Title
Racial and Ethnic Disparities in Glaucoma Surgery in the United States

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Publication Date
2023

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Racial and Ethnic Disparities in Glaucoma Surgery in the United States

A dissertation submitted in partial satisfaction

of the requirements for the degree

Doctor of Philosophy in Epidemiology

by

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2023

ABSTRACT OF THE DISSERTATION

Racial and Ethnic Disparities in Glaucoma Surgery

in the United States

by

Ken Kitayama

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2023

Professor Anne L. Coleman, Chair

Glaucoma is the leading cause of blindness in high-income countries like the United States (US) in adults aged 50 years and older. In the US, glaucoma is known to disproportionately affect racially and ethnically minoritized groups, such as Black, Latinx, and Asian/Pacific Islander individuals. Incisional glaucoma surgery remains a mainstay of treatment for severe or medically-uncontrolled glaucoma. Though studies have supported the longstanding clinical finding that Black patients are at increased risk for incisional glaucoma surgical failure, few studies have explored disparities in incisional glaucoma surgical outcomes within a racially and ethnically diverse and representative sample, or the structural inequities that contribute to these disparities.

The first study of this dissertation constructs a retrospective cohort using data from a 20% representative sample of 2016-2018 US fee-for-service Medicare beneficiaries who received

incisional glaucoma surgery (trabeculectomy, tube shunt, or EX-PRESS® shunt) to compare risk of surgical failure (defined as glaucoma surgical reoperation) by patient race and ethnicity. The final analytical sample included a total of 12,366 unique beneficiaries, and during the study period, there was a total of 1,590 incisional glaucoma surgical reoperation events, yielding a cumulative incidence of 12.9%. In this diverse and representative national cohort, Black, Latinx, and Asian/Pacific Islander patients had greater risk of reoperation compared to non-Latinx White beneficiaries. Thus, this representative cohort study of national Medicare beneficiaries elucidated new and persistent racial and ethnic disparities in incisional glaucoma surgical outcomes.

The second study examined racial and ethnic disparities in eye care provider networks by applying network science methods to Medicare claims data and determined whether network characteristics of treating surgeons were associated with risk of incisional glaucoma surgical failure. This study utilized the entire population of 2016 fee-for-service California (CA) Medicare beneficiaries aged 65 and older who received incisional glaucoma surgery. Overall, Asian/Pacific Islander patients were more likely to be treated by surgeons with fewer ties to other providers they had worked with previously and Black and Latinx beneficiaries tended to have treating surgeons who had fewer connections to other eye care providers and belonged to smaller, more isolated network clusters. Altogether, results from this second study point to these racial and ethnic disparities in eye care provider networks as possible manifestations of structural racism plaguing our present-day healthcare systems.

The third study estimated the proportion of the racial and ethnic disparity observed in glaucoma surgical outcomes that can be eliminated by theoretically intervening on socioeconomic status

(SES) on a national and statewide scale. Two retrospective cohorts were constructed using: (a) a nationally-representative 20% random sample of 2016-2018 US Medicare fee-for-service beneficiaries and (b) the entire population of 2016-2018 CA fee-for-service Medicare beneficiaries who received incisional glaucoma surgery. The SES mediator was dichotomized to low vs. non-low based on dual-eligibility for Medicaid coverage. Causal mediation analysis was used to estimate the proportion of the disparity eliminated after uniform assignment of SES to non-low for all. Results demonstrated that SES mediates racial and ethnic disparities in glaucoma surgical outcomes, though by varying amounts by individual racial and ethnic group. Furthermore, SES mediation of racial and ethnic disparities in glaucoma surgical outcomes was itself modified by local geographic regions and social contexts.

In conclusion, racial and ethnic disparities in glaucoma surgical outcomes persist and have extended to include a wider set of racially- and ethnically-minoritized groups, including Black, Latinx, and Asian/Pacific Islander populations. These disparities are partially driven by structural inequities in eye care provider networks and significant gaps in wealth. Racial and ethnic disparities are complex; future studies are needed to examine other downstream mediating structural inequities (such as other social determinants of health) that represent modifiable targets to intervene upon to achieve equity in glaucoma outcomes.

The dissertation of Ken Kitayama is approved.

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2023

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LIST OF ABBREVIATIONS

Adjusted hazard ratio (aHR)
Advanced Glaucoma Intervention Study (AGIS)
Angle closure glaucoma (ACG)
Argon laser trabeculoplasty (ALT)
California (CA)
Centers for Medicare and Medicaid Services (CMS)
Collaborative Initial Glaucoma Treatment Study (CIGTS)
Controlled direct effect (CDE)
Current Procedural Terminology 4 (CPT-4)
Fee-for-Service (FFS)
Hazard ratio (HR)
Intraocular pressure (IOP)
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)
International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)
Laser in Glaucoma and Ocular Hypertension Trial (LiGHT)
Master Beneficiary Summary File (MBSF)
Medicare Enrollment Database (EDB)
Mitomycin C (MMC)
Ocular hypertension (OHT)
Odds ratio (OR)
Open angle glaucoma (OAG)
Primary open angle glaucoma (POAG)
Primary Tube Versus Trabeculectomy (PTVT) Study
Proportion eliminated (PE)
Research Triangle Institute (RTI)
Risk ratio (RR)
Selective laser trabeculoplasty (SLT)
Social Security Administration (SSA)
Socioeconomic status (SES)
Standard Analytical Files (SAFs)
Total effect (TE)
Tube Versus Trabeculectomy (TVT) Study
Uncertainty interval (UI)
United States (US)

ACKNOWLEDGMENTS

I would like to express my sincere gratitude to my dissertation advisor, Dr. Anne L. Coleman, for her invaluable guidance, support, and mentorship throughout the process of preparing this dissertation and during the entire course of my doctoral studies. She has pushed me both clinically and scientifically to constantly improve and focus on what lies immediately ahead, reminding me that, "While you can't have everything at once, you *can* over a lifetime." I would also like to thank my committee members, Dr. Elizabeth Rose Mayeda, Dr. Aikihiro Nishi, and Dr. Yusuke Tsugawa for their illuminating instruction in the classroom in addition to their crucial direction and assistance with various aspects of this dissertation.

I greatly appreciate the financial support I have received during my doctoral studies at UCLA. I would like to acknowledge the Specialty Training and Advanced Research in Ophthalmology (EyeSTAR) Program in the UCLA Department of Ophthalmology for its support of my doctoral training. I would like to thank Dr. Joseph L. Demer, EyeSTAR Program Chair for his support and encouragement throughout my time in this program. I would also like to thank the Department of Epidemiology for awarding me with the HEALRISE (HEALth, Racism, Inequities, and Social Epidemiology) Scholarship, which has generously funded my research efforts.

I would like to earnestly thank my research collaborators, Dr. Fei Yu and Dr. Victoria L. Tseng for their time and expertise they shared with me in my preparation of this dissertation and during the entirety of my doctoral studies.

Finally, I would like to thank my family for their constant, loving support that has allowed me to pursue a path that has been immensely fulfilling and rewarding. For this, I am indebted most to my parents, Susana and Carlos Kitayama, who have both sacrificed so much to provide me with endless opportunities. This dissertation is dedicated in loving memory of my mother.

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PUBLICATIONS

Hofstetter AM, Vargas CY, Kennedy A, **Kitayama K**, Stockwell MS. Parental and provider preferences and concerns regarding text message reminder/recall for early childhood vaccinations. Prev Med. 2013;57(2):75-80.

Kitayama K, Stockwell MS, Vawdrey DK, Pena O, Catallozzi M. Parent perspectives on the design of a personal online pediatric immunization record. Clin Pediatr (Phila). 2014;53(3):238-242.

Leininger EC, **Kitayama K**, Kelley DB. Species-specific loss of sexual dimorphism in vocal effectors accompanies vocal simplification in African clawed frogs (Xenopus). J Exp Biol. 2015;218(Pt 6):849-857.

Ochoa A, 3rd, **Kitayama K**, Uijtdehaage S, Vermillion M, Eaton M, Carpio F, Serota M, Hochman ME: Patient and provider perspectives on the potential value and use of a bilingual online patient portal in a Spanish-speaking safety-net population. J Am Med Inform Assoc 2017, 24(6):1160-1164.

Kitayama K, Segura ER, Lake JE, Perez-Brumer AG, Oldenburg CE, Myers BA, Pourjavaheri P, Okorie CN, Cabello RL, Clark JL: Syphilis in the Americas: a protocol for a systematic

review of syphilis prevalence and incidence in four high-risk groups, 1980-2016. Syst Rev 2017, 6(1):195.

Carnero AM, **Kitayama K**, Diaz DA, Garvich M, Angulo N, Cama VA, Gilman RH, Bayer AM: Risk for interspecies transmission of zoonotic pathogens during poultry processing and pork production in Peru: A qualitative study. Zoonoses Public Health 2018, 65(5):528-539.

Huaman B, **Kitayama K**, Bayer AM, Condor DF, Segura P, Carcamo CP, Aral SO, Blanchard JF, Garcia PJ. Filling the gaps in the Peruvian care continuum for HIV-infected pregnant mothers: a case-control study in metropolitan Lima-Callao, Peru. Int J STD AIDS. 2020;31(10):982-988.

Kitayama K, Young AG, Ochoa A, Yu F, Wong KYS, Coleman AL. The agreement between an iPad visual field app and Humphrey frequency doubling technology in visual field screening at health fairs. J Glaucoma. 2021;30(9):846-850.

Emami S, **Kitayama K**, Coleman AL. Adjunctive steroid therapy versus antibiotics alone for acute endophthalmitis after intraocular procedure. Cochrane Database Syst Rev. 2022 Jun 6;6(6):CD012131.

Lee SY, Tseng VL, **Kitayama K**, Avallone TJ, Yu F, Pan D, Caprioli J, Coleman AL. Associations between Niacin Intake and Glaucoma in the National Health and Nutrition Examination Survey. J Glaucoma. 2023 Mar 20. doi: 10.1097/IJG.0000000000002216. Epub ahead of print.

Paul ME, Tseng VL, **Kitayama K**, Yu F, Coleman AL. Evaluating Discrepancies in Self-Reported Glaucoma and Electronic Health Records in the National Institutes of Health All of Us Database. Ophthalmol Glaucoma. 2023 Mar 15:S2589-4196(23)00061-3. doi: 10.1016/j.ogla.2023.03.003. Epub ahead of print.

Yao M, **Kitayama K**, Yu F, Tseng VL, Coleman AL. Association Between Myopia and Primary Open-Angle Glaucoma by Race and Ethnicity in Older Adults in the California Medicare Population. JAMA Ophthalmol. 2023 Apr 27:e231007. doi: 10.1001/jamaophthalmol.2023.1007. Epub ahead of print.

Chapter 1: Introduction and Background

1.1 Background

1.1.1 Pathophysiology of Glaucoma

Glaucoma refers to a heterogeneous group of optic neuropathies that are characterized by progressive degeneration of retinal ganglion cells, which are neurons of the central nervous system whose cell bodies are located in the inner layers of the retina and whose axons are situated in the optic nerve.[1] Glaucoma can be broadly categorized into two groups: open angle glaucoma (OAG) and angle closure glaucoma (ACG). These two forms of glaucoma are distinguished from one another according to the morphology of the anterior chamber angle and the anatomic location of the aqueous humor obstruction leading to hindered drainage out of the eye.[2]

As its name suggests, OAG is characterized by an open drainage angle; however, aqueous humor obstruction still occurs and is caused by increased resistance to aqueous outflow through the trabecular meshwork. Though the pathological mechanism behind OAG involves aqueous humor obstruction, intraocular pressure (IOP) is either increased only slightly or is within the normal range, and if elevated IOP is in fact present, it is usually painless.[3] Furthermore, the retinal ganglion cell loss observed in glaucoma causes progressive deterioration of visual fields, characteristically beginning with visual field loss in the midperiphery, usually progressing in a centripetal pattern until there remains only a central or peripheral island of intact vision in late stages of the disease.[1] In fact, as many as 30% to 50% of retinal ganglion cells may be damaged before defects begin to appear by standard visual field testing.[1,4,5] Thus, progression of OAG is often painless and asymptomatic, with about 50% of patients with OAG being unaware of their disease.[2,6-11]

On the other hand, ACG is caused by apposition of the iris, resulting in obstruction due to an anatomically closed angle (defined if at least 270º of the angle is occluded).[1] In less than a third of cases, patients with ACG may present with acute primary angle closure, a clinical condition characterized by inflammation, conjunctival hyperemia, corneal edema, a mid-dilated unreactive pupil, a shallow anterior chamber, and very high IOP.[1,3] However, in most cases, ACG has a chronic course and it is often asymptomatic until visual field defects are detected.[3,12]

1.1.2 Epidemiology of Glaucoma

It was estimated that 3 million people in the United States (US) had glaucoma in 2015, a figure that is expected to more than double to about 6.3 million people by 2050.[13] Globally, there were approximately 64.3 million cases of glaucoma in adults aged 40-80 years, with projections estimated to increase to about 111.8 million in 2040.[14] According to the Vision Loss Expert Group of the 2019 Global Burden of Disease Study, the worldwide age-standardized prevalence of glaucoma is approximately 2.04 per 1,000 population (95% uncertainty interval [UI]: 1.59 to 2.49).[15] Glaucoma is the leading cause of irreversible blindness in high income countries such as the US, accounting for approximately 28.2% (UI: 24.0-32.3%) of the age-standardized prevalence of blindness in 2020 in adults aged 50 years and older. Globally, glaucoma is also the number one cause of irreversible blindness, attributed to cause about 11.0% (UI: 9.3-12.8%) of the age-standardized prevalence of blindness in 2020 in adults aged 50 years and older.[15]

Glaucoma is a highly heritable and complex disease, with an estimated heritability of 70%.[16] In fact, first-degree relatives of individuals with glaucoma have a 22.0% lifetime risk for developing glaucoma, compared to 2.3% in those without family history of glaucoma, yielding a risk ratio for glaucoma of 9.2 (95% confidence interval [CI]: 1.2-73.9).[17] A number of individual genes have been found to be associated with monogenic, autosomal dominant inheritance patterns

of glaucoma; however, these single-gene or Mendelian forms of glaucoma account for only about 5% of primary open angle glaucoma (POAG)[18] and less than 10% of all glaucoma cases.[1] Recently, there have been a growing number of genome-wide association studies to look for glaucoma susceptibility loci; however, the 127 genome-wide significant loci that have been identified collectively explain only 9.4% of the POAG familial risk.[19]

Older age is another well-established risk factor for the development of glaucoma.[20-25] In fact, in a meta-analysis using population-based studies, Friedman et al. found that the prevalence of glaucoma in US adults 65 to 69 years of age was approximately 2.79% (95%CI: 2.54-3.04%) compared to 0.68% (95%CI: 0.59-0.78% in adults 40-49 years old, with estimates increasing to 7.74% (95%CI: 6.58-8.89%) in adults 80 years of age and older.[26] Further illustrating the relationship between older age and glaucoma development, a systematic review and meta-analysis by Rudnicka et al., found that the odds ratio per decade increase in age was 2.05 in White populations (95% CI: 1.91-2.18), 1.61 in Black populations (95% CI: 1.53-1.70), and 1.57 in Asian populations (95% CI: 1.46-1.68).[24]

Furthermore, racially and ethnically minoritized groups in the US are at greater risk for glaucoma, as demonstrated by a number of foundational epidemiologic studies primarily from the late 1980s to early 2000s (see Table 1.1).[8,27-31] Estimates from the Salisbury Eye Evaluation Glaucoma Study are greater than those of other studies given they examined older adults 73 years and older.[27] Based on these population-based estimates, there is widespread consensus that the prevalence of POAG in Black Americans is approximately four-fold higher compared to non-Latinx White individuals in the US.[30] The prevalence of glaucoma in Latinx individuals has also been found to be significantly higher than non-Latinx White individuals and similar to Black individuals in the US.[31]

Table 1.1 Glaucoma prevalence by race and ethnicity in US population-based studies

Study	Years	Location	Race and ethnicity	Prevalence (%)
Framingham Eye Study[28]	1973	Framingham, MA	White	3.3
Baltimore Eye Study[30]	1985-1988	Baltimore, MD	Black	4.7
			White	1.3
Beaver Dam Eye Study[29]	1988-1990	Beaver Dam, WI	White	2.1
Proyecto VER[8]	1997-1999	Nogales and Tucson, AZ	Latinx	2.0
Los Angeles Latinx Eye Study[31]	2000-2003	La Puente, CA	Latinx	4.7
Salisbury Eye Evaluation Glaucoma Study[26]	2001-2003	Salisbury, MD	Black	20.0
			White	8.5

Given the shifting demographics in the US, epidemiologic projections estimate that Latinx men 70 years and older will become the largest single demographic group with glaucoma by 2035, with the number of all Latinx POAG patients estimated to be 3.62 million, or approximately half of all POAG patients nationwide by that time.[32] Further compounding this disproportionality is the finding that a significant racial and ethnic disparity similarly exists in glaucoma underdiagnosis, with Black individuals having approximately 4.4 times (95% CI: 2.9-6.7) and Latinx individuals having approximately 2.5 times (95% CI: 1.5-4.3) greater odds of having undiagnosed and untreated glaucoma compared to non-Latinx White individuals.[9]

Related to this issue of underdiagnosis, Latinx and Black patients have been observed to be less likely to receive glaucoma testing compared to non-Latinx white patients.[33-35] In fact, in a recent retrospective cohort study using a nationally representative 5% random sample of Medicare beneficiaries from 2014 to 2016, Halawa and colleagues found that, compared to White counterparts, Black beneficiaries had lower counts of outpatient eye care visits (risk ratio [RR]: 0.92, 95% CI: 0.90-0.93), visual field tests (RR: 0.92, 95% CI: 0.90-0.94), more eye-related inpatient/emergency department encounters (RR: 2.42, 95%CI: 1.55-3.78), and more glaucoma

surgeries (RR: 1.14, 95% CI: 1.03-1.27).[36] Latinx beneficiaries experienced similar disparities in eye care utilization, with fewer outpatient eye care visits (RR: 0.97, 95%CI: 0.95-0.98) and fewer retinal nerve fiber layer optical coherence tomography tests (RR: 0.89, 95% CI: 0.86-0.93), but more eye-related inpatient/ED encounters (2.32, 95%CI: 1.18-4.57) and selective laser trabeculoplasty (SLT) (RR: 1.25, 95% CI: 1.11-1.42) as compared to non-Latinx White beneficiaries.[36] Furthermore, these racial and ethnic disparities in eye care utilization largely persisted after stratifying by socioeconomic status (SES), particularly for Black beneficiaries, suggesting that there may be other factors, such as consequences of systemic or structural racism, that may be an independent driver of these racial and ethnic disparities in this population.[36]

1.1.3 1.1.3 Treatment for Glaucoma

Topical medications remain the primary treatment option for glaucoma,[37] and they are divided into four main drug classes: prostaglandin analogues, beta-blockers, carbonic anhydrase inhibitors, and alpha-agonists. The goal of all four types of glaucoma medications is to lower and maintain control of IOP, since increased IOP remains the only modifiable risk factor for glaucoma, with disease progression typically stopping if pressures are lowered by 30-50% from baseline.[3] The choice of drug class for the initiation of therapy typically depends on cost, side effect profile, and dosing regimen. Potential systemic side effect profiles are often a concern when initiating topical glaucoma therapy in older adults given that they are at higher risk for experiencing adverse drug reactions due to changes in body consumption, serum albumin, total body water, and hepatic and renal drug clearance.[38] Dosing and medication burden are also important considerations when selecting an appropriate regimen for older adults who already manage complex drug schedules, further adding to issues related to medication adherence and persistence.[39] A patient's topical glaucoma medication regimen often requires adjustment(s) due to these aforementioned factors,

in addition to drug failure problems, as illustrated by the fact that two-thirds of patients require at least one modification to their glaucoma drops within the first 12 months of initiating treatment.[40]

Laser trabeculoplasty is an in-office procedure that can be used as initial or adjunctive therapy in patients with POAG.[37] Laser trabeculoplasty lowers IOP by improving aqueous outflow through the trabecular meshwork, which can be performed using argon or solid-state lasers, though more compact solid-state diode lasers have significantly replaced argon lasers given their equal IOP-lowering efficacy and safety.[37,41,42] Selective laser trabeculoplasty (SLT) involves the use of a 532 nm, Q-switched, frequency-doubled Nd:YAG laser that delivers less energy and is selectively absorbed by the pigmented cells in the trabecular meshwork, producing less thermal damage than the argon laser trabeculoplasty (ALT).[43] Most recently, the six-year outcomes for the Laser in Glaucoma and Ocular Hypertension (LiGHT) trial comparing initial treatment with SLT versus topical glaucoma treatment in POAG and ocular hypertension (OHT) demonstrated that SLT had lower glaucomatous disease progression, lower rates of incisional surgery, and lower rates of cataract surgery compared to the medication group.[44]

Incisional glaucoma surgery includes trabeculectomy and aqueous shunts. Trabeculectomy remains a mainstay surgical option for effective lowering of IOP, and is generally indicated when medications and appropriate laser therapy are insufficient to control disease progression.[37] However, trabeculectomy can be considered as initial therapy in some cases, as demonstrated by the Collaborative Initial Glaucoma Treatment Study (CIGTS), where trabeculectomy was more effective than initial medical therapy in lowering IOP and slowed progression of visual field defects in patients who presented with more advanced visual field loss.[45] The surgical technique behind trabeculectomy essentially provides an alternative path for aqueous humor to drain into the subconjunctival space and is often able to reduce IOP to the point where medical therapy is no

longer necessary.[37] Estimates of success rates over time range from 31% to 88% in different populations and with varying clinical definitions of success and failure.[37,46-49] A Cochrane Systematic Review conducted in 2005 demonstrated that intraoperative and postoperative use of antifibrotic agents such as mitomycin C (MMC) reduce the risk of subconjunctival scarring after trabeculectomy, leading to the recommendation that MMC be used intraoperatively.[50]

The Ex-PRESS shunt (Alcon Laboratories, Fort Worth, TX) is a non-valved, stainless steel implant which requires a procedure similar to trabeculectomy for implantation, though sclerotomy and iridectomy are not performed.[37] A number of randomized clinical trials[51-53] and retrospective studies[54-59] have reported similar IOP reduction and surgical success rates when comparing trabeculectomy with Ex-PRESS versus standard trabeculectomy. However, compared to standard trabeculectomy, Ex-PRESS shunt has been shown to have increased risk of postoperative complications, including greater endothelial cell loss[60] and early post-operative hypotony.[56,57,60]

All aqueous shunts (also referred to as tube shunts and glaucoma drainage devices) consist of a tube that diverts aqueous humor to an end plate that is surgically inserted within the subconjunctival space in the equatorial region of the eye.[37] Traditionally, aqueous shunts have been reserved for cases of medically uncontrolled glaucoma where trabeculectomy has failed to control IOP or is thought unlikely to succeed, though indications for its use have continued to broaden with a noted rise in shunt procedures along with a concurrent decline in trabeculectomies.[37] The five-year outcomes of the Primary Tube Versus Trabeculectomy (PTVT) Study were recently published, demonstrating that in eyes with medically uncontrolled glaucoma and no previous incisional ocular surgery, both trabeculectomy and aqueous shunts produced similar post-operative IOPs and no significant difference in the rate of surgical failures in the two surgical procedures.[61] Similarly, in the Tube Versus Trabeculectomy (TVT) Study, wherein

patients with previous trabeculectomy and/or cataract surgery and uncontrolled glaucoma, the rates of late postoperative complications and reoperation for complications were similar for both procedures after five years of follow-up.[62]

1.2 Summary of and gaps in the literature

1.2.1 Glaucoma surgical outcomes by race and ethnicity

Examining glaucoma surgical outcomes by race and ethnicity is challenging given the lack of racial and ethnic diversity in clinical trials for glaucoma. A systematic review and meta-analysis performed by Allison and colleagues included 105 clinical trials for POAG with a total of 33,428 POAG clinical trial participants; of these, 70.7% were White patients, 16.8% were Black patients, 3.4% were Latinx patients, and 9.1% were patients of other races/ethnicities, including Asian, Native Hawaiian or Pacific Islander, American Indian or Alaska Native, and unreported as defined by the US Census.[63] Thus, despite the fact that racially and ethnically minoritized groups have a higher prevalence of POAG, there has been a very low participation rate in POAG clinical trials for these groups. Furthermore, despite more recent measures intended to increase racial and ethnic diversity in clinical trial participants, there has not been a significant increase in clinical trial participation among Black individuals from 1994 to 2019 ($r^2 = 0.11$; $P = 0.17$).[63]

In a retrospective review of 500 patients treated with laser trabeculoplasty (ALT or SLT) at an academic institution in Toronto, Canada, Tzimis and colleagues examined patient characteristics that might be associated with 12-month outcomes. Study authors defined laser trabeculoplasty failure as subsequent incisional glaucoma surgery or an IOP decrease of 2 mmHg or less.[64] Study authors found no association between patient race (White versus non-White race) and laser trabeculoplasty failure in their multivariable logistic regression analysis (P=0.38).[64]

In a randomized trial of 174 consecutive POAG patients undergoing trabeculectomy and cataract surgery, Shin et al. examined use of adjunctive MMC in 174 eyes of 174 patients with an average follow-up time of 25.1 ± 5.5 months.[65] Surgical failure was defined as the need for an additional intraocular glaucoma procedure in addition to medical therapy to lower IOP to target pressure.[65] By this criterion, Black patients who underwent trabeculectomy surgery without MMC had 4.29 times the risk of surgical failure compared to White patients (hazard ratio [HR] 4.29, 95% CI: 1.40-13.16), and Black patients who were randomized to trabeculectomy with MMC had 1.28 times the risk of surgical failure compared to White patients (HR: 1.28, 95% CI: 0.35-4.64).[65] Thus, as mentioned previously, the use and appropriate dosing and titration of intraoperative antifibrotic agents such as MMC significantly reduces the risk of surgical failure in patients, and may represent an important intraoperative factor that can potentially reduce racial and ethnic disparities trabeculectomy outcomes.

In a retrospective case series of 71 consecutive patients with POAG who underwent primary combined trabeculectomy and cataract surgery, Morris et al. examined factors associated with increased risk for early surgical failure requiring suture release during the first month after surgery. Postoperative release of scleral flap closure suture is commonly performed for lowering IOP after trabeculectomy. In this analysis, study authors found that Black patients had 2.98 times the risk of early trabeculectomy failure requiring suture release compared to White patients (HR: 2.98, 95% CI: 1.01-8.82).[66]

The Advanced Glaucoma Intervention Study (AGIS) is an important randomized clinical trial in glaucoma surgery because of its practice-changing findings of race-treatment interactions between eyes of Black and White patients assigned randomly to surgical intervention sequences beginning either with ALT or trabeculectomy.[67] In AGIS, eyes were included if they failed medical

therapy for open-angle glaucoma and were randomly assigned to be managed with one of two surgical intervention sequences: ALT-trabeculectomy-trabeculectomy (ATT) or trabeculectomy-ALT-trabeculectomy (TAT), with the second and third interventions being offered in each sequence only after failure of the preceding intervention.[68] Eligible eyes had to be on maximum medical therapy and meet at least one of nine specified combinations of criteria for consistently elevated IOP, visual field defect due to glaucoma, and optic disc rim deterioration.[68] Late treatment failure, representing 242 (96%) of the 251 failures in the analysis, was defined as the eye again meeting the advanced glaucoma criteria for study eligibility at least six weeks or more after the most recent glaucoma surgery.[67] The AGIS investigators found that risk of failure of the initial surgical intervention was 79% greater for Black subjects than White subjects in the TAT sequence (RR: 1.79, 95% CI: 1.05-3.05), whereas risk of failure of the initial surgical intervention was 32% less for Black subjects than White subjects in the ATT sequence (RR: 0.68, 95% CI: 0.47-0.98).[67] Of note, study authors highlight that they limited AGIS failure analyses to the first intervention because there had been only small numbers of failures of the second and third interventions.[67] Thus, rather than examining failure rates of the entire TAT and ATT sequences, AGIS investigators essentially compared failure of primary ALT in Black versus White participants and primary trabeculectomy failure in Black versus White patients. Furthermore, it is important to note that adjunctive antifibrotics such as MMC were only used in a small number of primary trabeculectomies, under exceptional circumstances.[67] Nevertheless, it is interesting to note that AGIS essentially found reduced rates of failure in primary ALT for Black versus White participants, but increased rates of failure in primary trabeculectomy (without MMC or other antifibrotics) in Black versus White participants.

There is one study in the published literature that examined racial differences in trabeculectomy outcomes in Europe and South Africa. This particular analysis combined data from patients enrolled in two randomized double-masked clinical trials (CAT-152 study 0102 and CAT-152 study 0201) conducted in Europe and South Africa, following largely identical protocols.[69,70] Patients were adults 18 years or older who had uncontrolled glaucoma on maximal medical therapy, and either: (1) had first-time trabeculectomy (0102) or (2) had first- or second-time trabeculectomy (0201). The original purpose of the studies was to investigate the use of an antibody to transforming growth factor β_2, CAT-152 (lerdelimumab [Trabio, Cambridge Antibody Technology, Cambridge, United Kingdom]) to reduce bleb fibrosis and maintain bleb function, given that transforming growth factor β_2 has been implicated in scar formation.[71] In both clinical trials, surgical success was defined as an off-medication IOP of 6 to 16 mmHg at both 6 and 12 months after surgery. In the analysis of the data combined from both clinical trials, a negative relationship was found between Black race and surgical success; in other words, Black subjects were found to have 72% reduced risk of surgical success as compared to White counterparts (odds ratio [OR]: 0.28, 95% CI: 0.13-0.62).[71]

The only study comparing trabeculectomy failure in Asian and White patients in the US was undertaken by Law and colleagues in a case-control study of 29 eyes from 29 Asian patients matched to 29 eyes from 29 White patients on age, glaucoma subtype, preoperative IOP, gender, surgeon, ocular history, and glaucoma medications.[46] Study authors defined surgical success as: (1) final IOP >5 and <22 mmHg, (2) IOP reduction ≥20%, or final IOP ≤10 mm Hg, and (3) no need for additional glaucoma surgery, no loss of light perception visual acuity, or no surgical complications.[46] Mean follow-up time for Asian patients was 40.11±22.5 months, compared to 38.8±17.7 months for White patients. Kaplan-Meier survival analysis for surgical success was

performed, with a Log rank test statistic of *P*=0.46. The probabilities of trabeculectomy survival (continuing to meet definition of success criteria) at 12 and 48 months were 75.9 and 56.6% in the Asian American group and 82.8 and 66.6% in the Caucasian group, respectively.[46]

Most recently, five-year surgical outcomes of initial trabeculectomy with MMC were compared in Black and White patients in a retrospective matched cohort study published by Nguyen et al. Their examination of observational trabeculectomy outcomes included 135 eyes of 105 Black patients and 135 eyes of 117 White patients matched on age (within five years), surgeon, lens status, and follow-up time (within 1 year) from a single tertiary academic center.[72] Study authors defined qualified surgical success as follows (with increasingly stringent criteria for surgical success): criteria A, final IOP of 18 mm Hg or less with either 20% or greater reduction in IOP or reduction of at least 2 medications compared with the preoperative period; criteria B, final IOP of 15 mm Hg or less and either 25% or greater reduction in IOP or reduction of at least 2 medications; and criteria C, final IOP of 12 mm Hg or less and either 30% or greater reduction in IOP or reduction of at least 2 medications.[72] In the multivariable Cox proportional hazard regressions, Black patients had 1.37 times increased risk of trabeculectomy failure by criteria A compared to White patients (HR: 1.37, 95% CI: 0.89-2.14), Black patients had 1.73 times increased risk of trabeculectomy failure by criteria B compared to White patients (HR: 1.73, 95% CI: 1.20-2.48), and Black patients had 1.87 times increased risk of trabeculectomy failure by criteria C compared to White patients (HR: 1.87, 95% CI: 1.36-2.58).[72] Thus, in this retrospective matched cohort study of patients from a single tertiary academic medical center, Black patients were found to have increased risk for qualified surgical failure compared to White counterparts.

Salim and colleagues compared Ex-PRESS shunt outcomes in Black and White patients in a comparative case series of 36 eyes of 36 Black patients and 43 eyes of 43 White patients.[73]

Surgical success was defined as IOP between 5 and 18 mmHg, with or without glaucoma medications, without subsequent glaucoma surgery, or loss of light perception visual acuity.[73] Average follow-up was 31.9±9.8 months for Black patients and 30.7±8.6 months for White patients.[73] At 33 months of follow-up, surgical success was 80.0% in Black patients compared to 83.3% in White patients (P=1.00).[73] Thus, in this small case series, no significant difference in surgical failure for Ex-PRESS shunts were observed comparing Black and White patients. An examination of long-term outcomes of Ex-PRESS shunt surgery in Black and White patients was undertaken by Freedman et al. in a retrospective comparative study of 63 eyes of 50 Black patients and 44 eyes of 34 White patients.[74] Surgical success was defined as IOP between 5 and 18 mmHg, 20% reduction of IOP from baseline, with or without suture lysis or adjuvant medication, but no additional glaucoma surgery.[74] Mean follow-up time was 29 months (range: 12-81 months) for Black patients and 25 months (range: 12-66 months) for White patients.[74] Surgical success at 12 months was seen in 77.6% of Black patients compared to 95% of White patients, with the Log rank test indicating a significant difference in cumulative survival at 12 months (P=0.015), but no difference in cumulative survival at 2 years (P=0.462).[74]

In terms of aqueous shunt devices, the TVT study showed no association between race and ethnicity and cumulative probability of failure of tube versus trabeculectomy at five years[75] and the PTVT study similarly demonstrated no association between race and ethnicity and cumulative probability of failure of primary tube versus trabeculectomy at five years.[61]

As demonstrated by this exploration of the limited number of studies that have directly examined racial and ethnic differences in glaucoma surgical outcomes, a considerably large variety of definitions of surgical failure and surgical success are offered by each study. In fact, there exist almost as many definitions of success and failure as there are studies, with an examination of the

literature performed by Rotchford and King demonstrating that from 100 publications meeting literature search inclusion criteria, 92 distinct IOP-related definitions of success were identified.[76] This finding also motivated the World Glaucoma Association to make the following recommendation: "Utilizing consistent criteria for surgical success and definitions of postoperative complications and reoperations across clinical studies and trials is encouraged, so that outcomes across varied studies can be compared and/or combined."[77]

Furthermore, as demonstrated by this exploration of the literature on glaucoma surgical outcomes, very few studies have examined long-term outcomes of laser and incisional glaucoma surgeries in representative and racially/ethnically diverse populations in the US. Thus, a significant gap in the literature exists that requires further exploration to assess and describe racial and ethnic disparities that may exist in glaucoma surgical outcomes in a more diverse set of racial and ethnic groups, including non-Latinx White, Black, Latinx, and Asian populations.

1.2.2 Overview of Medicare administrative claims data

Medicare is the federal health insurance plan that offers coverage for individuals in the US aged 65 years and older, select individuals with disabilities younger than 65 years of age who have been receiving Social Security or Railroad Retirement Board benefits, and individuals with end-stage renal disease.[78] Medicare was officially established in 1965 and has grown in the number of beneficiaries covered over the last decades.[78] In 2020, an estimated 49.4 million[79] of the 52.4 million[80] adults aged 65 years and older were covered by Medicare, corresponding to approximately 94% coverage of older adults in the US. Administrative claims data from Medicare has been collected and used primarily for payment purposes,[78] but more recently, claims data has been leveraged to conduct a wide variety of health care research and surveillance studies to inform major health care and public policy decisions.[78,81,82]

Medicare coverage is broken into several parts. Part A, often referred to as "hospital insurance" covers care provided in the inpatient setting and may also cover care rendered in a skilled nursing facility, hospice, or home health care setting.[78] Part B, often referred to as "medical insurance" covers physician services (e.g., procedures, injections, and diagnostic tests) delivered in inpatient or outpatient settings, other outpatient care, medical supplies or durable medical equipment (e.g., oxygen tanks and wheelchairs), preventive services, and some home health care.[78] About 62.3% (n=39.0 million) of the 62.5 million Medicare beneficiaries in 2019 were enrolled in Parts A and/or B, with the remainder being enrolled in Medicare Advantage (Part C).[83] Part C claims are separate from CMS Medicare data files and can instead be accessed via specific employer group health plans.[78]

Fee-for-service claims are those submitted by professional providers, including physicians, physician assistants, optometrists, clinical social workers, and nurse practitioners.[84] Fee-for-service is defined by CMS as "a method in which doctors and other health care providers are paid for each service performed. Examples of services include tests and office visits."[85] The types of information contained in fee-for-service claims include billing codes for diagnosed medical conditions using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or Tenth Revision (ICD-10-CM) and billing codes for diagnostic and therapeutic procedures using Current Procedural Terminology 4 (CPT-4).[82] The Medicare Carrier File contains the fee-for-service claims submitted by professional providers and also includes claims from some organizational providers, including free-standing ambulatory surgical centers.[84] Data from the Carrier File is drawn from information from CMS claim form 1500, which is the uniform billing form used by professional providers for paper submission of claims.[86] The CMS Standard Analytical Files (SAFs) contain the final action claims for services rendered in one calendar year,

with separate SAFs created for each type of service (inpatient, outpatient, skilled nursing facility, home health, hospice, carrier, durable medical equipment).[87]

There are also limited demographic variables available in Medicare data. The Master Beneficiary Summary File (MBSF) base segment contains beneficiary enrollment information, including: date of birth, sex, race and ethnicity (obtained from CMS Common Medicare Environment) Zip code of beneficiary's mailing address (corresponding to the mailing address used for cash benefits and premium billing, obtained from Social Security Administration and Railroad Retirement Board Beneficiary Record Systems), race and ethnicity, Medicare Part A and Part B coverage, dual Medicare-Medicaid eligibility, and qualification for low-income subsidies for Medicare Part D (Medicare prescription drug coverage).[88]

The MBSF includes two separate variables for race and ethnicity. The first is taken from the Medicare Enrollment Database (EDB) and uses data that originates from Social Security Administration (SSA) records. Before 1980, the SSA collected voluntary race data using the following categories: White, Black, Other, and Unknown (for people who did not respond).[89] In subsequent years, CMS has made multiple efforts to address the issue of missing data, including sending a postcard survey to beneficiaries with a Hispanic surname or country of birth and use of race and ethnicity data from Medicaid sources for dual-eligible beneficiaries from 32 states.[89] Despite these efforts, it is recognized that the EDB race variable in the MBSF severely undercounts those who identify as Hispanic/Latinx, Asian American/Pacific Islander, and American Indian/Alaska Native.[90] Because of these shortcomings, the EDB race and ethnicity variable is usually only utilized to examine differences between Black and White patient populations. A second race and ethnicity variable was created in 2010 by the Research Triangle Institute (RTI) with the intention of reducing misclassification of Hispanic/Latinx and Asian/Pacific Islander

beneficiaries.[89] The RTI race and ethnicity variable applies a proprietary imputation algorithm that utilizes lists of Hispanic/Latinx and Asian/Pacific Islander names from the US Census together with simple geography (e.g., residence in Puerto Rico or Hawaii) to improve classification of these groups in the EDB race and ethnicity code.[89,91] Thus, CMS uses the RTI race and ethnicity variable when reporting on health disparities in the Medicare population and in studies that focus on Hispanic/Latinx and Asian/Pacific Islander populations.[89]

However, race and ethnicity data in Medicare has important limitations. In 2004, the National Academies of Sciences Engineering and Medicine analyzed the measurement and data needs required for studying the nature of disparities in health care and to develop strategies to eliminate disparities. In this report, the authors note an alarming limitation of the race and ethnicity data found in Medicare: "A further limitation in the racial and ethnic data contained in Medicare beneficiary files is that when CMS obtains the enrollee information from the SSA master beneficiary record, it receives information only on the retiree, not the retiree's spouse. Instead, the race of the beneficiary is simply assigned to the spouse."[92]

To investigate the possible misclassification of race and ethnicity in Medicare MBSF data, Jarrin and colleagues undertook an agreement study to compare the EDB and RTI race and ethnicity variable against a gold-standard source also available in the Medicare data warehouse: self-reported race and ethnicity coded in the home health Outcome and Assessment Information Set.[89] Among beneficiaries who self-identified as Hispanic/Latinx, the original EDB variable had low sensitivity (36.2) but high specificity (99.8), whereas the RTI race variable had higher sensitivity (90.8) and high specificity (98.8).[89] For beneficiaries who self-identified as non-Hispanic/Latinx Asian, Hawaiian Native, or other Pacific Islander, the RTI variable had higher sensitivity (74.7) compared to the EDB race and ethnicity variable (62.6), though both had

similarly high specificity (99.6-99.8).[89] Thus, the EDB race and ethnicity variable performs poorly in identifying beneficiaries who are Hispanic/Latinx (sensitivity, 36.2, kappa statistic (**κ**), 0.50), American Indian/Alaska Native (sensitivity, 42.9; **κ**, 0.44), and Asian American/Pacific Islander (sensitivity, 62.5; **κ**, 0.71). And though the RTI race and ethnicity variable performs better in identifying Hispanic/Latinx beneficiaries (sensitivity, 90.8; **κ**, 0.87), it nevertheless lacks validity for American Indian/Alaska Native (sensitivity, 43.0; **κ**, 0.44) and Asian American/Pacific Islander groups (sensitivity, 74.7; **κ**, 0.77).[89]

1.2.3 Previous studies of glaucoma surgical failure using Medicare data

The majority of previous studies that have utilized Medicare administrative claims data to explore racial and ethnic disparities in glaucoma surgery have focused on prevalence or incidence of glaucoma surgery to describe potential surgical undertreatment glaucoma in racially and ethnically minoritized groups (i.e., specifically, Black patients) using Medicare data from the 1990s.[93-97] An important caveat to consider is that these earlier studies compared observed rates of glaucoma surgery to expected rates of glaucoma surgery that were based on prevalence estimates from the aforementioned foundational population-based studies.[27,30] However, these early population-based surveys were by nature restricted to specific regional populations with sociodemographic characteristics—including race and ethnicity—that are not necessarily generalizable to the general US population.[98] This threat to external validity is further magnified by the significant demographic shifts favoring notably increased racial and ethnic diversity—both by state and nationwide—over the last decades.[99] Furthermore, another important limitation to these earlier studies is the residual confounding caused by glaucoma disease severity, given that racially and ethnically minoritized patients may be more likely to present with more severe disease, and thus may require additional glaucoma surgery.

However, ICD-10 codes now include a seventh digit to indicate the stage of glaucoma for that particular eye (with eye laterality encoded in the sixth ICD-10 code digit).[100] Glaucoma stage definitions encoded by the seventh digit disease modifier datapoint can take the following values: 1: mild or early stage glaucoma (optic nerve abnormalities consistent with glaucoma but no visual field abnormalities on any visual field test or abnormalities present only on short-wavelength automated perimetry or frequency doubling perimetry); 2: moderate stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field abnormalities in one hemifield and not within 5 degrees of fixation); 3: advanced, late, severe stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield); 4: indeterminate stage glaucoma (visual fields not performed yet or patient incapable of visual field testing or unreliable/uninterpretable visual field testing); 0: unspecified stage glaucoma (stage not recorded in chart).[100] However, it is important to note that adjustment for glaucoma disease severity is only possible beginning in October 2015, which is when ICD-10 codes were implemented into widespread clinical use.[101]

The only study to examine incisional glaucoma surgical failure in Medicare administrative claims data is presented in a paper recently published by Craven and colleagues.[102] In this study, investigators created a retrospective cohort using Medicare administrative claims data from 2005 through 2016 to compare reoperation rates for POAG patients treated with trabeculectomy, tube shunt, or Ex-PRESS shunt procedures. Study authors used Medicare 5% SAFs, which contain all service claims for a 5% random sample of Medicare fee-for-service beneficiaries.[102] Researchers can request data for a 5% or 20% random sample of Medicare beneficiaries, though in some situations 100% of Medicare beneficiaries can be requested for specific cohorts.[78] To select the

5% and 20% random samples, beneficiaries are selected based on the last two digits of their Medicare insurance claim number (which, in the vast majority of cases, corresponds to their social security number).[78] To allow for longitudinal follow-up of Medicare beneficiaries over multiple years (in those with continuous enrollment in Medicare FFS), information on all beneficiaries included in the 5% or 20% SAF random sample are provided for all years for which they received Medicare benefits (i.e., until death or disenrollment) included within the timeframe outlined in the investigators' data use agreement with CMS.[78]

Of note, investigators did not undertake a complete survival analysis approach to when defining their main outcome measures. They estimated cumulative rates of index failure and glaucoma reoperations over five years after incisional glaucoma surgery by surgical modality (trabeculectomy, tube shunt, Ex-PRESS shunt), but did not employ the log rank test to compare survival between groups, nor did they estimate the relative ratios of survival with hazard ratios evaluated with Cox proportional hazards models. Furthermore, the main objective of their study was to compare surgical failure among three different incisional glaucoma surgical modalities (trabeculectomy, tube shunt, Ex-PRESS shunt), and thus did not undertake explicit comparisons of outcomes by race and ethnicity to directly explore racial and ethnic disparities in surgical outcomes.

1.3 Overall objective

The purpose of this dissertation is to investigate potential racial and ethnic disparities in glaucoma surgical outcomes within a diverse and representative sample of Medicare beneficiaries, and to examine downstream factors that may contribute to these racial and ethnic disparities, including: (1) social network characteristics of patient-sharing networks of eye care providers, and

(2) individual patient SES as determined by dual-eligibility for Medicare-Medicaid coverage. These studies will be performed using Medicare administrative claims data from the Centers for Medicare & Medicaid services (CMS).

The first study will examine potential racial and ethnic disparities in glaucoma surgical outcomes in Medicare beneficiaries. This will be undertaken in a 20% representative sample of US Medicare fee-for-service beneficiaries. Time to surgical failure, defined as time to reoperation with an additional glaucoma surgical procedure, will be estimated and stratified by racial and ethnic subgroup.

Racial and ethnic disparities in health outcomes may occur through causes mediated through unintended forms of racism (whether interpersonal, institutional, or structural) that occur in healthcare systems. Thus, the second study will examine differences in patient-sharing networks of eye care providers as a potential target to reduce the racial and ethnic disparities observed in glaucoma surgical outcomes. Methods in social network analysis will be used to construct these patient-sharing networks of eye care providers using the Medicare administrative claims data. This time, the entire population of California (CA) Medicare fee-for-service beneficiaries will be utilized to construct complete patient-sharing networks of eye care providers. Specific network characteristics will be examined, such as the clustering coefficient and the popularity of each provider as determined by their network position, to differentiate networks caring for racially and ethnically minoritized populations versus those caring for predominantly non-Latinx White patients.

Racial and ethnic disparities in glaucoma surgical outcomes may also potentially be curbed by intervening on individual SES as another important downstream mediating factor. Studies have found that patients with glaucoma who have lower income and education levels have poorer visit

adherence and patients with glaucoma who have lower incomes and educational attainment are also more likely to report difficulty affording medications. Thus, rather than accounting for SES by modeling it as a confounder, as has been done in most epidemiologic studies examining racial and ethnic disparities in glaucoma, the third study will utilize methods in causal mediation analysis to examine SES as a mediator. This avoids methodologic pitfalls, including the potential introduction of collider stratification bias, while allowing for the estimation of causal effects that are meaningful from a policy perspective. These effects include the controlled direct effect (CDE), which estimates the residual racial and ethnic disparity that remains after uniform assignment of SES to the entire population, and the proportion eliminated (PE), or the proportion of the disparity eliminated after uniform assignment of SES.

Chapter 2: Racial and ethnic disparities in incisional glaucoma surgical outcomes in the United States: A retrospective cohort study using national Medicare data

2.1 Abstract

Purpose: To compare incisional glaucoma surgical outcomes by race and ethnicity of patients in a nationally-representative cohort.

Methods: A retrospective cohort was constructed using a 20% representative sample of 2016-2018 national fee-for-service Medicare beneficiaries with a claim for incisional glaucoma surgery (trabeculectomy, tube shunt, or EX-PRESS® shunt). We excluded beneficiaries with non-US residence, age <65 years, or missing eye laterality modifier code. The primary exposure was patient race and ethnicity, stratified into: Non-Latinx White, Black, Latinx, Asian/Pacific Islander, and Other. The primary outcome was reoperation with a new glaucoma surgical procedure and the secondary outcome was reoperation or revision of index surgery. Follow-up time extended through 2019. Time-to-event was modeled using Kaplan-Meier curves and Cox proportional hazards regression. A total racial and ethnic disparity model was designed that adjusted for age, sex, state fixed effects, and cohort year. A direct racial and ethnic disparity model was also designed that additionally adjusted for eligibility for dual-Medicaid and Part D low-income subsidies, 26 Chronic Conditions Warehouse comorbidities, glaucoma severity, and glaucoma subtype.

Results: The final analytical sample included a total of 12,366 unique beneficiaries. The largest racial and ethnic stratum was the non-Latinx White subgroup (n=8,510; 68.8%), followed by the Black subgroup (n=2,273; 18.4%), the Latinx subgroup (n=887; 7.2%), the Asian/Pacific Islander subgroup (n=409; 3.3%), and the Other race and ethnicity subgroup (n=287; 2.3%). During the study period, there was a total of 1,590 incisional glaucoma surgical reoperation events, yielding a cumulative incidence of 12.9%. The Kaplan-Meier curve demonstrated increased cumulative

proportion of surgery-free survival for non-Latinx White beneficiaries compared to other groups (p-value for Log-Rank Test = 0.001). Following covariate adjustment to estimate the total racial and ethnic disparity in surgical failure by reoperation, Black (adjusted hazard ratio [aHR]: 1.34, 95% confidence interval [CI]: 1.17-1.53), Latinx (aHR: 1.43, 95% CI: 1.19-1.71), and Asian/Pacific Islander (aHR: 1.49, 95% CI: 1.17-1.89) patients had greater risk of reoperation compared to non-Latinx White beneficiaries. Estimates from models assessing the direct racial and ethnic disparity on surgical failure were similar.

Conclusions: This representative cohort study of national Medicare beneficiaries elucidated new and persistent racial and ethnic disparities in incisional glaucoma surgical outcomes. Specifically, Black, Latinx, and Asian/Pacific Islander beneficiaries had increased risk of incisional glaucoma surgical failure compared to non-Latinx White beneficiaries. Future studies should examine possible mediating factors of these racial and ethnic disparities that may represent modifiable targets to intervene upon to achieve health equity.

2.2 Introduction

According to estimates from the 2020 Global Burden of Disease Study, glaucoma is the leading cause of blindness in high-income countries like the United States (US) in adults aged 50 years and older, accounting for 28.2% (95% uncertainty interval [UI] 24.0-32.3%) of age-standardized cases of blindness.[103] In the US, glaucoma is known to disproportionately affect racially and ethnically minoritized groups, such as Black and Latinx individuals, as demonstrated by a number of foundational epidemiologic studies primarily from the late 1980s to early 2000s.[8,27-31] Based on these population-based estimates, there is widespread consensus that the prevalence of primary open angle glaucoma (POAG)—the most common glaucoma subtype—in Black Americans is approximately four-fold higher compared to non-Latinx White individuals in the US.[30] The prevalence of glaucoma in Latinx groups has also been found to be significantly higher than non-Latinx white individuals and similar to Black individuals in the US.[31]

Given the shifting demographics in the US, epidemiologic projections estimate that Latinx men 70 years and older will become the largest single demographic group with glaucoma by 2035, with the number of all Latinx POAG patients estimated to be 3.62 million, or approximately half of all POAG patients nationwide by that time.[32] Not only do racially and ethnically minoritized groups have greater overall glaucoma prevalence, but Black, Latinx, and Asian/Pacific Islander patients have been found to have greater glaucoma disease severity at time of presentation as compared to non-Latinx White patients.[104]

Incisional glaucoma surgery—including trabeculectomy, Ex-PRESS® shunt (Alcon Laboratories, Fort Worth, TX), and aqueous shunts (also referred to as tube shunts and glaucoma drainage devices)—remains a mainstay surgical option for effective lowering of intraocular pressure, and is generally indicated when medications and appropriate laser therapy are insufficient

to control disease progression.[37] Early comparative studies published in the 1990s and early 2000s[65,66,105-108] and more recent investigations[72,109] have supported the strong clinical impression that Black patients are at increased risk for incisional glaucoma surgical failure. However, few studies have explored disparities in incisional glaucoma surgical outcomes within a racially and ethnically diverse and representative sample that reflects the epidemiologic shifts in glaucoma prevalence mentioned above. Thus, the aim of this study was to examine rates of incisional glaucoma surgical failure by racial and ethnic groups in a large and representative sample of national Medicare beneficiaries.

2.3 Methods

2.3.1 Study Population

The study population was drawn from the 20% representative sample of all Medicare beneficiaries with fee-for-service coverage of Medicare Parts A and B provided by the US Centers for Medicare and Medicaid Services (CMS). Assignment to the 20% random sample group is based on the last two digits of the Medicare Claim Account Number.[110] Fee-for-service claims are those submitted by professional providers, including physicians, physician assistants, optometrists, clinical social workers, and nurse practitioners.[84] The Medicare Carrier File contains the fee-for-service claims submitted by professional providers and also includes claims from some organizational providers, including free-standing ambulatory surgical centers.[84] Data from the Medicare Carrier File is drawn from information from CMS claim form 1500, which is the uniform billing form used by professional providers for paper submission of claims.[86] The CMS Standard Analytical Files (SAFs) contain the final action claims for services rendered in one calendar year,

with separate SAFs created for each type of service (inpatient, outpatient, skilled nursing facility, home health, hospice, carrier, durable medical equipment).[87]

A retrospective cohort of all Medicare beneficiaries with a claim for incisional glaucoma surgery, including trabeculectomy (all techniques), tube shunt (any model), or Ex-PRESS® shunt (Alcon Laboratories, Fort Worth, TX), from 2016 through 2018 was constructed with the Master Beneficiary Summary File (MBSF) and the Standard Analytic Files (SAF) of Part B Carrier Claim files provided by CMS. Claims filed for incisional glaucoma surgeries were identified by billing codes for diagnostic and therapeutic procedures using Current Procedural Terminology 4 (CPT-4) (Supplementary Table 2.1). If a beneficiary had multiple claims for incisional glaucoma surgery during the index period (2016-2018), then the earliest procedure defined the index surgery, index surgery date, and index eye. Only one eye per patient was included to preserve independence of observations. Beneficiaries with the following characteristics were excluded: age less than 65 years in 2016 or age 66 years or less in 2017 or 2018, residence outside of the 50 states of the US or the District of Columbia, and lack of Medicare Part A and Part B coverage. Exclusion criteria for age varied in 2016 (65 years) versus 2017 and 2018 (66 years) to ensure beneficiaries who received incisional surgery in 2017 or 2018 did not receive surgery in the immediately preceding year. Beneficiaries were also excluded if they did not have an International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code for any glaucoma associated with the claim for index incisional glaucoma surgery or if they have a missing laterality modifier for the index eye in the claims data for the index incisional glaucoma surgery. Finally, beneficiaries were also excluded if they did not contribute any follow-up time (i.e., they had no eye-related visits or failure events following their index incisional glaucoma surgery).

2.3.2 Exposure and covariate definitions

Race and ethnicity were the primary exposure for this study. The Research Triangle Institute (RTI) race and ethnicity variable was used given its greater level of agreement with self-reported race and ethnicity and higher sensitivity for identifying Asian/Pacific Islander and Latinx individuals.[89] The RTI race and ethnicity variable has the following coded values: Unknown, Non-Hispanic White, Black (or African-American), Other, Asian/Pacific Islander/Pacific Islander, Hispanic, and American Indian/Alaska Native. Given anticipated issues with small sample sizes, the race and ethnicity variable were aggregated into the following categories for the present analysis: Non-Latinx White, Black, Latinx, Asian/Pacific Islander/Pacific Islander, and Other (with the Other category including Unknown, American Indian/Alaska Native, and Other race and ethnicity groups). Currently, data from Medicare do not separate multiracial beneficiaries.[111]

Demographic variables that were examined during the index glaucoma surgery year (2016-2018) included age and sex. Age was analyzed as a categorical variable, beginning at 65 years, and binned into five-year age groups that truncated at age 90 years or greater. Beneficiary sex was categorized as male, female, and unknown, which was self-identified by applicants to Social Security.[112] For purposes of reporting descriptive distributions, US region of residence was extracted and categorized into the following groups: East, West, Midwest, and South. However, the individual US state of residence was used in all multivariable regression models.

Two proxy variables for socioeconomic status (SES) were constructed. The fee-for-service MBSF contains a set of variables that specify Medicare-Medicaid dual eligibility by calendar month throughout the coverage year. These variables specifically indicate coverage for beneficiaries entitled to Medicare (Part A and/or B benefits) and eligibility for some category of Medicaid benefits in the month (i.e., dual eligibility). A variable for dual Medicare-Medicaid

eligibility was constructed from a source variable that codes the number of months where the beneficiary had dual eligibility.[113] A dichotomous yes/no variable was created based on whether the beneficiary had at least one month of dual eligibility during the index surgery year.

A second proxy variable for SES was constructed based on whether the beneficiary qualified for a low-income subsidy (LIS) that covers some or all the costs for Medicare Part D benefit premiums and cost-sharing.[114] This program applies to beneficiaries up to 150% of the federal poverty line (FPL) and has higher asset limits than the Supplemental Security Income (SSI) program.[115] Eligibility for the LIS program for Part D captures a slightly higher income group as compared to dual Medicare-Medicaid enrollment criteria.[115] In the MBSF, this variable is coded on a month-by-month basis with code values delineating the percent of premium subsidy and copayment for which the beneficiary qualifies (Supplementary Table 2.2). A dichotomous yes/no variable for whether the beneficiary qualified for Part D LIS during the index surgery year was created, with the variable taking on the value of "yes" if the beneficiary had a code of 01 through 08 as per Supplementary Table 2.2 for at least one month during the year of the index surgery, indicating eligibility for a portion of premium subsidy and reduced copayment.

In terms of clinical covariates, a global measure of systemic comorbidities was estimated using the Charlson Comorbidity Index (CCI) score.[116] The CCI is a weighted index of systemic disease burden based on the presence or absence of 17 systemic comorbidities, which include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, cirrhosis, hepatic failure, immunosuppression, diabetes mellitus (DM) with or without complications, hemi/paraplegia, chronic renal disease, malignant neoplasms, multiple myeloma/leukemia, lymphomas, metastatic solid tumor, and AIDS.[116,117] Presence of each of

these diagnoses was determined by ICD-10 codes in claims filed during the index surgery year (Supplementary Table 2.3). The CCI produces a morbidity score that reflects mortality risk, adjusting for variable morbidity rates within a patient population.[116] The CCI score variable was then categorized into scores of 0, 1-2, 3-4, and ≥5.[118]

However, because of concerns regarding possible misclassification due to: (a) underdiagnosis of chronic conditions in one calendar year and (b) underdiagnosis of chronic medical conditions in racially and ethnically minoritized groups,[119] an additional set of variables was used to control for systemic disease burden. These 26 additional variables were drawn from the CMS Chronic Conditions Data Warehouse (CCW) and were derived utilizing validated algorithms with varying lookback periods for each condition predating the MBSF data for that year.[120] The CCW contains indicator variables for 27 chronic conditions, including glaucoma, which was excluded in this study given that all beneficiaries without an ICD-10 code associated with the claim for incisional glaucoma surgery were excluded. Algorithms used to define the 26 CCW variables utilized in the present analysis are found in Supplementary Table 2.4.[121]

Glaucoma disease severity for the index eye was assessed with the seventh digit incorporated into ICD-10 codes, with eye laterality encoded in the sixth ICD-10 code digit.[100] Glaucoma stage definitions encoded by the seventh digit disease modifier datapoint can take the following values: 1: mild or early stage glaucoma (optic nerve abnormalities consistent with glaucoma but no visual field abnormalities on any visual field test or abnormalities present only on short-wavelength automated perimetry or frequency doubling perimetry); 2: moderate stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field abnormalities in one hemifield and not within 5 degrees of fixation); 3: advanced, late, severe stage glaucoma (optic nerve abnormalities consistent with glaucoma and glaucomatous visual field

abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield); 4: indeterminate stage glaucoma (visual fields not performed yet or patient incapable of visual field testing or unreliable/uninterpretable visual field testing); 0: unspecified stage glaucoma (stage not recorded in chart).[100] However, it is important to note that adjustment for glaucoma disease severity is only possible beginning in October 2015, which is when ICD-10 codes were implemented into widespread clinical use.[101] Glaucoma subtype was also extracted from ICD-10 codes and was classified as: glaucoma suspect (H40.0*), open angle glaucoma (H40.1*), angle closure glaucoma (H40.2*), and other glaucoma (H40.3*, H40.4*, H40.5*, H40.6*, H40.8*). Eye laterality was assessed with the sixth digit of the ICD-10 code as a quality check to ensure random distribution of laterality of index eye by race and ethnicity. Year of index surgery (2016, 2017, or 2018) was also captured to assess for possible cohort effects.

2.3.3 Outcome definition

The primary outcome was time to failure of index incisional glaucoma surgery, defined as new glaucoma surgical reintervention (e.g., trabeculectomy, tube shunt placement, Ex-PRESS® shunt placement, iStent® placement, XEN® Gel Stent placement, Hydrus® microstent placement, cyclophotocoagulation, canaloplasty, goniotomy, trabeculotomy, and trabeculoplasty). The secondary outcome included new reoperations for glaucoma treatment—as in the primary outcome—in addition to revision of index surgery (e.g., trabeculectomy revision, device explantation, surgical revision of a tube shunt, or scleral reinforcement).

Start of follow-up time for each beneficiary began on the date of the index incisional glaucoma surgery during 2016-2018. Given that entry into the cohort could occur at any point during the index period (2016-2018), staggered entries or left censoring was permitted. Furthermore, censoring due to other endpoints was permitted, including death or loss of continuous

Medicare Part A or Part B coverage. Thus, the cohort represents an open population where individuals may enter at different times and exit for reasons outside of the outcome of interest or the end of the study. Time was assessed as duration of follow-up, measured as the time since the date of the index incisional glaucoma surgery to the primary outcome or secondary outcome or a censoring event.

Beneficiaries were assessed to ensure they continued to meet inclusion criteria at each year of follow-up (2016-2019). Beneficiaries were right censored if they died, lost continuous Part A or Part B coverage, or if their residence changed to one outside of the 50 US states and the District of Columbia. For beneficiaries who died, their censorship date was assigned as their death date found in the MBSF. For beneficiaries who lost continuous Part A or Part B coverage or whose residence changed to outside of the 50 US states and the District of Columbia, their censorship date was assigned as December 31st of the previous year during which the beneficiary retained continuous enrollment. Administrative censoring for all beneficiaries who survived without index incisional glaucoma surgical failure occurred at the date of the last claim date with an eye visit CPT code (92004, 92014, 92002, 92012, 99212, 99024) filed by an ophthalmologist, optometrist, or ambulatory surgical center, identified by the CMS provider specialty code (18, 41, 49), occurring on or before December 31, 2019. Differential follow-up was permitted, with those who received index incisional glaucoma surgery in 2016 having a maximum of four years of follow-up, those who received index surgery in 2017 having a maximum of three years of follow-up, and those who received index surgery in 2018 having a maximum of two years of follow-up.

Given that repeat incisional surgery is known to have variable surgical results[122] and is generally less successful than primary incisional surgery,[123,124] a sensitivity analysis was performed utilizing a cohort subset that received incisional glaucoma surgery in 2017 or 2018.

Beneficiaries in this 2017-2018 cohort who received incisional glaucoma surgery during a one-year lookback period extending through 2016 were excluded and the same primary and secondary outcome measures were assessed as above in a sensitivity analysis.

2.3.4 Statistical analyses

Figure 2.1 outlines the underlying assumptions about the data-generating process in a directed acyclic graph. The DAG depicted in Figure 2.1 assumes that remnants of historical racism, represented by node H,[125] is an unmeasured confounder that is a common cause for racial and ethnic disparities observed with respect to SES, sex differences in life expectancy, and other inequities by race and ethnicity that persist to the present day. However, with these remnants of historical racism as an unmeasured confounder, it is impossible to be able to estimate the total effect of race and ethnicity on glaucoma surgical failure. Instead, the direct effect of race and ethnicity on glaucoma surgical failure can still be estimated by conditioning on all measured covariates presented in the (age, sex, SES, systemic disease burden, and glaucoma disease severity). However, in accordance with updated guidance on the reporting of race and ethnicity in medical and science journals, it is important to recognize that "The reporting of race and ethnicity should not be considered in isolation but should be accompanied by reporting of other sociodemographic factors and social determinants, including concerns about racism, disparities, and inequities, and the intersectionality of race and ethnicity with these other factors."[126] Thus, by virtue of aiming to examine racial and ethnic disparities, the jurisdiction of this study includes the measurement of the biasing path created by remnants of historical racism discussed above; because in considering race, the intention is to capture the effect of these racial biases, whether internalized, interpersonal, or structural.

Descriptive statistics for baseline sociodemographic and clinical characteristics were assessed with frequency distributions and contingency tables for the entire cohort and stratified by racial and ethnic group. Crude differences in distributions of all characteristics by race and ethnicity were assessed with Chi-squared tests given that all variables were categorical. Time-to-event was modeled using Kaplan-Meier analysis. The log rank test of the null hypothesis of no difference in overall surgery-free survival was examined among the five racial and ethnic groups for the primary and secondary outcomes.[127]

Cox proportional hazards regression was employed for unadjusted and adjusted multivariable models to compare the risk of glaucoma surgical failure by racial and ethnic group, with non-Latinx White beneficiaries as the reference category. Two multivariable models were constructed: first, a model which estimated the total racial and ethnic disparity and adjusted for age, sex, US state of residence, and cohort year; and secondly, a model which estimated the direct racial and ethnic disparity and adjusted for age, sex, US state of residence, cohort year, glaucoma disease severity, type of glaucoma, systemic disease burden (assessed via 26 CCW variables), and SES (assessed via dual Medicaid coverage and eligibility for Part D low-income subsidies). The proportional hazards assumption was assessed visually using Kaplan-Meier curves. Additionally, a fully-saturated Cox proportional hazard regression with a race and ethnicity*log(time) interaction term was modeled to further assess possible violations of proportional hazards. Statistical analyses were performed using SAS version 9.4 (SAS Institute) and R, version 4.2.0 and R Studio, version 2022.06.0 (R Foundation for Statistical Computing). The study was approved by the Institutional Review Board of the University of California, Los Angeles (IRB#21-001951). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

2.4 Results

2.4.1 Baseline Cohort Characteristics

Distributions of sociodemographic and clinical characteristics for the cohort are presented in Table 2.1. A total of 13,420 unique beneficiaries with a Medicare claim listing a CPT code for incisional glaucoma surgery during 2016-2018 were identified and met the clinical exclusion criteria. However, of these, 1,054 (7.8%) were further excluded because they did not contribute any follow-up time (i.e., they did not have any eye care visits or failure events following the date of index incisional glaucoma surgery). Thus, the final analytical sample included a total of 12,366 beneficiaries. The largest racial and ethnic stratum was the non-Latinx White subgroup (n=8,510; 68.8%), followed by the Black subgroup (n=2,273; 18.4%), the Latinx subgroup (n=887; 7.2%), the Asian/Pacific Islander subgroup (n=409; 3.3%), and the Other race and ethnicity subgroup (n=287; 2.3%). The majority of beneficiaries identified as female sex (n=6,891; 55.7%) and did not qualify for dual-Medicaid coverage (n=10,491; 84.8%) nor Part D LIS (n=10,232; 82.7%). A plurality of beneficiaries was between 70-79 years old (n=5,580; 45.1%) and resided in the eastern US (n=5,542; 44.8%).

Beneficiaries from all racially- and ethnically-minoritized groups (Black, Asian/Pacific Islander, Latinx, and Other race and ethnicity individuals) tended to be younger and have lower SES (based on dual-Medicaid eligibility and qualifying for Part D low income subsidies) according to crude demographic distributions. Black and Latinx beneficiaries tended to have greater systemic disease burden based on CCI score, more severe glaucoma, and had a greater proportion of tube shunts, again based on crude distributions. The P-values for Chi-squared tests comparing distributions of baseline characteristics among the five racial and ethnic groups were all $P<0.0001$

for age, sex, dual Medicaid eligibility, qualification for Part D low-income subsidies, geographic region of residence, CCI score, type of index surgery, glaucoma severity, and glaucoma subtype. The P-value for the Chi-squared test comparing eye laterality by race and ethnicity was P=0.34 and the P-value for the Chi-squared test comparing year of index surgery by race and ethnicity was P=0.27.

2.4.2 Incisional Glaucoma Surgical Failure Incidence Rate

During the study period, there was a total of 1,590 incisional glaucoma surgical reoperation events among the 12,366 beneficiaries in the cohort, yielding a cumulative incidence of 12.9%. All beneficiaries in the cohort contributed a total of 23,282 person-years of follow-up time at risk for the primary outcome. Thus, the overall incidence rate for incisional glaucoma surgical reoperation events was 6.8 per 100 person-years at risk (95% confidence interval [CI]: 6.5-7.2 reoperation events per 100 person-years). For the secondary outcome of incisional glaucoma surgical reoperations or revisions, there was a total of 2,762 events among the 12,366 beneficiaries in the cohort, resulting in a cumulative incidence of 22.3%. All beneficiaries in the cohort contributed a total of 21,221 person-years of follow-up time at risk for the secondary outcome. Thus, the overall incidence rate for incisional glaucoma surgical reoperation or revision events was 13.0 per 100 person-years at risk (95% CI: 12.5-13.5 reoperation or revision events per 100 person-years).

The incidence rates of glaucoma surgical reoperation (primary outcome) and glaucoma surgical reoperation or revision (secondary outcome), stratified by racial and ethnic group, are presented in Tables 2.2 and 2.3, respectively. Forest plots of incidence rates of glaucoma surgical reoperation and glaucoma surgical reoperation or revision, stratified by racial and ethnic group and ordered by increasing incidence rate, are presented in Figures 2.2 and 2.3, respectively.

Asterisks in Figures 2.2 and 2.3 indicate when the 95% CI for incidence rate estimates are disjoint from the 95% CI for the non-Latinx White group. For both primary and secondary outcomes, Non-Latinx White individuals have the lowest incidence rate for both types of failure events amongst all racial and ethnic groups (6.07 reoperation events per 100 person-years, 95% CI: 5.70-6.46; 12.4 reoperation or revision events per 100 person-years, 95% CI: 11.8-12.9). The incidence rates for glaucoma surgical reoperation were greater in Black, Asian/Pacific Islander, Latinx, and Other race and ethnicity individuals. The 95% CIs for the incidence rates for the Black, Asian/Pacific Islander, and Latinx groups were disjoint from the 95% CI for the non-Latinx White group (Table 2.2 & Figure 2.2). The incidence rates for glaucoma surgical reoperation or revision were similarly greater in Black, Asian/Pacific Islander, Latinx, and Other race and ethnicity individuals. The 95% CIs for the incidence rates for the Black, Asian/Pacific Islander, and Latinx groups were again disjoint from the 95% CI for the non-Latinx White group (Table 2.3 & Figure 2.3).

2.4.3 Kaplan-Meier Survival Analysis

Figure 2.4 presents the Kaplan-Meier curve comparing the probability of reoperation-free survival, stratified by race and ethnicity, and demonstrates increased probability of surgery-free survival for non-Latinx White beneficiaries compared to other groups (Log Rank Test P-value < 0.0001). On visual inspection, the cumulative proportion of reoperation-free survival is similar for all five racial and ethnic groups through the first year of follow-up time, with curves beginning to deviate thereafter. The reoperation-free survival curve for the Other race and ethnicity subgroup does trend closely to the curve for the non-Latinx White subgroup, though the former has a much smaller sample size with coarser steps. Figure 2.5 presents the Kaplan-Meier curve comparing the probability of reoperation- or revision-free survival, stratified by race and ethnicity, and similarly demonstrates increased cumulative proportion of surgery-free survival for non-Latinx White

beneficiaries compared to other groups (Log Rank Test P-value < 0.0001). Again, on visual inspection, the cumulative proportion of reoperation- or revision-free survival is similar for all five racial and ethnic groups through the first year of follow-up time, with curves beginning to diverge thereafter. The reoperation- or revision-free survival curve for the Other race and ethnicity subgroup again appears to trend closely with the curve for the non-Latinx White subgroup, though the small sample size and coarse steps for the Other race and ethnicity subgroup makes for a difficult visual comparison.

2.4.4 Risk of Glaucoma Surgical Failure by Racial and Ethnic Group

Results of the Cox proportional hazards regressions are presented in Table 2.4. The unadjusted Cox proportional hazards regressions demonstrated increased risk of incisional glaucoma surgical failure by reoperation for all racially and ethnically minoritized groups (Black, Latinx, Asian/Pacific Islander, and Other race and ethnicity) compared to non-Latinx White beneficiaries. Following covariate adjustment to estimate the total racial and ethnic disparity in surgical failure by reoperation, Asian/Pacific Islander beneficiaries had 1.49 times the total estimated racial and ethnic disparity (adjusted hazard ratio [aHR]: 1.49, 95% CI: 1.17-1.89) compared to non-Latinx White beneficiaries, followed by Latinx beneficiaries (aHR: 1.43, 95% CI: 1.19-1.71) and Black beneficiaries (aHR: 1.34, 95% CI: 1.17-1.53), adjusting for age, sex, US state of residence, and cohort year. The Other race and ethnicity subgroup had similar risk of reoperation following index incisional glaucoma surgery compared to the non-Latino White group (aHR: 0.99, 95% CI: 0.71-1.38) in the model estimating the total racial and ethnic disparity in surgical failure by reoperation. Estimates for the direct racial and ethnic disparity for surgical failure by reoperation were similarly elevated for Asian/Pacific Islander (aHR: 1.41, 95% CI: 1.10-1.81), Latinx (aHR: 1.36, 95% CI: 1.12-1.65), and Black beneficiaries (aHR: 1.30, 95% CI: 1.13-

1.50) compared to non-Latinx White beneficiaries after adjusting for age, sex, CCW comorbidities, glaucoma severity, and glaucoma subtype.

Table 2.5 summarizes the results of the Cox proportional hazards regressions for the risk of incisional glaucoma surgical failure (reoperation or revision), stratified by race and ethnicity. The unadjusted models demonstrated increased risk of surgical reoperation or revision for Black (HR: 1.17, 95% CI: 1.06-1.29), Latinx (HR: 1.32, 95% CI: 1.15-1.51), Asian/Pacific Islander (HR: 1.28, 95% CI: 1.06-1.55), and Other race and ethnicity beneficiaries (HR: 1.19, 95% CI: 0.94-1.51) compared to non-Latinx White beneficiaries. The estimates for the total racial and ethnic disparity and direct racial and ethnic disparity remained elevated for Black, Latinx, and Asian/Pacific Islander beneficiaries, compared to non-Latinx counterparts, with the spread of the 95% CIs for the Asian/Pacific Islander subgroup suggesting increased risk, though containing the null value of 1.00 (Table 2.5).

The Cox proportional hazards model estimating the racial and ethnic disparity for incisional glaucoma reoperation was found to meet criteria for holding to the proportional hazards assumption, with the Wald Chi-squared test for the race and ethnicity*log(time) interaction term having a p-value of 0.06 (χ^2=3.52). On the other hand, the Cox proportional hazards model estimating the racial and ethnic disparity for incisional glaucoma reoperation and revision was found to violate the proportional hazards assumption, with the Wald Chi-squared test for the race and ethnicity*log(time) interaction term having a p-value of 0.0004 (χ^2=12.50). In the sensitivity analysis excluding beneficiaries who received incisional glaucoma surgery in 2016 with follow-up for incisional glaucoma surgical failure by reoperation through 2019 (i.e., one-year lookback period), a total of 4,974 beneficiaries were excluded (40.2%) and no racial or ethnic group was disproportionately excluded (p-value for Chi-squared test = 0.27). In this sensitivity analysis

accounting for a one-year lookback period, the hazard ratio estimates remained similar for the unadjusted, total racial and ethnic disparity, and direct racial and ethnic disparity models across Black, Asian/Pacific Islander, Latinx, and Other race and ethnicity groups (Supplementary Table 2.5).

2.5 Discussion

In this retrospective study constructed using a contemporary, representative, and racially and ethnically diverse cohort of national Medicare beneficiaries, there were racial and ethnic disparities in incisional glaucoma surgical outcomes. Specifically, Black, Latinx, and Asian/Pacific Islander beneficiaries who received incisional glaucoma surgery from 2016-2018 had increased incidence rates of incisional glaucoma surgical failure (by reoperation and reoperation or revision events) compared to non-Latinx White beneficiaries through 2019. Furthermore, non-Latinx White beneficiaries were found to have greater cumulative proportions of surgery-free survival time compared to Black, Latinx, and Asian/Pacific Islander beneficiaries for reoperation and reoperation or revision events. Finally, there were greater total racial and ethnic disparities and direct racial and ethnic disparities for Black, Latinx, and Asian/Pacific Islander beneficiaries compared to non-Latinx White beneficiaries in multivariable Cox proportional hazards regression models for reoperation and reoperation or revision outcomes.

This is the first study to examine racial and ethnic disparities in incisional glaucoma surgical outcomes in a cohort representative of multiple racially and ethnically minoritized groups with adequate sample sizes to allow for more meaningful disaggregation of race and ethnicity data. Accordingly, to our knowledge, this is one of the first studies describing increased risk of incisional glaucoma surgical failure in certain racial and ethnic groups, specifically Latinx and Asian/Pacific

Islander Medicare beneficiaries. This is of particular concern from both health disparities and public health perspectives given that, as mentioned previously, it is projected that Latinx patients will account for more than half of all POAG cases nationwide by the year 2035.[32] We did not find substantial disparities in the Other race and ethnicity individuals (a category which included American Indian/Alaska Native, Unknown, and Other race and ethnicity individuals) when compared to non-Latino White individuals. Of note, the Other race and ethnicity subgroup was the smallest in the study, including only 287 beneficiaries and representing 2.3% of the analytical sample. This racial and ethnic category represents a heterogeneous group of individuals and due to the small sample size, estimates are likely under-powered to detect differences.

Furthermore, it is important to emphasize that the racial and ethnic disparities in incisional glaucoma surgical failure presented here are observed within a cohort of beneficiaries enrolled in Medicare Parts A & B. Despite improvements in the safety net provided by the Affordable Care Act, nearly 27.1 million individuals were still uninsured in 2021, representing approximately 10.2% of the US population.[128] Though it is true that racially- and ethnically-minoritized individuals are more likely to be uninsured than non-Latinx White individuals, it has been shown that Medicare offers near universal coverage for older adults, with just 441,000, or less than 1%, of adults over age 65 being uninsured.[128] Thus, the racial and ethnic disparities in incisional glaucoma surgical outcomes reported here are likely representative of the entire US population aged 65 years and older, with perhaps only minor underestimations of failure rates for racially- and ethnically-minoritized individuals given the small number of uninsured older adults who are also more likely to come from communities of color. It is also worth noting that the racial and ethnic disparities in incisional glaucoma surgical outcomes reported here may be underestimated in Black and Latinx beneficiaries due to immediate differential loss to follow-up. Supplemental

Table 2.6 shows the distribution of study exclusion due to inability to contribute follow-up time after index surgery (i.e., no claims filed for eye care visit nor reoperation event following index surgery). Disproportionately greater proportions of Black (9.9%; 252 of 2,535 beneficiaries) and Latinx beneficiaries (8.0%; 77 of 966 beneficiaries) were excluded because of immediate loss to follow-up compared to non-Latinx White beneficiaries (6.8%; 627 of 9,174 beneficiaries) (P-value for Chi-squared test < 0.0001).

Results from the present analysis harmonize well with the limited contemporary data available on this topic. In a recently published retrospective cohort study using 2013-2019 data from the American Academy of Ophthalmology (AAO) Intelligent Research in Sight (IRIS®) Registry, Ciociola and colleagues similarly found that race and ethnicity were associated with failure of incisional glaucoma surgery.[109] The primary objective of their study was to compare the effectiveness of trabeculectomy and tube shunt surgery performed with concurrent phacoemulsification compared to stand-alone procedures. They found that stand-alone procedures for both trabeculectomy (69.8%) and tube shunt surgery (88.4%) were more commonly performed than either form of incisional glaucoma surgery combined with phacoemulsification.[109] Similar to the present analysis, study authors found that Black (HR: 1.82, 95% CI: 1.72-1.92), Latinx (HR: 1.53, 95% CI: 1.24-1.64), and an aggregated group of Asian/Pacific Islander or Other race and ethnicity patients (HR: 1.51, 95% CI: 1.37-1.66) had increased risk of reoperation with trabeculectomy alone compared to non-Latinx patients. However, they only observed increased risk of reoperation following stand-alone tube shunt surgery for Black (HR: 1.21, 95% CI: 1.11-1.30) patients, and not Latinx (HR: 1.10, 95% CI: 0.99-1.22) or Asian/Pacific Islander or Other race and ethnicity patients (HR: 1.06, 95% CI: 0.92-1.23).[109] However, it is important to note that

IRIS® Registry data represents a convenience sample and should not be considered representative of the general population.[129]

Comparison with the Ciociola study motivated a post-hoc analysis to examine racial and ethnic disparities in incisional glaucoma surgical failure stratified by type of surgery (trabeculectomy or tube shunt), the results of which are presented in Supplementary Tables 2.7 and 2.8. Similar to the Ciociola study, we found there to be increased risk of reoperation following trabeculectomy in Black (aHR: 1.52, 95% CI: 1.25-1.84), Latinx (aHR: 1.63, 95% CI: 1.25-2.13), and Asian/Pacific Islander beneficiaries (aHR: 1.73, 95% CI: 1.25-2.38), compared to non-Latinx beneficiaries, adjusting for age, sex, US state of residence, and cohort year (with estimates remaining similar in the direct racial and ethnic disparity model additionally adjusting for eligibility for dual-Medicaid, eligibility for Part D low-income subsidies, CCW comorbidities, glaucoma severity, and glaucoma subtype). Our results also suggested increased risk of reoperation following tube shunt surgery in Black (aHR: 1.22, 95% CI: 0.99-1.51) and Latinx (aHR: 1.27, 95% CI: 0.96-1.68) beneficiaries, though 95% CIs included the null value of 1.00, likely due to lack of statistical power from smaller sample sizes. Thus, this post-hoc analysis suggests that a greater proportion of the racial and ethnic disparity in incisional glaucoma surgical outcomes is caused by disparities in trabeculectomy outcomes compared to tube shunt outcomes. This is in line with evaluation of reoperation outcomes in the Tube Versus Trabeculectomy (TVT) Study, where the rate of reoperation for glaucoma was higher following trabeculectomy than tube shunt surgery.[130]

Defining surgical failure as reoperation events versus reoperation and revision events separately provided valuable insights in evaluating the use of these outcome definitions. A considerably large variety of definitions of surgical failure and surgical success are utilized in the growing body of literature on this topic. In fact, there exist almost as many definitions of success

and failure as there are studies, with an examination of the literature performed by Rotchford and King demonstrating that from 100 publications meeting literature search inclusion criteria, 92 distinct IOP-related definitions of success were identified.[76] This finding motivated the World Glaucoma Association to make the following recommendation: "Utilizing consistent criteria for surgical success and definitions of postoperative complications and reoperations across clinical studies and trials is encouraged, so that outcomes across varied studies can be compared and/or combined."[77] Though the primary (reoperation) and secondary (reoperation or revision) outcomes of the present study appear similar, they have nuanced differences highlighted by the results of the study. First, there are different clinical indications in addition to surgeon—and at times, patient—preferences that dictate whether revision of index surgery or reoperation with a new procedure is performed.[131] From an epidemiological methods perspective, it should be noted that in the present study, the proportional hazards assumption was maintained when examining the reoperations outcome, whereas it was violated when assessing reoperation or revision events. This may be because time to reoperation and time to revision have different natural histories that may present differently by race and ethnicity—not due to biological differences, as race and ethnicity are known to be sociopolitical constructs,[132] but rather due to disparities in social determinants of health. For example, racially- and ethnically-minoritized patients may find it more difficult to access or attend regular follow-up visits in the post-operative period, leading to fewer revision events and greater reoperation events, thereby explaining the dampened racial and ethnic disparity observed for reoperation or revision outcome events.

Our study has limitations. First, utilizing standard stratification-based approaches often entails examining racial and ethnic disparities after controlling for potential mediators, as in the estimations of the direct racial and ethnic disparities reported in the present analysis. However,

standard regression adjustment or restriction may overestimate or underestimate the potential impact of race and ethnicity on the outcome by introducing bias due to the presence of common causes of the mediator and outcome, resulting in collider-stratification bias when the mediator is controlled for via restriction or standard regression adjustment.[133-135] Thus, we believe the estimates with the most internal validity are those representing the total racial and ethnic disparity which are not subject to the potential bias-inducing confounding structure of unobserved common causes of mediators and outcomes found in the estimates for the direct racial and ethnic disparity on incisional glaucoma surgical outcomes. Second, there is always the possibility of information bias in the form of misclassification because of the coding errors associated with diagnostic and procedural codes utilized in administrative claims data. However, it is unlikely that this misclassification would be differential with respect to race and ethnicity, thus likely leading to bias toward the null.[136] Finally, race and ethnicity data in Medicare has important limitations. In 2004, the National Academies of Sciences Engineering and Medicine analyzed the measurement and data needs required for studying the nature of disparities in health care and to develop strategies to eliminate disparities. In this report, the authors note an alarming limitation of the race and ethnicity data found in Medicare: "A further limitation in the racial and ethnic data contained in Medicare beneficiary files is that when CMS obtains the enrollee information from the [Social Security Administration] SSA master beneficiary record, it receives information only on the retiree, not the retiree's spouse. Instead, the race of the beneficiary is simply assigned to the spouse."[92] Thus, the present analysis may be subject to exposure misclassification for race and ethnicity when SSA does not have information about a retiree's spouse who otherwise does not appear in the SSA master beneficiary record.

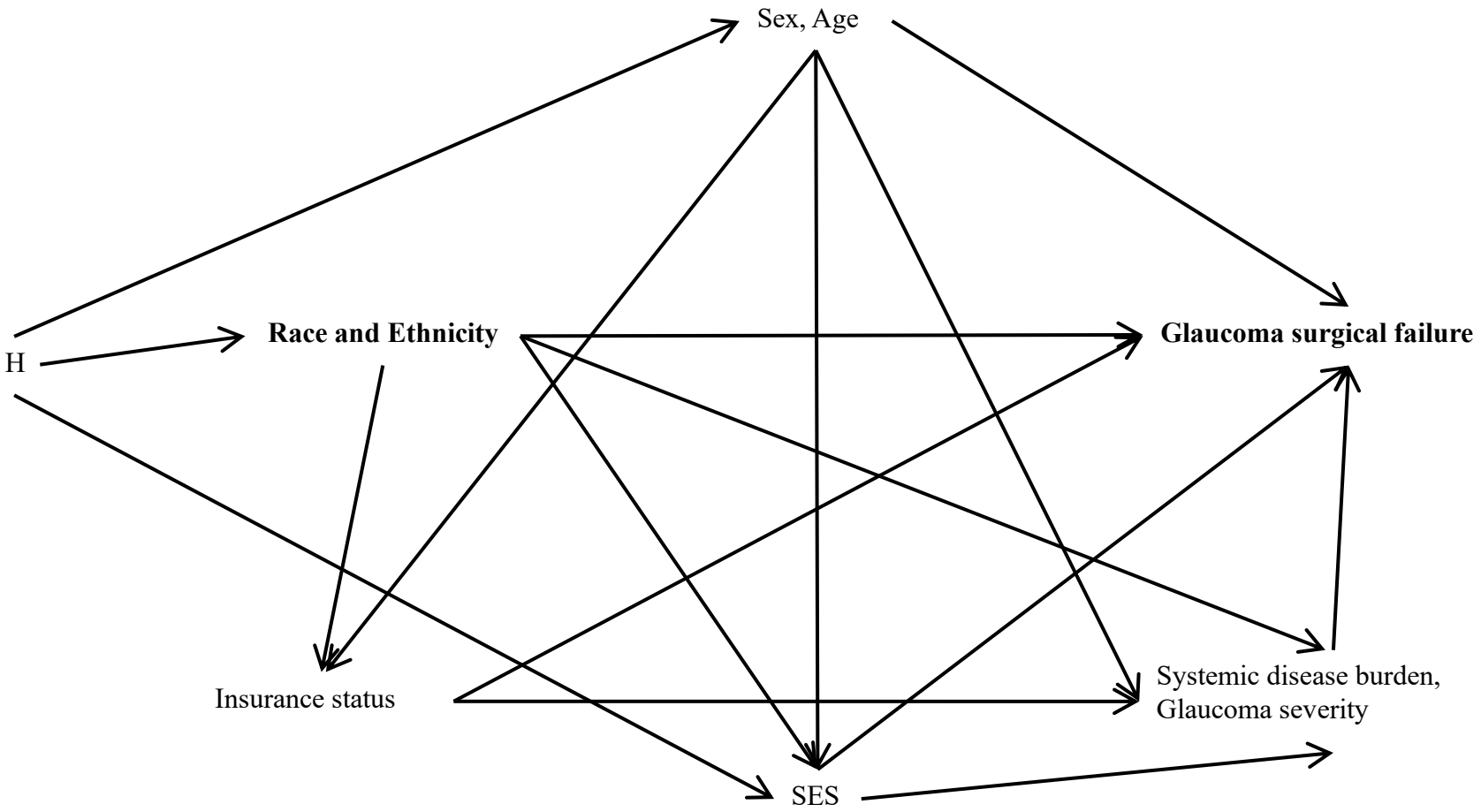
Examining glaucoma surgical outcomes by race and ethnicity is challenging, particularly given the lack of racial and ethnic diversity in clinical trials for glaucoma. A systematic review and meta-analysis performed by Allison and colleagues included 105 clinical trials for POAG with a total of 33,428 POAG clinical trial participants; of these, 70.7% were White patients, 16.8% were Black patients, 3.4% were Latino patients, and 9.1% were patients of other races/ethnicities, including Asian/Pacific Islander, Native Hawaiian or Pacific Islander, American Indian or Alaska Native, and unreported as defined by the US Census.[63] Thus, despite the fact that racially and ethnically minoritized groups have a higher prevalence of POAG, there has been a very low participation rate in POAG clinical trials for these groups. Furthermore, despite more recent measures intended to increase racial and ethnic diversity in clinical trial participants, there has not been a significant increase in clinical trial participation among Black individuals from 1994 to 2019 ($r^2 = 0.11$; $P = 0.17$).[63] Consequently, although observational studies have certain inferential limitations, for purposes of health disparities research, there are perhaps even greater limitations in clinical trials data given the lack of racial and ethnic diversity—both historically and presently—in participant recruitment.

The results of this study point to the persistence of racial and ethnic disparities in incisional glaucoma surgical outcomes that clearly involve multiple racially- and ethnically-minoritized groups, including Black, Latinx, and Asian/Pacific Islander Medicare beneficiaries. Though race and ethnicity are immutable factors, the racial and ethnic disparities described here likely lie upstream of structural racism mediators that may represent modifiable targets that can be intervened upon to achieve equity in surgical outcomes. Examples of such structural racism mediators include disparities in the SES of minoritized groups, disparities in the cumulative burden of chronic stress (i.e., allostatic load), or disparities in residential air pollution and environmental

justice. Additional studies examining the impact of such downstream mediators of the racial and ethnic disparities in incisional glaucoma surgical failure described here have the potential for substantial public health impact and require immediate attention.

2.6 Tables and Figures

Figure 2.1 Directed Acyclic Graph (DAG) summarizing assumptions behind data-generating process for this study.



H = remnants of historical racism (e.g., slavery, Jim Crow laws, discriminatory mortgage lending practices); SES = socioeconomic status

Table 2.1 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016-2018, 20% US Representative Sample

	All Patients		Non-Latinx White Patients		Black Patients		Latinx Patients		Asian/Pacific Islander Patients		Patients of Other Races & Ethnicities	
	N=12,366		N=8,510		N=2,273		N=887		N=409		N=287	
	N	%	N	%	N	%	N	%	N	%	N	%
Age in years												
65-69	2,103	17.0	1,196	14.1	528	23.2	193	21.8	84	20.5	102	37.4
70-74	2,787	22.5	1,775	20.9	590	26.0	250	28.2	91	22.2	81	29.7
75-79	2,793	22.6	1,893	22.2	553	24.3	186	21.0	107	26.2	54	19.8
80-84	2,305	18.6	1,707	20.1	373	16.4	123	13.9	66	16.1	36	13.2
85-89	1,661	13.4	1,345	15.8	168	7.4	91	10.3	45	11.0	*	*
90+	717	5.8	594	7.0	61	2.7	44	5.0	16	3.9	*	*
Sex												
Male	5,475	44.3	3,619	42.5	1,070	47.1	416	46.9	211	51.6	159	55.4
Female	6,891	55.7	4,891	57.5	1,203	52.9	471	53.1	198	48.4	128	44.6
Dual Medicaid Eligibility												
Yes	1,875	15.2	618	7.3	573	25.2	435	49.0	183	44.7	66	23.0
No	10,491	84.8	7,892	92.7	1,700	74.8	452	51.0	226	55.3	221	77.0
Part D Subsidies												
Yes	2,134	17.3	733	8.6	673	29.6	465	52.4	189	46.2	74	25.8
No	10,232	82.7	7,777	91.4	1,600	70.4	422	47.6	220	53.8	213	74.2
Geographic Region												
East	5,542	44.8	3,753	44.1	1,255	55.2	294	33.1	122	29.8	118	41.1
West	2,358	19.1	1,524	17.9	193	8.5	336	37.9	219	53.5	86	30.0
Midwest	2,500	20.2	2,004	23.5	334	14.7	72	8.1	38	9.3	52	18.1
South	1,966	15.9	1,229	14.4	491	21.6	185	20.9	30	7.3	31	10.8
CCI Score												
0	3,345	27.0	2,454	28.8	511	22.5	171	19.3	105	25.7	104	36.2
1-2	4,554	36.8	3,183	37.4	763	33.6	343	38.7	158	38.6	107	37.3
3-4	2,656	21.5	1,772	20.8	536	23.6	215	24.2	94	23.0	39	13.6
5+	1,811	14.6	1,101	12.9	463	20.4	158	17.8	52	12.7	37	12.9

* Cannot report cell size due to confidentiality

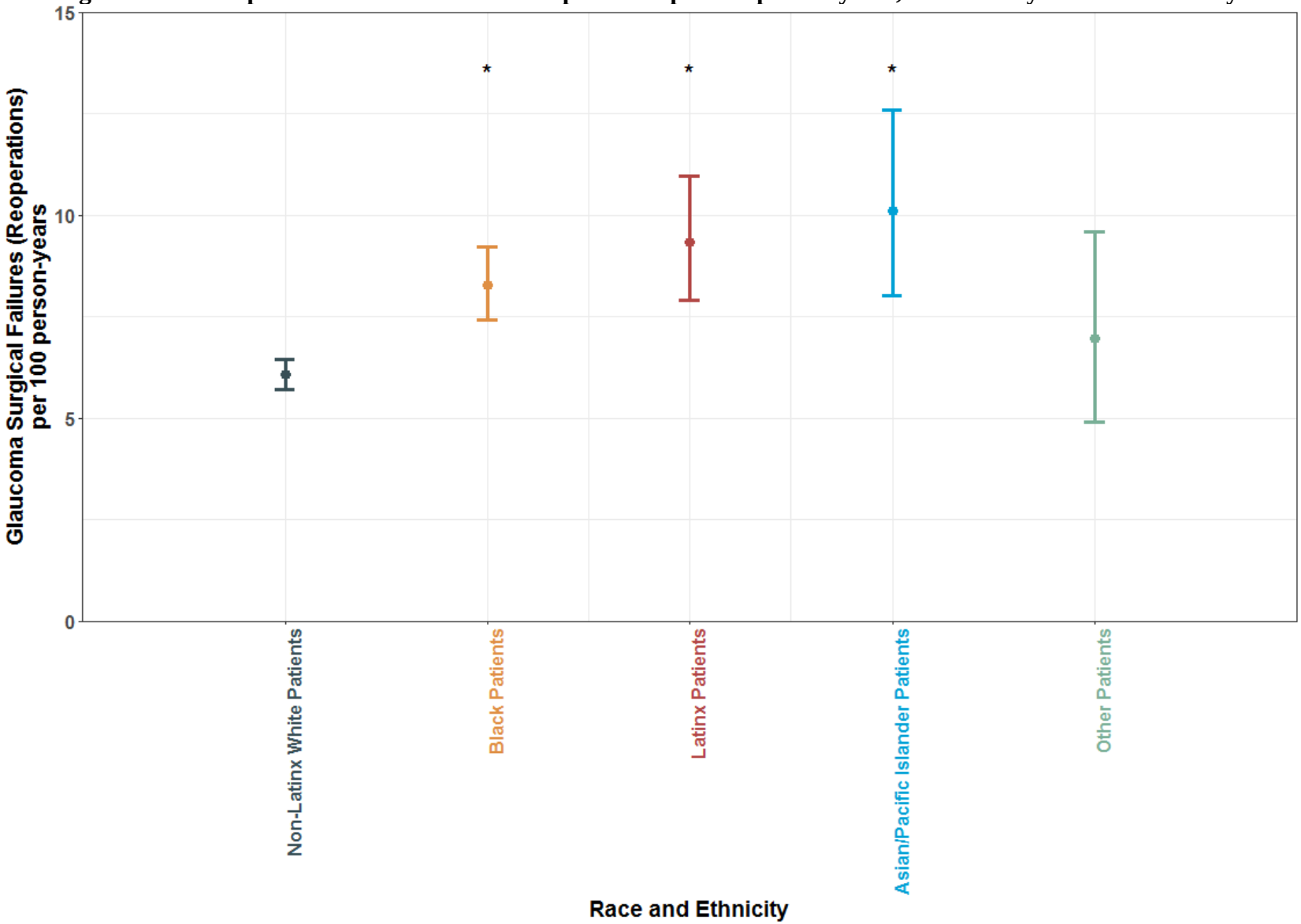
Table 2.1 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016-2018, 20% US Representative Sample												
	All Patients		**Non-Latinx White Patients**		**Black Patients**		**Latinx Patients**		**Asian/Pacific Islander Patients**		**Patients of Other Races & Ethnicities**	
	N=12,366		**N=8,510**		**N=2,273**		**N=887**		**N=409**		**N=287**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Index Surgery												
Trabeculectomy	5,864	47.4	4,139	48.6	1,002	44.1	373	42.1	219	53.5	131	45.6
Tube shunt	5,013	40.5	3,267	38.4	1,030	45.3	444	50.1	160	39.1	112	39.0
EX-PRESS shunt	1,489	12.0	1,104	13.0	241	10.6	70	7.9	30	7.3	44	15.3
Index eye												
Right	6,157	49.8	4,247	49.9	1,139	50.1	438	49.4	184	45.0	149	51.9
Left	6,209	50.2	4,263	50.1	1,134	49.9	449	50.6	225	55.0	138	48.1
Glaucoma severity												
Unspecified	1,636	13.2	1,090	12.8	260	11.4	154	17.4	78	19.1	54	18.8
Mild	707	5.7	558	6.6	92	4.0	29	3.3	13	3.2	15	5.2
Moderate	2,357	19.1	1,711	20.1	395	17.4	137	15.4	62	15.2	52	18.1
Severe	7,156	57.9	4,809	56.5	1,427	62.8	530	59.8	242	59.2	148	51.6
Indeterminate	510	4.1	342	4.0	99	4.4	37	4.2	14	3.4	18	6.3
Glaucoma subtype												
Glaucoma suspect	211	1.7	152	1.8	22	1.0	25	2.8	*	*	*	*
Open angle glaucoma	9,932	80.3	6,956	81.7	1,823	80.2	643	72.5	300	85.2	210	90.1
Angle closure glaucoma	663	5.4	334	3.9	174	7.7	80	9.0	52	14.8	23	9.9
Other glaucoma	1,560	12.6	1,068	12.5	254	11.2	139	15.7	*	*	*	*
Year of index surgery												
2016	4,974	40.2	3,398	39.9	959	42.2	359	40.5	157	38.4	101	35.2
2017	4,130	33.4	2,854	33.5	721	31.7	310	34.9	142	34.7	103	35.9
2018	3,262	26.4	2,258	26.5	593	26.1	218	24.6	110	26.9	83	28.9

* Cannot report cell size due to confidentiality

Table 2.2 Glaucoma surgical reoperation incidence rate, stratified by racial and ethnic group					
Racial and Ethnic Group	**Number of beneficiaries**	**Number of events**	**Person-years of follow-up**	**Incidence Rate per 100 Person-Years**	**95% Confidence Interval**
Non-Latinx White Patients	8,510	995	16,389	6.07	5.70-6.46
Black Patients	2,273	330	3,986	8.28	7.41-9.22
Latinx Patients	887	148	1,584	9.34	7.90-10.98
Asian/Pacific Islander Patients	409	80	791	10.12	8.02-12.59
Other Patients	287	37	532	6.95	4.89-9.58

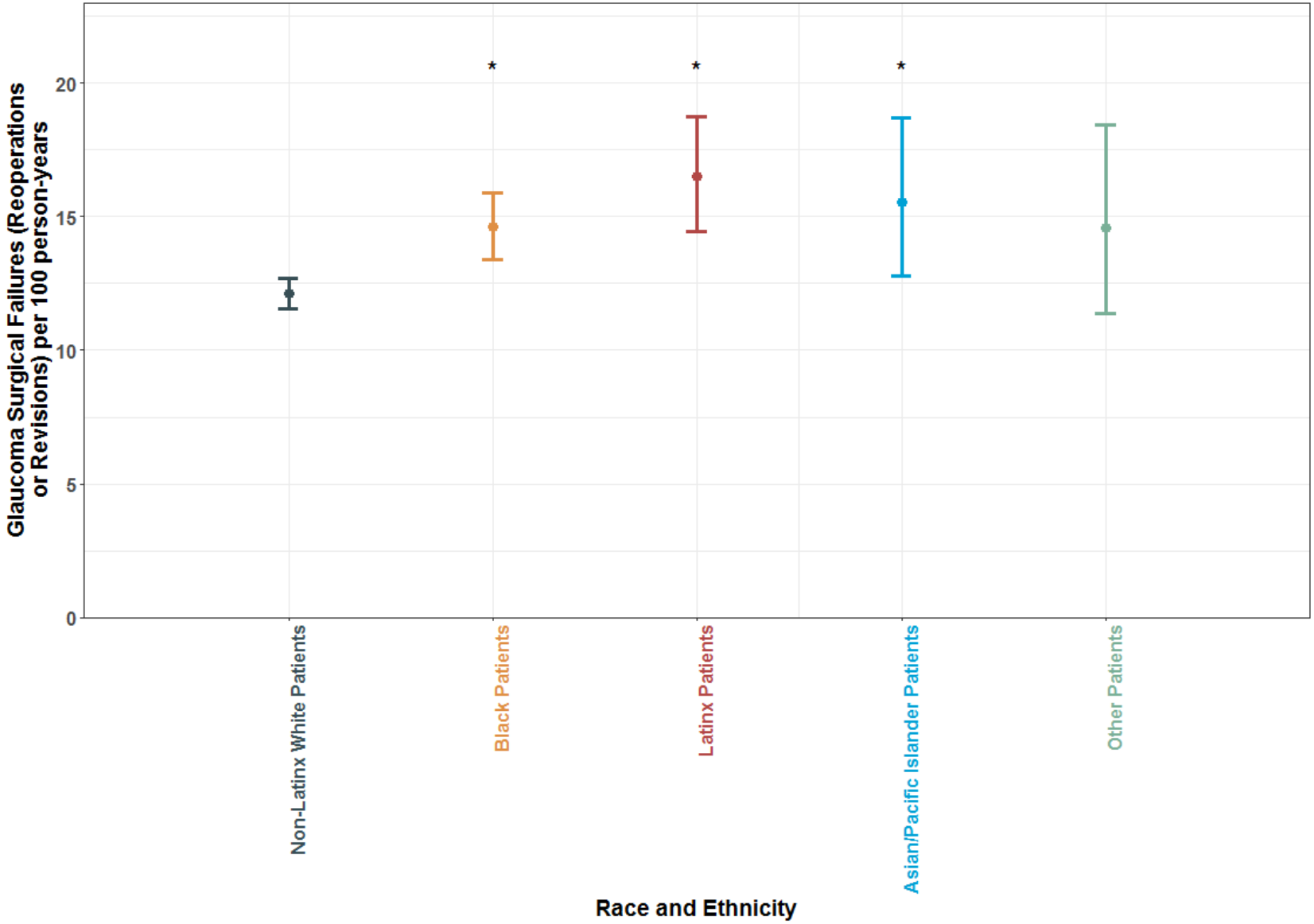
Table 2.3 Glaucoma surgical reoperation or revision incidence rate, stratified by racial and ethnic group					
Racial and Ethnic Group	**Number of beneficiaries**	**Number of events**	**Person-years of follow-up**	**Incidence Rate**	**95% Confidence Interval**
Non-Latinx White Patients	8,510	1,846	14,928	12.12	11.56-12.69
Black Patients	2,273	536	3,667	14.62	13.41-15.91
Latinx Patients	887	235	1,425	16.49	14.45-18.74
Asian/Pacific Islander Patients	409	112	721	15.53	12.79-18.69
Other Patients	287	70	480	48.59	11.37-18.44

Figure 2.2 Forest plot of incidence rates for reoperations per 100 person-years, stratified by race and ethnicity.



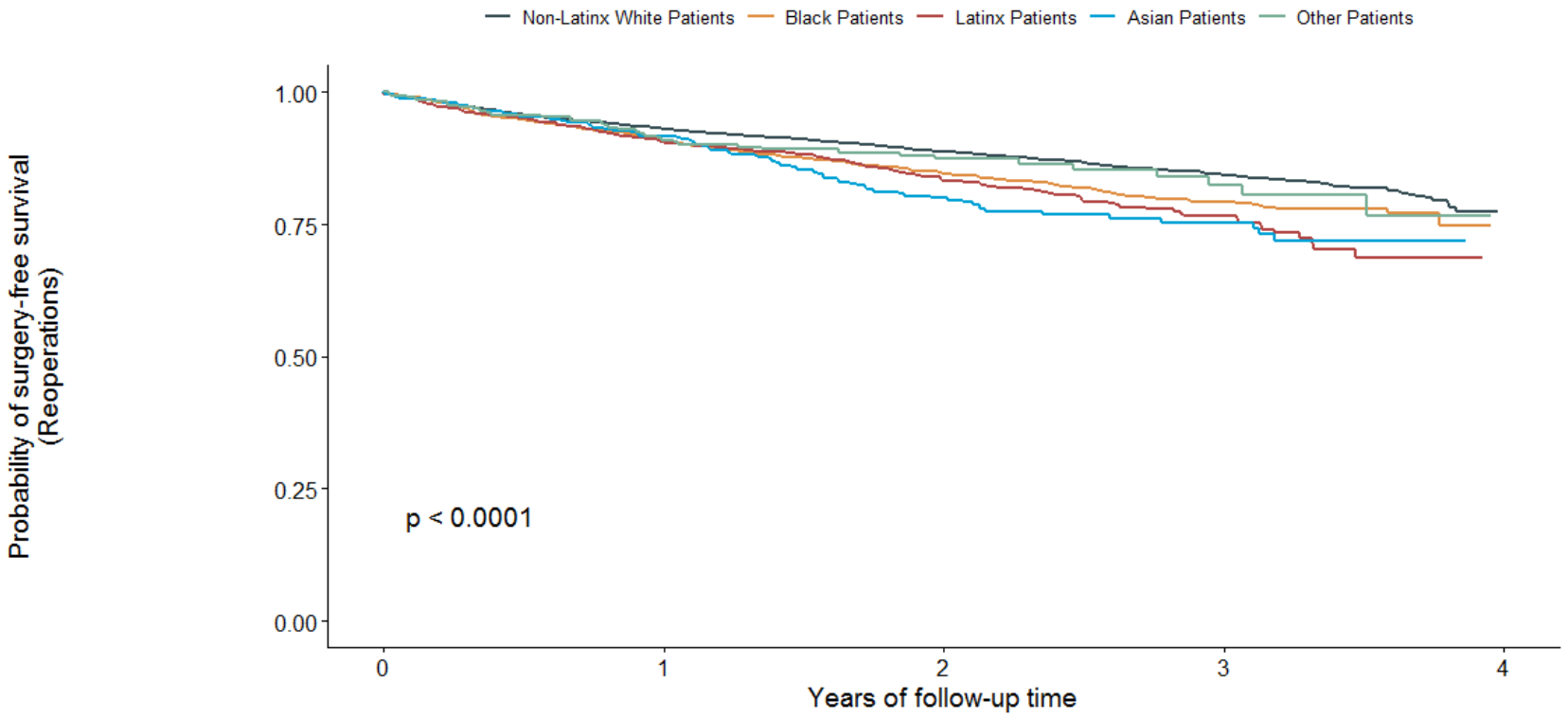
*Indicates 95% confidence interval (CI) is disjoint with 95% CI for Non-Latinx White

Figure 2.3 Forest plot of incidence rates for reoperations or revisions per 100 person-years, stratified by race and ethnicity.



*Indicates 95% confidence interval (CI) is disjoint with 95% CI for Non-Latinx White

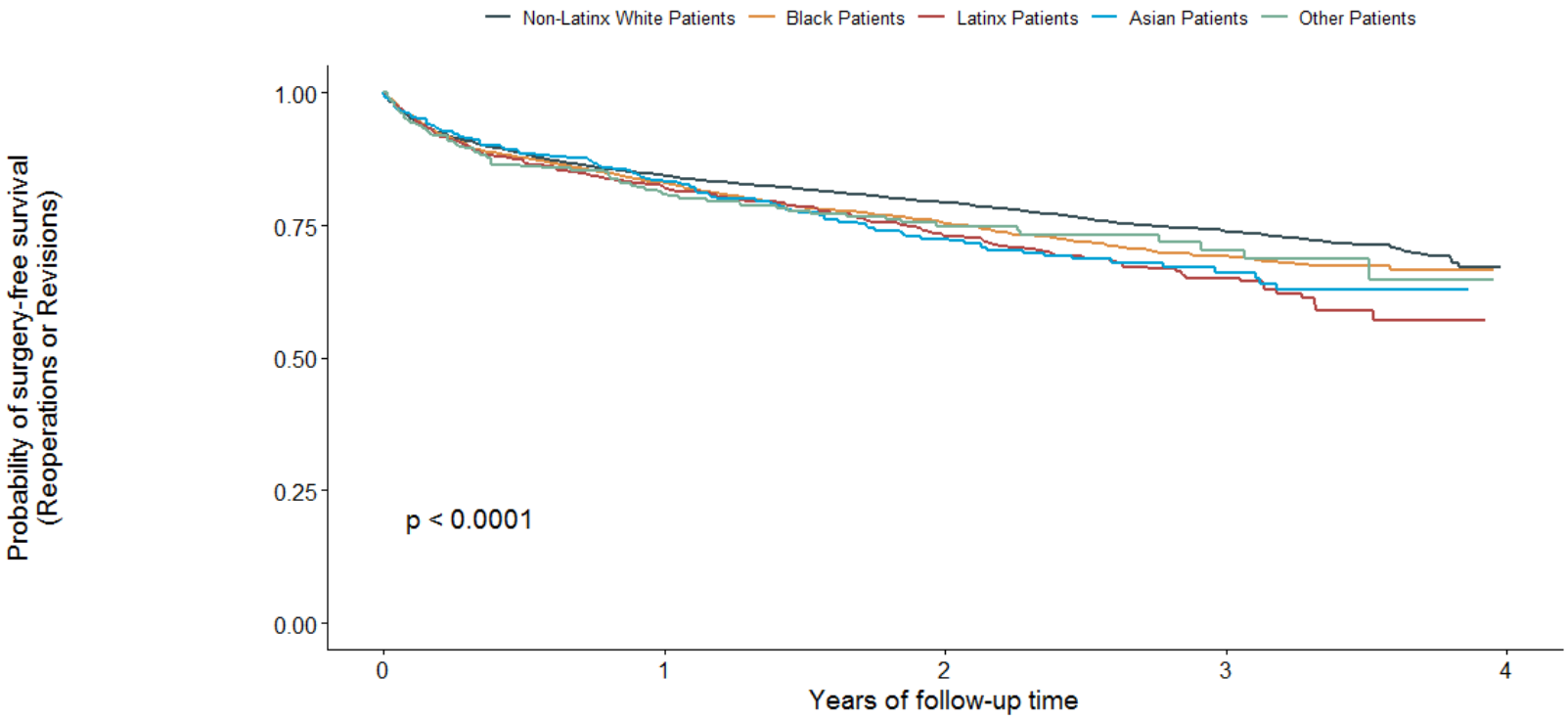
Figure 2.4 Kaplan-Meier curve for probability of surgery-free survival (reoperations), stratified by racial and ethnic group.



Number at risk

Non-Latinx White Patients	8510	6641	3953	1606	0
Black Patients	2273	1627	888	377	0
Latinx Patients	887	633	360	145	0
Asian Patients	409	330	189	76	0
Other Patients	287	219	123	47	0

Figure 2.5 Kaplan-Meier curve for probability of surgery-free survival (reoperations or revisions), stratified by racial and ethnic group.



Number at risk

Non-Latinx White Patients	8510	6030	3533	1406	0
Black Patients	2273	1492	803	337	0
Latinx Patients	887	568	317	122	0
Asian Patients	409	296	169	65	0
Other Patients	287	194	109	43	0

Table 2.4 Cox proportional hazards regressions estimating risk of incisional glaucoma surgery reoperation, by racial and ethnic group						
	Unadjusted		**Total Racial and Ethnic Disparity***		**Direct Racial and Ethnic Disparity****	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**	**Hazard Ratio**	**95% CI**
Non-Latinx White Patients	Ref	Ref	Ref	Ref	Ref	Ref
Black Patients	1.35	1.19-1.53	1.34	1.17-1.53	1.30	1.13-1.50
Latinx Patients	1.53	1.28-1.82	1.43	1.19-1.71	1.36	1.12-1.65
Asian/Pacific Islander Patients	1.67	1.33-2.09	1.49	1.17-1.89	1.41	1.10-1.81
Other Patients	1.14	0.82-1.58	0.99	0.71-1.38	0.96	0.69-1.34

*Model adjusts for: age, sex, US state of residence, cohort year.

**Model adjusts for: age, sex, US state of residence, cohort year, eligibility for dual-Medicaid, eligibility for Part D low-income subsidies, CCW comorbidities, glaucoma severity, and glaucoma subtype.

Table 2.5 Cox proportional hazards regressions estimating risk of incisional glaucoma surgery reoperation or revision, by racial and ethnic group						
	Unadjusted		**Total Racial and Ethnic Disparity***		**Direct Racial and Ethnic Disparity****	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**	**Hazard Ratio**	**95% CI**
Non-Latinx White Patients	Ref	Ref	Ref	Ref	Ref	Ref
Black Patients	1.17	1.06-1.29	1.17	1.05-1.29	1.16	1.04-1.30
Latinx Patients	1.32	1.15-1.51	1.29	1.12-1.49	1.31	1.12-1.52
Asian/Pacific Islander Patients	1.28	1.06-1.55	1.20	0.99-1.47	1.19	0.97-1.46
Other Patients	1.19	0.94-1.51	1.06	0.83-1.35	1.06	0.83-1.36
*Model adjusts for: age, sex, US state of residence, cohort year. **Model adjusts for: age, sex, CCI score, glaucoma severity, geographic region, cohort year dual Medicaid coverage						

Chapter 3: Racial and ethnic disparities in patient-sharing networks of eye care providers caring for California Medicare Beneficiaries who received incisional glaucoma surgery

3.1 Abstract

Purpose: To: (a) examine racial and ethnic disparities in eye care provider networks by applying network science methods to Medicare claims data and (b) determine whether network characteristics of treating surgeons are associated with risk of incisional glaucoma surgical failure.

Methods: The first part of this study involved a cross-sectional analysis of all 2016 California fee-for-service Medicare patients aged ≥65 years who received incisional glaucoma surgery. All providers who filed claims ±60 days from the date of surgery were aggregated to create a network of eye care providers (nodes) connected by shared patients (ties). Three provider network characteristics: (1) repeat-tie fraction (tendency for providers to have worked together in the past), (2) normalized degree centrality (a measure of network popularity), and (3) clustering coefficient (tendency for providers to assemble into tightly interconnected clusters around shared patients) were measured. Associations between surgeon network characteristics and beneficiary race and ethnicity were examined with logistic regression for dichotomized repeat-tie fraction (>0 vs. 0) and linear regression for log-transformed values of normalized degree centrality and clustering coefficient. Associations between surgeon network characteristics and incisional glaucoma surgical failure were assessed in the second part of this study using survival analysis with follow-up through 2019. To account for surgeon-specific random effects, frailty models using Cox proportional hazards regression were used to examine whether individual network characteristics were associated with risk of incisional glaucoma surgical failure.

Results: A total of 2,289 unique California Medicare beneficiaries who received incisional glaucoma surgery in 2016 were included in the analysis. Non-Latinx White beneficiaries comprised the largest group (n=1,244; 54.3%), followed by Latinx beneficiaries (n=440; 19.2%), Asian/Pacific Islander beneficiaries (n=331; 14.5%), Black beneficiaries (n=204; 8.9%), and beneficiaries of Other race and ethnicity (n=70; 3.1%). In total, there were 1,386 providers in the final patient-sharing network of eye care providers, of whom, 338 (24.4%) were treating surgeons. Asian/Pacific Islander beneficiaries had reduced odds of having a treating surgeon with a non-zero repeat tie fraction (adjusted odds ratio [aOR]: 0.75, 95% confidence interval [CI]: 0.57 to 0.99) compared to non-Latinx White beneficiaries. Black (adjusted e^{β}: 0.90, 95% CI: 0.78 to 1.03) and Latinx (adjusted e^{β}: 0.83, 95% CI: 0.74 to 0.92) beneficiaries had treating surgeons with lower normalized degree centrality compared to non-Latinx White beneficiaries. Latinx beneficiaries had treating surgeons with greater clustering coefficients than non-Latinx White beneficiaries (adjusted e^{β}: 1.17, 95% CI: 1.06 to 1.27). Finally, frailty models altogether showed no significant associations between network characteristics and glaucoma surgical failure, though data suggest a possible, albeit weak, dose-response relationship between increasing quartiles of normalized degree centrality and reduced surgical failure (Quartile 2 hazard ratio [HR]: 1.13, 95% CI: 0.80 to 1.61; Quartile 3 HR: 1.03, Quartile 3 95% CI: 0.70 to 1.50; Quartile 4 HR: 0.88, 95% CI: 0.55 to 1.40; fully adjusted model).

Conclusions: There were significant racial and ethnic disparities in network characteristics of treating surgeons for California Medicare beneficiaries who received incisional glaucoma surgery in 2016. Overall, Black and Latinx beneficiaries tended to have treating surgeons who had fewer connections to other eye care providers and belonged to smaller, more isolated network clusters. Altogether, results from the present study point to these racial and ethnic disparities in eye care

provider networks as possible manifestations of structural racism plaguing our present-day healthcare systems.

3.2 Introduction

There are many factors associated with disparities in care and outcomes, including causes mediated through unintended forms of structural and interpersonal racism in healthcare systems.[137] Underserved populations may obtain care from health systems that provide lower quality care. These benchmarks are determined by accepted measures of quality such as receiving care from a concentrated, smaller group of physicians, or being treated by physicians who are less likely to be board certified, or having more difficulty obtaining access to specialist providers.[138] Secondly, there may also be differences in the way patients are treated by physicians who themselves treat patients of various races, ethnicities and socioeconomic status (SES). For example, interpersonal racism in the form of implicit bias may impact physician referral patterns where referring physicians might assume that patients from a particular underserved group prefer not to travel far to see a specialist or may prefer to see specialists of a specific type.[137] Alternatively, physicians may perceive that specialists to whom they refer might be more or less willing to see underserved patients.

Biased physician referral patterns that result in the formation of inequitable patient-sharing networks may represent inadvertent manifestations of structural racism, limiting access to care to racially and ethnically minoritized individuals. To better understand these possible differential patterns of care by provider groups and referral practices, administrative claims data from Medicare can be used to examine these patterns of care which can be observed empirically. Methods from network science can be employed to construct patient-sharing networks of providers

to determine whether differences in observed patterns of patient sharing are significantly different based on race and ethnicity of the Medicare beneficiary.

There are particular physician network characteristics that are theorized to be advantageous with respect to patient care outcomes. For example, better cohesion amongst providers[139] or greater tendency for providers in a network to have worked together previously[140,141] may suggest improved communication or frequency of interactions that may be associated with enhanced patient outcomes. Thus, the purpose of the present study was to examine racial and ethnic disparities in structural network characteristics of patient-sharing networks of eye care providers in the perioperative period surrounding incisional glaucoma surgery. We assessed associations between beneficiary race and ethnicity and network characteristics of their treating surgeon, including factors related to network popularity, frequency of provider interaction, and whether surgeons belonged to network clusters that were smaller and more insular in structure. As a secondary outcome, we also examined whether these network characteristics were associated with risk of incisional glaucoma surgery failure.

3.3 Methods

3.3.1 Medicare Beneficiary Population

The study population was composed of all California Medicare fee-for-service beneficiaries who received incisional glaucoma surgery, including trabeculectomy (all techniques; Current Procedural Terminology 4 [CPT] codes: 66170, 6172), tube shunt (any model; CPT codes: 66179, 66180), or Ex-PRESS® shunt (Alcon Laboratories, Fort Worth, TX; CPT codes: 0192%, 66183), in 2016. This retrospective cohort was then followed up through 2019 using administrative data drawn from the Master Beneficiary Summary File (MBSF) and the Standard Analytic Files

(SAF) of Part B Carrier Claim files provided by the Centers for Medicare and Medicaid Services (CMS).

Exclusion criteria were as follows: age less than 65 years; missing International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code for any glaucoma associated with the claim for index incisional glaucoma surgery; missing laterality modifier for the index incisional glaucoma surgery; or no enrollment in Medicare Parts A and B. Given that repeat incisional surgery is known to have variable surgical results[122] and is generally less successful than primary incisional surgery,[123,124] beneficiaries were also excluded if they received incisional glaucoma surgery in 2015. For beneficiaries who had multiple claims for incisional surgery in 2016, the earliest procedure defined the index surgery, index surgery date, and index eye. Only one eye per patient was included to preserve independence of observations. Beneficiaries who did not contribute any follow-up time (i.e., they had no eye-related visits or failure events following their index incisional glaucoma surgery) were also excluded. Finally, beneficiaries were additionally excluded if their treating surgeon was found to not share patients with any other providers and thus did not figure in the patient-sharing network of eye care providers.

3.3.2 Eye Care Provider Network

Next, a patient-sharing network of eye care providers was constructed. To accomplish this, we constructed a claims window around the index surgery that began 60 days prior and extended 60 days beyond date of index surgery for each individual beneficiary in the cohort. Then, all eye care providers (i.e., ophthalmologists and optometrists) were identified based on Medicare Specialty Codes (Medicare Specialty Code 18 for ophthalmologists and Medicare Specialty Code 41 for optometrists) who billed for any services on the beneficiaries' behalf during this window.

We included claims filed by the treating surgeon (i.e., the surgeon who billed for the index incisional glaucoma surgery procedure used to identify the beneficiary for study inclusion), other treating ophthalmologists (comprehensive ophthalmologists and subspecialists), and optometrists during this window. After all eye care providers for a beneficiary's surgical episode were identified, they were aggregated together to create the bipartite physician referral network. Afterwards, unipartite projections of the bipartite networks were created so that eye care providers—represented by nodes—were directly connected, and with patients they shared—represented by ties—serving as the connections between them.

3.3.3 Network Characteristics

We examined three network characteristics that have been previously studied and theorized to influence delivery of care and patient outcomes, all measured for each eye care provider (node): (1) the repeat-tie fraction, (2) the normalized degree centrality, and (3) the clustering coefficient. The repeat-tie fraction reflects the tendency for physicians in a network to have worked together previously, and has been operationalized on the network level as the proportion of provider pairs in a network who has shared at least two patients.[141] Because network theory posits that communication between nodes improves as the frequency of interactions between them increases,[140] a high repeat-tie fraction is considered to be desirable in terms of patient care coordination.[141] In the present study, we chose to operationalize the repeat-tie fraction at the level of the individual provider (rather than at the level of the entire network), defining it as the fraction of ties to all other providers where at least two patients were shared. The repeat-tie fraction was then dichotomized to zero versus non-zero values, essentially distinguishing providers with at least one tie to another provider where more than one patient was shared to providers for whom ties to

all other providers were composed of sharing a single patient. This is similarly meant to be a proxy for ties to other providers with whom the provider of interest has worked previously.

A node's degree centrality is simply the number of ties it has extending to (or from) other nodes. A node's normalized degree centrality is simply the node's degree centrality divided by the maximum possible number of ties in the network (i.e., n-1). A node's normalized degree centrality is thought to represent the importance or popularity of a node within its network.[142] Finally, clustering refers to the tendency for physicians in a network to assemble into tightly interconnected clusters (cliques) around shared patients.[140,143] When members of a network are more heavily interconnected within their own clusters, they tend to be more insular and inward-looking and, therefore, may be less willing or able to access new knowledge and ideas from outside sources.[144,145] At the same time, however, clustering has also been hypothesized to be beneficial to patient care. For example, some have posited that networks with higher levels of clustering may indicate greater collaboration amongst physicians given that they are more likely to develop a shared sense of familiarity and trust with peers with whom they collaborate more regularly.[141,146-149] Furthermore, greater clustering within networks may also facilitate closer communication amongst clustered providers, allowing for more opportunities to interact with local colleagues.[141,150]

It is expected that the normalized degree centrality and the clustering coefficient will be right skewed, with most providers having values in the lower ranges. Thus, to better meet normal distribution criteria for parametric testing, the natural logarithms of these two network characteristics will also be analyzed separately. Histograms of original variables and log-transformed variables will be presented for data visualization.

3.3.4 Network Analysis

In social network analysis, data is visualized in the form of nodes and links. In the present study, nodes represent eye care providers, and the links between them represent patients who are under the shared care of both providers. After the network is constructed using the iGraph package in R (R Foundation for Statistical Computing, Vienna, Austria), the network will be visualized using the Fruchterman-Reingold algorithm which utilizes a force-directed graph method to minimize link crossing, allow for uniform link length, to prevent overlap, and promote symmetry.[151,152] Weights are applied to ties between nodes based on the number of shared patients between two providers. In the Fruchterman-Reingold algorithm, nodes connected with a highly weighted tie are placed closer to each other.

Network visualization will also be performed with the Kamada-Kawai algorithm to determine the optimal graphic structure of the networks under study. The Kamada-Kawai algorithm generates a matrix of shortest network path distances from each node to all other nodes in the network and repositions nodes to reduce the sum of the difference between the plotted distances and the network distances.[152,153] It thereby iteratively repositions nodes to reduce the number of ties that cross each other, while at the same time maximizing distance between nodes to minimize their overlap.[152] In the Kamada-Kawai algorithm, tie weights are operationalized such that larger values (i.e., greater number of ties between nodes) result in longer edges, which is opposite to the Fruchterman-Reingold algorithm.

Community detection will be undertaken using the Louvain method, which occurs in two phases. First, each node is analyzed individual to compute the modularity gain (a measure of the strength of division of a network into modules, clusters, or communities) if a connecting node were to be assigned to the same community.[154] This process is repeated until no further modularity gains

can be made. In the second phases, communities are condensed into nodes with edge weights and are all aggregated together.[155] For illustrative purposes, two Louvain clusters within the final network will be presented. The proportion of racially- and ethnically-minoritized patients shared within a cluster will be calculated for each cluster within the network. Then, for visualization purposes, the provider clusters serving at least 100 total beneficiaries will be ranked in the proportion of racially- and ethnically-minoritized beneficiaries served by each provider cluster. Then, the provider cluster serving the greatest proportion of racially- and ethnically-minoritized beneficiaries and the provider cluster serving the smallest proportion of racially- and ethnically-minoritized beneficiaries. Finally, because the provider network will be composed of: (a) surgeons who operated on beneficiaries in the cohort and (b) other ophthalmologists and optometrists who filed claims during the ±60-day window, nodes representing treating surgeons will be colored differently to distinguish their positions within the network.

3.3.5 Exposure and Covariate Definitions

Beneficiary race and ethnicity served as the exposure for the primary analysis examining the associations between beneficiary race and ethnicity and surgeon network characteristics. The Research Triangle Institute (RTI) race and ethnicity variable was used given its greater level of agreement with self-reported race and ethnicity and higher sensitivity for identifying Asian/Pacific Islander and Latinx individuals.[89] The RTI race and ethnicity variable has the following coded values: Unknown, Non-Hispanic White, Black (or African-American), Other, Asian/Pacific Islander/Pacific Islander, Hispanic, and American Indian/Alaska Native. Given anticipated issues with small sample sizes, the race and ethnicity variable were aggregated into the following categories for the present analysis: Non-Latinx White, Black, Latinx, Asian/Pacific Islander/Pacific Islander, and Other (with the Other category including Unknown, American

Indian/Alaska Native, and Other race and ethnicity groups). Currently, data from Medicare do not separate multiracial beneficiaries.[111]

Demographic variables that were examined during the index glaucoma surgery year (2016) included age and sex. Age was analyzed as a categorical variable, beginning at 65 years, and binned into five-year age groups that truncated at age 90 years or greater. Beneficiary sex was categorized as male, female, and unknown, which was self-identified by applicants to Social Security.[112] Two proxy variables for SES were constructed. A variable for dual Medicare-Medicaid eligibility was constructed from a source variable that codes the number of months where the beneficiary had dual eligibility.[113] A dichotomous variable was created based on whether the beneficiary had at least one month of dual eligibility during the index surgery year. A second proxy variable for SES was constructed based on whether the beneficiary qualified for a low-income subsidy (LIS) that covers some or all the costs for Medicare Part D benefit premiums and cost-sharing.[114] This program applies to beneficiaries up to 150% of the federal poverty line (FPL) and has higher asset limits than the Supplemental Security Income (SSI) program.[115] Eligibility for the LIS program for Part D captures a slightly higher income group as compared to dual Medicare-Medicaid enrollment criteria.[115]

In terms of clinical covariates, a global measure of systemic comorbidities was estimated using the CCI score.[116] The CCI is a weighted index of systemic disease burden based on the presence or absence of 17 systemic comorbidities, which include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, cirrhosis, hepatic failure, immunosuppression, diabetes mellitus (DM) with or without complications, hemi/paraplegia, chronic renal disease, malignant neoplasms, multiple myeloma/leukemia, lymphomas, metastatic

solid tumor, and AIDS.[116,117] Presence of each of these diagnoses was determined by ICD-10 codes in claims filed during the index surgery year. The CCI produces a morbidity score that reflects mortality risk, adjusting for variable morbidity rates within a patient population.[116] The CCI score variable was then categorized into scores of 0, 1-2, 3-4, and ≥5.[118]

Glaucoma disease severity for the index eye was assessed with the seventh digit incorporated into ICD-10 codes (mild, moderate, severe, indeterminate, or unspecified), with eye laterality encoded in the sixth ICD-10 code digit.[100] Eye laterality was assessed with the sixth digit of the ICD-10 code as a quality check to ensure random distribution of laterality of index eye by race and ethnicity.

For the secondary analysis, the three network characteristics (repeat-tie fraction, normalized degree centrality, and clustering coefficient) served as the exposure variables, with the log-transformed values replacing the latter two if found to violate normal distribution assumptions during data visualization.

3.3.6 Outcomes Definition

The outcomes for the primary aim will be the three network characteristics (repeat-tie fraction, normalized degree centrality, and clustering coefficient). For the secondary aim examining the effect of network characteristics on glaucoma surgical failure, a survival analysis was performed. The outcome was time to failure of index incisional glaucoma surgery, defined as new glaucoma surgical reintervention (e.g., trabeculectomy, tube shunt placement, Ex-PRESS® shunt placement, iStent® placement, XEN® Gel Stent placement, Hydrus® microstent placement, cyclophotocoagulation, canaloplasty, goniotomy, trabeculotomy, and trabeculoplasty). Start of follow-up time for each beneficiary began on the date of the index incisional glaucoma surgery during 2016. Censoring due to other endpoints was permitted, including death or loss of continuous

Medicare Part A or Part B coverage. Time was assessed as duration of follow-up, measured as the time since the date of the index incisional glaucoma surgery to the primary outcome or a censoring event.

Beneficiaries were assessed to ensure they continued to meet inclusion criteria at each year of follow-up (2016-2019). Beneficiaries were right censored if they died, lost continuous Part A or Part B coverage, or if their residence changed to one outside of the state of California. For beneficiaries who died, their censorship date was assigned as their death date found in the MBSF. For beneficiaries who lost continuous Part A or Part B coverage or whose residence changed to outside of California, their censorship date was assigned as December 31st of the previous year during which the beneficiary retained continuous enrollment. Administrative censoring for all beneficiaries who survived without index incisional glaucoma surgical failure occurred at the date of the last claim date with an eye visit CPT code (92004, 92014, 92002, 92012, 99212, 99024) filed by an ophthalmologist, optometrist, or ambulatory surgical center, identified by the CMS provider specialty code (18, 41, 49), occurring on or before December 31, 2019. Differential follow-up will be permitted, with those who received index incisional glaucoma surgery in 2016 having a maximum of four years of follow-up, those who received index surgery in 2017 having a maximum of three years of follow-up, and those who received index surgery in 2018 having a maximum of two years of follow-up.

3.3.7 Statistical Analyses

Figure 3.1 outlines the underlying assumptions about the data-generating process for the primary analysis examining the associations between beneficiary race and ethnicity and the network characteristics of their treating surgeons in Directed Acyclic Graph 1 (DAG 1). The DAG depicted in Figure 3.1 assumes that remnants of historical racism, represented by node H,[125] is an

unmeasured confounder that is a common cause for racial and ethnic disparities observed with respect to SES, sex differences in life expectancy, and other inequities by race and ethnicity that persist to the present day. But given that this study aimed to examine racial and ethnic disparities, measurement of the biasing path created by remnants of historical racism was considered to be essential to the driving motivations of the study. Thus, from DAG 1, it is clear that beneficiary demographic and socioeconomic characteristics (age, sex, SES) represent the minimal sufficient adjustment set for estimating associations between beneficiary race and ethnicity and the treating surgeon's network characteristics.

Figure 3.2 outlines the assumptions thought to drive the data-generating process for the secondary analysis examining the effect of network characteristics on glaucoma surgical failure. In this case, because we are exclusively interested in the impact of the treating surgeon's network characteristics on beneficiary surgical failure, most covariates (race and ethnicity, SES, CCI, and glaucoma severity) represent potential confounders that will be controlled for in regression models. Of note, the causal arrow between sex and network characteristics and the causal arrow between age and network characteristics was intentionally left out because, though unequal sex- and age-based distributions may exist in patient populations cared for by various providers, it is likely that this is due to sex and age being parents of variables that are themselves directly related to how patients are distributed amongst providers (rather than directly being due to sex and age). For example, it may be more likely for tertiary referral centers to see patients with more severe glaucoma, who, in turn, are likely to be older (and thus, more likely to be female, given observed differences in life expectancies), leading to uneven patient age and sex distributions amongst providers.

Descriptive statistics for baseline sociodemographic and clinical characteristics were assessed with frequency distributions and contingency tables for the entire cohort and stratified by racial and ethnic group. Crude differences in distributions of all characteristics by race and ethnicity were assessed with Chi-squared tests for categorical variables and t-tests for continuous variables. If continuous variables were found to have non-normal distributions, Wilcoxon rank sum tests were used instead of t-tests.

To examine possible associations between beneficiary race and ethnicity and the network characteristics of their treating surgeon, logistic regression and linear regression models were used. Logistic regression was used when assessing repeat-tie fraction as the outcome of interest, and linear regression was used when normalized degree centrality and clustering coefficient were the outcome variables. Unadjusted models were constructed first, which conceptually measure the total racial and ethnic disparity, together with the biasing paths representing downstream effects of structural and interpersonal racism that are remnants of historical processes such as slavery, Jim Crow laws, federal housing policies, and unfair lending policies and redlining.[125] Two multivariable models were additionally constructed: first, a model which estimated the total racial and ethnic disparity and adjusted for age, sex, and SES (dual-Medicaid eligibility and qualifying for Part D low-income subsidies); and secondly, a model which estimated the direct racial and ethnic disparity and additionally adjusted for CCI and glaucoma disease severity, thereby closing these mediating paths.

Finally, frailty models using Cox proportional hazards regression was employed for unadjusted and adjusted multivariable models to compare the risk of glaucoma surgical failure by each of the provider network characteristics. Given the exploratory nature of this analysis, unadjusted models were examined first, followed by two multivariable models: first, a model

adjusting for variables theorized to act as potential confounders, including race and ethnicity, SES, CCI, and glaucoma disease severity; and secondly, a fully-saturated model which additionally adjusted for age and sex. Frailty models were used to allow for a random intercept for cluster-specific random effects. Given that our survival analysis involved examining surgical failure in Medicare beneficiaries who shared the same treating surgeon with the same network characteristics, this hierarchical data structure required the use of frailty models to account for surgeon-specific random effects.[156] Log-normal distribution of shared frailty terms was assumed, which adopts a symmetric distribution for the shared frailty term. The network analysis for this study was carried out using R, version 4.2.0 (R Foundation for Statistical Computing) and R Studio, version 2022.06.0 (R Foundation for Statistical Computing), with all other statistical analysis performed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). The study was approved by the Institutional Review Board of the University of California, Los Angeles (IRB# 17-000914).

3.4 Results

3.4.1 Baseline Cohort Characteristics

Table 3.1 presents the distributions of baseline sociodemographic and clinical characteristics for the cohort, stratified by beneficiary race and ethnicity. A total of 2,289 unique California Medicare beneficiaries who received incisional glaucoma surgery in 2016 were included in the analysis. The racial and ethnic breakdown of the final analytical sample generally followed that of the total population of California aged 65 and older according to estimates from the American Community Survey.[157] Non-Latinx White beneficiaries comprised the largest group (n=1,244; 54.3%), followed by Latinx beneficiaries (n=440; 19.2%), Asian/Pacific Islander

beneficiaries (n=331; 14.5%), Black beneficiaries (n=204; 8.9%), and beneficiaries of Other race and ethnicity (n=70; 3.1%). A plurality of beneficiaries was aged between 70-79 years old (n=989; 43.2%). Most beneficiaries identified as female sex (n=1,221; 53.3%) and did not qualify for dual-Medicaid coverage (n=1,579; 69.0%) nor Part D low-income subsidies (n=1,552; 67.8%). As expected, beneficiaries from all racially- and ethnically-minoritized groups (Black, Asian/Pacific Islander, Latinx, and Other race and ethnicity individuals) tended to be younger and have lower SES (based on dual-Medicaid eligibility and qualifying for Part D low income subsidies) according to crude demographic distributions.

3.4.2 Network Graphs

In total, there were 1,386 providers in the final patient-sharing network of eye care providers. Of these, 338 (24.4%) were treating surgeons who performed the index incisional glaucoma surgery for the 2,294 beneficiaries in the cohort. Figure 3.3 represents the entire patient-sharing network of eye care providers using the Kamada-Kawai algorithm layout for optimized visualization of the entire network. Orange nodes represent treating surgeons and black nodes represent other eye care providers who shared patients with the treating surgeons and filed claims within the ±60-day window surrounding the date of index surgery.

For illustrative purposes, network graphs of two provider network clusters are presented. First, Figure 3.4 demonstrates the provider cluster caring for at least 100 patients with the highest proportion of non-Latinx White patients. It is a network of 89 total eye care providers with 16 (18.0%) treating surgeons caring for 494 total patients, 75.1% (n=371) of whom were non-Latinx White. This cluster has a global clustering coefficient of 0.25. In other words, if a node has ties to eight other nodes, two of those nodes would have ties to each other. On the other hand, Figure 3.5 represents the provider cluster caring for at least 100 patients with the lowest proportion of non-

Latinx White patients. It is a network of 50 total eye care providers with 14 (28.0%) treating surgeons caring for 522 total patients, 39.3% (n=205) of whom were non-Latinx White. This cluster has a global clustering coefficient of 0.41. In other words, if a node has ties to ten other nodes, four of those nodes would have ties to each other.

3.4.3 Network Characteristics

Table 3.2 presents the central tendencies and spread for each of the network characteristics (repeat-tie fraction, normalized degree centrality, and clustering coefficient), stratified by beneficiary racial and ethnic groups. Figure 3.6 and Figure 3.7 present histograms for the network characteristics measured as continuous values (normalized degree centrality and clustering coefficient) in both their native and log-transformed versions. According to crude distributions, Black (n=148, 72.6%) and Latinx (n=319, 72.5%) groups had greater proportions of beneficiaries with surgeons who had repeat-tie fractions greater than zero. As seen in Figures 3.6 and 6b, the distribution of continuous data for normalized degree centrality (Figure 3.6) and clustering coefficient (Figure 3.7) was generally right-skewed (i.e., a preponderance of smaller values) for all racial and ethnic groups. The log-transformed versions of normalized degree centrality (Figure 3.6) and clustering coefficient (Figure 3.7) have distributions that adhere more closely to normal assumptions. Of note, however, there were a total of 25 beneficiaries (1.1% of cohort) with surgeons who had a clustering coefficient of zero (i.e., treating surgeon had ties to other providers who had no ties to one another). These 25 beneficiaries are excluded from analyses utilizing the log-transformed clustering coefficient variable.

To better compare network characteristics of treating surgeons by beneficiary race and ethnicity, Table 3.3 presents regression models examining these associations. The non-Latinx White racial and ethnic group served as the reference category for all models. Table 3.3a focuses

on repeat-tie fraction, or the proportion of ties the treating surgeon had to other providers that was formed by sharing two or more patients. Latinx beneficiaries had 29% increased odds of non-zero repeat-tie fraction compared to non-Latinx White beneficiaries in the unadjusted model (odds ratio [OR] 1.29, 95% confidence interval [CI]: 1.01 to 1.64), though this association was no longer observed in the partially adjusted (OR: 1.16, 95% CI: 0.89 to 1.51) or fully adjusted models (OR: 1.16, 95% CI: 0.89 to 1.52). Asian/Pacific Islander beneficiaries had 26% reduced odds of non-zero repeat-tie fraction in partially adjusted (OR: 0.74, 95% CI: 0.57-0.98) and 25% reduced odds in fully adjusted models (OR:0.75, 95% CI: 0.57 to 0.99) compared to non-Latinx White counterparts.

Table 3.3b examines the association between beneficiary race and ethnicity and the treating surgeon's log-transformed normalized degree centrality in a set of linear regression models. To facilitate assimilation of results, model coefficients have been exponentiated to allow for interpretation on the ratio scale. Compared to non-Latinx White beneficiaries, Black beneficiaries had surgeons with 15% lower normalized degree centrality in the unadjusted model (e^{β}: 0.85, 95% CI: 0.75 to 0.98), though the association shifted toward the null in the partially adjusted (e^{β}: 0.90, 95% CI: 0.79 to 1.04) and fully adjusted models (e^{β}: 0.90, 95% CI: 0.78 to 1.03). Latinx beneficiaries had surgeons with 24% lower normalized degree centrality in the unadjusted model (e^{β}: 0.76, 95% CI: 0.69 to 0.84), and 17% lower normalized degree centrality in both the partially adjusted (e^{β}: 0.83, 95% CI: 0.74 to 0.92) and fully adjusted models (e^{β}: 0.83, 95% CI: 0.74 to 0.92) compared to non-Latinx White beneficiaries. On the other hand, Asian/Pacific Islander beneficiaries had surgeons with 16% higher normalized degree centrality in both the partially adjusted (e^{β}: 1.16, 95% CI: 1.03 to 1.30) and fully adjusted models (e^{β}: 1.16, 95% CI: 1.03 to 1.30) compared to non-Latinx White beneficiaries.

Finally, Table 3.3c examined the associations between beneficiary race and ethnicity and the treating surgeon's clustering coefficient. The linear regression coefficients were again log-transformed to facilitate their interpretation on the ratio scale. Compared to non-Latinx White beneficiaries, Latinx beneficiaries had surgeons with greater clustering coefficients in the unadjusted (e^{β}: 1.19, 95% CI: 1.10 to 1.30), partially adjusted (e^{β}: 1.16, 95% CI: 1.06 to 1.28), and fully adjusted models (e^{β}: 1.17, 95% CI: 1.06 to 1.27). On the other hand, Asian/Pacific Islander beneficiaries were found to have surgeons with smaller clustering coefficients compared to non-Latinx White beneficiaries in the unadjusted (e^{β}: 0.92, 95% CI: 0.84 to 1.01), partially adjusted (e^{β}: 0.90, 95% CI: 0.82 to 0.99), and fully adjusted models (e^{β}: 0.91, 95% CI: 0.82 to 0.99).

3.4.4 Risk of Glaucoma Surgical Failure

For the survival analysis, 95 additional beneficiaries were excluded because they received incisional glaucoma surgery in 2015, leaving an analytic sample of 2,194 beneficiaries. This survival cohort California Medicare beneficiaries contributed a total of 5,706 years of follow-up time. During follow-up through 2019, a total of 363 glaucoma reoperation events were observed, yielding an incidence rate of 6.4 reoperation events per 100 person-years (95% CI: 5.7 to 7.1 cases per 100 person-years). The 363 failure events among the 2,289 beneficiaries in the cohort also yielded a cumulative incidence of approximately 16.5%. Results from frailty models using Cox proportional hazards regressions examining whether network characteristics of treating surgeons was associated with risk of glaucoma surgical failure (defined as reoperation with an additional glaucoma surgery) are presented in Tables 3.6 and 3.7. As demonstrated by the hazard ratios with 95% CIs that symmetrically straddle the null value of 1.00 in Table 3.6, there was no significant association between glaucoma surgical failure and any of the network characteristics, including

repeat-tie fraction, log-transformed normalized degree centrality, and log-transformed clustering coefficient. To determine if there may be a dose-response relationship between network characteristics and glaucoma surgical failure, separate frailty models using Cox proportional hazards regression were constructed to determine whether increasing quartiles of each network characteristic was associated with surgical failure, the results of which are presented in Table 3.7. This analysis by quartiles of values for network characteristics also largely showed no association between the outcome of glaucoma surgical failure and repeat-tie fraction or clustering coefficient as exposures. However, the data do suggest a possible, albeit weak, dose-response relationship between increasing quartiles of degree centrality and reduced risk of glaucoma surgical failure when examining the trend in hazard ratio effect estimates (Quartile 2 HR: 1.13, Quartile 3 HR: 1.03, Quartile 4 HR: 0.88; fully adjusted model). Nevertheless, the relatively symmetric coverage of the 95% Cis for the hazard ratio effect estimates suggest no association between increasing quartiles of normalized degree centrality and glaucoma surgical failure (Quartile 2 95% CI: 0.80 to 1.61, Quartile 3 95% CI: 0.70 to 1.50, Quartile 4 95% CI: 0.55 to 1.40).

3.5 Discussion

This observational study utilizing Medicare administrative claims data and network science methods to construct patient-sharing networks of eye care providers is the first of its kind to examine possible associations with individual patient-level factors and ophthalmic outcomes. The present study found significant racial and ethnic disparities in network characteristics of treating surgeons for California Medicare beneficiaries who received incisional glaucoma surgery in 2016. Overall, Black and Latinx beneficiaries tended to have treating surgeons who had fewer connections to other eye care providers and belonged to smaller, more isolated network clusters.

Non-Latinx White and Asian/Pacific Islander beneficiaries, on the other hand, tended to be treated by surgeons who had more popular network positions with more ties to peer providers, while also belonging to larger, less isolated network clusters. Furthermore, our results suggest that beneficiaries treated by surgeons with greater normalized degree centrality (i.e., providers occupying more popular network positions with more patient-sharing ties to peer eye care providers) may have reduced risk of incisional glaucoma surgical failure. Altogether, results from the present study point to these racial and ethnic disparities in eye care provider networks as possible manifestations of structural racism plaguing our present-day healthcare systems.

Examining racial and ethnic disparities in patient-sharing networks of physicians has important public health and social justice implications. Prior work has shown that physicians of higher or lower quality tend to be connected to one another,[158,159] and that "high-status" physicians may be more likely to refer to one another.[160] This network phenomenon of homophily, or the tendency of individuals with similar characteristics to interact with one another, has been previously observed within physician networks. A large social network analysis utilizing 2006 Medicare administrative claims data of over 4.5 million beneficiaries and over 68,000 physicians undertaken by Landon and colleagues found that physicians are more likely to share patients with peers who have patient panels and practice locations that are similar to their own.[161] In fact, they found that connected physicians had more similar patient panels in terms of patient race or illness burden as compared to unconnected physicians. While our network analysis differed in scale and scope, our results nevertheless harmonize with these prior studies.

Network science methods have previously been used to examine the role of provider- and system-level factors that contribute to racial and ethnic disparities in surgical outcomes. Ghomrawi and colleagues led a study to determine whether patterns of interaction among physicians around

total hip replacement episodes differed in communities with low versus high concentrations of Black residents.[145] Study authors used national Medicare claims data from 2008 through 2011 to identify all fee-for-service beneficiaries who underwent total hip replacement. Using physician encounter data, they then mapped physician referral networks at the hospitals where the surgical procedures were performed. Investigators found that, after adjusting for number of acute care beds and number of medical specialists, hospital service areas with higher concentrations of Black residents were served by physician referral networks that had significantly higher within-network clustering and fewer external ties.

A previous study by Landon and colleagues examined whether disparities exist between Black and White Medicare beneficiaries in the observed patterns of patient sharing between primary care physicians (PCPs) and physicians in the six specialties to which patients were most frequently referred (cardiology, pulmonary disease, gastroenterology, orthopedic surgery, general surgery, and neurology).[137] Investigators used Medicare administrative claims data from 2009 to 2010 for beneficiaries seen by PCPs and selected high-volume specialists in 12 health care markets with at least 10% of the population identifying as Black. Study authors found that the mean PCP-specialist degree (i.e., the number of specialists with whom a PCP shares patients) was lower for Black patients than for White patients. For example, the mean PCP-cardiologist degree across all markets for White patients was 17.5 compared to 8.8 for Black patients.[137] Furthermore, specialist networks among White patients were much larger than those for Black patients. For instance, cardiology networks across all markets had 135 specialists for Black patient networks compared to 330 specialists for White patient networks. This difference was statistically significant and remained so even after equalizing the numbers of patients seen per PCP (123 for Black patient networks vs 211 for White patient networks).[137]

Upon deeper examination, it may not be surprising that the provider network characteristics were not associated with glaucoma surgical outcomes in the survival analysis using frailty models. Disparities in provider networks may be more likely to constitute barriers to healthcare access rather than healthcare quality. The smaller, more isolated provider networks that Black and Latinx beneficiaries were more likely to receive care from may not have poorer surgical outcomes, but they may be more difficult to access because of their insulated structure. Prior studies have pointed to the issue of healthcare access as being an important driver of disparities in glaucoma outcomes. In fact, when healthcare access issues are controlled for, as in a clinical research setting such as the African Descent and Glaucoma Evaluation Study (ADAGES), despite receiving less surgery and having higher mean treated intraocular pressure, Black patients had similar rates of visual field progression as compared to non-Hispanic White patients.[162] Furthermore, significant disparities in eye care utilization have been described among Black and Latinx Medicare beneficiaries with glaucoma, including lower ophthalmology visits and glaucoma testing.[36] Furthermore, disparities in these racial and ethnic groups persist after stratification by SES, suggesting that other drivers of systemic racism may be at work.

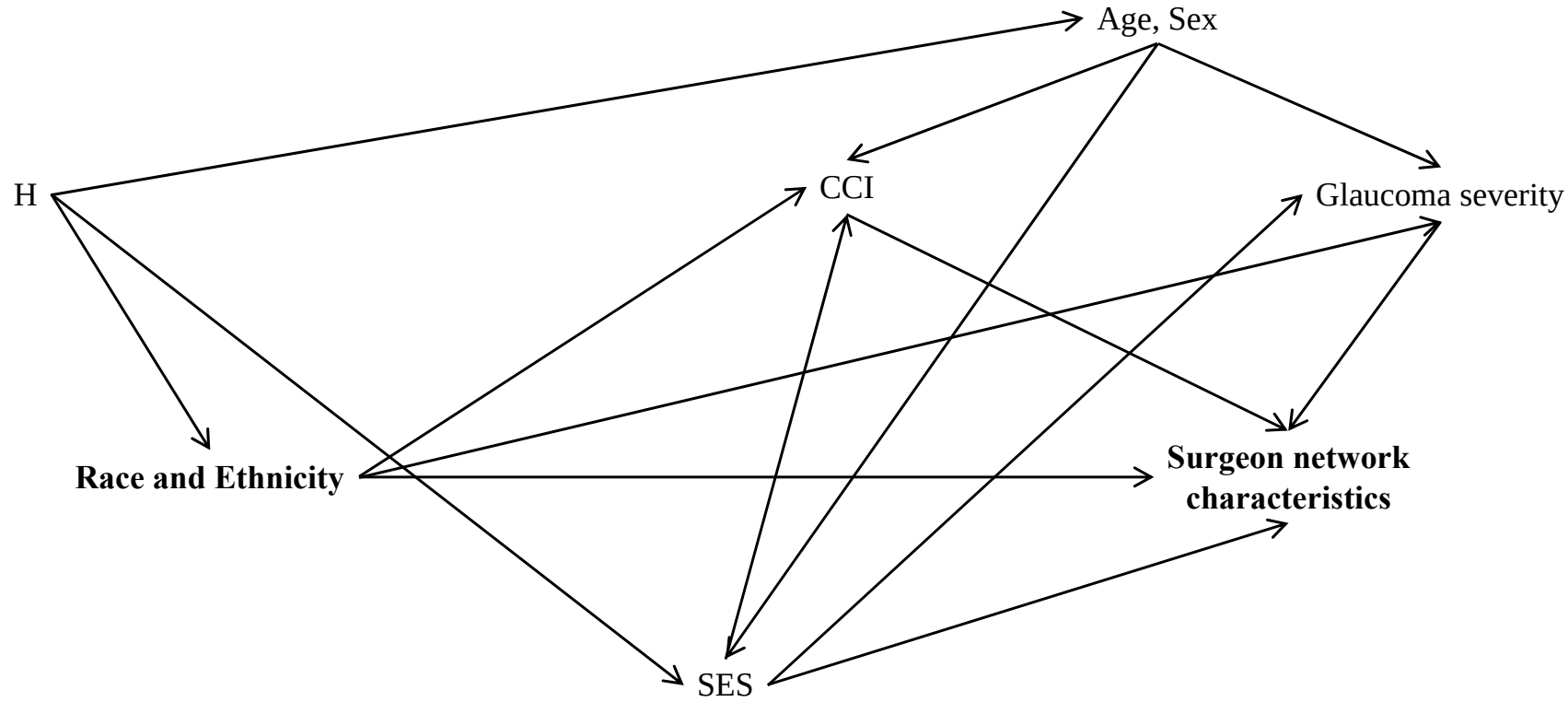
Our study must be considered within the context of several limitations. First, by constructing social networks of eye care providers based solely on referral networks constructed from claims data, we ignore other channels of provider interaction, thereby likely underestimating the number of internal and external ties the networks may have. Furthermore, lack of information about physician race and ethnicity is another important limitation, given that this may affect referral patterns. Additionally, our analysis was restricted entirely to California Medicare beneficiaries aged 65 years and older. It may be possible that patient-sharing relationships between

providers may differ for younger patients, a limitation that is particularly relevant given that racially and ethnically minoritized patients tend to have earlier onset of glaucoma.

Limitations notwithstanding, our study has important implications that aid in the understanding of the structural healthcare inequities that contribute to racial and ethnic disparities in glaucoma. Future studies utilizing larger samples of nationwide Medicare beneficiaries would benefit from greater statistical power to detect associations while additionally allowing for the exploration of whether these eye care provider networks are also subject to differences based on geographic region.

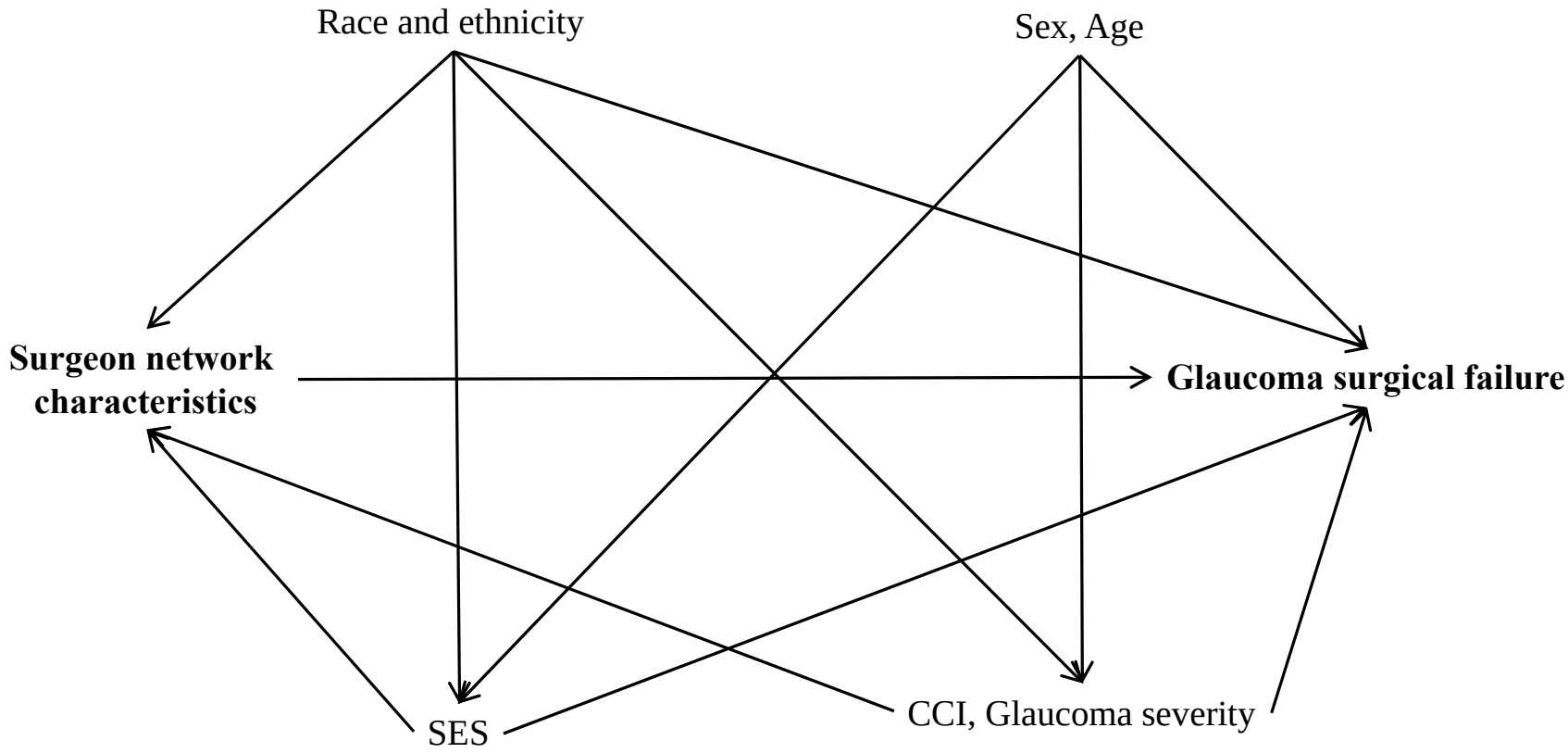
3.6 Tables and Figures

Figure 3.1 Directed Acyclic Graph 1 for analysis examining associations between beneficiary race and ethnicity and network characteristics of their treating surgeons.



H = remnants of historical racism (e.g., slavery, Jim Crow laws, discriminatory mortgage lending practices); SES = socioeconomic status; CCI = Charlson Comorbidity Index

Figure 3.2 Directed Acyclic Graph 2 for analysis examining associations between surgeon network characteristics and glaucoma surgical failure.



SES = socioeconomic status; CCI = Charlson Comorbidity Index

Table 3.1 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016, Entire California Population												
	All Patients		**Non-Latinx White Patients**		**Black Patients**		**Latinx Patients**		**Asian/Pacific Islander Patients**		**Patients of Other Races & Ethnicities**	
	N=2,289		N=1,244		N=204		N=440		N=331		N=70	
	N	%	N	%	N	%	N	%	N	%	N	%
Age in years												
65-69	389	17.0	154	12.4	50	27.5	97	22.0	69	24.3	19	32.8
70-74	475	20.8	232	18.6	49	26.9	105	23.9	66	23.2	23	39.7
75-79	514	22.5	278	22.3	44	24.2	96	21.8	80	28.2	16	27.6
80-84	456	19.9	266	21.4	39	21.4	73	16.6	69	24.3	*	*
85-89	320	14.0	206	16.6	*	*	57	13.0	*	*	*	*
90+	135	5.9	108	8.7	*	*	12	2.7	*	*	*	*
Sex												
Male	1,068	46.7	568	45.7	107	52.5	196	44.5	163	49.2	34	48.6
Female	1,221	53.3	676	54.3	97	47.5	244	55.5	168	50.8	36	51.4
Dual Medicaid Eligibility												
Yes	710	31.0	147	11.8	87	42.6	272	61.8	184	55.6	20	28.6
No	1,579	69.0	1,097	88.2	117	57.4	168	38.2	147	44.4	50	71.4
Part D Subsidies												
Yes	737	32.2	152	12.2	94	46.1	280	63.6	190	57.4	21	30.0
No	1,552	67.8	1,092	87.8	110	53.9	160	36.4	141	42.6	49	70.0
CCI Score												
0	569	24.9	341	27.4	39	19.1	89	20.2	78	23.6	22	46.8
1-2	804	35.1	446	35.9	64	31.4	165	37.5	104	31.4	25	53.2
3-4	534	23.3	278	22.3	52	25.5	101	23.0	88	26.6	*	*
5+	382	16.7	179	14.4	49	24.0	85	19.3	61	18.4	*	*
Index Surgery												
Trabeculectomy	1,056	46.1	553	44.5	98	48.0	191	43.4	172	52.0	42	100.0
Tube shunt	967	42.3	525	42.2	88	43.1	199	45.2	132	39.9	*	*
EX-PRESS shunt	266	11.6	166	13.3	18	8.8	50	11.4	27	8.2	*	*
Index eye												
Right	1,142	49.9	616	49.5	104	51.0	225	51.1	154	46.5	43	61.4
Left	1,147	50.1	628	50.5	100	49.0	215	48.9	177	53.5	27	38.6

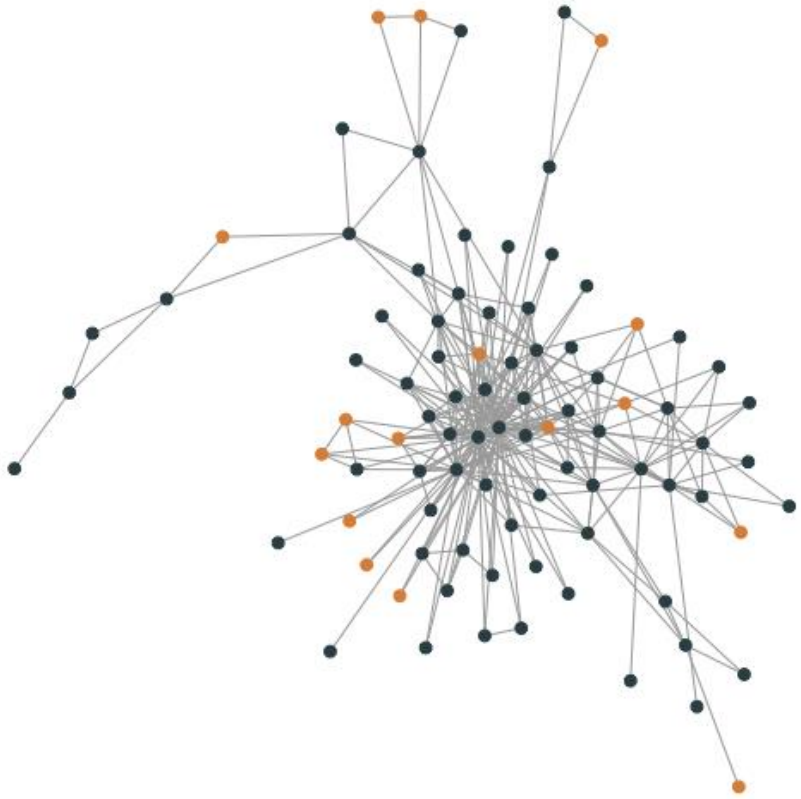
Table 3.1 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016, Entire California Population												
	All Patients		**Non-Latinx White Patients**		**Black Patients**		**Latinx Patients**		**Asian/Pacific Islander Patients**		**Patients of Other Races & Ethnicities**	
	N=2,289		N=1,244		N=204		N=440		N=331		N=70	
Glaucoma severity	N	%	N	%	N	%	N	%	N	%	N	%
Unspecified	658	28.7	338	27.2	54	27.6	135	30.7	104	32.5	27	49.1
Mild	87	3.8	57	4.6	*	*	16	3.6	*	*	*	*
Moderate	317	13.8	173	13.9	30	15.3	57	13.0	48	15.0	*	*
Severe	1,160	50.7	631	50.7	112	57.1	221	50.2	168	52.5	28	50.9
Indeterminate	67	2.9	45	3.6	*	*	11	2.5	*	*	*	*

* Cannot report cell size due to confidentiality

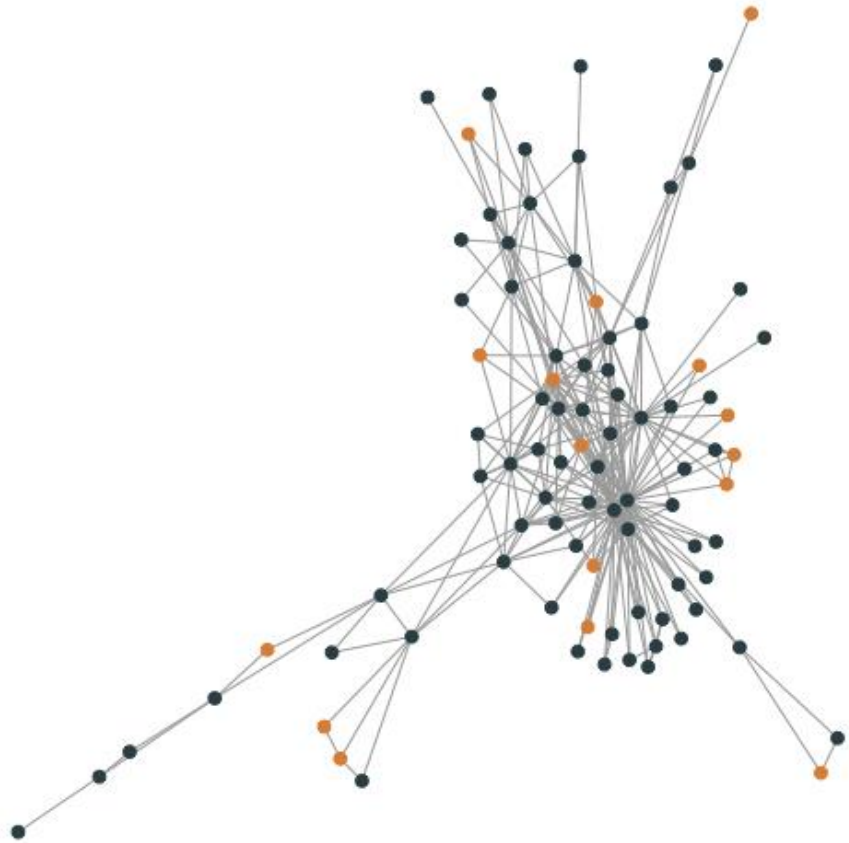
Figure 3.3 Network Graph of Patient-Sharing Network of Eye Care Providers

Orange nodes represent treating surgeons, black nodes represent other eye care providers (optometrists and ophthalmologists), and grey ties represent shared patients.

Figure 3.4 Least racially- and ethnically-minoritized group-serving provider cluster



(a) Kamada-Kawai layout

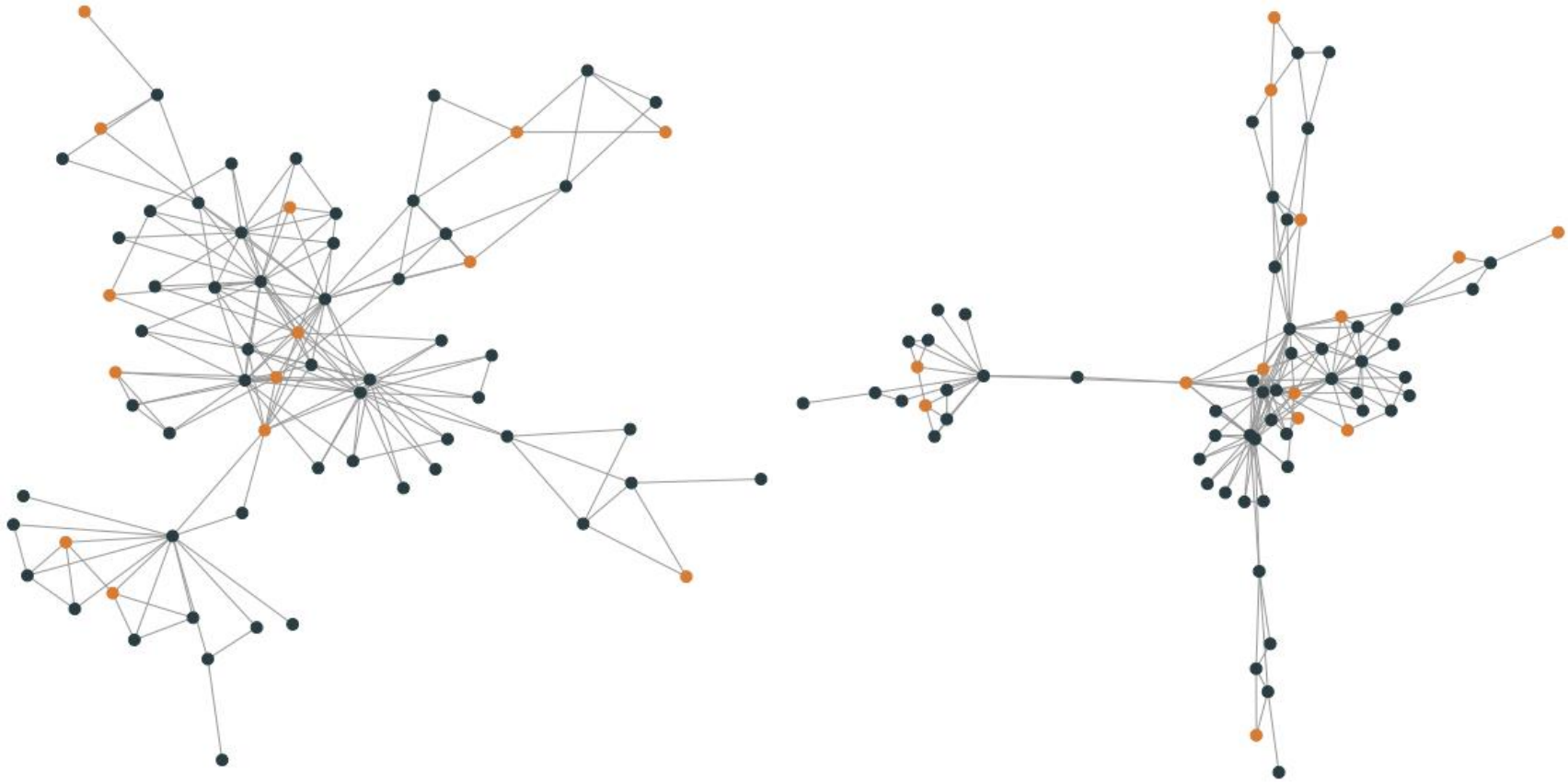


(b) Fruchterman-Reingold layout

Global clustering coefficient = 0.25
Number of patients = 494 (75.1% Non-Latinx White patients)
Number of eye care providers = 89
Number of treating surgeons = 16 (18.0%)

Orange nodes represent treating surgeons, black nodes represent other eye care providers (optometrists and ophthalmologists), and grey ties represent shared patients.

Figure 3.5 Most racially- and ethnically-minoritized group-serving provider cluster



(a) Kamada-Kawai layout

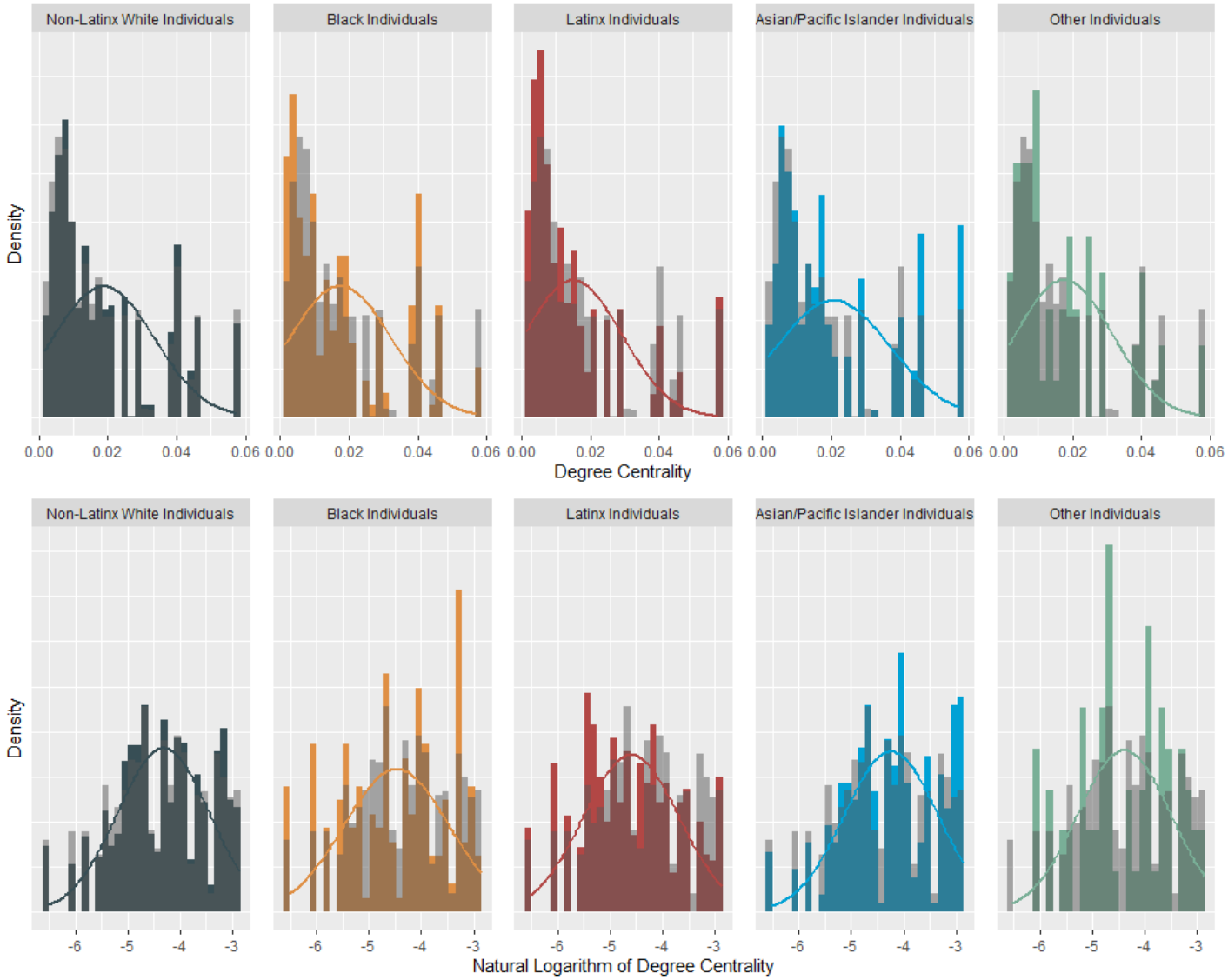
(b) Fruchterman-Reingold layout

Global clustering coefficient = 0.41
Number of patients = 522 (39.3% Non-Latinx White patients)
Number of eye care providers = 50
Number of treating surgeons = 14 (28.0%)

Orange nodes represent treating surgeons, black nodes represent other eye care providers (optometrists and ophthalmologists), and grey ties represent shared patients.

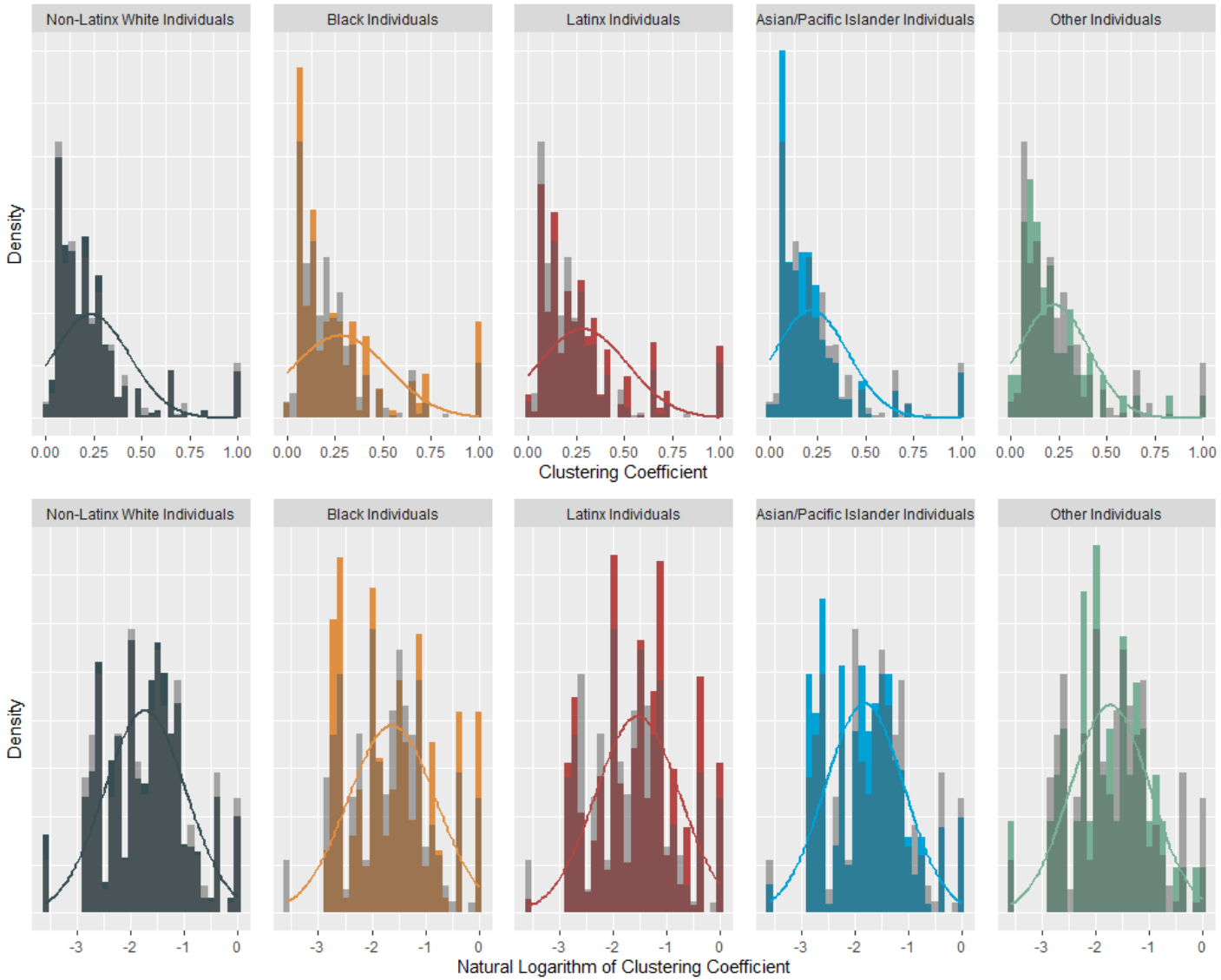
Table 3.2 Provider Network Characteristics Stratified by Beneficiary Race and Ethnicity											
Beneficiary Race and Ethnicity	**Sample Size**	**Repeat-Tie Fraction >0**		**Normalized Degree Centrality**		**Log-Transformed Normalized Degree Centrality**		**Clustering Coefficient**		**Log-Transformed Clustering Coefficient**	
	N	**n**	**%**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Non-Latinx White Patients	1,244	836	67.2	0.019	0.015	-4.321	0.875	0.233	0.200	-1.732	0.759
Black Patients	204	148	72.6	0.017	0.015	-4.478	1.006	0.275	0.253	-1.629	0.820
Latinx Patients	440	319	72.5	0.015	0.014	-4.589	0.904	0.278	0.228	-1.556	0.775
Asian Patients	331	207	62.5	0.021	0.017	-4.242	0.896	0.215	0.193	-1.814	0.735
Other Patients	70	44	62.9	0.017	0.014	-4.398	0.887	0.223	0.184	-1.736	0.741

Figure 3.6 Histograms with Normal Curves of Degree Centrality and Log-Transformed Degree Centrality, Stratified by Beneficiary Race and Ethnicity



Grey overlaid histogram represents distribution for entire cohort.

Figure 3.7 Histograms with Normal Curves of Clustering Coefficient and Log-Transformed Clustering Coefficient, Stratified by Beneficiary Race and Ethnicity



Grey overlaid histogram represents distribution for entire cohort.

Table 3.3 Logistic Regression Models Examining Association between Beneficiary Race & Ethnicity and Surgeon Repeat-Tie Fraction

Beneficiary Race & Ethnicity	Repeat-Tie Fraction >0					
	Unadjusted Model		Partially Adjusted Model*		Fully Adjusted Model**	
	OR	95% CI	OR	95% CI	OR	95% CI
Non-Latinx White Patients	Reference		Reference		Reference	
Black Patients	1.29	0.39 to 1.79	1.23	0.87 to 1.73	1.25	0.89 to 1.76
Latinx Patients	1.29	1.01 to 1.64	1.16	0.89 to 1.51	1.16	0.89 to 1.52
Asian/Pacific Islander Patients	0.82	0.63 to 1.05	0.74	0.57 to 0.98	0.75	0.57 to 0.99
Other Patients	0.83	0.50 to 1.36	0.81	0.49 to 1.34	0.80	0.48 to 1.32

*Partially adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility and eligibility for Part D low-income subsidies.
**Fully adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility, eligibility for Part D low-income subsidies Charlson Comorbidity Index score, and glaucoma disease severity.

Table 3.4 Linear Regression Models Examining Association between Beneficiary Race & Ethnicity and Surgeon Log-Transformed Normalized Degree Centrality

Beneficiary Race & Ethnicity	Log-Transformed Normalized Degree Centrality					
	Unadjusted Model		Partially Adjusted Model*		Fully Adjusted Model**	
	e^{β}	95% CI	e^{β}	95% CI	e^{β}	95% CI
Non-Latinx White Patients	Reference		Reference		Reference	
Black Patients	0.85	0.75 to 0.98	0.90	0.79 to 1.04	0.90	0.78 to 1.03
Latinx Patients	0.76	0.69 to 0.84	0.83	0.74 to 0.92	0.83	0.74 to 0.92
Asian/Pacific Islander Patients	1.08	0.97 to 1.21	1.16	1.03 to 1.30	1.16	1.03 to 1.30
Other Patients	0.93	0.75 to 1.15	0.97	0.78 to 1.20	0.97	0.78 to 1.21

*Partially adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility and eligibility for Part D low-income subsidies.
**Fully adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility, eligibility for Part D low-income subsidies Charlson Comorbidity Index score, and glaucoma disease severity.

Table 3.5 Linear Regression Models Examining Association between Beneficiary Race & Ethnicity and Surgeon Log-Transformed Clustering Coefficient

Beneficiary Race & Ethnicity	Log-Transformed Normalized Clustering Coefficient					
	Unadjusted Model		Partially Adjusted Model*		Fully Adjusted Model**	
	e^{β}	95% CI	e^{β}	95% CI	e^{β}	95% CI
Non-Latinx White Patients	Reference		Reference		Reference	
Black Patients	1.11	0.99 to 1.24	1.09	0.97 to 1.22	1.09	0.97 to 1.23
Latinx Patients	1.19	1.10 to 1.30	1.16	1.06 to 1.28	1.17	1.06 to 1.27
Asian/Pacific Islander Patients	0.92	0.84 to 1.01	0.90	0.82 to 0.99	0.91	0.82 to 0.99
Other Patients	1.00	0.83 to 1.20	0.98	0.81 to 1.18	1.00	0.83 to 1.20

*Partially adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility and eligibility for Part D low-income subsidies.
**Fully adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility, eligibility for Part D low-income subsidies Charlson Comorbidity Index score, and glaucoma disease severity.

Table 3.6 Cox Proportional Hazards Regressions Examining Risk of Glaucoma Surgical Failure by Surgeon Network Characteristics

Network Characteristic	Interval	Unadjusted Model		Partially Adjusted Model*		Fully Adjusted Model**	
		HR	95% CI	HR	95% CI	HR	95% CI
Repeat-Tie Fraction	>0 vs. 0	1.08	0.81 to 1.44	1.08	0.81 to 1.46	1.09	0.81 to 1.47
Log-Transformed Normalized Degree Centrality	1 unit increase	0.99	0.84 to 1.16	1.00	0.85 to 1.18	1.01	0.86 to 1.19
Log-Transformed Clustering Coefficient	1 unit increase	0.95	0.79 to 1.14	0.95	0.78 to 1.14	0.94	0.78 to 1.14

*Partially adjusted model controls for beneficiary race and ethnicity, eligibility for dual-Medicaid eligibility and eligibility for Part D low-income subsidies.

**Fully adjusted model controls for age, sex, eligibility for dual-Medicaid eligibility, eligibility for Part D low-income subsidies Charlson Comorbidity Index score, and glaucoma disease severity.

Table 3.7 Cox Proportional Hazards Regressions Examining Risk of Glaucoma Surgical Failure by Quartile of Surgeon Network Characteristics

Network Characteristic	Quartile	Unadjusted Model		Partially Adjusted Model*		Fully Adjusted Model**	
		HR	95% CI	HR	95% CI	HR	95% CI
Repeat-Tie Fraction	Quartile 1	Reference		Reference		Reference	
	Quartile 2	1.27	0.88 to 1.85	1.30	0.90 to 1.90	1.30	0.90 to 1.90
	Quartile 3	0.96	0.66 to 1.41	0.94	0.64 to 1.39	0.94	0.64 to 1.39
	Quartile 4	1.02	0.70 to 1.47	1.02	0.70 to 1.49	1.02	0.70 to 1.49
Normalized Degree Centrality	Quartile 1	Reference		Reference		Reference	
	Quartile 2	1.07	0.77 to 1.47	1.13	0.80 to 1.60	1.13	0.80 to 1.61
	Quartile 3	1.00	0.71 to 1.42	1.02	0.69 to 1.49	1.03	0.70 to 1.50
	Quartile 4	0.84	0.55 to 1.27	0.87	0.55 to 1.38	0.88	0.55 to 1.40
Clustering Coefficient	Quartile 1	Reference		Reference		Reference	
	Quartile 2	1.15	0.74 to 1.80	1.16	0.73 to 1.83	1.15	0.73 to 1.82
	Quartile 3	0.96	0.62 to 1.48	0.96	0.62 to 1.49	0.94	0.60 to 1.47
	Quartile 4	1.03	0.68 to 1.57	1.03	0.67 to 1.58	1.02	0.66 to 1.56

Chapter 4: Socioeconomic status mediates and modifies racial and ethnic disparities in incisional glaucoma surgical outcomes

4.1 Abstract

Purpose: To estimate the proportion of the racial and ethnic disparity observed in glaucoma surgical outcomes that can be eliminated by theoretically intervening on socioeconomic status (SES) on a national and statewide scale.

Methods: Two retrospective cohorts were constructed using: (a) a nationally-representative 20% random sample of 2016-2018 United States (US) Medicare fee-for-service beneficiaries and (b) the entire population of 2016-2018 California (CA) fee-for-service Medicare beneficiaries with a claim for incisional glaucoma surgery (trabeculectomy, tube shunt, or EX-PRESS shunt). Exclusion criteria were: residence outside of CA, age ≤64 years, or missing eye laterality modifier code. The primary exposure was race and ethnicity, stratified into: Non-Latinx White, Black, Latinx, Asian, and Other. The SES mediator was dichotomized to low vs. non-low based on dual-eligibility for Medicaid coverage. Time to failure event was defined as having a claim for a glaucoma surgery reoperation event. Follow-up time extended through 2019. Time-to-event was modeled using Cox proportional hazards with age and sex as covariates. The total effect (TE) estimated the entire racial and ethnic disparity on surgical failure. The controlled direct effect (CDE) estimated the remaining disparity after fixing SES to non-low for all, and the proportion eliminated (PE) estimated the proportion of the disparity eliminated after uniform assignment of SES to non-low for all.

Results: The final analytical sample included a total of 12,366 unique US beneficiaries for the US cohort and 5,985 unique CA beneficiaries for the CA cohort. In the US cohort, after uniformly assigning SES to non-low for the entire sample for CDE estimates, there remained significant

racial and ethnic disparities in glaucoma surgical failure for Black patients (CDE: 1.42, 95% CI: 1.23 to 1.65), Latinx patients (CDE: 1.36, 95% CI: 1.06 to 1.74), and Asian/Pacific Islander patients (CDE: 1.52, 95% CI: 1.11 to 2.08), with correspondingly minimal PE estimates. For the CA cohort, the racial and ethnic disparity for Black patients dissipated after uniform assignment of non-low SES (TE: 1.22, 95% CI: 0.97 to 1.55; CDE: 1.01, 95% CI: 0.84 to 1.37). The PE estimates suggest that theoretically intervening on SES would eliminate 97% of the disparity for Black patients in CA (PE: 0.97, 95% CI: -0.43 to 2.37).

Conclusions: Our results demonstrated that SES mediates racial and ethnic disparities in glaucoma surgical outcomes, though by varying amounts by individual racial and ethnic group. Furthermore, SES mediation of racial and ethnic disparities in glaucoma surgical outcomes is itself modified by local geographic regions and social contexts. Further studies are necessary to examine other mediating paths that may explain racial and ethnic disparities in glaucoma outcomes and in varying geographic and social environments.

4.2 Introduction

It is imperative to understand and recognize that the study and identification of racial and ethnic disparities in health outcomes are not immutable facts but are rather injustices that require intervention.[163] Racial and ethnic disparities in glaucoma surgical outcomes may potentially be ameliorated by intervening on important downstream intermediate or mediating factors that contribute to the disparity in failure rates for glaucoma surgery. One such potentially modifiable factor is an individual's SES. Recent studies have found that patients with glaucoma who have lower income and education levels had poorer visit adherence to seeing eye care providers;[164] furthermore, racially- and ethnically-minoritized glaucoma patients (who themselves were more likely to have lower income and lower educational attainment than non-Latinx White patients) were also more likely to report difficulty affording medications.[165]

Most epidemiologic studies examining racial and ethnic disparities in glaucoma account for SES by modeling it as a confounder and/or effect measure modifier.[36,162,165] However, treating SES as a confounder for racial and ethnic disparities in glaucoma outcomes presumes that SES is a common cause for both race and ethnicity and glaucoma surgical outcomes. Instead, we hypothesize that race and ethnicity may at least in part determine SES measures, thereby defining SES measures as potential mediators in the causal pathway for racial and ethnic disparities in glaucoma surgical outcomes (Figure 4.1).

In the last decade, methods in causal inference utilizing counterfactual approaches premised on a potential outcomes framework have uncovered limitations of previous analytical approaches to mediation analysis while proposing new methods for causal mediation analysis. These methods in causal mediation analysis allow for the examination of potential important downstream mediating factors that may contribute to racial and ethnic disparities in glaucoma

surgical outcomes without introducing bias. Thus, the purpose of this study was twofold: (1) first, to examine the racial and ethnic disparity that remains after uniform assignment of the SES mediator, a measure known as the controlled direct effect, and (2) second, to examine the proportion of the total racial and ethnic disparity that can be eliminated after uniform assignment of SES to all patients in the sample, a measure known as the proportion eliminated. We explored these aims in: (1) a nationally-representative cohort of US Medicare beneficiaries and (2) a statewide-representative cohort of CA Medicare beneficiaries to examine the causal mediation estimates from both national and statewide perspectives.

4.3 Methods

4.3.1 Study Population

The two study populations were drawn from: (a) a 20% representative sample of all Medicare beneficiaries with fee-for-service coverage of Medicare Parts A and B and (b) all California (CA) Medicare beneficiaries with fee-for-service coverage of Medicare Parts A and B, provided by the US Centers for Medicare and Medicaid Services (CMS). Two retrospective cohorts of all US and CA Medicare beneficiaries with a claim for incisional glaucoma surgery, including trabeculectomy (all techniques), tube shunt (any model), or Ex-PRESS® shunt (Alcon Laboratories, Fort Worth, TX), from 2016 through 2018 was constructed with the MBSF and the Standard Analytic Files (SAF) of Part B Carrier Claim files provided by CMS. Claims filed for incisional glaucoma surgeries were identified by billing codes for diagnostic and therapeutic procedures using Current Procedural Terminology 4 (CPT-4). If a beneficiary had multiple claims for incisional glaucoma surgery during the index period (2016-2018), then the earliest procedure defined the index surgery, index surgery date, and index eye. Only one eye per patient was included

to preserve independence of observations. Beneficiaries with the following characteristics were excluded: age less than 65 years in 2016 or age 66 years or less in 2017 or 2018, residence outside of the 50 states of the US or the District of Columbia, and lack of Medicare Part A and Part B coverage. Exclusion criteria for age varied in 2016 (65 years) versus 2017 and 2018 (66 years) to ensure beneficiaries who received incisional surgery in 2017 or 2018 did not receive surgery in the immediately preceding year. Beneficiaries were also excluded if they did not have an International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code for any glaucoma associated with the claim for index incisional glaucoma surgery or if they have a missing laterality modifier for the index eye in the claims data for the index incisional glaucoma surgery. Finally, beneficiaries were also excluded if they did not contribute any follow-up time (i.e., they had no eye-related visits or failure events following their index incisional glaucoma surgery).

4.3.2 Exposure and covariate definitions

Race and ethnicity were the primary exposure for this study. The Research Triangle Institute (RTI) race and ethnicity variable was used given its greater level of agreement with self-reported race and ethnicity and higher sensitivity for identifying Asian/Pacific Islander and Latinx individuals.[89] The RTI race and ethnicity variable has the following coded values: Unknown, Non-Hispanic White, Black (or African-American), Other, Asian/Pacific Islander/Pacific Islander, Hispanic, and American Indian/Alaska Native. Given anticipated issues with small sample sizes, the race and ethnicity variable were aggregated into the following categories for the present analysis: Non-Latinx White, Black, Latinx, Asian/Pacific Islander/Pacific Islander, and Other (with the Other category including Unknown, American Indian/Alaska Native, and Other race and ethnicity groups). Currently, data from Medicare do not separate multiracial beneficiaries.[111]

Demographic variables that were examined during the index glaucoma surgery year (2016-2018) included age and sex. Age was analyzed as a categorical variable, beginning at 65 years, and binned into five-year age groups that truncated at age 90 years or greater. Beneficiary sex was categorized as male, female, and unknown, which was self-identified by applicants to Social Security.[112] For purposes of reporting descriptive distributions, US region of residence was extracted and categorized into the following groups: East, West, Midwest, and South. However, the individual US state of residence was used in all multivariable regression models.

The SES mediator variable was constructed from a set of variables that specify Medicare-Medicaid dual eligibility by calendar month throughout the coverage year in the fee-for-service MBSF. These variables specifically indicate coverage for beneficiaries entitled to Medicare (Part A and/or B benefits) and eligibility for some category of Medicaid benefits in the month (i.e., dual eligibility). A variable for dual Medicare-Medicaid eligibility was constructed from a source variable that codes the number of months where the beneficiary had dual eligibility.[113] A dichotomous yes/no variable was created based on whether the beneficiary had at least one month of dual eligibility during the index surgery year.

4.3.3 Outcome definition

The primary outcome was time to failure of index incisional glaucoma surgery, defined as new glaucoma surgical reintervention (e.g., trabeculectomy, tube shunt placement, Ex-PRESS® shunt placement, iStent® placement, XEN® Gel Stent placement, Hydrus® microstent placement, cyclophotocoagulation, canaloplasty, goniotomy, trabeculotomy, and trabeculoplasty). Start of follow-up time for each beneficiary began on the date of the index incisional glaucoma surgery during 2016-2018. Given that entry into the cohort could occur at any point during the index period (2016-2018), staggered entries or left censoring was permitted. Furthermore, censoring due to

other endpoints was permitted, including death or loss of continuous Medicare Part A or Part B coverage. Time was assessed as duration of follow-up, measured as the time since the date of the index incisional glaucoma surgery to the primary outcome or secondary outcome or a censoring event.

Beneficiaries were assessed to ensure they continued to meet inclusion criteria at each year of follow-up (2016-2019). Beneficiaries were right censored if they died, lost continuous Part A or Part B coverage, or: (a) if their residence changed to one outside of the 50 US states and the District of Columbia for the US cohort or (b) if their residence changed to one outside of CA for the CA cohort. For beneficiaries who died, their censorship date was assigned as their death date found in the MBSF. For beneficiaries who lost continuous Part A or Part B coverage or whose residence changed to outside of the 50 US states and the District of Columbia for the US cohort or outside of CA for the CA cohort, their censorship date was assigned as December 31st of the previous year during which the beneficiary retained continuous enrollment. Administrative censoring for all beneficiaries who survived without index incisional glaucoma surgical failure occurred at the date of the last claim date with an eye visit CPT code (92004, 92014, 92002, 92012, 99212, 99024) filed by an ophthalmologist, optometrist, or ambulatory surgical center, identified by the CMS provider specialty code (18, 41, 49), occurring on or before December 31, 2019. Differential follow-up was permitted, with those who received index incisional glaucoma surgery in 2016 having a maximum of four years of follow-up, those who received index surgery in 2017 having a maximum of three years of follow-up, and those who received index surgery in 2018 having a maximum of two years of follow-up.

4.3.4 Causal Mediation Analysis

The potential population impact of intervening on these mediators can be validly evaluated using observational data when certain conditions are met.[133] Utilizing standard stratification-based approaches sometimes entail examining racial and ethnic disparities after controlling for potential mediators; however, standard regression adjustment or restriction may overestimate or underestimate the potential impact of race and ethnicity on the outcome by introducing bias due to the presence of common causes of the mediator and outcome, resulting in collider-stratification bias when the mediator is controlled for via restriction or standard regression adjustment (Figure 4.1).[133-135]

In mediation analysis where race and ethnicity is the primary exposure, the total effect (TE) can be decomposed into a direct effect, an indirect effect, and an interactive effect between the race and ethnicity exposure and the mediator.[166] The controlled direct effect (CDE) refers to the effect that race and ethnicity has on the outcome if everyone in the sample were uniformly assigned a specific level for the SES mediator of interest or the distribution of the SES mediator of interest were intervened upon.[133] The TE and CDE can then be used to estimate the proportion eliminated (PE), which represents the proportion of the TE that could be eliminated through either uniform assignment of the mediator or intervening on the distribution of the mediator.[133] Thus, the CDE and PE help to quantify the impact of interventions targeted at the SES mediator between race and ethnicity and the glaucoma surgical outcomes; furthermore, these mediators such as SES by definition contribute to racial and ethnic disparities in the outcome and are more likely to be more amenable to intervention than the primary race and ethnicity exposure variable. For the sake of real-world interventions, it is not realistic to assign the level or distribution of the mediator to be identical for an entire population. However, the PE from such an intervention is still helpful from

a health policy and public health perspective given that it represents an upper bound for the potential impact of the intervention under investigation.[133] Within this framework, the TE represents the racial and ethnic disparity that exists before theoretically intervening on a potential mediator; the CDE represents the remaining racial/ethnic disparity that exists after intervening on the potential mediator; and the PE represents the proportion of the racial/ethnic disparity that is eliminated by intervening on the potential mediator.[133,167]

In the case that the SES potential mediator under investigation is in actuality found to not act as a mediator between race and ethnicity and the glaucoma surgical outcome by means of race and ethnicity not being a parent of the SES mediator, there may still be an interaction between race and ethnicity and SES in how they affect the outcome, which still makes estimation of the CDE and PE a worthwhile exercise.[166] However, in this scenario, the PE will not necessarily fall between 0 and 1 (despite being referred to as a "proportion") because of the interaction between the race and ethnicity exposure and the potential mediator on the outcome.[168] Furthermore, investigation of potential mediators should be driven by the conceptual model underlying the presumed data-generating process rather than relying on the empirical approach involving the assessment of statistically significant associations between race and ethnicity and the potential mediator given that lack of such association may be due to lack of adequate power rather than a true absence of mediation.[133]

The following criteria must be met to appropriately estimate the CDE and the PE: (1) the assumptions of exchangeability and positivity must hold for the exposure, the potential mediator, and the selection mechanism that generated the analytical sample, (2) all fitted regression models must be correctly specified, (3) measurement error must not be present, and (4) the exposure, potential mediator, and the selection mechanism must be well-defined.[134,169,170] And to achieve

exchangeability, there must be no unmeasured confounding of the exposure-outcome relationship or the potential mediator-outcome relationship, and no unmeasured sources of selection bias.[133] And in order for positivity to hold, there must be a nonzero probability of each racial/ethnic group within every observed combination of the confounders and there must be a nonzero probability of each level of the potential mediator within every observed combination of the relevant confounders and the race and ethnicity exposure.[133]

A potential outcomes framework can be used to define the TE, CDE, and PE. Let R be race and ethnicity, Y the glaucoma surgical outcome, M the potential SES mediator, and C the additional covariates. For the identification of the TE, there are two assumptions that must hold: (1) the consistency assumption,[171] which states that amongst subjects with observed race and ethnicity $R = r$, the observed outcome Y is equal to the potential outcome $Y(r)$ (i.e., $Y(a) = Y$ when $R = r$) and (2) the no unmeasured confounders assumption,[171] which states that subjects with different observed races and ethnicities R, but the same confounder characteristics C, are compatible in the sense that

$$Y(r) \perp\!\!\!\perp R \mid C$$

for all race and ethnicity groups r. Both of these assumptions together are sufficient for identifying the conditional TE as:

$$\begin{aligned} & E[Y(r) - Y(r^*)|C] \\ & = E[Y(r)|C] - E[Y(r^*)|C] \\ & = E[Y(r)|R = r, C] - E[Y(r^*)|A = r^*, C] \\ & = E[Y|R = r, C] - E[Y|R = r^*, C] \end{aligned}$$

In order to estimate the CDE, the consistency assumption must again hold, but this time as the consistency assumption for race and ethnicity and the mediator on the outcome (such that amongst

the subgroup with observed race and ethnicity $R = r$ and observed mediator $M = m$, the observed outcome Y is equal to $Y(a, m)$) and the consistency assumption for the effect of the exposure on the mediator (such that amongst the subgroup with observed race and ethnicity $R = r$ the observed mediator M is equal to $M(a)$.[171] Furthermore, the assumption of no-unmeasured-confounders for the exposure-outcome relationship must again hold,

$$Y(r, m) \perp\!\!\!\perp R \mid C$$

However, to estimate CDE, stronger conditions for identification are required than for estimating TE because the CDE requires assessment of the effect of holding the mediator M fixed, which requires that all confounders of the association between mediator and outcome must be controlled,

$$Y(r, m) \perp\!\!\!\perp M \mid R, C$$

Thus, as long as the aforementioned assumptions hold, then the CDE can be identified by

$$\begin{aligned} & E[Y(r, m) - Y(r^*, m) | C] \\ & = E[Y(r, m) | C] - E[Y(r^*, m) | C] \\ & = E[Y(r, m) | R = r, M = m, C] - E[Y(r^*, m) | R = r^*, M = m, C] \\ & = E[Y | R = r, M = m, C] - E[Y | R = r^*, M = m, C] \end{aligned}$$

The PE, which again represents the proportion of the effect of race and ethnicity on the outcome that could be eliminated by intervening to set the mediator to some fixed level of m, can be estimated, on the difference scale, by

$$PE = \frac{TE - CDE}{TE}$$

Which represents the difference between the TE and the CDE fixing the SES mediator to level m (which measures the extent of the effect that is eliminated by fixing the SES mediator to level m) divided by the TE, to obtain a proportion. Of note, and as alluded to previously, the presence of an

interaction between race and ethnicity and the SES mediator may cause there to be a different PE for every value of m.[172]

The same principles hold for causal mediation analysis with survival data. In this case, we can let T_r denote the value of the time-to-event outcome observed when race and ethnicity R is set to r, and let M_r denote the value of the SES mediator observed when race and ethnicity R is set to r. Finally, T_{rm} would denote the value of the time-to-event outcome that would be observed had race and ethnicity R been set to r, and had the SES mediator M been set to m. As before, as long as the consistency assumption and the no unmeasured confounding assumption hold, then we can identify the conditional TE as:

$$\begin{aligned} & E[T(r)/T(r^*)|C] \\ & = E[T(r)|C]/E[T(r^*)|C] \\ & = E[T(r)|R = r, C]/E[T(r^*)|R = r^*, C] \\ & = E[T|R = r, C]/E[Y|R = r^*, C] \end{aligned}$$

In this case, the CDE comparing race and ethnicity r to r^* and fixing the mediator to level m on the mean survival time ratio scale is defined by:

$$CDE_{r,r^*}(m) = \frac{E[T_{rm}]}{E[T_{r^*m}]}$$

And the CDE within strata of $C = c$ is then defined by:

$$CDE_{r,r^*|c}(m) = \frac{E[T_{rm}|c]}{E[T_{r^*m}|c]}$$

Finally, for an arbitrary time-to-event variable V, let $\lambda v(t)$ and $\lambda v(t|c)$ denote the hazard and hazard conditional on covariates c at time t, or the instantaneous rate of the event conditional on $V \geq t$.[173] The causal effects can also be defined on the hazard ratio scale replacing $E[\cdot]$ with $\lambda[\cdot]$.

With M as a binary mediator following a logistic model with R as the race and ethnicity exposure and with C as additional covariates, we can define the mediator regression as:

$$logit[P(M = 1|r, c)] = \beta_0 + \beta_1 r + \beta_2' c$$

And we can define the outcome model as Cox proportional hazard:[173]

$$\lambda_T(t|r, m, c) = \lambda_T(t|0,0,0)e^{\gamma 1 r + \gamma 2 m + \gamma 3 rm + \gamma' 4 c}$$

If the assumption of no unmeasured confounding holds and the models for the continuous mediator and for the outcome are correctly specified, and Cox regression is employed the CDE can be defined as:[173]

$$\frac{\lambda_{T_{rm}}(t|c)}{\lambda_{T_{r^* m}}(t|c)} = e^{(\gamma 1 + \gamma 3 m)(r - r^*)}$$

And on the ratio scale, the PE is defined as follows:[172]

$$PE(m) = \frac{HR^{TE} - HR^{CDE}(m)}{HR^{TE} - 1}$$

Figure 4.2 depicts a directed acyclic graph 1 (DAG 1) representing the a priori assumptions behind the data-generating process for this study. Race and ethnicity are the primary exposure, with a presumed direct causal arrow to glaucoma surgical failure along with an indirect causal arrow through the SES mediator. Of note, DAG 1 in Figure 4.2 also includes a node labeled H, which represents an unmeasured confounder that is a common cause for race and ethnicity, SES, age, sex, and state of residence. This comes from the work of Jackson, who proposes that the racial and ethnic disparities observed with respect to SES, sex differences in life expectancy, and other inequities by race and ethnicity that persist to the present day are due to remnants of historical racism (e.g., slavery, Jim Crow laws, historical redlining practices, etc.). Although this H node is a mediator-outcome confounder, this backdoor path can be closed by conditioning on age and sex, as demonstrated in DAG 1. However, some may still raise concerns that this H node represents an

open backdoor path that confounds the exposure-mediator relationship, which would violate the assumptions to achieve conditional exchangeability for estimation of natural effects. Of note, the no-confounding assumption for the exposure-mediator relationship is not necessary to estimate the CDE. Nevertheless, to address these concerns, Supplementary Figure 4.1 presents a modified DAG 2 that combines the H and race and ethnicity nodes into a single racism node. We felt this was a fair transformation given that the H node in DAG 1 represents remnants of historical racism that cause present-day racial and ethnic disparities. In the simplified DAG 2, the no-confounding assumptions for the exposure-mediator, mediator-outcome, and exposure-outcome relationships are held after controlling for age and sex. In DAG 2, it is presumed that age, sex, and state of residence impact racism, and experiences of racism can impact SES.

The CMAverse package for R developed by Valeri and colleagues was used for reproducible causal mediation analysis.[174] Using the CMAverse package, we used the regression-based approach to estimate the TE, CDE, and the PE. The CDE was estimated via uniform assignment of non-low SES to the entire sample. Exposure-mediator interaction (i.e., effect measure modification of the racial and ethnic disparity by SES status) was specified in the regression models. The outcome regression had race and ethnicity as the exposure and conditioned on SES, age, sex, state of residence (for US cohort only), cohort year, and a race and ethnicity * SES interaction term. The mediator regression model was a logistic regression model with race and ethnicity as the exposure, SES as the outcome, and age, sex, state of residence (for US cohort only), and cohort year as covariates. Standard errors of the causal effects were obtained by the delta method, and confidence intervals were constructed by normal distribution approximation. Finally, a sensitivity analysis was also performed to estimate the causal effects using a more expansive definition of glaucoma surgical failure (reoperation with additional glaucoma surgery

procedure or revision of index glaucoma surgery) in both the US and CA cohorts to determine whether SES mediation of racial and ethnic disparities in surgical outcomes change by definition of surgical failure.

4.4 Results

4.4.1 Baseline Cohort Characteristics

Distributions of sociodemographic and clinical characteristics for the US cohort are presented in Table 4.1. The final analytical sample included a total of 12,366 unique US beneficiaries. The largest racial and ethnic stratum was the non-Latinx White subgroup (n=8,510; 68.8%), followed by the Black subgroup (n=2,273; 18.4%), the Latinx subgroup (n=887; 7.2%), the Asian/Pacific Islander subgroup (n=409; 3.3%), and the Other race and ethnicity subgroup (n=287; 2.3%). Most beneficiaries identified as female sex (n=6,891; 55.7%) and did not qualify for dual-Medicaid coverage (n=10,491; 84.8%). A plurality of beneficiaries was between 70-79 years old (n=5,580; 45.1%) and resided in the eastern US (n=5,542; 44.8%).

Table 4.2 presents the distributions of sociodemographic and clinical characteristics for the CA cohort. The final analytical sample included a total of 5,985 unique CA beneficiaries. The largest racial and ethnic stratum was the non-Latinx White subgroup (n=3,122; 52.2%), followed by the Latinx subgroup (n=1,180; 19.7%), the Asian/Pacific Islander subgroup (n=887; 14.8%), the Black subgroup (n=574; 9.6%), and the Other race and ethnicity subgroup (n=222; 3.7%). Most beneficiaries identified as female sex (n=3,170; 53.0%) and did not qualify for dual-Medicaid coverage (n=4,040; 67.5%). A plurality of beneficiaries was between 70-79 years old (n=2,652; 44.3%).

4.4.2 Incidence Rate of Glaucoma Surgical Failure by Race and Ethnicity and SES

For the US cohort, there was a total of 1,590 incisional glaucoma surgical reoperation events among the 12,366 beneficiaries in the cohort, yielding a cumulative incidence of 12.9%. All beneficiaries in the US cohort contributed a total of 23,282 person-years of follow-up time at risk for the primary outcome. Thus, the overall incidence rate for incisional glaucoma surgical reoperation events was 6.8 per 100 person-years at risk for the US cohort (95% confidence interval [CI]: 6.5-7.2 reoperation events per 100 person-years). For the CA cohort, there was a total of 836 incisional glaucoma surgical reoperation events among the 5,985 beneficiaries in the cohort, yielding a cumulative incidence of 14.0%. All beneficiaries in the CA cohort contributed a total of 11,491 person-years of follow-up time at risk for the primary outcome. Thus, the overall incidence rate for incisional glaucoma surgical reoperation events was 7.3 per 100 person-years at risk for the CA cohort (95% CI: 6.8-7.8 reoperation events per 100 person-years).

Table 4.3 summarizes the crude incidence rates of glaucoma surgical failure stratified by SES for each racial and ethnic group for the US cohort. The incidence rates ranged from 5.99 reoperation events per 100 person-years at risk for non-low SES non-Latinx White patients (95% CI: 5.61 to 6.39) to 10.43 reoperation events per 100 person-years at risk for low SES Asian/Pacific Islander patients (95% CI: 7.26-14.50). Figure 4.3 is a visual presentation of the glaucoma reoperation incidence rate data by SES stratum for each racial and ethnic group for the US cohort in a forest plot. In general, for the US cohort, the incidence rate for glaucoma reoperation was higher for the low-SES stratum for each racial and ethnic subgroup. The only exception was the Black race and ethnicity group, where the glaucoma reoperation incidence rate was higher in the non-low SES Black patient group (incidence rate [IR]: 8.53, 95% CI: 7.53-9.63) than in the low SES Black patient group (IR: 7.45, 95% CI: 5.80 to 9.43).

Table 4.4 summarizes the crude incidence rates of glaucoma surgical failure stratified by SES for each racial and ethnic group for the CA cohort. The incidence rates ranged from 5.34 reoperation events per 100 person-years at risk for low SES non-Latinx White patients (95% CI: 3.85 to 7.21) to 11.04 reoperation events per 100 person-years at risk for low SES Black patients (95% CI: 7.99 to 14.87). Figure 4.4 is a visual presentation of the glaucoma reoperation incidence rate data by SES stratum for each racial and ethnic group for the CA cohort in a forest plot. In general, for the CA cohort, the incidence rate for glaucoma reoperation was lower for the low-SES stratum for each racial and ethnic subgroup. The exceptions were the Black and Other race and ethnicity group. For the Black subgroup, the glaucoma reoperation incidence rate was higher in the low SES Black patient group (IR: 11.04, 95% CI: 7.99 to 14.87) than in the non-low SES Black patient group (IR: 7.32, 95% CI: 5.36 to 9.76). For the Other race and ethnicity subgroup, the glaucoma reoperation incidence rates were similar in the low SES Other patient group (IR: 9.00, 95% CI: 4.65 to 15.72) and the non-low SES Other patient group (IR: 8.57, 95% CI: 5.54 to 12.65).

4.4.3 Estimates of Causal Effects

Estimates for TE, CDE, and the PE are presented in Table 4.5 for the US cohort. The TE estimates demonstrated increased risk of glaucoma surgical failure for Black patients (TE: 1.35, 95% CI: 1.18 to 1.56), Latinx patients (TE: 1.40, 95% CI: 1.16 to 1.68), and Asian/Pacific Islander patients (TE: 1.52, 95% CI: 1.18 to 1.95) compared to non-Latinx White patients after adjusting for age, sex, US state of residence, and cohort year. There was no increased risk of surgical failure for the other race and ethnicity subgroup (TE: 0.95, 95% CI: 0.66 to 1.35). After uniformly assigning SES to non-low for the entire sample for CDE estimates, there remained significant racial and ethnic disparities in glaucoma surgical failure for Black patients (CDE: 1.42, 95% CI: 1.23 to 1.65), Latinx patients (CDE: 1.36, 95% CI: 1.06 to 1.74), and Asian/Pacific Islander

patients (CDE: 1.52, 95% CI: 1.11 to 2.08). Finally, PE estimates suggest that theoretically intervening on SES and uniformly assigning it as non-low for the entire sample would eliminate 1% of the racial and ethnic disparity for Asian/Pacific Islander patients (PE: 0.01, 95% CI: -0.47 to 0.49) and 11% of the disparity for Latinx patients (PE: 0.11, 95% CI: -0.40 to 0.62).

Table 4.6 presents the estimates for TE, CDE, and the PE for the CA cohort. The TE estimates suggested increased risk of glaucoma surgical failure for Black patients (TE: 1.22, 95% CI: 0.97 to 1.55), Latinx patients (TE: 1.15, 95% CI: 0.96 to 1.38), and Asian/Pacific Islander patients (TE: 1.20, 95% CI: 0.99 to 1.45) and Other patients (TE: 1.26, 95% CI: 0.90 to 1.77) compared to non-Latinx White patients after adjusting for age, sex, US state of residence, and cohort year. After uniformly assigning SES to non-low for the entire sample for CDE estimates, racial and ethnic disparities in glaucoma surgical failure remained for Latinx patients (CDE: 1.16, 95% CI: 0.90 to 1.52), Asian/Pacific Islander patients (CDE: 1.21, 95% CI: 0.93 to 1.59), and Other patients (CDE: 1.24, 95% CI: 0.83 to 1.86). However, the racial and ethnic disparity for Black patients dissipated after uniform assignment of non-low SES (CDE: 1.01, 95% CI: 0.84 to 1.37). Finally, PE estimates suggest that theoretically intervening on SES and uniformly assigning it as non-low for the entire sample would eliminate 5% of the racial and ethnic disparity for Other race and ethnicity patients (PE: 0.05, 95% CI: -1.03 to 1.13) and 97% of the disparity for Black patients (PE: 0.97, 95% CI: -0.43 to 2.37).

A sensitivity analysis was performed to determine whether the causal effects remain the same for a broader definition of surgical failure including both glaucoma reoperation events and revision of index surgery. The results of this sensitivity analysis are presented in Supplementary Table 4.1 for the US cohort and Supplementary Table 4.2 for the CA cohort. The results of the

sensitivity analysis for the US cohort are similar to the primary analysis, with no significant reductions of racial and ethnic disparities after intervening on the SES mediator.

However, the results of the sensitivity analysis for the CA cohort differ somewhat from the primary analysis. The TE estimates demonstrated increased risk of glaucoma surgical failure (reoperation and revision events) for Black patients (TE: 1.18, 95% CI: 0.99 to 1.41), Latinx patients (TE: 1.23, 95% CI: 1.08 to 1.41), and Asian/Pacific Islander patients (TE: 1.18, 95% CI: 1.02 to 1.36) and Other patients (TE: 1.32, 95% CI: 1.03 to 1.70) compared to non-Latinx White patients after adjusting for age, sex, US state of residence, and cohort year. After uniformly assigning SES to non-low for the entire sample for CDE estimates, racial and ethnic disparities in glaucoma surgical failure (reoperation and revision events) dissipated for most groups, including Black patients (CDE: 1.01, 95% CI: 0.80 to 1.27), Latinx patients (CDE: 1.10, 95% CI: 0.90 to 1.35), and Other patients (CDE: 1.24, 95% CI: 0.91 to 1.68). The disparity for Asian/Pacific Islanders did not change significantly after intervening on SES (CDE: 1.21, 95% CI: 0.99 to 1.47). Finally, PE estimates suggest that theoretically intervening on SES and uniformly assigning it as non-low for the entire sample would eliminate 24% of the racial and ethnic disparity for Other race and ethnicity patients (PE: 0.24, 95% CI: -0.49 to 0.97), 54% of the disparity for Latinx patients (PE: 0.54, 95% CI: -0.25 to 1.33), and 96% of the disparity for Black patients (PE: 0.96, 95% CI: -0.27 to 2.19).

4.5 Discussion

In this retrospective cohort study utilizing methods in causal mediation analysis, we found that SES mediates and modifies racial and ethnic disparities in glaucoma surgical outcomes, though by varying amounts depending on the individual racial and ethnic group, the geographic

region of residence, and the definition of surgical failure. After theoretically intervening on SES and uniformly assigning it to non-low for the entire sample did not result in significant reductions in the disparity in reoperation events for Black patients on a nation-wide scale, though in CA, this disparity could be eliminated by as much as 97%. Similarly, though intervening on SES did not result in curbing disparities in reoperation or revision events for Latinx patients nationally, examination of this theoretical SES intervention in the state of CA resulted in elimination of as much as 54% of the disparity for Latinx patients.

Examination of incidence rates of glaucoma reoperation events stratified by SES for each racial and ethnic subgroup demonstrates differing trends when comparing the US cohort to the CA cohort. In the US cohort, patients in the low SES stratum tended to have higher incidence rates of surgical failure compared to those in the non-low stratum for each racial and ethnic subgroup. In the CA cohort, on the other hand, there tended to be greater parity in incidence rate of reoperation events. However, the Black patient subgroup remained the exception in both cohorts. In the US cohort, Black non-low SES patients surprisingly had increased crude incidence rates of reoperation events compared to Black low SES patients.

This mirrors the recent literature published on the well-documented Black-White gap in infant and maternal health published in recent years. A recent study published by the National Bureau of Economic Research combined income tax data with birth, death, and hospitalization records for all infants born to first-time mothers from 2007 to 2016 in CA.[175] In this study, authors found that infants born to parents with higher income levels had lower rates of mortality and similarly, mothers with higher income levels had lower rates of maternal mortality. However, there was one group that did not confer the same protection from higher levels of income: Black mothers and infants.[175] Study authors also found that mothers with higher income tended to be older and to

have twins (indicating use of fertility treatments), leading to increased risk of poor birth outcomes. But despite these risks, infants born to higher income parents were also more likely to survive their first month and first year of life, leading authors to note that pregnancies for higher income women "are not only the riskiest, but also the most protected."[175] However, this protection conferred by higher income did not extend to Black mothers. Instead, authors found that the highest-income Black women had maternal and infant mortality rates as high as rates among low-income White women.[175] We found a similar phenomenon in our present analysis, where higher-income Black patients had similar—if not higher—glaucoma failure incidence rates (IR: 8.53, 95% CI: 7.53 to 9.63) as lower-income non-Latinx White patients (IR: 7.18, 95% CI: 5.67 to 8.97). It is clear that the effects of racism on glaucoma surgical outcomes go beyond SES, with other factors, such as disparities in exposure to air pollution[6] or persistent disparities due to historical redlining[176] perhaps contributing to the racial and ethnic inequities observed.

Interestingly, however, our results also suggest that intervening on SES could potentially lead to the elimination of racial and ethnic disparities within a more local, statewide context in CA. Our sensitivity analysis demonstrated that uniformly assigning non-low SES to the entire sample eliminated 96% of the racial and ethnic disparity for Black patients, reducing their risk of reoperation and revision events from 18% increased risk (TE: 1.18, 95% CI: 0.99 to 1.41) to 1% increased risk (CDE: 1.01, 95% CI: 0.80 to 1.27) compared to non-Latinx White patients. Similarly, intervening on SES eliminated 54% of the disparity for Latinx patients, reducing their risk of reoperation and revision events from 23% increased risk (TE: 1.23, 95% CI: 1.08 to 1.41) to 10% increased risk (CDE: 1.10, 95% CI: 0.90 to 1.35) and also eliminated 24% of the disparity for Other race and ethnicity patients, reducing their risk from 32 increased risk (TE: 1.32, 95% CI: 1.03 to 1.70) to 24% increased risk (CDE: 1.24, 95% CI: 0.91 to 1.68). Thus, our data suggest that

racial and ethnic disparities in glaucoma surgical outcomes operate differently depending on the geographic and social context (i.e., modification by geographic region and social environment).

Other studies have utilized methods in causal mediation analysis to investigate SES measures as a mediator for racial and ethnic disparities in other health outcomes. A study in New Zealand by Blakely and colleagues demonstrated that reducing SES disparities between Māori and European individuals greatly reduced ethnic inequalities in mortality.[177] Their study benefited from far greater sample sizes given their outcome of interest was all-cause mortality and they only analyzed disparities for one particular ethnic subgroup. Nevertheless, we similarly found there to be significant reductions in racial and ethnic disparities in glaucoma surgical outcomes after reducing SES disparities, but particularly for Black, Latinx, and Other race and ethnicity patients in CA.

Guadamuz and colleagues similarly used causal mediation to examine the mediating effects of SES factors on racial disparities in the treatment of diffuse large B-cell lymphoma. They found that between 31% and 38% of racial and ethnic disparities in chemo- and/or immune-therapy treatment were mediated by having private Medicare supplementation, leading study authors to conclude that more equitable access to Medicare supplementation may reduce racial and ethnic disparities in treatment.[178] Though we did not have access to private Medicare supplementation information in our data, we did observe a similar finding among dual Medicare-Medicaid beneficiaries in CA, where incidence rates for reoperation events were lower for dual-coverage enrollees compared to Medicare-only beneficiaries for non-Latinx White, Latinx, and Asian/Pacific Islander patients. It may be that the additional insurance benefits provided to dual Medicare-Medicaid beneficiaries reduce barriers to access and allow for improved outcomes for glaucoma reoperation events among CA beneficiaries.

The present study has limitations which provide an important lens through which to interpret our results. First, although our study benefits from use of Big Data sources, drawing from Medicare administrative claims data from both national and statewide cohorts, our causal mediation analyses are nevertheless underpowered. Power analysis in mediation models was explored by Fritz and MacKinnon who demonstrated that very large sample sizes are required, particularly for detecting small mediating effects.[179] Additionally, our SES proxy variable provides a crude estimation based on whether the Medicare beneficiary additionally qualified for Medicaid benefits for at least one month during the year of index surgery. A more nuanced SES variable could provide a more sensitive and/or specific measure to better capture the mediating effect of SES on racial and ethnic disparities in glaucoma surgical outcomes. Finally, racial and ethnic disparities in glaucoma outcomes are inherently complex, and are likely mediated through many causal mediating paths, including social determinants of health.[180] Thus, it will be important to examine other mediating paths that may account for greater proportions of these racial and ethnic disparities. Furthermore, as with most observational studies, there remains the possibility of potential unmeasured confounders given the complicated nature of the confounding structure of racial and ethnic disparities.

In conclusion, this study demonstrated that SES mediation of racial and ethnic disparities in glaucoma surgical outcomes is itself modified by other factors, including local geographic social contexts varying definitions of surgical failure. It is likely that racial and ethnic disparities in surgical outcomes are mediated by a variety of mediating paths, including those mediated through social determinants of health. Future studies are needed to examine these other downstream mediating factors that represent modifiable targets to intervene upon to achieve equity in glaucoma outcomes. Furthermore, harmonization of large datasets incorporating clinical outcomes data with

information on social determinants of health are crucial to more adequately understand these mediators of racial and ethnic disparities in vision outcomes, while also informing the design and implementation of policies and interventions aimed to curb them.

4.6 Tables and Figures

Figure 4.1 Illustration of collider bias induced by conditioning on a mediator (adapted from Richiardi et al., 2013)

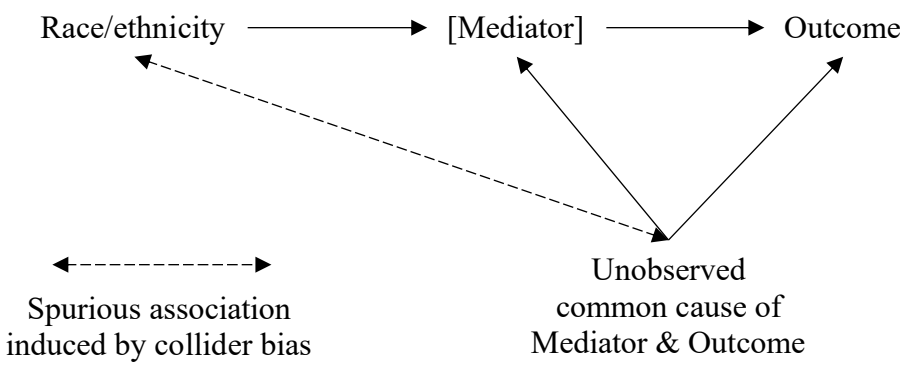
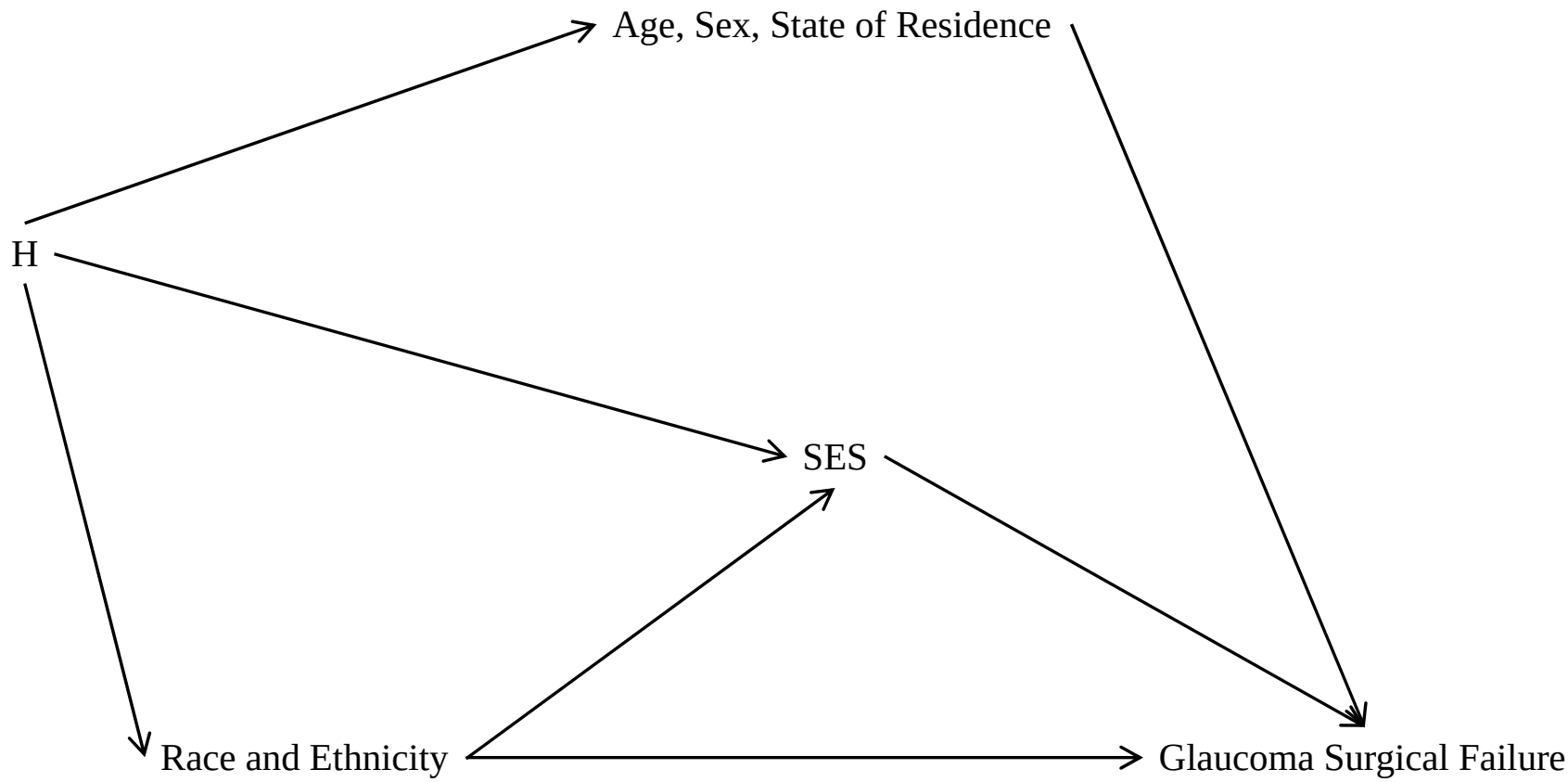


Figure 4.2 Directed Acyclic Graph 1 (DAG 1) summarizing assumptions behind data-generating process for this study.



H = remnants of historical racism (e.g., slavery, Jim Crow laws, discriminatory mortgage lending practices); SES = socioeconomic status

Table 4.1 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016-2018, 20% US Representative Sample												
	All Patients		**Non-Latinx White Patients**		**Black Patients**		**Latinx Patients**		**Asian/Pacific Islander Patients**		**Other Patients**	
	N=12,366		**N=8,510**		**N=2,273**		**N=887**		**N=409**		**N=287**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Age in years												
65-69	2,103	17.0	1,196	14.1	528	23.2	193	21.8	84	20.5	102	37.4
70-74	2,787	22.5	1,775	20.9	590	26.0	250	28.2	91	22.2	81	29.7
75-79	2,793	22.6	1,893	22.2	553	24.3	186	21.0	107	26.2	54	19.8
80-84	2,305	18.6	1,707	20.1	373	16.4	123	13.9	66	16.1	36	13.2
85-89	1,661	13.4	1,345	15.8	168	7.4	91	10.3	45	11.0	*	*
90+	717	5.8	594	7.0	61	2.7	44	5.0	16	3.9	*	*
Sex												
Male	5,475	44.3	3,619	42.5	1,070	47.1	416	46.9	211	51.6	159	55.4
Female	6,891	55.7	4,891	57.5	1,203	52.9	471	53.1	198	48.4	128	44.6
Dual Medicaid Eligibility												
Yes	1,875	15.2	618	7.3	573	25.2	435	49.0	183	44.7	66	23.0
No	10,491	84.8	7,892	92.7	1,700	74.8	452	51.0	226	55.3	221	77.0
Geographic Region												
East	5,542	44.8	3,753	44.1	1,255	55.2	294	33.1	122	29.8	118	41.1
West	2,358	19.1	1,524	17.9	193	8.5	336	37.9	219	53.5	86	30.0
Midwest	2,500	20.2	2,004	23.5	334	14.7	72	8.1	38	9.3	52	18.1
South	1,966	15.9	1,229	14.4	491	21.6	185	20.9	30	7.3	31	10.8
Year of index surgery												
2016	4,974	40.2	3,398	39.9	959	42.2	359	40.5	157	38.4	101	35.2
2017	4,130	33.4	2,854	33.5	721	31.7	310	34.9	142	34.7	103	35.9
2018	3,262	26.4	2,258	26.5	593	26.1	218	24.6	110	26.9	83	28.9

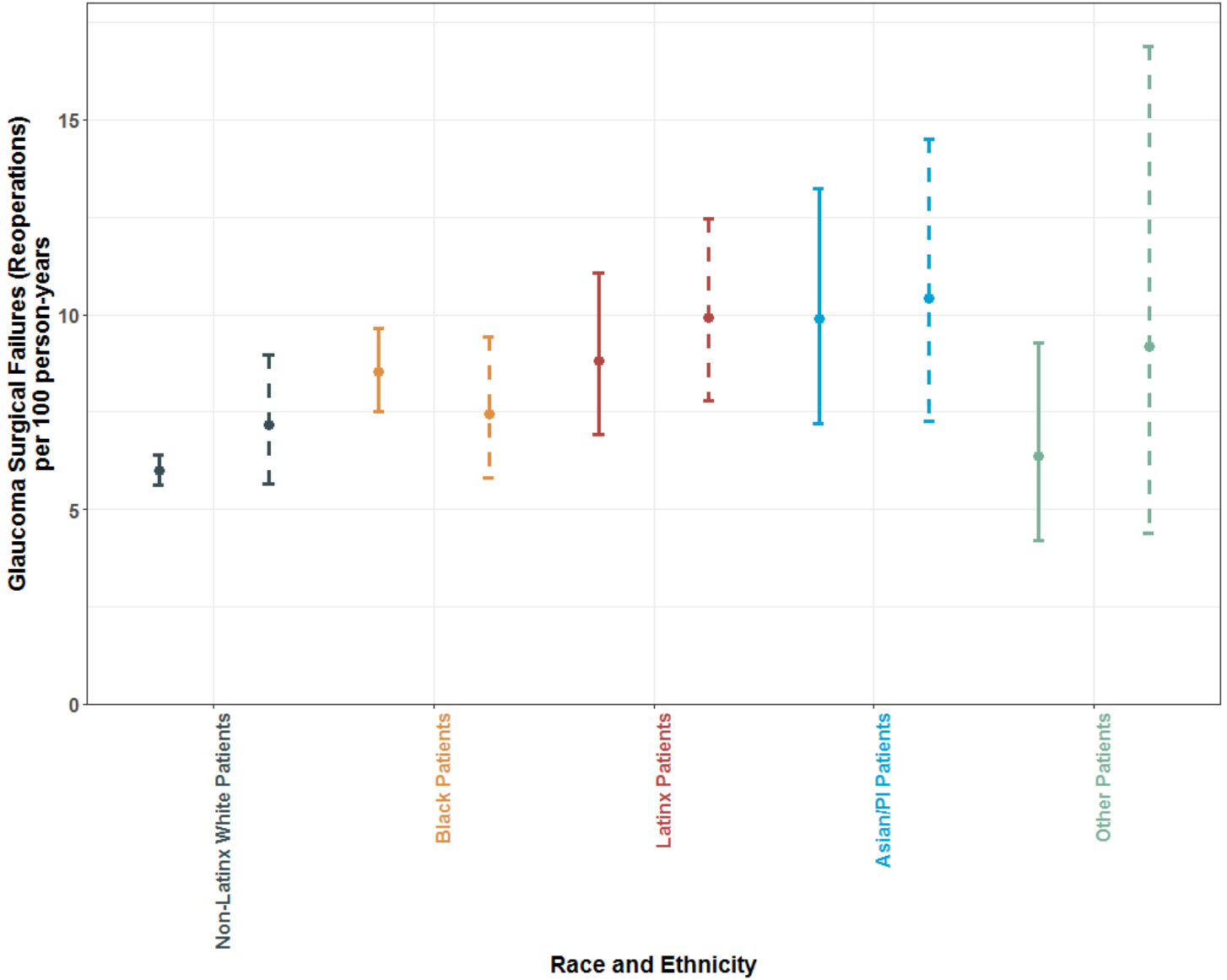
* Cannot report cell size due to confidentiality

Table 4.2 Baseline Demographic Cohort Characteristics, Medicare Beneficiaries who Received Index Incisional Glaucoma Surgery during 2016-2018, 20% CA Representative Sample												
	All Patients		**Non-Latinx White Patients**		**Black Patients**		**Latinx Patients**		**Asian/Pacific Islander Patients**		**Other Patients**	
	N=5,985		**N=3,122**		**N=574**		**N=1,180**		**N=887**		**N=222**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Age in years												
65-69	973	16.3	367	11.8	133	23.2	241	20.4	173	19.5	59	29.1
70-74	1,286	21.5	616	19.7	132	23.0	283	24.0	192	21.6	63	31.0
75-79	1,366	22.8	678	21.7	142	24.7	280	23.7	217	24.5	49	24.1
80-84	1,189	19.9	688	22.0	105	18.3	196	16.6	168	18.9	32	15.8
85-89	798	13.3	500	16.0	44	7.7	137	11.6	102	11.5	*	*
90+	373	6.2	273	8.7	18	3.1	43	3.6	35	3.9	*	*
Sex												
Male	2,815	47.0	1,437	46.0	289	50.3	520	44.1	451	50.8	118	53.2
Female	3,170	53.0	1,685	54.0	285	49.7	660	55.9	436	49.2	104	46.8
Dual Medicaid Eligibility												
Yes	1,945	32.5	411	13.2	225	39.2	735	62.3	495	55.8	79	35.6
No	4,040	67.5	2,711	86.8	349	60.8	445	37.7	392	44.2	143	64.4
Year of index surgery												
2016	2,380	39.8	1,287	41.2	214	37.3	464	39.3	343	38.7	72	32.4
2017	1,983	33.1	1,031	33.0	186	32.4	393	33.3	292	32.9	81	36.5
2018	1,622	27.1	804	25.8	174	30.3	323	27.4	252	28.4	69	31.1

* Cannot report cell size due to confidentiality

Table 4.3 Glaucoma surgical reoperation incidence rate, stratified by SES for each racial and ethnic group, US Cohort						
Racial and Ethnic Group	**SES stratum**	**Number of patients**	**Number of events**	**Person-years of follow-up**	**Incidence Rate**	**95% Confidence Interval**
Non-Latinx White Patients	**Non-low SES**	7,892	918	15,317	5.99	5.61 to 6.39
	Low SES	618	77	1,072	7.18	5.67 to 8.97
Black Patients	**Non-low SES**	1,700	261	3,060	8.53	7.53 to 9.63
	Low SES	573	69	926	7.45	5.80 to 9.43
Latinx Patients	**Non-low SES**	452	74	839	8.82	6.93 to 11.07
	Low SES	435	74	745	9.93	7.80 to 12.47
Asian/Pacific Islander Patients	**Non-low SES**	226	45	455	9.89	7.21 to 13.23
	Low SES	183	35	336	10.43	7.26 to 14.50
Other Patients	**Non-low SES**	221	27	423	6.38	4.20 to 9.28
	Low SES	66	10	109	9.17	4.40 to 16.87

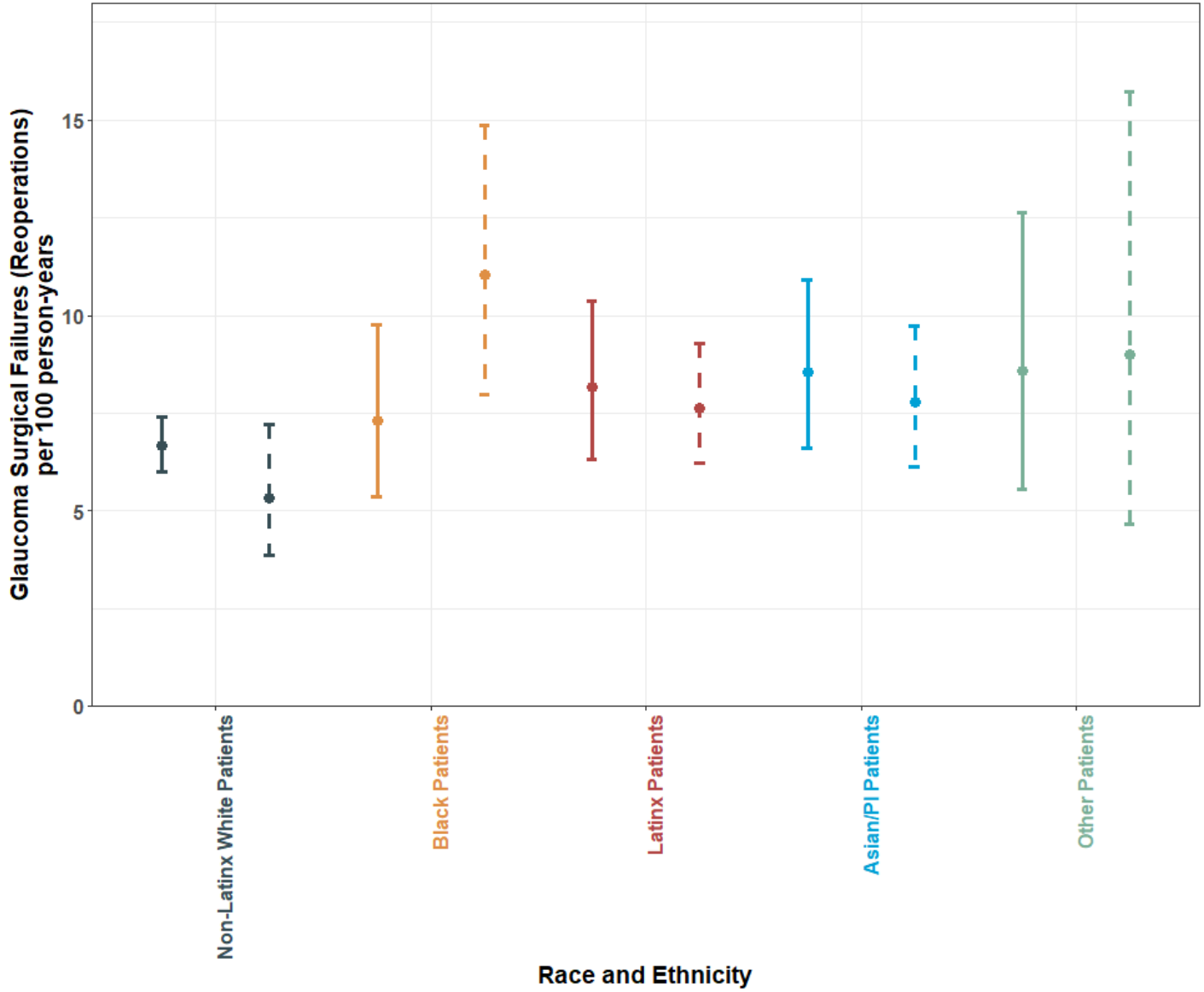
Figure 4.3 Forest plot of incidence rates of glaucoma reoperation stratified by SES for each racial and ethnic group, US cohort



*Solid lines reflect estimates for non-low SES and dashed lines reflect estimates for low SES strata; Asian/PI = Asian/Pacific Islander

Table 4.4 Glaucoma surgical reoperation incidence rate, stratified by SES for each racial and ethnic group, CA Cohort						
Racial and Ethnic Group	**SES stratum**	**Number of patients**	**Number of events**	**Person-years of follow-up**	**Incidence Rate**	**95% Confidence Interval**
Non-Latinx White Patients	**Non-low SES**	2,711	360	5,393	6.68	6.00 to 7.40
	Low SES	411	42	787	5.34	3.85 to 7.21
Black Patients	**Non-low SES**	349	46	628	7.32	5.36 to 9.76
	Low SES	225	43	389	11.04	7.99 to 14.87
Latinx Patients	**Non-low SES**	392	65	760	8.55	6.60 to 10.90
	Low SES	495	76	977	7.78	6.13 to 9.73
Asian/Pacific Islander Patients	**Non-low SES**	445	67	821	8.16	6.32 to 10.36
	Low SES	735	100	1,310	7.63	6.21 to 9.28
Other Patients	**Non-low SES**	143	25	292	8.57	5.54 to 12.65
	Low SES	79	12	133	9.00	4.65 to 15.72

Figure 4.4 Forest plot of incidence rates of glaucoma reoperation stratified by SES for each racial and ethnic group, CA cohort



*Solid lines reflect estimates for non-low SES and dashed lines reflect estimates for low SES strata; Asian/PI = Asian/Pacific Islander

Table 4.5 Causal mediation analysis estimates for SES as mediator for racial and ethnic disparities in glaucoma surgical failure, US cohort						
	TE	**95% CI**	**CDE**	**95% CI**	**PE**	**95% CI**
Non-Latinx White Patients	Reference					
Black Patients	1.35	1.18 to 1.56	1.42	1.23 to 1.65	-0.18	-0.47 to 0.10
Latinx Patients	1.40	1.16 to 1.68	1.36	1.06 to 1.74	0.11	-0.40 to 0.62
Asian/Pacific Islander Patients	1.52	1.18 to 1.95	1.52	1.11 to 2.08	0.01	-0.47 to 0.49
Other Patients	0.95	0.66 to 1.35	0.88	0.60 to 1.30	-1.18	-10.31 to 7.95

*TE = total effect; CDE = controlled direct effect; CI = confidence interval; PE = proportion eliminated

Table 4.6 Causal mediation analysis estimates for SES as mediator for racial and ethnic disparities in glaucoma surgical failure, CA cohort						
	TE	**95% CI**	**CDE**	**95% CI**	**PE**	**95% CI**
Non-Latinx White Patients	Reference					
Black Patients	1.22	0.97 to 1.55	1.01	0.74 to 1.37	0.97	-0.43 to 2.37
Latinx Patients	1.15	0.96 to 1.38	1.16	0.90 to 1.52	-0.13	-1.61 to 1.35
Asian/Pacific Islander Patients	1.20	0.99 to 1.45	1.21	0.93 to 1.59	-0.12	-1.25 to 1.01
Other Patients	1.26	0.90 to 1.77	1.24	0.83 to 1.86	0.05	-1.03 to 1.13

*TE = total effect; CDE = controlled direct effect; CI = confidence interval; PE = proportion eliminated

Chapter 5: Public health importance

Glaucoma is the leading cause of irreversible blindness in the US and worldwide, and racial and ethnic disparities in the screening, diagnosis, and treatment of glaucoma exist. Incisional glaucoma surgery remains a mainstay in treatment for glaucoma, though information on long-term additional surgery-free survival among racially and ethnically minoritized groups is lacking. With the rapidly aging US population, the incidence and prevalence of glaucoma will continue to increase, and sociodemographic shifts in the population are expected to cause there to be increased burden of glaucomatous disease in racially and ethnically minoritized populations. The studies outlined in this dissertation will contribute by providing information by investigating rates of incisional glaucoma surgical failure among a variety of racial and ethnic groups, and understanding the impact of structural inequities (patient-caring networks of eye care providers and individual disparities in SES) on racial and ethnic disparities in surgical outcomes as potential targets for intervention.

Chapter 6: Appendices

Supplementary Table 2.1 Current Procedural Terminology (CPT-4) codes for incisional glaucoma surgery reoperation or revision definitions.		
Outcome	**CPT-4 Code**	**Description of Claims-Based Variable**
Reoperation	66170	Fistulization of sclera for glaucoma; trabeculectomy ab externo in absence of previous surgery
Reoperation	66172	Trabeculectomy ab externo with scarring from previous ocular surgery or trauma (includes injection of antifibrotic agents)
Reoperation	66179	Aqueous shunt to extraocular equatorial plate reservoir; external approach; without graft
Reoperation	66180	Aqueous shunt to extraocular equatorial plate reservoir; external approach; with graft
Reoperation	0192T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach
Reoperation	66183	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach
Reoperation	0191T	Extracapsular cataract removal with insertion of intraocular lens prosthesis, manual or mechanical technique, complex, requiring devices or techniques not generally used in routine cataract surgery; with insertion of anterior segment aqueous drainage device without extraocular reservoir, internal approach, one or more.
Reoperation	66989	Extracapsular cataract removal with insertion of intraocular lens prosthesis, manual or mechanical technique, complex, requiring devices or techniques not generally used in routine cataract surgery; with insertion of anterior segment aqueous drainage device without extraocular reservoir, internal approach, one or more.
Reoperation	0376T	Extracapsular cataract removal with insertion of intraocular lens prosthesis, manual or mechanical technique; with insertion of anterior segment aqueous drainage device without extraocular reservoir, internal approach, one or more.
Reoperation	66991	Extracapsular cataract removal with insertion of intraocular lens prosthesis, manual or mechanical technique; with insertion of anterior segment aqueous drainage device without extraocular reservoir, internal approach, one or more.
Reoperation	0449T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; initial device.
Reoperation	66710	Ciliary body destruction; cyclophotocoagulation, transscleral.
Reoperation	66711	Ciliary body destruction; cyclophotocoagulation, endoscopic.

Supplementary Table 2.1 Current Procedural Terminology (CPT-4) codes for incisional glaucoma surgery reoperation or revision definitions.		
Outcome	**CPT-4 Code**	**Description of Claims-Based Variable**
Reoperation	66174	Transluminal dilation of aqueous outflow canal; without retention of device or stent.
Reoperation	66175	Transluminal dilation of aqueous outflow canal; with retention of device or stent.
Reoperation	65820	Goniotomy.
Reoperation	65850	Trabeculotomy ab externo.
Reoperation	65855	Trabeculoplasty by laser surgery.
Revision	66184	Revision of aqueous shunt to extraocular equatorial plate reservoir; without graft.
Revision	66185	Revision of aqueous shunt to extraocular equatorial plate reservoir; with graft.
Revision	65920	Removal of implanted material, anterior segment of eye.
Revision	67250	Scleral reinforcement (separate procedure); without graft.
Revision	67255	Scleral reinforcement (separate procedure); with graft.
Revision	66250	Revision or repair of operative wound of anterior segment, any type, early or late, major or minor procedure.

Supplementary Table 2.2 Cost Sharing Group Under Part D Low-Income Subsidy Codes	
Code	**Code Value**
00	Not Medicare enrolled for the month
01	Beneficiary enrolled in Parts A and/or B, and Part D; deemed eligible for LIS with 100% premium subsidy and no copayment
02	Beneficiary enrolled in Parts A and/or B, and Part D; deemed eligible for LIS with 100% premium subsidy and low copayment
03	Beneficiary enrolled in Parts A and/or B, and Part D; deemed eligible for LIS with 100% premium subsidy and high copayment
04	Beneficiary enrolled in Parts A and/or B, and Part D; enrolled in LIS with 100% premium subsidy and high copayment
05	Beneficiary enrolled in Parts A and/or B, and Part D; enrolled in LIS with 100% premium subsidy and 15% copayment
06	Beneficiary enrolled in Parts A and/or B, and Part D; enrolled in LIS with 75% premium subsidy and 15% copayment
07	Beneficiary enrolled in Parts A and/or B, and Part D; enrolled in LIS with 50% premium subsidy and 15% copayment
08	Beneficiary enrolled in Parts A and/or B, and Part D; enrolled in LIS with 25% premium subsidy and 15% copayment
09	Beneficiary enrolled in Parts A and/or B, and Part D; no premium or cost sharing subsidy
10	Beneficiary enrolled in Parts A and/or B, but not Part D enrolled; employer receives RDS subsidy
13	Beneficiary enrolled in Parts A and/or B, but not Part D enrolled. It is unknown whether the beneficiary has creditable prescription drug coverage elsewhere.
Null/Missing	Beneficiary was not found in cost sharing group data

Supplementary Table 2.3 Components of Charlson Comorbidity Index by International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) Codes	
Condition	**ICD-10 Codes**
Myocardial Infarction	I21.x, I22.x, I25.2x
Congestive Heart Failure	I09.9, I11.0, I13.2, I25.5, I42.0, I42.5-I42.9, I43.x, I50.x, P29.0
Peripheral Vascular Disease	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular Disease	I60.x-I69.x, H34.0, G45.x, G46.x
Dementia	F00.x-F03.x, F05.1, G30.x, G31.1
Chronic Pulmonary Disease/COPD	I27.8, I27.9, J40.x-J47.x, J60.x-J67.x, J68.4, J70.1, J70.3
Connective Tissue (Rheumatologic) disease	M05.x, M06.x, M31.5, M32.x-M34.x, M35.1, M35.3, M36.0
Peptic Ulcer Disease	K25.x-K28.x
Diabetes Mellitus w/o complications	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
Diabetes Mellitus w/ Complications (2pt)	E10.2-E10.5, E10.7, E11.2-E11.5, E11.7, E12.2-E12.5, E12.7, E13.2-E13.5, E13.7, E14.2-E14.5, E14.7
Chronic Renal Disease (2pt)	I12.0, I13.1, N03.2-N03.7, N05.2-N05.7, N18.x, N19.x, N25.0, Z49.0-Z49.2, Z94.0, Z99.2
Hemi/Paraplegia (2pt)	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, G83.9, I69.35x, I69.36x, I69.95x, I69.96x
Multiple Myeloma/Leukemia (2pt)	C90.x-C95.9x
Lymphomas (2pt)	C81.x-C88.x, C96.9, C96.z
Solid Tumor (Malignant neoplasms) (2pt)	C00.x- C76.x, C96.0-C96.6, C96.a
Solid Tumor (Metastatic) (6pt)	C77.x-C80.x
Mild liver disease	B18.x, K70.0-K70.3, K70.9, K71.3-K71.5, K71.7, K73.x, K74.x, K76.0, K76.2-K76.4, K76.8, K76.9, Z94.4
Moderate/severe liver disease (3pt)	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
AIDS (6pt)	B20.x-B22.x, B24.x

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
Acquired Hypothyroidism	1 year	E01.8, E02, E03.2, E03.3, E03.8, E03.9, E89.0 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes
Acute Myocardial Infarction	1 year	I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.4, I21.9, I21.A1, I21.A9, I22.0, I22.1, I22.2, I22.8, I22.9 (ONLY first or second DX on the claim)	At least 1 inpatient claim with DX code
Alzheimer's Disease	3 years	G30.0, G30.1, G30.8, G30.9 (any DX on the claim)	At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX code
Alzheimer's Disease and Related Disorders or Senile Dementia	3 years	F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F04, F05, F06.1, F06.8, G13.8, G30.0, G30.1, G30.8, G30.9, G31.01, G31.09, G31.1, G31.2, G94, R41.81, R54 (any DX on the claim)	At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX code
Anemia	1 year	D50.0, D50.1, D50.8, D50.9, D51.0, D51.1, D51.2, D51.3, D51.8, D51.9, D52.0, D52.1, D52.8, D52.9, D53.0, D53.1, D53.2, D53.8, D53.9, D55.0, D55.1, D55.2, D55.21, D55.29, D55.3, D55.8, D55.9, D56.0, D56.1, D56.2, D56.3, D56.4, D56.5, D56.8, D56.9, D57.00, D57.01, D57.02, D57.03, D57.09, D57.1, D57.20, D57.211, D57.212, D57.213, D57.218, D57.219, D57.3, D57.40, D57.411, D57.412, D57.413, D57.418, D57.419, D57.42, D57.431, D57.432, D57.433, D57.438, D57.439, D57.44, D57.451, D57.452, D57.453, D57.458, D57.459, D57.80, D57.811, D57.812, D57.813, D57.818, D57.819, D58.0, D58.1, D58.2, D58.8, D58.9, D59.0, D59.1, D59.10, D59.11, D59.12, D59.13, D59.19, D59.2, D59.3, D59.4, D59.5, D59.6, D59.8, D59.9, D60.0, D60.1, D60.8, D60.9, D61.01, D61.09, D61.1, D61.2, D61.3, D61.810, D61.811, D61.818, D61.82, D61.89, D61.9, D62, D63.0, D63.1, D63.8, D64.0, D64.1, D64.2, D64.3, D64.4, D64.81, D64.89, D64.9 (any DX on the claim)	At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX code
Asthma	1 year	J45.20, J45.21, J45.22, J45.30, J45.31, J45.32, J45.40, J45.41, J45.42, J45.50, J45.51, J45.52, J45.901, J45.902, J45.909, J45.990, J45.991, J45.998, J82.83 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP or Carrier claims with DX codes
	1 year	I48.0, I48.1, I48.11, I48.19, I48.2, I48.20, I48.21, I48.91 (ONLY first or second DX on the claim)	

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
Atrial Fibrillation			At least 1 inpatient claim **OR** 2 HOP/Carrier claims with DX codes
Benign Prostatic Hyperplasia	1 year	N40.0, N40.1, N40.2, N40.3, N42.83 (any DX on the claim) EXCLUSION: If any of the qualifying claims also have an ICD-10 diagnosis of D29.1, then EXCLUDE	At least 1 inpatient/SNF/HHA claim OR 2 HOP/Carrier claims with DX codes
Cancer, Female/Male Breast	1 year	C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, D05.00, D05.01, D05.02, D05.10, D05.11, D05.12, D05.80, D05.81, D05.82, D05.90, D05.91, D05.92, Z85.3 (any DX on the claim)	At least 1 inpatient/SNF claim **OR** 2 HOP/Carrier claims with DX codes
Cancer, Colorectal	1 year	C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, D01.0, D01.1, D01.2, Z85.038, Z85.040, Z85.048 (any DX on the claim)	At least 1 inpatient/SNF claim **OR** 2 HOP/Carrier claims with DX codes
Cancer, Endometrial	1 year	C54.1, C54.2, C54.3, C54.8, C54.9, D07.0, Z85.42 (any DX on the claim)	At least 1 inpatient/SNF claim **OR** 2 HOP/Carrier claims with DX codes
Cancer, Lung	1 year	C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, D02.20, D02.21, D02.22, Z85.110, Z85.118 (any DX on the claim)	At least 1 inpatient/SNF claim **OR** 2 HOP/Carrier claims with DX codes
Cancer, Prostate	1 year	C61, D07.5, Z85.46 (any DX on the claim)	At least 1 inpatient/SNF claim **OR** 2

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify** HOP/Carrier claims with DX codes
Cataract	1 year	H25.011, H25.012, H25.013, H25.019, H25.031, H25.032, H25.033, H25.039, H25.041, H25.042, H25.043, H25.049, H25.091, H25.092, H25.093, H25.099, H25.10, H25.11, H25.12, H25.13, H25.20, H25.21, H25.22, H25.23, H25.811, H25.812, H25.813, H25.819, H25.89, H25.9, H26.011, H26.012, H26.013, H26.019, H26.031, H26.032, H26.033, H26.039, H26.041, H26.042, H26.043, H26.049, H26.051, H26.052, H26.053, H26.059, H26.061, H26.062, H26.063, H26.069, H26.09, H26.101, H26.102, H26.103, H26.109, H26.111, H26.112, H26.113, H26.119, H26.121, H26.122, H26.123, H26.129, H26.131, H26.132, H26.133, H26.139, H26.20, H26.211, H26.212, H26.213, H26.219, H26.30, H26.31, H26.32, H26.33, H26.40, H26.411, H26.412, H26.413, H26.419, H26.491, H26.492, H26.493, H26.499, H26.8, H26.9, Q12.0, Z96.1 (ONLY principal DX on the claim)	At least 1 HOP or Carrier claim with DX codes
Chronic Kidney Disease	2 years	A18.11, A52.75, B52.0, C64.1, C64.2, C64.9, C68.9, D30.00, D30.01, D30.02, D41.00, D41.01, D41.02, D41.10, D41.11, D41.12, D41.20, D41.21, D41.22, D59.3, E08.21, E08.22, E08.29, E08.65, E09.21, E09.22, E09.29, E10.21, E10.22, E10.29, E10.65, E11.21, E11.22, E11.29, E11.65, E13.21, E13.22, E13.29, E74.8, I12.0, I12.9, I13.0, I13.10, I13.11, I13.2, I70.1, I72.2, K76.7, M10.30, M10.311, M10.312, M10.319, M10.321, M10.322, M10.329, M10.331, M10.332, M10.339, M10.341, M10.342, M10.349, M10.351, M10.352, M10.359, M10.361, M10.362, M10.369, M10.371, M10.372, M10.379, M10.38, M10.39, M32.14, M32.15, M35.04, N00.0, N00.1, N00.2, N00.3, N00.4, N00.5, N00.6, N00.7, N00.8, N00.9, N00.A, N01.0, N01.1, N01.2, N01.3, N01.4, N01.5, N01.6, N01.7, N01.8, N01.9, N01.A, N02.0, N02.1, N02.2, N02.3, N02.4, N02.5, N02.6, N02.7, N02.8, N02.9, N02.A, N03.0, N03.1, N03.2, N03.3, N03.4, N03.5, N03.6, N03.7, N03.8, N03.9, N03.A, N04.0, N04.1, N04.2, N04.3, N04.4, N04.5, N04.6, N04.7, N04.8, N04.9, N04.A, N05.0, N05.1, N05.2, N05.3, N05.4, N05.5, N05.6, N05.7, N05.8, N05.9, N05.A, N06.0, N06.1, N06.2, N06.3, N06.4, N06.5, N06.6, N06.7, N06.8, N06.9, N06.A, N07.0, N07.1, N07.2, N07.3, N07.4, N07.5, N07.6, N07.7, N07.8, N07.9, N07.A, N08, N13.1, N13.2, N13.30, N13.39, N14.0, N14.1, N14.2, N14.3, N14.4, N15.0, N15.8, N15.9, N16, N17.0, N17.1, N17.2, N17.8, N17.9, N18.1, N18.2, N18.3, N18.30, N18.31, N18.32, N18.4, N18.5, N18.6, N18.9, N19, N25.0, N25.1, N25.81, N25.89, N25.9, N26.1, N26.9, Q61.02, Q61.11, Q61.19, Q61.2, Q61.3, Q61.4, Q61.5, Q61.8, Q62.0, Q62.2, Q62.10, Q62.11, Q62.12, Q62.31, Q62.32, Q62.39, R94.4 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes
Chronic Obstructive Pulmonary Disease and Bronchiectasis	1 year	J40, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J47.0, J47.1, J47.9 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
Depression	1 year	F31.30, F31.31, F31.32, F31.4, F31.5, F31.60, F31.61, F31.62, F31.63, F31.64, F31.75, F31.76, F31.77, F31.78, F31.81, F32.0, F32.1, F32.2, F32.3, F32.4, F32.5, F32.9, F33.0, F33.1, F33.2, F33.3, F33.40, F33.41, F33.42, F33.8, F33.9, F34.1, F43.21, F43.23 (any DX on the claim)	At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX codes
Diabetes	2 years	E08.00, E08.01, E08.10, E08.11, E08.21, E08.22, E08.29, E08.311, E08.319, E08.321, E08.3211, E08.3212, E08.3213, E08.3219, E08.329, E08.3291, E08.3292, E08.3293, E08.3299, E08.331, E08.3311, E08.3312, E08.3313, E08.3319, E08.339, E08.3391, E08.3392, E08.3393, E08.3399, E08.341, E08.3411, E08.3412, E08.3413, E08.3419, E08.349, E08.3491, E08.3492, E08.3493, E08.3499, E08.351, E08.3511, E08.3512, E08.3513, E08.3519, E08.3521, E08.3522, E08.3523, E08.3529, E08.3531, E08.3532, E08.3533, E08.3539, E08.3541, E08.3542, E08.3543, E08.3549, E08.3551, E08.3552, E08.3553, E08.3559, E08.359, E08.3591, E08.3592, E08.3593, E08.3599, E08.36, E08.37X1, E08.37X2, E08.37X3, E08.37X9, E08.39, E08.40, E08.41, E08.42, E08.43, E08.44, E08.49, E08.51, E08.52, E08.59, E08.610, E08.618, E08.620, E08.621, E08.622, E08.628, E08.630, E08.638, E08.641, E08.649, E08.65, E08.69, E08.8, E08.9, E09.00, E09.01, E09.10, E09.11, E09.21, E09.22, E09.29, E09.311, E09.319, E09.321, E09.3211, E09.3212, E09.3213, E09.3219, E09.329, E09.3291, E09.3292, E09.3293, E09.3299, E09.331, E09.3311, E09.3312, E09.3313, E09.3319, E09.339, E09.3391, E09.3392, E09.3393, E09.3399, E09.341, E09.3411, E09.3412, E09.3413, E09.3419, E09.349, E09.3491, E09.3492, E09.3493, E09.3499, E09.351, E09.3511, E09.3512, E09.3513, E09.3519, E09.3521, E09.3522, E09.3523, E09.3529, E09.3531, E09.3532, E09.3533, E09.3539, E09.3541, E09.3542, E09.3543, E09.3549, E09.3551, E09.3552, E09.3553, E09.3559, E09.359, E09.3591, E09.3592, E09.3593, E09.3599, E09.36, E09.37X1, E09.37X2, E09.37X3, E09.37X9, E09.39, E09.40, E09.41, E09.42, E09.43, E09.44, E09.49, E09.51, E09.52, E09.59, E09.610, E09.618, E09.620, E09.621, E09.622, E09.628, E09.630, E09.638, E09.641, E09.649, E09.65, E09.69, E09.8, E09.9, E10.10, E10.11, E10.21, E10.22, E10.29, E10.311, E10.319, E10.321, E10.3211, E10.3212, E10.3213, E10.3219, E10.329, E10.3291, E10.3292, E10.3293, E10.3299, E10.331, E10.3311, E10.3312, E10.3313, E10.3319, E10.339, E10.3391, E10.3392, E10.3393, E10.3399, E10.341, E10.3411, E10.3412, E10.3413, E10.3419, E10.349, E10.3491, E10.3492, E10.3493, E10.3499, E10.351, E10.3511, E10.3512, E10.3513, E10.3519, E10.3521, E10.3522, E10.3523, E10.3529, E10.3531, E10.3532, E10.3533, E10.3539, E10.3541, E10.3542, E10.3543, E10.3549, E10.3551, E10.3552, E10.3553, E10.3559, E10.359, E10.3591, E10.3592, E10.3593, E10.3599, E10.36, E10.37X1, E10.37X2, E10.37X3, E10.37X9, E10.39, E10.40, E10.41, E10.42, E10.43, E10.44, E10.49, E10.51, E10.52, E10.59, E10.610, E10.618, E10.620, E10.621, E10.622, E10.628, E10.630, E10.638, E10.641, E10.649, E10.65, E10.69, E10.8, E10.9, E11.00, E11.01, E11.10, E11.11, E11.21, E11.22, E11.29, E11.311, E11.319, E11.321, E11.3211, E11.3212, E11.3213, E11.3219, E11.329, E11.3291, E11.3292, E11.3293, E11.3299, E11.331, E11.3311,	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
		E11.3312, E11.3313, E11.3319, E11.339, E11.3391, E11.3392, E11.3393, E11.3399, E11.341, E11.3411, E11.3412, E11.3413, E11.3419, E11.349, E11.3491, E11.3492, E11.3493, E11.3499, E11.351, E11.3511, E11.3512, E11.3513, E11.3519, E11.3521, E11.3522, E11.3523, E11.3529, E11.3531, E11.3532, E11.3533, E11.3539, E11.3541, E11.3542, E11.3543, E11.3549, E11.3551, E11.3552, E11.3553, E11.3559, E11.359, E11.3591, E11.3592, E11.3593, E11.3599, E11.36, E11.37X1, E11.37X2, E11.37X3, E11.37X9, E11.39, E11.40, E11.41, E11.42, E11.43, E11.44, E11.49, E11.51, E11.52, E11.59, E11.610, E11.618, E11.620, E11.621, E11.622, E11.628, E11.630, E11.638, E11.641, E11.649, E11.65, E11.69, E11.8, E11.9, E13.00, E13.01, E13.10, E13.11, E13.21, E13.22, E13.29, E13.311, E13.319, E13.321, E13.3211, E13.3212, E13.3213, E13.3219, E13.329, E13.3291, E13.3292, E13.3293, E13.3299, E13.331, E13.3311, E13.3312, E13.3313, E13.3319, E13.339, E13.3391, E13.3392, E13.3393, E13.3399, E13.341, E13.3411, E13.3412, E13.3413, E13.3419, E13.349, E13.3491, E13.3492, E13.3493, E13.3499, E13.351, E13.3511, E13.3512, E13.3513, E13.3519, E13.3521, E13.3522, E13.3523, E13.3529, E13.3531, E13.3532, E13.3533, E13.3539, E13.3541, E13.3542, E13.3543, E13.3549, E13.3551, E13.3552, E13.3553, E13.3559, E13.359, E13.3591, E13.3592, E13.3593, E13.3599, E13.36, E13.39, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.51, E13.52, E13.59, E13.610, E13.618, E13.620, E13.621, E13.622, E13.628, E13.630, E13.638, E13.641, E13.649, E13.65, E13.69, E13.8, E13.9 (any DX on the claim)	
Heart Failure	2 years	I09.81, I11.0, I13.0, I13.2, I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I50.9 (any DX on the claim)	At least 1 inpatient, HOP, or Carrier claim with DX code
Hip/Pelvic Fracture	1 year	M80.051A, M80.052A, M80.059A, M80.851A, M80.852A, M80.859A, M84.350A, M84.351A, M84.352A, M84.353A, M84.359A, M84.451A, M84.452A, M84.453A, M84.459A, M84.550A, M84.551A, M84.552A, M84.553A, M84.559A, M84.650A, M84.651A, M84.652A, M84.653A, M84.659A, S32.301A, S32.301B, S32.302A, S32.302B, S32.309A, S32.309B, S32.311A, S32.311B, S32.312A, S32.312B, S32.313A, S32.313B, S32.314A, S32.314B, S32.315A, S32.315B, S32.316A, S32.316B, S32.391A, S32.391B, S32.392A, S32.392B, S32.399A, S32.399B, S32.401A, S32.401B, S32.402A, S32.402B, S32.409A, S32.409B, S32.411A, S32.411B, S32.412A, S32.412B, S32.413A, S32.413B, S32.414A, S32.414B, S32.415A, S32.415B, S32.416A, S32.416B, S32.421A, S32.421B, S32.422A, S32.422B, S32.423A, S32.423B, S32.424A, S32.424B, S32.425A, S32.425B, S32.426A, S32.426B, S32.431A, S32.431B, S32.432A, S32.432B, S32.433A, S32.433B, S32.434A, S32.434B, S32.435A, S32.435B, S32.436A, S32.436B, S32.441A, S32.441B, S32.442A, S32.442B, S32.443A, S32.443B, S32.444A, S32.444B, S32.445A, S32.445B, S32.446A, S32.446B, S32.451A, S32.451B, S32.452A, S32.452B, S32.453A, S32.453B, S32.454A, S32.454B, S32.455A, S32.455B, S32.456A, S32.456B, S32.461A, S32.461B, S32.462A, S32.462B, S32.463A, S32.463B, S32.464A, S32.464B,	At least 1 inpatient or SNF claim with DX code

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
		S32.465A, S32.465B, S32.466A, S32.466B, S32.471A, S32.471B, S32.472A, S32.472B, S32.473A, S32.473B, S32.474A, S32.474B, S32.475A, S32.475B, S32.476A, S32.476B, S32.481A, S32.481B, S32.482A, S32.482B, S32.483A, S32.483B, S32.484A, S32.484B, S32.485A, S32.485B, S32.486A, S32.486B, S32.491A, S32.491B, S32.492A, S32.492B, S32.499A, S32.499B, S32.501A, S32.501B, S32.502A, S32.502B, S32.509A, S32.509B, S32.511A, S32.511B, S32.512A, S32.512B, S32.519A, S32.519B, S32.591A, S32.591B, S32.592A, S32.592B, S32.599A, S32.599B, S32.601A, S32.601B, S32.602A, S32.602B, S32.609A, S32.609B, S32.611A, S32.611B, S32.612A, S32.612B, S32.613A, S32.613B, S32.614A, S32.614B, S32.615A, S32.615B, S32.616A, S32.616B, S32.691A, S32.691B, S32.692A, S32.692B, S32.699A, S32.699B, S32.810A, S32.810B, S32.811A, S32.811B, S32.82XA, S32.82XB, S32.89XA, S32.89XB, S32.9XXA, S32.9XXB, S72.001A, S72.001B, S72.001C, S72.002A, S72.002B, S72.002C, S72.009A, S72.009B, S72.009C, S72.011A, S72.011B, S72.011C, S72.012A, S72.012B, S72.012C, S72.019A, S72.019B, S72.019C, S72.021A, S72.021B, S72.021C, S72.022A, S72.022B, S72.022C, S72.023A, S72.023B, S72.023C, S72.024A, S72.024B, S72.024C, S72.025A, S72.025B, S72.025C, S72.026A, S72.026B, S72.026C, S72.031A, S72.031B, S72.031C, S72.032A, S72.032B, S72.032C, S72.033A, S72.033B, S72.033C, S72.034A, S72.034B, S72.034C, S72.035A, S72.035B, S72.035C, S72.036A, S72.036B, S72.036C, S72.041A, S72.041B, S72.041C, S72.042A, S72.042B, S72.042C, S72.043A, S72.043B, S72.043C, S72.044A, S72.044B, S72.044C, S72.045A, S72.045B, S72.045C, S72.046A, S72.046B, S72.046C, S72.051A, S72.051B, S72.051C, S72.052A, S72.052B, S72.052C, S72.059A, S72.059B, S72.059C, S72.061A, S72.061B, S72.061C, S72.062A, S72.062B, S72.062C, S72.063A, S72.063B, S72.063C, S72.064A, S72.064B, S72.064C, S72.065A, S72.065B, S72.065C, S72.066A, S72.066B, S72.066C, S72.091A, S72.091B, S72.091C, S72.092A, S72.092B, S72.092C, S72.099A, S72.099B, S72.099C, S72.101A, S72.101B, S72.101C, S72.102A, S72.102B, S72.102C, S72.109A, S72.109B, S72.109C, S72.111A, S72.111B, S72.111C, S72.112A, S72.112B, S72.112C, S72.113A, S72.113B, S72.113C, S72.114A, S72.114B, S72.114C, S72.115A, S72.115B, S72.115C, S72.116A, S72.116B, S72.116C, S72.121A, S72.121B, S72.121C, S72.122A, S72.122B, S72.122C, S72.123A, S72.123B, S72.123C, S72.124A, S72.124B, S72.124C, S72.125A, S72.125B, S72.125C, S72.126A, S72.126B, S72.126C, S72.131A, S72.131B, S72.131C, S72.132A, S72.132B, S72.132C, S72.133A, S72.133B, S72.133C, S72.134A, S72.134B, S72.134C, S72.135A, S72.135B, S72.135C, S72.136A, S72.136B, S72.136C, S72.141A, S72.141B, S72.141C, S72.142A, S72.142B, S72.142C, S72.143A, S72.143B, S72.143C, S72.144A, S72.144B, S72.144C, S72.145A, S72.145B, S72.145C, S72.146A, S72.146B, S72.146C, S72.21XA, S72.21XB, S72.21XC, S72.22XA, S72.22XB, S72.22XC, S72.23XA, S72.23XB, S72.23XC, S72.24XA, S72.24XB, S72.24XC, S72.25XA, S72.25XB, S72.25XC, S72.26XA, S72.26XB, S72.26XC, S79.001A, S79.002A, S79.009A, S79.011A, S79.012A, S79.019A, S79.091A, S79.092A, S79.099A (any DX on the claim)	

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
Hyperlipidemia	1 year	E78.0, E78.00, E78.01, E78.1, E78.2, E78.3, E78.4, E78.41, E78.49, E78.5 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes
Hypertension	1 year	H35.031, H35.032, H35.033, H35.039, I10, I11.0, I11.9, I12.0, I12.9, I13.0, I13.10, I13.11, I13.2, I15.0, I15.1, I15.2, I15.8, I15.9, I67.4, N26.2 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes
Ischemic Heart Disease	2 years	I20.0, I20.1, I20.8, I20.9, I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.4, I21.A1, I21.A9, I22.0, I22.1, I22.2, I22.8, I22.9, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.7, I23.8, I24.0, I24.1, I24.8, I24.9, I25.10, I25.110, I25.111, I25.118, I25.119, I25.2, I25.3, I25.41, I25.42, I25.5, I25.6, I25.700, I25.701, I25.708, I25.709, I25.710, I25.711, I25.718, I25.719, I25.720, I25.721, I25.728, I25.729, I25.730, I25.731, I25.738, I25.739, I25.750, I25.751, I25.758, I25.759, I25.760, I25.761, I25.768, I25.769, I25.790, I25.791, I25.798, I25.799, I25.810, I25.811, I25.812, I25.82, I25.83, I25.84, I25.89, I25.9 (any DX on the claim)	At least 1 inpatient, SNF, HHA, HOP, or Carrier claim with DX code
Osteoporosis	1 year	M81.0, M81.6, M81.8 (any DX on the claim)	At least 1 inpatient/SNF/HHA claim **OR** 2 HOP/Carrier claims with DX codes
Rheumatoid Arthritis/ Osteoarthritis (RA/OA)	2 years	M05.00, M05.011, M05.012, M05.019, M05.021, M05.022, M05.029, M05.031, M05.032, M05.039, M05.041, M05.042, M05.049, M05.051, M05.052, M05.059, M05.061, M05.062, M05.069, M05.071, M05.072, M05.079, M05.09, M05.20, M05.211, M05.212, M05.219, M05.221, M05.222, M05.229, M05.231, M05.232, M05.239, M05.241, M05.242, M05.249, M05.251, M05.252, M05.259, M05.261, M05.262, M05.269, M05.271, M05.272, M05.279, M05.29, M05.30, M05.311, M05.312, M05.319, M05.321, M05.322, M05.329, M05.331, M05.332, M05.339, M05.341, M05.342, M05.349, M05.351, M05.352, M05.359, M05.361, M05.362, M05.369, M05.371, M05.372, M05.379, M05.39, M05.40, M05.411, M05.412, M05.419, M05.421, M05.422, M05.429, M05.431, M05.432, M05.439, M05.441, M05.442, M05.449, M05.451, M05.452, M05.459, M05.461, M05.462, M05.469, M05.471, M05.472, M05.479, M05.49, M05.50, M05.511, M05.512, M05.519, M05.521, M05.522, M05.529, M05.531, M05.532, M05.539, M05.541, M05.542, M05.549, M05.551, M05.552, M05.559, M05.561, M05.562, M05.569, M05.571, M05.572, M05.579, M05.59, M05.60, M05.611, M05.612, M05.619, M05.621, M05.622, M05.629, M05.631, M05.632, M05.639, M05.641, M05.642, M05.649, M05.651, M05.652,	At least 2 inpatient, SNF, HHA, HOP, or Carrier claims with DX codes

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
		M05.659, M05.661, M05.662, M05.669, M05.671, M05.672, M05.679, M05.69, M05.70, M05.711, M05.712, M05.719, M05.721, M05.722, M05.729, M05.731, M05.732, M05.739, M05.741, M05.742, M05.749, M05.751, M05.752, M05.759, M05.761, M05.762, M05.769, M05.771, M05.772, M05.779, M05.79, M05.7A, M05.80, M05.811, M05.812, M05.819, M05.821, M05.822, M05.829, M05.831, M05.832, M05.839, M05.841, M05.842, M05.849, M05.851, M05.852, M05.859, M05.861, M05.862, M05.869, M05.871, M05.872, M05.879, M05.89, M05.8A, M05.9, M06.00, M06.011, M06.012, M06.019, M06.021, M06.022, M06.029, M06.031, M06.032, M06.039, M06.041, M06.042, M06.049, M06.051, M06.052, M06.059, M06.061, M06.062, M06.069, M06.071, M06.072, M06.079, M06.08, M06.09, M06.0A, M06.1, M06.20, M06.211, M06.212, M06.219, M06.221, M06.222, M06.229, M06.231, M06.232, M06.239, M06.241, M06.242, M06.249, M06.251, M06.252, M06.259, M06.261, M06.262, M06.269, M06.271, M06.272, M06.279, M06.28, M06.29, M06.30, M06.311, M06.312, M06.319, M06.321, M06.322, M06.329, M06.331, M06.332, M06.339, M06.341, M06.342, M06.349, M06.351, M06.352, M06.359, M06.361, M06.362, M06.369, M06.371, M06.372, M06.379, M06.38, M06.39, M06.80, M06.811, M06.812, M06.819, M06.821, M06.822, M06.829, M06.831, M06.832, M06.839, M06.841, M06.842, M06.849, M06.851, M06.852, M06.859, M06.861, M06.862, M06.869, M06.871, M06.872, M06.879, M06.88, M06.89, M06.8A, M06.9, M08.00, M08.011, M08.012, M08.019, M08.021, M08.022, M08.029, M08.031, M08.032, M08.039, M08.041, M08.042, M08.049, M08.051, M08.052, M08.059, M08.061, M08.062, M08.069, M08.071, M08.072, M08.079, M08.08, M08.09, M08.0A, M08.1, M08.20, M08.211, M08.212, M08.219, M08.221, M08.222, M08.229, M08.231, M08.232, M08.239, M08.241, M08.242, M08.249, M08.251, M08.252, M08.259, M08.261, M08.262, M08.269, M08.271, M08.272, M08.279, M08.28, M08.29, M08.2A, M08.3, M08.40, M08.411, M08.412, M08.419, M08.421, M08.422, M08.429, M08.431, M08.432, M08.439, M08.441, M08.442, M08.449, M08.451, M08.452, M08.459, M08.461, M08.462, M08.469, M08.471, M08.472, M08.479, M08.48, M08.4A, M08.80, M08.811, M08.812, M08.819, M08.821, M08.822, M08.829, M08.831, M08.832, M08.839, M08.841, M08.842, M08.849, M08.851, M08.852, M08.859, M08.861, M08.862, M08.869, M08.871, M08.872, M08.879, M08.88, M08.89, M08.90, M08.911, M08.912, M08.919, M08.921, M08.922, M08.929, M08.931, M08.932, M08.939, M08.941, M08.942, M08.949, M08.951, M08.952, M08.959, M08.961, M08.962, M08.969, M08.971, M08.972, M08.979, M08.98, M08.99, M08.9A, M15.0, M15.1, M15.2, M15.3, M15.4, M15.8, M15.9, M16.0, M16.10, M16.11, M16.12, M16.2, M16.30, M16.31, M16.32, M16.4, M16.50, M16.51, M16.52, M16.6, M16.7, M16.9, M17.0, M17.10, M17.11, M17.12, M17.2, M17.30, M17.31, M17.32, M17.4, M17.5, M17.9, M18.0, M18.10, M18.11, M18.12, M18.2, M18.30, M18.31, M18.32, M18.4, M18.50, M18.51, M18.52, M18.9, M19.011, M19.012, M19.019, M19.021, M19.022, M19.029, M19.031, M19.032, M19.039, M19.041, M19.042, M19.049, M19.071, M19.072, M19.079, M19.09, M19.111, M19.112, M19.119, M19.121, M19.122, M19.129, M19.131, M19.132, M19.139, M19.141, M19.142, M19.149, M19.171, M19.172, M19.179, M19.19, M19.211, M19.212, M19.219, M19.221, M19.222, M19.229, M19.231,	

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
		M19.232, M19.239, M19.241, M19.242, M19.249, M19.271, M19.272, M19.279, M19.29, M19.90, M19.91, M19.92, M19.93, M45.0, M45.1, M45.2, M45.3, M45.4, M45.5, M45.6, M45.7, M45.8, M45.9, M47.011, M47.012, M47.013, M47.014, M47.015, M47.016, M47.019, M47.021, M47.022, M47.029, M47.10, M47.11, M47.12, M47.13, M47.20, M47.21, M47.22, M47.23, M47.24, M47.25, M47.26, M47.27, M47.28, M47.811, M47.812, M47.813, M47.814, M47.815, M47.816, M47.817, M47.818, M47.819, M47.891, M47.892, M47.893, M47.894, M47.895, M47.896, M47.897, M47.898, M47.899, M47.9, M48.8X1, M48.8X2, M48.8X3, M48.8X4, M48.8X5, M48.8X6, M48.8X7, M48.8X8, M48.8X9 (any DX on the claim)	
Stroke/Transient Ischemic Attack	1 year	G45.0, G45.1, G45.2, G45.8, G45.9, G46.0, G46.1, G46.2, G46.3, G46.4, G46.5, G46.6, G46.7, G46.8, G97.31, G97.32, I60.00, I60.01, I60.02, I60.10, I60.11, I60.12, I60.20, I60.21, I60.22, I60.30, I60.31, I60.32, I60.4, I60.50, I60.51, I60.52, I60.6, I60.7, I60.8, I60.9, I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I63.00, I63.011, I63.012, I63.013, I63.019, I63.02, I63.031, I63.032, I63.039, I63.09, I63.10, I63.111, I63.112, I63.113, I63.119, I63.12, I63.131, I63.132, I63.133, I63.139, I63.19, I63.20, I63.211, I63.212, I63.213, I63.219, I63.22, I63.231, I63.232, I63.233, I63.239, I63.29, I63.30, I63.311, I63.312, I63.313, I63.319, I63.321, I63.322, I63.323, I63.329, I63.331, I63.332, I63.333, I63.339, I63.341, I63.342, I63.343, I63.349, I63.39, I63.40, I63.411, I63.412, I63.413, I63.419, I63.421, I63.422, I63.423, I63.429, I63.431, I63.432, I63.433, I63.439, I63.441, I63.442, I63.443, I63.449, I63.49, I63.50, I63.511, I63.512, I63.513, I63.519, I63.521, I63.522, I63.523, I63.529, I63.531, I63.532, I63.533, I63.539, I63.541, I63.542, I63.543, I63.549, I63.59, I63.6, I63.8, I63.81, I63.89, I63.9, I66.01, I66.02, I66.03, I66.09, I66.11, I66.12, I66.13, I66.19, I66.21, I66.22, I66.23, I66.29, I66.3, I66.8, I66.9, I67.841, I67.848, I67.89, I97.810, I97.811, I97.820, I97.821 (any DX on the claim) EXCLUSION: If any of the qualifying claims have any of the following codes in any DX position then EXCLUDE: S01.90XA, S02.0XXA, S02.0XXB, S02.101A, S02.101B, S02.102A, S02.102B, S02.109A, S02.109B, S02.10XA, S02.10XB, S02.110A, S02.110B, S02.111A, S02.111B, S02.112A, S02.112B, S02.113A, S02.113B, S02.118A, S02.118B, S02.119A, S02.119B, S02.11GA, S02.11GB, S02.11HA, S02.11HB, S02.121A, S02.121B, S02.121D, S02.121G, S02.121K, S02.121S, S02.122A, S02.122B, S02.122D, S02.122G, S02.122K, S02.122S, S02.129A, S02.129B, S02.129D, S02.129G, S02.129K, S02.129S, S02.19XA, S02.19XB, S02.2XXA, S02.2XXB, S02.30XA, S02.30XB, S02.31XA, S02.31XB, S02.32XA, S02.32XB, S02.3XXA, S02.3XXB, S02.400A, S02.400B, S02.401A, S02.401B, S02.402A, S02.402B, S02.40AA, S02.40AB, S02.40BA, S02.40BB, S02.40CA, S02.40CB, S02.40DA, S02.40DB, S02.40EA, S02.40EB, S02.40FA, S02.40FB, S02.411A, S02.411B, S02.412A, S02.412B, S02.413A, S02.413B, S02.42XA, S02.42XB, S02.600A, S02.600B, S02.601A, S02.601B, S02.602A, S02.602B, S02.609A, S02.609B, S02.610A, S02.610B, S02.611A, S02.611B,	At least 1 inpatient claim OR 2 HOP/Carrier claims with DX codes

Supplementary Table 2.4 Chronic Conditions Warehouse (CCW) algorithms for 26 chronic conditions (glaucoma excluded)			
Algorithms	**Reference Period**	**Valid ICD-10 Codes**	**Number/Type of Claims to Qualify**
		S02.612A, S02.612B, S02.61XA, S02.61XB, S02.620A, S02.620B, S02.621A, S02.621B, S02.622A, S02.622B, S02.62XA, S02.62XB, S02.630A, S02.630B, S02.631A, S02.631B, S02.632A, S02.632B, S02.63XA, S02.63XB, S02.640A, S02.640B, S02.641A, S02.641B, S02.642A, S02.642B, S02.64XA, S02.64XB, S02.650A, S02.650B, S02.651A, S02.651B, S02.652A, S02.652B, S02.65XA, S02.65XB, S02.66XA, S02.66XB, S02.670A, S02.670B, S02.671A, S02.671B, S02.672A, S02.672B, S02.67XA, S02.67XB, S02.69XA, S02.69XB, S02.80XA, S02.80XB, S02.81XA, S02.81XB, S02.82XA, S02.82XB, S02.831A, S02.831B, S02.831D, S02.831G, S02.831K, S02.831S, S02.832A, S02.832B, S02.832D, S02.832G, S02.832K, S02.832S, S02.839A, S02.839B, S02.839D, S02.839G, S02.839K, S02.839S, S02.841A, S02.841B, S02.841D, S02.841G, S02.841K, S02.841S, S02.842A, S02.842B, S02.842D, S02.842G, S02.842K, S02.842S, S02.849A, S02.849B, S02.849D, S02.849G, S02.849K, S02.849S, S02.85XA, S02.85XB, S02.85XD, S02.85XG, S02.85XK, S02.85XS, S02.8XXA, S02.8XXB, S02.91XA, S02.91XB, S02.92XA, S02.92XB, S06.0X0A, S06.0X1A, S06.0X2A, S06.0X3A, S06.0X4A, S06.0X5A, S06.0X6A, S06.0X7A, S06.0X8A, S06.0X9A, S06.1X0A, S06.1X1A, S06.1X2A, S06.1X3A, S06.1X4A, S06.1X5A, S06.1X6A, S06.1X7A, S06.1X8A, S06.1X9A, S06.2X0A, S06.2X1A, S06.2X2A, S06.2X3A, S06.2X4A, S06.2X5A, S06.2X6A, S06.2X7A, S06.2X8A, S06.2X9A, S06.300A, S06.301A, S06.302A, S06.303A, S06.304A, S06.305A, S06.306A, S06.307A, S06.308A, S06.309A, S06.310A, S06.311A, S06.312A, S06.313A, S06.314A, S06.315A, S06.316A, S06.317A, S06.318A, S06.319A, S06.320A, S06.321A, S06.322A, S06.323A, S06.324A, S06.325A, S06.326A, S06.327A, S06.328A, S06.329A, S06.330A, S06.331A, S06.332A, S06.333A, S06.334A, S06.335A, S06.336A, S06.337A, S06.338A, S06.339A, S06.340A, S06.341A, S06.342A, S06.343A, S06.344A, S06.345A, S06.346A, S06.347A, S06.348A, S06.349A, S06.350A, S06.351A, S06.352A, S06.353A, S06.354A, S06.355A, S06.356A, S06.357A, S06.358A, S06.359A, S06.360A, S06.361A, S06.362A, S06.363A, S06.364A, S06.365A, S06.366A, S06.367A, S06.368A, S06.369A, S06.370A, S06.371A, S06.372A, S06.373A, S06.374A, S06.375A, S06.376A, S06.377A, S06.378A, S06.379A, S06.380A, S06.381A, S06.382A, S06.383A, S06.384A, S06.385A, S06.386A, S06.387A, S06.388A, S06.389A, S06.4X0A, S06.4X1A, S06.4X2A, S06.4X3A, S06.4X4A, S06.4X5A, S06.4X6A, S06.4X7A, S06.4X8A, S06.4X9A, S06.5X0A, S06.5X1A, S06.5X2A, S06.5X3A, S06.5X4A, S06.5X5A, S06.5X6A, S06.5X7A, S06.5X8A, S06.5X9A, S06.6X0A, S06.6X1A, S06.6X2A, S06.6X3A, S06.6X4A, S06.6X5A, S06.6X6A, S06.6X7A, S06.6X8A, S06.6X9A, S06.810A, S06.811A, S06.812A, S06.813A, S06.814A, S06.815A, S06.816A, S06.817A, S06.818A, S06.819A, S06.820A, S06.821A, S06.822A, S06.823A, S06.824A, S06.825A, S06.826A, S06.827A, S06.828A, S06.829A, S06.890A, S06.891A, S06.892A, S06.893A, S06.894A, S06.895A, S06.896A, S06.897A, S06.898A, S06.899A, S06.9X0A, S06.9X1A, S06.9X2A, S06.9X3A, S06.9X4A, S06.9X5A, S06.9X6A, S06.9X7A, S06.9X8A, S06.9X9A, OR Z51.89 as the principal DX Code then EXCLUDE.	

*SNF refers to skilled nursing facility; HHA refers to home health agency; HOP refers to hospital outpatient. Carrier claims refer to claim types 71 and 72 (not durable medical equipment [DME] claim types 81 or 82), and excludes any claims for which line item Berenson-Eggers Type of Service (BETOS) code variable equals D1A, D1B, D1C, D1D, D1E, D1F, D1G (which is DME), or O1A (which is ambulance services). The intent of the algorithm is to exclude claims where the services do not require a licensed health care professional. When two claims are required, they must occur at least one day apart

Supplementary Table 2.5 Cox proportional hazards regressions estimating risk of incisional glaucoma surgery reoperation (excluding beneficiaries who received index surgery in 2016), by racial and ethnic group						
	Unadjusted		**Total Racial and Ethnic Disparity***		**Direct Racial and Ethnic Disparity****	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**	**Hazard Ratio**	**95% CI**
Non-Latinx White Patients	Ref	Ref	Ref	Ref	Ref	Ref
Black Patients	1.36	1.15-1.63	1.40	1.16-1.68	1.37	1.12-1.67
Latinx Patients	1.43	1.12-1.83	1.36	1.05-1.76	1.29	0.98-1.70
Asian/Pacific Islander Patients	1.73	1.28-2.34	1.50	1.09-2.07	1.40	1.01-1.96
Other Patients	1.09	0.70-1.71	0.99	0.63-1.55	0.95	0.60-1.50
*Model adjusts for: age, sex, US state of residence, cohort year.						
**Model adjusts for: age, sex, US state of residence, cohort year, eligibility for dual-Medicaid, eligibility for Part D low-income subsidiies, CCW comorbidities, glaucoma severity, and glaucoma subtype.						

Supplementary Table 2.6 Distribution of exclusion due to immediate loss to follow-up by racial and ethnic group										
	Non-Latinx White beneficiaries		**Black beneficiaries**		**Latinx beneficiaries**		**Asian/Pacific Islander beneficiaries**		**Other beneficiaries**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Excluded due to immediate loss to follow-up	627	6.8%	252	9.9%	77	8.0%	22	5.0%	21	6.8%
Included	8547	93.2%	2283	90.1%	889	92.0%	414	95.0%	288	93.2%

Supplementary Table 2.7 Cox proportional hazards regressions estimating risk of reoperation following trabeculectomy, by racial and ethnic group						
	Unadjusted		**Total Racial and Ethnic Disparity***		**Direct Racial and Ethnic Disparity****	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**	**Hazard Ratio**	**95% CI**
Non-Latinx White Patients	Ref	Ref	Ref	Ref	Ref	Ref
Black Patients	1.52	1.27-1.81	1.52	1.25-1.84	1.50	1.22-1.84
Latinx Patients	1.66	1.29-2.13	1.63	1.25-2.13	1.58	1.19-2.10
Asian/Pacific Islander Patients	1.88	1.39-2.54	1.73	1.25-2.38	1.60	1.14-2.25
Other Patients	1.59	1.05-2.41	1.39	0.91-2.13	1.31	0.85-2.02

*Model adjusts for: age, sex, US state of residence, cohort year.

**Model adjusts for: age, sex, US state of residence, cohort year, eligibility for dual-Medicaid, eligibility for Part D low-income subsidies, CCW comorbidities, glaucoma severity, and glaucoma subtype.

Supplementary Table 2.8 Cox proportional hazards regressions estimating risk of reoperation following tube shunt, by racial and ethnic group						
	Unadjusted		**Total Racial and Ethnic Disparity***		**Direct Racial and Ethnic Disparity****	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**	**Hazard Ratio**	**95% CI**
Non-Latinx White Individuals	Ref	Ref	Ref	Ref	Ref	Ref
Black Individuals	1.22	1.01-1.49	1.22	0.99-1.51	1.13	0.90-1.42
Latinx Individuals	1.43	1.09-1.86	1.27	0.96-1.68	1.18	0.87-1.60
Asian/Pacific Islander Individuals	1.52	1.04-2.22	1.26	0.85-1.88	1.16	0.76-1.76
Other Individuals	0.70	0.36-1.36	0.61	0.31-1.19	0.58	0.30-1.14

*Model adjusts for: age, sex, US state of residence, cohort year.

**Model adjusts for: age, sex, US state of residence, cohort year, eligibility for dual-Medicaid, eligibility for Part D low-income subsidies, CCW comorbidities, glaucoma severity, and glaucoma subtype.

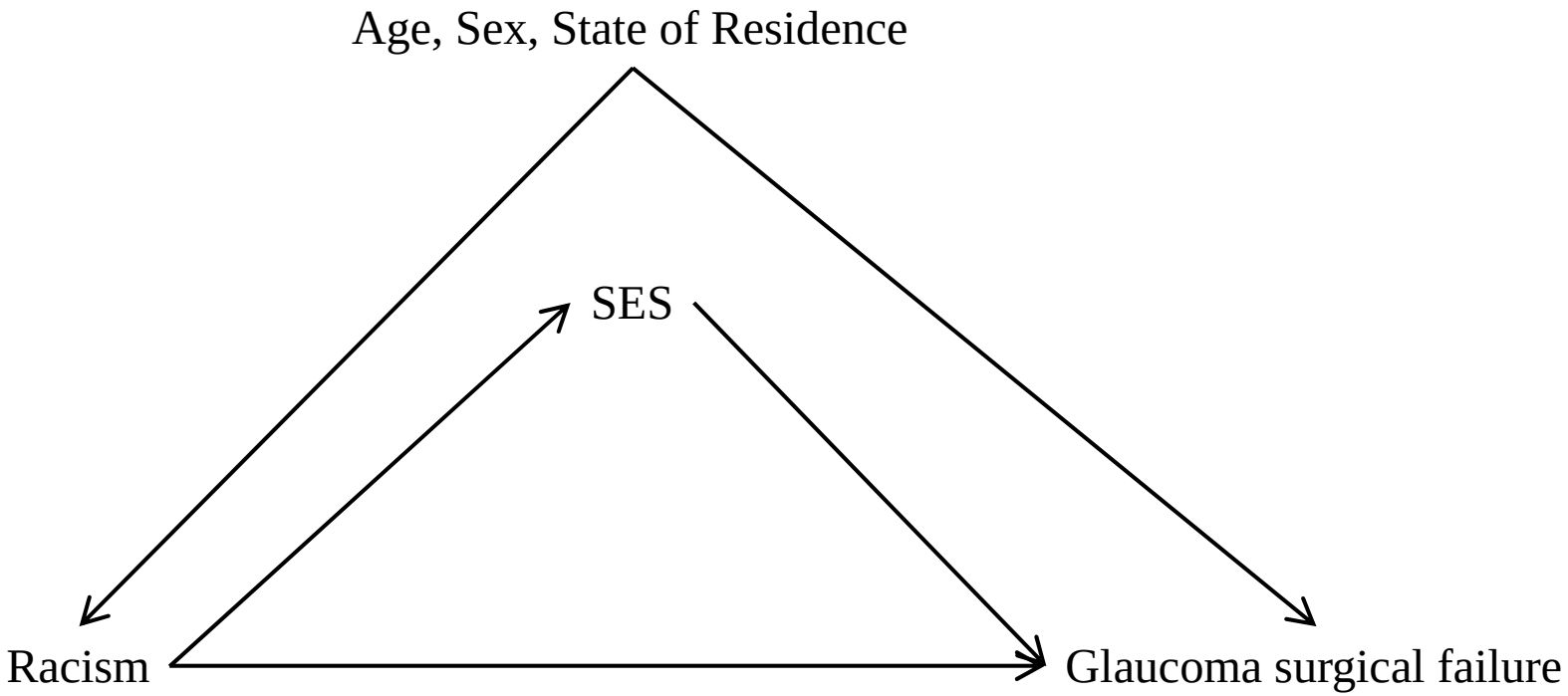
Supplementary Table 3.1 Linear Regression Models Examining Association between Beneficiary Race & Ethnicity and Surgeon Normalized Degree Centrality

	Normalized Degree Centrality					
Beneficiary Race & Ethnicity	**Unadjusted Model**		**Partially Adjusted Model**		**Fully Adjusted Model**	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Non-Latinx White Patients	Reference				Reference	
Black Patients	-0.0013	-0.0035 to 0.0010	-0.0008	-0.0031 to 0.0015	-0.0009	-0.0032 to 0.0014
Latinx Patients	-0.0036	-0.0051 to -0.0020	-0.0029	-0.0047 to -0.0011	-0.0029	-0.0047 to -0.0011
Asian/Pacific Islander Patients	0.0018	0.0000 to 0.0037	0.0024	0.0005 to 0.0044	0.0025	0.0005 to 0.0044
Other Individuals	-0.0012	-0.0048 to 0.0024	-0.0009	-0.0045 to 0.0028	-0.0009	-0.0046 to 0.0027

Supplementary Table 3.2 Linear Regression Models Examining Association between Beneficiary Race & Ethnicity and Surgeon Normalized Degree Centrality

	Normalized Degree Centrality					
Beneficiary Race & Ethnicity	**Unadjusted Model**		**Partially Adjusted Model**		**Fully Adjusted Model**	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Non-Latinx White Patients	Reference				Reference	
Black Patients	0.041	0.010 to 0.072	0.032	0.000 to 0.064	0.032	0.000 to 0.064
Latinx Patients	0.044	0.022 to 0.067	0.034	0.009 to 0.059	0.035	0.009 to 0.060
Asian/Pacific Islander Patients	-0.019	-0.044 to 0.007	-0.027	-0.055 to 0.000	-0.026	-0.054 to 0.001
Other Patients	-0.011	-0.061 to 0.040	-0.018	-0.069 to 0.033	-0.016	-0.066 to 0.035

Supplementary Figure 4.1 Simplified Directed Acyclic Graph 2 (DAG 2) for estimating natural effects (no uncontrolled-confounding of exposure-mediator, mediator outcome, and exposure-outcome relationships).



SES = socioeconomic status

Supplementary Table 4.1 Causal mediation analysis estimates for SES as mediator for racial and ethnic disparities in glaucoma surgical failure (reoperation and revision events), US cohort						
	TE	**95% CI**	**CDE**	**95% CI**	**PE**	**95% CI**
Non-Latinx White Patients	Reference					
Black Patients	1.17	1.05 to 1.31	1.22	1.09 to 1.37	-0.27	-0.70 to 0.15
Latinx Patients	1.27	1.10 to 1.47	1.29	1.06 to 1.55	-0.04	-0.57 to 0.49
Asian/Pacific Islander Patients	1.20	0.98 to 1.49	1.25	0.97 to 1.62	-0.22	-1.08 to 0.64
Other Patients	1.03	0.81 to 1.34	1.00	0.76 to 1.32	1.01	-6.27 to 8.33

*TE = total effect; CDE = controlled direct effect; CI = confidence interval; PE = proportion eliminated

Supplementary Table 4.2 Causal mediation analysis estimates for SES as mediator for racial and ethnic disparities in glaucoma surgical failure (reoperation and revision events), CA cohort						
	TE	**95% CI**	**CDE**	**95% CI**	**PE**	**95% CI**
Non-Latinx White Patients	Reference					
Black Patients	1.18	0.99 to 1.41	1.01	0.80 to 1.27	0.96	-0.27 to 2.19
Latinx Patients	1.23	1.08 to 1.41	1.10	0.90 to 1.35	0.54	-0.25 to 1.33
Asian/Pacific Islander Patients	1.18	1.02 to 1.36	1.21	0.99 to 1.47	-0.18	-1.11 to 0.75
Other Patients	1.32	1.03 to 1.70	1.24	0.91 to 1.68	0.24	-0.49 to 0.97

*TE = total effect; CDE = controlled direct effect; CI = confidence interval; PE = proportion eliminated

Chapter 7: References

1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA.* 2014;311(18):1901-1911.
2. Stein JD, Khawaja AP, Weizer JS. Glaucoma in Adults-Screening, Diagnosis, and Management: A Review. *JAMA.* 2021;325(2):164-174.
3. Jonas JB, Aung T, Bourne RR, Bron AM, Ritch R, Panda-Jonas S. Glaucoma. *Lancet.* 2017;390(10108):2183-2193.
4. Harwerth RS, Wheat JL, Fredette MJ, Anderson DR. Linking structure and function in glaucoma. *Prog Retin Eye Res.* 2010;29(4):249-271.
5. Quigley HA, Addicks EM, Green WR, Maumenee AE. Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage. *Arch Ophthalmol.* 1981;99(4):635-649.
6. Chua J, Baskaran M, Ong PG, et al. Prevalence, Risk Factors, and Visual Features of Undiagnosed Glaucoma: The Singapore Epidemiology of Eye Diseases Study. *JAMA Ophthalmol.* 2015;133(8):938-946.
7. McCann P, Hogg R, Wright DM, et al. Glaucoma in the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA): cohort profile, prevalence, awareness and associations. *Br J Ophthalmol.* 2020;104(11):1492-1499.
8. Quigley HA, West SK, Rodriguez J, Munoz B, Klein R, Snyder R. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. *Arch Ophthalmol.* 2001;119(12):1819-1826.
9. Shaikh Y, Yu F, Coleman AL. Burden of undetected and untreated glaucoma in the United States. *Am J Ophthalmol.* 2014;158(6):1121-1129 e1121.

10. 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.* 1991;109(8):1090-1095.

11. Topouzis F, Coleman AL, Harris A, et al. Factors associated with undiagnosed open-angle glaucoma: the Thessaloniki Eye Study. *Am J Ophthalmol.* 2008;145(2):327-335.

12. Ong EL, Baasanhu J, Nolan W, et al. The utility of symptoms in identification of primary angle-closure in a high-risk population. *Ophthalmology.* 2008;115(11):2024-2029.

13. National Eye Institute. Glaucoma Awareness Can Help Save Vision for Millions. https://www.nei.nih.gov/about/news-and-events/news/glaucoma-awareness-can-help-save-vision-millions. Published 2015. Accessed September 27, 2022.

14. 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.* 2014;121(11):2081-2090.

15. Blindness GBD, Vision Impairment C, Vision Loss Expert Group of the Global Burden of Disease S. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. *Lancet Glob Health.* 2021;9(2):e144-e160.

16. Wang K, Gaitsch H, Poon H, Cox NJ, Rzhetsky A. Classification of common human diseases derived from shared genetic and environmental determinants. *Nat Genet.* 2017;49(9):1319-1325.

17. Wolfs RC, Klaver CC, Ramrattan RS, van Duijn CM, Hofman A, de Jong PT. Genetic risk of primary open-angle glaucoma. Population-based familial aggregation study. *Arch Ophthalmol.* 1998;116(12):1640-1645.

18. Fingert JH. Primary open-angle glaucoma genes. *Eye (Lond).* 2011;25(5):587-595.

19. Youngblood H, Hauser MA, Liu Y. Update on the genetics of primary open-angle glaucoma. *Exp Eye Res.* 2019;188:107795.

20. European Glaucoma Prevention Study G, Miglior S, Pfeiffer N, et al. Predictive factors for open-angle glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study. *Ophthalmology.* 2007;114(1):3-9.

21. Kim KE, Kim MJ, Park KH, et al. Prevalence, Awareness, and Risk Factors of Primary Open-Angle Glaucoma: Korea National Health and Nutrition Examination Survey 2008-2011. *Ophthalmology.* 2016;123(3):532-541.

22. Kim M, Kim TW, Park KH, Kim JM. Risk factors for primary open-angle glaucoma in South Korea: the Namil study. *Jpn J Ophthalmol.* 2012;56(4):324-329.

23. 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.* 2003;44(9):3783-3789.

24. Rudnicka AR, Mt-Isa S, Owen CG, Cook DG, Ashby D. Variations in primary open-angle glaucoma prevalence by age, gender, and race: a Bayesian meta-analysis. *Invest Ophthalmol Vis Sci.* 2006;47(10):4254-4261.

25. Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: the Tajimi Study. *Ophthalmology.* 2006;113(9):1613-1617.

26. Friedman DS, Wolfs RC, O'Colmain BJ, et al. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol.* 2004;122(4):532-538.

27. Friedman DS, Jampel HD, Munoz B, West SK. The prevalence of open-angle glaucoma among blacks and whites 73 years and older: the Salisbury Eye Evaluation Glaucoma Study. *Arch Ophthalmol.* 2006;124(11):1625-1630.

28. Kini MM, Leibowitz HM, Colton T, Nickerson RJ, Ganley J, Dawber TR. Prevalence of senile cataract, diabetic retinopathy, senile macular degeneration, and open-angle glaucoma in the Framingham eye study. *Am J Ophthalmol.* 1978;85(1):28-34.

29. Klein BE, Klein R, Sponsel WE, et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology.* 1992;99(10):1499-1504.

30. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA.* 1991;266(3):369-374.

31. Varma R, Ying-Lai M, Francis BA, et al. Prevalence of open-angle glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study. *Ophthalmology.* 2004;111(8):1439-1448.

32. Vajaranant TS, Wu S, Torres M, Varma R. The changing face of primary open-angle glaucoma in the United States: demographic and geographic changes from 2011 to 2050. *Am J Ophthalmol.* 2012;154(2):303-314 e303.

33. Coleman AL, Yu F, Rowe S. Visual field testing in glaucoma Medicare beneficiaries before surgery. *Ophthalmology.* 2005;112(3):401-406.

34. Stein JD, Talwar N, Laverne AM, Nan B, Lichter PR. Racial disparities in the use of ancillary testing to evaluate individuals with open-angle glaucoma. *Arch Ophthalmol.* 2012;130(12):1579-1588.

35. 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.* 2017;124(10):1442-1448.

36. Halawa OA, Kolli A, Oh G, et al. Racial and Socioeconomic Differences in Eye Care Utilization among Medicare Beneficiaries with Glaucoma. *Ophthalmology.* 2022;129(4):397-405.

37. Gedde SJ, Vinod K, Wright MM, et al. Primary Open-Angle Glaucoma Preferred Practice Pattern(R). *Ophthalmology.* 2021;128(1):P71-P150.

38. Huang AR, Mallet L, Rochefort CM, Eguale T, Buckeridge DL, Tamblyn R. Medication-related falls in the elderly: causative factors and preventive strategies. *Drugs Aging.* 2012;29(5):359-376.

39. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J Geriatr Pharmacother.* 2007;5(4):345-351.

40. Reardon G, Kotak S, Schwartz GF. Objective assessment of compliance and persistence among patients treated for glaucoma and ocular hypertension: a systematic review. *Patient Prefer Adherence.* 2011;5:441-463.

41. Brancato R, Carassa R, Trabucchi G. Diode laser compared with argon laser for trabeculoplasty. *Am J Ophthalmol.* 1991;112(1):50-55.

42. Chung PY, Schuman JS, Netland PA, Lloyd-Muhammad RA, Jacobs DS. Five-year results of a randomized, prospective, clinical trial of diode vs argon laser trabeculoplasty for open-angle glaucoma. *Am J Ophthalmol.* 1998;126(2):185-190.

43. Kramer TR, Noecker RJ. Comparison of the morphologic changes after selective laser trabeculoplasty and argon laser trabeculoplasty in human eye bank eyes. *Ophthalmology.* 2001;108(4):773-779.

44. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. LiGHT trial: 6-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. *Ophthalmology.* 2022.

45. Musch DC, Gillespie BW, Lichter PR, Niziol LM, Janz NK, Investigators CS. Visual field progression in the Collaborative Initial Glaucoma Treatment Study the impact of treatment and other baseline factors. *Ophthalmology.* 2009;116(2):200-207.

46. Law SK, Modjtahedi SP, Mansury A, Caprioli J. Intermediate-term comparison of trabeculectomy with intraoperative mitomycin-C between Asian American and Caucasian glaucoma patients: a case-controlled comparison. *Eye (Lond).* 2007;21(1):71-78.

47. Kim HY, Egbert PR, Singh K. Long-term comparison of primary trabeculectomy with 5-fluorouracil versus mitomycin C in West Africa. *J Glaucoma.* 2008;17(7):578-583.

48. Wong MH, Husain R, Ang BC, et al. The Singapore 5-fluorouracil trial: intraocular pressure outcomes at 8 years. *Ophthalmology.* 2013;120(6):1127-1134.

49. Kirwan JF, Lockwood AJ, Shah P, et al. Trabeculectomy in the 21st century: a multicenter analysis. *Ophthalmology.* 2013;120(12):2532-2539.

50. Wilkins M, Indar A, Wormald R. Intra-operative mitomycin C for glaucoma surgery. *Cochrane Database Syst Rev.* 2005(4):CD002897.

51. de Jong L, Lafuma A, Aguade AS, Berdeaux G. Five-year extension of a clinical trial comparing the EX-PRESS glaucoma filtration device and trabeculectomy in primary open-angle glaucoma. *Clin Ophthalmol.* 2011;5:527-533.

52. Netland PA, Sarkisian SR, Jr., Moster MR, et al. Randomized, prospective, comparative trial of EX-PRESS glaucoma filtration device versus trabeculectomy (XVT study). *Am J Ophthalmol.* 2014;157(2):433-440 e433.

53. Wagschal LD, Trope GE, Jinapriya D, Jin YP, Buys YM. Prospective Randomized Study Comparing Ex-PRESS to Trabeculectomy: 1-Year Results. *J Glaucoma.* 2015;24(8):624-629.

54. Dahan E, Carmichael TR. Implantation of a miniature glaucoma device under a scleral flap. *J Glaucoma.* 2005;14(2):98-102.

55. Good TJ, Kahook MY. Assessment of bleb morphologic features and postoperative outcomes after Ex-PRESS drainage device implantation versus trabeculectomy. *Am J Ophthalmol.* 2011;151(3):507-513 e501.

56. Maris PJ, Jr., Ishida K, Netland PA. Comparison of trabeculectomy with Ex-PRESS miniature glaucoma device implanted under scleral flap. *J Glaucoma.* 2007;16(1):14-19.

57. Marzette L, Herndon LW. A comparison of the Ex-PRESS mini glaucoma shunt with standard trabeculectomy in the surgical treatment of glaucoma. *Ophthalmic Surg Lasers Imaging.* 2011;42(6):453-459.

58. Seider MI, Rofagha S, Lin SC, Stamper RL. Resident-performed Ex-PRESS shunt implantation versus trabeculectomy. *J Glaucoma.* 2012;21(7):469-474.

59. Sugiyama T, Shibata M, Kojima S, Ueki M, Ikeda T. The first report on intermediate-term outcome of Ex-PRESS glaucoma filtration device implanted under scleral flap in Japanese patients. *Clin Ophthalmol.* 2011;5:1063-1066.

60. Arimura S, Miyake S, Iwasaki K, et al. Randomised Clinical Trial for Postoperative Complications after Ex-PRESS Implantation versus Trabeculectomy with 2-Year Follow-Up. *Sci Rep.* 2018;8(1):16168.

61. Gedde SJ, Feuer WJ, Lim KS, et al. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 5 Years of Follow-up. *Ophthalmology.* 2022.

62. Gedde SJ, Herndon LW, Brandt JD, et al. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol.* 2012;153(5):804-814 e801.

63. 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.* 2021;4(5):e218348.

64. Tzimis V, Tze L, Ganesh J, et al. Laser trabeculoplasty: an investigation into factors that might influence outcomes. *Can J Ophthalmol.* 2011;46(4):305-309.

65. Shin DH, Hughes BA, Song MS, et al. Primary glaucoma triple procedure with or without adjunctive mitomycin. Prognostic factors for filtration failure. *Ophthalmology.* 1996;103(11):1925-1933.

66. 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.* 1999;117(9):1149-1154.

67. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within treatment groups. *Am J Ophthalmol.* 2001;132(3):311-320.

68. Ederer F, Gaasterland DE, Sullivan EK, Investigators A. The Advanced Glaucoma Intervention Study (AGIS): 1. Study design and methods and baseline characteristics of study patients. *Control Clin Trials.* 1994;15(4):299-325.

69. C. A. T. Trabeculectomy Study Group, Khaw P, Grehn F, et al. A phase III study of subconjunctival human anti-transforming growth factor beta(2) monoclonal antibody (CAT-152) to prevent scarring after first-time trabeculectomy. *Ophthalmology.* 2007;114(10):1822-1830.

70. C. A. T. Trabeculectomy Study Group. CAT-152 Trabeculectomy Study. *Ophthalmology.* 2007;114(10):1950.

71. C. A. T. Trabeculectomy Study Group, Grehn F, Hollo 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.* 2007;114(10):1831-1838.

72. 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.* 2018;136(10):1106-1113.

73. 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;6:955-962.

74. Freedman J, Ferri S. Long-term comparison using Ex-PRESS glaucoma shunt in black and white patients. *Can J Ophthalmol.* 2014;49(2):200-204.

75. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol.* 2012;153(5):789-803 e782.

76. Rotchford AP, King AJ. Moving the goal posts definitions of success after glaucoma surgery and their effect on reported outcome. *Ophthalmology.* 2010;117(1):18-23 e13.

77. World Glaucoma Association, Weinreb RN, Ramulu P, et al. *Glaucoma Surgery.* Amsterdam, The Netherlands: Kugler Publications; 2019.

78. Mues KE, Liede A, Liu J, et al. Use of the Medicare database in epidemiologic and health services research: a valuable source of real-world evidence on the older and disabled populations in the US. *Clin Epidemiol.* 2017;9:267-277.

79. Centers for Medicare & Medicaid Services. CMS Program Statistics - Medicare Total Enrollment. https://data.cms.gov/summary-statistics-on-beneficiary-enrollment/medicare-and-medicaid-reports/cms-program-statistics-medicare-total-enrollment. Published 2020. Accessed October 3, 2022.

80. United States Census Bureau. 2020: American Community Survey 5-year Estimates Subject Tables - S0101 | AGE AND SEX. https://data.census.gov/cedsci/table?t=Age%20and%20Sex&y=2020&tid=ACSST5Y2020.S0101. Published 2020. Accessed October 3, 2022.

81. Coleman AL, Greenland S. Glaucoma outcome studies using existing databases: opportunities and limitations. *J Glaucoma.* 1995;4(4):295-298.

82. Stein JD, Lum F, Lee PP, Rich WL, 3rd, Coleman AL. Use of health care claims data to study patients with ophthalmologic conditions. *Ophthalmology.* 2014;121(5):1134-1141.

83. Tarazi W, Welch WP, Nguyen N, et al. Medicare Beneficiary Enrollment Trends and Demographic Characteristics (Issue Brief No. HP-2022-08). *Office of the Assistant Secretary for Planning and Evaluation, US Department of Health and Human Services.* 2022;March 2022.

84. Research Data Assistance Center (ResDAC). Carrier (Fee-for-Service). https://resdac.org/cms-data/files/carrier-ffs. Accessed October 10, 2022.

85. HealthCare.gov. Fee for service. https://www.healthcare.gov/glossary/fee-for-service/. Accessed October 3, 2022.

86. Research Data Assistance Center (ResDAC). A-Z Glossary of Terms: CMS Form 1500. https://resdac.org/glossary#5061. Accessed October 10, 2022.

87. Research Data Assistance Center (ResDAC). Introduction to Medicare Utilization Data. http://resdac.umn.edu/sites/resdac.umn.edu/files/Introduction%20to%20Medicare%20Utilization%20Data%20(Slides).pdf. Accessed October 10, 2022.

88. Research Data Assistance Center (ResDAC). Master Beneficiary Summary File (MBSF) Base. https://resdac.org/cms-data/files/mbsf-base. Accessed October 10, 2022.

89. Jarrin OF, Nyandege AN, Grafova IB, Dong X, Lin H. Validity of Race and Ethnicity Codes in Medicare Administrative Data Compared With Gold-standard Self-reported Race Collected During Routine Home Health Care Visits. *Med Care.* 2020;58(1):e1-e8.

90. Filice CE, Joynt KE. Examining Race and Ethnicity Information in Medicare Administrative Data. *Med Care.* 2017;55(12):e170-e176.

91. Research Data Assistance Center (ResDAC). Research Triange Institute (RTI) Race Code. https://resdac.org/cms-data/variables/research-triangle-institute-rti-race-code. Accessed October 10, 2022.

92. National Research Council. In: Ver Ploeg M, Perrin E, eds. *Eliminating Health Disparities: Measurement and Data Needs.* Washington (DC): National Academies Press; 2004.

93. Javitt JC, McBean AM, Nicholson GA, Babish JD, Warren JL, Krakauer H. Undertreatment of glaucoma among black Americans. *N Engl J Med.* 1991;325(20):1418-1422.

94. Glynn RJ, Gurwitz JH, Bohn RL, Monane M, Choodnovskiy I, Avorn J. Old age and race as determinants of initiation of glaucoma therapy. *Am J Epidemiol.* 1993;138(6):395-406.

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

96. Devgan U, Yu F, Kim E, Coleman AL. Surgical undertreatment of glaucoma in black beneficiaries of medicare. *Arch Ophthalmol.* 2000;118(2):253-256.

97. Ostermann J, Sloan FA, Herndon L, Lee PP. Racial differences in glaucoma care: the longitudinal pattern of care. *Arch Ophthalmol.* 2005;123(12):1693-1698.

98. Gupta P, Zhao D, Guallar E, Ko F, Boland MV, Friedman DS. Prevalence of Glaucoma in the United States: The 2005-2008 National Health and Nutrition Examination Survey. *Invest Ophthalmol Vis Sci.* 2016;57(6):2905-2913.

99. Lee BA, Martin MJR, Matthews SA, Farrell CR. State-level changes in US racial and ethnic diversity, 1980 to 2015: A universal trend? *Demogr Res.* 2017;37:1031-1048.

100. American Academy of Ophthalmology (AAO). ICD-10 Glaucoma Reference Guide. https://www.aao.org/Assets/5adb14a6-7e5d-42ea-af51-3db772c4b0c2/636713219263270000/bc-2568-update-icd-10-quick-reference-guides-glaucoma-final-v2-color-pdf?inline=1. Published 2015. Accessed October 10, 2022.

101. Hellman JB, Lim MC, Leung KY, Blount CM, Yiu G. The impact of conversion to International Classification of Diseases, 10th revision (ICD-10) on an academic ophthalmology practice. *Clin Ophthalmol.* 2018;12:949-956.

102. Craven ER, Singh IP, Yu TM, Rhoten S, Sadruddin OR, Sheybani A. Reoperation Rates and Disease Costs for Primary Open-Angle Glaucoma Patients in the United States Treated with Incisional Glaucoma Surgery. *Ophthalmol Glaucoma.* 2022;5(3):297-305.

103. GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. *Lancet Glob Health.* 2021;9(2):e144-e160.

104. Halawa OA, Jin Q, Pasquale LR, et al. Race and Ethnicity Differences in Disease Severity and Visual Field Progression Among Glaucoma Patients. *Am J Ophthalmol.* 2022;242:69-76.

105. Ederer F, Gaasterland DA, Dally LG, et al. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race: 10-year results. *Ophthalmology.* 2004;111(4):651-664.

106. Ishida K, Netland PA. Ahmed Glaucoma Valve implantation in African American and white patients. *Arch Ophthalmol.* 2006;124(6):800-806.

107. Scott IU, Greenfield DS, Schiffman J, et al. Outcomes of primary trabeculectomy with the use of adjunctive mitomycin. *Arch Ophthalmol.* 1998;116(3):286-291.

108. Shin DH, Ren J, Juzych MS, et al. Primary glaucoma triple procedure in patients with primary open-angle glaucoma: the effect of mitomycin C in patients with and without prognostic factors for filtration failure. *Am J Ophthalmol.* 1998;125(3):346-352.

109. Ciociola EC, Yang SA, Hall N, et al. Effectiveness of Trabeculectomy and Tube Shunt with versus without Concurrent Phacoemulsification: Intelligent Research in Sight Registry Longitudinal Analysis. *Ophthalmol Glaucoma.* 2023;6(1):42-53.

110. Research Data Assistance Center (ResDAC). Medicare Sample Group Indicator. https://resdac.org/cms-data/variables/medicare-sample-group-indicator. Accessed March 3, 2023.

111. U.S. Department of Health and Human Services Office of Inspector General. Inaccuracies in Medicare's Race and Ethnicity Data Hinder the Ability To Assess Health Disparities. June 2022;OEI-02-21-00100.

112. Social Secuirty Administration (SSA). How do I change the sex identification on my Social Security record? https://www.ssa.gov/people/lgbtq/gender-identity.html. Accessed February 14, 2023.

113. Research Data Assistance Center (ResDAC). Months of Dual Eligibility. https://resdac.org/cms-data/variables/months-dual-eligibility. Accessed October 10, 2022.

114. Research Data Assistance Center (ResDAC). Monthly cost sharing group under Part D low-income subsidy - January. https://resdac.org/cms-data/variables/monthly-cost-sharing-group-under-part-d-low-income-subsidy-january. Accessed October 10, 2022.

115. Samson LW, Finegold K, Ahmed A, Jensen M, Filice CE, Joynt KE. Examining Measures of Income and Poverty in Medicare Administrative Data. *Med Care.* 2017;55(12):e158-e163.

116. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-383.

117. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol.* 1992;45(6):613-619.

118. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005;43(11):1130-1139.

119. Kim EJ, Kim T, Conigliaro J, Liebschutz JM, Paasche-Orlow MK, Hanchate AD. Racial and Ethnic Disparities in Diagnosis of Chronic Medical Conditions in the USA. *J Gen Intern Med.* 2018;33(7):1116-1123.

120. Chronic Conditions Data Warehouse (CCW). Chronic Conditions. https://www2.ccwdata.org/web/guest/condition-categories-chronic. Accessed March 3, 2023.

121. Chronic Conditions Data Warehouse (CCW). 27 CCW Chronic Conditions Algorithms: MBSF_CC_{YYYY} File. https://www2.ccwdata.org/documents/10280/19139421/ccw-chronic-condition-algorithms.pdf. Published 2023. Accessed March 3, 2023.

122. Coulon SJ, Vanner EA, Gedde SJ, Primary Tube Versus Trabeculectomy Study G. Outcomes of Glaucoma Reoperations in the Primary Tube Versus Trabeculectomy Study. *Ophthalmol Glaucoma.* 2023.

123. Law SK, Shih K, Tran DH, Coleman AL, Caprioli J. Long-term outcomes of repeat vs initial trabeculectomy in open-angle glaucoma. *Am J Ophthalmol.* 2009;148(5):685-695 e681.

124. Gedde SJ, Feuer WJ, Chen PP, et al. Comparing Treatment Outcomes from the Tube Versus Trabeculectomy and Primary Tube Versus Trabeculectomy Studies. *Ophthalmology.* 2021;128(2):324-326.

125. Jackson JW. Meaningful Causal Decompositions in Health Equity Research: Definition, Identification, and Estimation Through a Weighting Framework. *Epidemiology.* 2021;32(2):282-290.

126. Flanagin A, Frey T, Christiansen SL, Committee AMAMoS. Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals. *JAMA.* 2021;326(7):621-627.

127. Bland JM, Altman DG. The logrank test. *BMJ.* 2004;328(7447):1073.

128. Tolbert J, Drake P, Damico A. *Key Facts about the Uninsured Population.* Kaiser Family Foundation (KFF); December 19, 2022.

129. Centers for Disease Control and Prevention (CDC) - Vision and Eye Health Surveillance System (VEHSS). IRIS® Registry at a Glance. https://www.cdc.gov/visionhealth/vehss/data/ehr-registries/iris.html. Accessed March 3, 2023.

130. Saheb H, Gedde SJ, Schiffman JC, Feuer WJ, Tube Versus Trabeculectomy Study G. Outcomes of glaucoma reoperations in the Tube Versus Trabeculectomy (TVT) Study. *Am J Ophthalmol.* 2014;157(6):1179-1189 e1172.

131. Vinod K, Gedde SJ, Feuer WJ, et al. Practice Preferences for Glaucoma Surgery: A Survey of the American Glaucoma Society. *J Glaucoma.* 2017;26(8):687-693.

132. Witzig R. The medicalization of race: scientific legitimization of a flawed social construct. *Ann Intern Med.* 1996;125(8):675-679.

133. Howe CJ, Dulin-Keita A, Cole SR, et al. Evaluating the Population Impact on Racial/Ethnic Disparities in HIV in Adulthood of Intervening on Specific Targets: A Conceptual and Methodological Framework. *Am J Epidemiol.* 2018;187(2):316-325.

134. VanderWeele TJ. Marginal structural models for the estimation of direct and indirect effects. *Epidemiology.* 2009;20(1):18-26.

135. Richiardi L, Bellocco R, Zugna D. Mediation analysis in epidemiology: methods, interpretation and bias. *Int J Epidemiol.* 2013;42(5):1511-1519.

136. Rothman KJ, Greenland S, Lash TL. *Modern epidemiology.* 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008.

137. Landon BE, Onnela JP, Meneades L, O'Malley AJ, Keating NL. Assessment of Racial Disparities in Primary Care Physician Specialty Referrals. *JAMA Netw Open.* 2021;4(1):e2029238.

138. Bach PB, Pham HH, Schrag D, Tate RC, Hargraves JL. Primary care physicians who treat blacks and whites. *N Engl J Med.* 2004;351(6):575-584.

139. Mandl KD, Olson KL, Mines D, Liu C, Tian F. Provider collaboration: cohesion, constellations, and shared patients. *J Gen Intern Med.* 2014;29(11):1499-1505.

140. Dahlander L, McFarland DA. Ties That Last: Tie Formation and Persistence in Research Collaborations over Time. *Admin Sci Quart.* 2013;58(1):69-110.

141. Hollingsworth JM, Funk RJ, Garrison SA, et al. Differences between physician social networks for cardiac surgery serving communities with high versus low proportions of black residents. *Med Care.* 2015;53(2):160-167.

142. DuGoff EH, Fernandes-Taylor S, Weissman GE, Huntley JH, Pollack CE. A scoping review of patient-sharing network studies using administrative data. *Transl Behav Med.* 2018;8(4):598-625.

143. Newman M. *Networks: An Introduction.* Oxford University Press, Inc.; 2010.

144. Fleming L, Mingo S, Chen D. Collaborative Brokerage, Generative Creativity, and Creative Success. *Admin Sci Quart.* 2007;52:443-475.

145. Ghomrawi HMK, Funk RJ, Parks ML, Owen-Smith J, Hollingsworth JM. Physician referral patterns and racial disparities in total hip replacement: A network analysis approach. *PLoS One.* 2018;13(2):e0193014.

146. Gabbay J, le May A. Evidence based guidelines or collectively constructed "mindlines?" Ethnographic study of knowledge management in primary care. *BMJ.* 2004;329(7473):1013.

147. Brass DJ, Galaskiewicz J, Greve HR, Tsai W. Taking Stock of Networks and Organizations: A Multilevel Perspective. *The Academy of Management Journal.* 2004;47(6):795-817.

148. Barnett ML, Christakis NA, O'Malley J, Onnela JP, Keating NL, Landon BE. Physician patient-sharing networks and the cost and intensity of care in US hospitals. *Med Care.* 2012;50(2):152-160.

149. Funk RJ. MAKING THE MOST OF WHERE YOU ARE: GEOGRAPHY, NETWORKS, AND INNOVATION IN ORGANIZATIONS. *The Academy of Management Journal.* 2014;57(1):193-222.

150. Tortoriello M, Krackhardt D. Activating Cross-Boundary Knowledge: The Role of Simmelian Ties in the Generation of Innovations. *Academy of Management Journal.* 2010;53(1):167-181.

151. Fruchterman TMJ, Reingold EM. Graph drawing by force-directed placement. *Software, practice & experience.* 1991;21(11):1129-1164.

152. Christakis NA, Fowler JH. Social Network Visualization in Epidemiology. *Nor Epidemiol.* 2009;19(1):5-16.

153. Kamada T, Kawai S. An algorithm for drawing general undirected graphs. *Information Processing Letters.* 1989;31(1):7-15.

154. Blondel VD, Guillaume J-L, Lambiotte R, Lefebvre E. Fast unfolding of communities in large networks. *Journal of Statistical Mechanics: Theory and Experiment.* 2008;2008(10):P10008.

155. Smith NR, Zivich PN, Frerichs LM, Moody J, Aiello AE. A Guide for Choosing Community Detection Algorithms in Social Network Studies: The Question Alignment Approach. *Am J Prev Med.* 2020;59(4):597-605.

156. Austin PC. A Tutorial on Multilevel Survival Analysis: Methods, Models and Applications. *Int Stat Rev.* 2017;85(2):185-203.

157. Johnson H, McGhee E, Cuellar Mejia M. *California's Population.* Public Policy Institute of California (PPIC);2023.

158. Pollack CE, Wang H, Bekelman JE, et al. Physician social networks and variation in rates of complications after radical prostatectomy. *Value Health.* 2014;17(5):611-618.

159. McPherson M, Smith-Lovin L, Cook JM. Birds of a Feather: Homophily in Social Networks. *Annual Review of Sociology.* 2001;27(1):415-444.

160. Shortell SM. Patterns of referral among internists in private practice: a social exchange model. *J Health Soc Behav.* 1973;14(4):335-348.

161. Landon BE, Keating NL, Barnett ML, et al. Variation in patient-sharing networks of physicians across the United States. *JAMA.* 2012;308(3):265-273.

162. Melchior B, Valenzuela IA, De Moraes CG, et al. Glaucomatous Visual Field Progression in the African Descent and Glaucoma Evaluation Study (ADAGES): Eleven Years of Follow-up. *Am J Ophthalmol.* 2022;239:122-129.

163. Vyas DA, Eisenstein LG, Jones DS. Hidden in Plain Sight - Reconsidering the Use of Race Correction in Clinical Algorithms. *N Engl J Med.* 2020;383(9):874-882.

164. Acuff K, Delavar A, Radha Saseendrakumar B, Wu JH, Weinreb RN, Baxter SL. Associations between Socioeconomic Factors and Visit Adherence among Patients with Glaucoma in the All of Us Research Program. *Ophthalmol Glaucoma.* 2023.

165. Delavar A, Radha Saseendrakumar B, Weinreb RN, Baxter SL. Racial and Ethnic Disparities in Cost-Related Barriers to Medication Adherence Among Patients With Glaucoma Enrolled in the National Institutes of Health All of Us Research Program. *JAMA Ophthalmol.* 2022;140(4):354-361.

166. VanderWeele TJ. Policy-relevant proportions for direct effects. *Epidemiology.* 2013;24(1):175-176.

167. VanderWeele TJ, Robinson WR. On the causal interpretation of race in regressions adjusting for confounding and mediating variables. *Epidemiology.* 2014;25(4):473-484.

168. Suzuki E, Evans D, Chaix B, Vanderweele TJ. On the "proportion eliminated" for risk differences versus excess relative risks. *Epidemiology.* 2014;25(2):309-310.

169. Hernán MA, Robbins JM. *Causal Inference: What If.* Boca Raton: Chapman & Hall/CRC; 2020.

170. Howe CJ, Cain LE, Hogan JW. Are all biases missing data problems? *Curr Epidemiol Rep.* 2015;2(3):162-171.

171. VanderWeele TJ, Vansteelandt S. Conceptual issues concerning mediation, interventions and composition. *Statistics and Its Interface.* 2009;2(4):457-468.

172. VanderWeele TJ. *Explanation in Causal Inference: Methods for Mediation and Interaction.* New York, NY: Oxford University Press; 2015.

173. Valeri L, VanderWeele TJ. SAS macro for causal mediation analysis with survival data. *Epidemiology.* 2015;26(2):e23-24.

174. Shi B, Choirat C, Coull BA, VanderWeele TJ, Valeri L. CMAverse: A Suite of Functions for Reproducible Causal Mediation Analyses. *Epidemiology.* 2021;32(5):e20-e22.

175. Kennedy-Moulton K, Miller S, Persson P, Rossin-Slater M, Wherry L, Aldana G. Maternal and Infant Health Inequality: New Evidence from Linked Administrative Data. *National Bureau of Economic Research Working Paper Series.* 2022;No. 30693.

176. Hicks PM, Woodward MA, Niziol LM, et al. Seeing Red: Associations between Historical Redlining and Present-Day Visual Impairment and Blindness. *Ophthalmology.* 2023;130(4):404-412.

177. Blakely T, Disney G, Valeri L, et al. Socioeconomic and Tobacco Mediation of Ethnic Inequalities in Mortality over Time: Repeated Census-mortality Cohort Studies, 1981 to 2011. *Epidemiology.* 2018;29(4):506-516.

178. Guadamuz JS, Ozenberger K, Qato DM, et al. Mediation analyses of socioeconomic factors determining racial differences in the treatment of diffuse large B-cell lymphoma in a cohort of older adults. *Medicine (Baltimore).* 2019;98(46):e17960.

179. Fritz MS, Mackinnon DP. Required sample size to detect the mediated effect. *Psychol Sci.* 2007;18(3):233-239.

180. Elam AR, Tseng VL, Rodriguez TM, et al. Disparities in Vision Health and Eye Care. *Ophthalmology.* 2022;129(10):e89-e113.