Clinics in Surgery

Research Article
Published: 19 Aug, 2024

# The Evolution of Glaucoma Surgery Through Clinical Trials: From Past to Present

*Appelbaum J[1], Patel D[2], Greene L[3] and Allison K[4]**

[1]School of Medicine, New York Medical College, Valhalla, NY, USA

[2]Prevention of Blindness from Glaucoma and Age Related Macular Degeneration, NY, USA

[3]Northeastern University, Boston, MA, USA

[4]University of Rochester, Flaum Eye Institute, Rochester, NY, USA

## Abstract

In 2020, there were 52.7 million cases of Glaucoma and projections indicate a continued, predominantly driven by expected growth in Asia and Africa. The disease burden is particularly high in Black individuals and other racial/ethnic minorities. Presently, there are a number of surgical interventions available to help combat the effects of Glaucoma, including: Trabeculectomy, Glaucoma Drainage Devices (GDD), and Micro-Invasive Glaucoma Surgery (MIGS). MIGS has seen a 400% increase in procedures between 2012 to 2016. However, studies have found that non-Hispanic Black patients, compared with non-Hispanic White patients, were associated with an increased risk of reoperation. Given the growing popularity of MIGS procedures, and potential complications, researchers need to pay particular attention to creating a diverse study population in clinical trials studying these interventions.

This review consisted of publicly available data on MIGS and GDD clinical trials using ClinicalTrials.gov and PubMed from 1987 to 2020 that reported demographic subgroups including race and ethnicity. Microsoft Excel (Microsoft Corporation) and Python, version 3.10.12, were used for data collection and analysis. Data reporting and synthesis adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary outcomes was the prevalence of each demographic subgroup (White, Black, Hispanic/Latino, other race/ethnicity groups, and female or male) in each trial according to the trial start year, study region, mean age, and study sponsor. Participation rates are expressed as percentages.

A total of 67 clinical trials were included in this review, comprising 6,156 clinical trial participants (3,136 women [50.9%]). Overall, 69.1% were White, 16.2% were Black, 5.2% were reported as Hispanic/Latino patients, and 14.7% were individuals of other races/ethnicities. Black participation was even lower in MIGS clinical trials (13.0%) and in Europe (1.0%). Clinical trials in the United States, and sponsored by a Medical Device company, saw Black participation fall to 10.1%. A linear regression analysis was performed to assess significant trends between participation by Black individuals and the year the study began. There was a statistically significant increase of Black participation from 1987 to 2020 ($r^2$=0.198; P=0.023); however, no significant trend was established for clinical trials based in the U.S. ($r^2$=0.024; P=0.584). A 1-way analysis of variance was performed to assess the significance between participation by Black individuals and study region, sponsor type, and intervention type. Statistically significant differences were seen by region (P=0.000) and sponsor type (P=0.004) but not intervention type (P=0.332).

The results suggest that racial and ethnic minority groups have a significantly lower participation rate in MIGS clinical trials compared with White individuals. Additionally, these trends were more prevalent in studies in Europe in the United States that were sponsored by Medical Device companies.

Despite efforts to promote diversity in clinical trials, a significant increase in participation of Black individuals, who are affected impacted by both the disease and procedure-related complications, remains to be seen. This marked underrepresentation can raise concerns regarding the safety and effectiveness of approved surgical interventions. Consequently, there is a compelling need for expanded initiatives aimed at enhancing diversity in future MIGS and GDD clinical trials. As well as an imperative to advance the quality of race and ethnicity data reporting in future studies.

**OPEN ACCESS**

***Correspondence:***
*Karen Allison, University of Rochester, Flaum Eye Institute, Rochester, NY, USA,*

**Received Date**: *26 Jul 2024*
**Accepted Date:** *09 Aug 2024*
**Published Date:** *19 Aug 2024*

***Citation:***
*Appelbaum J, Patel D, Greene L, Allison K. The Evolution of Glaucoma Surgery Through Clinical Trials: From Past to Present. Clin Surg. 2024; 9: 3722.*

## Introduction

Glaucoma is a neurodegenerative eye condition that leads to damage of the optic nerve and is the leading cause of irreversible blindness globally. In 2020, 52.7 million individuals were impacted, and projections indicate a concerning rise with an estimated 111.8 million cases expected by 2040 for people aged 40 to 80, of which 79.8 million being Primary Open-Angle Glaucoma (POAG) and 32.0 million being Primary Angle-Closure Glaucoma (PACG). This sharp increase is predominantly driven by expected growth in Asia and Africa [1,2]. Presently, a vast array of therapeutics and interventions are available for treating glaucoma, depending on the sub-type, which range from pharmacologics to surgeries. Typically, these act to increase aqueous outflow or decrease aqueous production, ultimately leading to an overall decrease in Intraocular Pressure (IOP). Surgical management of glaucoma includes trabeculectomy, Glaucoma Drainage Devices (GDD), and Micro-Invasive Glaucoma Surgery (MIGS) [3-6].

Many of the modern glaucoma surgeries were conceived back in the 1960s; however, the genesis of these procedures can be traced to the 19th Century: When von Graefe discovered that iridectomy is an effective surgical method for acute glaucoma treatment [7,8]. Trabeculectomy, the gold standard in subconjunctival bleb-forming surgery, was first described by Sugar in 1961. Cairns and Watson modified this approach in 1968 and 1970 respectively, which now resembles the modern surgical technique [9,10]. In 1969, Molteno developed the first successful GDD with modern ones being introduced during the 1990s [8,11]. These include the Ahmed glaucoma valve, the Ahmed ClearPath, the Baerveldt glaucoma implant and the Molteno implant. For the purposes of this study, the term GDD will apply to all of the devices and implants summarized in Table 1.

GDD typically vary in their design, such as the size, shape, and material, while also being further subdivided into "valved" or "non-valved". Today, GDD surgery has traditionally been reserved for cases of refractory glaucoma where prior trabeculectomy has failed or is at high risk of failure. GDD is also indicated for cases of childhood glaucoma due to iridocorneal dysgenesis, aniridia, aphakia, juvenile rheumatoid arthritis and in Sturge-Weber syndrome [12]. Relative to trabeculectomy, patients who receive a GDD see lower probabilities of failure (29.8% *vs.* 46.9%) and reoperation rate (9% *vs.* 29%) [13].

Glaucoma surgery and device implants are not without its own set of complications [14]. Risks of trabeculectomy and GDD implantation include bleeding, inflammation, infection, cataract formation, corneal swelling, hypotony, and persistent IOP elevation resulting from scar tissue that limits outflow. In some cases, there is a need for additional intervention to address these negative outcomes [15].

For the past half century, and prior to the rise of MIGS, Glaucoma surgeries were largely unchanged, with a majority of those performed being trabeculectomies and GDD [16]. However, since the early 2000s, there has been a proliferation of alternative surgical interventions—some of which have established themselves in the mainstay of glaucoma treatment [16]. In 2017, there were 174,788 glaucoma surgeries performed: 22,862 trabeculectomies (13.1%), 19,991 GDD (11.4%), and 131,935 MIGS (75.5%). This follows a 400% increase in MIGS procedures seen between 2012 and 2016 in the United States, according to Medicare data [17,18]. This rapid increase in MIGS prevalence can be attributed to its ability to lower IOP while avoiding the long-term, postoperative difficulties that arise from more traditional and invasive glaucoma surgeries [19]. MIGS also show favorable economics in managing glaucoma, compared to SLT or medications alone, and is seen as an alternative to topical medication in its ability to address adherence challenges, adverse events, and quality-of-life issues [20,21].

The term MIGS was first seen in 2009 as an umbrella term for a group of devices and procedures to treat glaucoma that have 5 main features: ab interno microincision, rapid recovery, high safety profile, minimal disruption of anatomy and physiology, and lowering of IOP [22]. Devices such as the iStent inject® and the Hydrus® would fit neatly into this definition. However, others such as Trabectome®, the Kahook Dual Blade®, the XEN® Gel Stent, and cyclodestructive procedures that do not typically meet the 5 core descriptors but still retain good efficacy, a high safety profile, and a quick recovery [17]. For the purposes of this study, the term MIGS will apply to all of the devices and procedures summarized in Table 1.

The majority of MIGS procedures have primarily been studied to treat open-angle glaucoma subtypes (*e.g.*, Primary Open-Angle Glaucoma), and is considered to be a favorable option to address early stages of the disease: Bridging the treatment gap between medical therapies and more invasive surgeries [17,20]. Cantor et al. further supported that MIGS is a key option for early treatment of mild-to-moderate glaucoma, specifically for patients who experience side effects with topical medication, are contraindicated for other therapies, or are not candidates for invasive surgery [23].

Currently, there are very few studies that explore the changes in participant diversity among MIGS and GDD clinical trials. However, with the aim of improving the safety and effectiveness of medical interventions for all individuals, it is crucial to ensure a diverse range of participants in these trials. Steps have been taken to promote minority representation in clinical trials such as the 2007 FDA Amendments Act (FDAAA), 2012 FDA Safety and Innovation Act, and the Department of Health and Human Services Final Rule of 2017 [24,25]. Moreover, the FDA has released detailed guidelines on enhancing the diversity of clinical trial populations through less restrictive eligibility criteria, enrollment practices, and trial designs [26]. Yet, analysis of data clinical trial data since the FDAAA Final Rule has determined that compliance to these regulations still remains poor, potentially owing to a lack of enforcement by regulators [27].

There is growing concern regarding the lack of diversity, particularly in terms of race and ethnicity, within these research populations. To explore this issue, we have conducted a thorough investigation into the racial and ethnic disparities among MIGS and GDD clinical trials since 1987. The primary objective of our study was to perform a review and analysis of demographic data sourced from publicly available sources on completed, interventional MIGS and GDD clinical trials. Through this analysis, we aimed to assess the representation of racial and ethnic minority participants within these study populations.

## Methods

MIGS and GDD are umbrella terms that can cover many different types of surgeries. This review focuses on peer-reviewed evidence for the devices, implants, and procedures summarized in Table 1. This review included clinical trials on MIGS and GDD from English-language publications from ClinicalTrials.gov and

**Table 1:** Interventions included.

| Intervention Type | Intervention | # Of Trials |
|---|---|---|
| **GDD** | | **25** |
| | Ahmed® Implant | 13 |
| | Baerveldt® Implant | 5 |
| | Krupin® Eye Valve | 1 |
| | Molteno® Implant | 4 |
| | Ahmed® Implant \| Baerveldt® Implant | 2 |
| | Aurolab Aqueous Drainage Implant | 0 |
| **MIGS** | | **39** |
| | Cyclophotocoagulation (CPC) | 12 |
| | CyPass® Micro-Stent | 2 |
| | Hydrus® | 2 |
| | iStent® | 2 |
| | iTrack™ | 1 |
| | Trabectome® | 1 |
| | XEN® Gel Stent | 7 |
| | EX-PRESS® Glaucoma Filtration Device | 8 |
| | MINIject® | 2 |
| | iStent®, Hydrus® | 1 |
| | iStent® \| Kahook Dual Blade | 1 |
| | Gonioscopy-Assisted Transluminal Trabeculotomy (GATT) | 0 |
| | Kahook Dual Blade® | 0 |
| | OMNI® Surgical System | 0 |
| | PRESERFLO™ MicroShunt | 0 |
| | STREAMLINE® Surgical System | 0 |
| **Both** | | **3** |
| | Cyclophotocoagulation (CPC) \| Baerveldt® Implant \| Ahmed® Implant | 1 |
| | Cyclophotocoagulation (CPC) \| Ahmed® Implant | 2 |
| **Grand Total** | | **67** |

PubMed between 1987 to 2020. Keywords and filters used for this search on ClinicalTrials.gov included glaucoma, studies with results, completed, and interventional studies (clinical trials). Keywords and filters used for this search on PubMed included glaucoma and clinical trials. The search was performed on June 26th, 2023, and additional sources were incorporated up to September 06th, 2023, before the start of data extraction. This review was deemed exempt from institutional review board approval and informed consent because it collected and synthesized non-identifiable data from previously published studies and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline [28].

### Inclusion and exclusion criteria and data extraction

Studies were included if they met the following criteria: (1) MIGS and GDD clinical trials, (2) completed trials, (3) interventional studies, (4) publicly available studies with results, (5) institutional review board–approved studies, and (6) demographic subgroups including sex/gender and race. Studies were excluded that did not include (1) race, (2) sex or gender, (3) an intervention; that were (4) still ongoing, (5) still open to accrual, or (6) not published in English.

Extracted data included (1) medical intervention, (2) number of participants, (3) year the study started, (4) year the study ended, (5) region in which the studies were conducted, (6) study sponsor, (7) participant sex/gender, (8) ethnicity (if indicated), (9) race, and (10) age (if indicated). The geographic region of a study was defined using the United Nations classification, which includes Africa, Asia, Europe, Latin America and the Caribbean, North America, and Oceania [29]. We also added "multiregional" as a category to account for studies that encompassed more than 1 region. Race was captured using 3 categories: (1) White, (2) Black, and (3) other; ethnicity was recorded as Hispanic/Latino, if reported. Racial subgroups included as "other" consisted of Asian, Native Hawaiian or Pacific Islander, American Indian or Alaska Native, and unreported as defined by the US Census [30]. Sponsors for these trials were US-based or non–US-based, medical device companies, universities, medical centers, pharmaceutical companies, foundations, government agencies, or private citizens. These were organized as such into (1) US Foundations or Agencies, (2) US Medical Centers and Universities, (3) US Medical Device Companies, (4) US Pharmaceutical Companies, (5) Non-US Foundations or Agencies, (6) Non-US Medical Centers and Universities, (7) Non-US Medical Device Companies, (8) Private, and (9) Collaborators, which included more than one sponsor type working together, because some sponsors of more than 1 category worked together on 1 trial. Details on the sponsors for each of the trials are listed in Table 2.

### Statistical analysis

Statistical analyses were conducted using Microsoft Excel (Microsoft Corporation) and Python, v3.10.12. Demographic data from the study population were collected, and participation by sex/gender, race, and ethnicity of each trial was calculated as a percentage of total participants in the study. Trials were grouped according to the trial start year, the region in which the trial took place, and the type of study sponsor. Descriptive statistics were obtained for all collected data. Linear regression was performed to investigate a trend in Black participation by trial start year. A 1-way Analysis of Variance (ANOVA) was performed to assess the significance of the means for more than 2 groups, and then an independent-samples t-test was used to assess the differences between 2 groups and correct for multiplicity. Hypothesis tests were 2-sided. $P \leq 0.05$ was considered statistically significant for all analyses a priori.

## Results

The study selection process that was used in this review is depicted in Figure 1. A total of 540 studies were initially identified through a comprehensive search of randomized clinical trials using PubMed and ClinicalTrials.gov based on keywords. Subsequently, 79 studies were removed as duplicates, leaving 461 potentially eligible clinical trials. A final set of 394 studies were excluded based on inclusion and exclusion criteria. Studies were excluded owing to the lack of available demographic subgroup data that included race.

Ultimately, 67 clinical trials were included in this review of 6,156 clinical trial participants. Overall, 69.1% were White, 16.2% were Black, 14.7% were individuals of other races, 5.2% were reported as Hispanic/Latino, and 51.0% were female.

Characteristics of the trials are listed in Table 3. MIGS encompassed 39 of the 67 (58.2%) total reviewed trials and 70.3% of the total study population (1,943 women [53.6%]; 2,750 White participants [75.9%]). GDD encompassed 25 (37.3%) total reviewed trials and 45.0% of the total study population (1,096 women [47.2%];

**Table 2:** Types of sponsors.

| Sponsor | # Of trials |
|---|---|
| **COLLABORATORS** | **9** |
| Advanced Medical Optics (AMO) \| Stichting Wetenschappelijk Onderzoek Oogziekenhuis (SWOO) | 1 |
| Alcon Research \| Transcend Medical, Inc. | 1 |
| AqueSys, Inc. \| Allergan | 1 |
| Center for Sight, Georgetown University Medical Center \| Krieger Eye Institute, Sinai Hospital | 1 |
| European Science Exchange Program, the Royal Society \| Deutsche Forschungsgemeinschaft (DFG) | 1 |
| Federal University of Goiás \| Brazilian Center of Eye Surgery (CBCO) | 1 |
| JSEI Kirchgessner Ophthalmology Endowment Fund \| Naval Clinical Investigation Program | 1 |
| National Institutes of Health \| Research to Prevent Blindness | 1 |
| Research to Prevent Blindness \| National Eye Institute | 1 |
| **NON-US FOUNDATIONS OR AGENCIES** | **5** |
| CAPES/Ministry of Education of Brazil | 1 |
| Health Research Fund (FIS) of the Carlos III Health Institute (ISCIII) | 1 |
| Japan Society for the Promotion of Science (KAKENHI) | 1 |
| National Council of Technological and Scientific Development (CNPQ) | 1 |
| Swiss National Science Foundation | 1 |
| **NON-US MEDICAL CENTERS AND UNIVERSITIES** | **12** |
| Cairo University | 1 |
| Credit Valley EyeCare | 1 |
| Institute Catala de Retina | 1 |
| Khoo Teck Puat Hospital | 1 |
| Ophthalmologic Center Prof. Munteanu | 1 |
| Shahid Beheshti University of Medical Sciences | 1 |
| Sunnybrook and Women's College Health Sciences Centre | 1 |
| Swiss Vision Network | 1 |
| University Eye Hospital Tübingen | 2 |
| University of Montreal Health Centre | 1 |
| University of Witwatersrand, South Africa | 1 |
| **NON-US MEDICAL DEVICE COMPANIES** | **2** |
| iSTAR Medical | 2 |
| **PRIVATE** | **3** |
| Dr. Donato Errico | 1 |
| Dr. Enyr Saran Arcieri | 1 |
| Dr. Peter Netland | 1 |
| **US FOUNDATIONS OR AGENCIES** | **3** |
| New York Glaucoma Research Institute | 1 |
| Research to Prevent Blindness | 1 |
| Zanvyl and Isabelle Krieger Fellowship Fund | 1 |
| **US MEDICAL CENTERS AND UNIVERSITIES** | **15** |
| Cullen Eye Institute, Baylor College of Medicine | 1 |
| Duke University | 4 |
| Indiana University Medical Center | 1 |
| Kresge Eye Institute, Wayne State University School of Medicine | 1 |
| New York Eye and Ear Infirmary of Mount Sinai | 1 |
| Robert Cizik Eye Clinic | 1 |
| University of California, Los Angeles | 1 |
| University of California, San Francisco | 1 |
| University of Miami | 3 |
| University of Virginia | 1 |
| **US MEDICAL DEVICE COMPANIES** | **11** |
| Alcon Research | 1 |
| AqueSys, Inc. | 2 |
| Genentech, Inc. | 1 |
| Glaukos Corporation | 1 |
| iScience Interventional | 1 |
| Ivantis, Inc. | 3 |
| New World Medical, Inc. | 1 |
| Transcend Medical, Inc. | 1 |
| **US PHARMACEUTICAL COMPANIES** | **3** |
| Allergan | 3 |
| **Grand Total** | **63** |

1,356 White participants [58.4%]). Trials studying both intervention types encompassed 3 (4.5%) total reviewed trials and 4.1% of the total study population (102 women [48.6%]; 147 White participants [70.0%]).

The total number of participants along with demographic data extracted from each study by the trial start year, region, average age group, and type of study sponsor are displayed in Table 4. The region of each study is based on the United Nations classification of geographic region [29]; however, the Caribbean and Oceania were excluded from this table because clinical trials did not take place exclusively in those regions. There were, however, 11 multiregional studies.

Figure 2 compares the overall numbers of participants enrolled in the trials by race and ethnicity according to the trial start year based on the data from Table 4. Trial participation was evaluated in terms of trial start year in order to depict any trends in trial participation by race and ethnicity at the time of enrollment. Some years had very few trials compared with others, but including all years that trials were conducted from 1987 to 2020 was important for our analysis in order to evaluate for increases in participation by Black individuals during this time period.

Linear regression analysis demonstrates a slight increase in the Black participation rate ($r^2$=0.198, P=0.023); however, this significance is lost when looking at Black participation at an individual level. Moreover, there is no statistically significant increase of Black participation as a percentage when looking at US trials only or by trials at the individual region, sponsor type, or intervention type level. Black participants, Hispanic/Latino participants, and those categorized as others only surpassed 200 participants individually as their own subgroup in three individual years: The 3 years that had the greatest overall participants in these clinical trials.

The largest number of White participants occurred in 2012, with 694 of 948 (73.2%), whereas the number of Black participants at that time was 81 of 948 (8.5%). The year 2008 contained clinical trials with the largest number of Black participants at 116 of 361 (32.1%), with White participants at 214 of 361 (59.3%).

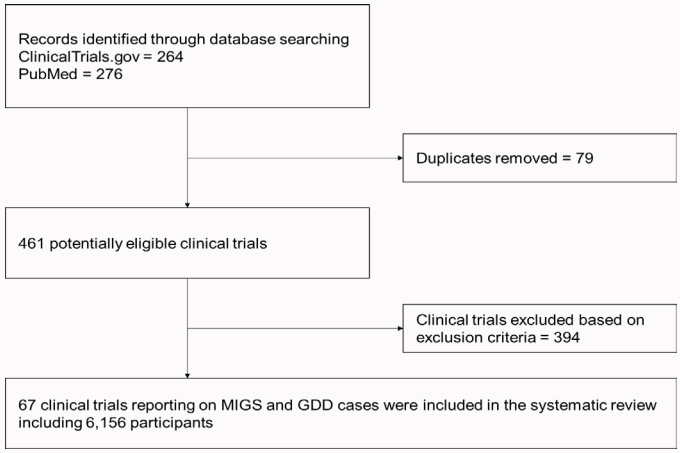


**Figure 1:** Study selection process using the PRISMA format.

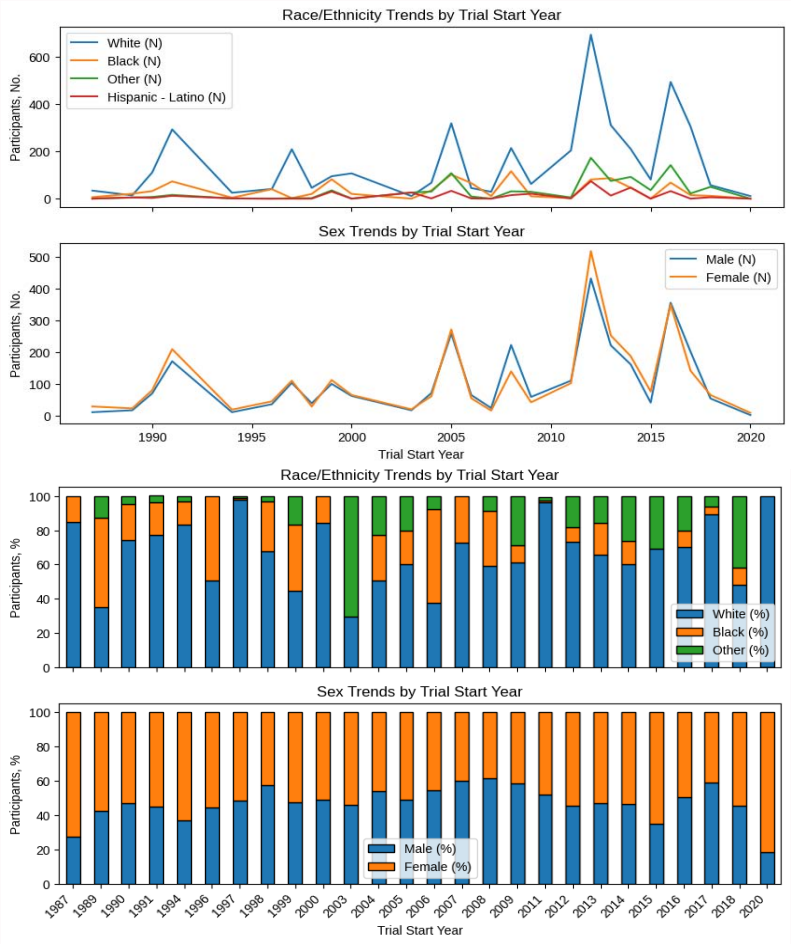


**Figure 2:** Demographic trends by start year.

Figure 3 compares the overall percentage of participants by race and ethnicity enrolled in the trials according to geographic region, based on data from Table 4. White participants were the largest racial subgroup in all regions except for Africa. In each region except for Africa and Latin America, White individuals comprised no less than 61.7% of trial participants, whereas Black individuals comprised no more than 23.4% of trial participation. White participation was greatest in Europe at 97.9% while North America saw the greatest amount of Black participation. Hispanic/Latino participation was greatest in Latin America at 23.8% and no more than 7.8% in any other region. There was a statistically significant association between the Black participation rate and the trial region ($\chi^2$=10.942; P=0.000).

Figure 4 compares the overall proportions of participants by race and ethnicity according to the type of study sponsor based on data from Table 4. Non-US Medical Centers and Universities had the highest White participation rate (946 of 1,102 [85.8%]), whereas US

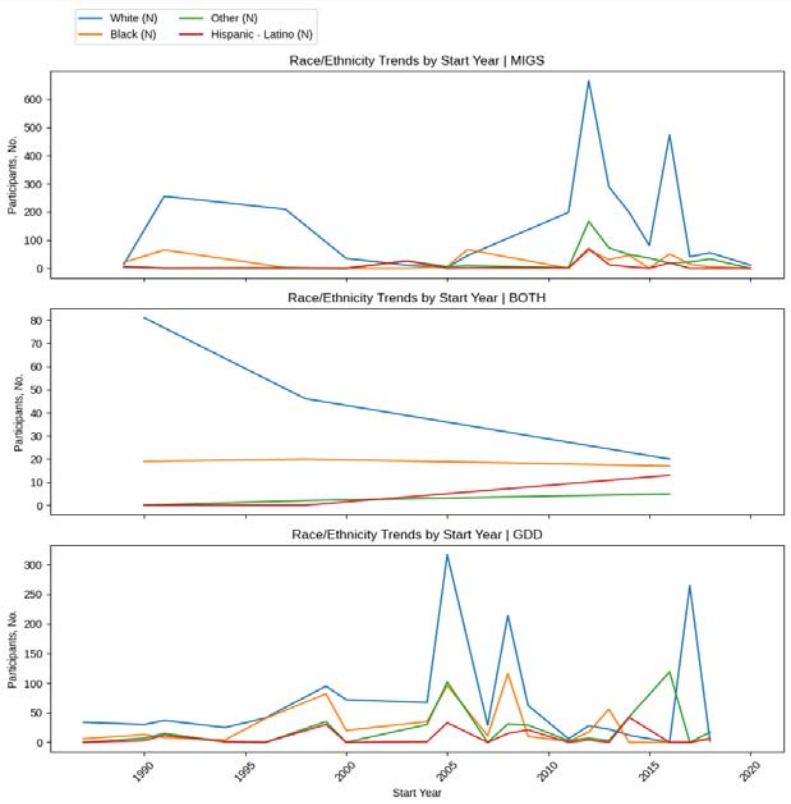


**Figure 2a:** Demographic trends by start year and intervention type.

| Start Year | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|
| 1987 | 1 | 40 | 34 (85.0) | 6 (15.0) | 0 (0.0) | 0 (0.0) | 11 (27.5) | 29 (72.5) |
| 1989 | 1 | 40 | 14 (35.0) | 21 (52.5) | 5 (12.5) | 5 (12.5) | 17 (42.5) | 23 (57.5) |
| 1990 | 2 | 150 | 111 (74.0) | 32 (21.3) | 7 (4.7) | 3 (2.0) | 70 (46.7) | 80 (53.3) |
| 1991 | 4 | 380 | 293 (77.1) | 73 (19.2) | 16 (4.2) | 12 (3.2) | 171 (45.0) | 209 (55.0) |
| 1994 | 1 | 30 | 25 (83.3) | 4 (13.3) | 1 (3.3) | 1 (3.3) | 11 (36.7) | 19 (63.3) |
| 1996 | 2 | 81 | 41 (50.6) | 40 (49.4) | 0 (0.0) | 0 (0.0) | 36 (44.4) | 45 (55.6) |
| 1997 | 2 | 213 | 209 (98.1) | 2 (0.9) | 2 (0.9) | 0 (0.0) | 103 (48.4) | 110 (51.6) |
| 1998 | 1 | 68 | 46 (67.6) | 20 (29.4) | 2 (2.9) | 0 (0.0) | 39 (57.4) | 29 (42.6) |
| 1999 | 1 | 212 | 95 (44.8) | 82 (38.7) | 35 (16.5) | 30 (14.2) | 100 (47.2) | 112 (52.8) |
| 2000 | 2 | 127 | 107 (84.3) | 20 (15.7) | 0 (0.0) | 0 (0.0) | 62 (48.8) | 65 (51.2) |
| 2003 | 1 | 37 | 11 (29.7) | 0 (0.0) | 26 (70.3) | 26 (70.3) | 17 (45.9) | 20 (54.1) |
| 2004 | 1 | 132 | 67 (50.8) | 35 (26.5) | 30 (22.7) | 1 (0.8) | 71 (53.8) | 61 (46.2) |
| 2005 | 3 | 529 | 319 (60.3) | 102 (19.3) | 108 (20.4) | 33 (6.2) | 258 (48.8) | 271 (51.2) |
| 2006 | 1 | 120 | 45 (37.5) | 66 (55.0) | 9 (7.5) | 1 (0.8) | 65 (54.2) | 55 (45.8) |
| 2007 | 1 | 40 | 29 (72.5) | 11 (27.5) | 0 (0.0) | 0 (0.0) | 24 (60.0) | 16 (40.0) |
| 2008 | 2 | 361 | 214 (59.3) | 116 (32.1) | 31 (8.6) | 15 (4.2) | 222 (61.5) | 139 (38.5) |
| 2009 | 2 | 101 | 62 (61.4) | 10 (9.9) | 29 (28.7) | 21 (20.8) | 59 (58.4) | 42 (41.6) |
| 2011 | 3 | 212 | 204 (96.2) | 2 (0.9) | 5 (2.4) | 1 (0.5) | 110 (51.9) | 102 (48.1) |
| 2012 | 6 | 948 | 694 (73.2) | 81 (8.5) | 173 (18.2) | 74 (7.8) | 431 (45.5) | 517 (54.5) |
| 2013 | 4 | 473 | 311 (65.8) | 87 (18.4) | 75 (15.9) | 13 (2.7) | 221 (46.7) | 252 (53.3) |
| 2014 | 6 | 348 | 210 (60.3) | 46 (13.2) | 92 (26.4) | 47 (13.5) | 161 (46.3) | 187 (53.7) |
| 2015 | 2 | 117 | 81 (69.2) | 0 (0.0) | 36 (30.8) | 0 (0.0) | 41 (35.0) | 76 (65.0) |
| 2016 | 5 | 704 | 494 (70.2) | 68 (9.7) | 142 (20.2) | 32 (4.5) | 355 (50.4) | 349 (49.6) |
| 2017 | 4 | 342 | 305 (89.2) | 15 (4.4) | 22 (6.4) | 0 (0.0) | 201 (58.8) | 141 (41.2) |
| 2018 | 3 | 119 | 57 (47.9) | 12 (10.1) | 50 (42.0) | 6 (5.0) | 54 (45.4) | 65 (54.6) |
| 2020 | 1 | 11 | 11 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (18.2) | 9 (81.8) |

**Figure 2b:** Table output – demographic trends by start year.

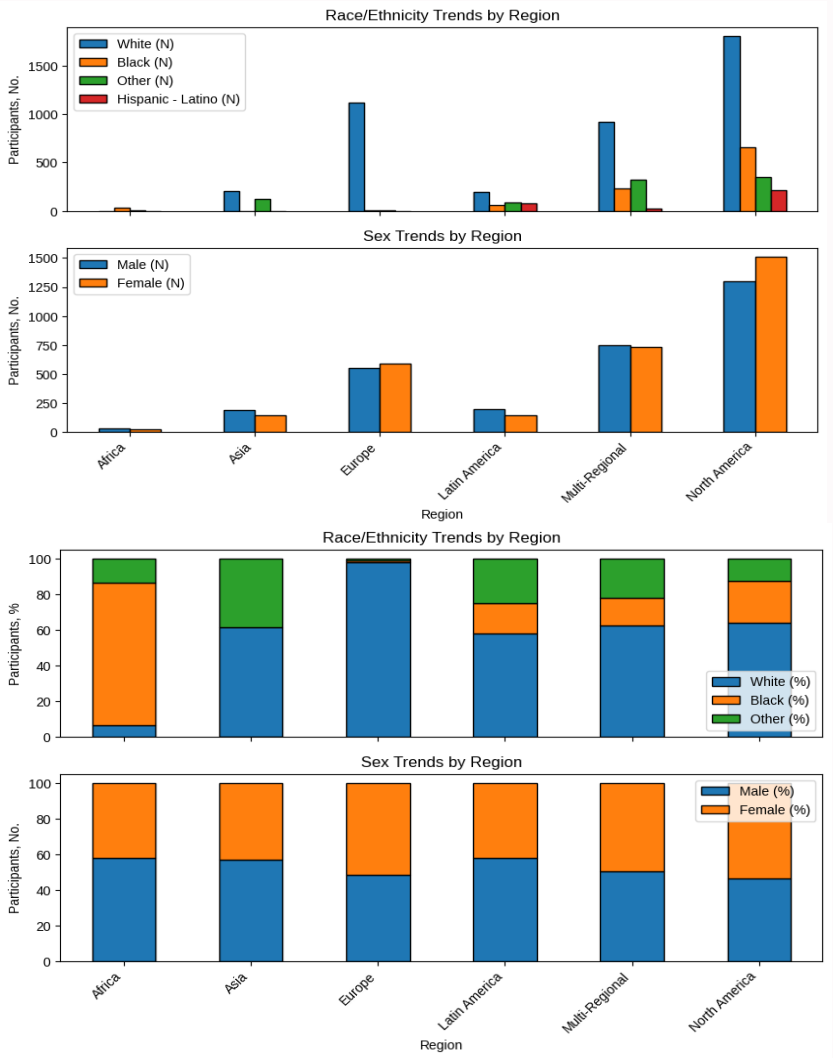


**Figure 3:** Demographic trends by region.

| Region | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|
| Africa | 2 | 45 | 3 (6.7) | 36 (80.0) | 6 (13.3) | 0 (0.0) | 26 (57.8) | 19 (42.2) |
| Asia | 4 | 334 | 206 (61.7) | 0 (0.0) | 128 (38.3) | 0 (0.0) | 190 (56.9) | 144 (43.1) |
| Europe | 15 | 1143 | 1119 (97.9) | 11 (1.0) | 12 (1.0) | 1 (0.1) | 553 (48.4) | 590 (51.6) |
| Latin America | 7 | 341 | 198 (58.1) | 58 (17.0) | 85 (24.9) | 81 (23.8) | 197 (57.8) | 144 (42.2) |
| Multi-Regional | 11 | 1481 | 923 (62.3) | 236 (15.9) | 324 (21.9) | 22 (1.5) | 749 (50.6) | 732 (49.4) |
| North America | 28 | 2812 | 1804 (64.2) | 659 (23.4) | 349 (12.4) | 218 (7.8) | 1300 (46.2) | 1512 (53.8) |

**Figure 3a:** Table output - demographics by region.

Medical Device Companies had the highest raw number of White participants (1,236). On the other hand, US Medical Centers and Universities had the highest Black participation rate and greatest number of Black individuals (575 of 1,580 [36.4%]). Moreover, US Pharmaceutical Companies and US Medical Device Companies saw a Black participation rate of 0.5% (1 of 202) and 7.5% (74 of 1,102) respectively. Individuals in the other race group had a higher participation rate compared with Black individuals in trials sponsored by Medical Device Companies and Pharmaceutical Companies as well as all non-US based sponsors. There was a statistically significant association between the Black participation rate and the sponsor type ($\chi^2$=3.266; P=0.004).

Figure 5 compares the overall proportions of participants by race and ethnicity according to the intervention type based on data from Table 4. Black participation rate was lowest in MIGS trials (421 of 3,625 [11.6%]) and highest in trials that studied both MIGS and GDD (56 of 210 [26.7%]); however, only 3 trials qualified for this group. From a regional perspective, North American trials saw the highest

**Table 3:** Characteristics of interventions in clinical trials.

| Intervention Type | No. of Trials | Total Pop | White N (%) | Black N (%) | Other N (%) | Hispanic - Latino N (%) | Male N (%) | Female N (%) |
|---|---|---|---|---|---|---|---|---|
| Both | 3 | 210 | 147 (70.0) | 56 (26.7) | 7 (3.3) | 13 (6.2) | 108 (51.4) | 102 (48.6) |
| GDD | 25 | 2321 | 1356 (58.4) | 523 (22.5) | 442 (19.0) | 168 (7.2) | 1225 (52.8) | 1096 (47.2) |
| MIGS | 39 | 3625 | 2750 (75.9) | 421 (11.6) | 455 (12.6) | 141 (3.9) | 1682 (46.4) | 1943 (53.6) |
| **Total** | 67 | 6156 | 4253 (69.1) | 1000 (16.2) | 904 (14.7) | 322 (5.2) | 3015 (49.0) | 3141 (51.0) |

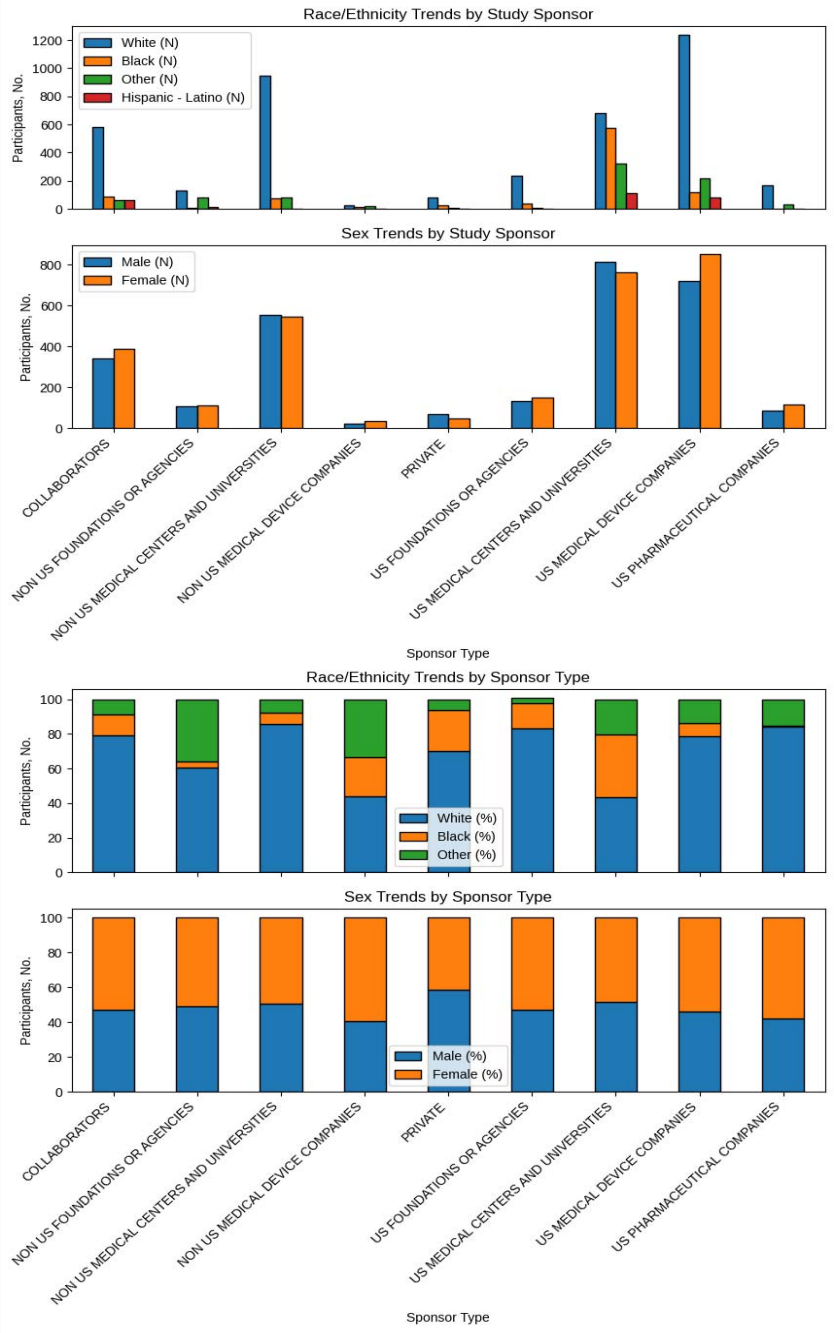


**Figure 4:** Demographic trends by sponsor type.

Black participation rate (206 of 971 [31.5%]) while multi-regional trials had the highest participation rate of individuals categorized as other (208 of 731 [28.5%]). Outside of Africa, Black participation was highest in MIGS trials in North America as well. On the other hand, White participation in GDD trials was highest in Asia (206 of 206 [100%]) and Europe (177 of 177 [100%]). Europe also saw the highest participation of White individuals in MIGS trials (942 of 966 [97.5%]). When looking at trials based in the US that were not sponsored by Medical Centers or Universities, Black participation in GDD and MIGS dropped to 20.6% (49 of 238) and 11.3% (143 of

| Sponsor Type | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|
| COLLABORATORS | 9 | 732 | 581 (79.4) | 85 (11.6) | 66 (9.0) | 66 (9.0) | 343 (46.9) | 389 (53.1) |
| NON US FOUNDATIONS OR AGENCIES | 5 | 219 | 133 (60.7) | 7 (3.2) | 79 (36.1) | 13 (5.9) | 108 (49.3) | 111 (50.7) |
| NON US MEDICAL CENTERS AND UNIVERSITIES | 12 | 1102 | 946 (85.8) | 74 (6.7) | 82 (7.4) | 0 (0.0) | 556 (50.5) | 546 (49.5) |
| NON US MEDICAL DEVICE COMPANIES | 2 | 57 | 25 (43.9) | 13 (22.8) | 19 (33.3) | 0 (0.0) | 23 (40.4) | 34 (59.6) |
| PRIVATE | 3 | 118 | 83 (70.3) | 28 (23.7) | 7 (5.9) | 4 (3.4) | 69 (58.5) | 49 (41.5) |
| US FOUNDATIONS OR AGENCIES | 3 | 281 | 234 (83.3) | 41 (14.6) | 8 (2.8) | 3 (1.1) | 133 (47.3) | 148 (52.7) |
| US MEDICAL CENTERS AND UNIVERSITIES | 15 | 1580 | 684 (43.3) | 575 (36.4) | 321 (20.3) | 112 (7.1) | 816 (51.6) | 764 (48.4) |
| US MEDICAL DEVICE COMPANIES | 11 | 1574 | 1236 (78.5) | 118 (7.5) | 219 (13.9) | 81 (5.1) | 722 (45.9) | 852 (54.1) |
| US PHARMACEUTICAL COMPANIES | 3 | 202 | 170 (84.2) | 1 (0.5) | 31 (15.3) | 0 (0.0) | 85 (42.1) | 117 (57.9) |

**Figure 4a:** Table output – demographics by sponsor type.

| | | | Participants, No. (%) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Race/ethincity | | | | Sex | |
| Variable | No. of Trials | Total Participants, No. | White | Black | Other | Hispanic/Latino | Male | Female |
| **Trial Start Year** | | | | | | | | |
| 1987 | 1 | 40 | 34 (85.0) | 6 (15.0) | 0 (0.0) | 0 (0.0) | 11 (27.5) | 29 (72.5) |
| 1989 | 1 | 40 | 14 (35.0) | 21 (52.5) | 5 (12.5) | 5 (12.5) | 17 (42.5) | 23 (57.5) |
| 1990 | 2 | 150 | 111 (74.0) | 32 (21.3) | 7 (4.7) | 3 (2.0) | 70 (46.7) | 80 (53.3) |
| 1991 | 4 | 380 | 293 (77.1) | 73 (19.2) | 16 (4.2) | 12 (3.2) | 171 (45.0) | 209 (55.0) |
| 1994 | 1 | 30 | 25 (83.3) | 4 (13.3) | 1 (3.3) | 1 (3.3) | 11 (36.7) | 19 (63.3) |
| 1996 | 2 | 81 | 41 (50.6) | 40 (49.4) | 0 (0.0) | 0 (0.0) | 36 (44.4) | 45 (55.6) |
| 1997 | 2 | 213 | 209 (98.1) | 2 (0.9) | 2 (0.9) | 0 (0.0) | 103 (48.4) | 110 (51.6) |
| 1998 | 1 | 68 | 46 (67.6) | 20 (29.4) | 2 (2.9) | 0 (0.0) | 39 (57.4) | 29 (42.6) |
| 1999 | 1 | 212 | 95 (44.8) | 82 (38.7) | 35 (16.5) | 30 (14.2) | 100 (47.2) | 112 (52.8) |
| 2000 | 2 | 127 | 107 (84.3) | 20 (15.7) | 0 (0.0) | 0 (0.0) | 62 (48.8) | 65 (51.2) |
| 2003 | 1 | 37 | 11 (29.7) | 0 (0.0) | 26 (70.3) | 26 (70.3) | 17 (45.9) | 20 (54.1) |
| 2004 | 1 | 132 | 67 (50.8) | 35 (26.5) | 30 (22.7) | 1 (0.8) | 71 (53.8) | 61 (46.2) |
| 2005 | 3 | 529 | 319 (60.3) | 102 (19.3) | 108 (20.4) | 33 (6.2) | 258 (48.8) | 271 (51.2) |
| 2006 | 1 | 120 | 45 (37.5) | 66 (55.0) | 9 (7.5) | 1 (0.8) | 65 (54.2) | 55 (45.8) |
| 2007 | 1 | 40 | 29 (72.5) | 11 (27.5) | 0 (0.0) | 0 (0.0) | 24 (60.0) | 16 (40.0) |
| 2008 | 2 | 361 | 214 (59.3) | 116 (32.1) | 31 (8.6) | 15 (4.2) | 222 (61.5) | 139 (38.5) |
| 2009 | 2 | 101 | 62 (61.4) | 10 (9.9) | 29 (28.7) | 21 (20.8) | 59 (58.4) | 42 (41.6) |
| 2011 | 3 | 212 | 204 (96.2) | 2 (0.9) | 5 (2.4) | 1 (0.5) | 110 (51.9) | 102 (48.1) |
| 2012 | 6 | 948 | 694 (73.2) | 81 (8.5) | 173 (18.2) | 74 (7.8) | 431 (45.5) | 517 (54.5) |
| 2013 | 4 | 473 | 311 (65.8) | 87 (18.4) | 75 (15.9) | 13 (2.7) | 221 (46.7) | 252 (53.3) |
| 2014 | 6 | 348 | 210 (60.3) | 46 (13.2) | 92 (26.4) | 47 (13.5) | 161 (46.3) | 187 (53.7) |
| 2015 | 2 | 117 | 81 (69.2) | 0 (0.0) | 36 (30.8) | 0 (0.0) | 41 (35.0) | 76 (65.0) |
| 2016 | 5 | 704 | 494 (70.2) | 68 (9.7) | 142 (20.2) | 32 (4.5) | 355 (50.4) | 349 (49.6) |
| 2017 | 4 | 342 | 305 (89.2) | 15 (4.4) | 22 (6.4) | 0 (0.0) | 201 (58.8) | 141 (41.2) |
| 2018 | 3 | 119 | 57 (47.9) | 12 (10.1) | 50 (42.0) | 6 (5.0) | 54 (45.4) | 65 (54.6) |
| 2020 | 1 | 11 | 11 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (18.2) | 9 (81.8) |
| **Region** | | | | | | | | |
| Africa | 2 | 45 | 3 (6.7) | 36 (80.0) | 6 (13.3) | 0 (0.0) | 26 (57.8) | 19 (42.2) |
| Asia | 4 | 334 | 206 (61.7) | 0 (0.0) | 128 (38.3) | 0 (0.0) | 190 (56.9) | 144 (43.1) |
| Europe | 15 | 1143 | 1119 (97.9) | 11 (1.0) | 12 (1.0) | 1 (0.1) | 553 (48.4) | 590 (51.6) |
| Latin America | 7 | 341 | 198 (58.1) | 58 (17.0) | 85 (24.9) | 81 (23.8) | 197 (57.8) | 144 (42.2) |
| Multi-Regional | 11 | 1481 | 923 (62.3) | 236 (15.9) | 324 (21.9) | 22 (1.5) | 749 (50.6) | 732 (49.4) |
| North America | 28 | 2812 | 1804 (64.2) | 659 (23.4) | 349 (12.4) | 218 (7.8) | 1300 (46.2) | 1512 (53.8) |
| **Sponsor** | | | | | | | | |
| US FOUNDATIONS OR AGENCIES | 3 | 281 | 234 (83.3) | 41 (14.6) | 8 (2.8) | 3 (1.1) | 133 (47.3) | 148 (52.7) |
| US MEDICAL CENTERS AND UNIVERSITIES | 15 | 1580 | 684 (43.3) | 575 (36.4) | 321 (20.3) | 112 (7.1) | 816 (51.6) | 764 (48.4) |
| US MEDICAL DEVICE COMPANIES | 11 | 1574 | 1236 (78.5) | 118 (7.5) | 219 (13.9) | 81 (5.1) | 722 (45.9) | 852 (54.1) |
| US PHARMACEUTICAL COMPANIES | 3 | 202 | 170 (84.2) | 1 (0.5) | 31 (15.3) | 0 (0.0) | 85 (42.1) | 117 (57.9) |
| NON US FOUNDATIONS OR AGENCIES | 5 | 219 | 133 (60.7) | 7 (3.2) | 79 (36.1) | 13 (5.9) | 108 (49.3) | 111 (50.7) |
| NON US MEDICAL CENTERS AND UNIVERSITIES | 12 | 1102 | 946 (85.8) | 74 (6.7) | 82 (7.4) | 0 (0.0) | 556 (50.5) | 546 (49.5) |
| NON US MEDICAL DEVICE COMPANIES | 2 | 57 | 25 (43.9) | 13 (22.8) | 19 (33.3) | 0 (0.0) | 23 (40.4) | 34 (59.6) |
| COLLABORATORS | 9 | 732 | 581 (79.4) | 85 (11.6) | 66 (9.0) | 66 (9.0) | 343 (46.9) | 389 (53.1) |
| PRIVATE | 3 | 118 | 83 (70.3) | 28 (23.7) | 7 (5.9) | 4 (3.4) | 69 (58.5) | 49 (41.5) |

**Table 4:** Participant demographic characteristics in clinical trials.

1,267) respectively. With respect to individual interventions, the Black participation rate did not exceed 9.1% in trials on the Trabectome®, iStent®, XEN® Gel Stent, iTrack™, and Hydrus®. Conversely, the Black participation rate in trials on the Krupin® Eye Valve, Molteno® Implant, and Baerveldt® Implant exceeded 26.0%. There was no statistically significant association between the Black participation rate and the trial intervention.

## Discussion

The results of our review of 67 MIGS and GDD clinical trials with 6,156 participants suggest that racial and ethnic minority groups have a significantly lower participation rate in MIGS clinical trials

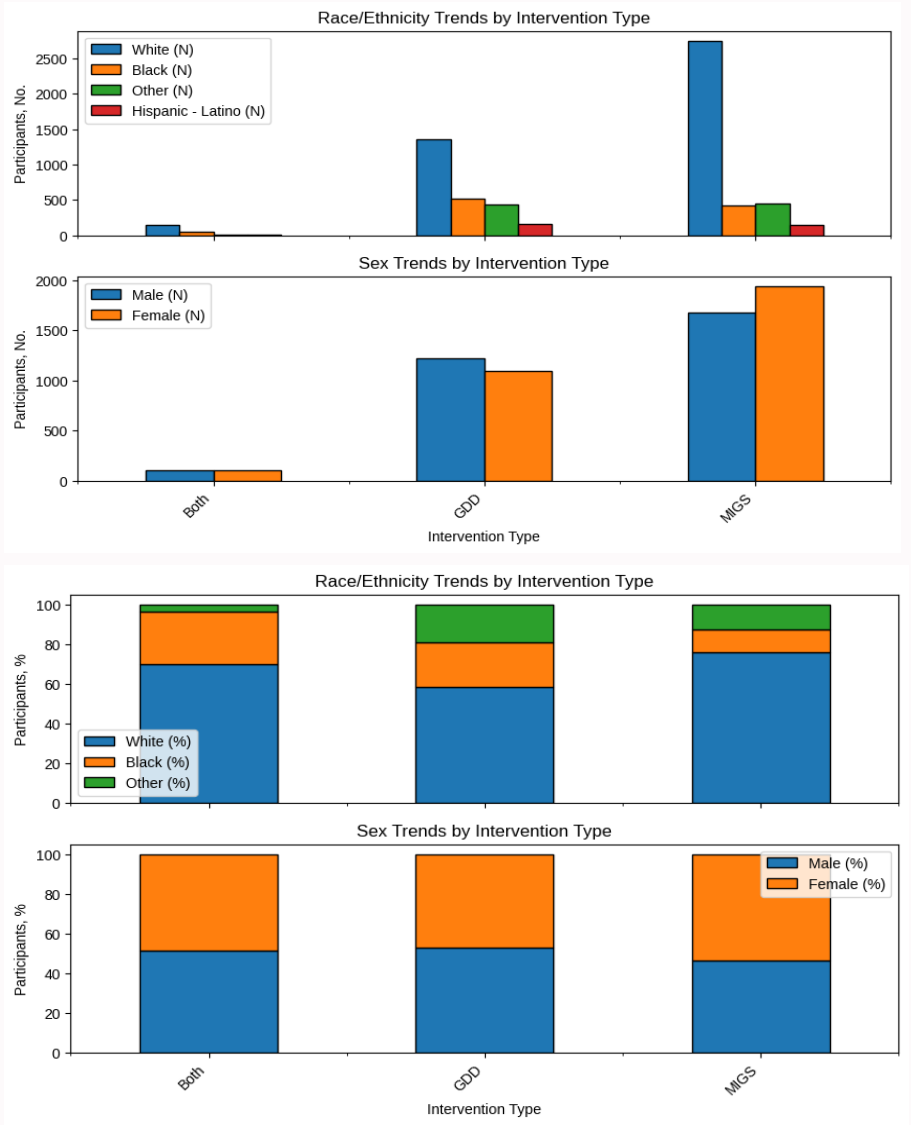


**Figure 5:** Demographic trends by intervention type.

compared with White individuals [31]. Additionally, these trends were more prevalent in studies in Europe and those sponsored by U.S. medical device companies. From 1987 to 2020, there was no significant evidence to suggest that there had been an increase in the participation of minority groups despite public policy taken to minimize this disparity.

## Lack of Black participant representation

According to the American Academy of Ophthalmology's IRIS® (Intelligent Research in Sight) Registry, a comprehensive eye disease clinical registry, there were 1,946,653 Glaucoma patients in 2022 [32]. Of that, 224,594 patients had received a surgical intervention or procedure, excluding those who only received Cataract surgery [33]. Nearly 40% of the surgical patients had underwent a MIGS procedure or received a GDD (*e.g.*, ExPress Shunt, XEN Gel Stent, Hydrus, iStent, Goniotomy, Cyclophotocoagulation) with 70.4% of these patients considered moderate to severe severity.

According to Figure 6 and 6a, 49.31% of the total surgical patients were classified as Non-Hispanic White, 18.08% classified as Non-Hispanic Black or African American, 8.73% classified as Hispanic/Latino, and 20.22% classified as Non-Hispanic Unknown [33]. Based on these figures, the percentage of White patients were over-represented (69.1% compared to 49.31%). Additionally, the percentage of Hispanic/Latino patients were under-represented in the clinical trials in this review (5.2% compared to 8.73%). The percentage of Non-Hispanic Black or African American were also under-represented in the clinical trials overall (18.08% compared to 16.2%). Moreover, this difference increases when looking at only MIGS trials (11.6%) or trials sponsored by US-based Medical Device Companies (7.5%). These trends are compounded by the fact that severe patients, according to the 2022 IRIS registry, were comprised of 23.25% and 9.06% Non-Hispanic Black or African American and Hispanic/Latino patients, respectively [33].

The majority of the clinical trials in this study included primarily White participants except for 9 trials that consisted of more Black participants. Of those, 2 trials were conducted in Africa and 4 were based in the US. It is estimated that the global prevalence of glaucoma for those aged 40 to 80 years is 3.54%. The highest prevalence of

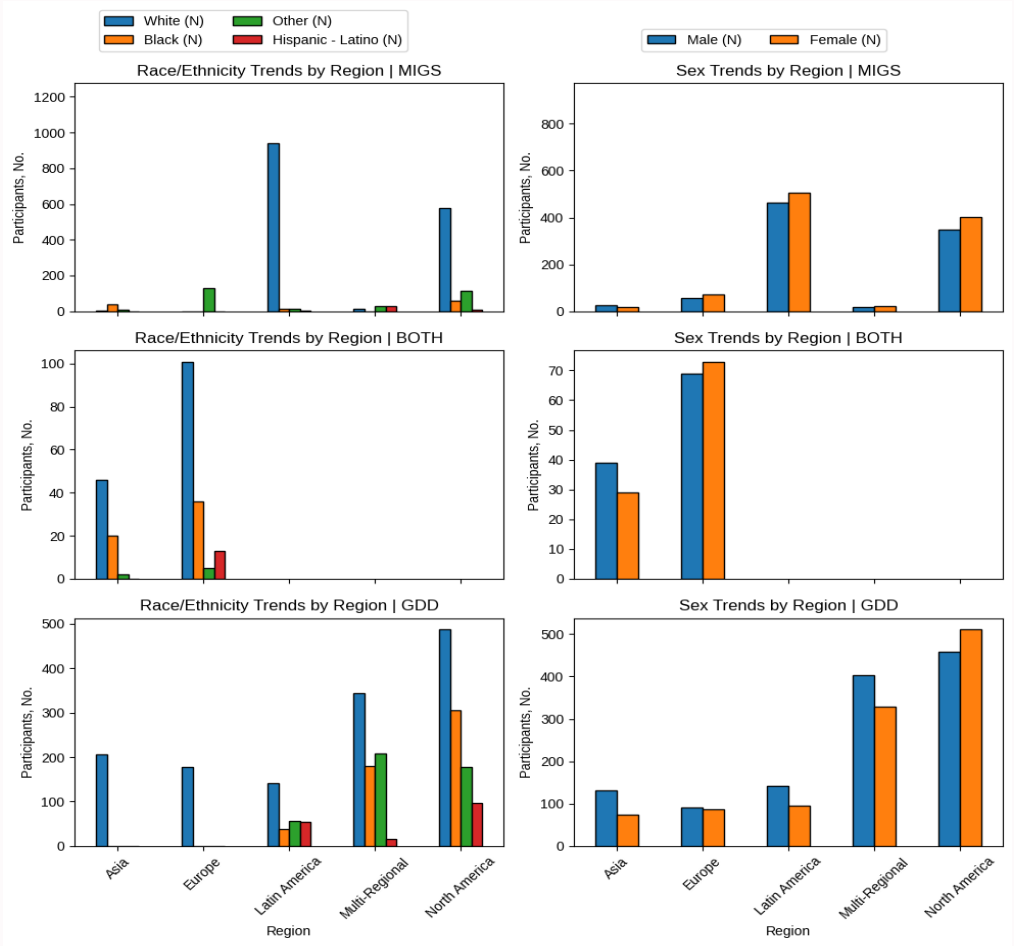


**Figure 5a:** Demographic trends by intervention type and region.

| Intervention Type | Intervention | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|---|
| Both | Cyclophotocoagulation (CPC) \| Ahmed® Implant | 2 | 168 | 127 (75.6) | 39 (23.2) | 2 (1.2) | 0 (0.0) | 84 (50.0) | 84 (50.0) |
| | Cyclophotocoagulation (CPC) \| Baerveldt® Implant \| Ahmed® Implant | 1 | 42 | 20 (47.6) | 17 (40.5) | 5 (11.9) | 13 (31.0) | 24 (57.1) | 18 (42.9) |
| GDD | Ahmed® Implant | 13 | 939 | 567 (60.4) | 110 (11.7) | 262 (27.9) | 86 (9.2) | 527 (56.1) | 412 (43.9) |
| | Ahmed® Implant \| Baerveldt® Implant | 2 | 514 | 316 (61.5) | 96 (18.7) | 102 (19.8) | 33 (6.4) | 248 (48.2) | 266 (51.8) |
| | Baerveldt® Implant | 5 | 667 | 343 (51.4) | 254 (38.1) | 70 (10.5) | 45 (6.7) | 367 (55.0) | 300 (45.0) |
| | Krupin® Eye Valve | 1 | 50 | 30 (60.0) | 13 (26.0) | 7 (14.0) | 3 (6.0) | 25 (50.0) | 25 (50.0) |
| | Molteno® Implant | 4 | 151 | 100 (66.2) | 50 (33.1) | 1 (0.7) | 1 (0.7) | 58 (38.4) | 93 (61.6) |
| MIGS | CyPass® Micro-Stent | 2 | 424 | 322 (75.9) | 45 (10.6) | 57 (13.4) | 15 (3.5) | 194 (45.8) | 230 (54.2) |
| | Cyclophotocoagulation (CPC) | 12 | 849 | 693 (81.6) | 138 (16.3) | 20 (2.4) | 5 (0.6) | 416 (49.0) | 433 (51.0) |
| | EX-PRESS® Glaucoma Filtration Device | 8 | 485 | 253 (52.2) | 114 (23.5) | 118 (24.3) | 1 (0.2) | 237 (48.9) | 248 (51.1) |
| | Hydrus® | 2 | 656 | 541 (82.5) | 60 (9.1) | 54 (8.2) | 44 (6.7) | 294 (44.8) | 362 (55.2) |
| | MINIject® | 2 | 57 | 25 (43.9) | 13 (22.8) | 19 (33.3) | 0 (0.0) | 23 (40.4) | 34 (59.6) |
| | Trabectome® | 1 | 37 | 11 (29.7) | 0 (0.0) | 26 (70.3) | 26 (70.3) | 17 (45.9) | 20 (54.1) |
| | XEN® Gel Stent | 7 | 574 | 490 (85.4) | 19 (3.3) | 65 (11.3) | 18 (3.1) | 243 (42.3) | 331 (57.7) |
| | iStent® | 2 | 133 | 101 (75.9) | 0 (0.0) | 32 (24.1) | 0 (0.0) | 74 (55.6) | 59 (44.4) |
| | iStent®\nHydrus® | 1 | 152 | 98 (64.5) | 4 (2.6) | 50 (32.9) | 27 (17.8) | 66 (43.4) | 86 (56.6) |
| | iStent® \| Kahook Dual Blade | 1 | 164 | 128 (78.0) | 23 (14.0) | 13 (7.9) | 4 (2.4) | 77 (47.0) | 87 (53.0) |
| | iTrack™ | 1 | 94 | 88 (93.6) | 5 (5.3) | 1 (1.1) | 1 (1.1) | 41 (43.6) | 53 (56.4) |

**Figure 5b:** Table output – demographics by intervention.

POAG in Africa (4.20%) and the highest prevalence of PACG in Asia (1.09%). Across ethnicities, people of African ancestry had the highest prevalence of glaucoma (6.11%) and POAG (5.40%) while Asians had the highest prevalence of PACG (1.20%). The odds ratio of POAG for individuals of African ancestry was 2.80 compared with individuals of European ancestry [1]. In this review, White participants outnumbered Black participants by approximately 4.2:1. This finding coincides with other studies that found that racial and

| Intervention Type | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|
| Both | 3 | 210 | 147 (70.0) | 56 (26.7) | 7 (3.3) | 13 (6.2) | 108 (51.4) | 102 (48.6) |
| GDD | 25 | 2321 | 1356 (58.4) | 523 (22.5) | 442 (19.0) | 168 (7.2) | 1225 (52.8) | 1096 (47.2) |
| MIGS | 39 | 3625 | 2750 (75.9) | 421 (11.6) | 455 (12.6) | 141 (3.9) | 1682 (46.4) | 1943 (53.6) |

**Figure 5c:** Table output – demographics by intervention type.

| Intervention Type | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|
| GDD | 6 | 238 | 157 (66.0) | 49 (20.6) | 32 (13.4) | 19 (8.0) | 101 (42.4) | 137 (57.6) |
| MIGS | 7 | 1267 | 988 (78.0) | 143 (11.3) | 136 (10.7) | 102 (8.1) | 568 (44.8) | 699 (55.2) |

**Figure 5d:** Table Output – Demographics by intervention type – US only and excluding medical centers and universities.

| Intervention Type | Region | No. of Trials | Total Pop | White | Black | Other | Hispanic - Latino | Male | Female |
|---|---|---|---|---|---|---|---|---|---|
| Both | Latin America | 1 | 68 | 46 (67.6) | 20 (29.4) | 2 (2.9) | 0 (0.0) | 39 (57.4) | 29 (42.6) |
| | North America | 2 | 142 | 101 (71.1) | 36 (25.4) | 5 (3.5) | 13 (9.2) | 69 (48.6) | 73 (51.4) |
| GDD | Asia | 1 | 206 | 206 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 132 (64.1) | 74 (35.9) |
| | Europe | 2 | 177 | 177 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 91 (51.4) | 86 (48.6) |
| | Latin America | 5 | 236 | 141 (59.7) | 38 (16.1) | 57 (24.2) | 55 (23.3) | 141 (59.7) | 95 (40.3) |
| | Multi-Regional | 4 | 731 | 344 (47.1) | 179 (24.5) | 208 (28.5) | 16 (2.2) | 402 (55.0) | 329 (45.0) |
| | North America | 13 | 971 | 488 (50.3) | 306 (31.5) | 177 (18.2) | 97 (10.0) | 459 (47.3) | 512 (52.7) |
| MIGS | Africa | 2 | 45 | 3 (6.7) | 36 (80.0) | 6 (13.3) | 0 (0.0) | 26 (57.8) | 19 (42.2) |
| | Asia | 3 | 128 | 0 (0.0) | 0 (0.0) | 128 (100.0) | 0 (0.0) | 58 (45.3) | 70 (54.7) |
| | Europe | 13 | 966 | 942 (97.5) | 11 (1.1) | 12 (1.2) | 1 (0.1) | 462 (47.8) | 504 (52.2) |
| | Latin America | 1 | 37 | 11 (29.7) | 0 (0.0) | 26 (70.3) | 26 (70.3) | 17 (45.9) | 20 (54.1) |
| | Multi-Regional | 7 | 750 | 579 (77.2) | 57 (7.6) | 116 (15.5) | 6 (0.8) | 347 (46.3) | 403 (53.7) |
| | North America | 13 | 1699 | 1215 (71.5) | 317 (18.7) | 167 (9.8) | 108 (6.4) | 772 (45.4) | 927 (54.6) |

**Figure 5e:** Table output – demographics by intervention type and region.

ethnic minority groups are underrepresented in clinical trials [34].

## Importance of a representative population

While MIGS show favorable efficacy and safety profiles, there are risks of reoperation and outcomes disparities between racial and ethnic populations [35]. Using data from the United States IRIS® Registry between 2013 and 2019, Yang et al. found that non-Hispanic Black patients, compared with non-Hispanic White patients, were associated with an increased risk of reoperation in all MIGS procedures, regardless of concurrent phacoemulsification, except for stand-alone ECP [35].

These findings are not exclusive to MIGS alone, as glaucoma surgical outcomes appear poorer in patients of African-Caribbean descent overall, relative to those of European descent, particularly for trabeculectomy [36]. This also supports the conclusions of the Advanced Glaucoma Intervention Study (AGIS), which demonstrated that Black patients have a higher failure rate following initial standard glaucoma interventions compared to White patients [37]. Chen et al. investigated the underlying mechanisms for these results and found that disparity in access and overall utilization of eye care potentiates the severity and progression of glaucoma and may partially explain the higher reoperation rate in Black patients [38]. Olivier et al. found that the Black population was more likely to undergo a MIGS procedure compared with White patients, while Hispanic patients were found to underutilize MIGS, even though there is a higher glaucoma prevalence within this group [39]. Given the higher utilization of MIGS procedures and greater postoperative complications seen in Black individuals, further research is needed to gain a better understanding of these disparities. This is compounded by reports demonstrating that glaucoma is 7 times more likely to cause blindness and 15 times more likely to cause visual impairment among Black individuals compared with White individuals [40-42].

The racial and ethnic landscape in the United States is evolving, with an increasing diversity index. This index rose from 54.9% in 2010 to 61.1% in 2020, with Asian and Hispanic populations experiencing the fastest growth [43,44]. Research shows that there is a clinical and ethical imperative to conduct studies involving a representative population that can be extrapolated to the target demographic. Disparities in healthcare access, utilization, and disease outcomes are exacerbated by the underrepresentation of minority groups in research studies. The lack of diversity raises concerns about the safety and efficacy of approved surgical interventions,

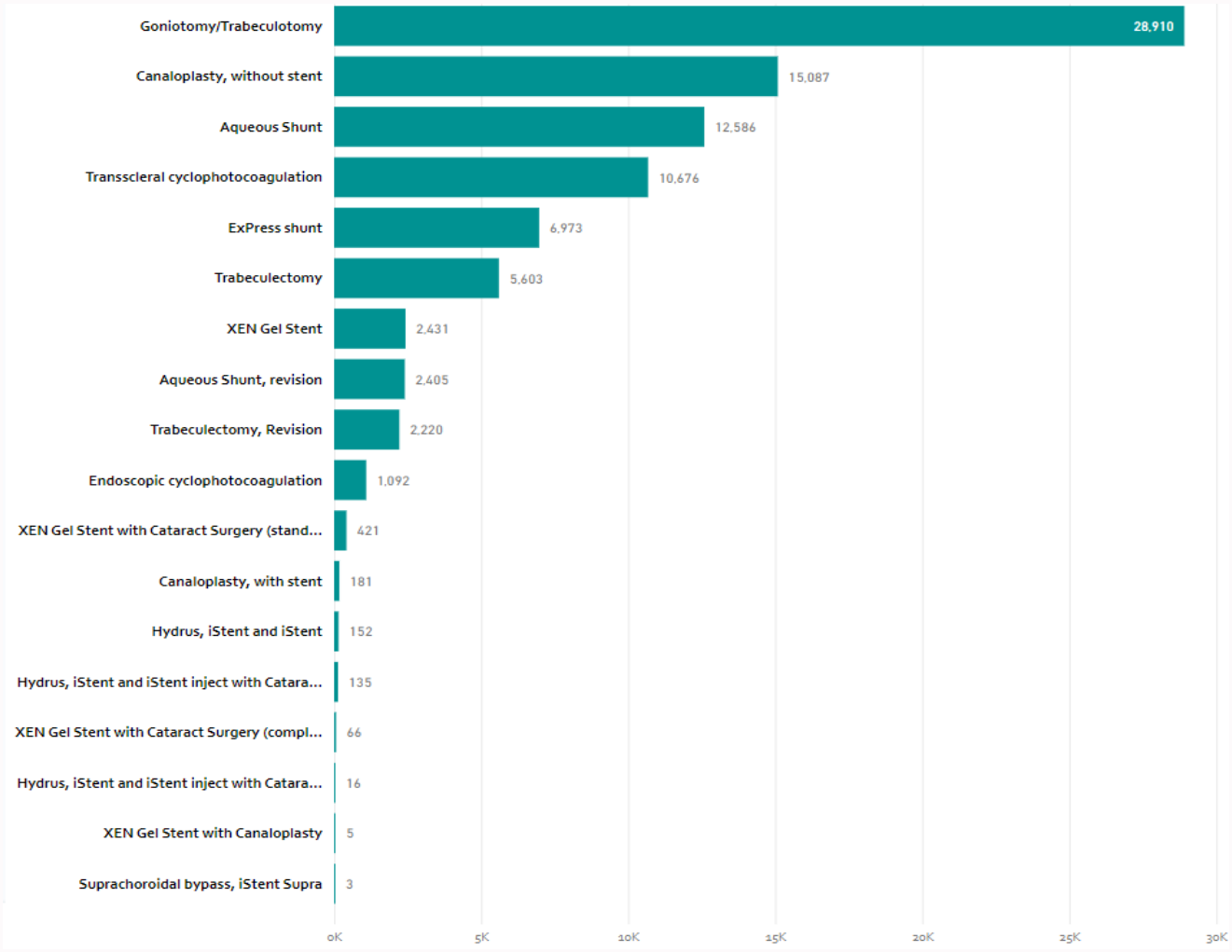


**Figure 6:** Glaucoma outcomes from the IRIS registry, glaucoma patients by procedure, MIGS and GDD, 2022.

highlighting the pressing need for expanded initiatives focused on promoting diversity in future clinical trials for MIGS and GDD. To foster broader representation, researchers must broaden the scope of their study populations by actively including more participants from minority groups [45].

## Overcoming the challenge to increase clinical trial diversity

Diversity in clinical trials is necessary for creating safe and effective treatments for everyone through generalizability. Yet, there are several challenges to increasing minority representation such as cultural barriers, linguistic barriers, and barriers accessing services [46]. These hurdles may be related to the structural or financial restriction of travel for evaluations, follow-ups, and administration of interventions, especially for those who may live in remote areas [47].

Mistrust in healthcare institutions as a result of prior unethical studies is a commonly cited source of lack of racial or ethnic minority participation of clinical trials; however, this may be a misconception as research has found very minor differences in the willingness of minorities to participate in clinical research compared to non-Hispanic whites. While mistrust is a reason for resistance of minority groups to enroll in a clinical trial, there is no significant evidence to suggest that mistrust alone is the only factor [48].

While the FDAAA and final rule demonstrate a contemporary focus on promoting clinical trial diversity, continued steps must be taken to increase representation of minority populations in these studies. Greater enforcement of regulations and increased compliance can increase transparency of data and reporting related to race and ethnicity in research. Removal of barriers to access, diversification of leadership roles, and greater involvement of key stakeholders in local communities may bridge the gap in the generalizability of clinical trials, ultimately improving the safety and effectiveness of approved surgical interventions.

## Reflection on glaucoma surgical interventions

Several medication classes are available which employ different mechanisms of action to achieve an IOP-lowering effect, such as decreasing production of aqueous humor or increasing aqueous humor outflow. Medications are therefore often combined to produce an additive IOP-lowering effect, particularly where monotherapy is insufficient [49]. As demonstrated in the Ocular Hypertension Treatment Study, medications are a valuable treatment option for delaying or preventing the onset of POAG in patients with elevated IOP [50].

Glaucoma surgery, such as trabeculectomy, GDDs, or MIGS, is typically recommended as a secondary option in glaucoma care or if

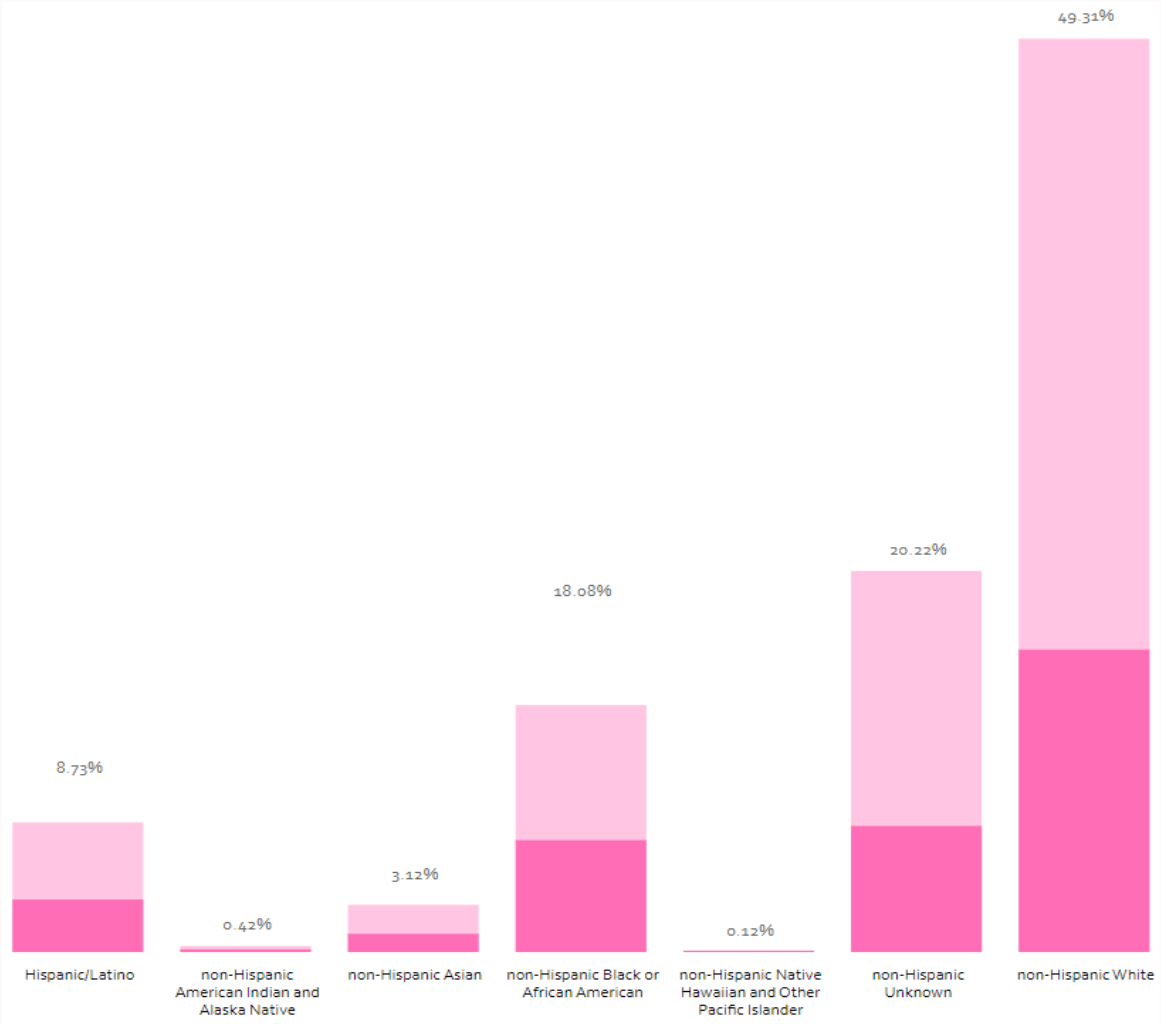


**Figure 6a:** Glaucoma outcomes from the IRIS registry, glaucoma surgical patients by race/ethnicity, MIGS or GDD only, 2022.

patients cannot tolerate medications. In cases of severe glaucoma or non-compliance with medication, surgery may be considered as the initial treatment option. Since the early 2000s, there have been several breakthrough studies that have shaped the landscape of Glaucoma surgery and. The Primary Tube Versus Trabeculectomy (PTVT) and Tube *vs.* Trabeculectomy (TVT) studies by Gedde et al. as well as Medication *vs.* Surgery studies have changed the overall paradigm regarding indications for surgical interventions [51]. These studies observed that surgical interventions resulted in reduced fluctuations in intraocular pressure, leading to enhanced stability.

After the 5 years of follow-up on the PTVT study, the results indicated that Trabeculectomy with MMC and tube shunt surgery produced similar IOPs, with no significant differences in the failure rates observed between the two groups [52]. Moreover, the 5-year follow-up on the TVT study demonstrated that tube shunt surgery had a higher success rate compared to trabeculectomy with MMC. While both groups saw similar decreases in IOP and use of medications at 5 years, Gedde et al. revealed that additional surgery was needed more frequently in the trabeculectomy group tube shunt group [53]. In one review looking at glaucoma medications compared to surgical interventions for POAG, the authors concluded that surgical groups saw a greater reduction of IOP compared to medication, and that there was some evidence that initial medication was associated with more glaucoma progression than surgery; however, it is recommended that this is investigated further with more contemporary medications and larger populations [54].

Research has demonstrated that surgical intervention can be just as effective as, if not more effective than, medications alone in achieving stabilized intraocular pressure and reducing variability over a 5-year follow-up period. The emergence of MIGS and real-world data on Trabeculectomy and GDDs has indicated that surgical intervention can bring benefits to numerous patients with glaucomatous conditions. These interventions should be regarded as an early treatment option, and it is advised that future studies include sufficient representation of patient populations, particularly those disproportionately affected by Glaucoma.

## Limitations

There are limitations to our study. First, not all of the included studies reported the start or end of the clinical trial. This was more prevalent in earlier studies but only encompassed 5 trials. Additionally, 3 studies did not provide age related data and 4 studies did not provide a sponsor. Second, a majority of the studies reviewed were from North American and Europe, particularly from the US, which may not be

entirely representative of the disease population globally. There were no trials that were exclusively done in the Caribbean nor Oceania. This limitation is likely related to the fact that data were extracted only from English-language publications. Third, we excluded trials that were still ongoing and open to accrual. In future meta-analyses, it should be a point of interest to study the prevalence of minorities in these types of trials. Last, our chosen studies did not always report ethnicity. Only 26 studies reported whether patients were Hispanic/Latino, which means that the prevalence of this demographic group could be underrepresented in the review. This limitation is representative of the disparity that is present in these clinical trials, as the Hispanic/Latino population is also greatly affected by this disease. Some of the trials included in this study included demographic descriptors that only allowed a participant to identify with 1 category and offered no insight into whether these participants considered themselves to be a part of more than 1 demographic subgroup. For example, some studies only allowed patients to identify as Hispanic/Latino and not Black or White. For future research, it is important to include this information in the study design and enrollment process in the analysis of these trials, as it may be pertinent to a participant's response to an intervention and future public health implications.

## Conclusion

It is evident that surgical procedures in glaucoma surgery result in increased stability and reduced variability in intraocular pressure. Black patients, who bear the highest burden of the disease, often present at a more advanced stage and are less adherent to medications for various reasons and should be prioritized for surgical intervention sooner rather than later. Nevertheless, the findings indicate that racial and ethnic minority groups have a notably lower participation rate in all glaucoma surgical trials, with MIGs being no exception. Black individuals participate in MIGS clinical trials at a significantly lower rate compared to their White counterparts.

Additionally, these trends were more prevalent in European studies and those sponsored by U.S. medical device companies. This underrepresentation raises concerns regarding the safety and effectiveness of approved surgical interventions. The absence of increased diversity of these clinical trials may suggest that the outcomes are not reflective of the broader population and reduces clear guidelines as to which procedures are more effective in certain populations. There is a compelling need for expanded initiatives aimed at enhancing diversity in future clinical trials as well as an imperative to advance the quality of race and ethnicity data reporting in future studies. It is understood that race is a social construct, but it is also understood that tissues react differently to treatment.

Future studies are encouraged to enhance the inclusivity of representative populations through various strategic initiatives that can involve government, public, or private entities. Furthermore, we encourage the continued identification of barriers to healthcare that limit minority representation and the diversity of clinical trials to ensure a well-represented participant pool in the future.

## References


1. 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):2081-90.
2. Zhang N, Wang J, Chen B, Li Y, Jiang B. Prevalence of primary angle closure glaucoma in the last 20 years: A meta-analysis and systematic review. Front Med (Lausanne). 2021;7:624179.
3. Sharaawy T, Bhartiya S. Surgical management of glaucoma: Evolving paradigms. Indian J Ophthalmol. 2011;59(Suppl):S123-30.
4. Rodriguez-Una I, Azuara-Blanco A, King AJ. Survey of glaucoma surgical preferences and post-operative care in the United Kingdom. Clin Exp Ophthalmol. 2017;45(3):232-40.
5. Mai DD, Ingram Z, Oberfeld B, Valle DSD. Combined microinvasive glaucoma surgery – A review of the literature and future directions. Semin Ophthalmol. 2023;38(6):529-36.
6. Taubenslag KJ, Kammer JA. Outcomes disparities between black and white populations in the surgical management of glaucoma. Semin Ophthalmol. 2016;31(4):385-93.
7. Sugar HS. Some recent advances in the surgery of glaucoma. Bull NY Acad Med. 1963;39(1):3-20.
8. Razeghinejad MR, Spaeth GL. A history of the surgical management of glaucoma. Optom Vis Sci. 2011;88(1)E39-47.
9. Watson PG, Jakeman C, Ozturk M, Barnett MF, Barnett F, Khaw KT. The complications of trabeculectomy (a 20-year follow-up). Eye (Lond). 1990;4:425-38.
10. Cairns JE. Trabeculectomy. Preliminary report of a new method. Am J Ophthalmol. 1968;66(4):673-9.
11. Molteno AC. New implant for drainage in glaucoma. Anim Trial. Br J Ophthalmol. 1969;53(3):161-8.
12. Agrawal P, Bhardwaj P. Glaucoma drainage implants. Int J Ophthalmol. 2020;13(8):1318-28.
13. Gedde SJ, Heuer DK, Parrish RK II. Review of results from the tube versus trabeculectomy study. Curr Opin Ophthalmol. 2010;21(2):123-8.
14. Gupta S, Jeria S. A review on glaucoma drainage devices and its complications. Cureus. 2022;14(9):e29072.
15. Gedde SJ, Herndon LW, Brandt JD, Budenz DL, Feuer WJ, Schiffman JC. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. Am J Ophthalmol. 2012;153(5):804-14.e1.
16. Lim R. The surgical management of glaucoma: A review. Clin Exp Ophthalmol. 2022;50(2):213-31.
17. Birnbaum FA, Neeson C, Valle DS. Microinvasive glaucoma surgery: An evidence-based review. Semin Ophthalmol. 2021;36(8):772-86.
18. Ma AK, Lee JH, Warren JL, Teng CC. GlaucoMap – distribution of glaucoma surgical procedures in the United States. Clin Ophthalmol. 2020;14:2551-60.
19. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. Am J Ophthalmol. 2007;143(1):9-22.
20. Ahmed IIK. MIGS and the FDA: What's in a Name? Ophthalmology. 2015;122(9):1737-9.
21. Berdahl JP, Khatana AK, Katz LJ, Herndon L, Layton AJ, Yu TM, et al. Cost-comparison of two trabecular micro-bypass stents versus selective laser trabeculoplasty or medications only for intraocular pressure control for patients with open-angle glaucoma. J Med Econ. 2017;20(7):760-66.
22. Saheb H, Ahmed IIK. Micro-invasive glaucoma surgery: Current perspectives and future directions. Curr Opin Ophthalmol. 2012;23(2):96-104.
23. Cantor L, Lindfield D, Ghinelli F, Świder AW, Torelli F, Steeds C, et al. Systematic literature review of clinical, economic, and humanistic outcomes following minimally invasive glaucoma surgery or selective laser trabeculoplasty for the treatment of open-angle glaucoma with or without cataract extraction. Clin Ophthalmol. 2023;17:85-101.

24. FDA. FDA's action plan for FDASIA Section 907: Questions and answers.

25. FDA. FDASIA section 907: Inclusion of demographic subgroups in clinical trials.

26. FDA. Enhancing the diversity of clinical trial populations—eligibility criteria, enrollment practices, and trial designs guidance for industry. 2020.

27. DeVito NJ, Bacon BA S, Ben Goldacre B. Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: A cohort study. Lancet (London, England). 2020;395(10221):361-9.

28. PRISMA. PRISMA Statement. 2023.

29. United Nations Statistics Division. N.d. Standard Country or Area Codes for Statistical Use (M49).

30. About the Topic of Race. 2022. United States Census Bureau. 1999.

31. Wu AM, Shen LQ. Racial disparities affecting black patients in glaucoma diagnosis and management. Semin Ophthalmol. 2023;38(1):65-75.

32. Hall NE, Chang EK, Samuel S, Gupta S, Klug E, Elze T, et al. Risk factors for glaucoma drainage device revision or removal using the IRIS registry. Am J Ophthalmol. 2022;240:302-20.

33. Glaucoma Outcomes from the IRIS Registry. American Academy of Ophthalmology. 2023.

34. Clark LT, Watkins L, Piña IL, Elmer M, Akinboboye O, Gorham M, et al. Increasing diversity in clinical trials: Overcoming critical barriers. Curr Probl Cardiol. 2019;44(5):148-72.

35. Yang SA, Ciociola EC, Mitchell W, Hall N, Lorch AC, Miller JW, et al. Effectiveness of microinvasive glaucoma surgery in the United States: Intelligent research in sight registry analysis 2013-2019. Ophthalmology. 2023;130(3):242-55.

36. Nagar AM, Maghsoudlou P, Wormald R, Barton K, Hysi P, Lim KS. Differences in the surgical outcomes of glaucoma surgery in patients of African Caribbean descent. Curr Eye Res. 2022;47(12):1567-77.

37. Williams AM, Huang W, Muir KW, Stinnett SS, Stone JS, Rosdahl JA. Identifying risk factors for blindness from primary open-angle glaucoma by race: A case–control study. Clin Ophthalmol. 2018;12:377-83.

38. Chen J, Vargas-Bustamante A, Mortensen K, Ortega AN. Racial and ethnic disparities in health care access and utilization under the affordable care act. Med Care. 2016;54(2):140-6.

39. Olivier MMG, Smith OU, Croteau-Chonka CC, VanderBeek BL, Maguire MG, Lum F, et al. Demographic and clinical characteristics associated with minimally invasive glaucoma surgery use: An Intelligent Research in Sight (IRIS®) registry retrospective cohort analysis. Ophthalmology. 2021;128(9):1292-9.

40. 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.

41. GBD 2019 Blindness and Vision Impairment Collaborators; Vision Loss Expert Group of the Global Burden of Disease Study. Trends in prevalence of blindness and distance and near vision impairment over 30 years: An analysis for the Global Burden of Disease Study. Lancet Glob Health. 2021;9(2):e130-43.

42. Unterlauft JD, Böhm MRR. [Role of the aging visual system in glaucoma]. Ophthalmologe. 2017;114(2):108-13.

43. Montazeri F, Wang M, Atkuru A, Estrada MM, Liu YA, Emami-Naeini P. Racial, ethnic, and gender diversity in United States ophthalmology clinical trials. Ophthalmol Sci. 2023;4(1):100402.

44. Khan MS, Shahid I, Siddiqi TJ, Khan SU, Warraich HJ, Greene SJ, et al. Ten-year trends in enrollment of women and minorities in pivotal trials supporting recent US Food and Drug administration approval of novel cardiometabolic drugs. J Am Heart Assoc. 2020;9(11):e015594.

45. Montazeri F, Komaki H, Mohebi F, Mohajer B, Mansournia MA, Shahraz S, et al. Editorial: Disparities in cancer prevention and epidemiology. Front Oncol. 2022;12:872051.

46. Alison M, Hoke MH, Williams JC. Lessons learned: Research with rural Mexican-American women. Nurs Outlook. 2005;53(3):141-6.

47. Murakami Y, Lee BW, Duncan M, Kao A, Huang JY, Singh K, et al. Racial and ethnic disparities in adherence to glaucoma follow-up visits in a county hospital population. Arch Ophthalmol. 2011;129(7):872-8.

48. Wendler D, Kington R, Madans J, Wye GV, Christ-Schmidt H, Pratt LA, et al. Are racial and ethnic minorities less willing to participate in health research? PLoS Med. 2006;3(2):e19.

49. Noecker RJ. The management of glaucoma and intraocular hypertension: Current approaches and recent advances. Ther Clin Risk Manag. 2006;2(2):193-206.

50. Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The ocular hypertension treatment study: A randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002;120(6):701-13; discussion 829-30.

51. Elizabeth CC, Yang SA, Hall N, Lorch AC, Miller JW, Friedman DS, 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.

52. Gedde SJ, Feuer WJ, Lim KS, Barton K, Goyal S, Ahmed II, et al. Treatment outcomes in the primary tube versus trabeculectomy study after 5 years of follow-up. Ophthalmology. 2022;129(12):1344-56.

53. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL, 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.e2.

54. Burr J, Azuara-Blanco A, Avenell A, Tuulonen A. Medical versus surgical interventions for open angle glaucoma. Cochrane Database Syst Rev. 2012;(9):CD004399.