Sir,

I was very interested in the report by Newsom and colleagues about screening for diabetic retinopathy.[1] This paper exemplifies the problems with screening tests evaluated in a 'clinical laboratory' rather than in the community. The authors have selected a patient group from a diabetic retinopathy screening clinic or a medical retina clinic. On the basis of this preselected sample they report a positive predictive value (PPV) of 0.98 and 0.99 for the detection of any retinopathy by digital colour photography and oral fluorescein angiography (OFA) respectively. However, the PPV of a screening test varies significantly with the prevalence of the disease in the population. In their study population the prevalence of any retinopathy is 91%; in the real world only approximately one-third of a population of people with diabetes have some retinopathy.[2] Thus, if applied to a screening programme, the PPV of digital colour photography is likely to be 0.72 and that of OFA 0.68 based on a prevalence of 0.33. The main comparator study they quote had a sample of 124 subjects and compared digital images with slit-lamp examination for the detection of sight-threatening diabetic retinopathy (STDR).[3] It is difficult to make meaningful comparisons of this study with Newsom *et al.*'s report, as they are measuring different end-points: any retinopathy by Newsom *et al.* and STDR by Kerr *et al.* Again, allowing for a realistic prevalence of 0.13 for STDR,[2] the PPV of digital imaging for STDR by Kerr *et al.*'s method would be 0.31.

Also, whilst it is expeditious to separate diabetic retinopathy and maculopathy in a study, this makes it difficult to extrapolate the results reported by Newsom *et al.* to a screening programme. A more meaningful end-point is the detection of STDR, as the aim of a screening programme is to identify treatable pathology. Results of pilot studies about screening tests need to be interpreted in the correct epidemiological context for them to be meaningful and to allow comparisons to be made across studies.

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Sir,

We are grateful for the comments of Mr Prasad, who commented that the screening test statistics may be affected by the demographic characteristics of a population. This issue of methodological standards is the subject of a widespread debate and has particular relevance in tests using continuous data.[1–3]

Our paper assessed the usefulness of both oral fluorescein angiography (OFA) and digital colour photography for diabetic retinopathy and diabetic maculopathy screening. The population was recruited from a screening programme and a retinal clinic giving a high prevalence of diabetic retinopathy within the test population.

The paper stressed that OFA should be considered as second-line screening test when diabetic retinopathy had been diagnosed and maculopathy was suspected. In this population a high prevalence of retinopathy would be expected and our population characteristics were comparable.

Further the sensitivity and specificity detected, in our study, for colour digital screening for diabetic retinopathy were comparable with previously reported data.[4] Our finding that digital colour photography by itself was relatively insensitive for detecting diabetic maculopathy may therefore be relevant to several screening programmes. It also should be noted that some are now using the negative predictive value (NPV) as the key measure of a screening test, as patients with disease who are screened negative have a strong case for compensation.

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Sir,

We read with interest the recent report by Chang *et al.* of late clouding of an acrylic intraocular lens (SC60B-OUV, Medical Developmental Research, FL) following routine phacoemulsification.[1] In view of the significant number of these lenses that have been implanted, they speculated whether their case was unique, in particular with regard to the late post-operative onset of the clouding.

Unfortunately, we are able to report that this problem is in our experience very common. In our unit we have implanted 140 of the same intraocular implants during 1998. Implantation of this type of implant was discontinued when lens changes were first noticed in a patient. It is also our experience that the clouding does not develop in the immediate post-operative period but several months later. The clouding appears to consist of tiny vacuoles within the material of the implant and these vacuoles typically have a lamellar distribution within the optic of the lens. The haptics remain unaffected. The most

common part of the implant affected appears to be just beneath the anterior and posterior surfaces of the lens. Less commonly the central substance of the lens is affected. There were no surface deposits found on the implants. We also found no benefit from topical steroids.

Clouding of acrylic implants (AcrySof) has been reported in the past,[2] and in these cases it was postulated that excessive warming of the implants prior to implantation accounted for the changes. It was thought that as the increased temperature of the implant material exceeded the glass transition temperature, microvacuoles were formed and subsequently became hydrated by the aqueous fluid. In our cases, however, none of the implants were preheated (the lenses folding easily at room temperature) and therefore this postulated mechanism for clouding is unlikely to be responsible in our patients.

We are currently performing a review of all 140 patients with this implant to assess both the scale of the problem with regard to the prevalence of lens haze and the impact of any haze on visual function. So far we have looked at 64 eyes with this lens. Twenty-one (33%) had no lens haze and 43 (67%) had lens haze. We graded the haze as mild in 34 (53%) and moderate in 9 (14%). Of the 34 with mild haze, 22 were asymptomatic and 12 were symptomatic. In the patients with moderate lens haze 4 were asymptomatic and 5 were symptomatic. Overall, therefore, 67% had lens haze, but only 27% had symptomatic lens haze. However, 3 patients (5%) had symptoms severe enough to warrant listing for lens exchange. The exchanged implants will then be analysed appropriately. When we have completed our review we hope to publish the data. Our findings, however, suggest that this is not an isolated or insignificant problem.

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Sir,

We read with great interest an article by Chang *et al.*[1] entitled 'Late clouding on an acrylic intraocular lens following routine phacoemulisfication'.

The authors have reported clouding of a foldable acrylic intraocular lens (IOL) made from poly-2-hydroxyethyl methacrylate polymer and discussed various possible mechanisms. Physical damage to foldable acrylic IOLs during folding has been reported to range from microtrauma to stress fractures. We speculate whether intralenticular protein deposition, calcium deposition or biofilm formation may have been responsible for late opacification of the acrylic IOL.

Proteins have been reported to bind to IOLs and change their biochemical properties on adsorption by denaturation or polarisation.[2] Protein deposition has been shown to vary depending upon the protein composition and concentration in the aqueous.[2,3] Proteinaceous biofilm has been demonstrated to occur in the surface of an IOL within hours of surgery.[4] In experimental studies on biofilm formation in rabbit eyes, protein disposition has been reported to vary on different IOL materials.[2,5] A biofilm is a dynamic structure with protein turnover through desorption and adsorption.[3] Physical changes during folding of an acrylic IOL may facilitate intralenticular protein deposition or biofilm formation. Calcium deposition in the foldable acrylic IOL may be another possible cause of cloudiness. Calcification of hydrogel IOLs and crystallisation on the IOL surface have been reported in the recent literature.[6,7] Protein deposition, calcium deposition and biofilm formation have been described to occur in contact lenses made from 2-hydroxyethyl methacrylate.[8] A possible defect in design or manufacturing as suggested by the authors may also contribute to the biochemical processes occurring in the IOL.

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Sir,

We are grateful for the interest shown by Sharma *et al.* We are not sure as to the aetiology of the clouding. Protein deposition could well be the cause but it would be unusual to have deposition just in the centre portion of the lens, as in this case. Therefore a defect in the design or manufacture still remains a good possibility.

As an update to our patient, she has since had a successful lens exchange with 6/9 aided vision. When explanted, the lens remained cloudy. The lens is now back in the hands of the manufacturer for analysis, as instructed by the Medical Devices Agency.

Further to our report to the Medical Devices Agency, they have received 27 reports of a similar problem of lens opacification with this particular lens type in the UK and 4 cases in France. As a result, use of this lens has been withdrawn from these two countries pending investigation.

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