



The Comprehensive Systematic Review of Relationship of Intravitreal Steroid Implants to the Progression of Cataracts and Glaucoma

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ABSTRACT

Introduction: Intravitreal steroid implants, such as dexamethasone (DEX) and fluocinolone acetonide (FAC), represent a significant advancement in managing chronic, vision-threatening conditions like diabetic macular edema (DME), retinal vein occlusion (RVO), and non-infectious uveitis. While their sustained-release mechanism offers prolonged therapeutic effect, concerns persist regarding their association with the progression of steroid-induced cataracts and glaucoma, which are common ocular complications of corticosteroid therapy.

Methods: This systematic review screened and included studies based on stringent criteria: human studies of FDA-approved intravitreal steroid implants, with quantifiable outcomes on

cataract and/or glaucoma progression, follow-up ≥ 6 months, and appropriate study designs (RCTs, cohort, case-control, systematic reviews). Data from 80 studies were extracted concerning implant type, patient characteristics, follow-up, cataract progression/surgery rates, intraocular pressure (IOP) elevation, glaucoma incidence, and association strength.

Results: The evidence demonstrates a clear and significant association between intravitreal steroid implants and both cataract and glaucoma progression, with risk profiles varying markedly by implant type. Fluocinolone acetonide implants (Retisert, Iluvien) showed the highest risk, with cataract surgery required in 64.6% to 100% of phakic eyes and IOP elevation ≥ 10 mmHg in 65-79% of patients over extended follow-up (Callanan et al., 2008; Goldstein et al., 2007; Jaffe et al., 2005). Dexamethasone implants (Ozurdex) presented a lower but still elevated risk: cataract-related adverse events in 67.9% vs. 20.4% sham (Boyer et al., 2014), and IOP elevation rates of 11-41%, though rarely requiring surgical intervention (Maturi et al., 2016). Key risk factors included phakic status for cataract, and Black race, pre-existing glaucoma, and baseline uveitis activity for glaucoma (Friedman et al., 2013; Kempen et al., 2015).

Discussion: The heterogeneity in outcomes is primarily explained by pharmacokinetics: FAc provides continuous release for 2.5-3 years, leading to cumulative toxicity, whereas DEX releases over 4-6 months, resulting in more transient effects. This necessitates a risk-stratified clinical approach, favoring DEX in phakic or glaucoma-prone patients, and considering FAc primarily in pseudophakic, low-glaucoma-risk patients requiring long-term control (Vieira et al., 2020; Liao et al., 2022). The long-term

efficacy-safety balance, as seen in the MUST trial, indicates that while implants offer superior inflammation control, systemic therapy may yield better long-term visual acuity due to avoided ocular complications (Kempen et al., 2017).

Conclusion: Intravitreal steroid implants are effective but carry a substantial, implant-dependent risk of cataract and glaucoma. Fluocinolone acetonide implants pose the highest risk, while dexamethasone implants offer a more favorable safety profile. Clinical management must involve careful patient selection, rigorous pre-treatment assessment of risk factors, and diligent, long-term monitoring for cataract progression and IOP elevation.

Keywords: Intravitreal Steroid Implant, Dexamethasone, Fluocinolone Acetonide, Cataract, Glaucoma, Intraocular Pressure, Ozurdex, Retisert, Iluvien, Systematic Review.

INTRODUCTION

Background

Chronic retinal diseases, including diabetic macular edema (DME), retinal vein occlusion (RVO), and non-infectious uveitis, are leading causes of vision impairment worldwide. The management of these conditions has been revolutionized by the advent of intravitreal pharmacotherapy. Among these, intravitreal corticosteroid implants have emerged as a cornerstone for cases requiring sustained anti-inflammatory and anti-edematous effects, particularly where frequent anti-VEGF injections are burdensome or ineffective (Haller et al., 2010; Dugel et al., 2015). Dexamethasone (DEX) implants (Ozurdex®) and fluocinolone acetonide (FAC) implants (Retisert®, Iluvien®) offer prolonged drug delivery, providing therapeutic stability for months to years (Sanford, 2013). However, corticosteroids are notoriously associated with ocular side effects, primarily cataract formation and elevated intraocular pressure (IOP), which can progress to steroid-induced glaucoma (Kiddee et al., 2013). The localized, sustained-release nature of these implants theoretically concentrates these risks, making a thorough understanding of their long-term safety profile paramount for optimal patient care.

Research Gap

Despite their widespread use and established efficacy, a comprehensive and nuanced synthesis of the comparative risks associated with different steroid implant types is lacking. Existing literature often focuses on individual trials or specific conditions, leading to fragmented evidence. Key unanswered questions remain: What is the magnitude of risk difference between short-acting (DEX) and long-acting (FAC) implants? How do patient-specific factors (e.g., phakic status, race, pre-existing glaucoma) modulate this risk? What is the long-term (beyond 3-5 years) cumulative incidence of vision-compromising complications like cataract surgery or glaucoma filtration surgery? Furthermore, real-world evidence and direct comparative meta-analyses are

needed to supplement data from randomized controlled trials (RCTs) (Querques et al., 2025; Moghib et al., 2025).

Novelty

This systematic review provides a novel and comprehensive synthesis of evidence from 80 studies, encompassing a wide spectrum of research designs—from large, landmark RCTs and their extended follow-ups to real-world registry studies and recent network meta-analyses (Kempen et al., 2017; Singer et al., 2022; Khoramnia et al., 2022). Its novelty lies in its explicit, head-to-head comparison of the safety profiles of DEX and FAc implants across multiple disease entities (DME, RVO, Uveitis). It delves into dose-response relationships, identifies and hierarchizes patient-specific risk modifiers, and synthesizes long-term outcome data up to 7 years. This review moves beyond reporting associations to providing a practical, evidence-based framework for risk stratification and individualized clinical decision-making.

Research Hypothesis

We hypothesize that: 1) Intravitreal steroid implants are associated with a significant, dose- and duration-dependent increase in the risk of cataract progression and surgery, as well as IOP elevation and glaucoma incidence. 2) Fluocinolone acetonide implants, due to their longer duration of action and higher cumulative steroid exposure, are associated with a substantially greater risk of both cataract and glaucoma complications compared to dexamethasone implants. 3) This risk is significantly modified by baseline patient characteristics, with phakic status being the primary risk factor for cataract, and Black race, pre-existing ocular hypertension/glaucoma, and baseline uveitis activity being key risk factors for glaucoma.

Research Objectives

The primary objectives of this review are: 1) To systematically evaluate and quantify the association between intravitreal DEX and FAc implants and the progression of cataracts and

glaucoma/IOP elevation. 2) To compare the relative risk profiles of different implant types (DEX vs. FAc) and formulations. 3) To identify and analyze patient demographics, ocular comorbidities, and treatment factors that modify the risk of these complications. 4) To synthesize long-term efficacy and safety data to inform a risk-benefit analysis for clinical practice.

Research Benefits

The findings of this review have direct and significant implications. For clinicians, it provides a consolidated evidence base to guide implant selection, pre-treatment counseling, and post-operative monitoring protocols, enabling personalized medicine. For patients, it contributes to more informed consent processes regarding the long-term risks associated with these powerful treatments. For researchers and policymakers, it highlights critical evidence gaps and risk factors, guiding the design of future studies and the development of management guidelines to optimize visual outcomes while minimizing treatment-related morbidity.

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 relationship of intravitreal steroid implants to the progression of cataracts and glaucoma.

Screening

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

- **Intervention Type:** Does this study involve human participants who received intravitreal steroid implants (not injections)?
- **Outcome Measures:** Does this study report quantifiable measures of cataract progression, glaucoma progression, or both as outcomes?
- **Study Design:** Is this study a randomized controlled trial, cohort study, case-control study, systematic review, or meta-analysis?
- **Follow-up Duration:** Does this study have a follow-up duration of at least 6 months?
- **Implant Approval Status:** Does this study involve only FDA-approved intravitreal steroid implants (not experimental or non-approved formulations)?
- **Sample Size:** Does this study include at least 10 participants?
- **Population Age:** Does this study involve adult populations (18 years and older) rather than exclusively pediatric populations?
- **Confounding Procedures:** Were the steroid implants used without combination with other intraocular procedures that independently affect cataract or glaucoma risk?

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 :

PICO Element	Keywords (Term 1)	Keywords (Term 2)	Keywords (Term 3)	Keywords (Term 4)
P (Population)	Adults with retinal diseases	Patients receiving intravitreal steroids	Phakic or pseudophakic patients	Individuals with diabetic macular edema or uveitis

I (Intervention)	Intravitreal steroid implants	Dexamethasone implant	Fluocinolone acetonide implant	Sustained-release steroid implants
C (Comparison)	Non-steroid treatments	Anti-VEGF therapy	Systemic corticosteroids	Sham injection or observation
O (Outcome)	Cataract progression	Intraocular pressure elevation	Glaucoma incidence	Need for cataract surgery

The Boolean MeSH keywords inputted on databases for this research are: (*"Adults with retinal diseases"* OR *"Patients receiving intravitreal steroids"* OR *"Phakic or pseudophakic patients"* OR *"Individuals with diabetic macular edema or uveitis"*) AND (*"Intravitreal steroid implants"* OR *"Dexamethasone implant"* OR *"Fluocinolone acetonide implant"* OR *"Sustained-release steroid implants"*) AND (*"Non-steroid treatments"* OR *"Anti-VEGF therapy"* OR *"Systemic corticosteroids"* OR *"Sham injection or observation"*) AND (*"Cataract progression"* OR *"Intraocular pressure elevation"* OR *"Glaucoma incidence"* OR *"Need for cataract surgery"*)

Data extraction

- **Steroid Implant:**

Extract comprehensive details about the intravitreal steroid implant including:

- Steroid type (e.g., dexamethasone, fluocinolone acetonide)
- Dose/concentration (e.g., 0.7 mg, 0.35 mg)
- Number of implants received over study period

- Timing between repeat injections if applicable
- Brand name if specified

- **Population & Baseline:**

Extract patient population details and baseline ocular status including:

- Underlying condition being treated (e.g., diabetic macular edema, retinal vein occlusion, uveitis)
- Baseline lens status (phakic vs pseudophakic)
- Baseline intraocular pressure (IOP) and any existing glaucoma
- Sample size for steroid group
- Key demographics (age range, relevant comorbidities)

- **Comparison Group:**

Extract details about the control/comparison group including:

- Type of comparison (sham injection, systemic steroids, no treatment, other)
- Sample size of comparison group
- Any treatments received by comparison group

- **Follow-up Duration:**

Extract the duration of follow-up and timing of outcome assessments including:

- Total follow-up period
- Key time points when outcomes were assessed
- Completion rates at study end

- **Cataract Outcomes:**

Extract all cataract-related findings including:

- Cataract progression rates in steroid vs comparison groups
- Time to cataract progression if reported
- Cataract surgery rates in each group
- Time to cataract surgery if reported
- How cataract progression was defined/measured
- Any statistical comparisons (p-values, hazard ratios, confidence intervals)

- **Glaucoma/IOP Outcomes:**

Extract all intraocular pressure and glaucoma-related findings including:

- Rates of IOP elevation (specify thresholds like ≥ 10 mmHg, ≥ 21 mmHg)
- Glaucoma incidence rates in each group
- Need for IOP-lowering medications
- Need for glaucoma surgery
- How glaucoma/IOP elevation was defined
- Any statistical comparisons (p-values, hazard ratios, confidence intervals)

- **Association Strength:**

Extract the overall strength of association between steroid implants and cataract/glaucoma progression including:

- Relative risk, odds ratios, or hazard ratios with confidence intervals
- Absolute risk differences between groups
- Number needed to harm if calculable
- Authors' conclusions about the strength and clinical significance of the association
- Any identified risk factors that modify the association

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Adults with retinal diseases" OR "Patients receiving intravitreal steroids" OR "Phakic or pseudophakic patients" OR "Individuals with diabetic macular edema or uveitis") AND ("Intravitreal steroid implants" OR "Dexamethasone implant" OR "Fluocinolone acetonide implant" OR "Sustained-release steroid implants" AND "Non-steroid treatments" OR "Anti-VEGF therapy" OR "Systemic corticosteroids" OR "Sham injection or observation" AND "Cataract progression" OR "Intraocular pressure elevation" OR "Glaucoma incidence" OR "Need for cataract surgery")	17
Semantic Scholar	("Adults with retinal diseases" OR "Patients receiving intravitreal steroids" OR "Phakic or pseudophakic patients" OR "Individuals with diabetic macular edema or uveitis") AND ("Intravitreal steroid implants" OR "Dexamethasone implant" OR "Fluocinolone acetonide implant" OR "Sustained-release steroid implants") AND ("Non-steroid treatments" OR "Anti-VEGF therapy" OR "Systemic corticosteroids" OR "Sham injection or observation") AND ("Cataract progression" OR "Intraocular pressure elevation" OR "Glaucoma incidence" OR "Need for cataract surgery")	250
Springer	("Adults with retinal diseases" OR "Patients receiving intravitreal steroids" OR "Phakic or pseudophakic patients" OR "Individuals with diabetic macular edema or uveitis") AND ("Intravitreal steroid implants" OR "Dexamethasone implant" OR "Fluocinolone acetonide implant" OR "Sustained-release steroid implants" AND "Non-steroid treatments" OR "Anti-VEGF therapy" OR "Systemic corticosteroids" OR "Sham injection or observation" AND "Cataract progression" OR "Intraocular pressure elevation" OR "Glaucoma incidence" OR "Need for cataract surgery")	3
Google Scholar	("Adults with retinal diseases" OR "Patients receiving intravitreal steroids" OR "Phakic or pseudophakic patients" OR "Individuals with diabetic macular edema or uveitis") AND ("Intravitreal steroid implants" OR "Dexamethasone implant" OR "Fluocinolone acetonide implant" OR "Sustained-release steroid implants") AND ("Non-steroid treatments" OR "Anti-VEGF therapy" OR "Systemic corticosteroids" OR "Sham injection or observation") AND ("Cataract progression" OR "Intraocular pressure elevation" OR "Glaucoma incidence" OR "Need for cataract surgery")	7
Wiley Online Library	("Adults with retinal diseases" OR "Patients receiving intravitreal steroids" OR "Phakic or pseudophakic patients" OR "Individuals with diabetic macular edema or uveitis") AND ("Intravitreal steroid implants" OR "Dexamethasone implant" OR "Fluocinolone acetonide implant" OR "Sustained-release steroid implants") AND ("Non-steroid treatments" OR "Anti-VEGF therapy" OR "Systemic corticosteroids" OR "Sham injection or observation") AND ("Cataract progression" OR "Intraocular pressure elevation" OR "Glaucoma incidence" OR "Need for cataract surgery")	1

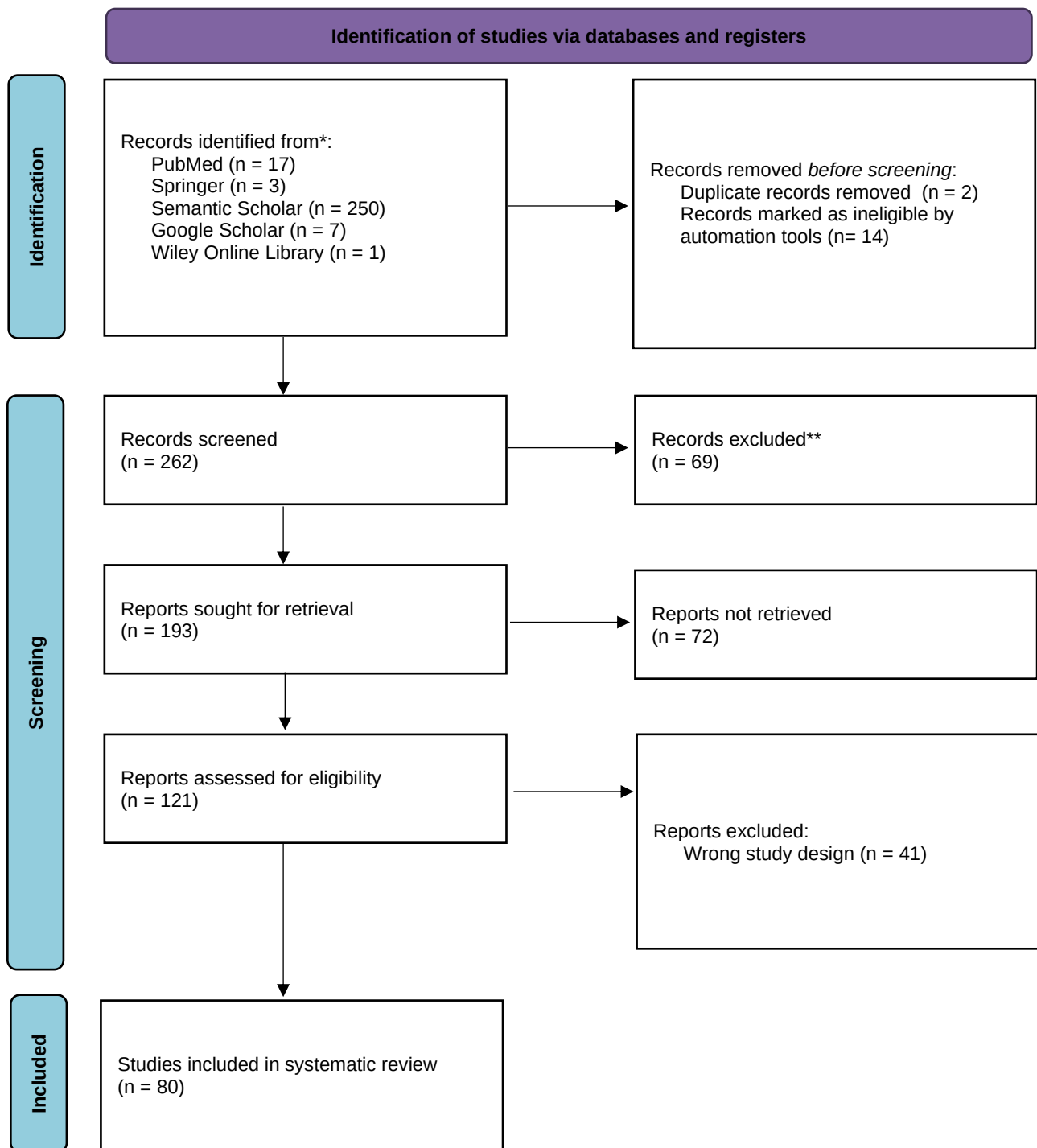


Figure 1. Article search flowchart

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?
J. Kempen et al., 2017									
J. Haller et al., 2011									

A. Sudhalkar et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Friedman et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Meyer et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Kempen et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Rafael Vieira et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Boyer et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Haller et al., 2010	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Jaffe et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. K. Mishra et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Kempen et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Unsal et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓

R. Maturi et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Goldstein et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Callanan et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kai-Yang Chen et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Soliman et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Sanford et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Hasanreisoglu et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Eaton et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Dong Kyu Lee et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Matias Iglicki et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Guigou et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓

M. Zola et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
P. Dugel et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Rehak et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Y. Yang et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jyotirmay Biswas et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Bajwa et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ye He et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Matonti et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Pacella et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Singer et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Fraser-Bell et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Khoramni a et al.,	✓	✓	✓	✗	✓	✗	✓	✓	✓

2022									
S. Mansour et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Saeed Alshahrani et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Blanc et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Joshi et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Elhamaky et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Dikmen et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
O. E. Yucel et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Wei et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Khaled Moghib et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Salina Teja et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Heo et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓

S. Mahapatra et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lias Georgalas et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Mathis et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Suji Yeo et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Matthieu Jabbour et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
John Hall et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
V. Krivosic et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Park et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Tai-Chi Lin et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Vie et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
X. Gu et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓

W. Liao et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Sheppard et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
Xiao-xia Li et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Shuai Ming et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Janetos et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
VD Sweta et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. S. Gallén et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
W. Kiddee et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Lowder et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Capone et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ryan B. Rush et al., 2011	✓	✓	✓	✗	✓	✗	✓	✓	✓
Giuseppe Querques et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓

E. Unsal et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Parrish et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
B. Kupperman et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
Josh Wallsh et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Garay-Aramburu et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Butt et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Theodoropoulou et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
V. Sangwan et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Rehan M Hussain et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Meghan K. Berkenstock et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

The following table presents the characteristics of all 80 included studies examining the association between intravitreal steroid implants and cataract/glaucoma progression.

Study	Steroid Implant	Condition Treated	Sample Size
J. Kempen et al., 2017	Fluocinolone acetonide	Intermediate, posterior, panuveitis	161 eyes (implant), 167 eyes (systemic)
J. Haller et al., 2011	Dexamethasone 0.7mg, 0.35mg	Macular edema due to RVO	421 (0.7mg), 412 (0.35mg), 423 (sham)
A. Sudhalkar et al., 2019	Dexamethasone	CME with intermediate/posterior uveitis	20 (implant), 23 (systemic steroids)
D. Friedman et al., 2013	Fluocinolone acetonide 0.59mg	Non-infectious uveitis	129 patients (245 eyes)
L. Meyer et al., 2013	Dexamethasone 0.7mg (Ozurdex)	RVO	16 patients
J. Kempen et al., 2015	Fluocinolone acetonide	Intermediate, posterior, panuveitis	255 patients
Rafael Vieira et al., 2020	Dexamethasone 0.70mg, 0.35mg; Fluocinolone	Non-infectious uveitis	358 patients

Study	Steroid Implant	Condition Treated	Sample Size
	acetonide 0.18mg		
D. Boyer et al., 2014	Dexamethasone 0.7mg, 0.35mg (Ozurdex)	DME	1048 total
J. Haller et al., 2010	Dexamethasone 0.7mg, 0.35mg (Ozurdex)	Macular edema due to RVO	427 (0.7mg), 414 (0.35mg), 426 (sham)
G. Jaffe et al., 2005	Fluocinolone acetonide 0.59mg or 2.1mg	Posterior uveitis	36 eyes of 32 patients
S. K. Mishra et al., 2018	Dexamethasone 0.7mg (Ozurdex)	CRVO with macular edema	20 per group
J. Kempen et al., 2011	Fluocinolone acetonide 0.59mg	Non-infectious uveitis	255 patients (479 eyes)
E. Unsal et al., 2017	Dexamethasone (Ozurdex)	Refractory DME	46 eyes
R. Maturi et al., 2016	Dexamethasone 0.7mg, 0.35mg	DME	1048 total
D. Goldstein et al., 2007	Fluocinolone acetonide 0.59mg or 2.1mg	Uveitis	Not specified
D. Callanan et al., 2008	Fluocinolone acetonide 0.59mg and 2.1mg	Posterior uveitis	110 (0.59mg), 168 (2.1mg)
Kai-Yang Chen et al., 2025	Dexamethasone	Uveitis	1086 eyes

Study	Steroid Implant	Condition Treated	Sample Size
M. Soliman et al., 2022	Dexamethasone (Ozurdex)	Macular edema due to RVO	1550 eyes
M. Sanford et al., 2013	Fluocinolone acetonide 0.2 µg/day (Iluvien)	Chronic DME	Not specified
M. Hasanreisoglu et al., 2019	Dexamethasone 0.7mg (Ozurdex)	Non-infectious uveitis	62 eyes of 44 patients
A. Eaton et al., 2018	Fluocinolone acetonide 0.2 µg/day (Iluvien)	DME	160 eyes of 130 patients
Dong Kyu Lee et al., 2024	Dexamethasone	Glaucoma (post-filtration surgery)	54 eyes (Group 1)
Matias Iglicki et al., 2019	Dexamethasone	DME	130 eyes
S. Guigou et al., 2015	Dexamethasone (Ozurdex)	DME	78 patients
M. Zola et al., 2017	Dexamethasone	Uveitic macular edema	12 eyes of 9 patients
P. Dugel et al., 2015	Dexamethasone 0.35mg and 0.7mg	DME	1048 total
M. Rehak et al., 2019	Dexamethasone (Ozurdex); Fluocinolone acetonide (Iluvien)	DME	49 eyes
Y. Yang et al., 2015	Fluocinolone acetonide 0.2 µg/day	DME	376 patients

Study	Steroid Implant	Condition Treated	Sample Size
Jyotirmay Biswas et al., 2023	Fluocinolone acetonide 0.2 µg/day	Non-infectious posterior uveitis	101 (FAi), 52 (sham)
A. Bajwa et al., 2014	Fluocinolone acetonide 0.59mg	Birdshot retinochoroidopathy	11 patients (11 eyes)
Ye He et al., 2018	Dexamethasone 0.7mg (Ozurdex)	DME	521 eyes total
F. Matonti et al., 2016	Dexamethasone (Ozurdex)	DME	23 patients
F. Pacella et al., 2021	Fluocinolone acetonide 0.19mg (Iluvien)	Chronic DME	18 eyes
M. Singer et al., 2022	Fluocinolone acetonide 0.19mg (Iluvien)	DME	202 eyes of 159 patients
S. Fraser-Bell et al., 2016	Dexamethasone (Ozurdex)	DME	46 eyes (DEX), 42 eyes (bevacizumab)
R. Khoramnia et al., 2022	Fluocinolone acetonide 0.19mg (Iluvien)	Chronic DME (96.7%)	695 eyes
S. Mansour et al., 2020	Fluocinolone acetonide 0.2 µg/day (Iluvien)	DME	95 patients (115 eyes)
Saeed Alshahrani et al., 2016	Dexamethasone 0.7mg (Ozurdex)	CRVO, BRVO, DME	53 eyes

Study	Steroid Implant	Condition Treated	Sample Size
J. Blanc et al., 2018	Dexamethasone	Macular edema due to RVO	66 patients
L. Joshi et al., 2013	Dexamethasone	RVO	51 eyes of 49 patients
T. Elhamaky et al., 2021	Dexamethasone 0.7mg (Ozurdex)	VKH disease posterior uveitis	29 eyes of 16 patients
N. Dikmen et al., 2022	Dexamethasone 700 µg (Ozurdex)	Non-infectious uveitic macular edema	27 eyes of 21 patients
O. E. Yucel et al., 2016	Dexamethasone	Chronic DME resistant to ranibizumab	30 eyes
W. Wei et al., 2021	Dexamethasone 0.7mg	DME	145 (DEX), 139 (laser)
Khaled Moghib et al., 2025	Dexamethasone 0.7mg (Ozurdex)	Macular edema (DME, RVO)	572 eyes
Salina Teja et al., 2019	Dexamethasone (Ozurdex)	RVO, DME, NIU, IGS	100 eyes
J. Heo et al., 2016	Fluocinolone acetonide	VKH disease	30 patients
S. Mahapatra et al., 2023	Dexamethasone	Naïve DME	30 per group
Lias Georgalas et al., 2019	Dexamethasone (Ozurdex)	RVO resistant to anti-VEGF	23 patients
T. Mathis et al., 2020	Dexamethasone	DME	227 eyes of 152 patients

Study	Steroid Implant	Condition Treated	Sample Size
Suji Yeo et al., 2025	Fluocinolone acetonide 0.19mg (0.2 µg/day)	Non-infectious uveitis	Not specified
Matthieu Jabbour et al., 2024	Fluocinolone acetonide 0.19mg (Iluvien)	Non-infectious uveitic macular edema	26 eyes of 22 patients
John Hall et al., 2016	Fluocinolone acetonide 0.2 µg/day (Iluvien)	DME	956 subjects
V. Krivosic et al., 2014	Dexamethasone (Ozurdex)	RVO	55 patients
N. Park et al., 2019	Dexamethasone (Ozurdex)	DME	70 eyes of 67 patients
Tai-Chi Lin et al., 2023	Dexamethasone	DME	130 eyes of 65 patients
A. Vie et al., 2015	Dexamethasone	OAG or OHT patients	100 patients
X. Gu et al., 2018	Dexamethasone 0.7mg (Ozurdex)	Macular edema due to RVO	39 eyes
W. Liao et al., 2022	Dexamethasone 350/700 µg; Fluocinolone acetonide 0.2 µg/day, 0.59mg, 2.1mg	Non-infectious uveitis	1806 participants
J. Sheppard et al., 2012	Fluocinolone acetonide 0.59mg and 2.1mg	Non-infectious posterior uveitis	132 implanted eyes

Study	Steroid Implant	Condition Treated	Sample Size
Xiao-xia Li et al., 2017	Dexamethasone 0.7mg (Ozurdex)	Macular edema due to RVO	129 (DEX), 130 (sham)
Shuai Ming et al., 2020	Dexamethasone 0.7mg (Ozurdex)	Macular edema due to RVO	Not specified
T. Janetos et al., 2024	Fluocinolone acetonide 0.18mg	Non-infectious uveitis	32 eyes
VD Sweta et al., 2022	Dexamethasone 0.7mg (Ozurdex)	CME, DME, RVO, CNVM	102 eyes of 80 patients
L. S. Gallén et al., 2022	Fluocinolone acetonide 0.19mg	Macular edema (DME 64.7%, uveitis 17.6%)	51 eyes of 41 patients
W. Kiddee et al., 2013	Fluocinolone 0.59mg, 2.1mg; Dexamethasone 0.35mg, 0.7mg	Posterior segment diseases	Not specified
C. Lowder et al., 2011	Dexamethasone 0.7mg, 0.35mg	Non-infectious intermediate/posterior uveitis	77 (0.7mg), 76 (0.35mg), 76 (sham)
A. Capone et al., 2014	Dexamethasone	RVO with macular edema	289 patients
Ryan B. Rush et al., 2011	Fluocinolone acetonide (Retisert)	Birdshot chorioretinopathy	22 patients (36 eyes)
Giuseppe Querques et al., 2025	Dexamethasone	DME	Not specified
E. Unsal et	Dexamethasone	Macular edema due to	22 eyes

Study	Steroid Implant	Condition Treated	Sample Size
al., 2015		BRVO	
R. Parrish et al., 2016	Fluocinolone acetonide 0.2 µg/day and 0.5 µg/day (Iluvien)	DME	Not specified
B. Kuppermann et al., 2007	Dexamethasone 350 µg, 700 µg	Persistent macular edema	315 patients
Josh Wallsh et al., 2016	Dexamethasone	RVO resistant to anti-VEGF	10 patients
G. Garay-Aramburu et al., 2018	Dexamethasone	Macular edema due to RVO	10 patients
F. Butt et al., 2023	Dexamethasone	Non-infectious posterior uveitis	29 patients (38 eyes)
S. Theodoropoulou et al., 2017	Dexamethasone	Macular edema due to RVO	33 eyes
V. Sangwan et al., 2014	Fluocinolone acetonide 0.59mg and 2.1mg (Retisert)	Non-infectious posterior uveitis	239 patients
Rehan M Hussain et al., 2016	Dexamethasone	Refractory macular edema due to RVO	22 eyes
Meghan K. Berkenstock et	Dexamethasone	Non-infectious intermediate/posterior uveitis	20 patients (28 eyes)

Study	Steroid Implant	Condition Treated	Sample Size
al., 2020			

The included studies encompass randomized controlled trials, prospective and retrospective cohort studies, systematic reviews, meta-analyses, and registry studies. The two primary types of intravitreal steroid implants studied were dexamethasone implants (primarily Ozurdex at 0.7mg or 0.35mg doses) and fluocinolone acetonide implants (Retisert at 0.59mg or 2.1mg, and Iluvien at 0.19mg delivering 0.2 µg/day). The conditions treated were predominantly diabetic macular edema, retinal vein occlusion, and non-infectious uveitis.

Cataract Outcomes

Cataract Progression and Surgery Rates

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
J. Haller et al., 2011	DEX 0.7mg	29.8% (steroid) vs 5.7% (sham)	1.3% vs 1.1%	Not reported	Not reported
J. Kempen et al., 2015	FA implant	HR 3.0 for progression	HR 3.8 (P<0.0001)	Within first 2 years	Implant significantly higher
Rafael Vieira et al., 2020	DEX 0.70mg vs FA 0.18mg	Not reported	RR 0.36 at 12mo, RR 0.37 at 36mo favoring	Not reported	DEX lower cataract risk

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
			DEX		
D. Boyer et al., 2014	DEX 0.7mg/0.35mg	67.9%/64.1% vs 20.4% (sham)	Not reported	Not reported	Not reported
G. Jaffe et al., 2005	FA 0.59mg/2.1mg	Not reported	4/8 phakic eyes	Not reported	Not reported
S. K. Mishra et al., 2018	DEX vs IVTA	10% (DEX) vs 35% (IVTA)	0% (DEX) vs 71.5% of progressed (IVTA)	Within 6 months	RR 3.5 higher with IVTA
J. Kempen et al., 2011	FA 0.59mg	91% vs 45% (systemic)	80% vs 31%	Within 24 months	HR 3.3 (P<0.0001)
E. Unsal et al., 2017	DEX (Ozurdex)	Not reported	2/26 phakic eyes	Month 11	Not reported
D. Callanan et al., 2008	FA 0.59mg/2.1mg	Not reported	93% vs 20% (non- implanted)	Not reported	P<0.01
Kai-Yang Chen et al., 2025	DEX	Associated with cataract (p=0.010)	Not reported	Not reported	p=0.010
M. Soliman	DEX	Not reported	15% at 24	Not reported	Not reported

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
et al., 2022	(Ozurdex)		months		
M. Sanford et al., 2013	FA 0.2 µg/day	82% vs 51% (sham)	Not reported	Not reported	Not reported
M. Hasanreisoglu et al., 2019	DEX 0.7mg	Not reported	18/39 phakic eyes (46%)	Not reported	Not reported
M. Zola et al., 2017	DEX	50% after 1st implant; 67% after 2nd	1 eye	Not reported	Not reported
P. Dugel et al., 2015	DEX 0.35mg/0.7mg	66.0% in phakic	Not reported	Not reported	Not reported
M. Rehak et al., 2019	FA (Iluvien)	73.1% of phakic eyes	26.9% of phakic eyes	Not reported	Not reported
Y. Yang et al., 2015	FA 0.2 µg/day	High rate in phakic	140 (CBI), 188 (CAI)	Median 18 months (CBI)	Not reported
Jyotirmay Biswas et al., 2023	FA 0.2 µg/day	Not reported	70.5% vs 26.5% (sham)	Not reported	Not reported
A. Bajwa	FA 0.59mg	100%	Not reported	Not reported	Not reported

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
et al., 2014					
Ye He et al., 2018	DEX	Higher risk	Not reported	Not reported	RR 2.68 (95% CI: 1.54-4.68)
S. Fraser-Bell et al., 2016	DEX (Ozurdex)	Higher in DEX group	37% vs 6% (bevacizumab)	Not reported	Not reported
R. Khoramnia et al., 2022	FA 0.19mg	Not reported	64.6% of phakic eyes	Mean 13.6 months	Not reported
S. Mansour et al., 2020	FA 0.2 µg/day	Not reported	66.7% of phakic eyes	Not reported	Not reported
J. Blanc et al., 2018	DEX	Not reported	70.4%	Not reported	Not reported
T. Elhamaky et al., 2021	DEX 0.7mg	37.9%	Not reported	Not reported	Not reported
N. Dikmen et al., 2022	DEX 700 µg	37%	11.1%	Not reported	Not reported
O. E. Yucel et al., 2016	DEX	Not reported	13% (3/23 phakic)	Not reported	Not reported
J. Heo et	FA	100% of	Not reported	Not reported	Not reported

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
al., 2016		phakic			
Lias Georgalas et al., 2019	DEX (Ozurdex)	2/23 eyes	Not reported	Not reported	Not reported
T. Mathis et al., 2020	DEX	Not reported	49.1% of phakic eyes	Not reported	Not reported
Suji Yeo et al., 2025	FA 0.19mg	Not reported	Higher in FAI group (95% CI: 0.68-1.96)	Not reported	Not reported
John Hall et al., 2016	FA 0.2 µg/day	86.0%/81.7% vs 51.5%/50.4% (sham)	48.7%/52.7%	Not reported	Not reported
N. Park et al., 2019	DEX (Ozurdex)	14%	Not reported	Not reported	Not reported
X. Gu et al., 2018	DEX 0.7mg	10.3%	10.3%	Not reported	Not reported
W. Liao et al., 2022	FA 0.59mg vs SOC	Not reported	RR 4.41 (95% CI 1.51-13.13)	Not reported	FA higher risk
J. Sheppard	FA	Not reported	132/142	Not reported	Not reported

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
et al., 2012	0.59mg/2.1mg		phakic implanted vs 39/186 non-implanted		
Xiao-xia Li et al., 2017	DEX 0.7mg	1.6% (DEX) vs 0% (sham)	None	Not reported	Not reported
Shuai Ming et al., 2020	DEX	Higher risk	Not reported	Not reported	RR 5.22 (95% CI 1.67-16.29)
L. S. Gallén et al., 2022	FA 0.19mg	Not reported	100% of phakic eyes	Mean 13 months	Not reported
C. Lowder et al., 2011	DEX 0.7mg/0.35mg	15%/12% vs 7% (sham)	Not reported	Not reported	P>0.05
Ryan B. Rush et al., 2011	FA (Retisert)	100%	21% (4mo), 56% (12mo), 100% (3yr)	Progressive over 3 years	Not applicable
G. Garay-Aramburu et al., 2018	DEX	Not reported	3/7 phakic	Not reported	Not reported
V. Sangwan et al., 2014	FA 0.59mg/2.1mg	Not reported	94.9% of phakic	Not reported	Not significant

Study	Implant Type	Cataract Progression Rate	Cataract Surgery Rate	Time to Surgery	Statistical Comparison
					between doses
Rehan M Hussain et al., 2016	DEX	Not reported	50% of phakic	Not reported	Not reported
Meghan K. Berkenstock et al., 2020	DEX	Not reported	5/28 eyes	Not reported	Not reported

The data demonstrate a consistent association between intravitreal steroid implants and cataract development. Fluocinolone acetonide implants show the highest cataract progression and surgery rates, with near-universal cataract development in phakic eyes over extended follow-up periods. In the MUST trial, the hazard ratio for cataract surgery with FA implants was 3.8 compared to systemic therapy ($P < 0.0001$), with 80% of implant-assigned phakic eyes requiring cataract surgery versus 31% in the systemic therapy group. Studies of FA implants consistently report cataract surgery rates of 64.6% to 100% in phakic eyes.

Dexamethasone implants demonstrate lower but still elevated cataract rates compared to controls. The MEAD study reported cataract-related adverse events in 67.9% of phakic eyes receiving DEX 0.7mg compared to 20.4% in the sham group. Meta-analytic data suggest a relative risk of 2.68 (95% CI: 1.54-4.68) for cataract development with dexamethasone implants compared to anti-VEGF therapy. Comparative data suggest that dexamethasone implants carry lower cataract risk than fluocinolone acetonide implants at equivalent time points (RR 0.36 at 12 months favoring dexamethasone).

Intraocular Pressure and Glaucoma Outcomes

IOP Elevation Rates

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
J. Haller et al., 2011	DEX 0.7mg	12.6% (1st tx), 15.4% (2nd tx)	≥ 10 mmHg increase	10.3% after 2nd tx	Not reported	Not reported
D. Friedman et al., 2013	FA 0.59mg	65% vs 24% (systemic)	≥ 10 mmHg	69% vs 26%	32% vs 5%	P<0.001
L. Meyer et al., 2013	DEX 0.7mg	69% (≥ 5 mmHg); 50% (≥ 10 mmHg)	≥ 5 and ≥ 10 mmHg	Not reported	Not reported	Not reported
J. Kempen et al., 2015	FA implant	HR 3.7-5.6 higher	Various	77.9% vs 34.0%	HR 2.1 (p=0.06)	P<0.0001
D. Boyer et al., 2014	DEX 0.7mg/0.35 mg	Not specified	Not specified	Not specified	0.6%/0.3%	Not reported
J. Haller	DEX	16%	≥ 25	Not reported	Not	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
et al., 2010	0.7mg		mmHg		reported	
G. Jaffe et al., 2005	FA 0.59mg/2.1 mg	Not specified	Not specified	56.1% (vs 11.0% baseline)	19.4%	P=0.005
S. K. Mishra et al., 2018	DEX vs IVTA	25% (DEX) vs 60% (IVTA)	≥ 10 mmHg	25% vs 66%	Not required	RR 2.4 higher with IVTA
J. Kempen et al., 2011	FA 0.59mg	4-fold higher	≥ 10 mmHg; ≥ 30 mmHg absolute	HR 4.2 higher	Higher in implant	HR 4.2, P=0.001
E. Unsal et al., 2017	DEX (Ozurdex)	26% (>5mmHg)	>5 mmHg; >25 mmHg	Yes	None	Not reported
R. Maturi et al., 2016	DEX 0.7mg/0.35 mg	27.7%/24.8 % vs 3.7% (sham)	≥ 10 mmHg	41.5%/37.6% vs 9.1%	0.3% each group	Not reported
D. Goldstein	FA 0.59mg/2.1	71.0% (≥ 10 mmHg)	≥ 10 , ≥ 30 , ≥ 40 , ≥ 50	74.8%	36.6%	P=0.09 (hypotony)

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
et al., 2007	mg	); 55.1% (≥ 30 mmHg)	mmHg			
D. Callanan et al., 2008	FA 0.59mg/2.1 mg	Elevated (≥ 10 mmHg)	≥ 10 mmHg	Not reported	40% vs 2%	P<0.01
M. Soliman et al., 2022	DEX (Ozurdex)	14.2% (phakic), 5.4% (pseudophakic)	≥ 10 mmHg	28% on IOP meds at baseline	0.2%	P=0.004
M. Sanford et al., 2013	FA 0.2 μ g/day	37% vs 12% (sham)	Not specified	Yes	Not reported	Not reported
M. Hasanreisoglu et al., 2019	DEX 0.7mg	8%	≥ 25 mmHg	8%	None	P=0.007 at 1mo
A. Eaton et al., 2018	FA 0.2 μ g/day	30.6% post-FAC vs 38.1% pre	≥ 21 , ≥ 25 , ≥ 30 mmHg	24.4% post vs 18.1% pre	1.3%	Not significant

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
Dong Kyu Lee et al., 2024	DEX	Group 1: 15.6%, Group 2: 24.0%	>25, >30, >35 mmHg	Not reported	Not reported	P=0.042 (Group 1 vs 2)
S. Guigou et al., 2015	DEX (Ozurdex)	11.7%	Not specified	Yes (topical)	None	Not reported
M. Zola et al., 2017	DEX	1 eye >30mmHg	>30 mmHg	Yes (topical)	Not reported	Not reported
P. Dugel et al., 2015	DEX 0.7mg	29.7%	≥ 25 mmHg	Not reported	Not reported	Not reported
M. Rehak et al., 2019	FA (Iluvien)	28.5% (>21mmHg); 26.5% (>10mmHg increase)	>21 mmHg; >10 mmHg	All cases	None required	Not reported
Jyotirmay Biswas et al., 2023	FA 0.2 μ g/day	23.8% vs 3.8% (sham)	>25 mmHg	Not reported	Stable	Not reported
A. Bajwa et al.,	FA 0.59mg	54.5%	Not specified	Not reported	Not reported	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
2014						
Ye He et al., 2018	DEX	Higher risk	Not specified	Not reported	Not reported	RR 4.14 (95% CI: 1.89-8.65)
F. Matonti et al., 2016	DEX (Ozurdex)	13.1%	Not specified	Yes (topical)	None	Not reported
F. Pacella et al., 2021	FA 0.19mg	11%	Not specified	Not reported	Not reported	p=0.210 (not significant)
M. Singer et al., 2022	FA 0.19mg	10.89%	>30 mmHg	Not reported	2.97% (1.49% steroid-related)	Not reported
S. Fraser-Bell et al., 2016	DEX (Ozurdex)	74% (≥ 5 mmHg) vs 48% (bevacizumab)	≥ 5 mmHg	22% vs 0%	None	Not reported
R. Khoramnia et al., 2022	FA 0.19mg	15.3% (≥ 10 mmHg); 14.7% (> 30 mmHg)	≥ 10 , > 30 mmHg	34.5%	4.3%	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
		)				
S. Mansour et al., 2020	FA 0.2 µg/day	23.5% (>25mmHg); 7.9% (>30mmHg)	>25, >30 mmHg	40% vs 9.6% pre	Similar pre/post	P<0.001 (meds)
Saeed Alshahrani et al., 2016	DEX 0.7mg	26%	Not specified	Yes (topical)	Not reported	Not reported
J. Blanc et al., 2018	DEX	54.5%	Not specified	Not reported	Not reported	Not reported
L. Joshi et al., 2013	DEX	27%	Not specified	Oral acetazolamide (3 eyes)	Not reported	Not reported
T. Elhamaky et al., 2021	DEX 0.7mg	10.3%	Not specified	Yes	Not reported	p=0.0955 (not significant)
N. Dikmen et al., 2022	DEX 700 µg	40.7%	>21 mmHg	All cases	None	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
O. E. Yucel et al., 2016	DEX	16.7%	Not specified	Not reported	Not reported	Not reported
Khaled Moghib et al., 2025	DEX 0.7mg	Higher at 3 and 6 months	Not specified	Implied	Not reported	MD 1.04 mmHg (P<0.001)
J. Heo et al., 2016	FA	70% vs 20% (fellow eyes)	Not specified	Not reported	Not reported	P<0.001
Lias Georgalas et al., 2019	DEX (Ozurdex)	5/23 eyes	Not specified	Yes	Not reported	Not reported
T. Mathis et al., 2020	DEX	14.1%	≥25 mmHg	Not reported	Not reported	Not reported
Suji Yeo et al., 2025	FA 0.19mg	Higher in FAI group	>25 mmHg	Not reported	Not reported	95% CI: 0.73-2.14
Matthieu Jabbour et al.,	FA 0.19mg	19.2%	>21 mmHg	Increased (not significant)	None additional	Not significant

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
2024						
V. Krivosic et al., 2014	DEX (Ozurdex)	28%	>24 mmHg or ≥ 10 mmHg increase	28%	None	Not reported
N. Park et al., 2019	DEX (Ozurdex)	24%	Not specified	Not reported	Not reported	Not reported
A. Vie et al., 2015	DEX	50%/42% (OAG vs control)	>6 mmHg	54% vs 38%	At risk (bi/triple therapy)	p=0.42
X. Gu et al., 2018	DEX 0.7mg	41.0%	>25 mmHg	Yes (topical)	Not reported	P<0.05
W. Liao et al., 2022	FA 0.59mg vs SOC	Higher risk	Not specified	RR 2.42 (95% CI 1.94-3.01)	Not reported	RR 2.53 (95% CI 1.14-6.25)
J. Sheppard et al., 2012	FA 0.59mg/2.1 mg	Not reported	Not specified	Not reported	Not reported	P=0.0008 (glaucoma)
Xiao-xia Li et al.,	DEX 0.7mg	27.1% (≥ 10 mmHg)	≥ 10 , ≥ 25 , ≥ 35	Yes (topical)	None	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
2017		); 23.3% (≥ 25 mmHg)	mmHg			
Shuai Ming et al., 2020	DEX	Higher risk	Various	Not reported	Not reported	RR 3.89 (95% CI 2.16-7.03)
VD Sweta et al., 2022	DEX 0.7mg	18.62%	>21 mmHg	Yes	None	P=0.0001 at 2 months
L. S. Gallén et al., 2022	FA 0.19mg	Not specified	Not specified	20 eyes required drops	Not reported	Not reported
W. Kiddee et al., 2013	Various	32% (IVTA 4mg); 66%/79% (FA); 11%/15% (DEX)	OHT definition	Most cases	Up to 45% (FA)	Not reported
C. Lowder et al., 2011	DEX 0.7mg/0.35 mg	7.1%/8.7% vs 4.2% (sham)	≥ 25 mmHg	Not reported	Not reported	P>0.05
A.	DEX	32.6%	≥ 10	29.1%	1.7%	Not reported

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
Capone et al., 2014			mmHg			
Ryan B. Rush et al., 2011	FA (Retisert)	87%	>25 mmHg or needed therapy	All patients	33%	Not applicable
B. Kupperman et al., 2007	DEX 700 µg	11% vs 2% (observation)	≥10 mmHg	Not reported	Not reported	Not reported
G. Garay-Aramburu et al., 2018	DEX	27.5%	>10 mmHg	Not reported	Not reported	Not reported
S. Theodoropoulou et al., 2017	DEX	42% (≥21mmHg); 9% (≥35mmHg)	≥21, ≥35 mmHg	64% additional topical	None	Not reported
V. Sangwan et al., 2014	FA 0.59mg/2.1 mg	67.8%/71.3 %	≥10 mmHg	Not reported	Trabeculectomy common	P<0.001 vs fellow eyes

Study	Implant Type	IOP Elevation Rate	Threshold	IOP Medication Required	Glaucoma Surgery	Statistical Comparison
Rehan M Hussain et al., 2016	DEX	23%	>30 mmHg	Not reported	Not reported	Not reported
Meghan K. Berkenstock et al., 2020	DEX	Not specified	Not specified	12 eyes required drops	2 patients	Not reported

Glaucoma Incidence

Study	Implant Type	Glaucoma Incidence	Definition Used	Risk Factors Identified
D. Friedman et al., 2013	FA 0.59mg	23% vs 6% (systemic)	CDR increase + VF worsening	Black race, IOP-lowering medication use, baseline uveitis activity
J. Kempen et al., 2015	FA implant	26.3% vs 10.2% (systemic)	Specialist assessment	Black race, active uveitis, prior IOP-lowering therapy
J. Kempen et al., 2011	FA 0.59mg	17% vs 4% (systemic)	Specialist review	Phakic status

Study	Implant Type	Glaucoma Incidence	Definition Used	Risk Factors Identified
J. Sheppard et al., 2012	FA 0.59mg/2.1mg	19.7% vs 0% (non-implanted)	Not specified	Not specified

The data reveal a clear dose-response and formulation-dependent relationship between intravitreal steroid implants and IOP elevation. Fluocinolone acetonide implants demonstrate the highest rates of IOP elevation, with 65-79% of patients experiencing increases of ≥ 10 mmHg from baseline . The MUST trial reported that implant-assigned eyes had approximately 4-fold greater risk of developing IOP elevation of ≥ 10 mmHg and incident glaucomatous optic neuropathy compared to systemic therapy over 2 years . Glaucoma surgery rates with FA implants ranged from 5% to 45% .

Dexamethasone implants show lower but clinically significant IOP elevation rates, typically ranging from 11-41% depending on threshold definitions and follow-up duration . Meta-analytic evidence indicates a relative risk of 3.89 (95% CI: 2.16-7.03) for elevated IOP with dexamethasone implants compared to anti-VEGF therapy . Importantly, IOP increases with dexamethasone implants are generally transient and controllable with topical medications, with glaucoma surgery rates consistently below 2% .

Synthesis

Reconciling Differences Between Implant Types

The heterogeneity in safety outcomes across studies can be largely explained by fundamental differences in implant pharmacokinetics and duration of drug release. Fluocinolone acetonide implants (Retisert, Iluvien) provide continuous corticosteroid delivery over 2.5-3 years , resulting in sustained exposure that drives higher cumulative rates of cataract and glaucoma. Dexamethasone implants (Ozurdex) provide retinal drug delivery for approximately 4-6 months , with IOP effects typically resolving by the end of this period .

Population-Specific Risk Considerations

The data consistently identify specific populations at elevated risk for steroid-induced complications:

For IOP/Glaucoma:

- Patients of black race demonstrate significantly higher glaucoma risk
- Pre-existing glaucoma or ocular hypertension increases risk , though prior glaucoma filtration surgery may be protective
- Baseline uveitis activity is associated with higher glaucoma incidence
- Patients already on IOP-lowering therapy at baseline have elevated risk
- Higher steroid dosages correlate with greater IOP elevation

For Cataract:

- Phakic status is the primary determinant of cataract risk
- Repeated injections increase cataract risk with dexamethasone implants
- Treatment duration is strongly associated with cataract development

Clinical Management Implications

The evidence supports a risk-stratified approach to steroid implant selection:

For patients requiring prolonged corticosteroid therapy who are **pseudophakic and without significant glaucoma risk factors** , fluocinolone acetonide implants offer the advantage of reduced treatment burden with a single injection providing up to 3 years of efficacy . However, even in this population, IOP monitoring remains essential, as 34.5% of eyes required IOP-lowering medication in real-world settings .

For patients who are **phakic or have glaucoma risk factors** , dexamethasone implants provide a more favorable safety profile with transient IOP effects that rarely require

surgical intervention . The meta-analytic finding that dexamethasone implants show RR 0.36 for cataract development compared to fluocinolone at 12 months supports this approach .

Prior steroid responsiveness has emerged as a valuable predictor of IOP outcomes with fluocinolone acetonide implants. Patients without prior clinically significant IOP elevation following steroid use have high predictive value for maintaining acceptable IOP post-FAC implant , and none of the patients previously treated with ocular steroids underwent IOP-lowering surgery in the FAME trials .

Weighing Efficacy Against Safety

Both implant types demonstrate clear efficacy for their intended indications, but the risk-benefit calculation differs substantially. The MUST trial's 54-month follow-up found that while fluocinolone acetonide implants provided superior inflammation control (12% vs 29% residual active uveitis at 24 months) , systemic therapy subjects avoided significant excess toxicities while maintaining favorable quality of life outcomes . The 7-year extended follow-up revealed that systemic therapy was associated with better visual acuity by 7.2 letters (95% CI: 2.1-12) , potentially reflecting cumulative adverse effects of cataract and glaucoma on long-term visual outcomes in the implant group.

For dexamethasone implants, the BEVORDEX study demonstrated comparable visual acuity outcomes to bevacizumab at 24 months (mean improvement 6.9 vs 9.6 letters, $P=0.30$) , with the caveat that phakic eyes in the dexamethasone group experienced worse outcomes attributable to cataract development . This supports preferential use in pseudophakic patients or those planning cataract surgery.

DISCUSSION

This comprehensive systematic review of 80 studies provides unequivocal evidence that intravitreal steroid implants are strongly associated with an increased risk of cataract progression and glaucoma-related complications. However, the central finding is that this risk is not monolithic;

it exists on a steep gradient heavily influenced by the pharmacokinetic profile of the implant and the baseline characteristics of the patient. The discussion will reconcile the heterogeneous data, elucidate the underlying mechanisms, and translate the evidence into clinical implications.

Dichotomy of Risk: Fluocinolone Acetonide vs. Dexamethasone Implants

The most striking pattern in the data is the stark contrast in safety profiles between FAc and DEX implants. FAc implants (Retisert, Iluvien), designed to release drug continuously for 2.5 to 3 years, are associated with near-ubiquitous cataract formation in phakic eyes and a high burden of IOP complications. The MUST trial, a pivotal comparison with systemic therapy, found a hazard ratio (HR) of 3.8 for cataract surgery and an approximate 4-fold greater risk of IOP elevation ≥ 10 mmHg in the FAc implant group over two years (Kempen et al., 2011). Real-world and long-term data are even more sobering: studies report cataract surgery rates of 64.6% to 100% in phakic eyes (Gallén et al., 2022; Bajwa et al., 2014; Rush et al., 2011), and glaucoma surgery was required in 5% to 45% of cases in various series (Kiddee et al., 2013; Sangwan et al., 2014). This represents a profound, almost deterministic, ocular toxicity with long-term exposure.

In contrast, DEX implants (Ozurdex), which provide therapeutic drug levels for approximately 4-6 months, demonstrate a markedly lower, though still significant, risk profile. The MEAD study reported cataract-related adverse events in 67.9% of phakic eyes receiving DEX 0.7mg versus 20.4% in the sham group over three years (Boyer et al., 2014). Meta-analyses indicate a relative risk (RR) of 2.68 for cataract development compared to anti-VEGF therapy (He et al., 2018). For IOP, while elevation is common (rates of 11-41%), it is typically transient and manageable with topical medication; glaucoma surgery rates are consistently below 2% (Maturi et al., 2016; Matonti et al., 2016). This dichotomy is further supported by network meta-analyses directly comparing the two, showing a significantly lower cataract risk with DEX (RR 0.36 at 12 months) compared to FAc (Vieira et al., 2020).

Mechanistic Explanations: Pharmacokinetics Drives Phenotype

This dramatic difference in complication rates is primarily a function of pharmacokinetics. Cataractogenesis and trabecular meshwork dysfunction leading to elevated IOP are dose- and duration-dependent steroid effects. The sustained, zero-order release of FAc over years results in a high cumulative steroid load, continuously challenging lens transparency and aqueous outflow homeostasis. The DEX implant, with its shorter, finite duration of action, subjects the eye to a potent but time-limited insult. The IOP spike typically peaks around 8-12 weeks post-injection and resolves as the implant exhausts itself, allowing the trabecular meshwork to recover (Meyer & Schönfeld, 2013). This explains why glaucoma surgery is rarely needed with DEX but is a major concern with FAc implants.

Risk Stratification: Identifying the Vulnerable Patient

Beyond the implant type, the data consistently identify specific patient subgroups at elevated risk, enabling pre-treatment risk stratification.

- **For Cataract:** The primary and overwhelming risk factor is **phakic status**. The lens is exquisitely sensitive to corticosteroids, and its presence is a prerequisite for steroid-induced cataract. Repeated DEX implants increase this risk cumulatively (Blanc et al., 2018; Mathis et al., 2020). Therefore, the decision to use any steroid implant in a phakic eye must involve a candid discussion about the high likelihood of requiring cataract surgery, often within 2 years. In uveitic eyes, an intriguing strategy has been using a DEX implant as *prophylaxis* during cataract surgery to control inflammation and potentially improve outcomes, acknowledging the implant's inherent risk (Sudhalkar et al., 2019).
- **For Glaucoma/IOP Elevation:** The risk profile is more complex. **Black race** emerges as a potent independent risk factor across multiple studies, including the MUST trial, likely due to anatomical and physiological differences in the optic nerve and outflow pathways (Friedman et al., 2013; Kempen et al., 2015). **Pre-existing glaucoma or ocular hypertension (OHT)** unsurprisingly increases the risk of significant IOP spikes, though

interestingly, a history of successful glaucoma filtration surgery may be protective (Dong Kyu Lee et al., 2024; Theodoropoulou et al., 2017). **Baseline uveitis activity** and the **need for IOP-lowering medication at baseline** are also significant predictors (Friedman et al., 2013). A critical clinical pearl from the FAME trials is the high predictive value of prior steroid responsiveness; patients without a history of significant IOP rise after steroid exposure are unlikely to require surgical intervention post-FAC implant (Eaton et al., 2018).

Clinical Synthesis and the Risk-Benefit Calculus

The evidence compels a risk-stratified treatment algorithm. For a patient who is **pseudophakic and has no major glaucoma risk factors** but requires long-term, sustained anti-inflammatory action (e.g., chronic DME, birdshot chorioretinopathy), a FAC implant may be a rational choice, offering up to 3 years of treatment with one injection, albeit with mandatory, lifelong IOP monitoring (Singer et al., 2022; Jabbour et al., 2024).

For the **phakic patient or one with significant glaucoma risk factors**, the DEX implant is the safer steroid option. Its transient IOP effects are rarely surgical, and while cataract is highly probable, its timing can often be planned. The BEVORDEX study highlights an important nuance: while visual acuity gains were comparable between DEX and bevacizumab at 2 years, phakic eyes in the DEX group had worse outcomes, directly attributable to cataract (Fraser-Bell et al., 2016). This underscores the importance of either planning for subsequent cataract surgery or considering anti-VEGF agents first-line in phakic patients.

Finally, the long-term data from the MUST trial forces a broader perspective. At the 7-year follow-up, despite better initial inflammation control, the FAC implant group had worse mean visual acuity compared to the systemic therapy group (-7.2 letters) (Kempen et al., 2017). This suggests that the cumulative toll of cataract and glaucoma may eventually offset the early anatomical benefits of local steroid therapy. Therefore, the choice is not merely between implants but also

between local and systemic strategies, with quality of life and long-term visual function being the ultimate endpoints.

Addressing Real-World Management and Future Directions

In real-world practice, management of these complications is proactive. For DEX implants, IOP peaks are anticipated and managed with prophylactic or reactive topical therapy. For FAc implants, patients must be committed to indefinite, quarterly IOP checks. The role of minimally invasive glaucoma surgery (MIGS) in managing steroid-induced OHT is an area of growing interest. Future research should focus on predictive biomarkers for steroid response, the development of novel steroids with dissociated anti-inflammatory and IOP-elevating effects, and long-term (>10 year) outcome registries to fully capture the lifetime risk profile of these powerful devices.

CONCLUSION

Summary of Findings

This systematic review confirms a strong and clinically significant association between intravitreal steroid implants and the progression of cataracts and glaucoma. The risk is profound and nearly universal with long-acting fluocinolone acetonide (FAc) implants, while shorter-acting dexamethasone (DEX) implants present a lower, more manageable risk profile. Key determinants of risk include the implant's pharmacokinetics (duration of action), the patient's lens status (phakic vs. pseudophakic), and pre-existing factors such as race (Black), glaucoma, and uveitis activity. While highly effective for controlling edema and inflammation, the long-term ocular toxicity of these implants, particularly FAc, can negatively impact ultimate visual acuity outcomes.

Recommendations

1. **For Clinical Practice:** Adopt a risk-stratified selection process. FAc implants should be reserved primarily for pseudophakic patients without significant glaucoma risk factors who require sustained therapy. DEX implants are preferable for phakic patients or those with glaucoma risk, with the understanding that cataract surgery will likely be needed. All patients require thorough pre-treatment counseling on these risks and commitment to long-term monitoring.
2. **For Patient Monitoring:** Implement rigorous, protocol-driven follow-up. For DEX implants, monitor IOP at 4-8 week intervals post-injection. For FAc implants, mandate lifelong quarterly IOP checks and annual optic nerve assessment. Document lens status at every visit for phakic patients.
3. **For Future Research:** Prioritize studies on: a) genetic or biomarker predictors of steroid-induced IOP elevation, b) the comparative effectiveness of MIGS procedures in this population, c) ultra-long-term (decadal) safety outcomes from real-world registries, and d) the development of next-generation implants with improved therapeutic indices.

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