To screen or not to screen? High-tech responses to a not-so-hamletic question

Loss of sight remains a largely unsolved problem in diabetes care, despite the advances in our understanding of the role of metabolic and blood pressure control in the pathogenesis of retinopathy [1–3], and encouraging results from randomized controlled drug trials, although not all of them were primarily aimed at its treatment [4–6]. The problem is that optimal glycaemic control is far from easy to achieve [7,8] and even, when it is, may still not necessarily prevent retinopathy [9]. Hence, there is a perceived need to screen for sight-threatening lesions in all patients with diabetes, in order to commence photocoagulation before any sight-diminishing symptoms have occurred [10].

To organize screening, however, is a major task that cannot be left to the initiative of individual carers. The problems are daunting. The number of patients with diabetes is expected to double between now and 2030 [11], while the number of doctors, especially eye doctors, grows more slowly and may even decrease as they develop an interest in other aspects of this ever-expanding profession, or become increasingly too expensive for either third-party payers or individual patients. In fact, screening programmes require political vision, leadership, organization and funding at a national or, at least, regional level. This, so far, has occurred in only a few places, including the United Kingdom, which has a National Plan for Screening in place.

Some of the problems of screening can at least be addressed by technology, with the development of non-mydriatic fundal cameras. This powerful tool was initially looked upon with some reservation, partly because the images captured on the Polaroid self-developing films did not offer either sufficient quality or durability. However, the advent of digital photography has resulted in a whole world of difference. Nowadays, the quality is such that both the sensitivity and specificity of digital fundal cameras are comparable to, if not better than, retinal examination by a specialist [12]. Photographs can be taken by nursing and/or technical personnel, and stored and graded in an asynchronous mode either locally or at remote centers via the Web. This saves expensive specialist time. As described by Massin et al. [13] in this issue, more than 75% of patients have no retinopathy when screened, and epidemiological data confirm that the vast majority of patients have no visible lesions on screening [14]. Photographic screening helps to focus specialists’ attention on those patients who are most in need, instead of wasting their time examining people who have normal retinas.

The benefits of this approach, as reflected by the OPHDIAT programme, are well described in this issue [13]. Screening by photography can be brought to patients who would normally have to make an effort to see an ophthalmologist, particularly in the case of inmates in a prison — one of the test sites in OPHDIAT — can raise a number of practical and economic issues. It can also create new professional skills, as retinal photographers and specialist nurses. As is the case in UK, ‘lay’ retinal graders can be specifically trained to read retinal photographs and will therefore save even more specialist’s time.

It is of course, a solution that will inevitably generate more problems at first, such as the initial surge of referrals for retinopathy and other ocular pathologies that are bound to arise with screening. This leads to the issue of quality assurance. Recognition of retinopathy must be reliable and reproducible, and any remote areas, where people with diabetes live should be reached regularly and in time. Photographs must be obtained quickly and painlessly, so that patients are more likely to keep coming back, and the reports need to be fed back rapidly to the referring physicians. It should also be possible to act quickly, in cases where further diagnostic and/or therapeutic action is necessary, as a result of the detection of retinopathy on screening. Patients need to be given appointments for follow-up screening visits, and a recall system should be in place to track those who fail to attend their appointments. Erginay et al. [15] describe how some of these items are addressed in OPHDIAT by setting standards for the rates of gradable photos, grading reproducibility and time taken to generate a report. The fact that almost all of the programme’s objectives were met in its first 2.5 years bode well for its future deployment.

Keywords: Diabetic retinopathy; Screening; Prevention; Non mydriatic camera

Mots clés : Rétinopathie diabétique ; Dépistage ; Prévention ; Caméra nonmydriatique
Nevertheless, OPHDIAT and other screening programmes must brace themselves for the challenges that lie ahead. New patients will rapidly become more numerous and could overwhelm the system. In addition to simply increasing manpower, a solution may be offered by image analysis using automated or, at least, assisted grading. This could range from the simple assessment of the absence/presence of retinopathy, which would skim some 60% or more of the workload off human graders, and might even allow appropriate manual checking of grading performance and lead to a system that could recognize individual lesions or clusters and perhaps eventually, to fully automated grading. This would be a wonderful achievement for information technology as applied to public medicine, if it proves to be technically feasible. After all, if ‘intelligent’ bombs today can be made to recognize their target through a camera while flying towards it and iris scanners put to regular use for identifying individuals, then the technology for pattern recognition may well be sufficiently developed for diagnosing retinopathy as well. It may also be that a change in the priorities used to allocate funds is the way towards realizing such visionary advances.

But, to come back down to earth, there are a few other tricks that may help to manage the growing numbers of diabetes patients, such as seeing them at longer time intervals. Based on their experience, the Liverpool group has suggested re-screening every three or more years, if no retinopathy is present [16]. There are reasons to disapprove of such long time-lags, as they may give patients the false impression that screening is not important, so that they may choose to miss appointments altogether, if they are arranged so far in the future. The OPHDIAT protocol calls for yearly screening, and our unit also screens yearly all patients taking insulin, whether type 1 or 2, and every two years for those taking oral agents or diet only.

Streamlining the procedure may also lead to taking as few photographs as possible and with dilated pupils, even with non-mydratic cameras. Most screening protocols recommend taking three, two or even one picture of the fundus — one centered on the macula, and the other(s) including the disc and part of the nasal field [13]. Mydriasis can be bothersome for patients, as it may impair their ability to drive for a few hours but, on the other hand, it can substantially reduce the proportion of non-gradable pictures. However, both concerns are addressed with the $2 \times 2$ approach of Apte et al. [17], which also published in this issue. By measuring the performance of one versus three photographs with and without mydriasis, this study concluded that, in line with OPHDIAT policy, three photos of undilated pupils may represent a working compromise. Considering, however, that 10% of pictures was not gradable in OPHDIAT [13] and, thus, required referral of those patients to an ophthalmologist, it is important to strike the right balance between improved performance at lower cost (mydriasis) and less immediate inconvenience versus a possibly higher referral rate.

Finally, the key question is: is screening worth? Will it truly reduce new cases of blindness due to diabetes? Some reports suggest that systematic screening, as was successfully implemented in Iceland [10] and Sweden [18,19], and economic simulations of it proved to be highly cost-effective, at least in the younger age groups [20,21]. However, the question cannot be answered definitively by a randomized controlled clinical trial. Although the benefits of systematic screening are unproven, to have a control group offered sham fundus examinations would be considered unethical, and such a clinical study would have to follow-up a massive study population for many years to properly measure an endpoint of blindness prevention. Thus, without such hard evidence, it would appear to be justifiable to resort to common-sense medicine. Screening for sight-threatening retinopathy remains the decent thing to do, as not to screen would be inhumane. Some countries are further ahead, to their credit, and others need to follow suit. Such programmes as OPHDIAT are to be commended, expanded and imitated — even plagiarized, if need be — until as many diabetic patients as possible are receiving appropriate eye care.

References


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20 March 2008
Available online 12 May 2008