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Sir,
Comment on 'The evidence informing the surgeon's selection of intraocular lens on the basis of light transmittance properties'

Recently Li *et al*[1] reviewed 'The evidence informing the surgeon's selection of intraocular lens on the basis of light transmittance properties'. The central argument of the article was that there was insufficient evidence to advocate the use of blue-light-filtering intraocular lenses (IOLs) over ultraviolet-only filtering IOLs. We would like to counter some of the conclusions in the article because the authors seem to have missed much of the relevant data.

For many years, and in multiple papers/venues (eg, refs 2–6), the senior authors (Nolan, Beatty) have argued that macular pigment (MP) helps prevent age-related macular degeneration due to its 'blue-light-filtering properties'. For example, Nolan *et al*[4] write 'MP …acts as a filter of short-wavelength visible (blue) light' and that 'AMD is attributable, at least in part, to oxidative stress and that irradiation with blue light induces oxidative stress in the retina'.

In Li *et al*,[1] they also address the question of whether blue-light filtering reduce phototoxicity. In the case of IOLs, however, the authors note that the 'hypothesized photoprotective benefits of implanting blue-light-fIltering IOLs at the time of cataract surgery is unlikely to be either proven or refuted, and the surgeon must make a decision based on a rationale rather than on an evidence base'.

Unlike for MP, the 'evidence base' in this case only refers to randomized control trials (RCTs) or case–control studies. As the authors note, however, RCTs are not appropriate for some experimental questions (eg, light damage studies). The actual 'best' experimental design is the one that is best matched to the specific question(s) being asked (that is why entire branches of medical biology rely on bench and laboratory study). The authors noted this in Sabour-Pickett *et al*.[7]

> '…RCTs have limitations…. many important findings have necessarily been the result of observational studies. Although lacking the benefit of a control group, large number of observational outcomes can provide highly reliable conclusions. The preference accorded to RCTs can, in some instances, result in the exclusion of evidence arising from other and valid sources. Experience demonstrates that studies with alternate designs should be seen as complementary to RCTs'.

Despite this view, Li *et al*[1] chose to ignore hundreds of such studies[8,9] that have used 'alternate' experimental designs and have assessed the potential for retinal damage due to short-wave light. Unlike for blue-filtering IOLs, when assessing the role of the MPs (blue-light-filtering pigments in the inner layer of the retina), the authors appear comfortable making the simple and direct inference that screening reduces such damage. Such inferences are common scientific practice, and have been made for the use of sun glasses, sun screens, originally putting UV chromophores in IOLs, and so on. It is unclear why the logic that applied for MP (screening actinic light) does not apply for blue-filtering IOLs, which actually screen more highly energetic, and hence actinic, light.

Selectively reviewing some data while neglecting other relevant empirical data is a common error in reviews and can lead to mistakes in interpretation. For example, the authors have often argued that the effects of chromatic aberration degrade visual function and that MP can limit those effects: 'MP augmentation results in optical image enhancement through a reduction of the deleterious effects of chromatic aberration…' (Nolan *et al*;[4] US prov. patent application number: 20160324800 A1). This relation actually has been empirically studied but was not cited by the authors. Engles *et al*[10] measured the relationship between MP and the deleterious effects of chromatic aberration and found no relation. The Engles *et al*[10] finding was not surprising. Careful modeling has shown that the optical effects of chromatic aberrations on visual function are minimal.[11]

The authors also argue that blue-filtering IOLs negatively affect visual function by reducing scotopic sensitivity. This also is unlikely. Sensitivity is not a static function. Rather, visual sensitivity can be adjusted quickly and over a wide range (especially with stabilized features of the eye such as constant filtering). Again, as the authors themselves note, MPOD at 460 nm ranges from near 100% transmission to about 10%, but yet the perception of blue is unaffected (the system compensates for the change in density over that log unit range).[12] The authors basically argue that the visual system can compensate for the natural lens and MP, but not a blue-filtering IOL (this is a violation of the principle of univariance; photoreceptors cannot ofcourse discriminate the source of filtering). Sensory adaptation is a basic principle and, as originally noted by Werner *et al*,[13] the dynamic range of the scotopic system (~4.0log) far exceeds possible filtering by a blue-filtering IOL (0.07log). There does appear to be some loss in scotopic sensitivity with age, but this loss is of neural, rather than optical, origin.[14] Nolan *et al*[15] notes:

> 'Reduced scotopic sensitivity has been demonstrated in some studies with the AcySof Natural IOL; however, this has generally been accepted to be of little visual or functional significance and does not affect patients' quality of life'.

A similar argument is the idea that a blue-filtering IOL will negatively influence circadian rhythms disrupting sleep. This also seems unlikely. Blue-filtering IOLs mimic a young lens. Hence, older patients are getting considerable more blue light after surgery than before (hence, based on their argument, sleep patterns should improve even with blue-filtering IOLs as shown empirically).[16] Further, light-entrained circadian rhythms are not simply driven by retinal melanopsin with its 460 nm peak (the rods and cones also feed into the retinohypothalamic tract;[17] and are not simply retinal (other 'peripheral clocks' contribute as well such as those in skin).[18] Like most aspects of the visual system, the melanopsin subsystem is not simply a passive detector, but can adjust for differing levels of constant intraocular

filtering. There are numerous empirical studies (not reviewed by Li *et al*) that find little or no effect of blue-absorbing IOLs on sleep quality.[19,20]

Li *et al* note that they 'included all studies involving patients (both male and female, above 16 years of age) undergoing cataract surgery and implantation of blue-light-filtering IOLs'. In fact, however, there are a number of studies, easily accessible, that directly compare clear and blue-filtering IOLs, which were not reviewed by the authors (eg, refs 21–24) including their own study.[15] The studies that the authors did not cite do show significant improvements with blue-filtering IOLs. For instance, the authors often tout how important increased MP is to retinal health and preventing ocular disease. Nolan *et al*[15] showed that, compared to a clear IOL, implanting a blue-absorbing IOL leads to increases in MP (a putative benefit). Hammond *et al*[24] tested visual function in patients who had a blue-filtering IOL implanted in one eye and a clear IOL implanted in the other (a contralateral design where visual function was tested 1 year after implantation). The experimenter was masked to IOL type and the order of testing was randomized. Glare disability, photostress recovery, and chromatic contrast were all improved significantly in the eye that contained the blue-absorbing IOL. Gray *et al*[21,22] compared driving performance under glare conditions in patients who had a blue-absorbing *vs* clear IOL and found improved driving performance when using a blue-filtering IOL.

The authors conclude their review by arguing that 'on the basis of currently available evidence, one cannot advocate for the use of blue-light-filtering IOLs over UV-only filtering IOLs'. The authors are certainly free to advocate as they wish. Their review, however, represents only the evidence they chose to present not the evidence that is currently available. In an earlier review published in *Eye* on the same topic (not referenced by the authors and including many studies not referenced by the authors), for instance, Downes[25] reached a quite different conclusion.

> '…there is good evidence in the literature that implantation of a BFIOL does not impair visual acuity, photopic, scotopic, or color vision, nor does it affect the sleep–wake cycle. In addition, there are some definite and theoretical benefits associated with implanting a BFIOL, including improved performance in glare but more importantly protection of the retina against short-wavelength light'.

Conflict of interest

The author declares no conflict of interest.

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Sir,
Response to 'Comment on The evidence informing the surgeon's selection of intraocular lens on the basis of light transmittance properties'

We thank Professor Hammond for his correspondence, which serves to strengthen our conclusion that there is no evidence base that can justify anyone to advocate for blue-blocking intraocular lenses (IOLs) over ultraviolet (UV)-only blocking IOLs.

Professor Hammond takes issue with our conclusion (that is, 'In terms of photoprotection, there is no Level 2b ([or higher) evidence in support of blue-filtering IOLs *vs* UV-only filtering IOLs.[1]') on the basis that we did not cite select publications, which he has now kindly brought to our attention. Accordingly, we would like to bring the Editor's attention to Table 1, which includes all of the publications alluded to by Professor Hammond, and which clearly illustrates that there remains no Level 2b evidence (or higher) in favour of blue-blocking IOLs over UV-only blocking IOLs.

Furthermore, not a single publication (ever) that has advocated for blue-blocking IOLs has measured MP, another prereceptoral filter that absorbs blue light and has profound implications for vision (as demonstrated by Professor Hammond's own work[2–4]) and for macular health.[5]

Accordingly, and in keeping with the findings of Professor Hammond and others, a study designed to comment upon the impact of blue-blocking IOLs *vs* UV-only blue-blocking IOLs that does not measure and account for MP not only fails to address the research question but even precludes the possibility of addressing the research question.

In conclusion, we thank Professor Hammond for the interest he has shown in our work, an interest, which copperfastens our contention that there is no evidence-based justification for implanting blue-blocking IOLs over UV-only blocking IOLs at the time of cataract surgery.

Conflict of interest

JMN and SB do consultancy work for nutraceutical companies, in a personal capacity, and as directors of Nutrasight Consultancy Limited. The remaining authors declare no conflict of interest.

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