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

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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

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to identify the potential mechanisms driving disparities in treatment and address overall potential bias in glaucoma management.

Keywords

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

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, 4] 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 20-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 are 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] Their 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, Kitnarong 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 or 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 conflicted 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.[57] 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% as 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 cost, 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 unequal 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 Ex-Press 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.

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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	23.9±2.8
Sommer et al, 1991[19]	Variety	20 (exact not provided)	21.48 ±6.46	18.69±3.23	24.15±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: 20.9	Travoprost 0.004% 8 AM: 26.8 10 AM: 25.0 4 PM: 24.0 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: 18.4 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 (18/33))	Bimatoprost, travoprost, and latanoprost	Bimatoprost: 17.0±14.7 Travoprost: 18.6±1.9 Latanoprost: 19.0±2.3	Bimatoprost: 25.9±2.5 Travoprost: 29.2±4.6 Latanoprost: 27.2±3.4	Bimatoprost: 18.7±1.9 Travoprost: 18.3±4.6 Latanoprost: 17.0±3.8	Bimatoprost: 28.3±2.8 Travoprost: 27.8±3.3 Latanoprost: 29.0±3.7

African descent (AD), Intraocular pressure (IOP)