural and remote areas (Figure 5 and Table 4) (Madden et al 2002).

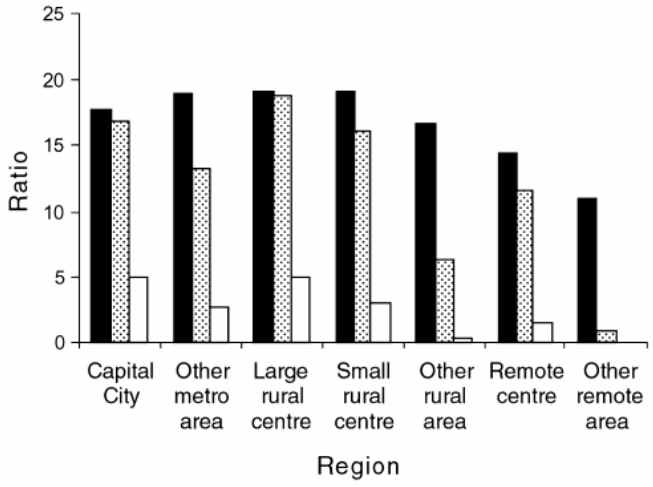

Figure 5 Distribution of optometrists and ophthalmologists in Australia, 1998-1999
■ patients per 100 population, ⊡ optometrists per 100,000 population, □ ophthalmologists per 100,000 population (Madden et al 2002)

Table 4 The proportion of ophthalmology practice sites and the proportion of the population in each setting (1995)

State/Territory	Capital city		Other major urban		Rural		Remote	
	Oph	Pop	Oph	Pop	Oph	Pop	Oph	Pop
New South Wales	77.6	62.3	7.5	11.6	14.2	24.6	0.7	1.5
Victoria	86.1	72.0	2.7	2.6	10.2	24.0	1.1	1.4
Queensland	60.3	45.9	25	20.5	13.8	29.9	0.8	3.7
South Australia	87.3	73.1	NA	NA	11.4	23.6	1.2	3.3
Western Australia	86.4	72.7	NA	NA	13.6	18.5	0.0	8.8
Tasmania	62.5	40.1	18.8	20.6	18.8	33.8	0.0	5.5
Australian Capital Territory	75.0	99.6	NA	NA	25.0	0.4	NA	NA
Northern Territory	100	46.4	NA	NA	0.0	6.8	0.0	46.8

NA = not applicable (Madden et al 2002)

Another technique for detecting DR is stereoscopic colour fundus photography in seven standard fields. This technique is accurate and reliable, however it is time consuming and requires highly skilled photographers and readers, and as such is not considered an ideal screening technique (Williams et al 2004). Fluorescein angiography is the most accurate method of identifying DR. This technique involves the injection of fluorescein dye into a vein in the arm, which circulates to the blood vessels at the back of the eye and photographs are taken for interpretation by an ophthalmologist. Fluorescein angiography is

not considered an ideal modality for screening for DR as it is invasive and may result in complications such as nausea, vomiting, allergic reactions, dizziness and chest pain (NHS 2000a; NHMRC 1997b).

Clinical Outcomes

There is a wealth of information and evidence that supports the effectiveness of screening for diabetic retinopathy in the diabetic population. Screening programs, which result in the early treatment of DR, may prevent substantial disability. A systematic literature review by Bachmann and Nelson (1998) assessed DR screening by ophthalmologists, general practitioners, opticians and technicians using mydriatic and non-mydriatic cameras in a district population of Britain. Pooled data suggested that screening by mydriatic camera by all practitioners was the most sensitive (88%) with other testing modalities ranging from 50 to 65 per cent. Reported screening sensitivity by an optician was 73 per cent and by a general practitioner was 56 per cent. Specificity estimates ranged between 90 to 100 per cent (Bachmann & Nelson 1998).

It has been suggested that the early detection and treatment of DR could prevent 77 per cent of blindness in the diabetic population, although no study has demonstrated a decline in the incidence of blindness directly attributable to a DR screening program. Of those screened, approximately four per cent would be correctly identified as needing treatment during the first screening round and this would decrease to one per cent in subsequent rounds. Of those individuals treated, six per cent would be prevented from going blind within one year of treatment and 34 per cent within 10 years of treatment (Bachmann & Nelson 1998).

Despite the well-established benefits of screening, population-based studies have found that even in urban areas such as Melbourne, where access to ophthalmologists would be greatly increased compared to rural settings, approximately 50 per cent of people with diabetes did not receive adequate DR screening (Harper et al 1998). Lee at al (2001) estimates that only 35 per cent of Victoria's rural diabetic population receive adequate eye examinations (Lee et al 2001). Rural residents are more likely to have consulted an optometrist, not an ophthalmologist (Madden et al 2002).

This report will examine the safety and effectiveness of screening a diabetic population for DR, utilising retinal photographs taken by trained health workers with either mydriatic or non-mydriatic cameras, which in turn are read by ophthalmologists.

Non-mydriatic retinal photography

Six studies reported on outcomes associated with *non-mydriatic* retinal photography for the detection of DR. Of these, three studies were conducted in rural locations, one in a remote location, one in a mixed rural and urban location and one in an urban location.

There were no studies available that assessed the impact of non-mydriatic retinal photography on patient management or on patient outcomes, for example blindness.

Diagnostic accuracy of non-mydriatic retinal photography

Four studies described the diagnostic accuracy of *non-mydriatic*, or physiological dilation, retinal photography for the detection of DR and of these, one study provided level I diagnostic evidence (rural setting), two studies provided diagnostic level II evidence (remote and, combined urban and rural locations) and one study provided level IV diagnostic evidence (urban location) (Table 5).

The high quality study by Gomez-Ulla et al (2002) conducted in a rural area of Spain, reported a good level of agreement between the gold standard of direct ophthalmoscopy and non-mydriatic retinal photography in determining the stage of diabetic retinopathy ($\kappa = 0.92$, 95%CI [0.9, 0.95]) (level I diagnostic evidence). There was complete agreement in the determination of patients without DR, 57/133 (49%), between the two techniques.

The good quality study by Diamond et al (1998) reported a much lower level of agreement between ophthalmoscopy and non-mydriatic retinal photography in determining the stage of diabetic retinopathy ($\kappa = 0.41$) (level II diagnostic evidence), however the comparator was *indirect* ophthalmoscopy rather than the direct method used by Gomez-Ulla et al (2002).

The good quality study (level II diagnostic evidence) by Scanlon et al (2003) reported a sensitivity of 86 per cent and a specificity of 77 per cent for the detection of referable or vision threatening DR using non-mydriatic retinal photography with a mobile unit in a rural and urban location. The positive predictive value for referable DR was 33%, indicating that out of 100 patients who test positive for DR, 33 would be correctly identified as positive. More importantly, this study reports a high negative predictive value (98%) for the detection of referable DR, indicating for every 100 patients screened for DR who test negative, that 98 of these individuals would be correctly identified as being negative. Recalculation of the data to include the detection of all DR (referable and non-referable) results in a sensitivity of 83 per cent, specificity of 65 per cent, and a positive and negative predictive value of 50 and 90 per cent, respectively.

The poor quality study (level IV diagnostic evidence) by Heaven et al (1992) referred only those patients with a suspect retinal photograph for further ophthalmic examination. Of the 100/639 (17.2%) patients referred for a follow-up examination there was agreement between ophthalmoscopy and retinal photography for the grade of DR in 94/200 (47%) of eyes. Ophthalmoscopy determined that a higher proportion of eyes had only background (non-vision threatening) DR compared to retinal photography (43% vs 28%). In addition ophthalmoscopy determined a lower proportion of eyes had maculopathy compared to retinal photography (23% vs 39%). However, the proportion of eyes reported to have more severe DR (pre-proliferative and proliferative DR), and therefore requiring immediate

treatment, were similar for the two techniques (10% and 12% for ophthalmoscopy and retinal photography, respectively).

Table 5 Diagnostic accuracy of non-mydriatic retinal photography

Study	Diagnostic level of evidence	Study design	Study population	Diabetic Retinopathy
Gomez-Ulla et al (2002) Galicia, Spain Examinations conducted in 2 peripheral hospitals Retinal photographs taken by a trained technician and sent electronically to a central location, where reviewed by an independent, blinded ophthalmologist	I	Cross classification of patients on *non-mydriatic* fundus photography and direct ophthalmoscopy	Rural population 140 eyes of 70 consecutive diabetic patients	Direct ophthalmoscopy No DR 57/133 (42.9%) Minimal NPDR 28/133 (21.1%) Moderate NPDR 28/133 (21.1%) Severe NPDR 7/133 (5.3%) PDR without HRC 5/133 (3.8%) PDR with HRC 1/133 (0.8%) Excluded patients 7/133 (5%) Retinal photography No DR 57/133 (42.9%) Minimal NPDR 29/133 (21.8%) Moderate NPDR 30/133 (22.6%) Severe NPDR 9/133 (6.8%) PDR without HRC 0/133 (0%) PDR with HRC 1/133 (0.8%) Excluded patients 7/133 (5%) (patients had poor image quality due to small size of the pupil, vitreous haemorrhage and lens opacity) Level of agreement on stage of DR between 2 techniques: Inter class correlation coefficient $\kappa = 0.92$ 95%CI [0.9, 0.95]

Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic Photographs taken by an ophthalmic photographer and indirect ophthalmoscopy by an ophthalmologist. Retinal photographs were reviewed by a blinded second ophthalmologist.	II	Cross classification of patients on *non-mydriatic* fundus photography and indirect ophthalmoscopy	Remote population 328 eyes in 164 NIDDM Aboriginal people	Detection of DR Combined ophthalmoscopy and retinal photography detected DR in 74/328 (22.6%) of eyes Ophthalmoscopy identified 44/74 (59.5%) eyes with DR Non-mydriatic photography identified 55/74 (74.3%) eyes with DR Level of agreement between 2 techniques: Correlation coefficient κ = 0.41, 95%CI not stated Prevalence of retinopathy 44/164 (26.8%) patients Treatment 35/74 (47.3%) of these eyes required laser treatment Ophthalmoscopy indicated a need for laser treatment in 18/35 (51.4%) eyes Non-mydriatic photography indicated a need for laser treatment in 30/35 (85.7%) eyes 13/35 (37%) of these were indicated for laser treatment by both non-mydriatic photography and ophthalmoscopy
Scanlon et al (2003) Gloucester, United Kingdom Examinations conducted in GP practices by mobile unit. Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis. Retinal photographs read by a blinded ophthalmologist.	II	Cross classification of patients on *non-mydriatic* fundus photography and direct ophthalmoscopy	Urban and rural population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy	Referable DR or VTR Sens 86.0%, 95%CI [80.9, 91.1] Spec 76.7%, 95%CI [74.5, 78.9] PPV 32.7%, 95%CI [28.4, 37.0] NPV 97.7%, 95%CI [96.8, 98.6] All DR [a] Sensitivity 82.9% Specificity 64.6% PPV 49.7% NPV 90%

Heaven et al (1992) Portsmouth, United Kingdom Examinations conducted in Diabetic Day Unit of hospital diabetic clinic Retinal photographs taken by an nurse technician Retinal photographs were reviewed by an independent ophthalmologist	IV	Only patients with a suspect *non-mydriatic* fundus photograph received ophthalmoscopy	Urban population 639 diabetic patients	Diabetic Retinopathy (patients) No DR 425/639 (66.5%) BDR 104/639 (16.3%) Ophthalmoscopy and retinal photography had agreed diagnosis in 94/200 (47%) eyes Retinal photography (eyes) No DR 43/200 (21.5%) BDR 56/200 (28%) Maculopathy 77/200 (38.5%) Pre PDR 19/200 (9.5%) PDR 5/200 (2.5%) Ophthalmoscopy (eyes) No DR 51/200 (25.5%) BDR 85/200 (42.5%) Maculopathy 45/200 (22.5%) Pre PDR 12/200 (6%) PDR 7/200 (3.5%) Referral for follow-up 110/639 (17.2%) patients 100/639 (15.6%) patients returned for follow-up examination Of these patients: 27/639 (4.2%) patients received laser photocoagulation

DR = diabetic retinopathy, NPDR = non-proliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, HRC = high-risk characteristics, NIDDM = non-insulin diabetes mellitus, PPV = positive predictive value, NPV = negative predictive value, VTR = vision threatening diabetic retinopathy, BDR = background diabetic retinopathy

[a] Values for all diabetic retinopathy have been calculated from the raw data by two independent researchers from the NHSU.

Quality of non-mydriatic retinal photographs

Diagnosis of some patients was not possible in several studies due to inadequate or poor image quality, or a lack of accessibility to eyes due to the presence of other pathology in the eye, such as cataracts, or a prosthesis. Five studies reported on the quality of, or the ability to take, non-mydriatic retinal photographs (Table 6). Diamond et al (1998) reported 87 per cent of images were excellent or adequate in a study undertaken on Aboriginal people in the remote Pilbara region of Australia. The study by Scanlon et al (2003) combined data from patients enrolled in the comparative arm of the study with data obtained from patients who had retinal photography alone. The technical failure rate in this study was reported to be 21 per cent. The number of poor or inadequate photographs in the remaining ranged from 9.2 to 21% of all images. The number of eyes that could not be photographed due to the presence of cataracts or a prosthesis ranged from 0.5 to 5.0%. Harper et al (1998) reported that 217 images were non-diagnostic or inadequate images, and 137 (63%) of these were due to the small pupil size of the patient, and that this situation may have been rectified if mydriasis had been employed.

Table 6 Quality of non-mydriatic retinal photographs

Study	Study population	Quality of photographs
Cummings et al (2001) North Carolina, United States Examinations conducted at a number of sites (hospitals, health departments, out-patient clinics and community health centres) with mobile imaging system Retinal photographs taken by a trained ophthalmic technician and sent electronically to a central location, where reviewed by an independent, blinded ophthalmologist	Rural population 193 diabetic patients	Quality of images 85% photographs rated as good or fair by retinal specialist 15% photographs rated as inadequate
Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic. Photographs taken by an ophthalmic photographer and ophthalmoscopy by an ophthalmologist. Retinal photographs were reviewed by a blinded second ophthalmologist.	Remote population 328 eyes in 164 NIDDM Aboriginal people	Quality of images (n= 328) Excellent 177/328 (54.2%) Adequate 108/328 (32.8%) Inadequate 43/328 (13%)
Gomez-Ulla et al (2002) Galicia, Spain Examinations conducted in 2 peripheral hospitals Retinal photographs taken by a trained technician and sent electronically to a central location, where reviewed by an independent, blinded ophthalmologist.	Rural population 140 eyes of 70 consecutive diabetic patients	7/140 (5%) eyes could not be photographed due to the presence of cataracts
Harper, CA et al (1998) La Trobe and Goulburn Valleys, Victoria, Australia Retinal photographs taken by an technician Retinal photographs were reviewed by an independent ophthalmologist	Rural population 2354 eyes in 1177 diabetic patients 209/1177(18%) IDDM 968/1177 (82%) NIDDM	Quality of images (eyes) Excellent 1496/2354 (63.5%) Adequate 630/2354 (26.7%) Non-diagnostic 217/2354 (9.2%) (137/2354 (6%) due to small pupils and 62/2354 (3%) due to media opacity) No photograph 11/2354 (0.5%) due to presence of prosthesis, or severe kyphosis

Scanlon et al (2003) Gloucester, United Kingdom Examinations conducted in GP practices by mobile unit Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs read by a blinded ophthalmologist	Urban and rural population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy 2062 diabetic patients received only non-mydriatic or mydriatic retinal photography	Quality of images (all images) Technical failure rate in 746/3597 (20.7%) patients, 95%CI [18.4, 21.0] Full accessibility to both eyes occurred in 1727/3597 (48%) patients

NIDDM = non-insulin dependent diabetes mellitus

Detection of diabetic retinopathy using non-mydriatic retinal photography

Two studies reported on the detection rate of DR in rural populations utilising non-mydriatic retinal photography (Table 7). Rates of DR detection ranged from 18 to 41%. Only those patients with a suspect fundus photograph were referred for follow-up examination by ophthalmoscopy. Harper et al (1998) reported that no DR was detected in the 122/1177 (10%) patients with an ungradable retinal photograph, who were referred for follow-up ophthalmoscopy.

Table 7 Detection of diabetic retinopathy using non-mydriatic retinal photography

Study	Study design	Study population	Diabetic Retinopathy
Cummings et al (2001) North Carolina, United States Examinations conducted at a number of sites (hospitals, health departments, out-patient clinics and community health centres) with mobile imaging system Retinal photographs taken by a trained ophthalmic technician and sent electronically to a central location, downloaded and reviewed by an independent, blinded ophthalmologist	Case series Only patients with a suspect *non-mydriatic* fundus photograph were referred for indirect ophthalmoscopy	Rural population 193 diabetic patients	79/193 (40.9%) patients with DR Mild or moderate NPDR 37/193 (19.2%) CIMO 15/79 (19%) PDR 4/79 (5%)
Harper, CA et al (1998) La Trobe and Goulburn Valleys, Victoria, Australia Retinal photographs taken by an technician Retinal photographs were reviewed by an independent ophthalmologist	Case series Only patients with an ungradable *non-mydriatic* fundus photograph were referred for indirect ophthalmoscopy	Rural population 2354 eyes in 1177 diabetic patients 209/1177(18%) IDDM 968/1177 (82%) NIDDM	No DR 704/1177 (60%) DR 209/1177 (18%) Ungradable 121/1177 (10%) OP 101/1177 (9%) Referral for follow-up 122/1177 (10%) patients with ungradable photographs were referred for follow-up examination. No DR was detected, however 27/122 (22%) had reduced visual acuity

DR = diabetic retinopathy, NPDR = non-proliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, NIDDM = non-insulin diabetes mellitus, IDDM = insulin dependent diabetes mellitus, OP = other pathology, CIMO = clinically insignificant macular oedema

Mydriatic retinal photography

Thirteen studies reported on outcomes associated with *mydriatic* retinal photography for the detection of DR, and of these, three studies were conducted in remote locations, three in rural locations, five in mixed rural and urban locations, one in an urban and one in an unknown location.

There were no studies available that assessed the impact of mydriatic retinal photography on patient management or on patient outcomes, for example blindness.

Diagnostic accuracy of mydriatic retinal photography

Three of the good quality studies (level II diagnostic evidence) reported values for the sensitivity and specificity of screening for DR utilising mydriatic retinal photography compared to direct ophthalmoscopy (Table 8). Scanlon et al (2003) reported on a mobile screening programme set in urban and rural locations. The sensitivity and specificity for referable or vision threatening DR were 88 and 86 per cent, respectively. The positive and negative predictive values were 45 and 98 per cent respectively. Recalculation of the data to include all DR (referable and non-referable) resulted in a sensitivity and specificity of 87 and 63 per cent, respectively. After recalculation, the positive predictive value increased to 50 per cent, and the negative predictive value decreased to 92 per cent (level II diagnostic evidence).

Griffith et al (1993) reported differences between sensitivity (94% versus 100%) and specificity (82% versus 64%) when an ophthalmologist or retinal specialist, respectively, read the retinal photographs taken from Native American Indians living in a rural setting, compared to the gold standard of direct ophthalmoloscopy. Both the ophthalmologist and retinal specialist recorded low positive predictive values (37% versus 31%), however the negative predictive values were reassuringly high (99% versus 100%) (level II diagnostic evidence).

The study by O'Hare et al (1996) in urban and rural England, compared screening by general practitioners or opticians using either direct ophthalmoscopy alone, ophthalmoscopy combined with retinal photography, or ophthalmoscopy combined with retinal photography with added assistance from an ophthalmologist in interpretation of the retinal photographs. When an ophthalmologist alone reviewed these photographs, the highest sensitivity, specificity and positive and negative predictive values were achieved for referrable, vision threatening DR (level II diagnostic evidence).

The good quality study by Evans et al (1997) reported the detection rate for vision threatening DR was similar for mydriatic retinal photography (87%) compared to direct ophthalmoscopy (100%). However, the detection rate for all types of DR decreased using mydriatic retinal photography (69%) compared to direct ophthalmoscopy (100%) (level II diagnostic evidence). Similarly the study by Diamond et al (1998), conducted in the remote Pilbara region of Australia, reported a 100 per cent agreement between mydriatic

retinal photography and indirect ophthalmoscopy for the detection of DR (level II diagnostic evidence).

Overall, sensitivity ranged from 58 to 100%, specificity from 63 to 99%, positive predictive values from 31 to 88% and negative predictive values from 92 to 100%, in the three good quality studies, which compared mydriatic retinal photography to the gold standard of direct ophthalmoscopy.

A further good quality study by Al Sabti et al (2003) conducted in a clinic in Kuwait, reported a good level of agreement between indirect ophthalmoscopy and mydriatic retinal photography for the determination of DR ($\kappa = 0.93$, 95%CI [0.83, 1.03]) (level II diagnostic level of evidence).

Table 8 Diagnostic accuracy of mydriatic retinal photography

Study	Diagnostic level of evidence	Study design	Study population	Diabetic retinopathy
Al Sabti et al (2003) Retina clinic, Kuwait Retinal photographs taken by the general practitioner or diabetologist Retinal photographs were reviewed by two masked independent retinal specialists	II	Cross classification of patients on *mydriatic* fundus photography and indirect ophthalmoscopy	92 eyes of 51 diabetic patients 5.8% IDDM 94.2% NIDDM	Ophthalmoscopy (eyes) No DR 6/92 (6.5%) Mild NPDR 59/92 (64.1%) Severe NPDR 11/92 (12%) PDR 5/92 (5.4%) HRC PDR 11/92 (12%) Digital photography (eyes) No DR 9/92 (9.8%) Mild NPDR 56/92 (60.9%) Severe NPDR 11/92 (12%) PDR 6/92 (6.5%) HRC PDR 10/92 (10.9%) Level of agreement $\kappa = 0.93$ 95%CI [0.83, 1.03] Concordance for DR was 95.6%, 4/92 eyes discordant in favour of ophthalmoscopy examination

Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic Photographs taken by an ophthalmic photographer and reviewed by a blinded second ophthalmologist Patients underwent indirect ophthalmoscopy after photography by an ophthalmologist	II	Cross classification of patients on *non-mydriatic* fundus photography and indirect ophthalmoscopy Subset of 136 eyes examined with *mydriatic* photography	Remote population 328 eyes in 164 NIDDM Aboriginal people Subset of this group, 136 eyes, examined with mydriatic photography	Mydriatic photography identified 9/136 (6.7%) eyes with retinopathy, which were within the group of 74/328 eyes detected by ophthalmoscopy or non-mydriatic photography. No new cases were detected by mydriatic photography and no cases were missed by mydriatic photography.
Evans et al (1997) Follow-up of study by O'Hare et al (1996) Somerset, United Kingdom Examinations held in mobile "clinic" parked outside of 23 general practice sites Retinal photographs were re-assessed (blinded to original diagnosis) 6 months after initial study where retinal photographs were taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist	II	Cross classification of patients on *mydriatic* fundus photography and direct ophthalmoscopy	Rural and urban population 1010 diabetic patients 517 examined by GP, 493 examined by optician	Sight threatening DR Ophthalmoscopy VTR 77/2014 (3.8%) eyes No VTR 1775/2014 (88%) eyes Retinal photography VTR 67/2014 (3.3%) eyes Detection rate using retinal photography 67/77 (87%) False positive rate 0.3% (5/1775) All diabetic retinopathy Ophthalmoscopy 375/2014 (18.6%) eyes Retinal photography 257/2014 (12.8%) eyes Detection rate of retinal photography 257/375 (69%) False positive rate = 1.6% (23/1477)

Griffith et al (1993) Yakima Native American Indian Reservation, Toppenish, Washington, USA Examinations took place in health centre Retinal photographs taken by trained technician. Direct ophthalmoscopy performed initially by primary care physician. Retinal photographs were reviewed by ophthalmologist or retinal specialists, and some images were read by both	II	Cross classification of patients on *mydriatic* (seven field non-stereoscopic) fundus photography and direct ophthalmoscopy	Rural population 188 Native American diabetic patients, with 243 visits to clinic 134 patients screened once, 53 patients screened twice, 1 patient screened three times	Ophthalmoscopy by primary care physician Sensitivity 100% Specificity 93%, 95%CI [88, 96] PPV 54%, 95%CI [37, 71] NPV 100% Retinal photography Read by ophthalmologist Sensitivity 94%, 95%CI [71, 100] Specificity 82%, 95%CI [75, 88] PPV 37%, 95%CI [22, 53] NPV 99%, 95%CI [96, 100] Read by retinal specialist Sensitivity 100% Specificity 64%, 95%CI [52, 74] PPV 31%, 95%CI [18, 47] NPV 100% Referral for follow-up 93/188 (49%) patients referred 83/93 (89%) referral visits completed
O'Hare et al (1996) Somerset, United Kingdom Examinations held in mobile "clinic" parked outside of 23 GP sites Retinal photographs taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist	II	Cross classification of patients on *mydriatic* fundus photography and direct ophthalmoscopy	Rural and urban population 1010 diabetic patients 517 examined by GP, 493 examined by optician	Ophthalmoscopy 205/1010 (20.3%) patients with DR 49/1010 (4.9%) with referrable DR Retinal photography read by ophthalmologist Non-referrable DR Sensitivity 58% Specificity 90% PPV 82% NPV 90% Referrable DR Sensitivity 71% Specificity 99% PPV 88% NPV 99%

Scanlon et al (2003) Gloucestershire, United Kingdom Examinations conducted in GP practices by mobile unit Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs were read by a blinded ophthalmologist	II	Cross classification of patients on *mydriatic* fundus photography and direct ophthalmoscopy	Urban and rural population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy	Referable DR only Sens 87.8%, 95%CI [83.0, 92.6] Spec 86.1%, 95%CI [84.2, 87.8] PPV 45.4%, 95%CI [40.2, 50.6] NPV 98.2%, 95%CI [97.4, 99] All DR [a] Sensitivity 87.3% Specificity 63.3% PPV 50.1% NPV 92.2%

IDDM = insulin dependent diabetes mellitus, NIDDM = non-insulin diabetes mellitus, DR = diabetic retinopathy, NPDR = non-proliferative diabetic retinopathy, PDR = proliferative diabetic retinopathy, HRC = high-risk characteristics, PPV = positive predictive value, NPV = negative predictive value, VTR = vision threatening diabetic retinopathy, [a] Values for all diabetic retinopathy have been calculated from the raw data by two independent researchers from the NHSU.

Quality of mydriatic retinal photographs

Eight studies reported on the quality of images using mydriatic retinal photography (two in a remote location, two in a rural location and four in a mixed rural and urban population) (Table 9). The study by Scanlon et al (2003) combined data from patients enrolled in the comparative arm of the study with data obtained from patients who had retinal photography alone. The number of poor or inadequate images ranged from 4 to 22%.

The study conducted by Mak et al (2003) in the remote Kimberly region of Australian reported that photographers who had undergone a training scheme and completed credentialing criteria such as administration of mydriatic drops, testing visual acuity, preparing and taking photographs, were more likely to take excellent or adequate photographs than non-credentialed photographers (Pearson χ^2 89.4, df=2, p=0.000). In addition, this study reported that of the 141/744 (19%) patients recommended for ophthalmic follow-up, only 33/141 (23%) had undergone this follow-up within the recommended time frame, highlighting the difficulties of screening and treating patients in remote locations. However, this is contrasted with the good quality study conducted by Griffith et al (1993) in a population of Native American Indians in a rural location, where 93/188 (49%) patients were referred for ophthalmic follow-up and of these 83/93 (89%) had attended their follow-up appointments.

Table 9 Quality of mydriatic retinal photographs

Study	Study population	Quality of photographs
Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic Photographs taken by an ophthalmic photographer and reviewed by a blinded second ophthalmologist Patients underwent indirect ophthalmoscopy after photography by an ophthalmologist	Remote population 328 eyes in 164 NIDDM Aboriginal people Subset of this group, 136 eyes, examined with mydriatic photography	Excellent 102/136 (75%), $p<0.0001$ Adequate 14/136 (10%), $p<0.0001$ Inadequate 20/136 (15%), $p = 0.76$
Evans et al (1997) Follow-up of study by O'Hare et al (1996) Somerset, United Kingdom Examinations held in mobile "clinic" parked outside of 23 general practice sites Retinal photographs were re-assessed (blinded to original diagnosis) 6 months after initial study. Retinal photographs were taken by trained technician/ driver and read by GP then assessed in a single blinded manner by ophthalmologist	Rural and urban population 1010 diabetic patients 517 examined by GP, 493 examined by optician	162/2014 (8%) of images too poor quality to use All of these patients were referred to an ophthalmologist

Gibbins et al (1994) Wales, United Kingdom Examinations held in general practices Retinal photographs were reviewed by ophthalmologist and general practitioner	Rural population 143 diabetic patients 29 (20%) IDDM	Gradable photographs were obtained for 137/143 (95.8%) patients
Jacob et al (1994) Exeter Health Authority Area, United Kingdom Mobile camera travelled to 17 general practices Retinal photographs taken by a trained technician and reviewed by an independent ophthalmologist	Mixed urban and rural population 1050 diabetic patients 170/1050 (16%) Type I 880/1050 (84%) Type II Of these 80/880 (9%) used insulin	81% of photographs were deemed good or excellent
Mak et al (2003) Kimberly region, Australia Examinations conducted in primary health care centres and clinics Retinal photographs taken by either trained nurses, Aboriginal health workers, a medical student and an ophthalmic photographer Retinal photographs were read by an ophthalmologist	Remote population 744 diabetic patients 566 Aboriginal 132 non-Aboriginal 46 unknown 669 individuals had one set of photographs, 66 had two and 4 had three sets	Of the 813 sets of images, only 680 (83.6%) were included for analysis 4 were excluded as were taken during workshop 77 had missing data 52 sets were taken from individuals with other eye pathology which interfered with adequate photography Of the remaining 680 photographs 427/680 (63%) were excellent 198/680 (29%) were adequate 55/680 (8%) were inadequate Of these 55 inadequate photographs, 39/55 (71%) were taken by a non-credentialed photographer Credentialed photographers were more likely to take adequate or excellent photographs than non-credentialed Pearson χ^2 89.4, df=2, p=0.000 Referral for follow-up 141/744 (19%) patients recommended for follow-up Of these only 33/141 (23.4%) had undergone follow-up within the recommended time frame

Owens et al (1998) Newport and Cardiff Brecon and Abergaveny, South and Mid Wales, United Kingdom Examinations held in general practices Retinal photographs taken by the study optometrist, two photographs per eye Retinal photographs were reviewed by two independent ophthalmologists	Urban and rural population 1210 eyes of 605 diabetic patients (266 Urban, 339 Rural 502 with NIDDM 111 with IDDM	1888/2420 (78%) images graded as excellent or good
Reda et al (2003) Waikato region, New Zealand Mobile screening unit Examinations conducted in community centres, marae (Maori community centres), medical centres, hospital outpatient clinics and a local prison Retinal photographs taken by a trained medical photographer, two photographs per eye Retinal photographs were read by an ophthalmologist	Rural population 8,172 diabetic patients screened one or more times 15,555 screening episodes during the period 1993 to 2001	957/15555 (6.2%) images not assessable
Scanlon et al (2003) Gloucestershire, United Kingdom Examinations conducted in GP practices by mobile unit Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs were read by a blinded ophthalmologist	Urban and rural population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy 2062 diabetic patients received only non-mydriatic or mydriatic retinal photography	Technical failure rate in 133/3602 (3.7%) patients, 95%CI [3.1, 4.3] Full accessibility of both eyes occurred in 2884/3602 (80.1%) patients

IDDM = insulin dependent diabetes mellitus, NIDDM = non-insulin diabetes mellitus

Detection of diabetic retinopathy using mydriatic retinal photography

Six studies reported on the detection rate of DR utilising mydriatic retinal photography (Table 10). The two studies by Jacob et al (1994) and Owens et al (1998) were designed as cross-classification studies, however neither study reported patient's ophthalmic results or the level of agreement between the two techniques. Therefore these studies have been considered as case series evidence. Of the remaining four studies, only those patients with a suspect fundus photograph were referred for follow-up examination by ophthalmoscopy.

Rates for the detection of DR ranged from 7.7 to 12.4% in an urban population, from 1.4 to 15.9% in a rural population, and 4.3% and 7.5% in a mixed rural/urban and remote population, respectively.

Only one study, by Villalpando et al (1997), reported on the clinically significant, positive association of duration of diabetes and the presence of severe DR ($p<0.01$).

The study by Gibbins et al (1994) reported on the DR rates as determined by a general practitioner in rural practices reading retinal photographs, as well as by an ophthalmologist's reading of the same photographs. This study also reported the comparison between the two readers, however this Horizon Scanning report is concerned with the safety and effectiveness of ophthalmologists, not the safety and effectiveness of other health workers, reading retinal photographs.[10]

Table 10 Detection of diabetic retinopathy utilising mydriatic retinal photography

Study	Study population	Diabetic Retinopathy	
Gibbins et al (1994) Wales, United Kingdom Examinations held in general practices Retinal photographs were reviewed by ophthalmologist and general practitioner	Rural population 143 diabetic patients 29 (20%) IDDM	Retinal photography, read by ophthalmologist No DR BDR BDRE PDDR PDR Total DR Retinal photography, read by GP No DR BDR BDRE PDDR PDR Total DR	 114/143 (79.7%) 13/143 (9.1%) 8/143 (5.6%) 0/143 (0%) 2/143 (1.4%) 23/143 (16.1%) 91/143 (63.6%) 11/143 (7.7%) 23/143 (16.1%) 5/143 (3.5%) 7/143 (4.9%) 46/143 (32.2%)

[10] Using the ophthalmologist's reading as the reference standard, a GP reading the same photographs produced a sensitivity of 20/23 (87%), 95%CI [66, 97] and specificity of 88/114 (77%), 95%CI [70, 85] for the detection of DR.

Jacob et al (1994) Exeter Health Authority Area, United Kingdom Mobile camera travelled to 17 general practices Retinal photographs taken by a trained technician and reviewed by an independent ophthalmologist	Mixed urban and rural population 1050 diabetic patients 170/1050 (16%) Type I 880/1050 (84%) Type II Of these 80/880 (9%) used insulin	Retinal photography 284/ 1050 (27%) with DR 76/170 (44%) of the Type I diabetics 37/80 (46%) of insulin using Type II diabetics Referral for follow-up 45/1050 (4.3%) referred for VTR 43/45 (95.6%) treated with laser
Owens et al (1998) Newport and Cardiff Brecon and Abergaveny, South and Mid Wales, United Kingdom Examinations held in general practices Retinal photographs taken by the study optometrist, two photographs per eye Retinal photographs were reviewed by two independent ophthalmologists	Urban and rural population 1210 eyes of 605 diabetic patients (266 Urban, 339 Rural 502 with NIDDM 111 with IDDM	Urban (patients) No DR 144/266 (54.1%), 95%CI [48.1, 60.1] BDR 85/266 (32.0%), 95%CI [26.4, 37.6] VTR 33/266 (12.4%), 95%CI [8.4, 16.4] Not graded 4/266 (1.5%) Rural (patients) No DR 193/339 (56.9%), 95%CI [51.7, 62.2] BDR 88/339 (26%), 95%CI [21.3, 30.6] VTR 54/339 (15.9%), 95%CI [12.0, 19.8] Not graded 4/339 (1.2%)
Reda et al (2003) Waikato region, New Zealand Mobile screening unit Examinations conducted in community centres, marae (Maori community centres), medical centres, hospital outpatient clinics and a local prison Retinal photographs taken by a trained medical photographer, two photographs per eye and read by an ophthalmologist	Rural population 8,172 diabetic patients screened one or more times 15,555 screening episodes during the period 1993 to 2001	No DR 12,132/15555 (78%) NVR 1,448/15555 (9.3%) VTR 474/15555 (3.1%) OP 544/15555 (3.5%) Prevalence of VTR by ethnicity Asian 1/105 (0.9%) European 258/10183 (2.5%) Indian 12/259 (4.6%) Maori 136/3161 (4.3%) Unknown 48/1233 (3.9%) Other 3/287 (1%) Pacific Is 16/327 (4.9%) Referral for follow-up 1201/8172 (14.7%) referred

Tennant et al (2000) Fort Vermilion, Alberta, Canada Retinal photographs taken by a trained ophthalmic photographer Images were downloaded, compressed and sent via satellite to a central reading location Retinal specialist read images in a masked manner	Remote population 199 eyes in 100 diabetic patients 93/100 (93%) patients with NIDDM	No DR 122/199 (61%) eyes Microaneurysms 70/199 (35%) eyes Retinal haemorrhage 51/199 (25.6%) eyes Hard exudate 31/199 (15.6%) eyes Cotton wool spots 22/199 (11%) CIMO 12/199 (6%) CSMO 15/199 (7.5%) or 10/100 (10%) of patients Referral for follow-up 10/100 (10%) patients with CSMO referred for laser treatment
Villalpando et al (1997) Mexico Examinations took place in a mobile "clinic" parked outside of a large primary care facility Retinal photographs taken by a trained medical photographer, two photographs per eye Retinal photographs were read by a blinded ophthalmologist in central location	Urban population 220 diabetic patients, 110 male and 110 female 97.6% NIDDM	No DR 134/220 (60.9%), 95% CI [54.5, 67.3] BDR 40/220 (18.2%), 95% CI [13.1, 23.3] PPDR 27/220 (12.3%), 95% CI [8.0, 16.6] PDR 17/220 (7.7%), 95% CI [4.2, 11.2] Ungradable 2/220 (0.9%), 95% CI [0.3, 2.1] Macular Oedema 18/220 (8.2%), 95% CI [4.6, 11.8] 19/220 (8.6%) patients required treatment Duration of diabetes was significantly associated with the presence of severe DR, $p<0.01$ [a]

IDDM = insulin dependent diabetes mellitus, NIDDM = non-insulin diabetes mellitus, DR = diabetic retinopathy, PDR = proliferative diabetic retinopathy, CSMO = clinically significant macular oedema, CIMO = clinically insignificant macular oedema, BDR = background diabetic retinopathy, BDRE = background diabetic retinopathy with exudates, PDDR = pre proliferative diabetic retinopathy, NVR = non-vision threatening diabetic retinopathy, VTR = vision threatening diabetic retinopathy, OP = other pathology

[a] multivariate analysis

Comparison between non-mydriatic and mydriatic retinal photography

Two studies (level II diagnostic evidence) reported on the effectiveness of non-mydriatic compared to mydriatic retinal photography (Table 11). The study by Scanlon et al (2003) conducted by a mobile clinic in urban and rural locations in England, reported that retinal photography with mydriasis was significantly more effective at detecting DR than non-mydriatic retinal photography, when using the same camera apparatus ($p<0.001$). Similarly, the study by Diamond et al (1998) in the remote Pilbara region of Australia, reported that retinal photographs with mydriasis were more likely to be

excellent or adequate for the diagnosis of DR when compared to non-mydriatic retinal photography (p<0.0001).

Table 11 Comparison between mydriatic and non-mydriatic retinal photography

Study	Diagnostic level of evidence	Study design	Study population	Outcome assessed
Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic Photographs taken by an ophthalmic photographer Patients underwent indirect ophthalmoscopy after photography by an ophthalmologist Retinal photographs were reviewed by a blinded second ophthalmologist	II	Cross classification of patients on *non-mydriatic* fundus photography and indirect ophthalmoscopy Subset of 136 eyes examined with *mydriatic* photography	Remote population 328 eyes in 164 NIDDM Aboriginal people Mean age = 48.2 years (range 16-81 years) Mean duration of diabetes = 7.5 years (range 1-35 years)	Quality of images Non-mydriatic (n= 328) Excellent 177/328 (54.2%) Adequate 108/328 (32.8%) Inadequate 43/328 (13%) Mydriatic (n= 136) Excellent 102/136 (75%) p<0.0001 Adequate 14/136 (10%) p<0.0001 Inadequate 20/136 (15%) p =0.76
Scanlon et al (2003) Gloucestershire, United Kingdom Examinations conducted in GP practices by mobile unit Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs were read by a blinded ophthalmologist	II	Cross classification of patients on non-*mydriatic*, *mydriatic* fundus photography and direct ophthalmoscopy	Urban and rural population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy 2062 diabetic patients received only non-mydriatic or mydriatic retinal photography	Detection rate of DR Non-mydriatic 10.6% Mydriatic 13.5% Difference 2.9% (p<0.001)

DR = diabetic retinopathy, GP = general practitioner, NIDDM = non-insulin dependent diabetes mellitus

Safety

Failure to detect diabetic retinopathy

Seven studies reported on safety, and more explicitly, the failure of retinal photography to detect diabetic retinopathy (Table 12). No studies reported on safety outcomes associated with pupil dilation, although most investigators advised patients not to drive immediately after a mydriatic examination of their pupils and that they may experience a transient degree of discomfort and blurring.

Mydriatic retinal photography failed to detect DR in 3/86 (3.5%) of cases in the study conducted by Al Sabti et al (2003) in Kuwait, to 118/375 (31%) of cases in the study by Evans et al in rural and urban England. The good quality study conducted by Diamond et al (1998) in the remote Pilbara region of Australia, reported that non-mydriatic retinal photography failed to detect 19/74 (25.7%) cases of DR, however in the same study, the gold standard, ophthalmoscopy, failed to detect 30/74 (40.5%) of DR cases.

One of the obvious safety outcomes in any screening study is the number of false positives and false negatives. Patients diagnosed as having DR with retinal photography should then undergo an examination by an ophthalmologist, which should detect any false positive patients, thus preventing the patient undergoing unnecessary laser surgery or treatment. However, false negatives are more worrying, as these patients will return to their communities with the false reassurance that they are disease free. These patients may not report back to clinicians for further eye examinations for up to two years, during which time irreversible damage may occur to the retina, with serious long-term consequences for the patient.

The number of false positives reported in the good quality studies (level II diagnostic evidence) ranged from 0.3 to 16% for the detection of vision threatening DR and from 1.6 to 37% for all DR, when mydriatic retinal photography is utilised. The number of false negatives reported in these studies ranged from 12 to 29% for the detection of vision threatening and from 0 to 42% for all DR when using mydriatic retinal photography. Only the study by Scanlon et al (2003) reported false positive and false negative rates for vision threatening (23% and 14%) and all DR (35% and 17%), respectively, when using non-mydriatic retinal photography.

In addition, a case series by Gibbins et al (1994) reported 18.2 per cent false positives and 21 per cent false negatives (2.1%) when mydriatic retinal photographs are read by general practitioners, compared to ophthalmologists (data not included in table).

Table 12 Failure to detect diabetic retinopathy

Study	Study design	Study design	Study population	Outcome assessed
Non-mydriatic retinal photography				
Diamond et al (1998) Pilbara region, Australia Examinations conducted in local health clinic Photographs taken by an ophthalmic photographer. Patients underwent indirect ophthalmoscopy after photography by an ophthalmologist. Retinal photographs reviewed by a blinded second ophthalmologist.	Diagnostic level of evidence II	Cross classification of patients on *non-mydriatic* fundus photography and indirect ophthalmoscopy Subset of 136 eyes examined with *mydriatic* photography	Remote population 328 eyes in 164 NIDDM Aboriginal people Mean age = 48.2 years (range 16-81 years) Mean duration of diabetes = 7.5 years (range 1-35 years)	False negative rate of ophthalmoscopy = 30/74 (40.5%) (cases of DR that were identified by retinal photography) False negative rate of non-mydriatic retinal photography = 19/74 (25.7%) (cases of DR that were identified by ophthalmoscopy)
Heaven et al (1992) Portsmouth, United Kingdom Examinations conducted in Diabetic Day Unit of hospital diabetic clinic Retinal photographs taken by an nurse technician Retinal photographs were reviewed by an independent ophthalmologist	Diagnostic level of evidence IV	Patients with a suspect *non-mydriatic* fundus photograph were referred for indirect ophthalmoscopy	Urban population 639 diabetic patients	False negative rate of non-mydriatic retinal photography = 6/639 (0.9%), not referred as suspect during study, however but found to have DR at ophthalmic follow-up
Mydriatic retinal photography				

Al Sabti et al (2003) Retina clinic, Kuwait Retinal photographs taken by a GP or diabetologist. Retinal photographs reviewed by two masked independent retinal specialists	Diagnostic level of evidence II	Cross classification of patients on *mydriatic* fundus photography and indirect ophthalmoscopy	92 eyes of 51 diabetic patients 5.8% IDDM 94.2% NIDDM Mean duration of diabetes 15.3 years, (range 3-35 years)	Mydriatic retinal photography False negative rate = 3/86 (3.5%)
Evans et al (1997) Follow-up of study by O'Hare et al (1996) Somerset, United Kingdom Examinations held in mobile "clinic" parked outside of 23 general practice sites Retinal photographs were re-assessed (blinded to original diagnosis) 6 months after initial study where retinal photographs taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist	Diagnostic level of evidence II	Cross classification of patients on *mydriatic* fundus photography and direct ophthalmoscopy	Rural and urban population 1010 diabetic patients 517 examined by GP, 493 examined by optician	Mydriatic retinal photography failed to detect 118/375 (31%) of DR cases detected by ophthalmoscopy Retinal photography Referable DR False positive rate 0.3% (5/1775) All diabetic retinopathy False positive rate = 1.6% (23/1477)

Griffith et al (1993) Yakima Native American Indian Reservation, Toppenish, Washington, USA Examinations took place in health centre. Retinal photographs taken by trained technician and reviewed by ophthalmologist or retinal specialists.	Diagnostic level of evidence II	Cross classification of patients on *mydriatic* (seven field non-stereoscopic) fundus photography and direct ophthalmoscopy	Rural population 188 Native American diabetic patients, with 243 visits to clinic 134 patients screened once, 53 patients screened twice, 1 patient screened three times	Diabetic retinopathy Ophthalmoscopy False Positive 7% False Negative 0% Retinal photography Read by ophthalmologist False Positive 18% False Negative 6% Read by retinal specialist False Positive 36% False Negative 0%
O'Hare et al (1996) Somerset, United Kingdom Examinations held in mobile "clinic" parked outside of 23 GP sites Retinal photographs taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist	Diagnostic level of evidence II	Cross classification of patients on *mydriatic* fundus photography and direct ophthalmoscopy	Rural and urban population 1010 diabetic patients 517 examined by GP, 493 examined by optician	Diabetic retinopathy Retinal photography Referrable DR False Positive 1% False Negative 29% Non-referrable DR False Positive 10% False Negative 42%

Both non-mydriatic and mydriatic retinal photography				
Scanlon et al (2003) Gloucestershire, United Kingdom Examinations conducted in GP practices by mobile unit Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs were read by a blinded ophthalmologist	Diagnostic level of evidence II	Cross classification of patients on non-*mydriatic*, *mydriatic* fundus photography and direct ophthalmoscopy	Rural and urban population 1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy 2062 diabetic patients received only non-mydriatic or mydriatic retinal photography	Referable DR Non-mydriatic photography False positive 318/1363 (23.3%) False negative 25/179 (14%) Mydriatic photography False positive 190/1369 (15.9%) False negative 22/180 (12.2%) All DR [a] Non-mydriatic photography False positive 384/1085 (35.4%) False negative 78/457 (17.1%) Mydriatic photography False positive 400/1089 (36.7%) False negative 58/460 (12.6%)

DR = diabetic retinopathy, IDDM= insulin dependent diabetes mellitus, NIDDM= non-insulin dependent diabetes mellitus, GP = general practitioner

[a] Values for all diabetic retinopathy have been calculated from the raw data by two independent researchers from the NHSU.

Potential Cost Impact

Cost Analysis

The study by Lee et al (2001) examined the costs of conducting a mobile screening programme in rural Victoria, Australia, utilising non-mydriatic retinal photography. Photographs were taken by trained non-medical staff and reported on by an ophthalmologist. This study aimed to screen those individuals with diabetes who had *not* had their eyes examined in the previous two years, a figure estimated to be 35 per cent of the rural diabetic population. Costs were categorised as either capital costs (purchase of camera, vehicle, analyser, computers, software and a printer) or as recurrent costs (staff salaries, vehicle running costs, equipment maintenance, Polaroid film and medical disposables).

As this study was performed in 2001, costs quoted were converted to $AUD for the first half of 2004 using the Consumer Price Index (ABS 2004). Charges to the Medicare Benefits Schedule for optometrist and ophthalmologist attendances were also updated to July 2004 (MBS 2004). The perspective used by the study was the costs realised by the Australian Health budget. After the introduction of the mobile screening programme, the study by Lee et al (2001) determined the cost per person tested would be $45 AUD, assuming that 80 per cent of people with diabetes were tested. The report also assumed that in this situation the mobile screening program was operating at 100 per cent

efficiency, ie. all available screening appointments were filled by patients. However, if the screening program operated at only 60 to 40 per cent efficiency, the cost per person tested would rise to $72 and $110 AUD respectively. In comparison, the cost of an initial visit to the optometrist would be $50.15 AUD (MBS item number # 10900) and a visit to the ophthalmologist as a result of a referral by a general practitioner would be $89.15 AUD (MBS item number # 104 and 23 respectively) (Lee et al 2001).

The cost-effectiveness of any screening programme depends on the disease prevalence, compliance to the programme, the sensitivity and specificity of the screening method and cost. A recent cost-effectiveness study by James et al (2000) compared a systematic screening programme, utilising a mobile unit visiting inner city general practices to perform mydriatic retinal photography, to opportunistic screening available through general practitioners, optometrists and diabetiologists using ophthalmology. Costs for this study have been converted to 2004 $AUD using the Purchasing Power Parities and Consumer Price Index (ABS 2004). The study by James et al (2000) was conducted in the city of Liverpool (United Kingdom) with an estimated DR prevalence of 14.1 per cent. Compliance, sensitivity, specificity and costs varied for the two different programmes. The cost per true positive detected of the systematic mobile screening programme was $474 (sensitivity 89%, specificity 86%, compliance 80%, annual cost $238,341) and of the opportunistic screening programme was $656 (combined sensitivity 63%, specificity 92%, compliance 78%, annual cost $228,081). The incremental cost-effectiveness of completely replacing the opportunistic screening programme was $73 per person. A sensitivity analysis revealed the effect of varying the prevalence of DR on the cost-effectiveness of screening. If the prevalence of DR fell, then the cost-effectiveness of both the opportunistic and systematic programmes was reduced. At all prevalence levels the systematic screening programme is more cost-effective than the opportunistic programme, despite the opportunistic programme being less expensive.

Compliance with screening programmes has a similar effect on the cost-effectiveness of detecting a true positive. The cost-effectiveness for the systematic programme improves when compliance increases from 30 per cent ($1105) to 100 per cent ($400). In addition, by increasing the number of individuals screened in the systematic programme the cost-effectiveness will improve despite increased overall costs. In this study, if the number of individuals screened increased to 6,000 it would cost a total of $317,473 and $340,436 for systematic and opportunistic screening, respectively. The cost per screen event for the systematic programme would fall from $59 to $52 and the cost-effectiveness would improve to $422. Systematic, compared to opportunistic screening, produces a saving of $98 per true positive case detected (James et al 2000).

Many of the papers included in this assessment for safety and effectiveness reported estimates of the cost of screening each patient based on the results of their studies. The good quality study by Griffith et al (1993) (diagnostic level of evidence II) estimated the costs of screening and diagnosing 100 patients by ophthalmology, retinal photography and ophthalmology by general practitioners. Referring all patients annually to an ophthalmologist would cost

$15,488, however performing retinal photography on the same patients would cost between $8698 to $10,092. It is unclear, however, if costs estimates for retinal photography include those associated with referring positive or suspect patients to an ophthalmologist. These costs are expressed in 2004 $AUD and did not include costs for transportation, training, equipment or other direct of indirect costs. Other studies such as Jacob et al (1994) and O'Hare et al (1996) (diagnostic level of evidence II) estimate the cost per patient screened to be $29 and $32, respectively in 2004 $AUD.

The current cost of purchasing a Canon digital retinal camera is approximately A$33,000. Accessories needed for the operation of a retinal camera as a mobile unit would include a flight case (A$1500), table (A$1500) and minimal software (A$8500). In addition a service contract for maintenance of a camera would cost approximately A$1000 per year in the city and A$1500 per year elsewhere (personal communication OptiMed, Canon Medical Camera Distributors).

Ethical Considerations

The possibility of screening for diabetic retinopathy using retinal photography raises a number of important ethical issues. First, the diverse results from studies comparing both mydriatic and non-mydriatic photography to ophthalmoscopy indicate that it will be difficult, if not impossible, to provide patients with precise information about the implications of their test results.

Second, once patients receive the results of testing they will be faced with difficult decisions about whether to proceed with further testing and treatment. Based on the best evidence available, 50-67 per cent of patients who test positive when screened using *non-mydriatic* retinal photography will turn out not to be diseased. People from remote and rural locations, especially Aboriginal and Torres Strait Islander peoples, may make unsettling journeys to regional centres for ophthalmoscopic testing which may turn out to be unnecessary.

Even for people who do have diabetic retinopathy, receiving a diagnosis will not always be a benefit. Some patients will find the experience of referral to an ophthalmologist in a regional centre, and perhaps transfer to a still more distant centre away from the support of family and friends distressing. Health workers will need to face the possibility that patients who screen positive may choose *not* to leave their communities for further testing or treatment.

The issues noted above focus on the ethical significance of screening for the individual patient. There are also societal issues to address. On a population level, if screening for diabetic retinopathy is offered to a rural or remote population the need to confirm the results of tests and/or treat disease will create extra financial and social burdens for service providers. Patients will need to be supported to travel to, and stay in regional centres.

Finally, the primary ethical justification for screening is that early detection and treatment will decrease mortality and morbidity below what it would have been had the disease not been detected and treated early. Similarly early detection and treatment should increase the patient's quality of life. Although many screening programs do meet this criterion, there are no long term data to demonstrate that this would be the case for using retinal photography to screen for diabetic retinopathy.

Training and Accreditation

Training

A person in Australia or New Zealand intending to become a specialist ophthalmologist must first complete an undergraduate medical degree and qualify to apply for registration with a State Medical Board or the Medical Council of New Zealand. To specialise in ophthalmology, the medical graduate must undertake the specialist postgraduate professional qualification, the Diploma of Fellowship of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO). The College sets the following pre-requisites for a person to be eligible to apply to enter its postgraduate program:

- possess medical qualifications registrable in Australia or New Zealand
- complete at least two years of postgraduate pre-vocational medical and surgical training (including the intern year) in hospitals approved by the College
- pass written and practical examinations in the basic ophthalmic sciences, conducted by the College (the Part I Fellowship Examination)
- apply and secure, through application to a hospital employing authority, appointment to an accredited ophthalmology training post (The College coordinates first year hospital appointments through the National Ophthalmology Matching Program).

A person who has satisfied these pre-requisites is eligible to apply for the College vocational training program by becoming a Trainee Associate Member of the College. Upon acceptance by the College of his/her application, the first year Trainee enters a training program that will take a minimum of four years to complete. During the first three years, the Trainee works in accredited vocational training posts. Specialist ophthalmologists (usually College Fellows) supervise the medical and surgical experience of each Trainee. After satisfactory completion of at least two years of vocational training as judged by the Censor-in-Chief, the Trainee is expected to sit and pass the Part II Fellowship Examination in Ophthalmology and Clinical Ophthalmic Pathology. Having passed the Part II Examination and satisfactorily completed at least three years in accredited posts, the Trainee is considered ready for the final year, where they are expected to broaden their specialist experience in final preparation for graduation and to function in the community as an independent ophthalmologist. The Trainee may work in a

specialist accredited post, or seek College approval to work in a specialist clinical or research position in Australia or overseas (RANZCO 2002).

There is no national, mandatory training program for non-ophthalmologists, such as general practitioners, practice nurses, diabetes educators and community health workers, to take non-mydriatic retinal photographs. Training appears to occur in an *ad hoc* manner depending on the type of screening program implemented by each State or health service. General practitioners undertake training during their medical training. In addition, the RANZCO runs a regular up-skilling program for general practitioners, which includes training on a user's needs basis, such as the detection of glaucoma or the treatment of penetrative eye injuries, but to date this program has not included training in the screening of DR (personal communication, RANZCO). Training general practitioners in small practices to use retinal cameras would be of little value as the technique is time consuming and requires regular use to maintain the skills acquired. Taking retinal photographs is a technical procedure, which is best performed by trained enrolled or registered nurses, Aboriginal health workers or dedicated retinal photographic technicians (personal communication, Dr Mak[11]).

The National Health Service (United Kingdom) has produced a set of guidelines for the suggested training and accreditation schedule for medical and non-medical personnel wishing to undertake retinal photography. The course would consist of five days intensive training including anatomy, basics of diabetic eye disease, technological aspects of screening including fundus photography, camera maintenance and screening for DR. All candidates would be expected to pass the exit examination and to produce high quality photographs of patient eyes (NHS 2000b).

Clinical Guidelines

The current National Health and Medical Research Council clinical guidelines for the management of diabetic retinopathy were written in 1997 and are currently under review. These guidelines recommend yearly or 2-yearly examination of all people with diabetes for diabetic retinopathy by trained personnel. Examinations should commence at time of diabetes diagnosis, however for children diagnosed prior to onset of puberty, examinations should commence at puberty. Where feasible, general practitioners, optometrists and physicians should be provided with appropriate and regular training to screen for diabetic retinopathy using a dilated fundus examination, combined with visual acuity assessment. Referral to an ophthalmologist may not be necessary if minimal non-proliferative diabetic retinopathy (NPDR) is detected and vision is normal. Referral to an ophthalmologist should occur if mild, moderate or severe NPDR is detected, if the fundus is unable to be examined, or if the patient's vision has deteriorated. Once minimal or mild NPDR is detected, patients should be examined every six to twelve months, and every three to six months if moderate or severe NPDR is detected. If proliferative

[11] Dr Mak is a public health physician, Communicable Disease Control, Health Department of Western Australia and Associate Professor and Head of Popualtion and Preventative Health, University of Notre Dame, Western Australia

diabetic retinopathy or macular oedema is detected the patient should be referred to an ophthalmologist immediately for treatment (NHMRC 1997b). Only 43 per cent of diabetics in the general Australian population received management that complied with these screening recommendations (OATSIH 2001).

In the Aboriginal and Torres Strait Islander diabetic population, screening is recommended annually due to the higher risk in this group. There are a number of barriers to screening this population for DR, including distance from facilities and lack of follow-up and referral due to long delays between visiting ophthalmologists (OATSIH 2001). The 1997 report on eye health in the Aboriginal and Torres Strait Islander community made three recommendations: (i) that regionally based non-mydriatic fundus cameras and portable laser equipment be made available by State and Territory governments to primary health care workers; (ii) that clinical practice guidelines include annual eye examinations in this community; and (iii) that a Medicare item number be provided for photographic screening for DR by health workers other than an ophthalmologist (Taylor 1997; McCarty 2003).

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon Scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

An Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, an Horizon Scanning Report is a ‘state of play’ assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of retinal photography undertaken by health workers and read by ophthalmologists, its present and potential use in the Australian public health system, and future implications of the use of this procedure.

Search Strategy used for the Report

The medical literature (Table 13) was searched utilising the search terms outlined in Table 14 to identify relevant studies and systematic reviews, until August 2004. In addition, major international health assessment databases were searched.

Table 13 Literature sources utilised in assessment

Source	Location
Electronic databases	
AustHealth	University library
Australian Medical Index	University library
Australian Public Affairs Information Service (APAIS) - Health	University library
Cinahl	University library
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	University library
Current Contents	University library
Embase	Personal subscription
Pre-Medline and Medline	University library
ProceedingsFirst	University library
PsycInfo	University library
Web of Science – Science Citation Index Expanded	University library
Internet	
Current Controlled Trials metaRegister	http://controlled-trials.com/
Health Technology Assessment international	http://www.htai.org
International Network for Agencies for Health Technology Assessment	http://www.inahta.org/
Medicines and Healthcare products Regulatory Agency (UK).	http://www.medical-devices.gov.uk/
National Library of Medicine Health Services/Technology Assessment Text	http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
National Library of Medicine Locator Plus database	http://locatorplus.gov
Trip database	http://www.tripdatabase.com
U.K. National Research Register	http://www.update-software.com/National/
US Food and Drug Administration, Center for Devices and Radiological Health.	http://www.fda.gov/cdrh/databases.html
Websites of Specialty Organisations	Dependent on technology topic area

Table 14 Search terms utilised

Search terms
MeSH
Diabetic retinopathy; health services, indigenous; rural health, rural population
Text words
Diabetic retinopathy; health services, indigenous; rural health, rural population
Limits
English

Availability and Level of Evidence

Seventeen studies were included in this report to assess the safety and effectiveness of trained health workers taking retinal photographs, which were then read by an ophthalmologist to detect the presence of diabetic retinopathy. Profiles of these studies are provided in Appendix B.

Six studies reported on outcomes associated with non-mydriatic retinal photography for the detection of retinopathy. Of these, four studies reported on the diagnostic accuracy of non-mydriatic retinal photography (one study was level I, two were level II and one was level IV diagnostic evidence) (Table 5). Five studies reported on the quality of, or the ability to take, non-mydriatic retinal photographs (Table 6) and two studies reported on the detection of DR using non-mydriatic retinal photography (Table 7).

Thirteen studies reported on outcomes associated with mydriatic retinal photography for the detection of retinopathy. Of these, six studies (all level II diagnostic evidence) reported on the diagnostic accuracy of mydriatic retinal photography (Table 8). Eight studies reported on the quality of, or the ability to take, mydriatic retinal photographs (Table 9) and six studies reported on the detection of DR using mydriatic retinal photography (Table 10).

Two studies reported on the effectiveness of non-mydriatic compared to mydriatic retinal photography (Table 11). Seven studies reported on safety, and more explicitly, the failure of retinal photography to detect diabetic retinopathy (Table 12). Two of these studies reported on outcomes of non-mydriatic retinal photography (one was level II and one was level IV diagnostic evidence). Four studies reported on the safety outcomes of mydriatic retinal photography (all level II diagnostic evidence). One study compared safety outcomes of both non-mydriatic and mydriatic retinal photography. Several studies reported on the sensitivity of retinal photography compared to the "gold standard" of ophthalmoscopy but didn't provide the raw data to enable the reporting of numbers of patients with a missed diagnosis. See Appendix B for diagnostic levels of evidence.

Sources of Further Information

The 1997 National Health and Medical Research Council clinical guidelines for the management of diabetic retinopathy are currently under review.

Conclusions

The current "gold standard" for the detection of diabetic retinopathy in Australia is an ophthalmoscopic examination performed by an ophthalmologist. There is a short supply of ophthalmologists in Australia, with the majority servicing well-populated urban centres. Retinal photography has been recognised as a viable alternative to direct or indirect ophthalmology.

Retinal photography may be performed with or without mydriasis, however it has been suggested that mydriasis may be a barrier to undertaking a screening programme. This report has assessed the safety and effectiveness of detecting diabetic retinopathy utilising trained health workers to take retinal photographs, which are in turn read by an ophthalmologist.

Three good quality studies assessed in this report described the detection of diabetic retinopathy using *non-mydriatic* retinal photography in remote, rural and urban populations. However, of these studies, only one reported on the diagnostic accuracy of the technique (Scanlon et al 2003). It would appear from this study that non-mydriatic retinal photography is more accurate at detecting referable or vision threatening diabetic retinopathy than it is for detecting all forms of diabetic retinopathy, with improved sensitivity, specificity, negative predictive values but a decreased positive predictive value.

Similarly, *mydriatic retinal photography* was more accurate at detecting referable or vision threatening retinopathy than *all* types of retinopathy (background, maculopathy, pre-proliferative and proliferative). A good level of agreement was reported between ophthalmoscopy and mydriatic retinal photography.

It is difficult to determine from the above results whether *mydriatic* or *non-mydriatic* retinal photography by trained health workers is the most effective tool for the diagnosis of diabetic retinopathy. To be effective, a diabetic retinopathy screening programme should aim to achieve a sensitivity of at least 60%, a requirement that both of these methods satisfies (NHMRC 1997). Two good quality studies compared both *mydriatic* and *non-mydriatic* retinal photography, using the same camera, to ophthalmoscopy. Scanlon et al (2003) reported that retinal photography with mydriasis was significantly more effective at detecting diabetic retinopathy than non-mydriatic photography ($p<0.001$). The rate for correctly identifying patients with referable diabetic retinopathy, the positive predictive value, increased from 33 to 45 per cent when mydriasis was utilised. Similarly, the study by Diamond et al (1998) in the remote Pilbara region of Australia, reported that retinal photographs with mydriasis were more likely to be excellent or adequate for the diagnosis of DR when compared to non-mydriatic retinal photography ($p<0.0001$).

There was great variation in the rate of false positive and false negative diagnoses of referable diabetic retinopathy utilising *mydriatic* retinal photography. Similar rates were reported with non-mydriatic retinal photography. However, false positive and false negative rates increased markedly for both types of retinal photography when detecting *all* types of retinopathy. It is unclear, therefore, that diabetic patients diagnosed with retinopathy by retinal photography should then undergo ophthalmoscopy for confirmation of the diagnosis, thus preventing unnecessary treatment. False negative rates for the detection of *all* types of diabetic retinopathy ranged from 13 to 42 per cent. False negative results may give false reassurance to the patient that they are disease free. These patients may not return to their clinicians for further examination for another two years, during which time

irreversible damage may occur to the retina, resulting in serious long-term consequences for the individual.

The number of inadequate or ungradable images is an issue with retinal photography, as patients who are unable to be diagnosed are treated as positive and referred to an ophthalmologist for further assessment. The number of ungradable images in both *mydriatic* and *non-mydriatic* studies ranged from 3.7 to 22%. Providing thorough training for health workers in the technique of taking retinal photographs, with or without mydriasis, is obviously important. The study by Mak et al (2003) reported that it was more likely an excellent or adequate photograph would be taken by a credentialed photographer than by a non-credentialed photographer (p=0.001).

There were no studies available that assessed the impact of either non-mydriatic or mydriatic retinal photography by trained health workers on patient management or on outcomes such as blindness. This is an area where research would be beneficial.

The cost-effectiveness of any screening programme depends on the disease prevalence, compliance to the programme, the sensitivity and specificity of the screening method and cost. The prevalence of diabetic retinopathy is particularly relevant for Aboriginal populations, where the prevalence of diabetes and therefore possibly diabetic retinopathy, is higher compared to other Australian populations. Two studies found that screening with either mydriatic or non-mydriatic retinal photography by a mobile clinic in rural areas was cost-effective.

The committee noted that the studies demonstrated a generally high negative predictive value but also a high rate of inadequate photography and a low positive predictive value. As a result, a significant number of referrals to ophthalmologists are likely to be generated for exclusion of DR. The technology is probably not suitable for general population screening but may be useful for screening of specific groups.

Appendix A Levels of Evidence

Designations of diagnostic levels of evidence

Level of evidence	Criteria
I	An independent, masked comparison with reference standard among an appropriate population of consecutive patients
II	An independent, masked comparison with reference standard among non-consecutive patients or confined to a narrow population of study patients
III	An independent, masked comparison with an appropriate population of patients, but reference standard not applied to all study patients
IV	Reference standard not applied independently or masked
V	Expert opinion with no explicit critical appraisal, based on physiology, bench research, or first principles

From:
Bandolier Extra. Evidence-based health care (2002). Evidence and diagnostics (Bandolier Extra 2002).

Designations of levels of evidence

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

Modified from:
National Health and Medical Research Council (1999). *A guide to the development, implementation and evaluation of clinical practice guidelines* (NHMRC 1999).

Appendix B Profiles of studies

Profiles of studies included in report

Study	Location	Study design	Study population	Study details	Outcome assessed
Al Sabti, K Raizada, S Wani, VB Al Ajmi, M Gayed, I Sugathan, TN (2003)	Retina clinic, Kuwait	Cross classification of patients on mydriatic fundus photography and indirect ophthalmoscopy Diagnostic level of evidence II	92 eyes of 51 diabetic patients 5.8% IDDM 94.2% NIDDM Mean duration of diabetes 15.3 years, (range 3-35 years)	Camera: Canon CF 60 UV digital *Mydriasis used* Patients underwent indirect ophthalmoscopy before retinal photography Retinal photographs taken by GP or diabetologist Retinal photographs reviewed by two masked independent retinal specialists	Detection of retinopathy Agreement between ophthalmology and retinal photography
Cummings, DM Morrissey, S Barondes, MJ Rogers, L Gustke, S (2001)	Rural North Carolina, United States Examinations conducted at different sites (hospitals, health departments, outpatient clinics and community health centres)	Case series Intervention level of evidence IV	316 patients 193 diabetic patients 123 non-diabetic patients	Camera: Canon CR5-45NM *Non-mydriatic* Retinal photographs taken by a trained ophthalmic technician, two photographs per eye Retinal photographs sent electronically to central location, downloaded and reviewed by an independent, blinded ophthalmologist	Detection of retinopathy Quality of images

Diamond, JP McKinnon, M Barry, C Geary, D McAllister, IL House, P Constable, IJ (1998)	Remote: Pilbara region, Western Australia, Australia Examinations conducted in local clinic	Cross classification of patients on non-mydriatic fundus photography and indirect ophthalmoscopy Diagnostic level of evidence II	328 eyes of 164 NIDDM diabetic Aboriginal people Mean duration of diabetes 7.5 years, (range 1-35 years)	Camera: Canon CR5-45NM *Non-mydriatic* Retinal photographs taken by an ophthalmic photographer Patients underwent indirect ophthalmoscopy after retinal photography by an ophthalmologist Retinal photographs were reviewed by a blinded second ophthalmologist	Detection of retinopathy Agreement between ophthalmology and retinal photography Quality of images
Evans, PMS Purewal, TS Hopper, A Slater, H Jones, DRL O'Hare, JP (1997) Follow-up of study by O'Hare et al (1996)	Rural and urban Somerset, United Kingdom Examinations conducted in mobile "clinic" parked outside of 23 general practice sites	Cross classification of patients on mydriatic fundus photography and direct ophthalmoscopy Diagnostic level of evidence II	1010 diabetic patients 517 examined by GP, 493 examined by optician	Camera: Canon CR5-45NM *Mydriasis used* Patients underwent retinal photography before ophthalmoscopy by GP or optician Retinal photographs taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist Retinal photographs were re-assessed 6 months later	Detection of retinopathy Agreement between original DR diagnosis using ophthalmology and retinal photography to diagnosis utilising retinal photographs alone 6 months later Quality of images

Gibbins, RL Kinsella, F Young, S Saunders, J Owens, DR (1994)	Rural Wales, United Kingdom Examinations conducted in general practices	Case series Patients with a suspect fundus photograph were referred for ophthalmoscopy Intervention level of evidence IV	143 diabetic patients 29 (20%) IDDM	Camera: Canon CR5-45NM *Mydriasis used* Retinal photographs taken by trained general practitioner Retinal photographs were reviewed by ophthalmologist and general practitioner	Agreement between GP and ophthalmologist's assessment of DR from retinal photographs Quality of images
Griffith, SP Freeman, WL Shaw, CJ Mitchell, WH Olden, CR Figgs, LD Kinyoun, JL Underwood, DL Will, JC (1993)	Rural Yakima Native American Indian Reservation, Toppenish, Washington, USA Examinations conducted in health centre	Cross classification of patients on mydriatic fundus photography and direct ophthalmoscopy Diagnostic level of evidence II	188 Native American diabetic patients 134 patients screened once, 53 patients screened twice, 1 patient screened three times	Camera: seven view non-stereoscopic mydriatic camera *Mydriasis used* Patients underwent direct ophthalmoscopy by primary care physician before retinal photography Retinal photographs taken by trained technician Retinal photographs were reviewed by ophthalmologist or retinal specialists	Detection of retinopathy Agreement between ophthalmology and retinal photography Referral for follow-up

Gomez-Ulla, F Fernandez, MI Gonzalez, F Rey, P Rodriguez, M Rodriguez-Cid, MJ Casanueva, FF Tome, MA Garcia-Tobio, J Gude, F (2002)	Rural Galicia, Spain Examinations conducted at 2 peripheral hospital sites	Cross classification of patients on non-mydriatic fundus photography and direct ophthalmoscopy Diagnostic level of evidence I	140 eyes of 70 consecutive diabetic patients	Camera: Canon CR5-45NM *Non-mydriatic* Patients underwent retinal photography before direct ophthalmoscopy Retinal photographs taken by a trained technician Retinal photographs were sent electronically to a central location where they were downloaded and reviewed by an independent, blinded ophthalmologist	Detection of retinopathy Agreement between ophthalmology and retinal photography
Harper, CA Livingston, PM Wood, C Jin, C Lee, SJ Keeffe, JE McCarty, CA Taylor, HR (1998)	Rural La Trobe and Goulburn Valleys, Victoria, Australia	Case series Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Intervention level of evidence IV	2354 eyes in 1177 diabetic patients 209/1177(18%) IDDM 968/1177 (82%) NIDDM Mean age 65 years (range 20-94 years) Mean duration diabetes 8 years (range 0-61 years)	Camera: Canon CR5-45NM *Non-mydriatic* Retinal photographs taken by an technician Retinal photographs were reviewed by an independent ophthalmologist	Detection of retinopathy Quality of images Referral for follow-up
Heaven, CJ Cansfield, J Shaw, KM (1992)	Urban Portsmouth, United Kingdom Examinations conducted in Diabetic Day Unit of hospital diabetic clinic	Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Diagnostic level of evidence IV	639 diabetic patients	Camera: Canon CR5-45NM *Non-mydriatic* Retinal photographs taken by an nurse technician Retinal photographs were reviewed by an independent ophthalmologist	Detection of retinopathy Referral for follow-up

Jacob, J Stead, J Sykes, J Taylor, D Tooke, JE (1994)	Exeter Health Authority Area, United Kingdom Mobile camera travelled to 17 general practices where examinations were held	Case series Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Intervention level of evidence IV	1050 diabetic patients 170 (16%) IDDM	Camera: Canon CR5-45NM *Mydriasis used* Retinal photographs and indirect/ direct ophthalmology taken by a trained technician Retinal photographs were reviewed by an independent ophthalmologist	Detection of retinopathy Quality of images Referral for follow-up
Mak, DB Plant, AJ McAllister, I (2003)	Remote Kimberly region, Western Australia, Australia Examinations conducted in primary health care centres and clinics	Case series Patients with a suspect fundus photograph were referred for follow-up Intervention level of evidence IV	744 diabetic patients 566 Aboriginal 132 non-Aboriginal 46 unknown 569 individuals had one set of photographs, 66 had two and 4 had three sets	Camera: Canon CR5-45NM *Mydriasis used* Retinal photographs taken by either trained nurses, Aboriginal health workers, a medical student and an ophthalmic photographer Retinal photographs were read by an ophthalmologist	Quality of images Referral for follow-up
O'Hare, JP Hopper, A Madhaven, C Charny, M Purewal, TS Harney, B Griffiths, J (1996)	Rural and urban Somerset, United Kingdom Examinations conducted in mobile "clinic" parked outside of 23 general practice sites	Cross classification of patients on mydriatic fundus photography and direct ophthalmoscopy Diagnostic level of evidence II	1010 diabetic patients 517 examined by GP, 493 examined by optician	Camera: Canon CR5-45NM *Mydriasis used* Patients underwent retinal photography before ophthalmoscopy by GP or optician Retinal photographs taken by trained technician/ driver Retinal photographs were read by GP then assessed in a single blinded manner by ophthalmologist	Detection of retinopathy Agreement between ophthalmology and retinal photography

Owens, DR Gibbins, RL Lewis, PA Wall, S Allen, JC Morton, R (1998)	Urban: Newport and Cardiff and Rural: Brecon and Abergaveny, South and Mid Wales, United Kingdom Examinations conducted in general practices	Case series Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Intervention level of evidence IV	1210 eyes of 605 diabetic patients 502 with NIDDM 111 with IDDM	Camera: Canon CR5-45NM *Mydriasis used* Patients underwent ophthalmoscopy by GP before retinal photography Retinal photographs taken by the study optometrist, two photographs per eye Retinal photographs were reviewed by two independent ophthalmologists	Detection of retinopathy Quality of images
Reda, E Dunn, P Straker, C Worsley, D Gross, K Trapski, I Whitcombe, S (2003)	Rural Waikato region, New Zealand Mobile screening unit Examinations conducted in community centres, marae (Maori community centres), medical centres, hospital outpatient clinics and a local prison	Case series Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Intervention level of evidence IV	8,172 diabetic patients screened one or more times 15,555 screening episodes during the period 1993 to 2001	Camera: initially a Kowa FX 50 R, currently a TopCon TRC 50X *Mydriasis used* Retinal photographs taken by a trained medical photographer, two photographs per eye Retinal photographs were read by an ophthalmologist	Detection of retinopathy Quality of images Referral for follow-up

Scanlon, PH Malhotra, R Thomas, G Foyt, C Kirkpatrick, JN Lewis-Barned, N Harney, B Aldington, SJ (2003)	Urban and rural Gloucestershire, United Kingdom Examinations conducted in GP sites	Cross classification of patients on mydriatic fundus photography and direct ophthalmoscopy Diagnostic level of evidence II and Case series Patients with a suspect fundus photograph were referred for indirect ophthalmoscopy Intervention level of evidence IV	1549 diabetic patients received both non-mydriatic and mydriatic retinal photography and ophthalmoscopy and 2062 diabetic patients received only non-mydriatic or mydriatic retinal photography	Camera: TopCon NRW5S Patients underwent *non-mydriatic* followed by *mydriatic* examination Retinal photographs taken by a nurse technician, one photograph for non-mydriatic, two photographs after mydriasis Retinal photographs were read by a blinded ophthalmologist	Detection of retinopathy Agreement between ophthalmology and retinal photography Quality of images Inter and intra-observer variability Referral rate to ophthalmologist
Tennant, MTS Rudnisky, CJ Hinz, BJ MacDonald, IM Greve, MDJ (2000)	Remote Fort Vermilion, Alberta, Canada	Case series Patients with a suspect fundus photograph were referred for ophthalmoscopy Intervention level of evidence IV	199 eyes in 100 diabetic patients 93/100 (93%) patients with NIDDM Mean age 55.4 years (range 9-82.7 years) Mean duration of diabetes 8.3 years (range 2 weeks to 40 years)	Camera: seven view non-stereoscopic mydriatic camera *Mydriasis used* Retinal photographs taken by a trained ophthalmic photographer Images were downloaded, compressed and sent via satellite to a central reading location Retinal specialist read images in a masked manner	Detection of retinopathy Referral for follow-up

Villalpando, CG Villalpando, EG Diaz, SM Martinez, DR Perez, BA Andrade, SI Stern, MP (1997)	Urban Mexico Examinations took place in a mobile "clinic" parked outside of a large primary care facility	Case series Patients with a suspect fundus photograph were referred for ophthalmoscopy Intervention level of evidence IV	220 diabetic patients, 110 male and 110 female 97.6% NIDDM Mean age men 62.4 ± 12.6 years, women 63.4 ±10.4 years Mean duration of diabetes for men 12.3 ± 10.1 years, women 11 ± 7.5 years	Camera: TopCon TRC 50X *Mydriasis used* Retinal photographs taken by a trained medical photographer, two photographs per eye Retinal photographs were read by a blinded ophthalmologist in central location	Detection of retinopathy Association between duration of diabetes and presence of DR

NIDDM = non-insulin dependent diabetes mellitus, IDDM = insulin dependent diabetes mellitus, GP = general practitioner

Profiles of studies not included in report

Study	Location	Study design	Study population	Study details	Outcome assessed
Bäcklund, LB Algvere, PV Rosenqvist, U (1998)	Urban Stockholm County, Sweden Examinations conducted in primary health care centres	Case series Intervention level of evidence IV	5340 diabetic patients	Camera: Canon CR5-45NM Mydriasis used Retinal photographs taken by trained ophthalmic nurse and GP Photographs were read by ophthalmic nurse or GP and only suspect photos were referred to an ophthalmologist	Detection of retinopathy

Ellingford, A (1992)	Urban Dundee, Scotland, United Kingdom	Case series Intervention level of evidence IV	2657 diabetic patients	Camera: Canon CR4-45NM Non-mydriatic (physiological dilation) examination of patients Retinal photographs taken by trained technician Photographs were read by diabetic physician and only suspect photos were referred to an ophthalmologist	Detection of retinopathy
Gutierrez, M Jovanovic, L Pettitt, DJ (2001)	Wisconsin, United States	Cross classification of patients on non-mydriatic retinal photography and seven field stereoscopic retinal photography	23 IDDM patients	Camera: Canon CR4-45NM Non-mydriatic (physiological dilation) examination of patients Retinal photographs taken by trained technician Photographs were read by the same trained technician who took the photographs and only suspect photos were referred to an ophthalmologist	Detection of retinopathy Agreement between non-mydriatic and seven field retinal photography

Leese, GP Newton, RW Jung, RT Haining, W Ellingford, A Tayside Mobile Screening Unit (1992)	Urban, rural and remote Tayside, Scotland, United Kingdom Examinations held in mobile "clinic"	Case series Intervention level of evidence IV	2112 diabetic patients	Camera: Canon CR4-45NM Non-mydriatic (physiological dilation) examination of patients Retinal photographs taken by trained technician Photographs were read by diabetic physician and only suspect photos were referred to an ophthalmologist	Detection of retinopathy Quality of images
McKenzie, A Grylls, J (1999)	Rural Kapiti GP Network, New Zealand	Case series Intervention level of evidence IV	300 diabetic patients	Mydriasis used Retinal photographs taken by optician Photographs were read by optician and only suspect photos were referred to an ophthalmologist	Detection of retinopathy
Rogers, D Bitner-Glindzicz, M Harris, C Yudkin, JS (1990)	Urban London, united Kingdom	Case series Intervention level of evidence IV	84 diabetic patients	Camera: Canon CR4-45NM Non-mydriatic (physiological dilation) examination of patients Retinal photographs taken by trained technician Photographs were read by the same trained personnel who took the photographs	Detection of retinopathy

Taylor, R (1996)	Urban and rural locations, United Kingdom Examinations held in mobile "clinic" parked outside of 12 sites: general practices (8) and general practices plus hospitals (4)	Case series Intervention level of evidence IV	64,905 diabetic patients, 49,667 screened at general practice sites and 15,238 screened at hospital sites	Camera: Canon CR5-45NM Mydriasis used in 10/12 sites for all patients, 1/12 sites used mydriasis for patients over the age of 50 years Retinal photographs taken by trained technician/ driver Photographs were read by health workers and only suspect photos were referred to an ophthalmologist	Detection of retinopathy

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