



AMERICAN GLAUCOMA SOCIETY

UNMET NEEDS IN THE DETECTION, DIAGNOSIS, MONITORING, TREATMENT, AND UNDERSTANDING OF PRIMARY OPEN ANGLE GLAUCOMA

Glaucoma is a common ophthalmic disorder characterized by typical optic nerve damage and vision loss. It is most commonly associated with elevated or dysregulated intraocular pressure (IOP), although there is evidence that other factors contribute to the disease. Glaucoma is a leading cause of irreversible blindness worldwide. Its prevalence in the United States is approximately 1,900 per 100,000 persons over age forty, and the condition is responsible for upwards of 9 million clinic visits each year.¹⁻³

³ In the United States, where annual spending on optic nerve disorders is estimated at \$5.8 billion annually,⁴ glaucoma is a significant public health concern. The American Glaucoma Society (AGS) and the American Society of Cataract and Refractive Surgery (ASCRS) are committed to bringing greater attention to the current challenges that exist in the detection, diagnosis, monitoring, treatment and understanding of open-angle glaucoma.

I. BACKGROUND

Individually and collectively, our organizations include and represent thousands of patients and the leading clinical and scientific experts in the fields of ophthalmology and glaucoma:

- **AGS** is composed of over 1,300 glaucoma specialists dedicated to sharing clinical and scientific information for the benefit of patients, colleagues, fellows and residents. Together with other health care organizations, the AGS serves as an important patient advocacy force to promote glaucoma awareness among policy makers and the general population.
- **ASCRS** is an international educational society with nearly 8,000 ophthalmic surgeons. Its mission is to empower anterior segment surgeons to improve the vision, outcomes and quality of life for their patients through innovative approaches to education, advocacy and philanthropy.

Members of these societies provide clinical care and conduct research aimed at better understanding, treating, and curing glaucoma. Despite significant recent advances, there are still substantial deficits in each of these categories, herein described as *unmet needs*.

II. SPECIFIC AREAS OF UNMET NEED

AGS and ASCRS work collaboratively with patients, providers, payors, and federal and state governments to better address the clinical burdens of glaucoma. We are also committed to advancing the state of the art in glaucoma treatment, with the support of the research community. A review of current evidence examining the diagnosis and management of glaucoma has identified key challenges to the effective treatment of glaucoma. Collectively, we urge researchers, clinicians, and other stakeholders to

implement strategies that address these gaps with the goal of increasing the effectiveness and efficiency of glaucoma treatment and clinical management.

The following **six key areas of unmet need** are listed in logical but arbitrary order, while the specific unmet needs listed in each numbered section below are given in priority order as determined by unanimous consent of the AGS Research Committee. This is a dynamic list that will be reviewed and updated regularly as needs are addressed and new unmet needs are identified, as specified in the attached Appendix.

1. Primary open angle glaucoma (POAG) manifests as a group of related neurodegenerative conditions acting through varying eye-specific pathophysiological processes that share some common elements: retinal ganglion cell axonal damage that is thought to occur primarily at the optic nerve head (ONH), which frequently results in clinical cupping of the ONH and the particular pattern of permanent visual field loss typical of the disease. The course of POAG can be relatively aggressive, manifesting in just a few years, but more commonly vision loss is slow, occurring over many years and even decades. Due to the complexity and diversity of POAG etiology and manifestation, coupled with the difficulty in clinical assessment of risk factors and detection of disease onset and progression, screening and management remain very challenging. In addition, there are significant numbers of patients in whom POAG goes undetected until significant permanent vision loss has occurred. Many patient populations do not have sufficient access to highly trained clinicians that can adequately manage POAG and its associated vision loss. Hence, **unmet needs in POAG screening and management** are:

- Improve glaucoma screening techniques and methods to ensure follow-up in those who screen positive. Attempt to minimize false positives and negatives. Develop strategies to best deploy screening in high-risk populations when appropriate.
- Improve telemedicine for glaucoma management such that it is viable for clinical practices
- Develop improved assessment and characterization of POAG, with a focus on disease definition and staging

2. The complexity of POAG etiology and its manifestations, coupled with the lack of methods to accurately quantify known risk factors and the insensitivity and variability of gold-standard visual function testing, combine to make it difficult to definitively diagnose POAG onset and accurately monitor its progression. While new imaging and diagnostic modalities have greatly improved eye care in recent years, these approaches have been slow to benefit POAG diagnosis and monitoring. As a result, the relationships between risk factors and POAG susceptibility, onset and progression require further investigation. Hence, **unmet needs in POAG diagnostics and monitoring** are:

- Develop robust, sensitive biomarkers for POAG susceptibility, onset and progression, with a focus on detecting disease early, and identifying those patients at greatest risk of progression
- Develop safe, accurate 24-hour IOP telemetry / monitoring technologies

- Develop new technologies to accurately and sensitively assess visual and RGC function, with a focus on early and reliable change detection using patient-friendly methods

3. While many POAG risk factors have been identified, the relationships between these risk factors and POAG susceptibility, onset and progression require further elucidation. Lowering IOP is the only accepted treatment for the disease and yet many patients with glaucoma never present with an elevated IOP. In addition, the pathways through which these factors act to damage RGC axons remain largely unknown. Hence, **unmet needs in understanding POAG pathophysiology** are:

- Develop an in depth understanding of non-IOP-related factors that contribute to POAG susceptibility, onset and progression, with a focus on:
 - Vascular perfusion/ocular perfusion pressure
 - Cellular and molecular pathways
 - Cerebrospinal fluid pressure
 - Ocular biomechanics
 - RGC soma and axonal health
 - Genetic factors
- Develop an in-depth understanding of IOP-related factors that contribute to POAG susceptibility, onset, and progression, with a focus on nocturnal IOP effects, IOP fluctuations, IOP control mechanisms, and their manifestations at the tissue, cellular and molecular levels
- Further develop high-fidelity model systems for studying POAG pathogenesis and treatment approaches

4. Therapeutics for lowering IOP, the only accepted clinical treatment for POAG, could be improved, especially in challenging patients that do not adequately respond to current therapies or those in which IOP is already within the normal range. In addition, there are many other potential pathways that could be targeted to slow or arrest POAG progression that do not involve modulating IOP. Hence, **unmet needs in POAG therapeutics** are:

- Develop methods to improve patient compliance and medication adherence, with a focus on sustained-release drug delivery systems that reduce the need for patient compliance/adherence and pharmacogenetic approaches to assess which drugs will work best in a particular patient
- Develop additional and/or more effective IOP-lowering therapies
- Develop non-IOP-related therapeutics, focused on:
 - Neuroprotection
 - Ocular blood pressure/flow/perfusion maintenance and modulation
 - Intracranial/cerebrospinal fluid pressure modulation
 - Neural regeneration and synaptogenesis

- Stem cell therapy / cell reprogramming
- Biomechanical reinforcement
- Develop new invasive and non-invasive surgical approaches or co-therapies that improve patient outcomes and reduce long-term failure rates

5. Maintenance and improvement of POAG patient quality of life is the eventual goal of clinical glaucoma management. Hence, **unmet needs in patient outcomes and quality of life** are:

- Improve vision rehabilitation among patients with advanced glaucoma-related vision loss
- Improve the definitions and characterization of clinically-relevant POAG progression and its direct impact on vision-related quality of life
- Develop a glaucoma specific Quality of Life (QoL) questionnaire that can be used to assist in measuring the true impact of this disease on patients. This QoL questionnaire could also help in standardizing further research efforts

6. To achieve the aforementioned goals, we will also need to improve the development of clinician-scientists, as well as further educate the public about glaucoma and the importance of regular clinical wellness visits with glaucoma screening.

As research and innovation in the field advances, it is vital that public health policy and coverage standards develop in parallel. We expect that efforts to overcome the clinical challenges outlined here will be a key marker of successful treatment and management of glaucoma.

References

1. Friedman DS, Wolfs RC, O'Colmain BJ, et al. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol.* 2004;122(4):532-538. doi:10.1001/archopht.122.4.532.
2. Schappert SM. Office Visits for Glaucoma: United States, 1991-92. *Vital and Health Statistics, Centers for Disease Control and Prevention / National Center for Health Statistics.* 1995; March, No. 262.
3. Lee PP, Walt JG, Doyle JJ, et al. A multicenter, retrospective pilot study of resource use and costs associated with severity of disease in glaucoma. *Arch Ophthalmol.* 2006;124(1):12-19. doi:10.1001/archopht.124.1.12.
4. Wittenborn JS, Zhang X, Feagan CW, et al. The economic burden of vision loss and eye disorders among the United States population younger than 40 years. *Ophthalmology.* 2013;120(9):1728-35. <https://doi.org/10.1016/j.ophtha.2013.01.068>.

APPENDIX

Unmet Needs in Open-Angle Glaucoma - Document Generation and Maintenance

The combined American Glaucoma Society (AGS) and American Society of Cataract and Refractive Surgery (ASCRS) consensus Unmet Needs Document for **open-angle glaucoma** includes all topics that are considered key concepts warranting investigation and execution in the following major categories:

- Detection
- Pathophysiology
- Epidemiology
- Treatment
- Patient and Provider Education

The purpose of the unmet needs document is to:

1. Articulate consensus unmet needs that must be addressed in order to improve our understanding and treatment of glaucoma in patients cared for by the membership of the AAO, AGS, and ASCRS;
2. Allow for change and reconsideration of needs over time. The topics included are to be reviewed by appropriate representative committees of each governing society and academy and modified to meet current unmet needs;
3. Serve as a method of documenting success in addressing prior unmet needs to allow for a public measure of accountability of grant efforts that were awarded to specifically address these consensus unmet needs;

Selection of Initial List of Unmet Needs

The 2020-2022 Research Committee and Chairs of the Education and Communications and Patient Care Committees of the American Glaucoma Society were charged with the generation of the initial consensus list of Unmet Needs for Open-Angle Glaucoma, which were then ratified by the Glaucoma Clinical Committee of the American Society of Cataract and Refractive Surgeons. The membership of the relevant committees are as follows:

The 2020-2022 Research Committee of the American Glaucoma Society:

Richard Lee, MD, PhD, Chair [Bascom Palmer Eye Institute, University of Miami]

J. Crawford Downs, PhD (author) [Dept. of Ophthalmology and Visual Sciences, University of Alabama - Birmingham]

David Fleischman, MD, MS (author) [Department of Ophthalmology, University of North Carolina at Chapel Hill]

Grace Richter, MD, MPH [Roski Eye Institute, University of Southern California]

Kathryn Bollinger, MD, PhD [Department of Ophthalmology, Augusta University]

Gustavo de Moraes, MD, MPH, PhD [Department of Ophthalmology, Columbia University]

Benjamin Frankfort, MD, PhD [Department of Ophthalmology, Baylor College of Medicine]

Ying Han, MD, PhD [Department of Ophthalmology, University of California San Francisco]

Yang Sun, MD, PhD [Department of Ophthalmology, Stanford University]

Yao Liu, MD, MS [Department of Ophthalmology, University of Wisconsin]

Tavé van Zyl, MD [Department of Ophthalmology, Yale School of Medicine]

The 2020-2022 Glaucoma Clinical Committee of the American Society of Cataract and Refractive Surgery:

Leon Herndon, MD, Chair [Duke Eye Center, Duke University]

Ike Ahmed, MD [Department of Ophthalmology, University of Toronto and Prism Eye Institute]

Jacob Brubaker, MD [Sacramento Eye Consultants]

Brian Francis, MD, MS [Doheny Eye Institute, UCLA Stein Eye Institute]

Davinder Grover, MD, MPH [Glaucoma Associates of Texas]

Paul Harasymowycz, MD [Department of Ophthalmology, University of Montreal and Bellevue Ophthalmology Clinics]

Sameh Mosaed, MD [Department of Ophthalmology, University of California Irvine]

Marlene Moster, MD [Wills Eye Institute, Thomas Jefferson University]

Robert Noecker, MD [Ophthalmic Consultants of Connecticut]

Tom Patrianakos, MD [Ophthalmology, Cook County Health]

Jody Piltz-Seymour, MD [Wills Eye Institute and University of Pennsylvania]

Nathan Radcliffe, MD [Mount Sinai Hospital and New York and Ear Infirmary of Mount Sinai]

Douglas Rhee, MD [Department of Ophthalmology and Visual Sciences, University Hospitals Cleveland Medical Center]

Amy Zhang, MD [Kellogg Eye Center, University of Michigan]

Manjool Shah, MD [Kellogg Eye Center, University of Michigan]

Oluwatosin Smith, MD [Glaucoma Associates of Texas]

Deborah Ristvedt, DO [Vance Thompson Vision]

The protocol for selecting topics was at the discretion of the respective Committee Chairs. The members of the AGS Research Committee each selected ten Unmet Needs, which were combined and categorized based on their respective major classifications. A short summary of the discussion of each topic was compiled, and the consensus Unmet Needs were approved by the AGS Research Committee Chair and by a vote of the full Research Committee. The document was then transferred to the ASCRS Glaucoma Clinical Committee for consideration and modification, then returned to the AGS Research Committee for final dispensation. Minor editing of the attached documents was performed by the 2021-2022 AGS Executive Vice President and the AGS Program Committee Chair prior to presentation to the AGS Board of Directors for approval at their November 2021 meeting.

All members partaking in the selection of the unmet needs are named above. Disclosures and interests are included within the document, where appropriate (no relevant disclosures are known). Maximal effort towards transparency must be protected throughout the evolution of the Unmet Needs Document.

Selecting Future Unmet Needs

The Research Committee of the American Glaucoma Society

The Glaucoma Clinical committee of the American Society of Cataract and Refractive Surgery

are charged with the annual review and editing of the Unmet Needs Document. Removal and additions of Unmet Needs should be explicitly documented and justified in a separate section.

Items of Unmet Needs that have been successfully addressed and removed from the standing document, and were completed by efforts supported by grants, should be explicitly mentioned within the document and archived for the combined records of the AGS and ASCRS as a monitor of progress in the advancement of addressing unmet needs in *open-angle glaucoma*.

Addressing Priority Unmet Needs

Unmet Needs are ranked based on the frequency of item selection by committee participants. The topic most frequently selected is listed first within its respective major category, and further needs are listed in order by frequency of selection by committee members.

Archiving Unmet Needs

Each document, with all voting members and disclosures, will be publicly archived for accounting. Grants awarded from ASCRS and AGS that were aimed at addressing an unmet need will be linked to the respective documents.