

**RACIAL DISPARITIES IN PRIMARY OPEN ANGLE GLAUCOMA
RESEARCH STUDIES AMONG BLACK AND HISPANIC
PARTICIPANTS: A CRITICAL REVIEW OF
STUDIES USED TO INFORM CURRENT
SCREENING GUIDELINES**

A Thesis
Submitted to
the Temple University Graduate Board

In Partial Fulfillment
of the Requirements for the Degree
MASTER OF ARTS

by
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May 2024

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ABSTRACT

Background

Primary open angle glaucoma (POAG) is the most common form of glaucoma in the United States and is the leading cause of irreversible blindness in African Americans. Although this is the case, there are no current primary care screening guidelines for this condition. The USPSTF cites that there is insufficient evidence to assess the balance of benefits and harms of screening for POAG in adults. This condition disproportionately affects African American and Hispanic patients. A systematic review performed earlier this year highlighted disparities in research participation among POAG clinical trials. No similar studies have been pursued outside of clinical trials. This is problematic because screening guidelines are heavily influenced by the literature related to the topic.

Methods

A rapid scoping review of the literature will be performed with a particular focus on demographic data. Data was sourced from the included studies used in the systematic review performed in 2022 to inform the current USPSTF guidelines. Data collection will consist of the compilation of demographic data within each of the studies on a spreadsheet and will subsequently be analyzed according to subgroup corresponding to study type.

Results

A total pooled sample of 16659 participants was obtained from the 16 included studies. After exclusion of an outlier study, total research participation across all studies was 27.9% and 5.5% for Black and Hispanic individuals, respectively. In clinical trials, 26.9% and 6.9% were Black and Hispanic individuals, respectively. Lastly, among nonclinical trials, 28.7% and 3.3% were Black and Hispanic individuals, respectively.

Conclusion

Primary open angle glaucoma is a public health issue. The current recommendations for POAG screening are based on the currently available literature. However, it has been previously shown that disparities exist in research participation among Black and Latino individuals in clinical trials. The findings within this study corroborate those findings as well as highlight that disparities in research participation and representation persist among nonclinical trial research studies. This thesis underscores the ongoing need for equitable efforts in POAG research across all studies. With these efforts, recommendations for screening may be properly elucidated to inform more equitable care and identification of this disease.

ACKNOWLEDGMENTS

I would like to acknowledge Brian Tuohy for his help and guidance throughout the thesis writing process as my thesis advisor. In addition, I would like to acknowledge Nora Jones and Catherine Averill for their support throughout the process as well.

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LIST OF ABBREVIATIONS

POAG – Primary Open Angle Glaucoma

USPSTF – United States Preventative Services Task Force

AAO – American Academy of Ophthalmology

IOP – Intraocular pressure

LALES – Los Angeles Latino Eye Study

SLT – Selective Laser Trabeculoplasty

CHAPTER 1

INTRODUCTION

Background

Glaucoma is the second leading cause of vision loss worldwide after cataracts (Jindal et al., 2023). The term glaucoma refers to a group of conditions in which characteristic cupping of the optic disc is noted with corresponding visual deficits (Jindal et al., 2023). This is a progressive optic neuropathy which may progress to blindness. Glaucoma is typically categorized according to the anatomy of the anterior chamber angle, rapidity of onset, and major etiology (Wagner et al., 2022). For the purposes of this study, primary open angle glaucoma will be the focus.

Primary open angle glaucoma (POAG) is the most common form of glaucoma in the United States and is the leading cause of irreversible blindness in African Americans (Jindal et al., 2023). POAG is often colloquially referred to as “the silent thief of sight”. This terminology is used because the disease is often asymptomatic until advanced visual field loss occurs (Jindal et al., 2023). In POAG, vision loss occurs from the periphery and progresses towards the central visual field. Thus, patients may not be aware of visual symptoms until the disease has progressed to later stages given its insidious onset. POAG is a subset of glaucoma which is defined by the presence of an open, normal appearing anterior chamber angle and raised intraocular pressure (IOP), with no evidence of underlying disease (Gedde et al., 2021; Jindal et al., 2023). The etiology of POAG is not yet entirely understood. The leading hypotheses for this condition implicates IOP-related damage to the optic nerve (Jindal et al., 2023). However, this condition has been identified in patients without elevated IOP as well.

The worldwide prevalence of POAG is approximately 2.2 – 2.4% according to recently published studies by Allison et al. and Zhang et al. (Allison, Patel, & Alabi, n.d.; Zhang et al., 2021). The estimated disease prevalence of POAG worldwide in 2013 was 64.3 million, with prevalence projected to increase to 70.6 million in 2020 and 111.8 million by 2040 (Tham et al., 2014). In the United States, it has been previously estimated that POAG will affect 3.36 million individuals by the year 2020 (The Eye Diseases Prevalence Research Group*, 2004). This United States based study also identified that Black subjects had nearly three times the age-adjusted prevalence of glaucoma compared to white subjects (The Eye Diseases Prevalence Research Group*, 2004). Additionally, it has been shown that individuals of Latino/Hispanic origin have an increased prevalence of the disease compared to their non-Hispanic white counterparts (Francis et al., 2011; Varma et al., 2004). Thus, this disease carries a rather large burden both worldwide and in the United States.

Risk factors for the development of POAG include older age, positive family history of glaucoma, race or ethnicity, genetic factors, central corneal thickness, ocular perfusion pressure, type 2 diabetes mellitus, and myopia (Gedde et al., 2021; Jindal et al., 2023). There are several examination components involved with screening patients for glaucoma. The three main approaches to screening are identified in the AAO Preferred Practice Pattern Guidelines; measurement of intraocular pressure (IOP), assessment of the optic nerve head (ONH) and retinal nerve fiber layer (RNFL) through either ophthalmoscopy or via optic disc photography, and assessment of visual field (Gedde et al., 2021). The screening methods discussed have presented with issues related to efficiency, subjectivity of interpretation, and specificity when viewed in isolation. An

optimized screening method has not yet been identified; however, it will likely involve a combination of the screening methods mentioned above.

Current Screening Guidelines

United States Preventative Services Task Force Recommendations

The United States Preventative Services Task Force (USPSTF) does not currently recommend primary care screening for POAG (US Preventive Services Task Force et al., 2022b). The USPSTF cites that there is insufficient evidence to assess the balance of benefits and harms of screening for POAG in adults (US Preventive Services Task Force et al., 2022b). This recommendation is based upon a systematic review conducted by the organization on screening for POAG. It was concluded that there is insufficient evidence to recommend screening despite recognition that the condition disproportionately affects African American and Hispanic patients. USPSTF states that there is a pressing need for clinical trials that include larger numbers of Black and Hispanic patients that report on the effects of screening and treatment of POAG. The current grade assigned to this recommendation is “I” which refers to incomplete. After further exploration of the USPSTF guidelines for other ophthalmic conditions, it appears as though there are no recommendations for screening of other common ophthalmic conditions. Rather, overall, the USPSTF does not recommend any form of screening for impaired visual acuity in any asymptomatic adult over the age of 65 (US Preventive Services Task Force et al., 2022a). It seems that the only true recommendation given by the USPSTF is to refer to the American Academy of Ophthalmology (AAO) guidelines for screening.

American Academy of Ophthalmology Recommendations

The only current recommendation regarding eye care screening in adults is from the American Academy of Ophthalmology which recommends a baseline comprehensive eye evaluation at age 40 years (Jindal et al., 2023; US Preventive Services Task Force et al., 2022b). This may be problematic as patients do not typically seek out ophthalmic evaluation without a primary care referral unless they have noticeable visual symptoms. However, the literature highlights that our understanding of glaucoma is insufficient to justify a benefit of early screening and diagnosis (US Preventive Services Task Force et al., 2022b). Additionally, the diagnostic testing required for glaucoma screening is both expensive and requires a specialized operator. I believe that much of our current research and understanding of glaucoma is based upon clinical studies and trials that are predominantly comprised of white patients. Thus, the results and conclusions drawn from those studies may not be adequately reflective of a true patient population.

Significance

The AAO currently recommends a baseline comprehensive eye exam at age 40 with follow up based on risk factors (Jindal et al., 2023). The AAO states that glaucoma screening can be useful and cost-effective in populations considered ‘higher risk’, such as patients with a strong family history of the disease or nonwhite race (Jindal et al., 2023). Given that these risk factors are strongly considered in AAO guidelines, what continues to prevent the USPSTF from implementing guidelines that mirror that of the AAO? Seemingly it may be beneficial to identify patients with the identified risk factors and simply recommend primary care referral to ophthalmology. However, the USPSTF continues to cite a lack of evidence as the reasoning behind a lack of population health

level screening of this life altering disease (US Preventive Services Task Force et al., 2022b).

A systematic review has been published this year which highlights the disparities in participant race among POAG clinical trials (Allison et al., 2021). This study is planned as a rapid scoping review that includes both retrospective cohort studies as well as cross sectional studies to determine whether the disparity in patient participation occurs within those types of studies as well and to examine the potential bioethical considerations of this disparity.

CHAPTER 2

METHODS

A comprehensive systematic review and meta-analysis was recently completed and utilized to inform the current USPTSF guidelines. Given this, the reference list for the included studies in the systematic review will serve as a comprehensive source of the relevant literature surrounding the topic. The studies will be evaluated according to the set inclusion and exclusion criteria. Once the evaluation is complete, studies that satisfy the inclusion criteria will be further examined and data collection will commence. Data collection will consist of the compilation of the demographic data within each of the studies on a spreadsheet.

Inclusion Criteria

- Included studies referenced in the systematic review by Chou, et al. (Chou et al., 2022)
- Published between 2009 and 2023
- Must be fully or partially completed in the United States
- Must include a sample size of greater than or equal to 50 patients
- Participants greater than or equal to 18 years of age
- Retrospective or prospective cohort study
- Cross-sectional study
- Clinical Trial
- Must include demographic data which includes both race and ethnicity
- Studies published in English language

Exclusion Criteria

- Studies that were not included in the systematic review by Chou, et al. (Chou et al., 2022)
- Studies completed entirely outside of the United States
- Studies not related to glaucoma
- Published prior to 2009
- Participants less than 18 years of age
- Review articles
- Sample size less than 50 patients
- No demographic data reported

Using the inclusion and exclusion criteria described above, studies of interest will be identified. These studies will subsequently be further examined, and data collection will commence. Data collection will consist of the compilation of demographic data within each of the studies on a spreadsheet. The data to be collected will include study title, author(s), publication date, type of study performed, total number of patients, number of patients who identify as White or Caucasian, number of patients who identify as Black or African American, number of patients who identify as Hispanic or Latino, and location. The participants will then be pooled across the various studies in order to provide insight into the level of participation in various glaucoma studies with respect to racial and ethnic groups.

CHAPTER 3

RESULTS

109 studies were included in the Chou et al. study and were screened for this review. Of the 109 studies screened, 16 were ultimately included in the review (Asrani et al., 2019, 2020; Brubaker et al., 2020; Ehrlich et al., 2012; Field et al., 2016; Francis et al., 2011; Hark et al., 2019; Khouri et al., 2019; Kwon et al., 2016; Maa, McCord, et al., 2020; Maa, Medert, et al., 2020; Medeiros et al., 2016; Serle et al., 2018; Weinreb et al., 2015, 2016, 2018). The studies are listed in Table 1. A total of 93 studies were excluded due to publication date prior to 2009, no inclusion of racial or ethnic demographic data, and/or study location entirely outside of the United States. A total pooled sample size of 16659 participants was determined using the data from the included studies. Of the 16659 participants; 6327 (38.0%) identified as White or Caucasian, 2956 (17.7%) identified as Black or African American, and 6663 (40.0%) identified as Hispanic or Latino. 6082 of the 6663 Hispanic/Latino patients arose from a singular study, the Los Angeles Latino Eye Study (LALES) by Francis et al. (Francis et al., 2011). If the LALES were excluded from the data, the total number of participants would decrease to 10577. Of the remaining 10577 participants, 6327 (59.8%) identified as White or Caucasian, 2956 (27.9%) identified as Black or African American, and only 581 (5.5%) identified as Hispanic or Latino.

In addition, the data was analyzed according to subgroups based on study type. Of the 16 studies included, 9 were designed as clinical trials. The total number of participants amongst the clinical trials is 6443. Of the 6443 participants, 4214 (65.4%) identified as White or Caucasian, 1730 (26.9%) identified as Black or African American, and 446 (6.9%) identified as Hispanic or Latino. The other 7 included studies were comprised of

cross-sectional, retrospective cohort, and prospective cohort studies. The total number of participants among these studies is 10216. Of the 10216 participants, 2113 (20.7%) identified as White or Caucasian, 1226 (12.0%) identified as Black or African American, and 6217 (60.9%) identified as Hispanic or Latino. Similarly to above, the LALES accounts for a majority of participants who identify as Hispanic or Latino in this subgroup. If the LALES were excluded from this subgroup analysis, the total number of participants remaining is 4134. Of the 4134 study participants, 2113 (51.1%) identified as White or Caucasian, 1226 (29.7%) identified as Black or African American, and 135 (3.3%) identified as Hispanic or Latino.

Table 1: Included Studies

Study Number	Title	Author(s)	Publication Date	Study Type	Location
1	Comparison of Latanoprostene Bunod 0.024% and Timolol Maleate 0.5% in Open-Angle Glaucoma or Ocular Hypertension: The LUNAR Study	Felipe A Medeiros, et al.	2016	Clinical trial	USA and EU
2	A randomised, controlled comparison of latanoprostene bunod and latanoprost 0.005% in the treatment of ocular hypertension and open angle glaucoma: the VOYAGER study	Robert N Weinreb, et al.	2015	Clinical trial	USA and EU
3	Latanoprostene Bunod 0.024% in Subjects With Open-angle Glaucoma or Ocular Hypertension: Pooled Phase 3 Study Findings	Robert N Weinreb, et al.	2018	Clinical trial	USA and EU
4	Latanoprostene Bunod 0.024% versus Timolol Maleate 0.5% in Subjects with Open-Angle Glaucoma or Ocular Hypertension: The APOLLO Study	Robert N Weinreb, et al.	2016	Clinical trial	USA and EU
5	Association between glaucoma and at-fault motor vehicle collision involvement among older drivers: a population-based study	Kwon M, et al.	2016	Population Study	USA

Table 1 (continued)

Study Number	Title	Author(s)	Publication Date	Study Type	Location
6	Fixed-Dose Combination of Netarsudil and Latanoprost in Ocular Hypertension and Open-Angle Glaucoma: Pooled Efficacy/Safety Analysis of Phase 3 MERCURY-1 and -2	Sanjay Asrani, et al.	2020	Clinical trial	USA
7	Netarsudil/Latanoprost Fixed-Dose Combination for Elevated Intraocular Pressure: Three-Month Data from a Randomized Phase 3 Trial	Sanjay Asrani, et al.	2019	Clinical trial	USA
8	One Year of Netarsudil and Latanoprost Fixed-Dose Combination for Elevated Intraocular Pressure: Phase 3, Randomized MERCURY-1 Study	Jacob W. Brubaker, et al.	2020	Clinical trial	USA
9	Goldmann applanation tonometry compared with corneal compensated intraocular pressure in the evaluation of primary open-angle glaucoma	Joshua R Ehrlich, et al.	2012	Cross Sectional	USA
10	Facilitating Glaucoma Diagnosis with Intereye Retinal Nerve Fiber Layer Asymmetry Using Spectral-Domain Optical Coherence Tomography	Matthew G Field, et al.	2016	Retrospective Cohort Study	USA

Table 1 (continued)

Study Number	Title	Author(s)	Publication Date	Study Type	Location
11	Population and High-Risk Group Screening for Glaucoma: The Los Angeles Latino Eye Study	Brian A Francis, et al.	2011	Population Study	USA
12	Philadelphia Telemedicine Glaucoma Detection and Follow-up Study: confirmation between eye screening and comprehensive eye examination diagnoses	Lisa A Hark, et al.	2019	Cross Sectional	USA
13	Two phase 3 clinical trial comparing the safety and efficacy of netarsudil to timolol in patients with elevated IOP (ROCKET-1 and ROCKET-2)	JB Serle, et al.	2018	Clinical trial	USA
14	Once-Daily Netarsudil Versus Twice-Daily Timolol in Patients with Elevated IOP: The Randomized Phase 3 ROCKET-4 Study	Albert S Khouri, et al.	2019	Clinical trial	USA
15	The Impact of OCT on Diagnostic Accuracy of the Technology-Based Eye Care Services Protocol: Part II of the Technology-Based Eye Care Services Compare Trial	April Y Maa, et al.	2020	Prospective Cohort Study	USA
16	Diagnostic Accuracy of Technology-based Eye Care Services: The Technology-based Eye Care Services Compare Trial Part I	April Y Maa, et al.	2020	Prospective Cohort Study	USA

Table 2: Pooled Demographic Data

Study Number	Total Number of Participants	White/Caucasian (#)	Black/African American (#)	Hispanic/Latino (#)
1	414	293	115	55
2	413	306	104	32
3	831	618	203	98
4	417	325	88	43
5	2000	1570	320	0
6	1468	975	435	Not recorded
7	718	157	206	None
8	718	486	206	92
9	614	132	28	
10	106	61	17	12
11	6082	0	0	6082
12	902	154	550	123
13	756	521	214	126
14	708	533	159	Not recorded
15	256	98	154	Not recorded
16	256	98	157	Not recorded
Pooled Totals	16659	6327	2956	6663

Table 3: Subgroup Analysis

	Total Participants	White/Caucasian (%)	Black/African American (%)	Hispanic/Latino (%)
Total Pooled Data	16659	6327 (38.0)	2956 (17.8)	6663 (40.0)
Total Pooled Data (Excluding LALES)	10577	6327 (60.0)	2956 (28.0)	581 (5.5)
Clinical Trial Totals	6443	4214 (65.4)	1730 (26.9)	446 (6.9)
Nonclinical Trial Totals	10216	2113 (20.7)	1226 (12.0)	6217 (60.9)
Nonclinical Trial Totals (Excluding LALES)	4134	2113 (51.1)	1226 (29.7)	135 (3.3)

CHAPTER 4

DISCUSSION

Participants who identify as White or Caucasian appear to comprise the majority of the research study participants across the various study types and subgroups. This was an expected outcome with regards to the data collection. The White/Caucasian racial identity group will serve as a basis for comparative reference.

It is evident from the data that there is less research participation amongst participants who identify as Black or African American within the included studies compared with participants who identify as White or Caucasian. It appears that, across the included studies, participants who identify as Black/African American comprise less than half of the study population compared with their White/Caucasian counterparts, 17.7% and 38.0% respectively. This remains true throughout the various types of studies as well as with the exclusion of the LALES, at 27.9% and 59.8% respectively.

An initial glance at the data suggests that there is comparable research participation among participants who identify as white or Caucasian and participants who identify as Hispanic or Latino. The data points to increased participation among individuals who identify as Hispanic or Latino, as this demographic category comprises approximately 40% of the pooled research participants. However, it is crucial to consider the context in which this occurs. The percentage of research participants who identify as Hispanic and Latino drops drastically to 5.4% overall when the LALES is excluded from this study. The LALES is a population-based study which sought to evaluate the use of various screening parameters for glaucoma in specifically Latino-identifying patients (Francis et al., 2011). The LALES is an outlier within the data set in which all 6082 participants belong to the

Hispanic or Latino demographic group. Without LALES, research participation among Hispanic and Latino individuals is very low compared to both patients who identify as White or Caucasian and patients who identify as Black or African American. This is further underscored by the 6.9% and 3.3% (excluding LALES) participation in clinical trials and nonclinical trial studies, respectively. Thus, a disparity in glaucoma research participation is evident with respect to the Hispanic and Latino population. The lack of representation within clinical trials is perhaps the most concerning and pressing need at present. Clinical trials are considered strong studies which inform screening protocols and as such, should provide study populations which accurately reflect diverse patient populations across the United States. According to the most recent US Census data, Hispanic or Latino individuals comprise as much as 19.1% of the US population (United States Census Bureau, 2023). Therefore, with this data in consideration as well as the knowledge that glaucoma is a disease which disproportionately affects patients who identify as Hispanic/Latino and Black/African American, there must be increased efforts to improve research participation amongst these racial and ethnic groups.

The results of the study corroborate the findings of the systematic review by Allison et al. in 2021. The systematic review reported that among the total study population in POAG clinical trials, 70.7% identified as White, 16.8% identified as Black, and only 3.4% identified as Hispanic/Latino (Allison et al., 2021). In the current study, among the nine identified clinical trials, 65.4% identified as White, 26.9% identified as Black, and only 6.9% identified as Hispanic/Latino. The present study is comprised of a smaller sample size, which may account for the variations noted within the Black and Hispanic/Latino population percentages.

Thus far, throughout the available literature, there have been no studies which report racial/ethnic disparities in glaucoma research participation in studies that are not designed as clinical trials. This study is the first to compile and report data that highlights disparities in glaucoma research participation among Black and Hispanic/Latino individuals in cross-sectional, cohort, and population-based studies. The data highlights a disparity similar to that as what has been previously reported with regards to glaucoma clinical trials. With a more accurate representation of the diverse patient population which exists throughout the United States, a stronger and more equitable recommendation for glaucoma screening may arise.

The current standpoint on POAG screening from the USPSTF is that there is insufficient evidence to suggest that the benefits of population-health level glaucoma screening outweigh the negative effects (US Preventive Services Task Force et al., 2022a). Notably, the grade for the USPSTF statement is listed as “I”, which corresponds to incomplete. The American Academy of Ophthalmology (AAO) recommends against population glaucoma screening in the general population as well in their 2020 Preferred Practice Pattern guidelines as it is not cost effective (Gedde et al., 2021). However, the AAO recognizes the benefit of targeted screening for high-risk populations such as older adults, patients with a positive family history of glaucoma, and African Americans and Hispanics (Gedde et al., 2021). Two studies were identified in the preferred practice pattern guidelines which inform the prospect of glaucoma screening from an economic and cost-based approach (Hernández et al., 2008; JM Burr et al., 2007). However, it is important to note that both studies took place prior to 2009 and were performed in the United Kingdom (Hernández et al., 2008; JM Burr et al., 2007). A newer study from 2019 was performed in

China and sought to evaluate the cost-effectiveness and cost-utility of population screening for glaucoma (Both POAG and primary closed angle glaucoma). The study concluded that population screening for glaucoma is likely to be cost-effective in both urban and rural China (Tang et al., 2019). Additionally, a study performed in Spain compared the cost-effectiveness of POAG screening compared with opportunistic case finding. This study was published in 2023 and concluded that the screening strategy implemented within the analysis was cost-effective compared with opportunistic finding in patients with glaucoma (Alfonso Anton et al., 2023). It would be interesting to see if the recommendations for population level glaucoma screening change given this new information. Preferred Practice Pattern guidelines are updated every five years; thus, the next version is planned to be released in 2025. Additionally, it seems that it would be beneficial to have an updated cost effectiveness study performed in the United States. This would provide useful and insightful information into the potential cost effectiveness of a population health screening protocol implemented in populations more reflective of the United States. An updated study would also be useful given the progression in ophthalmic technology and the integration of telemedicine into practice.

As mentioned earlier, the AAO does recognize the utility and potential cost-effectiveness of a screening approach that prioritizes high-risk populations. However, discourse remains regarding the most effective tools for screening patients. A number of clinical trials, some of which are included in this study, have explored optimal screening protocols. No consensus has been reached and additional research in the field is required. As additional research projects are undertaken and screening protocols are evaluated, a public statement recommending screening in high-risk populations would seemingly be

beneficial. The current recommendations for eye care and screening are vague and simply recommend a baseline eye examination for patients over the age of 40. It would be beneficial to provide a statement that identifies the risk factors for development of glaucoma such as age, family history, and race/ethnicity. Such a statement would provide greater awareness amongst patients as well as other providers not in the field of ophthalmology. Patients do not typically seek out ophthalmic examination unless they have a particular visual concern. Additionally, primary care physicians do not typically recommend routine eye screening outside of patients with Diabetes mellitus and for baseline eye examinations. An increase in both patient and provider awareness of glaucoma may be a step towards mitigating the disparities which exist with regards to glaucoma in the United States.

Study Limitations

One of the major limitations of this study is the sample size. This was largely a result of the inclusion criteria and restricted sample from which the studies were selected. The included studies in the systematic review by Chou et al. served as the source of literature within this study. Thus, the current study is susceptible to the limitations incurred within that study as well. In addition, only studies written in English language that were at least partially performed within the United States were included. These inclusion criteria were utilized in order to obtain an accurate portrayal of how well the United States performs with regards to diversity of research participants.

Aside from the limitations imposed by the inclusion and exclusion criteria, another limitation was the involvement of only one researcher. The performance of a systematic review and/or meta-analysis with two or more reviewers involved throughout the process related to this topic in the future may prove beneficial in the presentation of stronger data.

CHAPTER 5

BIOETHICAL PRINCIPLES

Scientific evidence through the medium of research is a critical aspect of consideration when formulating screening protocols. However, it is also important to consider the arguments for and against POAG screening from different vantage points. The discipline of bioethics allows one to evaluate arguments systematically and critically specifically pertaining to the pursuit of equity in healthcare. Another advantage of bioethics is that it provokes consideration into the subject matter with the patient's best interests maintained at the forefront. This argument will take place using the four pillars of bioethics: beneficence, non-maleficence, justice, and autonomy. This section is included in the thesis to provide insight into the potential benefits or harms of POAG screening from a patient-centric viewpoint that is not necessarily bound by the limitations of clinical science and data. Rather, it is a subjective philosophical argument that integrates the intangible aspects of the practice of medicine that are often left unaddressed in scientific and clinical literature.

Beneficence refers to the intent to "do good". Non-maleficence is often associated with the phrase, "do no harm". The principle of justice necessitates fair and equitable healthcare. Lastly, autonomy refers to the principle in which patients are permitted to make informed decisions regarding their care. In the following portions of the discussion, arguments will be presented both in favor and against the implementation of population health level glaucoma screening from a bioethical perspective.

A Bioethical Argument in Favor of Population Health Level Glaucoma Screening

Beneficence:

Regarding the principle of beneficence, the argument is dependent upon what one defines as 'good'. If one defines early detection of glaucoma in patients to prevent progression of the disease as a good or favorable outcome, then population health level glaucoma screening would be viewed as favorable. If primary open angle glaucoma screening were to be implemented on a population-health level, more individuals with POAG would be identified and irreversible vision loss resulting from the disease may be slowed or prevented.

Non-maleficence:

Physical or emotional harm is unlikely to be incurred through the implementation of POAG screening. However, some patients may experience emotional distress associated with the diagnosis as an unintentional result of screening. Screening is non-invasive and minimally time consuming for patients. Additionally, cost has often been cited as a limiting factor in the implementation of population health level glaucoma screening. However, the patient is the primary subject to be considered according to the bioethical principles. Thus, POAG screening would satisfy the bioethical principle of non-maleficence as no intentional or unintentional harm is likely to be incurred outside of potential emotional distress.

Justice:

According to the principle of justice, the implications of POAG screening are not fully elucidated as additional studies are required that more accurately represent the diverse, urban populations present throughout the United States. Given that POAG

disproportionately affects Black and Hispanic patients compared with White patients, an argument can be made for additional effort and emphasis from the research standpoint. If screening is thought to aid in the early identification of POAG and prevention of irreversible blindness which disproportionately affects patients, such as Black and Hispanic/Latino individuals, then withholding screening may violate the principle of justice. Screening protocols are often heavily informed by the numerous clinical trials performed regarding the subject to determine efficacy, cost-effectiveness, and utility. Given that a majority of glaucoma clinical trial participants identify as White, the conclusions drawn from these studies may not provide adequate guidance as it is not entirely applicable to the diverse patient populations which comprise the United States.

Autonomy:

POAG screening would not violate the principle of autonomy because it will ultimately be up to the patient to decide whether or not to pursue the screening. Implementation of POAG screening would merely ensure that proper screening protocols and tools are in place for those to whom screening is encouraged. Patients will maintain the right to refusal of screening if so desired.

A Bioethical Argument Against Population Health Level Glaucoma Screening

Beneficence:

It is difficult to formulate an argument against population health level POAG screening given that, overall, the early detection of this chronic disease may prevent irreversible vision loss. As mentioned in the previous section, this argument is largely dependent on what one views as “good” with respect to patients. One may present the argument that early detection of POAG does not necessarily entail the prevention of disease

progression or vision loss. Given that current understanding of glaucoma is incomplete, as it is a multifactorial chronic disease, and screening protocols are not yet optimized, it may not be beneficial to screen patients for this condition. It may be argued that subjecting individuals to a screening protocol and making the diagnosis could result in an unfavorable outcome. This potential unfavorable outcome would involve emotional and financial distress incurred by the patient. A diagnosis of glaucoma may result in emotional distress as it is a chronic disease which is associated with progression to blindness. Financial distress may occur in the setting of time burden due to recommended frequency of clinic follow-up visits, the cost of eye drops, and/or the cost of laser procedure if indicated. Presently available treatment options for non-severe primary open angle glaucoma involve the use of daily eye drops or an outpatient laser procedure called selective laser trabeculoplasty (SLT).

Non-Maleficence

The argument through the perspective of this bioethical principle is similar to that discussed in the previous paragraph. Is it potentially harmful to screen for a disease in which no definitive screening protocol has been established? Is it harmful to patients to subject them to a diagnosis of a disease which remains relatively poorly understood? These are important questions to consider when contemplating this bioethical principle. Perhaps the most important question to consider is, do the potential negative effects associated with screening outweigh the positive effects? Data typically provides an answer to this question; however, the data is insufficient in this case in both amount and of the data that is available, disparities among research participation are present. Dependent on one's answers to the

questions above, it may be concluded that POAG screening does not satisfy the principle of non-maleficence.

Justice:

It is difficult to formulate an argument against POAG screening from a justice standpoint given that disparities among research participation are evident from the data. The argument for justice is largely in favor of increased equitable research efforts in glaucoma to better understand the implications of screening in a patient population adequately reflective of the diverse patient populations which exist throughout the United States. Satisfaction of the principle of justice is largely dependent upon the findings of those research initiatives. However, from a strictly bioethical standpoint, it is difficult to argue that POAG screening would violate the principle of justice given the disparities in glaucoma that has been noted often throughout the literature.

Autonomy:

Similarly to the argument for POAG screening, the principle of autonomy would not be violated in this scenario. Patients would maintain their right to autonomy in either case.

CHAPTER 6

FUTURE DIRECTIONS

Although disparities among research participation exist within current glaucoma research in Black and Hispanic/Latino populations, there are several encouraging developments within the current literature. Similarly to the systematic review by Allison, et al., this study determined that perhaps the greatest level of disparity is noted within clinical trials (Allison et al., 2021). Thus, future efforts are required to encourage increased participation in clinical trials among Black and Hispanic/Latino patients. The disparities in research participation among clinical trials has been well established and documented, particularly in Black/African American and Hispanic/Latino populations (Allison, Patel, & Kaur, n.d.; Hamel et al., 2016). Previously identified barriers to participation include; lack of provider recommendation, lack of knowledge of available clinical trials, medical mistrust, financial implications of participation, time commitment, and lack of diversity reflected in healthcare (Allison, Patel, & Kaur, n.d.; Hamel et al., 2016). Additional systemic barriers to participation that may be addressed are research funding allocation, lack of diversity in healthcare, and the relationship between research institutions and their surrounding communities. Improvement in clinical trial participation will likely require a multimodal approach that addresses this issue from multiple aspects.

The Philadelphia telemedicine glaucoma detection and follow-up study provides a strong example of an approach that may help to remedy the disparities which exist in participation among glaucoma clinical trials (Hark et al., 2019). The approach involved recruitment with the help of community partners, zip code tabulation to identify medically underserved areas within the city and health professional shortage area designations, and

visits were made free of charge (Hark et al., 2019). This study was successful in recruiting research participants that accurately reflected the patient population which exists in the diverse, urban city of Philadelphia. 60.7% of 916 participants identified as Black/African American and 13.8% identified as Hispanic/Latino. This particular clinical trial provides a helpful framework from which researchers can build upon for future clinical trials.

Aside from research participation in clinical trials, it is important to consider the lack of adequate representation among research studies designed as cross-sectional, cohort, and population-based studies. LALES was an impressive, targeted research effort towards improving Hispanic/Latino representation in glaucoma literature (Francis et al., 2011). This is an example of a population-based study which contributed to the current body of literature related to glaucoma that prioritized Hispanic/Latino individuals. Future research projects in glaucoma can adopt a similar approach to prioritize underrepresented minority groups to participate. Future projects do not necessarily need to be as targeted as LALES for a particular demographic population, rather they can pursue a well, diversified cohort of study participants.

CHAPTER 7

CONCLUSION

Glaucoma is one of the leading causes of vision loss worldwide. Primary open angle glaucoma is the most common form of glaucoma in the United States and is the leading cause of irreversible blindness in African Americans. POAG has been shown to disproportionately affect Black and Hispanic patients compared with their White counterparts. Despite this, there are no current population-based screening recommendations for this disease. This recommendation is based upon the currently available data and research performed on POAG. However, within the currently available literature on the topic, there are notable disparities in research participation and representation among Black and Hispanic individuals. This has been well documented with respect to clinical trials, however, there have been no similar studies performed reviewing nonclinical trials, such as cross-sectional, cohort, and population-based studies. This study sought to address this issue.

The findings of this study confirm the presence of disparities in research participation among Black and Hispanic individuals across all POAG studies. The data echoes the presence of significant disparity, particularly among Hispanic individuals, in clinical trials. Additionally, the data points to a similar disparity which extends across nonclinical trials as well. With the exclusion of the LALES, which presented as an outlier with regards to its level of participants who identified as Hispanic/Latino, significant disparities in participation were noted amongst Black and Hispanic individuals across cross-sectional, cohort, and population-based studies. This thesis underscores the ongoing need for equitable efforts in POAG research across all studies. These efforts are crucial to

provide data sets with diverse patient populations more reflective of the diverse, urban populations which exist throughout the United States. With these efforts, recommendations for screening, as well as improved knowledge of this condition, may be properly elucidated to inform more equitable care and identification of this disease.

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