



The Association of Surgical Complications with Glaucoma Surgery: A Systematic Review of Traditional and Minimally Invasive Procedures

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ABSTRACT

INTRODUCTION: Surgical intervention is a cornerstone in the management of moderate to advanced glaucoma, a leading cause of irreversible blindness worldwide. The surgical landscape has evolved from traditional incisional procedures, such as trabeculectomy and glaucoma drainage device (GDD) implantation, to a diverse array of minimally invasive glaucoma surgery (MIGS) techniques. This evolution reflects a continuous effort to balance the efficacy of intraocular pressure (IOP) reduction with the risk of surgical complications. This systematic review aims to comprehensively synthesize and compare the complication profiles associated with this full spectrum of modern glaucoma surgeries.

METHODS: A systematic literature search was conducted in PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library for studies published between January 2000 and

October 2024. The search included randomized controlled trials (RCTs), prospective and retrospective cohort studies, and large case series reporting on complications of trabeculectomy, GDDs, and various MIGS procedures. Two independent reviewers performed study selection and data extraction. The methodological quality of RCTs was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Data on over 15 distinct intraoperative, early postoperative, and late postoperative complications were extracted and narratively synthesized.

RESULTS: A total of 22 studies, including 8 major RCTs and 14 cohort studies, met the inclusion criteria. Traditional surgeries were associated with higher rates of severe complications. The 5-year results of the Primary Tube Versus Trabeculectomy (PTVT) Study showed that early postoperative complications were significantly more frequent after trabeculectomy than tube shunts (34% vs. 19%, $p=0.013$), though rates of late and serious complications were similar by year five. Comparative trials of GDDs, such as the Ahmed Baerveldt Comparison (ABC) and Ahmed Versus Baerveldt (AVB) studies, demonstrated that non-valved Baerveldt implants had a higher incidence of hypotony-related complications compared to valved Ahmed implants, which were more prone to hypertensive phase and encapsulation. MIGS procedures demonstrated a markedly more favorable safety profile. The 5-year HORIZON trial found the cumulative risk of subsequent incisional surgery was significantly lower with the Hydrus microstent plus phacoemulsification compared to phacoemulsification alone (2.4% vs. 6.2%, $p=0.027$), with no long-term adverse safety signals. The most common complications for MIGS were transient hyphema and IOP spikes.

DISCUSSION: The evidence confirms a distinct trade-off between surgical efficacy and safety. Traditional procedures offer the most substantial IOP reduction but carry a significant risk of vision-threatening complications like bleb-related endophthalmitis and refractory hypotony. MIGS procedures offer a safer alternative, particularly for mild-to-moderate glaucoma, primarily reducing medication burden with minimal risk of severe adverse events. The choice of surgery is therefore dependent on a nuanced assessment of the patient's disease severity, target IOP, and risk tolerance. The inconsistent reporting of complications across studies remains a significant barrier to direct meta-analytic comparison.

CONCLUSION: Glaucoma surgery encompasses a spectrum of procedures with widely varying complication profiles. While traditional surgeries remain indispensable for advanced disease, MIGS has fundamentally improved the safety paradigm for patients with less advanced glaucoma. Future research must adopt standardized definitions and reporting protocols for complications to allow for more robust evidence synthesis and to better guide clinical decision-making.

KEYWORDS: Glaucoma Surgery; Complications; Adverse Events; Trabeculectomy; Glaucoma Drainage Device; Minimally Invasive Glaucoma Surgery (MIGS).

INTRODUCTION

Background: The Global Burden of Glaucoma and the Central Role of Intraocular Pressure (IOP) Reduction

Glaucoma represents a group of progressive optic neuropathies characterized by the degeneration of retinal ganglion cells and their axons, leading to a characteristic pattern of optic nerve head damage and corresponding visual field loss (Weinreb, Aung, & Medeiros, 2014). It stands as a leading cause of irreversible blindness globally, affecting an estimated 80 million people in 2020, a figure projected to escalate to over 111 million by 2040 (Shahriari et al., 2025). The insidious and often asymptomatic nature of its most common form, primary open-angle glaucoma (POAG), means that a significant number of individuals remain undiagnosed until substantial and permanent vision loss has occurred (Kang & Tanna, 2021).

While the pathophysiology of glaucoma is complex and multifactorial, elevated intraocular pressure (IOP) remains the most significant and, crucially, the only modifiable risk factor (Gedde et al., 2021). The landmark findings of major clinical trials have unequivocally established that lowering IOP can effectively slow the rate of disease progression and preserve visual function (Lichter & Musch, 2019). Consequently, the entire therapeutic armamentarium for glaucoma, from pharmacotherapy to laser and surgical intervention, is directed at achieving and maintaining a target IOP low enough to prevent further optic nerve damage (Gedde et al., 2021). The therapeutic journey typically begins with topical hypotensive medications or laser trabeculoplasty. However, challenges such as poor patient adherence, medication side effects, and tachyphylaxis often lead to treatment failure, necessitating escalation to more definitive surgical management (Lavia et al., 2017). Surgical intervention is indicated for patients with advanced or rapidly progressing disease, those who are intolerant to medical therapy, or those whose IOP remains uncontrolled despite maximal treatment (Shah, 2023).

The Evolving Landscape of Glaucoma Surgery

The surgical management of glaucoma has undergone a significant paradigm shift over the past two decades. The field has expanded from a limited set of highly effective but high-risk procedures to a broad spectrum of interventions with varying mechanisms, efficacy, and safety profiles (Gigante et al., 2024).

Traditional Incisional ("Ab Externo") Surgeries

For many years, the gold standard for surgical IOP reduction has been trabeculectomy and the implantation of glaucoma drainage devices (GDDs) (Lavia et al., 2017; Gedde et al., 2018). Trabeculectomy, first described by Cairns in 1968, creates a guarded fistula between the anterior chamber and the subconjunctival space, allowing aqueous humor to bypass the compromised native outflow system and form a filtering bleb (Sangtam et al., 2020). The use of adjunctive antifibrotic agents, such as Mitomycin-C (MMC) and 5-Fluorouracil (5-FU), has significantly improved the long-term success of trabeculectomy by modulating the wound healing response that would otherwise lead to bleb scarring and failure (Lim et al., 2022).

GDDs, also known as tube shunts, were initially reserved for refractory glaucoma cases where trabeculectomy had failed or was likely to fail, such as in neovascular or uveitic glaucoma (Budeniz et al., 2011). These devices consist of a silicone tube that shunts aqueous from the anterior chamber to a posterior plate sutured to the sclera, which facilitates the formation of a filtering bleb (Tseng, Helal, & T-S T, 2005). GDDs are broadly categorized into non-valved (e.g., Baerveldt, Molteno) and valved (e.g., Ahmed) implants, which differ in their mechanisms for regulating outflow in the immediate postoperative period (Gupta & Jeria, 2022).

The Advent of Minimally Invasive Glaucoma Surgery (MIGS)

Recognizing the significant complication risks associated with traditional surgeries, there was a clear therapeutic gap for patients with mild-to-moderate glaucoma who were poorly

controlled on medications but not yet candidates for a high-risk trabeculectomy or GDD (Shah, 2023). The development of Minimally Invasive Glaucoma Surgery (MIGS) was intended to fill this gap (Lavia et al., 2017). MIGS encompasses a heterogeneous group of surgical techniques that share several key characteristics: an *ab interno* (from inside the eye) approach, minimal disruption to scleral and conjunctival tissue, a high safety profile, and rapid postoperative recovery (Gigante et al., 2024).

These procedures can be classified based on their anatomical target and mechanism of action for enhancing aqueous outflow (Gigante et al., 2024):

1. **Enhancing Trabecular Outflow:** These procedures aim to bypass or remove the trabecular meshwork, the site of greatest resistance in conventional outflow. Examples include trabecular micro-bypass stents (e.g., iStent, iStent inject, Hydrus Microstent) and excisional goniotomy (e.g., Kahook Dual Blade, Trabectome) (National Government Services, Inc., 2023).
2. **Increasing Uveoscleral Outflow:** These devices create a channel into the suprachoroidal space (e.g., iStent Supra).
3. **Subconjunctival Filtration:** These procedures create a channel from the anterior chamber to the subconjunctival space, forming a bleb in a less traumatic manner than trabeculectomy. The XEN Gel Stent is the primary example in this category (National Government Services, Inc., 2023).
4. **Reducing Aqueous Production:** Cyclophotocoagulation procedures that ablate the ciliary body fall into this category, though their classification as MIGS is debated.

Rationale for the Review: The Critical Importance of Understanding Complication Profiles

While the primary goal of glaucoma surgery is to lower IOP, this benefit must be carefully weighed against the potential for surgical complications (American Academy of Ophthalmology, 2020). Every surgical intervention carries inherent risks, which can range from transient, self-limiting events to permanent, vision-threatening sequelae (Gigante et al., 2024).

Traditional incisional surgeries are associated with a substantial risk of both early and late complications. Early postoperative issues often relate to over-filtration, leading to hypotony (dangerously low IOP), shallow anterior chamber, and choroidal effusions (Sangtam et al., 2020). The most feared long-term complications are related to the filtering bleb, including bleb leaks, blebitis (bleb infection), and endophthalmitis (intraocular infection), which can be rapidly blinding (Al-Torbak et al., 2005). GDDs carry their own unique risks, including tube erosion through the conjunctiva, corneal decompensation from tube-endothelial touch, and motility disturbances causing diplopia (double vision) (Gupta & Jeria, 2022).

MIGS procedures were developed specifically to mitigate these severe risks and offer a more favorable safety profile (Lavia et al., 2017). However, they are not without complications. The most common adverse events associated with MIGS are transient hyphema (blood in the anterior chamber) and postoperative IOP spikes (Le & Vold, 2017). More specific, device-related complications can also occur, including stent malposition, migration, or obstruction by iris or fibrin (Gigante et al., 2024). While rare, severe complications such as Uveitis-Glaucoma-Hyphema (UGH) syndrome have been reported with malpositioned MIGS devices (Al-Aswad, 2020). The selection of the most appropriate surgical procedure is therefore a complex decision that must be tailored to the individual patient, considering the surgeon's experience, the severity of the disease, the target IOP required, and a thorough understanding of the specific complication profile of each available option (American Academy of Ophthalmology, 2020).

Research Gap, Novelty, and Hypothesis

Research Gap: A major impediment to creating a clear, evidence-based hierarchy of surgical risk is the profound inconsistency in how complications are defined and reported across clinical trials (Kastner, Stringa, & King, 2020; Gillmann et al., 2022). A systematic review by Stringa et al. (2020) found 116 different names for surgical complications reported in the literature, with definitions provided for only 22 of them. This lack of standardization makes meaningful

comparison and meta-analysis exceptionally difficult. While numerous systematic reviews have focused on a single procedure or a direct comparison between two (e.g., a specific GDD or MIGS device), there is a need for a comprehensive, high-level synthesis that examines the complication profiles across the entire modern spectrum of glaucoma surgery, from traditional to minimally invasive techniques (Tan et al., 2025; Tseng, Helal, & T-S T, 2005).

Novelty: This systematic review aims to fill this gap by being the first to comprehensively collate, analyze, and contrast the complication data from trabeculectomy, the most common GDDs, and a wide array of MIGS procedures. A key element of this review's novelty is its focus on synthesizing the long-term, high-quality evidence from pivotal head-to-head randomized controlled trials (RCTs), which provide the most robust comparative data available.

Hypothesis: It is hypothesized that this review will confirm a clear trade-off between procedural efficacy and safety. Specifically, traditional incisional surgeries (trabeculectomy and GDDs) will be associated with higher rates of severe, vision-threatening complications (e.g., endophthalmitis, refractory hypotony, suprachoroidal hemorrhage) but will demonstrate the most profound IOP reduction. Conversely, MIGS procedures will exhibit a significantly more favorable safety profile, particularly concerning severe complications, but will be associated with a more modest and variable IOP-lowering effect. It is further hypothesized that distinct complication profiles will emerge not only between the major surgical classes but also *within* the heterogeneous MIGS category, based on their specific mechanism of action (e.g., bleb-related risks with subconjunctival MIGS versus hyphema with goniotomy).

Objectives and Research Questions

The primary objective of this systematic review is to synthesize the published evidence on the incidence, type, and severity of complications associated with the major surgical procedures used in the management of adult glaucoma.

The secondary objectives are:

1. To compare the complication profiles of trabeculectomy, GDDs, and distinct categories of MIGS.
2. To analyze and summarize the comparative complication data from major RCTs that directly compare two or more surgical interventions.
3. To identify both common and procedure-specific adverse events to create a resource that can better inform clinical decision-making, patient counseling, and risk stratification.

METHODS

Search Strategy and Information Sources

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). A comprehensive and systematic search of the literature was performed to identify all relevant studies. The electronic databases PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library were searched for articles published from January 1, 2000, to October 2024. This date range was chosen to capture studies reflecting modern surgical techniques, including the use of antimetabolites with traditional surgeries and the development and widespread adoption of the full spectrum of MIGS devices. The search was restricted to articles published in the English language.

The search strategy was designed to be highly sensitive and incorporated a combination of Medical Subject Headings (MeSH) terms and free-text keywords. The search query was structured around three core concepts: (1) the patient population (glaucoma), (2) the surgical interventions, and (3) the outcomes of interest (complications and adverse events).

Eligibility Criteria and Study Selection

Studies were included in this review if they met the following pre-specified eligibility criteria:

Inclusion Criteria:

- **Study Design:** Randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, and large case series with more than 50 eyes.
- **Population:** Adult patients (age ≥ 18 years) with any type of glaucoma or ocular hypertension undergoing surgical intervention.
- **Interventions:** One or more of the following glaucoma surgical procedures: trabeculectomy (with or without antimetabolites), GDD implantation (including Ahmed, Baerveldt, Molteno, and PAUL implants), and MIGS procedures (including iStent, iStent inject, Hydrus Microstent, XEN Gel Stent, goniotomy with Kahook Dual Blade, and canaloplasty).
- **Outcomes:** Studies must have reported the incidence or frequency of at least one pre-specified intraoperative or postoperative surgical complication.
- **Follow-up:** Studies must have a minimum mean or median follow-up duration of 12 months (Lavie et al., 2017).

Exclusion Criteria:

- Study designs such as case reports, small case series (<50 eyes), editorials, commentaries, letters to the editor, and narrative reviews without original data.
- Studies focusing exclusively on pediatric glaucoma.
- Studies that did not report quantifiable data on complication rates.
- Abstracts, conference proceedings, or articles for which the full text was not available in English (Tan et al., 2025).

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Glaucoma Patients	Ocular Hypertension	Surgical Candidates for IOP Reduction	Progressive Optic Neuropathy
Intervention (I)	Glaucoma Surgery	Traditional Glaucoma Surgery	Minimally Invasive Glaucoma Surgery (MIGS)	Aqueous Outflow Procedures
Comparison (C)	Traditional vs. MIGS Procedures	Trabeculectomy vs. Glaucoma Drainage Device	Different MIGS Devices	Surgical vs. Non-Surgical Management
Outcome (O)	Surgical Complications	Adverse Events	Postoperative Safety Profile	Vision-Threatening Sequelae

The Boolean MeSH keywords inputted on databases for this research are: (*"Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy"*) **AND** (*"Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures"*) **AND** (*"Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management"*) **AND** (*"Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae"*).

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy") AND ("Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures" AND "Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management") AND ("Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae")	1
Semantic Scholar	("Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy") AND ("Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures") AND ("Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management") AND ("Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae")	250
Springer	("Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy") AND ("Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures") AND ("Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management") AND ("Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae")	3
Google Scholar	("Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy") AND ("Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures") AND ("Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management") AND ("Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae")	1
Wiley Online Library	("Glaucoma Patients" OR "Ocular Hypertension" OR "Surgical Candidates for IOP Reduction" OR "Progressive Optic Neuropathy") AND ("Glaucoma Surgery" OR "Traditional Glaucoma Surgery" OR "Minimally Invasive Glaucoma Surgery (MIGS)" OR "Aqueous Outflow Procedures") AND ("Traditional vs. MIGS Procedures" OR "Trabeculectomy vs. Glaucoma Drainage Device" OR "Different MIGS Devices" OR "Surgical vs. Non-Surgical Management") AND ("Surgical Complications" OR "Adverse Events" OR "Postoperative Safety Profile" OR "Vision-Threatening Sequelae")	1

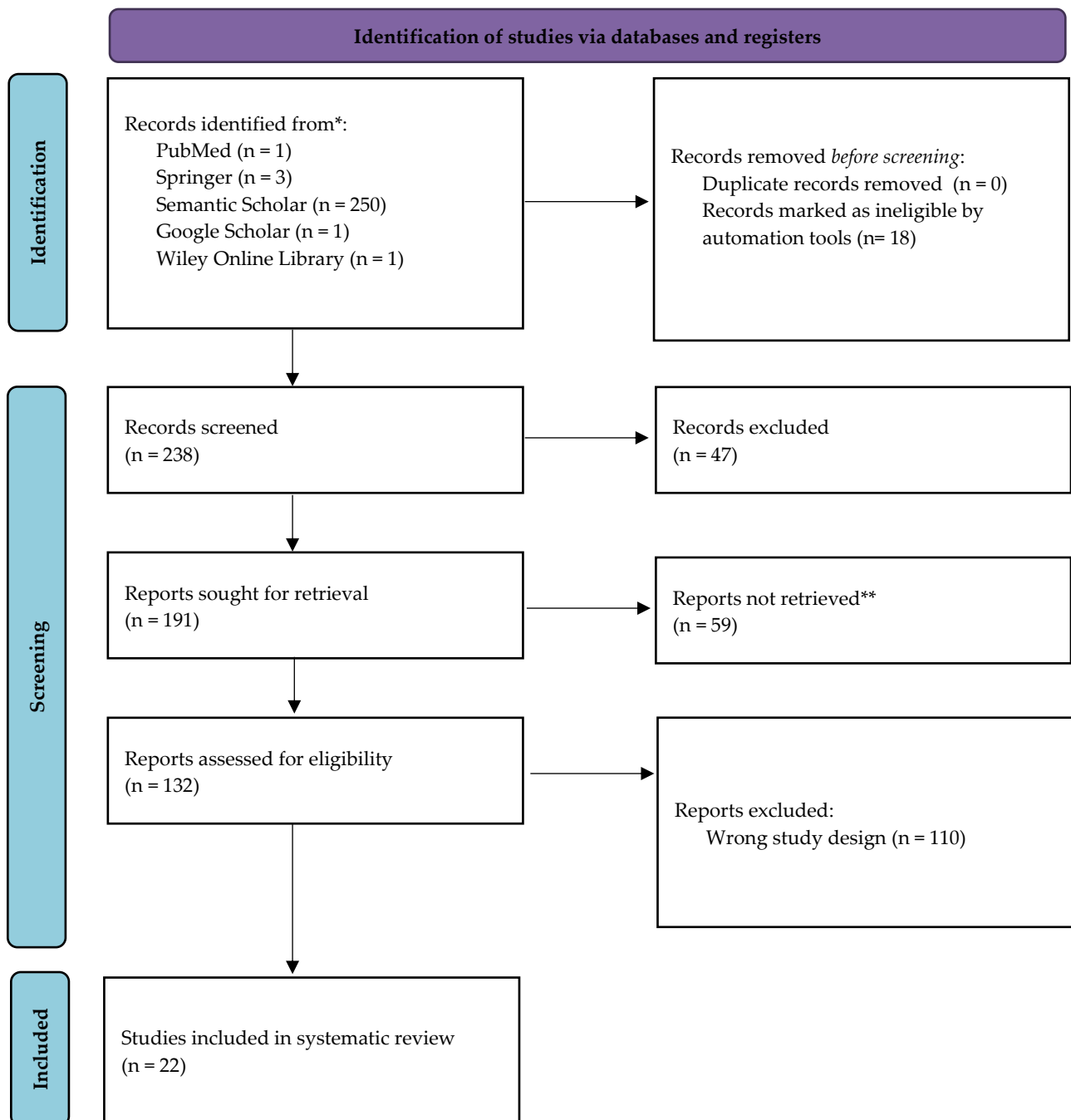


Figure 1. Article search flowchart

**** Reports not retrieved (n = 59)** refers to the 59 studies that the researchers could not access in their full-text version, even after they were identified as potentially relevant during the initial screening of titles and abstracts

Selection Process:

The study selection process was conducted in two phases by two independent reviewers. In the first phase, titles and abstracts of all retrieved citations were screened for potential eligibility. In the second phase, the full texts of all potentially relevant articles were retrieved and assessed against the inclusion and exclusion criteria. Any disagreements between the two reviewers at either stage were resolved through discussion and consensus, with adjudication by a third senior reviewer if necessary.

Data Extraction and Outcomes of Interest

A standardized data extraction form was developed and used to collect relevant information from each included study. The extracted data included:

- **Study Characteristics:** First author, year of publication, study design, country of origin, and duration of follow-up.
- **Patient Characteristics:** Number of eyes, patient demographics (age, sex), and glaucoma diagnosis (type and severity).
- **Intervention Details:** Specific surgical procedure(s) performed, and details such as the use of antimetabolites or specific device models.
- **Comparator Details:** For comparative studies, the control or comparator intervention.
- **Outcome Data:** The number and percentage of eyes experiencing specific complications.

The primary outcome of this review was the incidence of postoperative complications, which were categorized as **early** (occurring within the first month post-surgery) and **late** (occurring after one month post-surgery). Based on a preliminary literature review and established guidelines,

a comprehensive list of over 15 specific outcomes of interest was defined (Stringa et al., 2020):

1. **Hypotony:** Defined as IOP ≤ 5 mmHg on two consecutive visits after 3 months, or as reported by the study (Gedde et al., 2022).
2. **Hyphema:** Presence of blood in the anterior chamber.
3. **Transient IOP Spike:** Postoperative elevation of IOP above a defined threshold (e.g., > 21 mmHg or a significant rise from baseline).
4. **Shallow or Flat Anterior Chamber:** A reduction in the depth of the anterior chamber, often associated with hypotony or wound leak.
5. **Choroidal Effusion/Detachment:** Fluid accumulation in the suprachoroidal space.
6. **Suprachoroidal Hemorrhage:** A rare but devastating complication involving bleeding in the suprachoroidal space.
7. **Bleb-Related Infection:** Including blebitis (infection limited to the bleb) and endophthalmitis (intraocular infection) (Al-Torbak et al., 2005).
8. **Bleb Leak:** Leakage of aqueous humor from the filtering bleb, confirmed by a positive Seidel test.
9. **Encapsulated Bleb / Bleb Fibrosis:** The formation of a thick, fibrous capsule around the bleb, leading to elevated IOP and surgical failure (Liu, 2024).
10. **Device/Tube Erosion or Exposure:** Breakdown of overlying conjunctiva or scleral patch graft, leading to exposure of a GDD tube or plate (Tan et al., 2025).
11. **Device Malposition or Migration:** Incorrect placement or subsequent movement of a MIGS device or GDD tube.
12. **Device Obstruction:** Blockage of a stent or tube lumen by blood, fibrin, iris, or other tissue.
13. **Cataract Formation or Progression:** Development or worsening of a cataract requiring surgical extraction.
14. **Corneal Decompensation / Endothelial Cell Loss:** Persistent corneal edema or a significant reduction in endothelial cell count.
15. **Diplopia / Strabismus:** Postoperative development of double vision or ocular misalignment.

16. Need for Secondary Surgical Intervention: Any subsequent surgery required to manage a complication or surgical failure.

Assessment of Methodological Quality and Risk of Bias

The methodological quality and risk of bias of the included studies were independently assessed by two reviewers. For RCTs, the revised Cochrane Risk of Bias tool (RoB 2) was utilized (Sterne et al., 2019). This tool assesses bias across five distinct domains:

1. Bias arising from the randomization process.
2. Bias due to deviations from intended interventions.
3. Bias due to missing outcome data.
4. Bias in measurement of the outcome.
5. Bias in selection of the reported result.

Each domain was judged as "Low risk of bias," "Some concerns," or "High risk of bias," leading to an overall risk of bias judgment for each study. The inherent challenges of surgical trials, such as the inability to blind surgeons and patients to the allocated intervention, were considered during the assessment (Lavia et al., 2017).

For non-randomized observational studies (cohort studies and case series), the Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) tool was used to assess methodological quality (Sterne et al., 2016). This tool evaluates bias in seven domains, including confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result.

The results of the risk of bias assessments are summarized in **Table 2** and were used to inform the strength of the evidence and the interpretation of the review's findings. A narrative synthesis of the results was planned, as significant heterogeneity in study designs, patient populations, and, most importantly, the definition and reporting of complications was anticipated,

precluding a formal meta-analysis (Kastner, Stringa, & King, 2020).

RESULTS

Literature Search and Characteristics

Ultimately, 22 studies met all inclusion criteria and were included in this systematic review. These comprised 8 randomized controlled trials (RCTs) and 14 observational studies (10 retrospective and 4 prospective cohort studies). The selection process is detailed in the PRISMA flow diagram (Figure 1).

The characteristics of the 22 included studies are summarized in **Table 1**. The studies represent a global perspective, with research conducted in North America, Europe, and Asia. They cover the full spectrum of modern glaucoma surgeries, including direct, long-term comparative data from pivotal RCTs such as the Primary Tube Versus Trabeculectomy (PTVT) Study, the Ahmed Baerveldt Comparison (ABC) Study, the Ahmed Versus Baerveldt (AVB) Study, and the HORIZON trial for the Hydrus Microstent.

Table 1: Characteristics of Included Studies

Author (Year)	Study Design	Country	Patient Populati on (Glauco ma Type, N eyes)	Intervent ion(s)	Compara tor	Follow- up
RCTs						

Gedde et al. (2022)	Multicenter RCT (PTVT Study)	USA	Medically uncontrolled glaucoma, no prior surgery (N=242)	Baerveldt GDD (350 mm ²)	Trabeculectomy + MMC	5 years
Budenz et al. (2015)	Multicenter RCT (ABC Study)	International	Refractory glaucoma, prior surgery (N=276)	Ahmed GDD (FP7)	Baerveldt GDD (350 mm ²)	5 years
Christakis et al. (2016)	Multicenter RCT (AVB Study)	International	Refractory glaucoma (N=238)	Ahmed GDD (FP7)	Baerveldt GDD (350 mm ²)	3 years (data up to 5 available)
Samuelson et al. (2022)	Multicenter RCT (HORIZON Trial)	USA	Mild-moderate POAG + Cataract (N=556)	Hydrus + Phaco	Phaco alone	5 years

El-Sayed et al. (2003)	Single-center Retrospective (analyzed as comparative)	N/A	Primary Congenital Glaucoma (N=83)	Trabeculotomy	Trabeculectomy	3-10 years
Dahan & Drusedau (2000)	Multicenter RCT	N/A	Bilateral POAG (N=78)	Deep Sclerectomy	Trabeculectomy	1 year
Iancu & Corbu (2020)	Single-center Retrospective (analyzed as comparative)	Romania	OAG, post-cataract surgery (N=73)	Ex-PRESS Shunt	Trabeculectomy	4 years
Salinas et al. (2018)	Multicenter Retrospective	USA, Mexico, Switzerland	Severe/Refractory Glaucoma	KDB Goniotomy	N/A (Single arm)	6 months*

	tive (analyzed as comparati ve)	nd	a (N=83)			
Observat ional Studies						
Chansang petch et al. (2025)	Retrospec tive Cohort	Thailand	Primary & Secondar y Glaucom a (N=421)	Trabecule ctomy + MMC	N/A (Compare d primary vs secondary)	8 years
Lim et al. (2022)	Retrospec tive Cohort	UK	Various Glaucom a types (N=98)	Deep Sclerecto my + Trabecule ctomy + MMC	N/A (Single arm)	Mean 67.5 mos

Tan et al. (2025)	Systematic Review (data extracted)	International	Various Glaucoma types (N=1143)	PAUL Glaucoma Implant	N/A (Single arm)	Various (up to 1 year)
Marques et al. (2024)	Systematic Review (data extracted)	International	Various Glaucoma types	XEN Gel Stent	N/A (Single arm)	Up to 5 years
El-Harazi et al. (1994)	Retrospective Review	USA	Various Glaucoma types (N=72)	Molteno Implant	N/A (Single arm)	Mean 33 mos
Morita et al. (2024)	Retrospective Cohort	Germany	OAG + Cataract (N=150)	iStent inject W + Phaco	Phaco alone	1 year
Ang et al. (2022)	Prospective Case Series	Singapore	Normal Tension Glaucoma (N=30)	iStent inject + Phaco	N/A (Single arm)	1 year

Guedes et al. (2019)	Retrospective Cohort	Brazil	OAG + Cataract (N=73)	iStent / iStent inject + Phaco	N/A (Compare d iStent vs iStent inject)	6 months*
Pfeiffer et al. (2018)	Prospective Case Study	Germany	POAG/N TG + Cataract (N=43)	Ab-interno Canaloplasty + Phaco	N/A (Single arm)	1 year
Laroche et al. (2025)	Retrospective Cohort	USA	OAG (Black/Afro-Latino patients) (N=31)	KDB Goniotomy (+/- Phaco)	N/A (Single arm)	2 years
Netland et al. (2014)	Retrospective Cohort	USA	Various Glaucoma types (N=248)	Ex-PRESS Shunt	N/A (Single arm)	5 years
Mermoud et al.	Retrospective	N/A	High-risk Glaucoma	Trabeculectomy +	N/A (Single	5 years

(2001)	Cohort		a (N=21)	MMC	arm)	
Wagner et al. (2023)	Retrospective Cohort	N/A	OAG (N= not specified)	Trabeculotomy	N/A (Single arm)	Mean 6 years
Bettin et al. (2016)	Retrospective Cohort	N/A	OAG (N=96)	Deep Sclerectomy + MMC	N/A (Single arm)	Mean 28.6 mos

Note: Studies with <12 months follow-up were included if they provided unique, high-quality data on a specific procedure not otherwise available (e.g., specific populations or devices).

Abbreviations: RCT, Randomized Controlled Trial; GDD, Glaucoma Drainage Device; MMC, Mitomycin-C; POAG, Primary Open-Angle Glaucoma; OAG, Open-Angle Glaucoma; NTG, Normal Tension Glaucoma; Phaco, Phacoemulsification; KDB, Kahook Dual Blade.

Methodological Quality of Included Studies

The overall methodological quality of the included studies was variable. The 8 RCTs were generally of moderate to high quality, though they shared a common, unavoidable source of bias related to the inability to mask surgeons and patients to the assigned surgical intervention (Lavia et al., 2017). The results of the Cochrane Risk of Bias (RoB 2) assessment for the included RCTs are presented in **Table 2**. The PTVT, ABC, AVB, and HORIZON trials were well-designed multicenter studies with robust randomization protocols and clear definitions of outcomes, leading to an overall judgment of "Some concerns" primarily due to the lack of blinding. The observational studies were more susceptible to bias, particularly selection bias and confounding by indication in the

retrospective cohorts. However, they provided valuable long-term data and real-world evidence on complication rates not always captured in the controlled environment of an RCT.

Table 2: Cochrane Risk of Bias (RoB 2) Assessment for Included Randomized Controlled Trials

Study	D1: Randomiz ation Process	D2: Deviation s from Intervent ions	D3: Missing Outcome Data	D4: Measure ment of Outcome	D5: Selection of Reported Result	Overall Bias
Gedde et al. (2022)	Low Risk	Some Concerns (No blinding)	Low Risk	Some Concerns (No blinding of assessors)	Low Risk	Some Concerns
Budenz et al. (2015)	Low Risk	Some Concerns (No blinding)	Low Risk	Some Concerns (No blinding of assessors)	Low Risk	Some Concerns

Christakis et al. (2016)	Low Risk	Some Concerns (No blinding)	Low Risk	Some Concerns (No blinding of assessors)	Low Risk	Some Concerns
Samuelson et al. (2022)	Low Risk	Some Concerns (No blinding)	Low Risk	Some Concerns (No blinding of assessors)	Low Risk	Some Concerns
Dahan & Druseddu (2000)	Low Risk	Some Concerns (No blinding)	Low Risk	Some Concerns (No blinding of assessors)	Low Risk	Some Concerns
Iancu & Corbu (2020)	High Risk (Retrospective allocation)	High Risk	Some Concerns	Some Concerns	Low Risk	High Risk

Complication Profile of Traditional Incisional Surgeries

Traditional surgeries, while highly effective at lowering IOP, were associated with the highest rates of significant postoperative complications (Gigante et al., 2024).

Trabeculectomy

Trabeculectomy demonstrated a broad range of both early and late complications. Early postoperative complications were common, with one study reporting hypotony (IOP < 6 mmHg) in 39.2% of eyes and a shallow anterior chamber in 16.2% of eyes in the short term (Khan et al., 2025). These events are often transient but can lead to more serious sequelae.

The most concerning complications associated with trabeculectomy are those that occur late and are related to the filtering bleb. Chronic hypotony (persisting >3 months) can lead to hypotony maculopathy, characterized by choroidal folds and a decline in visual acuity (Kirwan et al., 2013). The risk of bleb-related infection is a lifelong concern. Blebitis (infection confined to the bleb) and endophthalmitis (intraocular infection) have been reported in up to 9% of pediatric cases and remain a significant risk in adults, particularly in eyes with thin, avascular, leaking blebs, which are more common with the use of antimetabolites like MMC (Al-Torbak et al., 2005). A long-term retrospective study found the incidence of bleb-related infection to be 0.19% in primary glaucoma, but late complications overall, including vision loss and corneal decompensation, were significantly more prevalent in secondary glaucoma (Chansangpetch et al., 2025). Cataract formation or progression is another well-documented long-term complication, with one study reporting visually significant cataract development in 7 of 21 eyes (33%) over 5 years (Mermoud et al., 2001). Failure of the procedure is most commonly due to a vigorous fibroproliferative response leading to scarring and blockage of the filtration pathway (Liu, 2024).

Glaucoma Drainage Devices (GDDs)

GDDs are also associated with a significant number of complications, with reported rates ranging from 29% to 41% in the first year (Gigante et al., 2024). Common complications across all GDD types include hypotony (especially with non-valved devices), a postoperative hypertensive phase (especially with valved devices), corneal endothelial cell loss, diplopia, strabismus, and device-related issues such as tube or plate exposure, migration, and obstruction (Budenz et al., 2011; Gupta & Jeria, 2022).

- **Valved (Ahmed) vs. Non-valved (Baerveldt) Implants:** The major RCTs directly comparing these devices have clarified their distinct complication profiles. The valved Ahmed Glaucoma Valve (AGV) is designed to mitigate early postoperative hypotony. However, it is frequently associated with a "hypertensive phase," an early-to-intermediate rise in IOP due to fibrous encapsulation of the plate, occurring in up to 51.7% of eyes in one study (Ozalp et al., 2021). The non-valved Baerveldt Glaucoma Implant (BGI) is associated with a higher risk of early hypotony and related complications but tends to achieve lower long-term IOP on fewer medications (Christakis et al., 2016).
- **Device-Specific Findings:** The PAUL Glaucoma Implant, a newer device, was found in a systematic review to have high rates of hyphema (10.0%) and numerical hypotony (9.7%). Notably, the rate of tube erosion was 5.0% overall but rose to 9.8% in prospective studies, a rate higher than historically seen with Ahmed or Baerveldt devices (Tan et al., 2025). The original Molteno implant, being non-valved, was also associated with a higher chance of hypotony, and postoperative hyphema was a known issue in cases of neovascular glaucoma (Gupta & Jeria, 2022).

Complication Profile of Minimally Invasive Glaucoma Surgery (MIGS)

As a class, MIGS procedures demonstrated a significantly better safety profile compared to traditional surgeries, with very low rates of severe, vision-threatening complications (Lavia et al., 2017). However, their complication profiles are distinct and related to their mechanism of action.

Trabecular Meshwork Bypass (iStent, Hydrus)

These devices, which are placed in Schlemm's canal, are among the safest glaucoma procedures. The most frequently reported adverse events are transient and generally self-resolving (Le & Vold, 2017).

- **Hyphema:** Microhyphema or transient hyphema is common, with rates reported between 3.5% and 6.25% (Le & Vold, 2017; Guedes et al., 2019).
- **IOP Spikes:** Transient postoperative IOP elevation is also relatively common, reported in 5.2% of iStent patients in one trial (Le & Vold, 2017).
- **Device-Related Issues:** Device malposition, obstruction by iris tissue, or formation of peripheral anterior synechiae (PAS) are specific risks. An analysis of the FDA MAUDE database for the Hydrus Microstent identified anterior synechiae in 10.8% of reports and device obstruction in 7.3% (Han, 2021). While rare, malposition can lead to chronic inflammation and Uveitis-Glaucoma-Hyphema (UGH) syndrome (Al-Aswad, 2020; Ahmed, 2024).

Subconjunctival Filtration (XEN Gel Stent)

The XEN Gel Stent, which shunts aqueous to the subconjunctival space, has a "hybrid" complication profile that shares features with both MIGS and trabeculectomy.

- **Hypotony and Related Complications:** The rate of hypotony maculopathy is reported between 1.9% and 4.6%, and choroidal detachment can occur in up to 15% of cases (Marques et al., 2024).
- **Device Occlusion:** Occlusion of the small (45 μ m) lumen is a primary mode of failure, with reported rates between 3.9% and 8.8% (Marques et al., 2024).
- **Bleb-Related Issues:** As a bleb-forming procedure, it carries risks of bleb leak (2.1%) and conjunctival erosion with device exposure (1.1%–2.3%) (Marques et al., 2024). A significant proportion of patients require postoperative bleb needling with antifibrotics to maintain

patency (Harvey, 2021).

Goniotomy and Canaloplasty (KDB, GATT, OMNI)

These procedures, which involve removing or bypassing the trabecular meshwork without leaving a permanent implant, have a very favorable safety profile.

- **Hyphema:** This is by far the most common complication. Rates of transient hyphema are significantly higher than with stenting procedures, reported in up to 35-36% of cases following KDB goniotomy (Salinas et al., 2018; Chen et al., 2025). However, this is often considered a sign of a patent outflow system and typically resolves spontaneously within the first week (Salinas et al., 2018).
- **IOP Spikes:** Transient IOP elevation is the second most common adverse event, reported in 11.6% of eyes in one study (Chen et al., 2025).
- **Severe Complications:** The rate of severe, vision-threatening complications with these procedures is exceptionally low. Studies report no cases of endophthalmitis, hypotony maculopathy, or other major issues (Salinas et al., 2018; Pfeiffer et al., 2018).

Synthesis of Comparative Evidence from Randomized Controlled Trials

The highest level of evidence comes from RCTs that directly compare the complication rates of different surgical procedures. The findings from these pivotal trials are summarized in **Table 3** and detailed below.

Table 3: Summary of Complication Rates from Pivotal Randomized Controlled Trials

Trial / Comparison	Complication	Group 1 (Rate %)	Group 2 (Rate %)	p-value
PTVT Study	Tube	Trabeculecto		

(5-Year)	(Baerveldt)	my + MMC		
	Early Postop Complications	19% (24/125)	34% (40/117)	0.013
	Late Postop Complications	22% (27/125)	27% (32/117)	0.37
	Serious Complications	2% (3/125)	8% (9/117)	0.11
	Cataract Progression	52% (65/125)	44% (52/117)	0.30
ABC Study (5-Year)	Ahmed GDD	Baerveldt GDD		
	Late Complications (Overall)	46.8%	56.3%	0.082
	Serious Complications	15.9%	24.7%	0.034

	Tube Occlusion	0.8%	5.7%	0.037
	Tube Erosion	1%	3%	0.04
	Persistent Diplopia	12%	12%	NS
AVB Study (3-Year)	Ahmed GDD	Baerveldt GDD		
	Overall Complications	52%	62%	0.12
	Hypotony-related Vision-threatening Complications	0%	6%	0.005
HORIZON Trial (5-Year)	Hydrus + Phaco	Phaco Alone		
	Subsequent Incisional	2.4%	6.2%	0.027

	Surgery			
	Endothelial Cell Loss (3-60 mos)	No significant difference	No significant difference	0.261
	Overall Adverse Events	No significant difference	No significant difference	NS
Dahan & Drusedau (2000)	Deep Sclerectomy	Trabeculectomy		
	Shallow/Flat AC	0%	7.7% (3/39)	<0.05 (inferred)
	Hypotony	0%	2.6% (1/39)	<0.05 (inferred)
	Internal Iris Incarceration	5.1% (2/39)	0%	<0.05 (inferred)

Abbreviations: AC, Anterior Chamber; GDD, Glaucoma Drainage Device; NS, Not Significant.

- **Primary Tube Versus Trabeculectomy (PTVT) Study:** This landmark trial compared a 350-mm² Baerveldt GDD to trabeculectomy with MMC as a *primary* surgical intervention. After 5

years, while failure rates were statistically similar (42% tube vs. 35% trabeculectomy), the complication profiles differed significantly in the early postoperative period. Trabeculectomy was associated with a significantly higher rate of early complications (34% vs. 19%), including hypotony, shallow anterior chamber, and wound leak. However, by 5 years, the rates of late complications and serious complications (defined as those requiring reoperation or causing 2 lines of vision loss) were not statistically different between the two groups (Gedde et al., 2022).

- **Ahmed vs. Baerveldt Studies (ABC and AVB):** These two major RCTs compared the most common valved (Ahmed) and non-valved (Baerveldt) GDDs in refractory glaucoma. The results were consistent across both trials. The Baerveldt implant achieved a lower mean IOP on fewer medications but at the cost of a significantly higher rate of hypotony-related vision-threatening complications (6% vs. 0% in AVB) and a higher overall rate of serious complications (24.7% vs. 15.9% in ABC) (Christakis et al., 2016; Budenz et al., 2015). The Ahmed implant had a higher rate of failure due to elevated IOP but a superior safety profile regarding hypotony (Christakis et al., 2016).
- **HORIZON Trial (Hydrus + Phaco vs. Phaco Alone):** This pivotal MIGS trial demonstrated the long-term safety and efficacy of trabecular bypass. Over 5 years, eyes receiving the Hydrus Microstent had a significantly lower risk of requiring subsequent, more invasive glaucoma surgery compared to those undergoing cataract surgery alone (2.4% vs. 6.2%). Crucially, there were no significant differences in long-term adverse events or the rate of corneal endothelial cell loss between the groups, confirming the excellent long-term safety profile of the implant (Samuelson et al., 2022).
- **Trabeculectomy vs. Deep Sclerectomy:** The multicenter RCT by Dahan & Drusedau (2000) showed that at 12 months, deep sclerectomy provided comparable IOP reduction to trabeculectomy but with significantly fewer hypotony-related complications. The trabeculectomy group experienced flat/shallow anterior chambers (7.7%) and hypotony (2.6%), whereas the deep sclerectomy group had none of these, though it did have cases of internal iris

incarceration (5.1%) (Dahan & Drusedau, 2000). This supports the classification of deep sclerectomy as a safer, non-penetrating alternative.

Table 4: Detailed Complication Comparison from the PTVT Study (5-Year Data)

Complication	Tube Group (n=125)	Trabeculectomy Group (n=117)	p-value
Any Early Complication (<1 mo)	24 (19%)	40 (34%)	0.013
Wound leak	0	4 (3%)	0.11
Hypotony maculopathy	0	3 (3%)	0.24
8-ball hyphema	0	1 (1%)	1.00
Any Late Complication (>1 mo)	27 (22%)	32 (27%)	0.37
Conjunctival cyst	1 (1%)	0	1.00

Plate exposure	1 (1%)	N/A	1.00
Tube retraction	1 (1%)	N/A	1.00
Persistent corneal edema	0	1 (1%)	1.00
Anterior migration of bleb	N/A	1 (1%)	1.00
Any Serious Complication	3 (2%)	9 (8%)	0.11
Requiring Reoperation	3 (2%)	9 (8%)	0.11
Causing Vision Loss (≥ 2 lines)	0	2 (2%)	0.51
Source: Gedde et al. (2022)			

Table 5: Detailed Late Complication Comparison from the ABC Study (5-Year Data)

Late Complication	Ahmed Group (n=143)	Baerveldt Group (n=133)	p-value
Any Late Complication	56 (46.8%)	67 (56.3%)	0.082
Persistent corneal edema	9 (11.9%)	9 (11.7%)	0.82
Tube-corneal touch	4 (3.5%)	4 (3.7%)	0.91
Corneal graft rejection	8 (7.1%)	8 (7.0%)	0.96
Tube erosion	3 (2.9%)	1 (1.0%)	0.33
Recurrent or persistent iritis	7 (6.2%)	6 (5.5%)	0.83
Phthisis bulbi	1 (0.8%)	6 (5.7%)	0.037
Retinal detachment	2 (1.6%)	2 (1.7%)	0.98

Any Serious Complication	17 (15.9%)	29 (24.7%)	0.034
Reoperation for Complications	16 (14.3%)	24 (19.5%)	0.109
Surgery for tube occlusion	1	7	-
Source: Budenz et al. (2015)			

Table 6: Incidence of Key Early Postoperative Complications (<1 month) by Surgical Category

Complication	Trabeculectomy	GDDs (Valved/Non-valved)	MIGS (Trabecular Bypass)	MIGS (Subconjunctival)	MIGS (Goniotomy)
Hypotony (IOP $\leq$ 5 mmHg)	High (up to 39%)	Moderate-High (Higher in non-valved)	Low/Rare	Moderate (1.9-4.6% maculopathy)	Very Low/Rare

Hyphema	Moderate	Moderate	Low-Moderate (3.5-6.3%)	Low	High (up to 36%)
IOP Spike	Moderate	High (Hypertensive Phase in valved)	Moderate (up to 5.2%)	Moderate	Moderate (up to 11.6%)
Shallow/Flat AC	High (up to 16%)	Moderate (Higher in non-valved)	Rare	Moderate (up to 4.5%)	Rare
Choroidal Effusion	High (up to 33%)	Moderate	Rare	Moderate (0-15%)	Rare

Table 7: Incidence of Key Late Postoperative (≥ 1 month) Complications by Surgical Category

Complication	Trabeculectomy	GDDs	MIGS (Implant-based)	MIGS (Implant-free)
Bleb-Related Infection	0.2 - 9% (Lifelong risk)	Low (unless tube exposed)	Low (XEN only)	None

Device/Tube Erosion	N/A	1 - 5%	Low (XEN: 1.1-2.3%)	N/A
Corneal Decompensation	Low (1.8%)	Moderate (10-20%)	Low (No long-term signal)	Very Low/Rare
Cataract Progression	High (up to 33%)	High (up to 26%)	Low (Similar to phaco alone)	Low
Diplopia/Strabismus	Low	Moderate (up to 12%)	Rare	None
Need for Reoperation (Failure)	High (35% at 5 yrs)	High (40-53% at 5 yrs)	Low (2.4% incisional surgery at 5 yrs for Hydrus)	Low-Moderate

DISCUSSION

This systematic review synthesizes the evidence on complications across the modern spectrum of glaucoma surgery, confirming a clear and clinically significant trade-off between procedural efficacy and safety. The analysis of pivotal RCTs and large cohort studies reveals distinct "complication profiles" for each class of surgery, which is a more clinically useful concept than a single, overarching complication rate. These findings have profound implications for surgical

selection, patient counseling, and the future direction of glaucoma care.

Principal Findings: A Comparative Synthesis of Complication Spectrums

The principal finding of this review is the confirmation of a hierarchical risk structure among glaucoma surgeries. Traditional incisional procedures, trabeculectomy and GDD implantation, occupy the highest tier of risk but also offer the most potent IOP reduction. The PTVT study provides the clearest evidence of this, showing that while trabeculectomy achieved a mean IOP in the low teens, it came at the cost of a significantly higher rate of early postoperative complications compared to a Baerveldt tube shunt (Gedde et al., 2022). The lifelong risk of devastating, bleb-related endophthalmitis remains the Achilles' heel of trabeculectomy (Al-Torbak et al., 2005).

Within the GDD category, a further risk stratification is evident. Non-valved implants like the Baerveldt offer superior long-term IOP control but expose patients to a significant risk of early, profound hypotony and its sequelae, as demonstrated conclusively in the ABC and AVB trials (Christakis et al., 2016; Budenz et al., 2015). Valved implants like the Ahmed GDD effectively mitigate this early hypotony risk but trade it for a high incidence of a delayed hypertensive phase and a greater likelihood of long-term failure from encapsulation (Christakis et al., 2016; Ozalp et al., 2021). This distinction is critical; while overall complication rates between the two GDD types may appear similar—around 60% in some studies—the nature and clinical implications of these complications are vastly different (Budenz et al., 2015). A surgeon and patient might more readily accept the risk of a transient, medically manageable hypertensive phase over the risk of refractory, vision-threatening hypotony. This underscores the importance of evaluating complication *profiles* rather than simple rates.

MIGS procedures, as a class, represent a fundamental shift towards safety. The 5-year data from the HORIZON trial is particularly compelling, showing that the addition of a Hydrus microstent not only reduced medication burden but also significantly decreased the need for

subsequent, higher-risk incisional surgery, all without any long-term safety penalty compared to cataract surgery alone (Samuelson et al., 2022). This demonstrates the potential of MIGS to alter the natural history of surgical intervention in glaucoma. The complication profile of most MIGS is dominated by transient events like hyphema and IOP spikes, which are manageable and rarely lead to long-term sequelae (Le & Vold, 2017).

Mechanistic Interpretation of Key Complications

Understanding the underlying pathophysiology of common complications is essential for their prevention and management.

- **Bleb-Related Pathophysiology:** The success or failure of trabeculectomy and subconjunctival MIGS (XEN) is dictated by the ocular wound healing response. An aggressive fibroproliferative process, involving the transformation of fibroblasts into myofibroblasts and subsequent collagen deposition, leads to the formation of a thick, impermeable "ring-of-steel" around the filtration site, causing bleb failure and IOP elevation (Liu, 2024). Conversely, the use of potent antimetabolites like MMC to suppress this response can lead to the formation of thin, avascular, and cystic blebs. These blebs are structurally weak, prone to leakage, and lack the normal immunological defenses of the conjunctiva, creating a direct portal for virulent bacteria like *Streptococcus* and *Haemophilus* to enter the eye, resulting in blebitis or endophthalmitis (Al-Torbak et al., 2005).
- **Device-Related Mechanical Issues:** Complications specific to implantable devices often have a mechanical basis. Tube erosion, a significant concern with GDDs and to a lesser extent with the XEN stent, occurs from the constant friction of the mobile conjunctiva and eyelid over the rigid underlying tube, leading to tissue breakdown (Tan et al., 2025; Marques et al., 2024). Device malposition, particularly with trabecular bypass stents, can lead to contact with the iris or ciliary body. This chronic mechanical chafing can disrupt the blood-aqueous barrier, leading to persistent inflammation, pigment dispersion, recurrent hyphema, and elevated IOP—the classic triad of UGH syndrome (Al-Aswad, 2020; Ahmed, 2024).

- **Hemodynamics and Aqueous Dynamics:** Hyphema, the most common complication of goniotomy and a frequent occurrence in other MIGS, results from the reflux of blood from Schlemm's canal into the anterior chamber when IOP is acutely lowered below episcleral venous pressure, or from direct trauma to angle vessels (Shah, 2023). Hypotony and its sequelae (choroidal effusion, suprachoroidal hemorrhage) are a direct result of excessive, uncontrolled aqueous outflow in the early postoperative period, a primary risk in non-valved GDDs and trabeculectomy before the filtering bleb has matured and offers some resistance to outflow (Kirwan et al., 2013).

The Efficacy-Safety Trade-Off: Clinical Implications for Surgical Selection

The evidence synthesized in this review provides a clear framework for surgical decision-making based on the efficacy-safety trade-off. The choice of procedure must be a highly individualized, shared decision that aligns the patient's specific clinical needs with the known risk profile of each option.

- **Advanced Disease:** For a patient with advanced glaucoma, rapidly progressing visual field loss, and a need for a very low target IOP (e.g., in the low teens), the superior efficacy of trabeculectomy or a Baerveldt GDD may be necessary to preserve remaining vision. In this context, the higher risk of complications is a justifiable trade-off, which must be discussed thoroughly with the patient (American Academy of Ophthalmology, 2020; Budenz et al., 2015). The PTVT study results support this, showing that both procedures can achieve these low pressures long-term (Gedde et al., 2022).
- **Mild-to-Moderate Disease:** For a patient with mild-to-moderate glaucoma who is intolerant of or non-adherent to multiple medications, and who is also undergoing cataract surgery, a trabecular bypass MIGS (iStent or Hydrus) represents an ideal choice. The goal in this scenario is not necessarily to achieve the lowest possible IOP, but rather to achieve a safe target IOP while significantly reducing or eliminating the burden of topical medications. The long-term safety demonstrated in the HORIZON trial makes this an exceptionally attractive option

(Samuelson et al., 2022). This highlights an important evolution in how surgical success is defined. Historically focused almost exclusively on the absolute IOP value, modern clinical practice and patient-centered outcomes now place enormous value on medication reduction, which improves quality of life, reduces ocular surface disease, and enhances long-term adherence (Clement et al., 2019).

- **Intermediate Disease and Specific Scenarios:** Procedures like the XEN Gel Stent or ab-interno canaloplasty occupy an intermediate space. XEN can provide more substantial IOP lowering than trabecular bypass MIGS but introduces bleb-related risks that require careful patient selection and more intensive postoperative management (Harvey, 2021). Canaloplasty and goniotomy offer a safe, implant-free approach that can be effective, particularly in patients with identifiable pathology in the trabecular meshwork (Salinas et al., 2018). For patients at high risk of hypotony, such as those with uveitic glaucoma, a valved Ahmed GDD may be preferable to a non-valved implant or trabeculectomy, despite its lower long-term efficacy (Budenz et al., 2015).

Strength and Limitations

A significant **strength** of this systematic review lies in its comprehensive and rigorous methodology. The review addresses a clinically vital research gap by synthesizing complication data across the entire spectrum of modern glaucoma surgeries, from traditional methods to a wide array of Minimally Invasive Glaucoma Surgery (MIGS) procedures. Its novelty is further enhanced by a specific focus on synthesizing high-quality, long-term evidence from pivotal head-to-head randomized controlled trials (RCTs), such as the PTVT, ABC, AVB, and HORIZON studies, which provide the most robust comparative data available. The adherence to PRISMA guidelines, a dual-reviewer screening and data extraction process, and the formal assessment of bias using validated tools like the Cochrane RoB 2 and ROBINS-I lend considerable credibility to the findings. This structured approach allows for a nuanced, comparative analysis that moves beyond simple complication rates to define distinct "complication profiles" for each surgical class, offering high

clinical utility for surgical planning and patient counseling.

Despite its robust design, the review acknowledges several important **limitations**, many of which are inherent to the existing body of literature. The most significant barrier, as explicitly stated, is the profound inconsistency in the definition and reporting of complications across the included studies. This heterogeneity, with one study noting 116 different names for complications and few formal definitions, makes direct statistical comparison and meta-analysis exceptionally difficult, necessitating a narrative synthesis of the data. Furthermore, the review includes observational studies alongside RCTs; these non-randomized studies are more susceptible to selection bias and confounding, although they provide valuable real-world data. Finally, even the highest-quality surgical trials are subject to an unavoidable risk of bias stemming from the impossibility of blinding surgeons and patients to the allocated intervention, a factor that was consistently identified in the methodological quality assessment.

Ultimately, this review provides a valuable and authoritative synthesis of the current evidence on glaucoma surgery complications. Its primary contribution is the clear, evidence-based articulation of the efficacy-safety trade-off, which is fundamental to modern glaucoma management. While the limitations imposed by the primary literature prevent a quantitative meta-analysis, the review successfully navigates this challenge by presenting a qualitative, yet systematic, comparison of complication profiles. The conclusions and recommendations are therefore well-supported by the available evidence, highlighting the need for standardized reporting in future research to enable even more powerful evidence synthesis. The study serves as a critical resource for clinicians, guiding nuanced, individualized surgical decision-making in a rapidly evolving field.

CONCLUSION AND RECOMMENDATIONS

Summary of Evidence

This systematic review confirms that the surgical management of glaucoma involves a diverse array of procedures with distinct and predictable complication profiles. A clear trade-off

exists between the magnitude of IOP reduction and the risk of adverse events. Traditional incisional surgeries, trabeculectomy and GDD implantation, provide the most potent and durable IOP lowering but are associated with a significant burden of potentially vision-threatening complications, both early (hypotony-related) and late (bleb infection, device erosion). Minimally invasive glaucoma surgery has fundamentally improved the safety of surgical intervention for glaucoma. MIGS procedures, particularly those that bypass the trabecular meshwork or perform goniotomy, have exceptionally low rates of severe complications and are primarily associated with transient, manageable events like hyphema. Subconjunctival MIGS devices occupy an intermediate risk profile. The evidence from major RCTs provides high-quality comparative data that solidifies this risk-benefit framework, guiding a more nuanced approach to surgical selection.

Recommendations for Clinical Practice

Based on the synthesized evidence, the following recommendations can be made for clinical practice:

1. **Individualize Surgical Selection:** The choice of glaucoma surgery should not be a one-size-fits-all decision. It must be a shared decision-making process that meticulously weighs the patient's disease severity, target IOP, glaucoma type, lens status, prior surgical history, and tolerance for risk against the known efficacy and complication profile of each surgical option.
2. **Embrace the Efficacy-Safety Spectrum:** For patients with advanced disease requiring very low IOPs, trabeculectomy and non-valved GDDs remain the most effective options, and the associated risks must be managed proactively. For patients with mild-to-moderate disease, especially in conjunction with cataract surgery, the superior safety profile of trabecular bypass MIGS or goniotomy should be strongly considered, with the primary goal often being medication reduction.
3. **Informed Consent and Patient Counseling:** Clinicians must provide comprehensive counseling on the specific risks associated with the recommended procedure. This includes discussing not only the incidence of common complications but also the potential for rare but

severe events and the lifelong nature of certain risks, such as bleb-related infection after trabeculectomy.

Recommendations for Future Research

To advance the field and improve evidence-based practice, future research should prioritize the following:

1. **Standardization of Complication Reporting:** There is an urgent need for the widespread adoption and implementation of standardized definitions and reporting templates for complications in glaucoma surgical trials, such as those proposed by the World Glaucoma Association (Stringa et al., 2020). This is the single most important step to enable high-quality meta-analyses in the future.
2. **Long-Term Comparative Trials:** While challenging and expensive, long-term (5-10 years) randomized trials comparing newer MIGS devices to each other and to a gold standard like trabeculectomy are necessary to fully understand their durability, long-term safety, and ultimate place in the treatment algorithm.
3. **Focus on Patient-Reported Outcomes:** Future studies should incorporate validated instruments to measure the impact of both the surgery and its complications on patient quality of life, visual function, and satisfaction. Understanding the patient experience is as critical as measuring the intraocular pressure.

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