in her joints. However, 6 months later, she developed bilateral scleritis. The etanercept was stopped, and her joints flared. She was given a cycle of rituximab with resolution of scleritis and improvement of the arthritis. Six months later, she is in remission, for both arthritis and scleritis.

**CASE 3**
A 56-year-old male with a history of chronic obstructive airway disease, ischaemic heart disease, excess alcohol intake and RA had problems complying with taking his medication. He presented with scleritis and a flare of synovitis. Initial treatment of analgesics and high-dose oral prednisolone was ineffective. Because of poor compliance with therapy, and many medical problems, it was considered too risky to use cyclophosphamide or a TNFi. A cycle of rituximab was therefore given. One month later, his eyes became quiet and synovitis resolved. He has remained well for the past 6 months.

Eye involvement in rheumatic diseases can lead to residual damage and even blindness. Immunosuppressive drugs (steroids, azathioprine, ciclosporin, mycophenolate, cyclophosphamide and tacrolimus) are the mainstay of therapy with variable efficacy. TNFi agents may also be effective in suppressing inflammation in eyes as well as joints. However, their high cost, contra-indications or development of adverse effects and lastly unresponsiveness in some patients limit their use in these situations.

Rituximab is an anti-CD20 chimeric human/mouse monoclonal antibody that depletes pre-B cells. It has been used with success in various rheumatological disorders including RA, systemic lupus erythematosus and antineutrophil cytoplasmic antibodies-positive vasculitis. In Europe, it is currently licensed for use in RA after failure of a TNFi. Until now, there have been only five individual case reports of inflammatory eye disease successfully treated with rituximab. Two of these had Wegener granulomatosis, and one each with Sjögren syndrome, Behçet disease and primary refractory anterior uveitis. A comprehensive literature search has failed to reveal any case of scleritis associated with rheumatoid arthritis treated with rituximab.

We present the first report of scleritis associated with RA treated successfully with rituximab. In our hands, rituximab has proven to be a highly effective therapy in scleritis associated with RA in patients who have proven refractory to, or who cannot tolerate, conventional treatment with cyclophosphamide or a TNFi. We believe that rituximab should be given serious consideration for use in patients with inflammatory eye conditions secondary to RA or other rheumatological disorders, who have proven refractory to other modalities. However, there is a paucity of literature, thus warranting more trials to define the optimal place of rituximab in such conditions.

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**MAILBOX**

Cataract surgery and mortality

We read with interest the paper by Blundell *et al.* which compared mortality among people who had undergone cataract surgery in Bristol in 2000–2001 with the mortality in the general population of England and Wales, and of the Bristol region.

We have some concerns about the sample and interpretation of the results.

The authors provide a pooled standardised mortality ratio (SMR) of 0.88 (95% CI 0.79 to 0.99) for all age mortality among those having cataract surgery compared with the general population. This pooled estimate hides the mortality ratio (SMR) by age group only demonstrates decreased mortality in the older population groups. They hypothesise that within these older age groups, individuals with comorbidity that would affect their mortality may be less likely to have cataract surgery, thus artificially lowering the SMR measured in our study. They go on to state that only longitudinal studies should be used to examine the relationship between mortality and cataract.

In our study, we have only investigated mortality in the proportion of the population with cataract who have undergone cataract surgery. While this method cannot give us the complete picture of the relationship between cataract and mortality, it still represents an important patient group that deserves study. Understanding in a pragmatic way the survival of people undergoing surgery at different ages has value. It

**AUTHORS’ RESPONSE**

We acknowledge the points made by Lindfield *et al.* and thank them for taking an interest in our article. Their letter highlights that our subanalysis of standardised mortality ratio (SMR) by age group only demonstrates decreased mortality in the older population groups. They hypothesise that within these older age groups, individuals with comorbidity that would affect their mortality may be less likely to have cataract surgery, thus artificially lowering the SMR measured in our study. They go on to state that only longitudinal studies should be used to examine the relationship between mortality and cataract.

In our study, we have only investigated mortality in the proportion of the population with cataract who have undergone cataract surgery. While this method cannot give us the complete picture of the relationship between cataract and mortality, it still represents an important patient group that deserves study. Understanding in a pragmatic way the survival of people undergoing surgery at different ages has value.
informs practical issues of relevance to service delivery—for example in determining quality-adjusted life years (QALYs) per cataract operation.

In our article we have compared our results only with those from previous similarly designed studies,\(^1\) studies that have the same limitations and biases as our own. These would be as affected by lower take-up rates of surgery by older infirm people as in our study. Despite this, the results from previous studies show a higher rate of mortality postcataract surgery when compared with a national population, while our study shows a lower mortality. This change over time is not explained by Lindfield et al’s hypothesis and should not be overlooked.

We recognise and accept that our study has limitations, and our methodology cannot deliver “absolute truth” on this subject. However, our findings investigate in a “real world” context the mortality of those who present for cataract surgery. The results demonstrate a change from earlier studies which could be representative of changes in provision of cataract surgery in the UK. Our findings may be relevant in practical issues of service delivery and stress the importance of re-evaluating knowledge in the light of changing practice.

**Promise and potential pitfalls of anti-VEGF drugs in retinopathy of prematurity**

Only rarely does a new treatment offer a real sea change. An example in the field of neonatology is the use of exogenous surfactant for hyaline membrane disease.\(^1\) For the eye, anti-vascular endothelial growth factor (VEGF) drugs may be the therapeutic advance of our time, revolutionising the treatment of vasoproliferative retinopathies including age-related macular degeneration and diabetic retinopathy. In his informative editorial, Sears suggests that anti-VEGF therapy may play a similar role in retinopathy of prematurity.\(^2\)

Retinopathy of prematurity (ROP) is a vasoproliferative disease, and it is therefore not surprising that there is increasing enthusiasm for anti-VEGF drugs.\(^3\) \(^\text{3}\) Even with the best treatment available, laser photocoagulation of the peripheral retina, some eyes still lose vision. Anti-VEGF therapy does not ablate retinal tissue; hence, if the fibrovascular process is not too advanced at the time of treatment, retinal architecture and function might be preserved. ROP is now an important cause of blindness in children in middle-income countries and an increasing problem in India and China.\(^4\) In such low-resource situations, anti-VEGF drugs are appealing, as the intravitreal injection can be administered in the nursery without specialised equipment. However, earlier ROP studies show spontaneous regression in approximately two-thirds of eyes reaching current treatment criteria, albeit sometimes with visually disabling consequences. We must be certain that any new therapy has at least as good a cost–benefit profile as established treatments.

Experimental studies demonstrate that VEGF has key roles in development beyond retinal vasculogenesis.\(^5\) VEGF regulates angiogenesis in other organs; in the nervous system, it is neurotropic and neuroprotective, and maintains the blood–brain barrier,\(^6\) in the lungs, it plays an important role in alveolarisation.\(^7\) Critically, VEGF is active when anti-VEGF agents would be required to treat ROP. Plus disease, present in severe ROP, is associated with blood–ocular barrier breakdown and may lead to greater systemic absorption of anti-VEGF preparations than in adults or experimental animal models.

Neonatology has its share of disasters and from ad hoc introduction of new therapies that “seemed a good idea at the time.” Examples include the uncontrolled use of oxygen in the 1940s, which led to the first epidemic of ROP, and the higher rates of cerebral palsy in premature babies given systemic steroids to shorten ventilatory support in the 1980–1990s. The notable feature in both these examples was that these treatments were introduced for short-term gains without considering possible longer-term harm.

Anti-VEGF treatment has been used with good results in babies with ROP.\(^8\) \(^\text{8}\) However, we would advocate extreme caution before introducing a new, unproven therapy, particularly as recent randomised clinical trials have shown the safety and effectiveness of laser photocoagulation. There is an urgent need for well-designed, adequately powered randomised clinical trials in which ocular, neurological and pulmonary long-term outcomes are carefully documented. A thorough understanding of the systemic side effects is essential before wide implementation of this new, potentially helpful treatment. We must not look back in a few years and be faced with the knowledge that, with careful planning and research, we could have avoided doing harm.

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