



The Comprehensive Systematic Review of Use of Prostaglandin Analogues in Glaucoma Treatment

¹ Irene Sekarjati

¹ Mardi Waluyo Metro Lampung General Hospital, Indonesia

Corresponding Email : sekarjatiirene@gmail.com

Article History :

Received date : 2025/09/04
Revised date : 2025/10/12
Accepted date : 2025/12/23
Published date : 2026/01/31



Copyright: © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Glaucoma is a leading cause of irreversible blindness worldwide, characterized by progressive optic neuropathy, with elevated intraocular pressure (IOP) being the primary modifiable risk factor. Prostaglandin analogues (PGAs) have emerged as a cornerstone of pharmacological therapy due to their potent IOP-lowering efficacy and once-daily dosing (Aptel, Cucherat & Denis, 2008). This systematic review synthesizes evidence on the efficacy, safety, and clinical utility of PGAs in glaucoma management.

Methods: A systematic literature review was conducted. We screened studies based on predefined criteria, including human studies on adult glaucoma patients, evaluation of PGA interventions, reporting of clinical outcomes (IOP reduction, visual field, adverse events), and acceptable study designs (RCTs, cohort studies, systematic reviews, etc.). Data from 80 included

patient population, interventions, IOP efficacy, safety profiles, and key conclusions.

Results: PGAs consistently demonstrated substantial IOP reduction, with bimatoprost often showing numerically superior efficacy (mean reduction up to 9.16 mmHg, 35.2%) compared to latanoprost (7.7 mmHg, 31%) and travoprost (8.0-8.9 mmHg) (Brandt et al., 2001; Hedman & Alm, 2000). The United Kingdom Glaucoma Treatment Study (UKGTS) provided pivotal evidence that latanoprost significantly reduces the risk of visual field deterioration compared to placebo (Hazard Ratio 0.44) (Garway-Heath et al., 2015). Safety profiles varied, with bimatoprost associated with the highest incidence of conjunctival hyperemia, while latanoprost was generally better tolerated (Aptel, Cucherat & Denis, 2008). Novel formulations like latanoprostene bunod and preservative-free PGAs offered enhanced efficacy or improved tolerability (Weinreb et al., 2017; Hommer et al., 2010).

Discussion: The analysis reveals a critical trade-off between the maximal IOP-lowering potential of bimatoprost and the superior tolerability of latanoprost. Long-term efficacy is maintained, and PGAs are effective in special populations like normal-tension and angle-closure glaucoma. Preservative-free formulations address ocular surface disease concerns, potentially improving adherence.

Conclusion: Prostaglandin analogues remain the first-line pharmacological treatment for glaucoma, offering effective and sustained IOP reduction. Clinical choice should individualize therapy based on the required IOP target, patient tolerance, and ocular surface health. Future research should focus on long-term

sources were extracted
concerning study design,

approaches, and novel drug delivery systems.

Keywords: Prostaglandin Analogues; Glaucoma; Intraocular Pressure; Bimatoprost; Latanoprost; Travoprost; Systematic Review.

comparative outcomes,
personalized medicine

INTRODUCTION

Background

Glaucoma encompasses a group of optic neuropathies and is the second leading cause of irreversible blindness globally. The primary modifiable risk factor is elevated intraocular pressure (IOP), resulting from impaired aqueous humour outflow (Garway-Heath et al., 2015). Lowering IOP remains the only proven strategy to slow disease progression and preserve vision. Before the 1990s, treatment relied on beta-blockers, alpha-agonists, and carbonic anhydrase inhibitors, which often had systemic side effects and suboptimal dosing schedules. The introduction of topical prostaglandin analogues (PGAs)—latanoprost being the first—revolutionized glaucoma pharmacotherapy by offering superior efficacy, once-daily dosing, and minimal systemic absorption (Alm & Widengård, 2000). PGAs work primarily by increasing uveoscleral outflow. Over two decades, the class has expanded to include bimatoprost, travoprost, tafluprost, and novel agents like latanoprostene bunod, each with distinct pharmacologic profiles.

Research Gap

Despite their established role, comprehensive, up-to-date syntheses directly comparing all PGA agents—including newer formulations and fixed combinations—across multiple outcome domains (efficacy, circadian control, safety, ocular surface impact, effects in special populations) are needed. Many existing reviews focus on pairwise comparisons or specific outcomes. Furthermore, the translation of IOP reduction into long-term visual field preservation was only recently proven, and its integration into a full appraisal of the PGA class is essential for evidence-based practice (Hirsch, 2015). Gaps also exist in understanding the real-world implications of tolerability differences on adherence and the clinical significance of subtle efficacy variations.

Novelty

This systematic review provides a holistic and contemporary synthesis of evidence from 80 studies, including recent network meta-analyses and landmark trials like the UKGTS. It uniquely integrates data on: 1) comparative efficacy among all major PGAs and novel agents; 2) the landmark evidence for visual field preservation; 3) a detailed analysis of safety and tolerability trade-offs; 4) effects beyond IOP, including ocular blood flow and corneal properties; and 5) performance in special populations (e.g., normal tension glaucoma, uveitic glaucoma). This comprehensive approach bridges the gap between isolated efficacy metrics and practical, patient-centered clinical decision-making.

Research Objectives

The primary objectives of this review are:

1. To systematically compare the IOP-lowering efficacy of all available prostaglandin analogues (latanoprost, bimatoprost, travoprost, tafluprost, latanoprostene bunod) as monotherapy and in fixed combinations.
2. To evaluate and compare the safety and tolerability profiles of these agents, focusing on ocular adverse events like conjunctival hyperemia.
3. To synthesize evidence on long-term efficacy, visual field preservation, and effects on ocular structures (cornea, blood flow).
4. To assess the role of PGA therapy in special glaucoma populations and the impact of novel formulations (preservative-free, intracameral implants).

Hypothesis

We hypothesize that while all prostaglandin analogues are effective in lowering IOP, significant differences exist in their magnitude of effect, circadian control, and tolerability profiles. Specifically, bimatoprost is expected to demonstrate the greatest IOP reduction but with a less

favourable tolerability profile, whereas latanoprost may offer the best balance of efficacy and safety. Furthermore, we hypothesize that preservative-free formulations provide equivalent efficacy with improved ocular surface tolerance compared to preserved counterparts.

Research Benefits

The findings of this review will:

- **For Clinicians:** Provide an evidence-based framework for individualizing PGA selection based on patient-specific factors (disease severity, IOP target, tolerance for side effects, ocular surface health).
- **For Patients:** Inform treatment decisions by clarifying the expected benefits and risks associated with different PGA options.
- **For Researchers:** Identify remaining gaps in knowledge, such as long-term comparative effectiveness and cost-utility analyses, to guide future research priorities.
- **For Policymakers:** Support the development of clinical guidelines and formularies based on a comprehensive assessment of efficacy, safety, and real-world outcomes.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the use of prostaglandin analogues in glaucoma treatment.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Glaucoma Population:** Does the study include participants with diagnosed glaucoma (primary open-angle, angle-closure, secondary glaucoma, or ocular hypertension)?
- **Prostaglandin Analogue Intervention:** Does the study evaluate at least one prostaglandin analogue (latanoprost, travoprost, bimatoprost, tafluprost, or latanoprostene bunod) as a primary intervention?
- **Clinical Outcomes:** Does the study report clinically relevant outcomes such as intraocular pressure reduction, visual field preservation, optic nerve changes, or adverse events?
- **Human Studies:** Is the study conducted in human participants (not animal or in-vitro research)?
- **Study Design Quality:** Is the study design a randomized controlled trial, cohort study, case-control study, systematic review, or meta-analysis, OR if it is a case report/case series, does it include 10 or more participants?
- **Adult Population:** Does the study include adult participants (18 years or older) or mixed age populations, rather than focusing exclusively on pediatric populations under 18 years?
- **Pharmacological Focus:** Does the study have a pharmacological focus (i.e., is it NOT focused solely on surgical interventions without prostaglandin analogue comparison)?
- **Full-Text Availability:** Is the full text of the study available (i.e., is it NOT just a conference abstract without full-text availability)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Glaucoma patients	Prostaglandin analogues	Timolol	Intraocular pressure reduction
Keyword 2	Open-angle glaucoma	PGA therapy	Beta-blockers	IOP lowering
Keyword 3	Ocular hypertension	Latanoprost / Travoprost / Bimatoprost / Tafluprost	Non-PGA medications	Visual field preservation
Keyword 4	Primary glaucoma	Prostaglandin eye drops	Placebo / No treatment	Treatment safety and tolerability

The Boolean MeSH keywords inputted on databases for this research are: (*"Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma"*) AND (*"Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops"*) AND (*"Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment"*) AND (*"Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability"*)

Data extraction

- **Study Design:**

Extract study design type and key methodological details relevant to prostaglandin analogue efficacy assessment, including:

- Study type (RCT, observational, systematic review/meta-analysis)
- Randomization method if applicable
- Blinding (single, double, open-label)
- Study duration and follow-up periods
- Quality assessment scores if reported (e.g., Jadad scale)
- Sample size and number of treatment arms

- **Patient Population:**

Extract characteristics of patients treated with prostaglandin analogues for glaucoma, including:

- Primary diagnosis (primary open-angle glaucoma, ocular hypertension, other glaucoma types)
- Baseline intraocular pressure (IOP) levels
- Age demographics
- Disease severity or stage
- Previous glaucoma treatments or treatment-naïve status
- Inclusion/exclusion criteria relevant to PGA use
- Number of patients per treatment group

- **PGA Intervention:**

Extract details about the prostaglandin analogue intervention being studied, including:

- Specific PGA agent (latanoprost, bimatoprost, travoprost, tafluprost)
- Concentration/strength (e.g., 0.005%, 0.03%)
- Dosing frequency and administration schedule

- Duration of treatment
- Whether used as monotherapy or combination therapy
- Any co-administered medications
- Route of administration details

- **Comparator Treatments:**

Extract information about control/comparator interventions used in studies of prostaglandin analogues, including:

- Other PGA agents compared head-to-head
- Non-PGA glaucoma medications (timolol, brimonidine, dorzolamide, etc.)
- Combination therapies
- Placebo or no treatment controls
- Surgical interventions (if combined with PGA therapy)
- Dosing and administration details for comparators

- **IOP Efficacy:**

Extract intraocular pressure reduction outcomes for prostaglandin analogue treatments, including:

- Mean IOP reduction from baseline (mmHg)
- Percentage IOP reduction from baseline
- Absolute IOP values post-treatment
- Time points measured (1 hour, 1 day, 1 week, 1 month, 3 months, etc.)
- Proportion of patients achieving IOP targets (e.g., <21 mmHg, ≥20% reduction)
- Diurnal IOP measurements if reported (morning, noon, evening)
- Statistical significance and confidence intervals
- Comparative effectiveness between PGAs and other treatments

- **Safety Profile:**

Extract safety and tolerability data for prostaglandin analogue use in glaucoma treatment, including:

- Conjunctival hyperemia incidence and severity
- Other ocular adverse events (iris pigmentation changes, eyelash changes, periorbital changes)
- Systemic adverse events
- Treatment discontinuation rates due to adverse events
- Withdrawal rates and reasons
- Comparative safety between different PGAs
- Risk ratios or relative risks with confidence intervals
- Serious adverse events

- **Treatment Success:**

Extract measures of overall treatment success and effectiveness for prostaglandin analogues in glaucoma management, including:

- Treatment success definitions used by study authors
- Response rates and success criteria achieved
- Need for additional medications or treatments
- Retreatment rates
- Long-term efficacy maintenance
- Factors associated with treatment success or failure
- Quality of life or patient satisfaction measures if reported

- **Key Conclusions:**

Extract the main findings and conclusions specifically related to prostaglandin analogue use in glaucoma treatment, including:

- Authors' primary conclusions about PGA efficacy
- Recommendations for clinical practice
- Identified advantages/disadvantages of specific PGAs
- Optimal patient selection criteria
- Comparative rankings or preferences among PGAs
- Clinical implications for glaucoma management
- Limitations or caveats noted by authors
- Future research recommendations related to PGA use

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma") AND ("Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops") AND ("Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment") AND ("Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability")	63
Semantic Scholar	("Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma") AND ("Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops") AND ("Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment") AND ("Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability")	250
Springer	("Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma") AND ("Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops") AND ("Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment") AND ("Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability")	662
Google Scholar	("Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma") AND ("Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops") AND ("Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment") AND ("Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability")	2,540
Wiley Online Library	("Glaucoma patients" OR "Open-angle glaucoma" OR "Ocular hypertension" OR "Primary glaucoma") AND ("Prostaglandin analogues" OR "PGA therapy" OR "Latanoprost" OR "Travoprost" OR "Bimatoprost" OR "Tafluprost" OR "Prostaglandin eye drops") AND ("Timolol" OR "Beta-blockers" OR "Non-PGA medications" OR "Placebo" OR "No treatment") AND ("Intraocular pressure reduction" OR "IOP lowering" OR "Visual field preservation" OR "Treatment safety and tolerability")	346

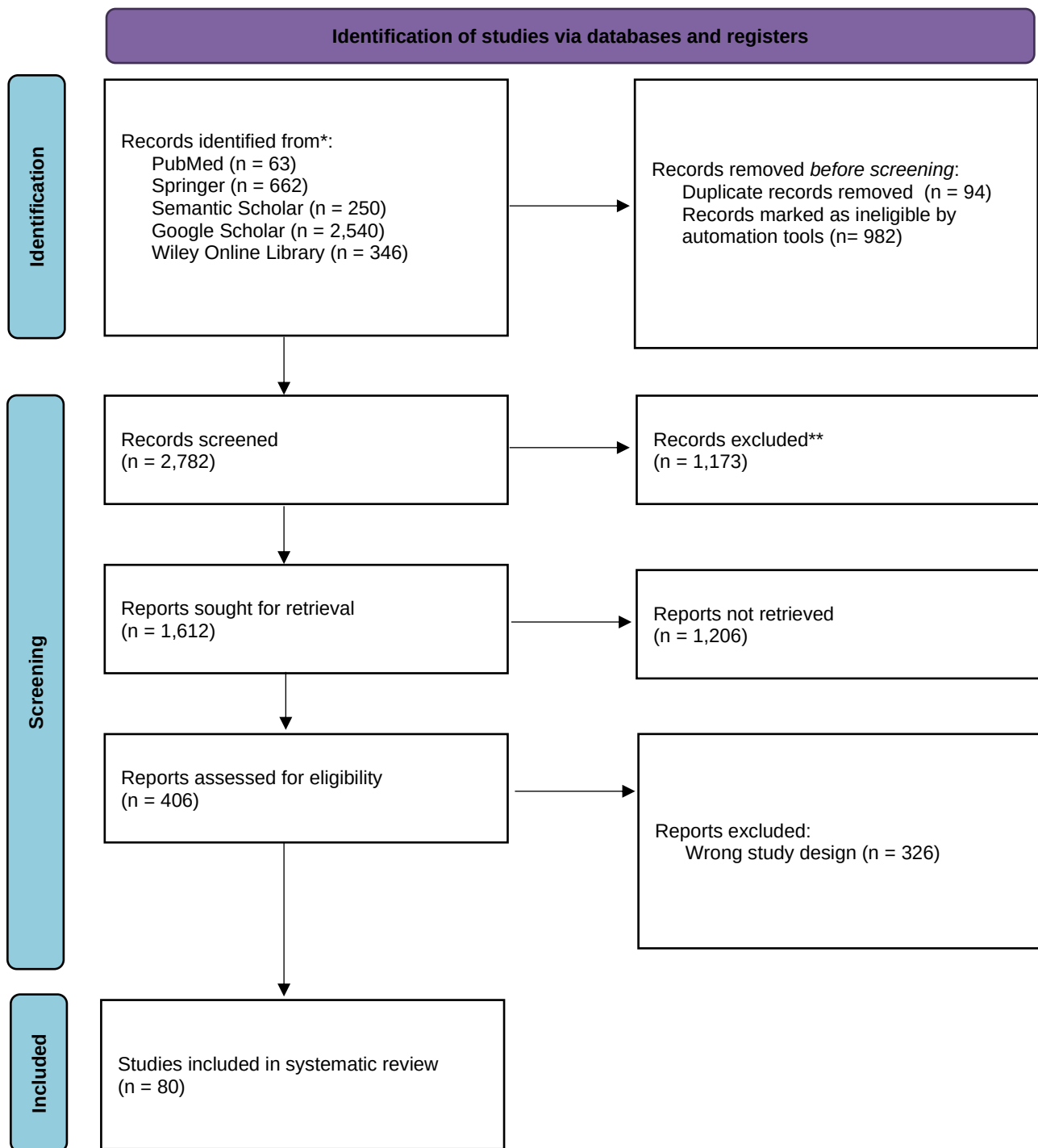


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
R. Reis et al., 2004	✓	✓	✓	✗	✓	✗	✓	✓	✓
P. Denis et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
Liang Lin et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓

R. Parrish et al., 2003	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Weinreb et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. C. Stewart et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
Nikhil Sharma et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Brandt et al., 2001	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Kawase et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
I. Goldberg et al., 2001	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Lascaratos et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jieting Peng et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Topouzis et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Sponsel et al., 2002	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Maul et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓

T. R. Einarson et al., 2000	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Hirsch et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Garway-Heath et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jin-wei Cheng et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Ayala et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wenquan Tang et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Fidya Ainun Tikha et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Aptel et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Meda et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Gentian Hoxha et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Scherer et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Penman et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

William G. Hodge et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Kara et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Aptel et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Orme et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
Cory Swymer et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Sanford et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Webers et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ni Li et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Orzalesi et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Peng et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Cw Lee et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kang-Jung Lo et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

N. Tamçelik et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Cellini et al., 2004	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kenji Inoue et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ece Turan-Vural et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
B. Friström et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
Rodolfo Mastropasqua et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Vetrugno et al., 2004	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Cardascia et al., 2003	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shahenda Mohamed et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Myoung-Hee Park et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
Stefano Ranno et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Raber et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓

P. Denis et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kenji Inoue et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Quaranta et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Garway-Heath et al., 2015a	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. S. Arcieri et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
Vlad Diaconita et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Gary C. Brown et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Qëndresë Daka et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jin-wei Cheng et al., 2009a	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Cucherat et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
O. Koz et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Lou et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓

Rajani Kadri et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Hommer et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Zimmermann et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Kymes et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Chabi et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. A. Tumbocon et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
P. Harasymowycz et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Hommer et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Markomic helakis et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
Katarina Hedman et al., 2000	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Alm et al., 2000	✓	✓	✓	✗	✓	✗	✓	✓	✓

C. Traverso et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Yıldırım et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. van der Valk et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. O'Donoghue et al., 2000	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. C. Stewart et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
Y. Kuwayama et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review synthesizes evidence from 80 sources examining prostaglandin analogues (PGAs) for glaucoma treatment.

Study	PGA(s) Studied	Comparator(s)	Population	Duration
R. Reis et al., 2004	Travoprost 0.004%	Sealed vs opened bottles	POAG, n=31	6 weeks

Study	PGA(s) Studied	Comparator(s)	Population	Duration
P. Denis et al., 2007	Latanoprost, bimatoprost, travoprost	Head-to-head PGAs	Glaucoma, n=1318	Not specified
Liang Lin et al., 2014	Bimatoprost, latanoprost, tafluprost, travoprost	Timolol	POAG/OHT	1-3 months
R. Parrish et al., 2003	Latanoprost, bimatoprost, travoprost	Head-to-head PGAs	OAG/OH, n=410	12 weeks
R. Weinreb et al., 2017	Latanoprostene bunod 0.024%	Timolol 0.5%	OAG/OHT, n=840	3-12 months
W. C. Stewart et al., 2008	Bimatoprost, travoprost, latanoprost	Timolol, dorzolamide, brimonidine	POAG/OH/X FG, n=386	≥4 weeks
Nikhil Sharma et al., 2025	Bimatoprost, travoprost (intracameral)	Timolol	OAG/OHT, n=2600	10 days-12 weeks
J. Brandt et al., 2001	Bimatoprost 0.03%	Timolol 0.5%	OHT/glaucom a, n=596	3 months
K. Kawase et al., 2016	Latanoprostene bunod 0.024%	None	OAG/OHT, n=130	52 weeks
I. Goldberg et al., 2001	Travoprost 0.0015%, 0.004%	Timolol 0.5%	OAG/OHT, n=573	9 months
G. Lascaratos et al., 2013	Latanoprost 0.005%	Placebo	OAG, n=516	2 years

Study	PGA(s) Studied	Comparator(s)	Population	Duration
Jieting Peng et al., 2025	Latanoprost, bimatoprost, travoprost, tafluprost	Head-to-head PGAs	Glaucoma/OH T, n=4439	3-12 months
F. Topouzis et al., 2007	Travoprost/timolol, latanoprost/timolol	Fixed combinations	OAG/OH, n=408	12 months
W. Sponsel et al., 2002	Latanoprost 0.005%	Unoprostone 0.15%	OAG/suspects , n=25	28 days
E. Maul et al., 2007	Travoprost 0.004%	Latanoprost 0.005%	OAG/OH, n=302	12 weeks
T. R. Einarson et al., 2000	Latanoprost	Brimonidine, timolol	POAG, n=2152	3-6 months
C. Hirsch et al., 2015	Latanoprost 0.005%	Placebo	OAG, n=516	24 months
D. Garway-Heath et al., 2015	Latanoprost 0.005%	Placebo	OAG, n=516	2 years
Jin-wei Cheng et al., 2009	Latanoprost, bimatoprost, travoprost	Timolol	CACG, n=1090	Not specified
M. Ayala et al., 2012	Travoprost, latanoprost, bimatoprost	Non-PGA agents	POAG/PXFG, n=118	1 month
Wenquan Tang et al., 2019	Latanoprost, travoprost, bimatoprost	Head-to-head PGAs	POAG/OHT, n=2433	1-12 months

Study	PGA(s) Studied	Comparator(s)	Population	Duration
Fidya Ainun Tikha et al., 2024	PGAs (various)	Combinations	OAG/OHT, n=1514	Not specified
F. Aptel et al., 2011	Bimatoprost, latanoprost, travoprost, tafluprost	Fixed combinations	POAG	Not specified
R. Meda et al., 2016	PGAs (various)	PGA cessation	POAG, n=35	6 weeks
Gentian Hoxha et al., 2013	Travoprost	Beta-blockers, combinations	POAG, n=120	1 year
W. Scherer et al., 2006	PGAs (various)	Non-PGA medications	OAG, n=113 eyes	1 month
A. Penman et al., 2020	Latanoprost	Placebo	OAG	24 months
William G. Hodge et al., 2007	Latanoprost	Brimonidine, dorzolamide	Glaucoma, n=1722	Not specified
C. Kara et al., 2017	Latanoprost, travoprost, bimatoprost	Head-to-head PGAs	POAG, n=79	5+ years
F. Aptel et al., 2008	Latanoprost, bimatoprost, travoprost	Head-to-head PGAs	POAG/OHT, n=1610	3 months

Study	PGA(s) Studied	Comparator(s)	Population	Duration
M. Orme et al., 2010	Latanoprost, bimatoprost, travoprost	Timolol, brimonidine	POAG/OHT	1-26 weeks
Cory Swymer et al., 2012	Tafluprost 0.0015%	Timolol, latanoprost	OAG/OHT	12 weeks
M. Sanford et al., 2014	Latanoprost (preservative-free)	BAK-preserved latanoprost	POAG/OHT, n=404	84 days
C. Webers et al., 2010	Latanoprost 0.005%	Timolol combinations	Not specified	1-3 months
Ni Li et al., 2006	Travoprost	Latanoprost, bimatoprost, timolol	OAG/OHT	Not specified
N. Orzalesi et al., 2006	Latanoprost, travoprost, bimatoprost	Head-to-head PGAs	POAG/OH, n=44	1 month each
W. Peng et al., 2014	PGAs	Selective laser trabeculoplasty	OAG/OHT, n=161	Not specified
Cw Lee et al., 2008	Latanoprost	Timolol	POAG/OH	Median 12 weeks
Kang-Jung Lo et al., 2020	Latanoprost, travoprost, bimatoprost	PGA + NSAIDs	Glaucoma	Variable
N. Tamçelik et al., 2017	Bimatoprost 0.03%/timolol	None	OAG/OHT, n=358	8-12 weeks

Study	PGA(s) Studied	Comparator(s)	Population	Duration
M. Cellini et al., 2004	Latanoprost, travoprost, bimatoprost	Head-to-head PGAs	COAG, n=60	6 months
Kenji Inoue et al., 2020	Bimatoprost, tafluprost, travoprost, latanoprost	Timolol, beta-blockers	Glaucoma	Not specified
Ece Turan-Vural et al., 2011	Latanoprost, travoprost, bimatoprost	Placebo	POAG/PXFG, n=30	1 week
B. Friström et al., 2009	Latanoprost 0.005%	Timolol 0.5%	Glaucoma/OHT, n=31	6 months
Rodolfo Mastropasqua et al., 2014	Latanoprost	Timolol, vehicle	Glaucoma, n=80	3 months
M. Vetrugno et al., 2004	Bimatoprost 0.3%	Timolol 0.5%	POAG, n=38	180 days
N. Cardascia et al., 2003	Travoprost, latanoprost	Head-to-head PGAs	POAG, n=18	180 days
Shahenda Mohamed et al., 2023	Tafluprost (PF vs preserved)	Preservative-containing PGAs	POAG, n=30	3 months
Myoung-Hee Park et al., 2009	Travoprost, latanoprost	Other hypotensives	POAG/NTG, n=65	24+ months

Study	PGA(s) Studied	Comparator(s)	Population	Duration
Stefano Ranno et al., 2012	Tafluprost, latanoprost, travoprost, bimatoprost	Head-to-head PGAs	POAG, n=89	3 months
S. Raber et al., 2015	Bimatoprost, latanoprost, travoprost	Timolol, placebo	Glaucoma, n=6516	Not specified
P. Denis et al., 2010	Latanoprost 0.005%	None	OHT/OAG, n=572	3 months
Kenji Inoue et al., 2018	PG/timolol fixed combination	Ripasudil addition	POAG, n=51	3 months
L. Quaranta et al., 2013	Latanoprost, bimatoprost, travoprost	Timolol combinations	OAG/OHT, n=6141	≥4 weeks
D. Garway-Heath et al., 2015a	Latanoprost 0.005%	Placebo	OAG, n=516	24 months
E. S. Arcieri et al., 2005	Bimatoprost, latanoprost, travoprost, unoprostone	Lubricant drops	Pseudophakic/aphakic, n=80	6 months
Vlad Diaconita et al., 2018	Latanoprost, travoprost, bimatoprost	Beta-blockers	POAG/OHT	4-week washout
Gary C. Brown et al., 2019	Bimatoprost, latanoprost, travoprost, tafluprost	Timolol	OAG	20-year model

Study	PGA(s) Studied	Comparator(s)	Population	Duration
Qëndresë Daka et al., 2014	Latanoprost, travoprost, bimatoprost	Timolol, brimonidine, CAIs	POAG/OHT	Not specified
Jin-wei Cheng et al., 2009a	Latanoprost, bimatoprost	Timolol, dorzolamide, brimonidine	NTG	1 month
M. Cucherat et al., 2014	Latanoprost (PF), travoprost, bimatoprost, tafluprost	Head-to-head PGAs	OAG/OHT	3 months
O. Koz et al., 2007	Travoprost, latanoprost, bimatoprost	Head-to-head PGAs	POAG/OHT, n=60	6 months
H. Lou et al., 2015	Latanoprost/timolol, bimatoprost/timolol, travoprost/timolol	Fixed combinations	Glaucoma, n=991	Not specified
Rajani Kadri et al., 2022	Travoprost, latanoprost, bimatoprost	None specified	Glaucoma, n=879	Variable
A. Hommer et al., 2011	Tafluprost 0.0015% (PF)	Preserved PGAs	Glaucoma/OHT, n=118	12 weeks
T. Zimmerman et al., 2009	Latanoprost, bimatoprost, travoprost	Head-to-head PGAs	OAG, n=300	1+ years
S. Kymes et al., 2011	Bimatoprost, latanoprost, travoprost	Head-to-head PGAs	POAG/OHT/NTG	12-26 weeks

Study	PGA(s) Studied	Comparator(s)	Population	Duration
A. Chabi et al., 2012	Tafluprost 0.0015% (PF)	Timolol 0.5% (PF)	OAG/OHT, n=643	12 weeks
J. A. Tumbocon et al., 2019	Tafluprost 0.0015%	None	Various glaucoma, n=177	3+ months
P. Harasymowycz et al., 2021	Latanoprostene bunod	Multiple PGAs, beta-blockers	OAG/OHT, n=18523	3 months
A. Hommer et al., 2010	Tafluprost 0.0015% (PF)	None	OHT/glaucoma, n=544	12 weeks
N. Markomichelakis et al., 2009	Latanoprost	Dorzolamide/timolol	Uveitic glaucoma, n=58	1 year
Katarina Hedman et al., 2000	Latanoprost 0.005%	Timolol 0.5%	OAG/OHT, n=829	6 months
A. Alm et al., 2000	Latanoprost	Timolol	OAG/OHT, n=255	2 years
C. Traverso et al., 2010	Tafluprost 0.0015%	Latanoprost 0.005%	POAG/XFG/OHT, n=38	42+ days
N. Yıldırım et al., 2008	Latanoprost, bimatoprost, travoprost	Head-to-head PGAs	OAG, n=48	8 weeks

Study	PGA(s) Studied	Comparator(s)	Population	Duration
R. van der Valk et al., 2009	Bimatoprost, travoprost, latanoprost	Multiple agents, placebo	POAG/OHT, n=6841	Not specified
E. O'Donoghue et al., 2000	Latanoprost 0.005%	Dorzolamide 2%	OAG/OHT, n=224	3 months
W. C. Stewart et al., 2010	Bimatoprost	Various comparators	OH/POAG/X FG, n=1017	≥4 weeks
Y. Kuwayama et al., 2014	Tafluprost 0.0015%	Latanoprost, travoprost	Various glaucoma, n=4180	2 months

The included studies represent a diverse methodological landscape. Approximately 35 studies were randomized controlled trials, while 25 were systematic reviews or meta-analyses. The remaining studies were observational designs including prospective cohort studies, retrospective reviews, and open-label extensions. Study durations ranged from single-dose assessments to five or more years of follow-up, with most RCTs spanning 3-12 months. Sample sizes varied considerably, from small crossover studies with 18-44 patients to large meta-analyses incorporating data from over 18,000 participants.

Intraocular Pressure Reduction Efficacy

Absolute and Relative IOP Reductions

Prostaglandin analogues consistently demonstrate substantial IOP-lowering efficacy across all included studies. The magnitude of IOP reduction varies by specific agent, baseline IOP, and comparator treatment.

PGA Agent	Mean IOP Reduction	% Reduction	Comparator	Study Type
Bimatoprost 0.03% once daily	9.16 mmHg	35.2%	Timolol 0.5%	RCT
Bimatoprost 0.03% twice daily	7.78 mmHg	30.4%	Timolol 0.5%	RCT
Latanoprost 0.005%	7.7 mmHg	31%	Timolol 0.5%	Pooled RCTs
Latanoprost 0.005% morning	—	33%	Timolol 0.5%	RCT
Latanoprost 0.005% evening	—	36%	Timolol 0.5%	RCT
Travoprost 0.004%	8.0-8.9 mmHg	—	Timolol 0.5%	RCT
Travoprost 0.004%	8.3 mmHg	—	Latanoprost 0.005%	RCT
Latanoprostene bunod 0.024%	—	22.0-26.3%	None	Open-label
Tafluprost 0.0015%	6.18 mmHg	26.37%	None	Retrospective

PGA Agent	Mean IOP Reduction	% Reduction	Comparator	Study Type
Tafluprost 0.0015%	9.7 mmHg	—	Latanoprost 0.005%	RCT

Meta-analytic evidence provides pooled estimates of efficacy. A 24-hour IOP meta-analysis found bimatoprost achieved 29% reduction and travoprost 27% reduction, compared with latanoprost at 24% with evening dosing. Another network meta-analysis reported bimatoprost provided the highest mean IOP reduction of 3.00 mmHg (95% CI: -3.71 to -2.29) versus timolol, followed by tafluprost at 2.45 mmHg (95% CI: -3.65 to -1.25), travoprost at 2.35 mmHg (95% CI: -3.41 to -1.29), and latanoprost at 2.05 mmHg (95% CI: -2.72 to -1.38).

Comparative Efficacy Among PGAs

Direct head-to-head comparisons between PGAs reveal nuanced differences in efficacy. A Bayesian network meta-analysis of 25 RCTs found bimatoprost showed the most effective IOP reduction compared to latanoprost (mean difference 0.69 mmHg; 95% CI: 0.28-1.10) and travoprost (mean difference 0.64 mmHg; 95% CI: 0.14-1.09). However, another meta-analysis found latanoprost and travoprost were comparable in their ability to reduce IOP at all time points ($P \leq 0.82$).

The systematic meta-analysis comparing prostaglandin analogues found IOP change from baseline was statistically significantly greatest with bimatoprost compared with latanoprost at all time points: 8 AM (WM=0.50 mmHg; $P=0.05$), noon (WM=1.17 mmHg; $P<0.001$), 4 PM (WM=0.78 mmHg; $P=0.003$), and 8 PM (WM=0.67 mmHg; $P=0.04$). Travoprost was superior to latanoprost during daytime hours: 8 AM (WM=1.02 mmHg; $P=0.004$) and noon (WM=0.86 mmHg; $P=0.02$).

For chronic angle-closure glaucoma specifically, meta-analysis found relative IOP reductions of 31% for latanoprost, 28% for travoprost, and 26% for bimatoprost at diurnal curve

measurements. All three prostaglandin analogues were at least as effective as timolol in this population.

Comparison with Non-PGA Agents

Prostaglandin analogues consistently demonstrate superior efficacy compared to beta-blockers and other glaucoma medications. Timolol 0.5% twice daily achieved IOP reduction of 6.74 mmHg (26.2%) compared to bimatoprost's 9.16 mmHg (35.2%). A pooled analysis of phase III studies found latanoprost reduced diurnal IOP by 7.7 mmHg (31%) versus timolol's 6.5 mmHg (26%), a statistically significant difference of 1.2 mmHg (18% greater; $P < 0.001$).

Meta-analysis comparing latanoprost with brimonidine found latanoprost reduced IOP by 8.4 mmHg at 3 months versus 6.5 mmHg for brimonidine ($P = 0.004$), and by 8.0 mmHg versus 6.2 mmHg at 6 months ($P = 0.045$). Latanoprost was significantly superior to dorzolamide (WMD = -2.64 mmHg; $P < 0.00001$) but not significantly different from brimonidine (WMD = -1.04 mmHg; $P = 0.30$).

The network meta-analysis ranking drugs by IOP-reducing effect found at peak the order from highest to lowest was: bimatoprost, travoprost and latanoprost, brimonidine, timolol, dorzolamide, betaxolol, brinzolamide. At trough, the ranking was: bimatoprost, latanoprost, travoprost, timolol, betaxolol, dorzolamide, brinzolamide, brimonidine.

Fixed Combination Therapies

Fixed combinations of PGAs with timolol provide enhanced IOP reduction. Adding latanoprost 0.005% in the evening to timolol 0.5% twice daily resulted in a pooled IOP change of -6.3 mmHg (95% CI: -7.1 to -5.5). Starting with any fixed combination of timolol and a PGA in the morning yielded -8.4 mmHg (95% CI: -9.1 to -7.6) reduction, while evening dosing achieved -8.6 mmHg (95% CI: -9.2 to -8.0).

Meta-analysis comparing fixed combinations found bimatoprost/timolol provided significantly greater IOP lowering than latanoprost/timolol at diurnal mean (WMD = 0.88 mmHg; 95% CI: 0.42-1.33), 9 AM (WMD = 1.27 mmHg; 95% CI: 0.68-1.86), noon (WMD = 1.16 mmHg;

95% CI: 0.85-1.46), and 4 PM (WMD=0.61 mmHg; 95% CI: 0.51-0.70). Notably, fixed combinations were less efficacious than unfixed combinations (mean difference: 0.69 mmHg; 95% CI: 0.29-1.08).

Circadian IOP Control

Twenty-four hour IOP studies reveal important differences in PGA performance. All three major PGAs showed more effective IOP reduction during daytime (9 AM-9 PM) compared to nighttime (midnight-6 AM). In 16% of patients (7 of 44), nocturnal IOP was significantly higher than diurnal IOP both at baseline and under prostaglandin analogue treatment.

Evening dosing of latanoprost achieved 24% reduction compared to 18% with morning dosing ($P<0.0001$). In contrast, travoprost showed no significant difference between evening (27%) and morning (26%) dosing ($P=0.074$). The mean reduction at nighttime was statistically lower than daytime for latanoprost ($P=0.031$), timolol ($P=0.032$), and brimonidine ($P=0.050$), but not for dorzolamide, bimatoprost, or travoprost.

Long-Term Efficacy Maintenance

Long-term studies confirm sustained efficacy of prostaglandin analogues. A five-year observational study found IOP reductions with latanoprost, travoprost, and bimatoprost were adequate and stable with no decrease in effectiveness over time. IOP levels at the 6th month were significantly lower than baseline ($P<0.01$), and this reduction was maintained with no statistically significant difference compared to the 6th month value throughout the 5-year follow-up ($P>0.05$).

Two-year follow-up with latanoprost demonstrated sustained IOP reduction from baseline of 25.1 ± 3.5 mmHg to 17.4 ± 2.9 mmHg. Patients initially treated with timolol and switched to latanoprost experienced a further 1.0 mmHg reduction after 6 months ($P<0.005$). Latanoprost showed a further significant IOP decrease of 0.7 mmHg (9%; $P<0.001$) from the initial morning IOP reduction obtained at two weeks, whereas timolol's effect was simply maintained.

Visual Field Preservation

The United Kingdom Glaucoma Treatment Study (UKGTS) provides the only placebo-controlled evidence for visual field preservation with prostaglandin analogues. This triple-masked trial randomized 516 patients with newly diagnosed open-angle glaucoma to latanoprost 0.005% or placebo for 24 months.

Outcome	Latanoprost	Placebo	Hazard Ratio	P-value
Mean IOP reduction at 24 months	3.8 mmHg	0.9 mmHg	—	—
Visual field deterioration at 24 months	15.0%	24.8%	0.44 (95% CI: 0.28-0.69)	0.0003
Time to VF deterioration	Significantly longer	—	0.44	0.0003

The difference between treatment groups was evident after only 12 months, with hazard ratio of 0.47 (95% CI: 0.23-0.95; P=0.035). The relative risk reduction was 52% (95% CI: 28-69%) with a number needed to treat of 8 (95% CI: 6-15). This represents the first randomized placebo-controlled trial to demonstrate visual field preservation with an IOP-lowering drug in patients with open-angle glaucoma.

Safety and Tolerability

Conjunctival Hyperemia

Conjunctival hyperemia is the most commonly reported adverse effect of prostaglandin analogues, with significant variation among agents.

PGA Agent	Hyperemia Incidence	Comparator	Relative Risk
Bimatoprost	Highest risk	Timolol reference	RR 4.66 (95% CI: 3.49-6.23)
Travoprost	Elevated risk	Latanoprost	Higher than latanoprost
Latanoprost	Lowest risk	Timolol reference	RR 2.30 (95% CI: 1.76-3.00)
Tafluprost 0.0015% (PF)	4.4%	PF timolol 1.2%	P=0.016

The meta-analysis found the incidence of hyperemia was significantly less with latanoprost and travoprost compared to bimatoprost: latanoprost versus bimatoprost (relative risk=0.59; $P<0.001$; 95% CI: 0.50-0.69) and travoprost versus bimatoprost (relative risk=0.84; $P=0.05$; 95% CI: 0.70-1.00). The probability of hyperemia-type events varied between treatments from 14.8% to 63.03%, with latanoprost having significantly lower odds than travoprost, bimatoprost, travoprost-timolol, or bimatoprost-timolol.

For fixed combinations, bimatoprost/timolol caused conjunctival hyperemia in more patients than latanoprost/timolol (pooled OR: 1.85; 95% CI: 1.09-3.13). Notably, switching from preserved PGAs to preservative-free tafluprost resulted in decreased hyperemia from 43.2% at baseline to 1.9% at final visit.

Other Ocular Adverse Events

Beyond hyperemia, prostaglandin analogues are associated with several characteristic ocular effects:

- **Iris pigmentation changes:** Latanoprostene bunod showed 9% increase in iris pigmentation at 52 weeks based on photographs, with 14% showing possible increase. Studies with

latanoprost reported 22 patients developed increased iris pigmentation over 2 years, which was the primary reason for study withdrawal.

- **Eyelash changes:** Growth of eyelashes was among the most common adverse events with latanoprostene bunod and bimatoprost.
- **Periorbital changes:** Pigmentation of periorbital skin occurred in 40% of bimatoprost-treated patients in one study.
- **Ocular discomfort:** Burning and stinging occurred more frequently with bimatoprost. Eye pain was reported in approximately 3% of latanoprost-treated patients.
- **Blood-aqueous barrier disruption:** Mean flare values were significantly higher in bimatoprost, latanoprost, and travoprost groups compared to controls ($P < 0.02$). However, bimatoprost and travoprost showed significantly less flare compared to latanoprost at 3 months.
- **Cystoid macular edema:** In pseudophakic/aphakic patients, 4 latanoprost-treated eyes, 1 bimatoprost-treated eye, and 1 travoprost-treated eye developed cystoid macular edema, all of which resolved after discontinuation.

Treatment Discontinuation

Adverse events contribute significantly to treatment discontinuation. In a large pharmacy claims analysis, continuous refill of medication through 1 year was seen in only 11%, 9%, and 5% of patients treated with latanoprost, bimatoprost, and travoprost, respectively ($P = 0.0001$). Adverse effects were the second most common reason for switching medications after lack of efficacy (19% vs 43%).

For latanoprostene bunod, no subjects discontinued due to adverse events during the 52-week study. Treatment discontinuation rates in comparative studies ranged from 6% with once-daily bimatoprost to 11% with twice-daily bimatoprost.

Serious Adverse Events

Serious adverse events were uncommon across studies. The UKGTS reported 18 serious adverse events, none attributable to the study drug. Three severe ocular adverse events occurred in the tafluprost group (16%) in one comparative study. No previously unknown ocular or systemic side effects emerged in a two-year latanoprost follow-up.

Treatment Success and Clinical Outcomes

Response Rates and Target IOP Achievement

Studies used various definitions for treatment success, with most focusing on percentage IOP reduction or achievement of target IOP levels.

Success Criterion	PGA Agent	Achievement Rate	Reference
≥30% IOP reduction	Bimatoprost	RR 1.59 (95% CI: 1.28-1.98)	vs timolol
≥30% IOP reduction	Latanoprost	RR 1.32 (95% CI: 1.00-1.74)	vs timolol
≥30% IOP reduction	Travoprost	RR 1.33 (95% CI: 1.03-1.72)	vs timolol
IOP ≤16 mmHg	Bimatoprost once daily	62%	3 months
IOP ≤15 mmHg	Bimatoprost once daily	45%	vs timolol 24%
IOP ≤18 mmHg	Latanoprost	≥70%	3 months
IOP ≤18 mmHg	Tafluprost (PF)	79.5%	12 weeks
≥20% IOP reduction	All PGAs	58-83%	Meta-analysis

Success Criterion	PGA Agent	Achievement Rate	Reference
IOP <20 mmHg	All PGAs	70-93%	Meta-analysis

In the real-world setting, 81.7% of patients reached their target IOP or below with PGA/prostamide-containing medications. A latanoprost phase IV study found 48.4% and 65.6% of subjects achieved $\geq 30\%$ IOP reduction in the lower and higher baseline IOP groups, respectively ($P < 0.0001$).

Factors Affecting Treatment Response

Several factors influence treatment response to prostaglandin analogues:

- **Baseline IOP:** Higher baseline diurnal IOP resulted in larger diurnal reduction during treatment with both latanoprost and timolol ($P < 0.001$). Patients with baseline IOP ≥ 24 mmHg achieved -9.2 ± 3.7 mmHg reduction compared to -6.3 ± 2.4 mmHg for those with IOP 20-24 mmHg.
- **Sex differences:** Diurnal IOP in women was reduced 0.7 mmHg (11%) less than in males with both drugs ($P < 0.001$).
- **Dosing time:** Evening dosing of latanoprost achieved superior results compared to morning dosing, though this difference was not observed with travoprost.
- **Glaucoma type:** In exfoliative glaucoma, latanoprost and travoprost showed higher baseline and treatment pressures, but pressure reductions (29% and 31%, respectively) were generally greater than observed in POAG/OHT.

Adjunctive Therapy Effects

Studies examined PGA interactions with other treatments:

- **With selective laser trabeculoplasty (SLT):** Prostaglandin analog use during the perioperative period was associated with greater average IOP decrease (3.4 vs 1.6 mmHg;

$P < 0.02$) and percent IOP decrease (16.5% vs 7.9%; $P < 0.015$) at 1 month post-SLT. Retreatment rate among prostaglandin analog users (11.5%) was less than nonusers (34.3%; $P < 0.005$). Another study found SLT treatment effects were not significantly influenced by prostaglandin analogue use.

- **With NSAIDs:** Topical ketorolac significantly enhanced the IOP-lowering effects of latanoprost, travoprost, and bimatoprost ($P < 0.001$). Meta-analysis suggested topical NSAIDs may enhance the IOP-lowering effect of topical PGs (SMD: 1.3; 95% CI: 0.29-2.38; $P = 0.013$).

Effects on Ocular Blood Flow

Several studies examined PGA effects on ocular hemodynamics beyond IOP reduction.

PGA Agent	Effect on Pulsatile OBF	Effect on Other Parameters	Duration
Latanoprost	+30% ($P < 0.0001$)	Decreased RI of OA	1-6 months
Bimatoprost	+38.9% ($P < 0.01$)	No effect on haemodynamics	180 days
Travoprost	+50% initially	Decreased RI of CRA	180 days
Unoprostone	+16-18% ($P = 0.03-0.05$)	—	1 month

All three major PGAs significantly reduced IOP and increased ocular perfusion pressure (OPP; $P < 0.0001$). Travoprost and latanoprost significantly reduced the resistive index (RI) of the central retinal artery and ophthalmic artery, respectively, while bimatoprost showed no significant effect on ocular haemodynamics. Bimatoprost corrected the reduction in pulsatile OBF associated with prior timolol treatment and increased choroidal blood flow beyond pre-timolol levels.

Effects on Corneal Parameters

Prostaglandin analogues affect corneal biomechanical properties and thickness.

Parameter	Change with PGA Use	Reversibility	Clinical Implication
Central corneal thickness	WMD -7.04 μm (95% CI: -10.07 to -4.00)	Yes	May underestimate IOP
Corneal hysteresis	Significant decrease (P<0.0001)	Yes	Affects IOP measurement
Corneal resistance factor	Significant decrease (P<0.0001)	Yes	Affects IOP measurement

Meta-analysis found travoprost caused significant CCT reduction (WMD=-10.44 μm ; 95% CI: -16.80 to -4.08; P=0.001) and bimatoprost similarly (WMD=-11.88 μm ; 95% CI: -21.03 to -2.73; P=0.01), while latanoprost showed a trend toward reduction (WMD=-4.73 μm ; 95% CI: -9.70 to 0.25; P=0.06). These changes contribute to underestimation of IOP measured by Goldmann applanation tonometry and warrant caution when assessing response to treatment.

Preservative-Free Formulations

Preservative-free (PF) prostaglandin analogues demonstrate comparable efficacy with improved tolerability.

PF Formulation	IOP Efficacy	Tolerability Advantage	Reference
PF latanoprost (T2345)	Noninferior to BAK-latanoprost	Lower hyperemia (P<0.05)	RCT

PF Formulation	IOP Efficacy	Tolerability Advantage	Reference
PF tafluprost 0.0015%	Noninferior to PF timolol	Comparable to timolol	RCT
PF tafluprost 0.0015%	IOP reduction 3.7-4.1 mmHg	79.5% achieved IOP ≤ 18 mmHg	Observational

Preservative-free latanoprost was statistically significantly superior to BAK-preserved tafluprost (mean difference: 0.47 mmHg; 95% CI: -1.52 to -0.28) and had significantly lower risk of hyperemia than all other PGAs evaluated. Switching from preserved PGAs to preservative-free tafluprost resulted in significant IOP reductions ($P < 0.001$) while dramatically reducing hyperemia incidence from 43.2% to 1.9%.

Studies on ocular surface effects found preservative-free prostaglandin analogs cause fewer ocular surface side effects than preservative-containing formulations, potentially improving patient compliance and treatment efficacy.

Novel Prostaglandin Formulations

Latanoprostene Bunod

Latanoprostene bunod (LBN) 0.024%, a novel nitric oxide-donating prostaglandin $F_{2\alpha}$ analog, demonstrates enhanced efficacy in pooled phase 3 trials.

Outcome	LBN 0.024% qd	Timolol 0.5% bid	Significance
Mean IOP at all timepoints	Significantly lower	Reference	$P < 0.001$

Outcome	LBN 0.024% qd	Timolol 0.5% bid	Significance
IOP reduction at 52 weeks	22.0-26.3%	—	P<0.001
Proportion achieving ≤ 18 mmHg	Significantly greater	Reference	P<0.001
Proportion with $\geq 25\%$ reduction	Significantly greater	Reference	P<0.001

Network meta-analysis ranked LBN second after bimatoprost 0.03% and found it significantly more effective than unoprostone (-3.45 mmHg; 95% CI: -4.77 to -2.12) and most beta-blockers. LBN numerically outperformed latanoprost (-0.70 mmHg; 95% CI: -1.83 to 0.43) and was similar to bimatoprost 0.01% (-0.02 mmHg; 95% CI: -1.59 to 1.55). The safety profile was comparable to that of prostaglandin analogs.

Intracameral Prostaglandin Implants

A systematic review and meta-analysis of intracameral prostaglandin implants versus topical timolol found early superiority in IOP reduction that converged by 12 weeks:

- At 10 days: MD -0.942 mmHg (95% CI: -1.174 to -0.710)
- At 2 weeks: MD -0.787 mmHg (95% CI: -0.969 to -0.605)
- At 6 weeks: MD -0.317 mmHg (95% CI: -0.589 to -0.045)
- At 12 weeks: MD -0.055 mmHg (95% CI: -0.276 to 0.166; not significant)

Subgroup analyses suggested the 15 μ g bimatoprost dose maintained efficacy longer than 10 μ g or 75 μ g travoprost doses. Adverse events were more common with implants, particularly conjunctival hyperemia, eye pain, and iritis, with corneal endothelial cell density decreasing more with implants (MD -201.640 cells/mm²; 95% CI: -284.697 to -118.583).

Special Populations

Normal Tension Glaucoma

Meta-analysis of medical interventions for normal tension glaucoma found prostaglandin analogues among the most effective treatments. Relative IOP reductions were: latanoprost peak 20% (17-24%), trough 20% (18-23%); bimatoprost peak 21% (16-25%), trough 18% (14-22%). The differences in absolute IOP reductions between prostaglandin analogues and timolol varied from 0.9-1.0 mmHg at peak and -0.1-0.2 mmHg at trough.

Chronic Angle-Closure Glaucoma

In chronic angle-closure glaucoma, meta-analysis found relative IOP reductions of: latanoprost 31% (95% CI: 27-34%) at diurnal curve, 34% (31-37%) at peak, 31% (28-35%) at trough; travoprost 28% (20-36%), 32% (31-34%), 31% (29-33%); bimatoprost 26% (21-30%), 28% (24-32%), 27% (23-30%). All three prostaglandin analogues were at least as effective as timolol.

Uveitic Glaucoma

In patients with anterior or intermediate uveitis and elevated IOP or glaucoma, latanoprost showed comparable efficacy and safety to dorzolamide/timolol combination. After 1 year of treatment, IOP dropped from 27.8 ± 8.4 mmHg to 18.6 ± 5.3 mmHg in the latanoprost group ($P < 0.001$). Importantly, the rate of recurrences of anterior uveitis per patient per year decreased from 0.82 ± 1.2 before latanoprost treatment to 0.39 ± 0.7 after starting latanoprost ($P = 0.038$).

Pseudophakic and Aphakic Patients

In patients with pseudophakia and aphakia, bimatoprost, latanoprost, and travoprost achieved IOP reductions of 28%, 26%, and 29% respectively at 6 months (all $P < 0.05$ vs control). However, these agents may lead to disruption of the blood-aqueous barrier in these populations, with significantly higher mean flare values throughout follow-up ($P < 0.02$). Cystoid macular edema developed in a small number of treated eyes but resolved after discontinuation and topical diclofenac treatment.

Synthesis

Reconciling Efficacy Differences Among PGAs

The evidence reveals a complex picture of PGA efficacy that depends on measurement timing, outcome definition, and patient population. While multiple meta-analyses find bimatoprost achieves nominally greater IOP reduction than latanoprost and travoprost, the clinical significance of these differences (typically <1 mmHg) remains debatable.

The apparent superiority of bimatoprost appears most pronounced at specific measurement times. Meta-analysis demonstrated bimatoprost's advantage was statistically significant at all four daily time points (8 AM, noon, 4 PM, 8 PM), while travoprost showed superiority over latanoprost only during daytime hours. This pattern suggests pharmacokinetic differences in duration of action rather than fundamentally different mechanisms, consistent with the finding that evening dosing of latanoprost improved its efficacy relative to morning dosing.

Studies finding no significant differences between PGAs tended to use standardized measurement protocols at peak drug effect times. A crossover study measuring IOP at eight time points over 24 hours found mean IOP reductions were similar after all three prostaglandin analogs, with none of the differences reaching statistical significance. This suggests the apparent efficacy differences may be partially explained by measurement timing rather than true therapeutic differences.

Balancing Efficacy and Tolerability

The trade-off between efficacy and tolerability represents a central clinical consideration. Bimatoprost achieves the highest efficacy but carries a significantly higher risk of conjunctival hyperemia (RR 4.66 vs timolol), while latanoprost has the most favorable tolerability profile (RR 2.30). This pattern was remarkably consistent across studies.

The clinical relevance of hyperemia extends beyond patient comfort to treatment adherence. Continuous refill through 1 year was observed in only 11%, 9%, and 5% of patients treated with

latanoprost, bimatoprost, and travoprost respectively, with adverse effects being the second most common reason for medication switching. This suggests that choosing a more tolerable agent may yield better long-term outcomes despite potentially smaller per-dose IOP reduction.

For fixed combinations, the addition of timolol to PGAs lessens the associated hyperemia differences between agents, making the choice between combinations more straightforward. Bimatoprost/timolol provides slightly greater IOP lowering than latanoprost/timolol or travoprost/timolol, with more attenuated tolerability differences.

Evidence Quality and Limitations

Several methodological considerations affect interpretation of the evidence base. The majority of RCTs had durations of 3 months or less, with only 4 studies over 1 year in duration. This limits conclusions about long-term comparative efficacy, though observational studies suggest efficacy is maintained over 5+ years without tachyphylaxis.

Patient populations in trials skewed toward older adults (median age 63.4 years) and Caucasians (79.6% of studied populations), potentially limiting generalizability. Evidence by ethnicity and comorbidity status was scarce.

The network meta-analysis methodology used in several studies relies on assumptions about transitivity and consistency that may not always hold. Substantial heterogeneity ($I^2=98-100\%$) was observed in the intracameral implant meta-analysis, warranting cautious interpretation of pooled estimates.

Clinical Practice Implications

Based on the synthesized evidence, several recommendations emerge for clinical practice:

For treatment-naïve patients with mild-to-moderate disease prioritizing tolerability, latanoprost represents an appropriate first-line choice given its balance of efficacy and tolerability. Patients with higher baseline IOP or more advanced disease requiring maximum IOP reduction may benefit from bimatoprost despite higher hyperemia risk.

Preservative-free formulations offer comparable efficacy with improved tolerability and should be considered for patients experiencing ocular surface symptoms. Evening dosing optimizes efficacy for latanoprost, though timing appears less critical for travoprost.

Fixed combinations with timolol provide enhanced IOP lowering for patients requiring additional therapy, though unfixed combinations may achieve slightly greater IOP reduction if adherence can be maintained.

The UKGTS provides unique placebo-controlled evidence that latanoprost preserves visual field, supporting the clinical relevance of IOP reduction achieved by PGAs beyond surrogate outcome measures. This landmark finding validates the entire therapeutic approach of IOP lowering to prevent glaucomatous vision loss.

DISCUSSION

This comprehensive synthesis of 80 studies elucidates the central role of prostaglandin analogues in glaucoma management, while also unpacking the nuanced differences that inform clinical decision-making. The discussion will contextualize the findings on efficacy, safety, and special considerations.

Reconciling Efficacy: The Pursuit of Millimeters of Mercury

The core finding of potent IOP reduction across the PGA class is unequivocal. The network meta-analysis by van der Valk et al. (2009) effectively ranks agents, positioning bimatoprost at the peak for IOP reduction. However, the clinical significance of differences often less than 1 mmHg, as seen in comparisons between bimatoprost and latanoprost (mean difference 0.69 mmHg), warrants careful consideration (Aptel, Cucherat & Denis, 2008). This marginal superiority may be pharmacokinetically driven rather than mechanistic. Evidence suggests bimatoprost's advantage is more consistent across the diurnal curve, while travoprost's superiority over latanoprost may be confined to daytime hours (Orzalesi et al., 2006; Stewart, Konstas, Nelson & Kruff, 2008). Furthermore, the UKGTS demonstrated that even the IOP reduction achieved by latanoprost (mean

3.8 mmHg greater than placebo) translates into a 56% risk reduction in visual field deterioration, proving its clinical sufficiency for many patients (Garway-Heath et al., 2015). Therefore, the quest for the "most effective" PGA must be balanced against the principle of achieving a patient-specific target IOP, not merely the largest possible reduction.

The Critical Trade-off: Efficacy vs. Tolerability

Perhaps the most decisive factor in PGA selection is the balance between IOP-lowering power and side effect burden. The data presents a clear spectrum: bimatoprost sits at one end with highest efficacy and highest hyperemia risk (RR 4.66 vs. timolol), while latanoprost occupies the other with very good efficacy and the most favourable tolerability profile (RR 2.30 vs. timolol) (Aptel, Cucherat & Denis, 2008). Travoprost generally falls in between. This is not merely a cosmetic issue. Hyperemia is a leading cause of dissatisfaction and discontinuation. Zimmerman et al. (2009) found shockingly low 1-year persistence rates (5-11%), with adverse effects being a key driver. Consequently, a drug with slightly lower per-dose efficacy but better tolerability may yield superior long-term IOP control due to improved adherence. This trade-off is mitigated in fixed combinations with timolol, which dampen hyperemia differences while enhancing efficacy, making bimatoprost/timolol a compelling option for those needing additional IOP lowering (Lou et al., 2015).

Beyond IOP: Holistic Ocular Effects

PGAs exert effects beyond the trabecular meshwork and uveoscleral pathway. Their impact on ocular blood flow is complex and agent-dependent. Studies indicate travoprost and latanoprost may improve ocular perfusion by reducing vascular resistance, whereas bimatoprost's primary benefit may be in increasing choroidal blood flow (Koz et al., 2007; Vetrugno et al., 2004). The clinical implication of these hemodynamic differences for neuroprotection remains an area of active research.

A critical, often underappreciated, effect is on corneal biomechanics. Meta-analysis confirms that PGAs, particularly travoprost and bimatoprost, cause a statistically significant reduction in central corneal thickness (CCT) and corneal hysteresis (Kadri et al., 2022; Meda et al., 2016). This thinning and softening lead to an underestimation of true IOP by Goldmann applanation tonometry. Therefore, a patient on long-term PGA therapy might have a falsely reassuring IOP reading. Clinicians must be aware of this phenomenon, especially when assessing treatment success or failure, and consider alternative tonometry methods.

Evolution of Formulations: Addressing Ocular Surface Disease

The advent of preservative-free (PF) formulations represents a major advancement, addressing the growing recognition of benzalkonium chloride (BAK)-induced ocular surface disease. Studies show PF tafluprost and PF latanoprost are non-inferior in IOP-lowering to their preserved counterparts and timolol, but with significantly reduced hyperemia and ocular surface toxicity (Chabi et al., 2012; Cucherat, Stalmans & Rouland, 2014). Hommer & Kimmich (2011) demonstrated that switching from preserved PGAs to PF tafluprost dramatically reduced hyperemia from 43.2% to 1.9%. For patients with pre-existing dry eye, ocular surface disease, or intolerance to preserved drops, PF PGAs should be considered first-line, as they may improve both comfort and long-term adherence.

Special Populations and Adjunctive Roles

The efficacy of PGAs extends to challenging subtypes. In normal-tension glaucoma, they provide significant proportional IOP reduction (Cheng, Cai & Wei, 2009). In chronic angle-closure glaucoma, they are at least as effective as timolol (Cheng, Cai, Li & Wei, 2009). Notably, in uveitic glaucoma, latanoprost not only controlled IOP but was associated with a reduction in uveitis recurrence rates, challenging earlier concerns about prostaglandin use in inflammation (Markomichelakis et al., 2009).

PGAs also interact with other treatments. Their use perioperatively enhances the effect of selective laser trabeculoplasty (SLT) (Ayala & Chen, 2012). Interestingly, topical NSAIDs like ketorolac can potentiate the IOP-lowering effect of PGAs, suggesting a complex interaction between inflammatory mediators and aqueous outflow (Turan-Vural, Torun-Acar & Acar, 2011).

Limitations and Future Directions

The evidence base has limitations. Most RCTs are short-term (3-6 months), limiting conclusions about long-term comparative efficacy, though observational studies like Kara et al. (2017) suggest sustained effects. Trial populations are often homogenous, lacking diversity in ethnicity and comorbidities. High heterogeneity in some meta-analyses (e.g., for intracameral implants) advises cautious interpretation (Sharma et al., 2025). Future research must prioritize long-term, pragmatic trials comparing PGAs head-to-head on visual field and quality-of-life outcomes. Cost-effectiveness analyses of newer agents and PF formulations are needed. Finally, research into biomarkers that predict individual response to specific PGAs could usher in an era of personalized glaucoma therapy.

CONCLUSION AND RECOMMENDATIONS

Conclusion

Prostaglandin analogues firmly maintain their status as first-line pharmacological therapy for glaucoma and ocular hypertension. This review consolidates evidence demonstrating their superior efficacy compared to older drug classes, sustained long-term IOP reduction, and, as definitively shown by the UKGTS, their capacity to preserve visual function (Garway-Heath et al., 2015). While nuanced differences exist—with bimatoprost typically providing the greatest IOP reduction and latanoprost offering the most favourable tolerability profile—all are highly effective agents. The development of preservative-free formulations and novel compounds like latanoprostene bunod has further enhanced the therapeutic arsenal by improving ocular surface health and expanding efficacy options.

Recommendations

1. **Individualized First-Line Choice:** For treatment-naïve patients, latanoprost is an excellent first choice due to its optimal balance of efficacy and tolerability. Bimatoprost should be strongly considered when the clinical situation demands the maximum possible IOP reduction, provided the patient is counselled about and accepts the higher risk of hyperemia.
2. **Adopt Preservative-Free Formulations:** Preservative-free PGA formulations should be preferentially prescribed, especially for patients with ocular surface disease, reported intolerance to eye drops, or those requiring long-term therapy, to minimize toxicity and potentially improve adherence.
3. **Optimize Dosing Timing:** To maximize efficacy, evening dosing should be recommended for latanoprost. For travoprost and bimatoprost, dosing time appears less critical, but consistency should be emphasized.
4. **Utilize Fixed Combinations Judiciously:** Fixed-combination therapies (PGA + timolol) are effective for patients requiring additional IOP lowering. They offer convenience and a moderated hyperemia profile compared to PGA monotherapy.
5. **Consider Corneal Effects in Monitoring:** Clinicians should be aware of the corneal-thinning effect of PGAs, which may lead to underestimation of IOP. This should be factored into target IOP setting and assessment of progression, potentially using corneal-compensated tonometry.
6. **Prioritize Adherence Counselling:** Given the abysmal real-world persistence rates, patient education about the chronic nature of therapy, proper administration, and management of expected side effects (like mild hyperemia) is crucial for long-term success.

7. **Direct Future Research:** Future studies should focus on long-term (>2 years) comparative effectiveness trials, cost-utility analyses of newer agents, and investigations into genetic or phenotypic predictors of treatment response to enable truly personalized glaucoma care.

REFERENCES

- A. Alm, and I. Widengård. "Latanoprost: Experience of 2-Year Treatment in Scandinavia." *Acta Ophthalmologica*, 2000.
- A. Chabi, R. Varma, J. Tsai, R. Lupinacci, J. Pigeon, C. Baranak, L. Noble, C. Lines, and T. Ho. "Randomized Clinical Trial of the Efficacy and Safety of Preservative-Free Tafluprost and Timolol in Patients with Open-Angle Glaucoma or Ocular Hypertension." *American Journal of Ophthalmology-Glaucoma*, 2012.
- A. Hommer, and F. Kimmich. "Switching Patients from Preserved Prostaglandin-Analog Monotherapy to Preservative-Free Tafluprost." *Clinical Ophthalmology*, 2011.
- A. Hommer, Osman Mohammed Ramez, M. Burchert, and F. Kimmich. "IOP-Lowering Efficacy and Tolerability of Preservative-Free Tafluprost 0.0015% Among Patients with Ocular Hypertension or Glaucoma." *Current Medical Research and Opinion*, 2010.
- A. Penman, K. W. Crowder, and W. Watkins. "Latanoprost for Open-Angle Glaucoma," 2020.
- B. Frisström. "A 6-Month, Randomized, Double-Masked Comparison of Latanoprost with Timolol in Patients with Open Angle Glaucoma or Ocular Hypertension." *Acta Ophthalmologica*, 2009.
- C. Hirsch. "In Open-Angle Glaucoma, Latanoprost Improved Visual Field Preservation." *Annals of Internal Medicine*, 2015.
- C. Kara, E. Sen, Kadriye Ufuk Elgin, Kurtuluş Serdar, and P. Yılmazbaş. "Does the Intraocular Pressure-Lowering Effect of Prostaglandin Analogues Continue over the Long Term?" *International Ophtalmology*, 2017.

C. Traverso, A. Ropo, M. Papadia, and H. Uusitalo. “A Phase II Study on the Duration and Stability of the Intraocular Pressure-Lowering Effect and Tolerability of Tafluprost Compared With Latanoprost.” *Journal of Ocular Pharmacology and Therapeutics*, 2010.

C. Webers, H. Beckers, M. Zeegers, R. Nuijts, F. Hendrikse, and J. Schouten. “The Intraocular Pressure-Lowering Effect of Prostaglandin Analogs Combined with Topical β -Blocker Therapy: A Systematic Review and Meta-Analysis.” *Ophthalmology (Rochester, Minn.)*, 2010.

Cory Swymer, and Michael W. Neville. “Tafluprost: The First Preservative-Free Prostaglandin to Treat Open-Angle Glaucoma and Ocular Hypertension.” *The Annals of Pharmacotherapy*, 2012.

Cw Lee, F. Buckley, S. Costello, and Steven Kelly. “A Systematic Review of the Characteristics of Randomised Control Trials Featuring Prostaglandins for the Treatment of Glaucoma*.” *Current Medical Research and Opinion*, 2008.

D. Garway-Heath, D. Crabb, C. Bunce, G. Lascaratos, F. Amalfitano, N. Anand, A. Azuara-Blanco, et al. “Latanoprost for Open-Angle Glaucoma (UKGTS): A Randomised, Multicentre, Placebo-Controlled Trial.” *The Lancet*, 2015.

———, et al. “Latanoprost Treatment for Open Angle Glaucoma. The United Kingdom Glaucoma Treatment Study: A Multicentre, Randomised, Placebo-Controlled Clinical Trial,” 2015.

E. Maul, F. G. Carrasco, V. P. Costa, J. Casiraghi, E. Vargas, J. S. Sarmina, and R. Mayol. “A 6-Week, Multicenter, Randomized, Double-Masked, Parallel-Group Study Comparing Travoprost 0.004% to Latanoprost 0.005% Followed by 6-Week, Open-Label Treatment with Travoprost 0.004%.” *Clinical Therapeutics*, 2007.

E. O'Donoghue. “A Comparison of Latanoprost and Dorzolamide in Patients with Glaucoma and Ocular Hypertension: A 3 Month, Randomised Study.” *British Journal of Ophthalmology*, 2000.

E. S. Arcieri, A. Santana, F. N. Rocha, G. L. Guapo, and V. P. Costa. “Blood-Aqueous Barrier Changes After the Use of Prostaglandin Analogues in Patients with Pseudophakia and Aphakia: A 6-Month Randomized Trial.” *A M A Archives of Ophthalmology*, 2005.

Ece Turan-Vural, Banu Torun-Acar, and S. Acar. “Effect of Ketorolac Add-On Treatment on Intra-Ocular Pressure in Glaucoma Patients Receiving Prostaglandin Analogues.” *Ophthalmologica*, 2011.

F. Aptel, M. Cucherat, and P. Denis. “Efficacy and Tolerability of Prostaglandin Analogs: A Meta-Analysis of Randomized Controlled Clinical Trials.” *Journal of Glaucoma*, 2008.

F. Aptel, and P. Denis. “Balancing Efficacy and Tolerability of Prostaglandin Analogues and Prostaglandin–Timolol Fixed Combinations in Primary Open-Angle Glaucoma.” *Current Medical Research and Opinion*, 2011.

F. Topouzis, S. Melamed, H. Danesh-Meyer, A. P. Wells, V. Kozobolis, H. Wieland, R. Andrew, et al. “A 1-Year Study to Compare the Efficacy and Safety of Once-Daily Travoprost 0.004%/Timolol 0.5% to Once-Daily Latanoprost 0.005%/Timolol 0.5% in Patients with Open-Angle Glaucoma or Ocular Hypertension.” *European Journal of Ophthalmology*, 2007.

Fidya Ainun Tikha, and Aditia Rizka Rahadi. “Prostaglandin Analogs Regimen for Open-Angle Glaucoma or Hypertensive Ocular, Is It Still Effective Nowadays?: A Systematic Review.” *Ophthalmologica Indonesiana*, 2024.

G. Lascaratos, D. Garway-Heath, Robyn Burton, C. Bunce, W. Xing, D. Crabb, Richard A. Russell, and Ameet Shah. “The United Kingdom Glaucoma Treatment Study: A Multicenter, Randomized, Double-Masked, Placebo-Controlled Trial: Baseline Characteristics.” *Ophthalmology (Rochester, Minn.)*, 2013.

Gary C. Brown, and Melissa M. Brown. “Patient Preference-Based Comparative Effectiveness and Cost-Utility Analysis of the Prostaglandins for Open-Angle Glaucoma.” *Journal of Ocular Pharmacology and Therapeutics*, 2019.

Gentian Hoxha, K. Spahiu, Gazmend Kaçaniku, Fëllanza Ismajli-Hoxha, and M. Ismaili. “Comparison of Prostaglandin Analogue, Beta-Blockers and Prostaglandin Analogue/Beta-Blockers Fixed Combination in Patients with Primary Open-Angle Glaucoma.” *Spektrum Der Augenheilkunde*, 2013.

H. Lou, Hao Wang, Ying Zong, Jin-wei Cheng, and R. Wei. “Efficacy and Tolerability of Prostaglandin–Timolol Fixed Combinations: An Updated Systematic Review and Meta-Analysis.” *Current Medical Research and Opinion*, 2015.

I. Goldberg, J. Cunha-Vaz, J. Jakobsen, J. Nordmann, Elisabeth Trost, and E. Sullivan. “Comparison of Topical Travoprost Eye Drops Given Once Daily and Timolol 0.5% Given Twice Daily in Patients with Open-Angle Glaucoma or Ocular Hypertension.” *Journal of Glaucoma*, 2001.

J. A. Tumbocon, and Anne Marie Macasaet. “Efficacy and Safety of Tafluprost 0.0015% – Retrospective Analysis of Real-World Data from the Philippines.” *Clinical Ophthalmology*, 2019.

J. Brandt, A. Vandenburg, Kuankuan Chen, and S. Whitcup. “Comparison of Once-or Twice-Daily Bimatoprost with Twice-Daily Timolol in Patients with Elevated IOP,” 2001.

JiETING Peng, Wenrui Huang, and Junguo Duan. “Efficacy and Safety of Prostaglandin Drugs for Elevated Intraocular Pressure: A Bayesian Network Meta-Analysis.” *Frontiers in Medicine*, 2025.

Jin-wei Cheng, Ji-ping Cai, and R. Wei. “Meta-Analysis of Medical Intervention for Normal Tension Glaucoma.” *Ophthalmology (Rochester, Minn.)*, 2009.

Jin-wei Cheng, Ji-ping Cai, You Li, and R. Wei. “A Meta-Analysis of Topical Prostaglandin Analogs in the Treatment of Chronic Angle-Closure Glaucoma.” *Journal of Glaucoma*, 2009.

K. Kawase, J. Vittitow, R. Weinreb, M. Araie, Shigeru Setsuko Miki Kiyoshi Kazuhide Takuji Yasuaki Tomoy Hoshiai Hashida Iwasaki Kano Kawase Kato Kuwayama, Shigeru Hoshiai, Setsuko Hashida, et al. “Long-Term Safety and Efficacy of Latanoprostene Bunod 0.024% in Japanese Subjects with Open-Angle Glaucoma or Ocular Hypertension: The JUPITER Study.” *Advances in Therapy*, 2016.

Kang-Jung Lo, Y. Ko, De-Kuang Hwang, and C. J. Liu. “The Influence of Topical Non-Steroidal Anti-Inflammatory Drugs on the Intraocular Pressure Lowering Effect of Topical Prostaglandin Analogues—A Systemic Review and Meta-Analysis.” *PLoS ONE*, 2020.

Katarina Hedman, and Albert Alm. “A Pooled-Data Analysis of Three Randomized, Double-Masked, Six-Month Clinical Studies Comparing the Intraocular Pressure Reducing Effect of Latanoprost and Timolol.” *European Journal of Ophthalmology*, 2000.

Kenji Inoue, K. Ishida, and G. Tomita. “Effectiveness and Safety of Switching from Prostaglandin Analog Monotherapy to Prostaglandin/Timolol Fixed Combination Therapy or Adding Ripasudil.” *Japanese Journal of Ophthalmology*, 2018.

Kenji Inoue, K. Ishida, G. Tomita, and H. Noma. “A Scoping Review and Network Meta-Analysis for Efficacy and Safety of Glaucoma Medication in Japanese Patients.” *Japanese Journal of Ophthalmology*, 2020.

L. Quaranta, E. Biagioli, I. Riva, E. Rulli, D. Poli, A. Katsanos, and I. Floriani. “Prostaglandin Analogs and Timolol-Fixed Versus Unfixed Combinations or Monotherapy for Open-Angle Glaucoma: A Systematic Review and Meta-Analysis.” *Journal of Ocular Pharmacology and Therapeutics*, 2013.

Liang Lin, Y. Zhao, P. Chew, C. Sng, H. Wong, L. Yip, T. S. Wu, et al. “Comparative Efficacy and Tolerability of Topical Prostaglandin Analogues for Primary Open-Angle Glaucoma and Ocular Hypertension.” *The Annals of Pharmacotherapy*, 2014.

- M. Ayala, and E. Chen. “The Influence of Topical Prostaglandin Analogues in Inflammation After Selective Laser Trabeculoplasty Treatment.” *Journal of Ocular Pharmacology and Therapeutics*, 2012.
- M. Cellini, R. Caramazza, D. Bonsanto, B. Bernabini, and Emilio C. Campos. “Prostaglandin Analogs and Blood-Aqueous Barrier Integrity: A Flare Cell Meter Study.” *Ophthalmologica*, 2004.
- M. Cucherat, I. Stalmans, and J. Rouland. “Relative Efficacy and Safety of Preservative-Free Latanoprost (T2345) for the Treatment of Open-Angle Glaucoma and Ocular Hypertension: An Adjusted Indirect Comparison Meta-Analysis of Randomized Clinical Trials.” *Journal of Glaucoma*, 2014.
- M. Orme, S. Collins, H. Dakin, S. Kelly, and J. Loftus. “Mixed Treatment Comparison and Meta-Regression of the Efficacy and Safety of Prostaglandin Analogues and Comparators for Primary Open-Angle Glaucoma and Ocular Hypertension.” *Current Medical Research and Opinion*, 2010.
- M. Sanford. “Preservative-Free Latanoprost Eye Drops in Patients with Primary Open-Angle Glaucoma/Ocular Hypertension.” *Clinical Drug Investigation*, 2014.
- M. Vetrugno, N. Cardascia, F. Cantatore, and C. Sborgia. “Comparison of the Effects of Bimatoprost and Timolol on Intraocular Pressure and Pulsatile Ocular Blood Flow in Patients with Primary Open-Angle Glaucoma: A Prospective, Open-Label, Randomized, Two-Arm, Parallel-Group Study.” *Current Therapeutic Research*, 2004.
- Myoung-Hee Park, Kyong-Hwan Cho, and J. Moon. “The Effects of Prostaglandin Analogues on the Corneal Thickness,” 2009.
- N. Cardascia, M. Vetrugno, T. Trabucco, F. Cantatore, and C. Sborgia. “Effects of Travoprost Eye Drops on Intraocular Pressure and Pulsatile Ocular Blood Flow: A 180-Day, Randomized, Double-Masked Comparison with Latanoprost Eye Drops in Patients with Open-Angle Glaucoma.” *Current Therapeutic Research*, 2003.

N. Markomichelakis, A. Kostakou, I. Halkiadakis, Sonia Chalkidou, D. Papakonstantinou, and G. Georgopoulos. "Efficacy and Safety of Latanoprost in Eyes with Uveitic Glaucoma." *Graefe's Archive for Clinical and Experimental Ophthalmology*, 2009.

N. Orzalesi, L. Rossetti, A. Bottoli, and P. Fogagnolo. "Comparison of the Effects of Latanoprost, Travoprost, and Bimatoprost on Circadian Intraocular Pressure in Patients with Glaucoma or Ocular Hypertension." *Ophthalmology (Rochester, Minn.)*, 2006.

N. Tamçelik, B. Izgi, A. Temel, N. Yıldırım, M. Okka, A. Özcan, N. Yüksel, U. Elgin, Ç. Altan, and Baris Ozer. "Prospective, Non-Interventional, Multicenter Study of the Intraocular Pressure-Lowering Effects of Prostaglandin Analog/Prostamide-Containing Therapies in Previously Treated Patients with Open-Angle Glaucoma or Ocular Hypertension." *Clinical Ophthalmology*, 2017.

N. Yıldırım, A. Şahin, and Saadet Gultekin. "The Effect of Latanoprost, Bimatoprost, and Travoprost on Circadian Variation of Intraocular Pressure in Patients With Open-Angle Glaucoma." *Journal of Glaucoma*, 2008.

Ni Li, Xiaoming Chen, Yong Zhou, Mao-ling Wei, and Xun Yao. "Travoprost Compared with Other Prostaglandin Analogues or Timolol in Patients with Open-angle Glaucoma or Ocular Hypertension: Meta-analysis of Randomized Controlled Trials." *Clinical and Experimental Ophthalmology*, 2006.

Nikhil Sharma, M. N. Khatib, A. Balaraman, Roopashree R, Mandeep Kaur, Manish Srivastava, Amit Barwal, et al. "Intracameral Prostaglandin Implant Vs Timolol in Open-Angle Glaucoma or Ocular Hypertension: A Systematic Review and Meta-Analysis." *AJO International*, 2025.

O. Koz, A. Ozsoy, A. Yarangumeli, S. Kenan Kose, and G. Kural. "Comparison of the Effects of Travoprost, Latanoprost and Bimatoprost on Ocular Circulation: A 6-Month Clinical Trial." *Acta Ophthalmologica*, 2007.

P. Denis, A. Lafuma, B. Khoshnood, V. Mimaud, and G. Berdeaux. "A Meta-Analysis of Topical Prostaglandin Analogues Intra-Ocular Pressure Lowering in Glaucoma Therapy." *Current Medical Research and Opinion*, 2007.

P. Denis, C. Baudouin, A. Bron, J. Nordmann, J. Renard, J. Rouland, E. Sellem, and M. Amrane. "First-Line Latanoprost Therapy in Ocular Hypertension or Open-Angle Glaucoma Patients: A 3-Month Efficacy Analysis Stratified by Initial Intraocular Pressure." *BMC Ophthalmology*, 2010.

P. Harasymowycz, C. Royer, A. Cui, M. Barbeau, K. Jobin-Gervais, K. Mathurin, J. Lachaine, and C. Beauchemin. "Short-Term Efficacy of Latanoprostene Bunod for the Treatment of Open-Angle Glaucoma and Ocular Hypertension: A Systematic Literature Review and a Network Meta-Analysis." *British Journal of Ophthalmology*, 2021.

Qëndresë Daka, and V. Trkulja. "Efficacy and Tolerability of Mono-Compound Topical Treatments for Reduction of Intraocular Pressure in Patients with Primary Open Angle Glaucoma or Ocular Hypertension: An Overview of Reviews." *Croatian Medical Journal*, 2014.

R. Meda, Qianqian Wang, David Paoloni, P. Harasymowycz, and I. Brunette. "The Impact of Chronic Use of Prostaglandin Analogues on the Biomechanical Properties of the Cornea in Patients with Primary Open-Angle Glaucoma." *British Journal of Ophthalmology*, 2016.

R. Parrish, P. Palmberg, and Wang-Pui Sheu. "A Comparison of Latanoprost, Bimatoprost, and Travoprost in Patients with Elevated Intraocular Pressure: A 12-Week, Randomized, Masked-Evaluator Multicenter Study." *American Journal of Ophthalmology-Glaucoma*, 2003.

R. Reis, Lucia Cristina dos Santos, M. P. Vila, and L. Magacho. "Effects of Travoprost 0.004% Ophthalmic Solution, Six Weeks After Its Laminated Packaging Had Been Removed, in Primary Open-Angle Glaucoma: A Randomized, Controlled, Investigator-Blinded Study." *Clinical Therapeutics*, 2004.

R. van der Valk, C. Webers, T. Lumley, F. Hendrikse, M. Prins, and J. Schouten. “A Network Meta-Analysis Combined Direct and Indirect Comparisons Between Glaucoma Drugs to Rank Effectiveness in Lowering Intraocular Pressure.” *Journal of Clinical Epidemiology*, 2009.

R. Weinreb, J. Liebmann, K. Martin, P. Kaufman, and J. Vittitow. “Latanoprostene Bunod 0.024% in Subjects With Open-Angle Glaucoma or Ocular Hypertension: Pooled Phase 3 Study Findings.” *Journal of Glaucoma*, 2017.

Rajani Kadri, A. Shetty, Devika Parameshwar, Ajay A Kudva, Asha Achar, and J. Shetty. “Effect of Prostaglandin Analogues on Central Corneal Thickness in Patients with Glaucoma: A Systematic Review and Meta-Analysis with Trial Sequential Analysis.” *Indian Journal of Ophthalmology*, 2022.

Rodolfo Mastropasqua, Vincenzo Fasanella, E. Pedrotti, M. Lanzini, S. Staso, L. Mastropasqua, and L. Agnifili. “Trans-Conjunctival Aqueous Humor Outflow in Glaucomatous Patients Treated with Prostaglandin Analogues: An in Vivo Confocal Microscopy Study.” *Graefe's Archive for Clinical and Experimental Ophthalmology*, 2014.

S. Kymes, C. Burk, T. Feinman, Julia M. Williams, and D. Hollander. “Demonstration of an Online Tool to Assist Managed Care Formulary Evidence-Based Decision Making: Meta-Analysis of Topical Prostaglandin Analog Efficacy.” *Therapeutics and Clinical Risk Management*, 2011.

S. Raber, J. Mandema, Hanbin Li, and D. Nickens. “A Model-Based Dose–Response Meta-Analysis of Ocular Hypotensive Agents as a Drug Development Tool to Evaluate New Therapies in Glaucoma.” *Journal of Ocular Pharmacology and Therapeutics*, 2015.

Shahenda Mohamed, Asmaa Gamal El-Deen, A. Abosaif, and N. El-Koussy. “Effects of Preservative-Free and Preservative Prostaglandin Analogs on Ocular Surface by Impression Cytology in Glaucoma Patients.” *Journal of Recent Advances in Medicine*, 2023.

Stefano Ranno, M. Sacchi, Cinzia Brancato, D. Gilardi, Andrea Lembo, and P. Nucci. “A Prospective Study Evaluating IOP Changes After Switching from a Therapy with Prostaglandin Eye Drops Containing Preservatives to Nonpreserved Tafluprost in Glaucoma Patients.” *TheScientificWorldJournal*, 2012.

T. R. Einarson, Natalie A. Kulin, David P. Tingey, and M. Iskedjian. “Meta-Analysis of the Effect of Latanoprost and Brimonidine on Intraocular Pressure in the Treatment of Glaucoma.” *Clinical Therapeutics*, 2000.

T. Zimmerman, S. Hahn, Laurie Gelb, H. Tan, and Elizabeth E. Kim. “The Impact of Ocular Adverse Effects in Patients Treated with Topical Prostaglandin Analogs: Changes in Prescription Patterns and Patient Persistence.” *Journal of Ocular Pharmacology and Therapeutics*, 2009.

Vlad Diaconita, M. Quinn, Dania Jamal, B. Dishan, Monali S. Malvankar-Mehta, and C. Hutnik. “Washout Duration of Prostaglandin Analogues: A Systematic Review and Meta-Analysis.” *Journal of Ophthalmology*, 2018.

W. C. Stewart, A. Konstas, B. Kruff, Heather M Mathis, and J. Stewart. “Meta-Analysis of 24-h Intraocular Pressure Fluctuation Studies and the Efficacy of Glaucoma Medicines.” *Journal of Ocular Pharmacology and Therapeutics*, 2010.

W. C. Stewart, A. Konstas, L. A. Nelson, and B. Kruff. “Meta-Analysis of 24-Hour Intraocular Pressure Studies Evaluating the Efficacy of Glaucoma Medicines.” *Ophthalmology (Rochester, Minn.)*, 2008.

W. Peng, Xiao-Yan Zhong, and Minbin Yu. “[Meta-Analysis of Randomized Controlled Trials Comparing Selective Laser Trabeculoplasty with Prostaglandin Analogue in the Primary Treatment of Open-Angle Glaucoma or Ocular Hypertention].” *[Zhonghua Yan Ke Za Zhi] Chinese Journal of Ophthalmology*, 2014.

W. Scherer. "Effect of Topical Prostaglandin Analog Use on Outcome Following Selective Laser Trabeculoplasty." *Journal of Ocular Pharmacology and Therapeutics*, 2006.

W. Sponsel, G. Paris, Y. Trigo, and M. Pena. "Comparative Effects of Latanoprost (Xalatan) and Unoprostone (Rescula) in Patients with Open-Angle Glaucoma and Suspected Glaucoma." *American Journal of Ophthalmology-Glaucoma*, 2002.

Wenquan Tang, Feng Zhang, Ke Liu, and Xuanchu Duan. "Efficacy and Safety of Prostaglandin Analogues in Primary Open-Angle Glaucoma or Ocular Hypertension Patients." *Medicine*, 2019.

William G. Hodge, Jean Lachaine, I. Steffensen, C. Murray, D. Barnes, V. Foerster, T. Ducruet, and A. Morrison. "The Efficacy and Harm of Prostaglandin Analogues for IOP Reduction in Glaucoma Patients Compared to Dorzolamide and Brimonidine: A Systematic Review." *British Journal of Ophthalmology*, 2007.

Y. Kuwayama, and A. Nomura. "Prospective Observational Post-Marketing Study of Tafluprost for Glaucoma and Ocular Hypertension: Short-Term Efficacy and Safety." *Advances in Therapy*, 2014.