Effectiveness bulletin

Complications of diabetes: screening for retinopathy and management of foot ulcers

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This paper is based on *Effective Health Care*, volume 5, number 4,[1] which is based on two systematic reviews undertaken to inform national clinical practice guidelines for type 2 diabetes.[2 3] The first part of the article looks at screening for diabetic retinopathy and the second at the prevention and treatment of diabetic foot ulcers.

Two of the most common complications of diabetes are visual problems caused by retinopathy, and problems with the feet, particularly persistent ulcers. These result from microvascular and macrovascular complications, often exacerbated by chronically raised blood glucose levels. Around 2% of the UK population are believed to have diabetes, of whom perhaps 200 000 have type 1 (insulin dependent) diabetes, and more than a million have type 2 (non-insulin dependent) diabetes.[4]

Screening for diabetic retinopathy

Diabetic retinopathy is the leading cause of blindness in people of working age in industrialised countries.[5] Twenty years after diagnosis, almost all of those with type 1 diabetes and 60% of those with type 2 diabetes will have some degree of retinopathy.[6] The condition is due to small blood vessels in the retina becoming blocked, swollen, or leaky, which causes oedema (swelling) and haphazard growth of new fragile vessels. This process can continue for years without causing visual symptoms or visual impairment; during this period, retinopathy can only be detected by eye examination. If left untreated, bleeding and scarring will lead to progressive loss of vision.

The condition can, however, be treated by laser photocoagulation, and large trials have shown that this type of treatment can prevent blindness if it is given before significant visual loss has occurred.[7 8] Meta-analysis of studies of screening, followed by treatment of sight threatening retinopathy, shows a high level of effectiveness.[9 10] This cuts the frequency of severe visual loss or blindness among people with diabetes to less than half the level found among untreated controls (relative risk 0.39, 95% CI 0.28 to 0.55).

It is clear that regular examination of the eyes is necessary to detect and treat diabetic retinopathy before it becomes sight threatening. Such a screening programme can also be cost effective: US studies suggest that the cost of screening and subsequent treatment can be lower than the cost of dealing with the blindness that could be expected without screening.[11–13] It has been estimated that systematic screening for diabetic retinopathy could prevent around 260 new cases of blindness each year among people aged under 70 in England and Wales.[14]

The systematic review on which the bulletin is based included 20 studies, the majority of which were undertaken in the UK.[7 8 15–32] Table 1 shows a summary of the UK studies.

SCREENING METHODS

The effectiveness of screening for prevention of blindness depends on the method used, the competence of the screener, the screening interval, and organisational or other factors which affect the uptake of screening. There are two main types of screening method, ophthalmoscopy and retinal photography, which may be further subdivided (table 2). Either method is currently used with or without mydriasis (dilation of the pupils with eye drops).

RETINAL PHOTOGRAPHY

Retinal photography allows the screening process to be separated from assessment and provides lasting records of patients' retinas. It can be done in a range of settings, from clinics to mobile converted vans; the photographs can then be assessed by suitably trained readers. Mydriasis significantly improves the quality of the photographs and increases the sensitivity of screening; one study reported that mydriasis improved sensitivity from 61% to 81%.[23] However, the camera flash is less comfortable for the patient after mydriasis (flash rated "comfortable" by 80% rather than 90%) and temporary visual impairment may render some patients unable to drive safely or read small print for several hours after treatment.[33]

Some retinal photographs are unclear and cannot be assessed. The reported rate for this form of technical failure ranges from 3.7% to 22%[17 23 32]; it is less frequent when mydriasis is used. There may be further improvements with digital systems.

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Table 1 Screening for diabetic retinopathy in the UK (all studies included people with type 1 and type 2 diabetes). Studies in alphabetical order by name of first author

First author	Screening method	Screener	Number screened	Severity of retinopathy	Sensitivity % (95% CI)	Specificity % (95% CI if reported)	Comparison ("gold standard")	Comments
Burnett[15]	Ophthalmoscopy: no details given	Optometrists	536	Referable	100	94 (90 to 98)	Ophthalmoscopy by ophthalmologist	Screeners (community optometrists) trained and accredited, paid £20 for each examination
Buxton[8]	Direct ophthalmoscopy	GP	2350	Sight-threatening	53 (44 to 62)	91 (90 to 92)	Ophthalmoscopy by trained clinical assistant	Cost effectiveness studies based on same data
		Optician	307		48 (26 to 70)	94 (92 to 97)		
		Hospital doctor	416		67 (50 to 84)	96 (94 to 98)		
	Polaroid camera, no mydriasis	Ophthalmologist in GP practice or hospital clinic, photos read by ophthalmologist	2799	Sight-threatening	56 (49 to 72)	97 (96 to 98)		5% of photos unusable, 90% "assessable"
Forrest[16]	Ophthalmoscopy	Diabetologist	282	Any	51 (35 to 68)	99 (97 to 100)	Five field stereoscopic fundus photography	Confidence intervals reported only for diabetologist, any retinopathy
		Nurse			50	99		
		Diabetologist		Sight-threatening	27	99		
		Nurse			55	92		
Gibbins[17]	35mm camera, mydriasis	GP.	143	Any	87 (66 to 97)	77 (70 to 85)	Same photos assessed by ophthalmologist	Sensitivity based on "good quality" photos — 78% of total
				Proliferative	100	96 (92 to 99)		
Gibbins[18]	Direct ophthalmoscopy	GP	613 in first phase of study,	Any	63 (56 to 69)	75 (70 to 80)	Photos assessed by trained graders	
		Optician			74 (67 to 81)	80 (75 to 85)		
		GP		Sight-threatening	66 (54 to 77)	94 (91 to 96)		
		Optician			82 (68 to 92)	90 (87 to 93)		
	35mm camera, mydriasis	GP	644 in second phase.	Any	79 (74 to 85)	73 (68 to 79)	Same photos assessed by trained graders	
		Optometrist			88 (83 to 93)	68 (62 to 74)		
		Diabetologist			73 (66 to 79)	93 (89 to 96)		
		GP		Sight-threatening	87 (77 to 94)	85 (81 to 88)		
		Optometrist			91 (79 to 87)	83 (79 to 87)		
		Diabetologist			89 (79 to 95)	91 (88 to 94)		
Harding[19]	35mm camera, mydriasis	Ophthalmological clinical assistant	358	Sight-threatening	89 (80 to 98)	86 (82 to 90)	Slit lamp biomicroscopy by retinal specialist	3.75% of photos "unobtainable"
	Direct ophthalmoscopy	Ophthalmologist			65 (51 to 79)	97 (95 to 99)		
O'Hare[7]	Direct ophthalmoscopy	Optician		Referable	73	93	Ophthalmoscopy by ophthalmologist	Only opticians using both methods achieve BDA criteria
	Direct ophthalmoscopy plus photo with mydriasis.	GP	517		60	98		
		Optician	493		88	99		
Taylor[20]	Polaroid camera	District retinal screener	197	Any	72 (66 to 78)	88 (85 to 91)	Seven field stereo photography (118 patients, randomly selected)	Results for referable retinopathy consistently meet BDA criteria.
	Digital camera		534	Referable	90 (86 to 94)	97 (95 to 99)		
	Polaroid plus ophthalmoscopy		Unclear	Any	74 (68 to 80)	96 (94 to 98)		Patients preferred digital; 2.6% discomfort versus 17% with polaroid
				Referable	85 (80 to 90)	98 (96 to 100)		
				Any	92 (86 to 98)	92 (86 to 98)		
				Referable	95 (91 to 99)	97 (95 to 99)		
Williams[21]	35mm or polaroid camera, no mydriasis	Ophthalmological clinical assistant	62	Any	96 (88 to 99)	98 (87 to 100)	Ophthalmoscopy by ophthalmologist	Unusually high levels of accuracy—but a small study

OPHTHALMOSCOPY

In most studies of screening using ophthalmoscopy alone, direct ophthalmoscopes were used.[7 8 18 19 23 26 28 30] The sensitivity of this method was often found to be low, even in the hands of experts, although specificity was high, usually 90–100% (table 1). This means that when retinopathy is detected, the result is likely to be correct.

An important reason for the lack of sensitivity of the direct ophthalmoscope is that it offers a small field of view. This instrument is now rarely used by ophthalmologists; its place has been taken by the slit lamp biomicroscope and handheld lens, which offer a much wider field of view.

A recent London study of optometrists, accredited after specialist training, found much higher levels of accuracy.[15] Participants used mydriasis but it was not clear what type of ophthalmoscope was used. The positive predictive value (PPV) for referable eye disease was 79% (that is, 79% of patients referred had retinopathy requiring treatment) and the negative predictive value (NPV) was 100% (no cases were missed).

Using ophthalmoscopy in combination with retinal photography shows promising results and can provide a high degree of accuracy in the hands of ophthalmologists or optometrists.[7 20 34] Reported sensitivity falls below acceptable levels when screening is done by GPs.[7 8]

Table 2 Screening methods used for diabetic retinopathy

Screening tool (method type)	Varieties	Gold standard	Comment
Ophthalmoscope (ophthalmoscopy)	Direct, indirect	Slit-lamp biomicroscopy	An ophthalmoscope allows the user to see into the eye
Retinal (fundus) camera (retinal photography)	Digital, 35mm, polaroid; mobile or fixed	Multiple (usually 5 or 7) field stereo photography	These are specialised cameras, used to produce colour photographs of the retina. Digital cameras require less flash and allow the picture to be viewed on a computer screen

Table 3 Potentially beneficial treatments for foot ulcers

Intervention	*Mode of action*	*Comment*
Total contact casting	A plaster cast which redistributes weight on the foot	One small RCT showed benefit[60]
Growth factors (CT-102, RGDpm, rhPDGF)	Substances derived from human tissue which can stimulate growth	5 RCTs found growth factors helped uninfected ulcers to heal faster.[61–65] No UK marketing authorisation
Granulocyte-colony stimulating factor (G-CSF)	Enhances ability to fight infection	G-CSF reduced infection and enhanced healing of severely infected diabetic foot ulcers in patients treated with antibiotics in one small RCT.[66] Not currently licensed for this indication
2% ketanserin ointment	Believed to improve local blood supply	Two RCTs suggested benefit.[67*] No UK marketing authorisation
Iamin gel	Applied immediately after debridement	One small RCT suggested possible benefits.[68] No UK marketing authorisation
Debridement with cadexomer iodine	Might promote healing better than standard treatment	Evidence from one small study.[69]

*Janssen H, Rooman R, Donecker P, *et al*. Topical ketanserin accelerates the wound healing process in decubitus, arterial and diabetic skin ulcers. Unpublished.

FEATURES OF A SCREENING PROGRAMME

Wide variation exists in sensitivity of screening by different professional groups (table 1). In general, it appears that more experienced professionals such as specialist ophthalmologists are likely to be more accurate, whatever the method used. Consistently good results have been reported in US studies of trained graders assessing photographs in specialist centres.[21 23 25]

In the UK, retinal photography in mobile screening units may offer a practical and effective option.[19 35 36] The level of training required to operate the camera has not been clearly defined, however, and considerable experience is likely to be required to read the photographs accurately. Whatever screening method is used, quality control is essential.

The consensus among expert groups in Europe is that yearly screening is appropriate.[37 38] The chronic disease management programme (CDMP) for diabetes in primary care requires a full review of the patients' health, including their eyes, at least annually.

COSTS AND COST EFFECTIVENESS

Any system of screening requires initial investment in equipment, training, and administration, and will have ongoing organisation and personnel costs. Mobile screening, using a van equipped with a fundus camera, has been proposed as an effective and inexpensive option. Reported costs are £10–13 per patient screened and just over £1000 per patient requiring laser treatment.[9 35] This included the salary of the photographer, depreciation and running costs for van and camera, and costs of film and processing.[39] Screening by accredited optometrists in London was reported to cost £12.62 per case (including training and quality audit costs), plus a £20 fee to the optometrists.[15] The cost of each case identified (2.3% of patients screened) was £581.

The potential costs of failure to offer effective screening should be weighed against the costs of providing such a service. These could include not only the cost of looking after people with avoidable blindness but also litigation costs if such people were to pursue legal action against the health authority for negligence.

RECOMMENDATIONS FOR POLICY

- Adequate evidence exists that screening should be provided for all people with diabetes who are not being treated for retinopathy
- The service needs to be organised efficiently at a local level to ensure adequate population coverage
- Screening can be provided effectively by accredited optometrists, reimbursed on a per capita basis, or by mobile retinal photography, operating in various locations as necessary.

Foot problems associated with diabetes

At some time in their life, 15% of people with diabetes develop foot ulcers associated with peripheral neuropathy (nerve damage) or ischaemia (lack of blood supply), or both.[40] In a local population study of 1077 patients with diabetes, 7.4% had foot ulcers or had experienced them; 40% of these were neuropathic, 24% ischaemic, and 36% mixed.[41] Recurrence rates for diabetic foot ulcers are 35–40% over three years and 70% over five years.[42] These ulcers can have serious consequences. They are highly susceptible to infection, which may spread rapidly, causing overwhelming tissue destruction.[43]

PREVENTION

Several trials were identified in the systematic review which showed that various interventions could be effective in preventing ulcers or reducing amputation rates, or both.[44–51] For example, a large randomised controlled trial in a Liverpool diabetes clinic showed that amputation rates among people at high risk of foot ulcers could be significantly reduced by a foot protection programme.[44] Patients with type 2 diabetes and foot deformities, history of foot ulceration, or significant vascular or neuropathic disease were randomised to the intervention—weekly clinics providing chiropody, hygiene, hosiery, protective shoes, and education—or usual care. At two years the ulcer rate in the intervention group was non-significantly reduced to 2.4% compared with 3.5% in the usual care group ($p=0.14$). Amputations, however, were reduced threefold, with seven in the intervention group and 23 among controls ($p<0.04$).

Callus formation often precedes the development of neuropathic ulcers.[40] Callus tends to form at pressure points in shoes, compounded by effects of neuropathy on patterns of weight bearing. These problems can be reduced through provision of orthoses—usually custom made insoles designed to redistribute weight on the foot—and/or therapeutic shoes.[52 53]

TREATMENT

Infection is a major problem with foot ulcers and a main cause of amputation following ulceration. Systemic antibiotics are regarded as part of standard treatment for invasive infections associated with diabetic foot ulcers. However, available trials of antibiotics for foot ulcers are uninformative and further research is required.

Table 3 shows which treatments have been shown to be potentially beneficial in the treatment of foot ulcers. The review found no evidence that any particular type of wound dressing was more effective than any other (Baker N. Allevyn vs Sorbsan in the treatment of diabetic foot ulcers, unpublished data; and Vandeputte J, Gryson L. Diabetic foot infection controlled by immuno-modulating hydrogel containing 65% glycerine—presentation of a clinical trial, unpublished data),[54–58] but suggested that adhesive dressings intended to improve debridement should be avoided.[59]

IMPLICATIONS

- Multidisciplinary interventions, such as education to increase patients' knowledge about foot care, podiatry, and therapeutic shoes, can improve the condition of the feet and help to reduce ulcer and amputation rates
- Various treatments are used for diabetic foot ulcers, but evidence for their effectiveness is generally poor.

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