

EDITORIAL

Changing Trends of Blindness: The Initial Harvest From Translational Public Health and Clinical Research in Ophthalmology

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ALL OPHTHALMOLOGISTS AND VISION RESEARCHERS are aware of the profound adverse effects of blindness on our patients' health and quality of life. From a societal perspective, visual loss comes with an exorbitant price tag, with an estimated global cost of nearly \$3 trillion for the 733 million people living with low vision and blindness worldwide.¹ With unceasing population growth and aging demographics, these numbers are expected to spiral upward. In this issue of the Journal, however, contemporary surveillance data from 2 large population-based studies shed some light on our battle against blindness and offer hope that the tide may be turning because of new public health initiatives and novel clinical treatments that have been translated from research in recent years.^{2,3}

Based on national registry data over the last decade, there is now evidence of a substantial decline in the incidence of blindness in 2 developed countries. Skaat and associates showed that the incidence of blindness in Israel halved from 1999 to 2008.² Although several common causes of blindness contributed to this finding, much of the decline could be explained by the reduced blindness resulting from age-related macular degeneration (AMD). Results of the study by Bloch and associates support this observation, showing a 50% reduction in the incidence of blindness attributable to AMD from 2000 through 2010 in Denmark.³ Notably, the bulk of this reduction occurred after 2006, suggesting a temporal relation to the introduction of intravitreal anti-vascular endothelial growth factor (VEGF) therapy for neovascular AMD. Similar results can be expected in the United States and many countries in which anti-VEGF therapy is used widely and is likely to have a major impact. For example, based on computer modeling of data from clinical trials and population-based studies, Bressler and associates showed that anti-VEGF

therapy could reduce the incidence of blindness by approximately 70% within 2 years among non-Hispanic white Americans.⁴

The expanding role of intravitreal anti-VEGF therapy in ophthalmology is truly revolutionary. Over the last decade, it has been proven and used as an effective treatment for an array of blinding retinal diseases, including neovascular AMD,⁵ diabetic retinopathy,⁶ and retinal vein occlusion.⁷ These conditions, before the anti-VEGF era, were the major contributors to blindness in many developed countries, and now their treatment paradigms have shifted momentarily. AMD treatment alone is evidently illustrative.⁸ Not so long ago, neovascular AMD was considered untreatable. Then, the advent of photodynamic therapy surpassed argon laser as the predominant treatment choice with an aim to preserve vision in patients with neovascular AMD. Now, the aim of anti-VEGF treatment is not just to maintain, but also to improve, vision in a significant proportion of patients. Similar trends are seen in the management of macular edema related to diabetic retinopathy and retinal vein occlusion.^{6,7}

Nevertheless, it is important to recognize reasons other than anti-VEGF therapy that also may contribute to the declining incidence of blindness. One such example would be better recognition of the importance of visual impairment and better delivery and access to universal health care systems, particularly in developed countries like Denmark and Israel. Blindness resulting from cataract, for instance, is now much less common because of readily available modern cataract surgery to the general community. Second, improvements in the care and management of diabetes likely account for the reduced visual loss resulting from diabetic retinopathy. New medications to treat hyperglycemia and hypertension, coupled with the development of educational and surveillance programs, play major roles in the decrease in vision-threatening retinopathy over the last decade.^{9,10} Third, the fall in glaucoma-related blindness may be linked to enhanced diagnosis, monitoring, and treatment of glaucoma. Whereas national screening campaigns aid in early diagnosis, technological advances in optic nerve head and retinal nerve fiber layer analysis allow more precise monitoring of glaucoma progression.¹¹ In addition, effective control of intraocular pressure now can

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be achieved in most patients with topical therapies (e.g., prostaglandin analogs) and laser therapies. The development of combination eye drops and the use of selective laser trabeculoplasty, whether as a primary, adjunctive, or replacement therapy, help to mitigate problems with patient compliance. Finally, the success of antismoking campaigns in linking smoking with blindness also may have contributed in reducing the overall incidence of vision loss.¹² Taken together, all these changes in public health measures and clinical practice are central to the declining trend for blindness seen in developed countries.

Although the lowering incidence of blindness may represent a triumph in translational public health and medical research, several uncertainties remain. For example, it is unclear whether the number of people affected by blindness also is reducing in developing countries, where access to health care generally is poor and where the prevalence of diabetes is expected to increase as their populations become more sedentary and obese.¹³ It is estimated that in China and India alone, the number of people with diabetes will be well over 200 million in the next 2 decades.¹⁴ It is debatable whether the health care systems in these countries are in place to cope with the expected increase in diabetes-related ocular complications. Even in developed countries, although the clinical efficacy of intravitreal anti-VEGF therapy is indisputable, its cost effectiveness has been a focal point of controversy. Based on a study model comparing ranibizumab and bevacizumab, 2 principal anti-VEGF agents used for neovascular AMD, ranibizumab is cost effective at current pricing only if it is at least 2.5-fold more efficacious than bevacizumab.¹⁵ As it turns out, unsurprisingly, this is not the case. The lack of a significant difference in efficacy for treating neovascular AMD, as

demonstrated in the Comparison of AMD Treatments Trial,¹⁶ seriously challenges the considerable cost differential between these 2 agents. Moreover, a recent report by the Department of Health and Human Services indicates that Medicare could save more than \$1 billion and patients could save \$275 million in copayments in just 2 years if bevacizumab replaces ranibizumab as the primary treatment of neovascular AMD in the United States.¹⁷ With expanding indications of anti-VEGF therapy for other eye diseases (e.g., diabetic retinopathy, retinal vein occlusion), the cost of this treatment could be astronomical and could add unsustainable stress to the finite resources of the health care system. Cost is not the sole issue in play. The choice of anti-VEGF agents also is complicated by possible systemic and ocular safety concerns, for which the current literature provides more questions than answers.¹⁸ Future studies are expected to address some of these issues, especially in relation to safety profile, optimal dosing regimen, and the use of alternative new antiangiogenic agents (eg, VEGF-Trap).

Nonetheless, the declining incidence of blindness can be considered a public health success and is related to the substantial funding for translational research carried out in ophthalmology over the past decades. It offers a glimpse of hope in our battle against blinding eye diseases, although this battle is far from over. Further funding is needed for research into new cost-effective preventative, diagnostic, and therapeutic strategies. These public health endeavors must continue and should extend to the developing countries where the rate of blindness is expected to be higher. We cannot afford complacency, especially with close to 1 billion people worldwide expected to experience visual impairment by 2020.¹

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