Review Article

Journal of Optometry and Ophthalmology Research

Managing Glaucoma in an Evolving Clinical Landscape

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Received: May 08, 2026; **Accepted:** May 18, 2026; **Published:** May 25, 2026

ABSTRACT

Glaucoma continues to affect patients at a rate overwhelming to current care models, a problem particularly evident in rural and underserved communities. This necessitates reevaluation of the current glaucoma management approach and opens the door for the development of collaborative care frameworks that leverage the complementary skills of optometrists and ophthalmologists. As our understanding of glaucoma continues to evolve, ongoing research consistently identifies new risk factors, mechanisms, and therapeutic targets. Emerging technologies, including home tonometry, wearable perimetry devices, and polygenic risk score, have the potential to reshape glaucoma screening, monitoring and treatment. Similarly, systemic conditions like obstructive sleep apnea and hypertension, as well as medications including glucagon-like peptide-1 receptor agonists, calcium channel blockers, nicotinamide, and pyruvate, warrant consideration in glaucoma. New insight into glaucoma pathophysiology combined with access to novel screening, monitoring, and treatment modalities, positions eyecare providers to deliver more comprehensive, patient-centered care. By combining new discoveries and technology with interprofessional collaboration, we are positioned to transform glaucoma care from a traditionally reactive approach toward a more proactive, preventive model.

Keywords: Glaucoma, evolving approach, technology, tonometry, perimetry

Introduction

Tens of millions worldwide are affected by glaucoma, including over 4 million Americans, and despite available and effective therapies, glaucoma is still a leading cause of blindness. Unfortunately, the US optometric and ophthalmic workforce remains unevenly distributed and frankly insufficient. In 2022 in the US, glaucoma prevalence was 5.2% among patients older than 65, and 2.6% in patients older than 40 [1,2]. Reports from 2023 estimated that the full-time ophthalmology workforce (all specialties) totaled 16,778, while optometrist numbers were higher at just above 40,000 [3]. Geographically, 61% of US counties had no ophthalmologists, 24.2% had no optometrists and 24% had neither, with rural locations often suffering the most from pronounced gaps in access to glaucoma care [4]. In the US, the Veteran's Affair (VA) department reports that the majority of US veterans suffering from glaucoma are located in rural areas and hence greatly underserved [5]. In short, glaucoma prevalence creates major demand on a workforce that is too small and unevenly distributed to address the unmet need. So, rather than asking "how do we catch up?" the focus must be redirected towards adjusting our approach to disease management, so that together optometrists and ophthalmologists may serve this population more effectively.

Expanding Role of Optometrists in Glaucoma Care

This mismatch between disease burden and provider availability means that many patients are diagnosed and monitored in settings where optometrists are essential for early detection, longitudinal surveillance, and timely referral, especially in regions with limited specialist coverage. The role of optometry in glaucoma will continue to expand as both patient population and scope of practice grow and evolve. Both co-management models and primary management in early/moderate disease will continue to become more common, benefiting patients with minimal access to care or those with early disease that may have previously been low priority in overflowing glaucoma clinics. As collaborative frameworks, such as digital care and telemedicine continue to

Citation: Coy Steel, Andy Renschler MD, Brian Stagg MD MS, Barbara M Wirostko MD. Managing Glaucoma in an Evolving Clinical Landscape. J Opto Opht Res. 2026. 2(2): 1-6. DOI: doi.org/10.61440/JOOR.2026.v2.11

be developed and refined, eyecare providers can and should leverage several emerging resources to optimize the quality and quantity of care that can be provided.

Driven by an incomplete understanding of the pathophysiology and genetics of the disease, modern glaucoma management is progressing. As we continue to gain a deeper understanding of the pathophysiology that drives progression, we also develop technology and techniques that are making diagnosis and timely treatment more effective. Traditionally, disease diagnosis and monitoring relied on infrequent, in-office, one time point intraocular pressure (IOP) and visual field evaluation. We now know that this is inadequate and leads to overflowing clinics where patients often slip through cracks. Research has confirmed that the majority of Americans with glaucoma do not even complete yearly VFs as recommended by our association guidelines [6]. However, promising new resources including home tonometry, wearable visual field perimeters and glaucoma polygenic risk scores (PRS) have potential to transform the traditional approach to management, effectively reducing long-term impact and improving patient outcomes by managing proactively and preventively rather than reactionary.

Emerging Technology

Home Tonometry

Goldman applanation tonometry measured in clinic has long been considered the gold-standard measure of IOP and glaucoma control. However, infrequent clinic measurements only capture a single point along a patient's diurnal/nychthemeral IOP curve. IOP fluctuation, in addition to magnitude, is linked to vision loss, and patients with glaucoma often experience their highest IOP spikes outside of office hours (between the hours of 4-6 AM) in the early morning [7,8]. Previously, clinicians lacked the ability to characterize IOP variation conveniently [7,9]. Now, home tonometry devices like the iCare HOME2 (iCare USA, Raleigh, NC) enable more accurate characterization of true IOP variation sufficient enough to influence management decisions, and their implementation into clinical practice should be thoroughly considered [10].

Though proven to be effective resources, further research into optimal use monitoring timelines can help outline best practice guidelines and facilitate more widespread use. Recent data (both published and unpublished by our group at Moran and Wilmer) show that even 24 hours of IOP data fails to fully characterize variability due to environmental and behavioral influences[11]. Preliminary findings show that multi-(7-10) day monitoring periods better capture both true magnitude and variability of IOP, which provides clinicians with more information and helps to guide both magnitude- and variability-informed decisions (manuscript pending). A more complete understanding of diurnal rhythm also allows clinicians to incorporate timing into individual care plans to fully optimize the effects of pressure-lowering therapies[10]. Our Moran data, showing that peak IOP in early waking hours (4-6 am) was effectively lowered by selective laser trabeculoplasty (SLT), has further helped explain why perhaps the LiGHT study showed less progression on VFs over 6 years despite similar IOPs in office with SLT versus topical drops (manuscript in press) [12]. Current monitoring practices based on infrequent office-based measurements fail to fully characterize IOP (potentially delaying progression identification) and miss what may be the critical IOP, the out of office time [13]. A transition towards remote monitoring enables data-informed care for patients and might allow clinicians to not only treat more patients but provide better care.

Wearable VF Perimetry

Following a similar trend, traditional in office visual field (VF) perimetry protocols are being challenged with the emergence of wearable VF perimetry devices. Traditionally, visual field loss has been monitored in clinics along the same infrequent timeline as IOP. Although the AAO preferred practice guidelines suggest yearly VF testing at a minimum, patients often complete VF tests at a rate so infrequent (<1/year) that timely detection of VF loss/progression is impossible or at least highly unlikely [6,9]. In its current form, completion of the test requires time, space, and money. Patient cooperation is also impacted by the uncomfortable nature of the test. Combined, each of these factors contribute to longer testing intervals. Higher VF testing frequency is proven to reduce time to detect progression and more effectively identify those at risk of rapid progression. However, the logistics behind current testing practices have limited the ability to translate this knowledge into clinical practice [14,15]. The current solution to this problem is wearable VF perimeters which can be administered not only at home but more frequently. Studies have demonstrated and modeled that more frequent testing and clustering for testing can in fact detect progression more rapidly thus enabling early intervention [16-19].

These innovative new devices enable more frequent testing by improving ease of use and comfort and decreasing cost. They also eliminate the need for VFs to be conducted in person, which enables more frequent, at home monitoring. Initial results are promising in studies comparing wearable perimeters to traditional Humphrey VF testing, supporting their use as valuable adjuncts to traditional methods (manuscript pending) [20]. Furthermore, because VF testing relies upon subjective patient response, and the algorithms underlying various devices make inter-device comparisons inaccurate, progression detection relies upon clinician interpretation (manuscript pending). Accordingly, consistency within a given platform may be more important than continuing to adhere to traditional "gold-standard" monitoring protocols. Either way, this emerging technology provides options to clinicians in rural or resource-limited settings and simultaneously makes adhering to monitoring guidelines more feasible.

PRS Scores

Glaucoma polygenic risk scores (PRS) represent another exciting new tool in glaucoma management. These screening tools can help predict a patient's risk prior to any evidence of disease. They quantify genetic predisposition and are valuable as screening and progression prediction tools [21]. Further, when used in parallel with traditional measures such as IOP, central corneal thickness (CCT), family history, and findings on clinical exam, PRS can help improve risk stratification and potentially guide treatment frequency and intensity (work ongoing at the Moran: IRB_00192805). Early studies have shown associations with high risk PRS and increased maximum IOP, family history, and incisional procedures [13,22]. Similarly, ocular hypertension patients demonstrated an increased likelihood of progression to

POAG with higher PRS scores[23]. Despite many promising findings, there are several limitations worth considering when incorporating a PRS with clinical practice. Limitations include generalizability to a wide range of ethnicities, cost, accessibility, and ethical implications underlying all genetic testing [24,25]. While PRS scores appear to be a promising improvement to current risk stratification and screening capabilities, they have not yet proven to be sufficient on their own, which highlights the importance of using this tool in conjunction with clinical risk factors such as family history, IOP, and visual field loss [23,26]. However, if used appropriately, and with continued development, they may soon transform glaucoma management.

Additional Contributors to Glaucoma Progression - Factors to Consider

Systemic Conditions

Additional factors worth considering when a patient's glaucomatous disease is progressing despite standard of care include systemic comorbidities. Screening for these conditions may improve diagnosis and management. For example, obstructive sleep apnea (OSA) is associated with more than a two-fold increase of open-angle glaucoma at 3, 5, and 10 years after an OSA diagnosis [27]. Despite fundamentally being a respiratory disorder, OSA disrupts circadian regulation and may contribute to glaucoma progression through both vascular and mechanical mechanisms [28,29]. We are currently collecting data using home tonometry to characterize IOP fluctuations in patients with POAG and OSA [30].

While elevations in IOP are closely monitored in glaucoma, blood pressure is equally important. Blood pressure and IOP interact to influence ocular perfusion pressure (OPP), which determines optic nerve and retinal perfusion [31]. Elevations in IOP and low blood pressure can both decrease OPP. It's worth noting that OPP is dynamic; both magnitude and duration of nocturnal hypotension have been associated with accelerated glaucoma progression - presumably due to sustained reductions in optic nerve perfusion [32]. Emerging evidence also suggests that long-term blood pressure variability may worsen visual outcomes in patients with glaucoma, independent of mean blood pressure [33]. These findings highlight a critical point: The optic nerve is susceptible to insult from additional factors beyond elevated IOP, particularly fluctuations in IOP, hypoxia and blood pressure instability.

Medication Effects

In addition to the systemic health factors and their relationship with glaucoma, new information regarding the impact of systemic therapeutics on optic nerve health and IOP is worth noting. Observational and preliminary studies have demonstrated anti-inflammatory and neuroprotective effects of glucagon-like peptide 1 receptor agonists (GLP-1RAs), suggesting a potential therapeutic impact on optic nerve health and vision preservation [34,35]. Animal and human studies have demonstrated neuroprotective effects via anti-inflammatory mechanisms impacting IOP and retinal ganglion cells through cAMP-dependent and nitric oxide pathways reducing CSF production and improved trabecular meshwork outflow[35–43]. These mechanisms may account for otherwise unexplained IOP reductions observed in multiple patients who started GLP-1RAs for non-glaucoma indications (manuscript in press), though further research is needed for a more comprehensive understanding.

Additionally, calcium channel blockers (CCBs) are another class of medications to be aware of when treating glaucoma patients. Recently, studies have shown an IOP-independent mechanism that might potentiate vision loss by inducing structural damage on the retina [44,45]. Previously thought to be neuroprotective, the hypotensive effects of CCBs might ultimately compromise blood flow to highly metabolic retinal cells, thus altering the ocular perfusion pressure [46]. Conversely, oral supplementation with nicotinamide and pyruvate may reduce early mitochondrial damage and metabolic deficits in retinal ganglion cells (RGC), reducing optic nerve degeneration. We await the results of the clinical trials currently being conducted assessing the role of these oral supplements on glaucomatous progression independent of IOP lowering (National Clinic Trials: NCT05275738, NCT05405868).47 Together, these two metabolites boost metabolism in struggling RGCs, effectively reducing neurodegeneration evidenced by improved visual field outcomes and inner retinal function [48–51]. Though not traditionally associated with the disease, each of the medications mentioned above appear to have unique implications for glaucoma. At a minimum, they are worth discussing with glaucoma patients and may eventually help explain unexpected stability or progression, respectively.

Personalized Glaucoma Management and Future Directions

Deeper insight into the pathophysiology of glaucoma and greater access to novel screening, monitoring and treatment modalities enable optometrists and ophthalmologists to provide excellent, comprehensive care. These improvements allow for more personalized, frequent, and convenient glaucoma treatment. However, with increasing patient data, interpretation challenges may need to be addressed. Synthesizing days- to weeks-worth of at-home IOP data, or monthly visual fields into targeted treatment plans will take time and may initially increase clinician workload. Potentially, there may be room for integration of AI and predictive analytics into clinical workflow and progression detection. Nearly 90% of clinicians are interested in digital support to improve glaucoma decision making [52]. As we develop these programs, it is critical that they integrate into clinical workflows and are designed to address the needs of practicing clinicians [53]. Additionally, remote monitoring and combined care frameworks could create systems conducive to tele-ophthalmology and improve access to care.

Conclusion

To illustrate the value of these newer methods of monitoring glaucoma, we present the case of a 64-year-old white male with severe bilateral pigment dispersion glaucoma, obstructive sleep apnea (OSA) not on CPAP, and controlled hypertension demonstrating the efficacy of an approach that utilizes the principles outlined. While monitoring diurnal IOP via home tonometry due to his severe glaucoma status and remote residence, it was noted that he exhibited clinically significant IOP declines on two separate occasions following initiation and later reinitiation of a GLP-1RA. At a follow up visit, inquiry into his OSA status while reviewing systemic comorbidities resulted in a formal sleep evaluation and subsequent use of a CPAP machine for management. Continued IOP monitoring with home tonometry revealed further significant reduction in diurnal IOP fluctuation after sufficient OSA treatment led to fewer apneic events. The combined integration of these interventions with data gathered using remote monitoring techniques has helped delay further surgical intervention and improved ocular health and quality of life.

This case illustrates how integrating modern diagnostics (home tonometry and sleep apnea monitors), addressing systemic comorbidities (OSA), and leveraging emerging therapeutic insights (GLP-1 RA) meaningfully altered the course of severe glaucoma by delaying/avoiding surgery in a high-risk patient. As this frontier continues to evolve, implementing a more encompassing approach with the available resources will reshape routine glaucoma care.

Historically, glaucoma management has been largely reactive. Today, we are uniquely positioned to transform glaucoma care with the adoption of a more proactive, anticipatory model. Advances in ophthalmic technology and research are guiding this transition: PRS may offer utility in screening and risk stratification, while remote monitoring technologies, including home tonometry and wearable visual field devices, better characterize disease dynamics and variability. Furthermore, there is increasing evidence stressing the importance of comprehensive evaluation and management beyond the eye. Continued progress will depend on further research and implementation into real-world practice.

Glaucoma remains a chronic, blinding disease with no cure and growing incidence that significantly outpaces provider workforce. Expanding provider capacity at the necessary rate is not possible, so, glaucoma care must evolve. By leveraging emerging resources and scientific discoveries, we can limit its impact. Similarly, combined-care models can help improve care delivery, extend reach to more patients, and optimize the capability of both optometrists and ophthalmologists. During this exciting time in the world of glaucoma, a comprehensive approach based on current evidence and new technology offers the most practical path forward.

Financial Support: This work was supported by an Unrestricted Grant from Research to Prevent Blindness, New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.

Conflict of Interest: No conflicting relationship exists for any author.

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