Screening for diabetic retinopathy

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Throughout the industrialized world the complications of diabetic retinopathy remain the major cause of preventable visual loss in persons of working age. A reduction by one-third or more in new blindness due to diabetes has been adopted as one of the key 5-year targets in the St Vincent declaration,[1] and the best way to achieve this aim is a national strategy of screening for diabetic retinopathy. In this article we review the rationale and supporting evidence for a screening programme for diabetic retinopathy. We also debate the arguments for and against the screening modalities that are currently used in the UK.

WHY SCREEN FOR DIABETIC RETINOPATHY AT ALL?

One of the prime motivating factors behind the development of a screening programme for diabetic retinopathy is the efficacy of laser photocoagulation treatment in preventing visual loss. The beneficial effect of laser treatment was established by two large randomized clinical trials—the Diabetic Retinopathy Study and the Early Treatment Diabetic Retinopathy Study (ETDRS). The essential findings of these trials were that, compared with no treatment, laser photocoagulation prevented visual loss in patients with proliferative diabetic retinopathy and macular oedema by about 50%.[2,3] The ETDRS also served to identify points in the natural history of diabetic retinopathy at which laser photocoagulation treatment should be applied. From epidemiological data we know that patients are usually symptom-free at these threshold levels of retinopathy: retinopathy may be well advanced before visual deterioration is noticed. That patients are generally symptom-free when they should receive preventive treatment is a strong argument for establishing a screening programme.

WHAT EVIDENCE IS THERE THAT SCREENING CAN REDUCE BLINDNESS?

In general, the progression of retinopathy is orderly and the prevalence and severity of retinopathy is related to duration of diabetes.[4–6] To date no randomized controlled trial has been conducted to assess the efficacy of screening for diabetic retinopathy: the practical difficulties of conducting such a study would be enormous. The impact of a national screening programme in the UK has been estimated by use of mathematical models based on what is known about the disease's natural history, and these models indicate that an annual screening programme could yield worthwhile health gains.[7,8] These findings are supported by the results of observational studies which point to substantial reductions in the incidence of new blindness due to diabetic retinopathy after the introduction of screening programmes.[9,10]

Mathematical models have also been used to examine the cost-effectiveness of annual and semi-annual screening intervals in patients with diabetes. These analyses come to broadly similar conclusions. Annual screening for diabetic retinopathy in all patients with type 1 diabetes is cost-effective (provided the screening modality is sufficiently sensitive), when the economic impact of a person's blindness is balanced against the health costs incurred by treatment and screening.[11–14] The economic argument for annual screening of all patients with type 2 diabetes is less convincing. The two analyses that have specifically investigated this area concluded that only those patients with type 2 diabetes who require insulin, or in whom retinopathy has been previously detected, warrant annual screening.[12,15] Neither of these mathematical models, however, allows for the additional administrative costs of running several different screening programmes for patients with type 2 diabetes. The economic argument for the annual screening of all patients with type 2 diabetes might have been more persuasive if these costs had been taken into consideration.

WHAT IS THE BEST SCREENING METHOD?

For any screening programme to function effectively it must fulfil certain basic criteria. Firstly, the screening test must have sufficiently high sensitivity (true positive rate) to ensure that substantial numbers of patients with sight-threatening retinopathy are not missed. Secondly, it must have sufficiently high specificity (true negative rate) to ensure that ophthalmic departments are not overwhelmed with unnecessary referrals. The British Diabetic Association proposed that any screening programme for diabetic retinopathy should have at least 80% sensitivity and specificity, and it is against these figures that any screening modality for diabetic retinopathy must be judged. A survey

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conducted across England and Wales during 1996 revealed that the provision of diabetic retinopathy screening services was uneven, with different screening modalities being employed.[16] Though there is now general acknowledgment that we need a national strategy for diabetic retinopathy screening, debate continues on how this screening should be performed. Direct ophthalmoscopy alone has no role in a screening programme since the method consistently fails to meet the 80% sensitivity and specificity targets.[17–20] There are two principal candidates—retinal photography (in one of its many guises), and screening by optometrists using the indirect ophthalmoscope or the slit lamp biomicroscope. As yet no randomized trial has been conducted to compare these options. One study did use a mathematical model to analyse the effectiveness of various screening strategies but did not include optometrist screeners.[12] To date, only one large systematic review has addressed this issue.[21] The authors concluded that the most effective screening modality for diabetic retinopathy was retinal photography through dilated pupils. Unfortunately this comparison is flawed, because they used data from studies in which most optometrists used the direct ophthalmoscope. This is important since the authors conceded that indirect ophthalmoscopy was an effective screening strategy in trained hands. Subsequently, further evidence has emerged on the effectiveness of optometrist screeners using slit lamp biomicroscopy.[22] The widely assumed superiority of photographic screening over optometrists using appropriate equipment therefore remains unproven.

The effectiveness of an individual screening modality to deliver the desired sensitivity and specificity targets for detecting diabetic retinopathy is not, in itself, sufficient justification for adopting that modality. It must in addition be acceptable and convenient for patients, be sensitive to local needs and have inbuilt quality control mechanisms. We will now briefly review each of the screening modalities currently in use, outlining their merits and disadvantages. The principal advantages and disadvantages of each technique are summarized in Table 1.

Retinal photography

Fundus photography, without mydriasis, utilizing 45° Polaroid colour prints was the first retinal photographic technique to be applied to diabetic retinopathy screening. Whilst Polaroid photography offered an instant hard-copy image of the retina, concerns were soon raised about the adequacy of the technique to detect sight-threatening retinopathy in the peripheral retina, particularly when the pupils were small.[23] These concerns were borne out by a large comparative study which revealed sensitivities as low as 35% with this technique.[19] In contrast, retinal photography through dilated pupils using 35 mm transparencies has proved highly effective, achieving sensitivities and specificities of 89% and 86%, respectively.[18] But this method of retinal photography likewise has limitations. Lenticular and corneal opacities, a poor tear film and patient movement can all render the acquired image useless for grading purposes. The technique thus has an associated technical failure rate of about 8%. In addition, the processing and storage of large numbers of transparencies can be costly in resources. The use of digital imaging systems may be part of the answer to these difficulties. The instant image acquisition afforded by a digital system has the potential to reduce the technical failure rate, and the electronic image facilitates easy storage and cataloguing.[24] Controlled studies evaluating the latest digital systems in this role have been very promising, with reported sensitivities and specificities of around 90%.[25,26]

Retinal photography through dilated pupils using 35 mm transparencies, or digital imaging, is therefore an effective technique for diabetic retinopathy screening. But whatever the imaging system employed, retinal photography has several inherent weaknesses as a screening tool. First, it requires special equipment and a pool of trained personnel and equipment, which mean high capital set-up costs. Second, concern has been expressed that, as in other screening programmes, there might be difficulties in maintaining the motivation of screening staff.[27] Finally, there is the problem of how to deliver the service to those patients who need to be screened. One solution is to mount camera systems in mobile vans. Whilst this option does have the advantage of flexibility, a large administrative team is required to coordinate the programme and it also demands purchase and maintenance of a fleet of vehicles. An alternative would be to locate several fixed camera systems within the target community. If careful consideration was given to the location and access to these facilities, such a system might work well in urban areas. It would be less suitable for rural populations, and even in urban areas the number required to ensure high attendance rates might be prohibitively high.

Optometrist screening

Use of an optometrist practice based scheme to screen for diabetic retinopathy has several potential advantages. The practices have long flexible opening hours and their proximity to the populace facilitates easy access. Optometrists who offer home visits can even screen housebound patients. In Sheffield, a system has proved popular with patients, with over 90% of our 6500 target patients presenting for screening annually. This contrasts sharply with the high non-attendance rates of our hospital-based diabetic eye and general diabetic clinics. Furthermore, the screening itself is performed by personnel who

Table 1 **Advantages and disadvantages of different modalities for diabetic retinopathy screening**

Screening modality	*Advantages*	*Disadvantages*
Retinal photography	Effective technique if mydriatic photography is performed with either 35 mm transparencies or digital systems Retinal image can be used in patient education Hard copy can be incorporated into patient record Amenable to audit	High capital set-up costs Difficulties in reaching all patients who need to be screened Need to provide regular training for graders Potential problem retaining motivated personnel for grading
Optometrist screeners	Effective technique if indirect ophthalmoscope/slit lamp biomicroscope used Accessible, convenient service Offers holistic package of eye care to the patient	Requires an elaborate quality control mechanism for the system to be audited
Combined modalities	Effective techniques Retinal image can be used in patient education Hard copy can be incorporated into patient record Amenable to audit Accessible, convenient service Offers holistic package of eye care to the patient Utilizes the well trained, motivated workforce that optometrists represent	High capital set-up costs Camera systems might have to rotate around practices, potentially limiting accessibility of the service

can offer a holistic package of care, since they are in a position to screen for non-diabetic eye disease as well. The ability of an optometrist to detect sight-threatening retinopathy obviously depends on which instrument is used to examine the retina. In the early studies with optometrist screeners, all used the direct ophthalmoscope. Although the results were encouraging,[28–30] we now know that, even when done by an experienced optometrist, screening by this method is unacceptable.[19] The results with the slit lamp biomicroscope have been much more impressive, yielding sensitivities and specificities as high as 80% and 95%, respectively.[22,31] With an associated technical failure rate of less than 1%, these results compare favourably with retinal photography. The one crucial weakness of a screening programme with optometrist screeners is the need for an elaborate quality control mechanism if it is to be audited effectively.[32] This means either re-examination of a substantial number of patients or secondary photography with the ETDRS gold standard 7 field stereo images. In our experience the secondary wave of screening for quality assurance is poorly attended, with non-attendance rates of over 50% (unpublished). This failure to attend seriously undermines the audit process. Furthermore, since the expected prevalence of sight-threatening eye disease in the screened population is low, a substantial proportion of the screened population must be audited to obtain meaningful data. Add this to the high non-attendance rate, and we calculate that one-fifth of our original screening population would need to be secondarily screened. This is obviously not practicable and is the principal obstacle to use of optometrists in screening for diabetic retinopathy.

Combined modalities

The remaining option for diabetic retinopathy screening is to combine screening modalities and site camera systems within optometrist practices. Such a system might offer both the desired accessibility and a holistic package of eye care amenable to audit.[33] Combination of screening modalities is not a new idea. Previous studies have shown that sensitivities of around 90% can be achieved by optometrists using ophthalmoscopy and dilated fundus photography,[34,35] and these figures are all the more impressive when one considers that they were achieved with the direct ophthalmoscope. Optometrists also represent an available, well trained and motivated work force. With minimal training they could perform many of the tests that, in a purely photographic screening programme, would have to be delegated to a team of photographers and graders. Recruitment of this workforce might overcome the potential difficulties of training and retaining personnel to grade retinal photographs. One disadvantage of a combined modality programme is that the capital set-up costs may be of the same magnitude as those of a purely photographic system. Furthermore, if these costs are not to be prohibitive the camera systems might have to rotate around optometrist practices, thus nullifying the accessibility that is one of the strengths of an optometrist-based system.

CONCLUSION

No single modality satisfies all the requirements for a screening programme. Currently the preferred method for screening is a retinal photographic service based on digital

systems. In any one region, the screening programme that is adopted is likely to be a compromise between efficacy of the method, the existing infrastructure and local expertise.

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