Journal of Glaucoma Publish Ahead of Print
DOI:10.1097/IJG.0000000000002027

Glaucoma Treatment Outcomes in Open-Angle Glaucoma Patients of African Descent

Brent Siesky[1], PhD, Alon Harris[1], MS, PhD, FARVO, Aditya Belamkar[2], BS, Ryan Zukerman[3], BA, Avery Horn[4], Alice Verticchio Vercellin[1], MD, PhD, Kristen Ann V. Mendoza[5], MD, Paul A. Sidoti[1], MD, Francesco Oddone[6], MD, PhD

[1] Department of Ophthalmology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY, USA

[2] Indiana University School of Medicine, Indianapolis, IN, USA

[3] Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, FL, USA

[4] Darien High School, Darien, CT, USA

[5] New York Eye and Ear Infirmary of Mount Sinai, New York, NY, USA

[6] IRCCS - Fondazione Bietti, Rome, Italy

Address for correspondence and reprints:
Alon Harris, MS, PhD, FARVO
Professor of Ophthalmology
Vice Chair of International Research and Academic Affairs
Director of the Ophthalmic Vascular Diagnostic and Research Program at Mount Sinai Hospital
Icahn School of Medicine at Mount Sinai

1468 Madison Avenue, Annenberg 22-86
New York, NY 10029
T: 212-241-0250
F: 212-241-5764
C: 317-529-1033
palonharris@gmail.com

Contributors: All authors made a substantial contribution to the article. Each author participated in drafting or revising the manuscript and approved submission of this version for publication.

Conflict of interest: There are no conflicts of interest.

Financial disclosures: Alon Harris would like to disclose that he received remuneration from AdOM, Qlaris, Luseed, and Cipla for serving as a consultant and he serves on the board of AdOM, Qlaris, and Phileas Pharma. Alon Harris holds an ownership interest in AdOM, Luseed, Oxymap, Qlaris, Phileas Pharma, InLed, and QuLent. All relationships listed above are pursuant to Icahn School of Medicine's policy on outside activities. The contribution of the author Francesco Oddone was supported by Fondazione Roma and by the Italian Ministry of Health. None of the other authors listed have any financial disclosures.

Funding: Alon Harris is supported by NIH grant (R01EY030851), NSF DMS (1853200/2021192), NIYEI Foundation grant, and in part by a Challenge Grant award from Research to Prevent Blindness, NY.

Keywords: African descent, blacks, glaucoma, open-angle glaucoma, topical medications, trabeculectomy, laser trabeculoplasty, adherence, access to care

Running head: Treatment outcomes in open-angle glaucoma patients of African descent

Abstract

Open angle glaucoma (OAG), characterized by structural changes to the optic nerve head and retinal nerve fiber layer, is a progressive multifactorial optic neuropathy and leading cause of irreversible blindness globally. Currently intraocular pressure is the only modifiable risk factor; however, others have been identified including genetics and race. Importantly, OAG is much more prevalent in persons of African descent (AD) compared to those of European descent (ED). OAG patients of AD are also known to have a more severe course of the disease, a finding potentially explained by structural and/or vascular differences within eye tissues. In addition, disparities in treatment outcomes have been identified in OAG patients of AD. Specifically, prostaglandin analogues have been suggested to be more effective in patients of AD than in those ED, while beta-adrenergic receptors have been suggested to be less effective, although the evidence is inconsistent. Being of AD has also been identified as a risk factor for trabeculectomy failure while laser trabeculoplasty, has been conversely found to be very effective in lowering IOP in patients of AD. Alternative surgical options including Ex-Press shunt implantation, viscocanalostomy, and canaloplasty are promising in equivalence but require further research to properly evaluate disparity in outcomes. In addition to treatment outcomes, social disparities affecting clinical care also exist for persons of AD in the form of reduced adherence, access, and choice. Overall, data suggests the need for properly designed prospective trials with AD populations as a primary focus to identify the potential mechanisms driving disparities in treatment and address overall potential bias in glaucoma management.

Introduction

Open-angle glaucoma (OAG) describes a family of multifactorial progressive optic neuropathies characterized by retinal ganglion cell loss and subsequent alterations to the optic nerve head and retinal nerve fiber layer.[1] The disease is a leading cause of irreversible blindness with a global prevalence for populations aged 40 to 80 estimated to be 3.54%.[1, 2] While OAG is known to be a multifactorial disease, the only currently approved treatment approach is the reduction of intraocular pressure (IOP). Although lowering IOP is known to be effective in delaying or preventing disease onset for many, a significant percentage of patients will continue to experience disease progression even with lowered IOP.[1, 3] Other identified OAG risk factors include: advanced age, positive family history, male gender, myopia, pseudoexfoliation, cup-to-disk-ratio, genetics, and being of African descent (AD).[4-10]

Glaucoma is a disease with significant disparities and disproportionate impact. Persons of AD have specifically been estimated to have a 2.8 times higher prevalence of glaucoma than persons of European descent (ED), with the prevalence in some age groups rising up to 6 times higher.[2, 11] A recently published 9-year follow up analysis of the Ocular Hypertension Study found that the cumulative incidence of OAG was 55.2% in AD participants and 42.7% in participants of all other races.[12] In general, OAG patients of AD have younger disease onset, more rapid progression, and overall worse outcomes compared to their ED counterparts. [13, 14]

The physiological mechanisms related to OAG disparities have yet to be fully elucidated, however, some ocular structural and vascular differences between races have been identified. Persons of AD have been found to have larger optic disc areas, different optic disc structure, greater cup-to-disc ratios, and thinner retinal nerve fiber layers and corneas in comparison to persons of ED.[11, 15, 16] Differences in IOP between groups have been conflicted in the literature,

with higher IOP reported in AD, yet no discrepancies have been identified in outflow facility, aqueous flow, and uveoscleral flow between OAG patients of AD and ED.[11, 16] The importance of vascular health and contribution of ocular blood flow has been suggested in patients of AD due to higher incidences of hypertension and other systemic vascular diseases. [13, 17] Within the eye reduced blood flow biomarkers in retinal and retrobulbar vessels were found that were associated with glaucomatous structural changes in the optic nerve head and macula in patients of AD but not ED despite similar IOP and visual fields. [17, 18] The extent to which differences in baseline ocular structure, IOP, and/or vascular health in persons of AD alter the course of therapeutic interventions in the management of OAG has yet to be established.

There are significant OAG disease disparities affecting persons of AD, yet the rational for elevated risk and worse treatment outcomes is not well described. Pilot data and conjecture point to potential structural and/or vascular susceptibilities alongside more limited access, therapeutic choice, and adherence to treatment for persons of AD. Importantly, interventional effectiveness appears to differ by therapeutic approach in persons of AD. Generally, the mechanisms of elevated risk and differential response to treatments remain poorly defined with an absence of studies focusing on outcomes for OAG patients of AD as a primary goal. Herein we review the available literature on patterns and differences in therapeutic outcomes for OAG patients of AD to find opportunities to improve disease management and reduce the outsized disease burden they experience.

Methods

PubMed, Embase, Ovid, Scopus, and Trip searches were conducted through December 1, 2021, to evaluate all pertinent articles, abstracts, and related research. Key words utilized in varying combinations include: glaucoma, open-angle glaucoma, race, African, African

American, African descent, black, European, European descent, white, Asian, Hispanic, Latin America, beta blockers, alpha-2 agonists, carbonic anhydrase inhibitors, prostaglandin analogues, cholinergic agonists, ROCK inhibitors, melanin, access to care, adherence, travoprost, latanoprost, timolol, surgical intervention, trabeculectomy, Ex-Press shunt, viscocanalostomy, canaloplasty, laser trabeculoplasty, argon laser trabeculoplasty, selective laser trabeculoplasty, treatment, therapy, and outcomes. Only articles available in English were considered for review.

Topical Drug Therapies

Differences in response to topical antiglaucoma therapies in different races has been studied as early as the 1990s (Table 1). The Baltimore Eye Study found that AD patients with OAG receiving treatment had average IOP measurements equivalent to those patients not receiving treatment, while ED patients with OAG receiving treatment had lower IOP than those not receiving treatment.[19] Similarly, the Ocular Hypertension Treatment Study found a nonsignificant trend that suggested that glaucoma medical therapy was less effective in AD patients than ED patients.[3] Despite these suggestive baseline findings, comparative data of specific topical treatments and their efficacy over time between races are anemic.

Within the available literature, most studies compare the efficacy of prostaglandin analogues to beta blockers, with racial differences in treatment outcomes considered as a secondary outcome. One study comparing travoprost (0.0015% and 0.004%) to latanoprost and timolol in patients with OAG or ocular hypertension (OHT) found that travoprost 0.004% was significantly more effective at reducing IOP in AD patients than travoprost 0.0015%, latanoprost or timolol, but found no difference in the IOP–lowering efficacy in the nonblack patients between travoprost 0.0015% and 0.004% and no significant difference between travoprost 0.0015% and latanoprost for either AD patients or non-AD patients.[20] In a follow-up report of

two studies specifically comparing AD and non-AD patients, the authors found that the IOP-reductive effect of travoprost was significantly greater in AD patients than non-AD patients both with and without adjustment for age, central corneal thickness, diagnosis, iris color, and sex. [21] Comparatively, timolol had a greater effect in non-AD patients, although this difference was only significant at one measured timepoint. [21] These findings were similar to those from Higginbotham et al., who found bimatoprost, a prostaglandin analogue, to be equally effective in AD and non-AD patients, while timolol showed lower efficacy in AD patients. [22] The mechanistic explanation(s) for these observed differences are not currently known.

The efficacy of latanoprost was also compared with that of timolol in a heterogenous population of 1,389 OAG or OHT patients where both latanoprost and timolol significantly reduced mean diurnal IOP across all racial groups (AD, ED, Asian descent, and Latin American descent (LAD) patients). [23] The data also specifically demonstrated that Asian and LAD patients had a significantly larger mean diurnal IOP reduction with treatment compared to ED patients. [23] Similarly, Pitnarong et al. studied the efficacy of latanoprost and timolol maleate in AD and ED patients finding latanoprost was more effective at lowering IOP in AD patients than ED patients. [24] It is important to note, however, that this finding was only reported at one of two measured timepoints from the study protocol.[24] Finally, a study comparing prostaglandin analogues and topical nonselective beta-adrenergic antagonists in self-identified AD and ED populations found no statistically significant differences in efficacy between races. [25]

More recently, the Prostaglandin Efficacy and Safety Study Undertaken by Race specifically examined the efficacy of three different prostaglandin analogues (latanoprost, travoprost, and bimatoprost) among patients from different ethnic groups (ED and Other) to determine differences in medication effectiveness. In an 83 patient cohort, the study found no

statistical difference in IOP lowering effect between any of the three drugs or two ethnic groups studied.[26] A similar study utilizing the same three prostaglandin analogues also found no racial differences in responses to topical therapy.[27]

While there is insufficient evidence to determine whether different races have varied responses to prostaglandin analogue therapy, it has recently been suggested that genetic variants may play a role in the IOP response to these drugs with research largely focusing on genetic polymorphisms of the prostaglandin F2α gene in populations of Asian descent.[28-31] Further research into potential genetic determinants of drug response variability for AD populations may help better contextualize past research on differences in drug efficacy. For instance, it has also been suggested that individual variations in ocular melanin might contribute to racial differences in topical drug efficacy. Research has shown that there are statistically significant differences in melanin content in patients with different eye color.[32] In addition, it has also been determined that melanin has the ability to act as a drug reservoir and can impact the pharmacokinetics of ocular drugs.[33] However, only a handful of studies have specifically evaluated the effects of ocular melanin on antiglaucoma drugs, with none studying prostaglandin analogues.[34-36]

Ultimately, potential racial differences in response to topical glaucoma therapy are poorly understood and exacerbated by the fact that drug efficacy is primarily studied in ED populations. Further research specifically designed to examine drug efficacy in persons of AD, as opposed to its evaluation as a secondary outcome based on study demographics, is required. The underlying physiological and/or pathological rational for differences in topical treatments in persons of AD remain poorly described, with potential genetic variants affecting hypotensive response and considerations of other non-IOP risk pathways including ocular structural and hemodynamic mechanisms. As new topical treatments including ROCK-inhibitors are brought to market a

clear understanding of potential differential in efficacy for persons of AD should be established if the drug's foundational studies are primarily conducted in ED populations.

Surgical Interventions

Similar to proposed differences in treatment outcomes with topical drug therapies, there are scarce and conflicting results regarding surgical outcomes between glaucoma patients of AD and ED.[11, 37] In overall review of the current literature, there is no conclusive evidence suggesting that any procedure is more effective in controlling IOP for patients of AD than standard trabeculectomy, which is a primary option for clinicians.[37] However, this procedure does possess risks for AD patients, necessitating a discussion of other interventional approaches including the Ex-PRESS shunt, viscocanalostomy, canaloplasty, and laser trabeculoplasty. Surgical interventions may have the added benefit of avoiding adherence and accessibility issues related to repeated office visits, consistent access to medication, and other chronic treatment obstacles that disproportionately affects persons of AD.

Trabeculectomy

Trabeculectomy, also known as filtration surgery, is the primary surgical option in lowering IOP for medically uncontrolled patients. Overall, the literature strongly suggests that AD is associated with a significant independent prognostic risk factor for failure of this procedure at both short- and long-term follow-ups.[37-45] It is important to note that some studies have found no significant difference in mean IOP between AD and ED patients following trabeculectomy, but these are largely in the minority.[46, 47] A recent study focused on trabeculectomy with mitomycin c matched, by age, surgeon, lens status, and follow-up time, 135 eyes of 105 AD patients with 135 eyes of 117 ED patients. The group found that AD was associated with a higher failure rate when surgical success was based on lower final IOPs.[43] Furthermore, patients of AD were found to

have significantly higher incidence of bleb leaks and require additional glaucoma surgeries significantly more often than patients of ED.[43] The disparity in clinical outcomes between these demographics may be present also in minimally invasive glaucoma surgeries, as found in a study by Rahmatnejad et al. that showed how African American patients who underwent gonioscopy-assisted transluminal trabeculotomy had a significantly higher rate of failure compared to their white counterparts.[42] Interestingly, a study conducted in an AD population found evidence to suggest the prevalence of hypotony maculopathy may be substantially lower in this population than in the ED population.[48] While no physiological mechanism has yet been described to elucidate this discrepancy in treatment outcomes, it has been suggested that the conjunctiva of AD persons may contain a greater number of macrophages and fibroblasts and a lesser number of mast cells and goblet cells compared to the conjunctiva of ED persons.[44] A locally increased number of macrophages may predispose AD persons to a greater risk of trabeculectomy failure through excessive wound healing.[44] Further research may be needed to evaluate anatomical and physiological differences between the anterior eyes of AD and ED glaucoma patients to improve treatment outcomes for this primary surgical option.

Laser Trabeculoplasty

Laser trabeculoplasty is an effective, non-invasive intervention targeting the trabecular meshwork that can reduce IOP in patients with medically uncontrolled glaucoma. The two primary types of laser trabeculoplasty are argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT). The relationship between treatment outcomes of SLT and AD has yet to be identified in the literature.[37] A 14-year study following patients with SLT found that race had no impact on treatment outcomes.[49] However, another study comparing patients of AD and those of Indian ancestry found that 90% of AD eyes saw a sustained 20% reduction in IOP at 12

months in comparison to 50% of Indian eyes.[50] Additionally, the mean decrease in IOP was 42.4% at 12 months among AD eyes versus 27.8% among Indian eyes, a difference between subgroups that was found to be highly significant.[50] It is important to note that a 28.8% mean decrease in IOP was identified in ED eyes, however, this subgroup was too small for statistical analysis.[50] Interestingly, the study described distinct patterns of response among AD and Indian eyes; AD eyes showed a uniform response pattern while Indian eyes showed a gradual response pattern.[50] A short-term study conducted in Omani patients also found a comparable gradual pattern in patients of Indian ancestry.[51] These findings indicate a noteworthy difference between patients of AD, Indian ancestry, and potentially ED that must be investigated further. Overall, disparities in treatment outcomes for SLT may not disfavor patients of AD.

In comparison, the literature is much more conducted regarding the relationship between ALT outcomes and race. Certain studies have found no relationship between treatment outcomes for ALT and AD, [49,52] while others have found a negative relationship.[37, 53] The Advanced Glaucoma Intervention Study (AGIS) conducted noteworthy research on ALT and trabeculectomy by randomly assigning patients to either an ALT-trabeculectomy-trabeculectomy (ATT) sequence or a trabeculectomy-ALT-trabeculectomy (TAT) sequence. The second and third interventions were offered to patients upon failure of the prior intervention. Interestingly, AD patients displayed better visual field, visual acuity, and vision parameter scores on ATT than TAT, but ED patient displayed better parameter scores on TAT than ATT at 7-year follow-up.[54] Similarly, at 10-years, AD patients in the ATT sequence showed better long-term visual function outcomes while this finding was reflected in ED patients in the TAT sequence.[55] Additionally, AD patients displayed a lower risk for failure in the ATT treatment sequence but a higher risk for failure in the TAT treatment sequence than ED patients.[56] AD patients were also found to have increased

risk of failure of trabeculectomy regardless of if it was a first or second intervention, indicating that their success in the ATT sequence may be dependent on ALT treatment outcomes. [45, 56] Overall, the AGIS results demonstrate a clear benefit in long-term treatment outcomes for patients of AD from initial ALT. This may be important for clinicians to consider in developing more individualized treatment plans for their patients. Trabeculectomy, although a very popular surgical option, has consistently been shown to be a poor alternative for AD patients. Laser trabeculoplasty may provide for better outcomes in this demographic.

Ex-Press Shunt

The Ex-Press shunt is a glaucoma filtration device that is surgically implanted under the conjunctiva to shunt aqueous humor from the anterior chamber. While the device may not be as commonly used as trabeculectomy, it is still an important surgical option for reducing IOP. In patients of AD, trabeculectomy and the Ex-Press shunt have been shown to both significantly reduce IOP and the number of glaucoma medications taken, with no significant difference in the findings between the two surgical interventions.[57] Additionally, the cumulative number of postoperative interventions defined as laser suture lysis or 5-fluorouracil injection, was significantly greater for AD patients receiving trabeculectomy as compared to those receiving the Ex-Press shunt. While the Ex-Press shunt may be a convincing alternative for AD patients, outcomes in this subgroup as compared to ED patients have not been widely studied. Two studies utilizing Kaplan-Meier analysis to evaluate surgical success rates found similar outcomes between AD and ED patients at long-term follow-ups.[58, 59] Interestingly, however, Freedman and Ferri found the surgical success rates for AD patients were significantly lower at 12 months but no longer significantly different at 24 months as compared to ED patients.[59] They concluded that AD patients may experience failure earlier on while ED patients experience failure later to

eventually show similar outcomes at long-term follow-up.[59] It may be important to further understand these trends in outcomes to better evaluate differences in demographics.

Viscocanalostomy and Canaloplasty

Viscocanalostomy and canaloplasty are both non-penetrating surgeries for the reduction of IOP in glaucomatous eyes but have yet to be proven superior to trabeculectomy.[37] Viscocanalostomy has been found to have a high success rate in AD patients with outcomes similar to ED patients after 5 years and only slightly worse after 10 years. [37,60] Canaloplasty has been found, by comparing two studies conducted at the same medical center, to have a lower success rate in AD patients than in ED patients.[37,61,62] While these surgical alternatives may be promising, properly designed studies are needed that specifically focus on outcomes in AD populations to properly evaluate their efficacy and role in glaucoma management.

Alternative Surgical Options

Another surgical option for managing elevated IOP is the usage of tube shunts. The most common devices utilized are the Molteno, Baerveldt, and Ahmed implants. In the Tube Versus Trabeculectomy (TVT) Study, the 5-year treatment outcomes of tube shunt (350-mm^2 Baerveldt glaucoma implant) were compared to trabeculectomy with mitomycin C. Importantly, race was not associated with treatment failure either univariately or in a multivariate analysis.[63] Further research is necessary to draw definitive conclusions from the literature on the correlation between race and treatment outcomes.[37] Similarly, cyclodestructive procedures do not have strong evidence to suggest a predictive relationship.[37] Newer procedures such as the trabecular microbypass techniques, iStent, and phacoemulsification have been shown to be effective and safe for AD patients with glaucoma but do require further studies to draw informed conclusions.[64]

Adherence Patterns

Patients of AD face a greater disease burden with worse clinical outcomes, and differences in patient adherence to medical therapy between populations has been suggested to play an important role in defining these varied outcomes. Less-frequent dosing regimens have been indicated to improve adherence, yet nonadherence rates have still been reported to be as high as 80%.[65] In fact, the Glaucoma Adherence and Persistency Study determined that more than 90% of glaucoma patients fail to continuously refill their prescribed therapies during the first year of treatment, and less than 60% of patients continue refilling prescriptions past one year.[66] When examining OAG disparities in persons of AD, adherence to medical therapy is often discussed as a primary concern but data remains limited on the actual drivers of the more limited compliance.

Within the literature, significant differences in medication adherence rates between AD and ED patients have been identified, with AD patients being less likely to be fully adherent than ED patients.[67] In fact, AD race was identified as the only significant independent predictor of adherence, even when controlling for age, education, gender, income, IOP, number of medications, and severity of disease.[67] Race alone was found to predict 11% of adherence patterns while race and income together predicted 19%.[67] Additionally, AD and LAD—two significant American minority groups—have been found to be significantly associated with poor adherence to medical therapy and to be much more likely to not attend follow-up visits.[68] Electronic monitoring data for eyedrop usage has also shown minority race and ethnicity to predict lower adherence rates.[69] Specifically, non-white race has been associated with a 40% reduced odds of maintaining adherent behavior as compared to white patients.[70] Overall, AD patients have been found to have lower adherence rates than ED patients and be much more

likely to miss doses and visits, with some studies estimating that ED patients may be as much as three times more likely than AD patients to be more than 80% adherent in medication usage.[71-73]

While there may be a variety of individual factors influencing poor adherence to medical therapy in persons of AD, underlying systemic health disparities cannot be ruled out given the outsized burden of their comorbidities. Poor health literacy is another issue that has been identified as a potential mechanism for lower rates of adherence in minority populations.[71, 72, 74] Finally, it should be noted that adherence is also related to access to care and consistent availability of chronic medications. Therefore, identifying ways to increase availability of therapeutics in high-risk communities may lead to improved adherence in minority populations.[73] Finally, it is crucial to highlight that there is strong evidence that communication in racially discordant medical interactions is usually less productive and positive in content and tone than in racially concordant interactions.[75-77] Therefore, the poor adherence noted among minority groups may also be influenced by physician-patient discordance in race, suggesting health care professionals should be educated and focus on improving communications in racially discordant settings.

Access to Care

Unequal access to care among racial groups is an important concern in discussing differential treatment outcomes and disease burden. Importantly, AD patients have been found to be 67% less likely as ED patients to utilize eye care services in a Medicare study population.[78] As AD patients are known to face a greater disease burden, less access to care may result in undertreatment and worse clinical outcomes.[78] Additionally, AD Medicaid patients had much greater odds of not receiving testing than ED Medicaid patients, while Medicaid patients irrespective of race or ethnicity have been found to receive less glaucoma testing as compared to

commercial insurance patients.[79] These findings are particularly troubling as AD patients have a much greater risk for blindness due to glaucoma and there are many more AD patients on Medicaid than ED patients.[79] These issues regarding racial differences in access to care are systemic in nature and afflict other minority populations as well, particularly those of Latin American descent.[80,81] Finally it has been reported that AD patients on Medicare may have higher rates of surgery than any other group.[82]

Barriers to care in OAG patients of AD may include lack of knowledge about glaucoma, utilization issues, insurance status, transportation, prescription costs, and issues related to doctor-patient communication and relationships.[83-85] While multiple programs and initiatives have been created to address these barriers, reports of their success are varied.[86-89] These programs are also challenged by insufficient resource allocation and participant recruitment.[89] Early access to glaucoma screening, care, and treatment can improve treatment outcomes drastically, yet the stalled nature of progress suggests new additional solutions must be identified for these racial disparities to be significantly and promptly reduced.

Compounding issues of inequal access to clinical care, racial and ethnic disparities have also been identified in ophthalmology clinical trials. A cohort study of 31 clinical trials over a 20-year period, from 2000 to 2020, identifying 13 medications and 18,410 participants found that the enrollment of AD and Latin American descent participants showed significant increases from the first decade (2000-2010) to the second decade (2010-2020) in glaucoma drug trials.[90] However, the enrollment incidence ratio is expected to continue to worsen by 2050, implicating an underrepresentation of these groups and an overrepresentation of ED participants.[90] A recent meta-analysis of 105 clinical trials confirms these representative disparities, noting no significant increase in AD persons participation from 1994 to 2019.[91] These trends indicate poor

representation of minority populations in glaucoma, and other ophthalmic conditions, clinical trials. This may help explain racial disparities in treatment outcomes as new drugs are often not well tested in minority populations. The overrepresentation of ED participants may mask the effect of these drugs on the underrepresented minority populations as well as reducing the statistical power for analysis of results in these populations.

Overall, clinicians must acknowledge the intertwined nature of treatment, physiology, and systemic societal issues creating a lack of access and choice, poorer adherence, and worse outcomes in OAG for persons of AD. Review of the literature compels for the creation of studies specifically designed for and occurring within AD populations, with a primary focus on identifying translatable methods of improving access to care, adherence, and availability of therapeutic choice.

Discussion

Patients of AD are known to have a greater incidence of OAG, worse disease severity, and poorer treatment outcomes compared to patients of ED. Despite carrying an outsized disease burden for many decades, the mechanisms behind AD OAG disparities remain poorly understood. Pilot work has identified differences in certain baseline ocular structural and vascular biomarkers between OAG patients of AD and ED, however their relationship to disease progression is uncertain. Currently there is a lack of properly designed longitudinal studies focusing on AD populations with AD outcomes as a primary focus over the chronic course of the disease.

When targeting therapy, discrepancies in response and efficacy to topical medications and surgical interventions have been identified. Generally, among topical therapeutics prostaglandin analogues have been found to be more effective while beta-adrenergic antagonists

have been found to be less effective in OAG patients of AD compared to those of ED. No comparative data on newer therapeutics including rho-associated protein kinase inhibitors, or ROCK inhibitors, are yet available. When considering surgical interventions trabeculectomy is a standard procedure for lowering IOP, however, AD has commonly been shown to be a prognostic risk factor for surgical failure. Alternative surgical options including ExPress shunt implantation, viscocanalostomy, and canaloplasty may be promising for AD patients, yet the literature on the racial differences in outcomes for these options is scarce. Similarly, newer alternatives such as trabecular microbypass techniques and cyclodestructive procedures also require further study to properly evaluate outcomes and potential racial disparities. In comparison, laser trabeculoplasty has been shown to be at least equally beneficial in AD patients as compared to ED patients.

A significant consideration of elevated risk in poorer communities may be limited therapeutic choice, especially in terms of surgical interventions. Limited access to therapeutics and difficulty in maintaining adherence also especially affect communities of AD. Higher baseline IOP for patients of AD is also a potential consideration in treatment efficacy, as are potential structural and hemodynamic influences. Perhaps the largest hindrance of progress is the lack of studies specifically designed for persons of AD with focus on primary endpoints in AD populations. Currently, studies investigating endpoints for OAG patients of AD are most often underpowered sub-analysis of ED studies that were not designed for determining outcomes in AD populations.

Racial disparities may further indicate that glaucoma is not a single pathological entity but instead describes a family of pathologies with similar presentation, and elevated risk for persons of AD. Increased risk may be related to bias in treatment approach, limited access, lack

of therapeutic choice, lower chronic medication adherence, and overall bias in glaucoma studies that focus on ED populations as the primary treatment population. To improve treatment outcomes and reduce disease disparity and burden, our understanding of glaucoma pathology must improve both individuals and specifically within high risk populations. To accomplish this properly designed prospective research evaluating AD outcomes as a primary goal is required to better understand disparities in disease progression and treatment bias. Social issues must also be considered in the design of research to mitigate potential bias including access to participation and the role of caregiver education to improve racial concordance in patient-physician interactions. Looking forward, creating awareness of the differential risk experienced by persons of AD and identifying all possible pathways to reduce disease disparities should be at the forefront of glaucoma research.

References

1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA*. May 14 2014;311(18):1901-11. doi:10.1001/jama.2014.3192

2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. Nov 2014;121(11):2081-90. doi:10.1016/j.ophtha.2014.05.013

3. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol*. Jun 2002;120(6):701-13; discussion 829-30. doi:10.1001/archopht.120.6.701

4. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Arch Ophthalmol*. Jan 2003;121(1):48-56. doi:10.1001/archopht.121.1.48

5. Ramdas WD, Wolfs RC, Hofman A, de Jong PT, Vingerling JR, Jansonius NM. Ocular perfusion pressure and the incidence of glaucoma: real effect or artifact? The Rotterdam Study. *Invest Ophthalmol Vis Sci*. Aug 29 2011;52(9):6875-81. doi:10.1167/iovs.11-7376

6. Ekstrom C. Risk factors for incident open-angle glaucoma: a population-based 20-year follow-up study. *Acta Ophthalmol*. Jun 2012;90(4):316-21. doi:10.1111/j.1755-3768.2010.01943.x

7. Le A, Mukesh BN, McCarty CA, Taylor HR. Risk factors associated with the incidence of open-angle glaucoma: the visual impairment project. *Invest Ophthalmol Vis Sci*. Sep 2003;44(9):3783-9. doi:10.1167/iovs.03-0077

8. Czudowska MA, Ramdas WD, Wolfs RC, et al. Incidence of glaucomatous visual field loss: a ten-year follow-up from the Rotterdam Study. *Ophthalmology*. Sep 2010;117(9):1705-12. doi:10.1016/j.ophtha.2010.01.034

9. Kapetanakis VV, Chan MP, Foster PJ, Cook DG, Owen CG, Rudnicka AR. Global variations and time trends in the prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. *Br J Ophthalmol*. Jan 2016;100(1):86-93. doi:10.1136/bjophthalmol-2015-307223

10. Zukerman R, Harris A, Vercellin AV, Siesky B, Pasquale LR, Ciulla TA. Molecular Genetics of Glaucoma: Subtype and Ethnicity Considerations. *Genes (Basel).* Dec 31 2020;12(1):55. doi: 10.3390/genes12010055. PMID: 33396423; PMCID: PMC7823611.

11. Racette L, Wilson MR, Zangwill LM, Weinreb RN, Sample PA. Primary open-angle glaucoma in blacks: a review. *Surv Ophthalmol*. May-Jun 2003;48(3):295-313. doi:10.1016/s0039-6257(03)00028-0

12. Kass MA, Heuer DK, Higginbotham EJ, et al. Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-up. *JAMA Ophthalmol*. Apr 15 2021;[volume]:[issue]:10.1001/jamaophthalmol.2021.0341

13. Hulsbeck A, Harris A, Siesky B, et al. Vascular considerations in glaucoma patients of African and European descent. *Acta Ophthalmol*. Aug 2014;92(5):e336-40. doi:10.1111/aos.12354

14. Wilson R, Richardson TM, Hertzmark E, Grant WM. Race as a risk factor for progressive glaucomatous damage. *Ann Ophthalmol*. Oct 1985;17(10):653-9.

15. Girkin CA, McGwin G, Jr., Xie A, Deleon-Ortega J. Differences in optic disc topography between black and white normal subjects. *Ophthalmology*. Jan 2005;112(1):33-9. doi:10.1016/j.ophtha.2004.07.029

16. Beltran-Agullo L, Alaghband P, Rashid S, et al. Comparative human aqueous dynamics study between black and white subjects with glaucoma. *Invest Ophthalmol Vis Sci*. Dec 9 2011;52(13):9425-30. doi:10.1167/iovs.10-7130

17. Siesky B, Harris A, Racette L, et al. Differences in ocular blood flow in glaucoma between patients of African and European descent. *J Glaucoma*. Feb 2015;24(2):117-21. doi:10.1097/IJG.0b013e31829d9bb0

18. Siesky B, Harris A, Carr J, et al. Reductions in Retrobulbar and Retinal Capillary Blood Flow Strongly Correlate With Changes in Optic Nerve Head and Retinal Morphology Over 4 Years in Open-angle Glaucoma Patients of African Descent Compared With Patients of European Descent. *J Glaucoma*. Sep 2016;25(9):750-7. doi:10.1097/IJG.0000000000000520

19. Sommer A, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open-angle glaucoma among white and black Americans. The Baltimore Eye Survey. *Arch Ophthalmol*. Aug 1991;109(8):1090-5. doi:10.1001/archopht.1991.01080080050026

20. Netland PA, Landry T, Sullivan EK, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol*. Oct 2001;132(4):472-84. doi: 10.1016/s0002-9394(01)01177-1. PMID: 11589866.

21. Netland PA, Robertson SM, Sullivan EK, et al. Response to travoprost in black and nonblack patients with open-angle glaucoma or ocular hypertension. *Advances in therapy*. May-Jun 2003;20(3):149-63. doi:10.1007/bf02850202

22. Higginbotham EJ, Schuman JS, Goldberg I, et al. One-year, randomized study comparing bimatoprost and timolol in glaucoma and ocular hypertension. *Arch Ophthalmol*. Oct 2002;120(10):1286-93. doi:10.1001/archopht.120.10.1286

23. Hedman K, Larsson LI. The effect of latanoprost compared with timolol in African-American, Asian, Caucasian, and Mexican open-angle glaucoma or ocular hypertensive patients. *Surv Ophthalmol*. Aug 2002;47 Suppl 1:S77-89. doi:10.1016/s0039-6257(02)00310-7

24. Kitnarong N, Zhao Y, Netland PA, Kent AR. Efficacy of latanoprost and timolol maleate in black and white patients. *Advances in therapy*. Jul-Aug 2004;21(4):209-13. doi:10.1007/BF02850153

25. Mansberger SL, Hughes BA, Gordon MO, et al. Comparison of initial intraocular pressure response with topical beta-adrenergic antagonists and prostaglandin analogues in African American and white individuals in the Ocular Hypertension Treatment Study. *Arch Ophthalmol*. Apr 2007;125(4):454-9. doi:10.1001/archopht.125.4.454

26. Birt CM, Buys YM, Ahmed II, Trope GE. Prostaglandin efficacy and safety study undertaken by race (the PRESSURE study). *J Glaucoma*. Sep 2010;19(7):460-7. doi:10.1097/IJG.0b013e3181c4aeac

27. Parrish RK, 2nd, Palmberg P, Sheu WP. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. *Am J Ophthalmol*. May 2003;135(5):688-703. doi:10.1016/s0002-9394(03)00098-9

28. Gao LC, Wang D, Liu FQ, et al. Influence of PTGS1, PTGFR, and MRP4 genetic variants on intraocular pressure response to latanoprost in Chinese primary open-angle glaucoma

patients. *European journal of clinical pharmacology*. Jan 2015;71(1):43-50. doi:10.1007/s00228-014-1769-8

29. Cui XJ, Zhao AG, Wang XL. Correlations of AFAP1, GMDS and PTGFR gene polymorphisms with intra-ocular pressure response to latanoprost in patients with primary open-angle glaucoma. *Journal of clinical pharmacy and therapeutics*. Feb 2017;42(1):87-92. doi:10.1111/jcpt.12468

30. Zhang P, Jiang B, Xie L, Huang W. PTGFR and SLCO2A1 Gene Polymorphisms Determine Intraocular Pressure Response to Latanoprost in Han Chinese Patients with Glaucoma. *Current eye research*. Dec 2016;41(12):1561-1565. doi:10.3109/02713683.2016.1143013

31. Sakurai M, Higashide T, Takashima M, Sugiyama K. Association between genetic polymorphisms of the prostaglandin F2 alpha receptor gene and response to latanoprost. *Ophthalmology*. Jun 2007;114(6):1039-45. doi:10.1016/j.ophtha.2007.03.025

32. Menon IA, Wakeham DC, Persad SD, Avaria M, Trope GE, Basu PK. Quantitative determination of the melanin contents in ocular tissues from human blue and brown eyes. *Journal of ocular pharmacology*. Spring 1992;8(1):35-42. doi:10.1089/jop.1992.8.35

32. Menon IA, Wakeham DC, Persad SD, Avaria M, Trope GE, Basu PK. Quantitative determination of the melanin contents in ocular tissues from human blue and brown eyes. *Journal of ocular pharmacology*. Spring 1992;8(1):35-42. doi:10.1089/jop.1992.8.35

33. Bahrpeyma S, Rimpelä A-K, Hagström M, Urtti A. Ocular melanin binding of drugs: in vitro binding studies. *Acta Ophthalmologica*. 2019;97(S263)doi:https://doi.org/10.1111/j.1755-3768.2019.5366

34. Nagata A, Mishima HK, Kiuchi Y, Hirota A, Kurokawa T, Ishibashi S. Binding of antiglaucomatous drugs to synthetic melanin and their hypotensive effects on pigmented and nonpigmented rabbit eyes. *Japanese journal of ophthalmology*. 1993;37(1):32-8.

35. Katz IM, Berger ET. Effects of iris pigmentation on response of ocular pressure to timolol. *Survey of Ophthalmology*. 1979/05/01/ 1979;23(6):395-398. doi:https://doi.org/10.1016/0039-6257(79)90234-0

36. Araie M, Takase M, Sakai Y, Ishii Y, Yokoyama Y, Kitagawa M. Beta adrenergic blockers: ocular penetration and binding to the uveal pigment. *Japanese journal of ophthalmology*. 1982;26(3):248-63.

37. Taubenslag KJ, Kammer JA. Outcomes Disparities between Black and White Populations in the Surgical Management of Glaucoma. *Semin Ophthalmol*. 2016;31(4):385-93. doi:10.3109/08820538.2016.1154163

38. Group CATTS, Gedde SF, Ho... G, et al. Factors affecting the outcome of trabeculectomy: an analysis based on combined data from two phase III studies of an antibody to transforming growth factor beta2, CAT-152. *Ophthalmology*. Oct 2007;114(10):1831-8. doi:10.1016/j.ophtha.2007.06.028

39. Borisuth NS, Phillips B, Krupin T. The risk profile of glaucoma filtration surgery. *Curr Opin Ophthalmol*. Apr 1999;10(2):112-6. doi:10.1097/00055735-199904000-00006

40. Morris DA, Peracha MO, Shin DH, Kim C, Cha SC, Kim YY. Risk factors for early filtration failure requiring suture release after primary glaucoma triple procedure with adjunctive mitomycin. *Arch Ophthalmol*. Sep 1999;117(9):1149-54. doi:10.1001/archopht.117.9.1149

41. Shin DH, Hughes BA, Song MS, et al. Primary glaucoma triple procedure with or without adjunctive mitomycin. Prognostic factors for filtration failure. *Ophthalmology*. Nov 1996;103(11):1925-33. doi:10.1016/s0161-6420(96)30406-5

42. Rahmatnejad K, Pruzan NL, Amanullah S, et al. Surgical Outcomes of Gonioscopy-assisted Transluminal Trabeculotomy (GATT) in Patients With Open-angle Glaucoma. *J Glaucoma*. Dec 2017;26(12):1137-1143. doi:10.1097/IJG.0000000000000802

43. Nguyen AH, Fatehi N, Romero P, et al. Observational Outcomes of Initial Trabeculectomy With Mitomycin C in Patients of African Descent vs Patients of European Descent: Five-Year Results. *JAMA Ophthalmol*. Oct 1 2018;136(10):1106-1113. doi:10.1001/jamaophthalmol.2018.2897

44. Broadway D, Grierson I, Hitchings R. Racial differences in the results of glaucoma filtration surgery: are racial differences in the conjunctival cell profile important? *Br J Ophthalmol*. Jun 1994;78(6):466-75. doi:10.1136/bjo.78.6.466

45. Investigators A. The Advanced Glaucoma Intervention Study (AGIS): 11. Risk factors for failure of trabeculectomy and argon laser trabeculoplasty. *Am J Ophthalmol*. Oct 2002;134(4):481-98. doi:10.1016/s0002-9394(02)01658-6

46. Nazarali S, Damji KF. Ab interno trabeculectomy with Trabectome: outcomes in African American versus Caucasian patients. *Can J Ophthalmol*. Aug 2018;53(4):361-364. doi:10.1016/j.jcjo.2017.10.018

47. Stewart WC, Reid KK, Pitts RA. The results of trabeculectomy surgery in african-american versus white glaucoma patients. *J Glaucoma*. Winter 1993;2(4):236-40.

48. Singh K, Byrd S, Egbert PR, Budenz D. Risk of hypotony after primary trabeculectomy with antifibrotic agents in a black west African population. *J Glaucoma*. Apr 1998;7(2):82-5.

49. Tzimis V, Tze L, Ganesh J, et al. Laser trabeculoplasty: an investigation into factors that might influence outcomes. *Can J Ophthalmol*. Aug 2011;46(4):305-9. doi:10.1016/j.jcjo.2011.06.005

50. Goosen E, Coleman K, Visser L, Sponsel WE. Racial Differences in Selective Laser Trabeculoplasty Efficacy. *J Curr Glaucoma Pract*. Jan-Apr 2017;11(1):22-27. doi:10.5005/jp-journals-10008-1216

51. Al Busaidi A, Shenoy K, Panchatcharam SM, Al-Mahaini A. Short-Term Efficacy of Selective Laser Trabeculoplasty in Omani Eyes with Glaucoma: A Single Institutional Study. *Clin Ophthalmol*. 2020;14:2631-2638. doi:10.2147/OPTH.S269508

52. Krupin T, Patkin R, Kurata FK, et al. Argon laser trabeculoplasty in black and white patients with primary open-angle glaucoma. *Ophthalmology*. Jun 1986;93(6):811-6. doi:10.1016/s0161-6420(86)33683-7

53. Schwartz AL, Lotz BC, Schwartz MA. Long-term follow-up of argon laser trabeculoplasty for uncontrolled open-angle glaucoma. *Arch Ophthalmol*. Oct 1985;103(10):1482-4. doi:10.1001/archopht.1985.01050100058018

54. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes within race: Seven-year results. *Ophthalmology*. Jul 1998;105(7):1146-64. doi:10.1016/s0161-6420(98)97013-0

55. Lederer F, Gaasterland DA, Dally LG, et al. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race: 10-year results. *Ophthalmology*. Apr 2004;111(4):651-64. doi:10.1016/j.ophtha.2003.09.025

56. Investigators A. The Advanced Glaucoma Intervention Study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within treatment groups. *Am J Ophthalmol*. Sep 2001;132(3):311-20. doi:10.1016/s0002-9394(01)01028-5

57. Dib Bustros Y, Fechtner R, A SK. Outcomes of Ex-PRESS and Trabeculectomy in a Glaucoma Population of African Origin: One Year Results. *J Curr Glaucoma Pract*. May-Aug 2017;11(2):42-47. doi:10.5005/jp-journals-10028-1221

58. Salim S, Du H, Boonyaleephan S, Wan J. Surgical outcomes of the Ex-PRESS glaucoma filtration device in African American and white glaucoma patients. *Clin Ophthalmol*. 2012;6:955-62. doi:10.2147/OPTH.S32282

59. Freedman J, Ferri S. Long-term comparison using Ex-PRESS glaucoma shunt in black and white patients. *Can J Ophthalmol*. Apr 2014;49(2):200-4. doi:10.1016/j.jcjo.2013.09.021

60. Grieshaber MC, Peckar P, Pienaar A, Koerber N, Stegmann R. Long-term results of up to 12 years of over 700 cases of viscocanalostomy for open-angle glaucoma. *Acta Ophthalmol*. Jun 2015;93(4):362-7. doi:10.1111/aos.12513

61. Grieshaber MC, Pienaar A, Olivier J, Stegmann R. Canaloplasty for primary open-angle glaucoma: long-term outcome. *Br J Ophthalmol*. Nov 2010;94(11):1478-82. doi:10.1136/bjo.2009.163170

62. Grieshaber MC, Fraenkl S, Schoetzau A, Flammer J, Orgul S. Circumferential viscocanalostomy and suture canal distension (canaloplasty) for whites with open-angle glaucoma. *J Glaucoma*. Jun-Jul 2011;20(5):298-302. doi:10.1097/IJG.0b013e3181e3d46e

63. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL; Tube versus Trabeculectomy Study Group. Treatment outcomes in the Tube Versus Trabeculectomy (TVT)

study after five years of follow-up. *Am J Ophthalmol.* 2012 May;153(5):789-803.e2. doi: 10.1016/j.ajo.2011.10.026. Epub 2012 Jan 15. PMID: 22245458; PMCID: PMC4460

64. Bargoud AR, Lira J, An S, Walsman SM, Herndon LW, Khouri AS. Trabecular Microbypass Stent and Phacoemulsification in African American Patients With Open-angle Glaucoma: Outcomes and Effect of Prior Laser Trabeculoplasty. *J Glaucoma*. Jan 2021;30(1):89-93. doi:10.1097/IJG.0000000000001692

65. Olthoff CM, Schouten JS, van de Borne BW, Webers CA. Noncompliance with ocular hypotensive treatment in patients with glaucoma or ocular hypertension: an evidence-based review. *Ophthalmology.* 2005 Jun;112(6):953-61. doi: 10.1016/j.ophtha.2004.12.035. PMID: 15885795.

66. Quigley HA, Friedman DS, Hahn SR. Evaluation of practice patterns for the care of open-angle glaucoma compared with claims data: the Glaucoma Adherence and Persistency Study. *Ophthalmology*. Sep 2007;114(9):1598-606. doi:10.1016/j.ophtha.2007.03.042

67. Dreer LE, Girkin C, Mansberger SL. Determinants of medication adherence to topical glaucoma therapy. *J Glaucoma*. Apr-May 2012;21(4):234-40. doi:10.1097/IJG.0b013e31821dac86

68. Murakami Y, Lee BW, Duncan M, et al. Racial and ethnic disparities in adherence to glaucoma follow-up visits in a county hospital population. *Arch Ophthalmol*. Jul 2011;129(7):872-8. doi:10.1001/archophthalmol.2011.163

69. Cook PF, Schmiege SJ, Mansberger SL, Kammer J, Fitzgerald T, Kahook MY. Predictors of adherence to glaucoma treatment in a multisite study. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine*. Feb 2015;49(1):29-39. doi:10.1007/s12160-014-9641-8

70. Newman-Casey PA, Blachley T, Lee PP, Heisler M, Farris KB, Stein JD. Patterns of Glaucoma Medication Adherence over Four Years of Follow-Up. *Ophthalmology*. 2015/10/01/ 2015;122(10):2010-2021. doi:https://doi.org/10.1016/j.ophtha.2015.06.039

71. Friedman DS, Okeke CO, Jampel HD, et al. Risk factors for poor adherence to eyedrops in electronically monitored patients with glaucoma. *Ophthalmology*. Ju[illegible]2009;11[illegible]6):1097-105. doi:10.1016/j.ophtha.2009.01.021

72. Sleath B, Blalock SJ, Covert D, Skinner AC, Muir K[illegible], Robi[illegible]AL. Patient race, reported problems in using glaucoma medications, and adhere[illegible]e. *ISRN o[illegible]thalmology*. 2012;2012:902819. doi:10.5402/2012/902819

73. Hark LA, Leiby BE, Waisbourd M[illegible]et al. A[illegible]herence to Follow-up Recommendations Among Individuals in the Philadelph[illegible]a Glauc[illegible]a Detection and Treatment Project. *J Glaucoma*. Aug 2017;26(8):697-701. doi:1[illegible]1097/ij[illegible].0000000000000716

74. Hoevenaars JG, S[illegible]oten JS, van de[illegible]Borne B, Beckers HJ, Webers CA. Socioeconomic differences in glaucon[illegible]patients' k[illegible]owledge, need for information and expectations of treatments. *A[illegible]a ophthalm[illegible]gi[illegible]Scandinavica*. Feb 2006;84(1):84-91. doi:10.1111/j.1600-0420.2005.[illegible]0587.x

75. [illegible]Johnson R[illegible]toter D, Powe NR, Cooper LA. Patient race/ethnicity and quality of patient-physi[illegible]a communication during medical visits. *Am J Public Health*. 2004 Dec;94(12):2084-90. doi: 10.[illegible]105/ajph.94.12.2084. PMID: 15569958; PMCID: PMC1448596

76. Siminoff LA, Graham GC, Gordon NH. Cancer communication patterns and the influence of patient characteristics: disparities in information-giving and affective behaviors. *Patient Educ Couns.* 2006 Sep;62(3):355-60. doi: 10.1016/j.pec.2006.06.011. Epub 2006 Jul 24. PMID: 16860520

77. Oliver MN, Goodwin MA, Gotler RS, Gregory PM, Stange KC. Time use in clinical encounters: are African-American patients treated differently? *J Natl Med Assoc.* 2001 Oct;93(10):380-5. PMID: 11688918; PMCID: PMC2594073.

78. Wang F, Javitt JC, Tielsch JM. Racial variations in treatment for glaucoma and cataract among Medicare recipients. *Ophthalmic Epidemiol*. Jun 1997;4(2):89-100. doi:10.3109/09286589709057101

79. Elam AR, Andrews C, Musch DC, Lee PP, Stein JD. Large Disparities in Receipt of Glaucoma Care between Enrollees in Medicaid and Those with Commercial Health Insurance. *Ophthalmology*. Oct 2017;124(10):1442-1448. doi:10.1016/j.ophtha.2017.05.003

80. Varma R, Mohanty SA, Deneen J, Wu J, Allen SP, Group L. Burden and predictors of undetected eye disease in Mexican-American: the Los Angeles Latino Eye Study. *Med Care*. May 2008;46(5):497-506. doi:10.1097/MLR.0b013e31816080fe

81. Manuel JI. Racial/Ethnic and Gender Disparities in Health Care Use and Access. *Health Serv Res*. Jun 2018;53(3):1407-1429. doi:10.1111/1475-6773.12705

82. Osterhaus J, Sloan FA, Kerndon L, Lee PP. Racial differences in glaucoma care: the longitudinal pattern of care. *Arch Ophthalmol*. 2005;123(12):1693-1698. doi:10.1001/archopht.123.12.1693

83. Cower EW, Silverman E, Cassard SD, Williams SK, Baldonado K, Friedman DS. Barriers to attending an eye examination after vision screening referral within a vulnerable population. *J Health Care Poor Underserved*. Aug 2013;24(3):1042-52. doi:10.1353/hpu.2013.0134

84. Gwira JA, Vistamehr S, Shelsta H, et al. Factors associated with failure to follow up after glaucoma screening: a study in an African American population. *Ophthalmology*. Aug 2006;113(8):1315-9. doi:10.1016/j.ophtha.2006.04.017

85. Dreer LE, Girkin CA, Campbell L, Wood A, Gao L, Owsley C. Glaucoma medication adherence among African Americans: program development. *Optom Vis Sci*. Aug 2013;90(8):883-97. doi:10.1097/OPX.0000000000000009

86. Quigley HA, Park CK, Tracey PA, Pollack IP. Community screening for eye disease by laypersons: the Hoffberger program. *Am J Ophthalmol*. Mar 2002;133(3):386-92. doi:10.1016/s0002-9394(01)01380-0

87. Hark L, Waisbourd M, Myers JS, et al. Improving Access to Eye Care among Persons at High-Risk of Glaucoma in Philadelphia--Design and Methodology: The Philadelphia Glaucoma Detection and Treatment Project. *Ophthalmic Epidemiol*. 2016;23(2):122-130. doi:10.3109/09286586.2015.1099682

88. Owsley C, Rhodes LA, McGwin G, Jr., et al. Eye Care Quality and Accessibility Improvement in the Community (EQUALITY) for adults at risk for glaucoma: study rationale and design. *Int J Equity Health*. Nov 18 2015;14:135. doi:10.1186/s12939-015-0213-8

89. Sapru S, Bertold J, Crews JE, et al. Applying RE-AIM to evaluate two community-based programs designed to improve access to eye care for those at high-risk for glaucoma. *Eval Program Plann*. Dec 2017;65:40-46. doi:10.1016/j.evalprogplan.2017.06.006

90. Lerkowitz ST, Groth SL, Gangaputra S, Patel S. Racial/Ethnic Disparities in Ophthalmology Clinical Trials Resulting in US Food and Drug Administration Drug Approvals From 2000 to 2020. *JAMA Ophthalmol*. Apr 22 2021;doi:10.1001/jamaophthalmol.2021.0857

91. Allison K, Patel DG, Greene L. Racial and Ethnic Disparities in Primary Open-Angle Glaucoma Clinical Trials: A Systematic Review and Meta-analysis. *JAMA Netw Open*. May 3 2021;4(5):e218348. doi:10.1001/jamanetworkopen.2021.8348

Table 1: Racial Discrepancies in Response to Topical Therapies

		AD Patients		Non-AD Patients	
	Drug	Treated IOP (mm Hg)	Untreated/Baseline IOP (mm Hg)	Treated IOP (mm Hg)	Untreated/Baseline IOP (mm Hg)
Kass et al, 2002[3]	Variety	19.3±2.3	23.9±3.2	19.3±2.1	23.1±2.8
Sommer et al, 1991[19]	Variety	20 (exact not provided)	21.48 ±6.46	18.69±3.23	24.13±5.23
Netland et al, 2001[20]	Travoprost (0.004% and 0.0015%), latanoprost 0.005%, and timolol 0.5%	Travoprost 0.004% 8 AM: 18.8 10 AM: 16.7 4 PM: 16.6 Travoprost 0.0015% 8 AM: 19.4 10 AM: 18.8 4 PM: 17.8 Latanoprost 8 AM: 19.7 10 AM: 18.3 4 PM: 18.3 Timolol 8 AM: 22.3 10 AM: 21.0 4 PM: 20	Travoprost 0.004% 8 AM: 26.8 10 AM: 25.0 4 PM: 24 Travoprost 0.0015% 8 AM: 26.1 10 AM: 25.0 4 PM: 24.3 Latanoprost 8 AM: 27.6 10 AM: 25.9 4 PM: 25.2 Timolol 8 AM: 27.2 10 AM: 25.4 4 PM: 24.8	Travoprost 0.004% 8 AM: 20.0 10 AM: 18.6 4 PM: 18 Travoprost 0.0015% 8 AM: 19.4 10 AM: 18.2 4 PM: 18.2 Latanoprost 8 AM: 19.3 10 AM: 18.0 4 PM: 18.6 Timolol 8 AM: 20.3 10 AM: 19.6 4 PM: 19.6	Travoprost 0.004% 8 AM: 26.8 10 AM: 25.2 4 PM: 24.7 Travoprost 0.0015% 8 AM: 26.4 10 AM: 24.7 4 PM: 24.1 Latanoprost 8 AM: 26.6 10 AM: 25.0 4 PM: 24.9 Timolol 8 AM: 26.9 10 AM: 25.4 4 PM: 24.6
Netland et al, 2003[21] (Pooled data)	Travoprost 0.004%, latanoprost 0.005%, and timolol 0.5%	Travoprost 8 AM: 18.9 10 AM: 16.8 4 PM: 16.7	Travoprost 8 AM: 27.0 10 AM: 25.2 4 PM: 24.3	Travoprost 8 AM: 20.2 10 AM: 18.9 4 PM: 18.6	Travoprost 8 AM: 27.0 10 AM: 25.4 4 PM: 24.9
Kitnarong et al, 2004[24]	Latanoprost 0.005% and timolol 0.5%	Timolol 8 AM: 19.2±6.3 10 AM: 17.1±3.7 Latanoprost 8 AM: 16.1±3.7 10 AM: 15.8±3.1	Timolol 8 AM: 24.8±7.2 10 AM: 24.2±7.6 Latanoprost 8 AM: 23.4±6.8 10 AM: 25.8±6.1	Timolol 8 AM: 17.1±3.3 10 AM: 16.2±4.5 Latanoprost 8 AM: 17.5±3.5 10 AM: 16.7±2.8	Timolol 8 AM: 21.7±3.4 10 AM: 21.9±2.6 Latanoprost 8 AM: 22.7±2.2 10 AM: 22.6±3.1
Mansberger et al, 2007[25]	Nonselective β-adrenergic antagonists, prostaglandin analogues	β-adrenergic antagonists: 19.6±2.8 Prostaglandins: 17.5±3.8	β-adrenergic antagonists: 25.8±3.0 Prostaglandins: 25.3±3.9	β-adrenergic antagonists: 19.6±3.0 Prostaglandins: 18.3±3.5	β-adrenergic antagonists: 26.0±2.8 Prostaglandins: 24.5±3.4
Birt et al, 2010[26] (Treated: 24-week data) (AD patients a portion of Other	Bimatoprost, travoprost, and latanoprost	Bimatoprost: 17.0±14.7 Travoprost: 18.6±1.9 Latanoprost:	Bimatoprost: 25.9±2.5 Travoprost: 29.2±4.6 Latanoprost:	Bimatoprost: 18.7±1.9 Travoprost: 18.3±4.6 Latanoprost:	Bimatoprost: 28.3±2.8 Travoprost: 27.8±3.3 Latanoprost:

(18/33))		19.0±2.3	27.2±3.4	17.0±3.8	29.0±3.7

African descent (AD), Intraocular pressure (IOP)