Potential Harms of Posterior Chamber Phakic IOL: A Systematic Review and Meta-Analysis of Complication Incidence

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• TOPIC: To estimate the incidence of complications after posterior chamber phakic intraocular lens implantation and to evaluate temporal and geographic variation in reported outcomes.

• CLINICAL RELEVANCE: PCPIOLs are widely used for refractive correction, yet uncertainty persists regarding the true frequency of mechanical, anterior-segment, and posterior-segment complications. Reliable incidence estimates are essential for patient counseling and postoperative management.

• METHODS: This systematic review and meta-analysis included randomized and nonrandomized trials and observational studies involving adults undergoing posterior chamber phakic intraocular lens implantation. PubMed, Scopus, WANFANG Data, and China National Knowledge Infrastructure were searched through May 2024 without language or date restrictions. The primary outcome was the incidence of IOL explantation. Secondary outcomes included the onset of IOL rotation or displacement, anterior capsular opacification, cataract formation, iris atrophy, retinal detachment, macular oedema, pupillary block, glaucoma, pupil ovalisation, intraocular infection, endothelial failure, and iris cyst. Risk of bias was assessed using a modified Newcastle–Ottawa Scale. Incidence was modeled as events per 1,000 person-years using negative binomial regression with robust variance. The protocol was registered in PROSPERO (CRD42024527190).

• RESULTS: A total of 214 studies (45,027 eyes) were included, most involving the V4c model of the Implantable Collamer Lens (92.7%). Rotation or displacement occurred at 4.2 per 1,000 person-years and explantation at 3.1 per 1,000 person-years, corresponding to approximately about 2 rotated lenses and explantations per 100 eyes followed for 5 years, assuming constant hazards. Anterior segment events were less frequent, and posterior events were rare (retinal detachment, 0.4; macular edema, 0.3 per 1,000 person-years). Complication rates decreased in more recent studies and were lower in Asian cohorts.

• CONCLUSIONS: PCPIOL implantation is associated with a low incidence of complications, and vision-threatening events appear to be very rare. However, predominantly short follow-up and high risk of bias likely lead to underestimation of late events. These incidence estimates support early postoperative assessment of centration, axis alignment, and vault, and long-term endothelial and anterior segment monitoring. (Am J Ophthalmol 2026;285: 73–82.

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INTRODUCTION

Posterior chamber phakic intraocular lenses (PCPIOLs) are an established surgical option for the correction of refractive error in phakic eyes. By positioning the lens in the ciliary sulcus, PCPIOLs can provide excellent optical quality while avoiding the tissue removal inherent to corneal ablative procedures.[1] A key intrinsic advantage is the preservation of the crystalline lens,

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thereby maintaining its natural accommodative and optical functions and avoiding vitreoretinal side effects that may occur after clear lens extraction.[2] Earlier phakic IOLs (angle-fixated, iris-supported) were abandoned due to safety concerns such as corneal decompensation and uveitis–glaucoma–hyphema syndrome,[3,4] whereas PCPIOLs have gained wide acceptance. Contemporary devices in routine use include the Collamer-based Implantable Collamer Lens (ICL, Staar Surgical, USA), the hydrophilic acrylic Eyecryl Phakic (BioTech Healthcare GmbH, Switzerland), and the hydrophilic acrylic Implantable Phakic Contact Lens (IPCL, Caregroup Sight Solution, India).[5]

Despite favorable refractive outcomes, concerns about possible harms remain. Concerns traditionally focus on early mechanical events (eg, rotation or displacement, particularly in toric designs, intraocular pressure spikes and pupillary block) and later anterior segment complications such as anterior capsular opacification, cataract formation, iris atrophy, and endothelial cell loss.[1,6,7] Vault sizing is critical, low vaulting predisposes to anterior subcapsular cataract, while high vaulting increases risks of angle crowding, pupillary block, pigment dispersion, and rotation.[8-11] Posterior segment events, especially retinal detachment in highly myopic eyes, have also been reported as sight-threatening complications.[12]

Interpreting risk is challenging because existing studies are small and heterogeneous. Moreover, many reports are from Asia and published in Chinese, limiting their accessibility in prior reviews. Previous systematic reviews have mainly emphasized refractive efficacy or single complications, without providing pooled incidence estimates across the spectrum of harm outcomes.

To address these gaps, we conducted a systematic review and meta-analysis of both English- and Chinese-language studies to estimate the incidence of complications after PCPIOL implantation.

METHODS

We conducted and report this systematic review and meta-analysis in accordance with the methodological recommendations outlined in the Cochrane Handbook and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[13,14] We prospectively registered the study protocol in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42024527190. Given the nature of this meta-analysis involving previously published studies, no ethical approval was required.

• **OUTCOMES:** The primary outcome was the incidence of IOL explantation because it reflects clinically significant failure that integrates multiple potential complications (vaulting, cataract, pigment dispersion). Secondary outcomes included the onset of IOL rotation or displacement, anterior capsular opacification, cataract formation, iris atrophy, retinal detachment, macular oedema, pupillary block, glaucoma, pupil ovalisation, intraocular infection, endothelial failure, and iris cyst.

• **ELIGIBILITY CRITERIA:** According to the Patients, Intervention, Comparator, Outcomes, Study type (PICOS) approach,[13] eligible studies included eyes from male and female patients with a refractive error—myopia, hyperopia, or astigmatism—who underwent posterior chamber phakic intraocular lens (PCPIOL) implantation. As this study was a meta-analysis of incidence, no comparator group was required. No minimum follow-up duration was imposed to allow for a broader inclusion of available evidence. Eligible studies included randomized controlled trials (RCTs), non-randomized controlled trials (NRCTs), and observational designs such as cohort studies, case-control studies, and case series. We chose this broad eligibility for study designs to capture more evidence as observational studies have several advantages to identifying harms over RCTs. Comparative studies assessing different PCPIOL surgical techniques were eligible, as were those comparing PCPIOLs with other refractive procedures, provided that outcome data specific to posterior chamber lenses could be extracted. Studies were also eligible if their primary endpoint was refractive outcomes but postoperative follow-up data included the presence or absence of complications. Non-clinical outcome studies explicitly reporting statements such as "no postoperative complications were observed" or "no lens removal was required" were also considered for inclusion.

We excluded studies if they were case reports, case series with fewer than 5 eyes, conference abstracts, posters, letters, narrative reviews, meta-analyses, or purely descriptive surgical technique papers. Duplicate publications and multiple reports from the same patient cohort were also excluded, with preference given to the most recent or most comprehensive publication. We also applied the following exclusion criteria pertaining to PICO: studies focusing on bilensectomy or explant series ICL; studies on pediatric patients, ICL implantation following keratoplasty, laser-assisted in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK), or posterior scleral reinforcement, and studies combining ICL implantation with other ocular surgeries; articles reporting only postoperative anatomical or biometric changes (eg, vaulting abnormalities, gonioscopic findings) without clinically relevant complications or need for surgical reintervention; and studies evaluating PCPIOL models that are no longer commercially available. We included only studies published from the year 2000 onward and those published in English or Chinese.

• **DATA SOURCES:** We performed two separate literature searches for English and Chinese language articles: one in PubMed and Scopus, one in WANFANG Data and China National Knowledge Infrastructure (CNKI). Dupli-

cates were removed across databases within each search, however across searches we only checked for duplicates among the Chinese language papers (ie, Chinese language articles indexed in English databases) to ensure we did not double-count Chinese language studies. No manual hand-searching of conference proceedings, grey literature or journal issues was undertaken. At this stage, no limits were applied regarding date, language, or publication status. The search strategy combined relevant keywords, including "posterior chamber phakic intraocular lenses," "PCIOLs," "posterior chamber pIOLs," "implantable Collamer lens," "ICL," "Eyecryl," and "implantable phakic contact lens," "IPCL." These same search terms were translated into Chinese for use in Chinese-language databases (File 1, supplementary materials). The final search was completed in May 2024.

• **STUDY SELECTION AND DATA EXTRACTION:** From each eligible study, we extracted data on publication details (first author, year), study characteristics (design, setting), follow-up duration, and country of origin. English-language studies were extracted by two reviewers (M.B., M.L.P.), and Chinese-language studies by three reviewers (vs.F.C., S.N., Y.Z.). Data were collected using Qualtrics software and automatically exported to Excel. A third reviewer verified concordance and comparability of the extracted data (R.Q. for English studies; vs.F.C. for Chinese studies). Follow-up duration was standardized by converting all reported time units into months. When the original studies expressed follow-up in years, weeks, days, or hours, values were converted to months using the following assumptions: 1 year = 12 months, 1 month = 4.345 weeks, 1 month = 30.44 days, and 1 day = 24 hours. For incidence analyses, follow-up in months was subsequently converted to years and multiplied by the number of eyes to obtain person-years at risk. Although we did not stratify the time periods in analyses, for better description of studies, we classified the follow-up into five categories: immediate-term (<1 month), short-term (1 to <6 months), medium-term (6 to <12 months), long-term (≥12 months), and not reported (NA). Moreover, the specific PCPIOL model used, number of included eyes, mean age, baseline refractive error (including mean and SD, as well as proportions for different refractive error categories when available), and postoperative vault measures were extracted.

We classified harms and complications reporting into three categories: (1) reported specific harms/complications, (2) explicitly stated that no harms/complications occurred (coded as zero events), and (3) no mention of harms/complications (coded as not reported, NR). Harms were recorded when reported, including cases of IOL explantation, IOL rotation or displacement, anterior capsular opacification, cataract formation, iris atrophy, retinal detachment, macular oedema, pupillary block, glaucoma, pupil ovalisation, intraocular infection, endothelial failure, and iris cyst. When outcome data were unavailable for a specific variable, the study was excluded from the pooled analysis for that endpoint. Studies providing subgroup analyses (eg, based on refractive error, vault, or surgical technique variations) had all available subgroup data extracted and treated as independent entries in the database. In comparative studies assessing PCPIOL vs other refractive procedures, only data pertaining to PCPIOLs were included when extractable.

• **QUALITY ASSESSMENT:** We assessed the potential risk of bias of the included studies using a modified Newcastle–Ottawa Scale, as adapted by Cochrane Eyes and Vision,[15,16] to evaluate common epidemiological biases across a variety of study types. The tool comprises five domains: selection bias, measurement bias (exposure), measurement bias (outcome), confounding in analyses, and reporting bias. Each domain was rated as low, moderate, or high risk of bias according to predefined criteria. An overall risk of bias judgement was determined by combining the assessments from all individual domains. A study was classified as having an overall high risk of bias if at least one domain was rated as high risk, regardless of the ratings in other domains. If three or more domains were rated as moderate risk, the study was also considered to have a high overall risk of bias. Studies with all domains rated as low risk were classified as having an overall low risk of bias. If one or two domains were rated as moderate risk and none as high risk, the overall classification was moderate. Risk of bias was independently assessed by two reviewers for English-language studies (M.B., M.L.P.) and by two reviewers for Chinese-language studies (vs.F.C., S.N.), with a third senior reviewer (R.Q. for English studies; Y.Z. for Chinese studies) verifying consistency. Disagreements were resolved through discussion and consensus, with arbitration by the senior reviewer when required.

• **STATISTICAL ANALYSIS:** We generated descriptive summaries of study and patient characteristics. Continuous variables, including mean age and preoperative refractive error, were pooled using inverse-variance random-effects meta-analyses of means with 95% CIs, whereas categorical variables were summarized as counts and percentages.

For harm outcomes, each study or eligible subgroup contributed the number of events and the person-time at risk, calculated as eye-years from the number of eyes multiplied by the follow-up duration (converted to years). We estimated incidence rates using over-dispersed count regression with negative binomial generalized linear models in a frequentist framework, applying a log link and including person-years as an exposure term. Clustering by study was used to account for non-independence of multiple entries from the same source. We combined estimates from all included studies with relevant data, regardless of study type. Given the complexity of analyzing harms, we present a detailed description of our justification and approaches to meta-analyses in File 2, Supplementary materials.

For a clearer clinical interpretation, incidence rates expressed per 1000 person-years can be translated into approximate cumulative risks over time. For example, a rate of 3 events per 1000 person-years implies that, if the underlying hazard remains stable, one would expect roughly 3 events in 1000 eyes observed for 1 year, or approximately 3 events in 100 eyes over a 10-year period. As a sensitivity analysis, we re-fitted the same models under a Bayesian framework to assess the robustness of estimates and quantify uncertainty using credible intervals. As a second sensitivity analyses, we applied two alternative approaches to the handling of studies classified as "no mention of harms/complications" in the initial coding scheme. In the primary analysis, these studies were treated as having missing data for that outcome (ie, excluded from the pooled estimate for that complication). In the sensitivity analysis, the same studies were instead assumed to have experienced zero events for that outcome and were included in the pooled estimates accordingly.

We conducted exploratory meta-regressions to investigate potential associations between complication rates and study-level covariates, including follow-up length, year of publication, mean baseline refractive error, PCPIOL model and country. A *P*-value <.05 was considered statistically significant. Analyses were conducted in StataNow (Version 19.5. College Station, TX, USA: StataCorp, 2025).

RESULTS

A total of 16,438 records were identified from the following databases: PubMed ($n = 4892$), Scopus ($n = 5024$), WANFANG Data ($n = 2309$), CNKI ($n = 4213$). Five researchers (M.B., vs.F.C., S.N., M.L.P., Y.Z.) conducted screening of titles and abstracts. After screening titles and abstracts, 621 articles underwent full-text review. Conflicts were resolved through consensus (Figure 1).

Finally, we included 214 studies providing 258 ICL datasets with 45,027 eyes in analyses. Included studies comprised 19 randomized clinical trials, 14 non-randomized

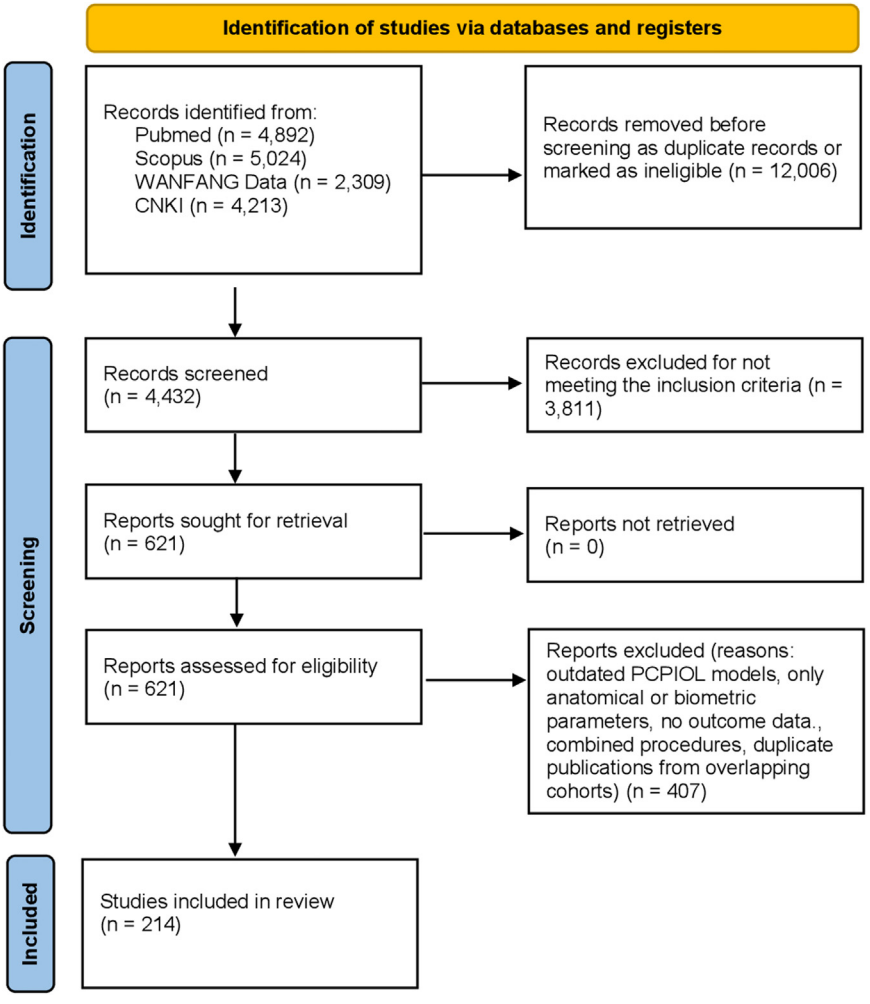

FIGURE 1. PRISMA flow diagram of study selection. Flow of records through identification, screening, eligibility assessment, and final inclusion in the meta-analysis.

clinical trials, 25 prospective observational studies, 8 cohort studies, 8 case-control studies, 19 case series, and 121 retrospective hospital record analyses. In total, 42 studies included more than one study arm, of which 39 had two arms and 3 had three arms, while the remaining 172 studies had a single arm; these arms were analyzed independently and treated as separate studies in the quantitative synthesis.

Most were conducted in China ($n = 123$), followed by Spain ($n = 18$), Japan ($n = 12$), Egypt ($n = 10$), and India ($n = 9$). Additional studies came from Turkey ($n = 8$), Germany ($n = 5$), Korea ($n = 4$), the United States ($n = 4$), and Portugal ($n = 3$), and the Czech Republic ($n = 2$). Eight countries - Arabia, Argentina, Croatia, Iraq, Italy, Thailand, the United Kingdom, and Vietnam - were represented by a single study, for a total of 206 single-country studies. In addition, five studies were conducted across multiple countries, and three did not report the exact country of origin.

• **QUALITY ASSESSMENT:** Overall, the large majority of the studies (204, 95.3%) were judged at high risk of bias, with 9 (4.2%) at moderate risk, and only 1 (0.5%) at low risk (File 3, Supplementary materials). In the selection bias domain, most studies were at moderate (117; 54.7%) or high risk (45; 21.0%), largely due to small sample sizes and single-centre designs. Measurement bias for exposure was consistently low (100%) as expected in studies of surgical interventions following people post procedure. Conversely, outcome measurement bias was high (122; 57.0%) or moderate (47; 22.0%) in the majority of studies, mainly due to poor or absent reporting of adverse event detection, or to studies that merely reported no complications without specifying the detection methods or providing detailed outcome data. Risk of confounding in analyses was predominantly high (120; 56.1%) or moderate (82; 38.3%), typically reflecting a lack of multivariable analysis or only minimal statistical adjustment in the non-randomized studies. Reporting bias was high in 126 (58.9%) and moderate in 75 (35.0%) studies, most often due to the absence of a study protocol.

• **DEMOGRAPHIC DATA:** The total number of eyes included across all studies was 45,027, with a mean age of the patients of 28.6 (95% CI: 28.0 to 29.2) years. The reported follow-up duration across studies had a median of 12 (IQR 6-13.2) months. Follow-up was stratified into four predefined categories: immediate term (< 1 month; 13 studies, 1060 eyes, 2.4%), short term (1 to < 6 months; 32 studies, 2754 eyes, 6.1%), medium term (6 to < 12 months; 46 studies, 4901 eyes, 10.9%), and long term (≥ 12 months; 115 studies, 15,547 eyes, 34.5%). In 8 studies (20,765 eyes, 46.1%), the follow-up period could not be determined, which may bias incidence estimates toward underestimation of late events.

The majority of cases involved the ICL V4c (EVO) model (41,743 eyes; 92.7%), followed by the ICL (2164 eyes; 4.8%), the IPCL (766 eyes; 1.7%), and the Eyecryl (354 eyes; 0.8%). The pooled mean refractive error across studies was − 8.8 diopters (95% CI: −9.5 to − 8.1). The pooled mean postoperative vault was 496 μm (95% CI: 477 to 515).

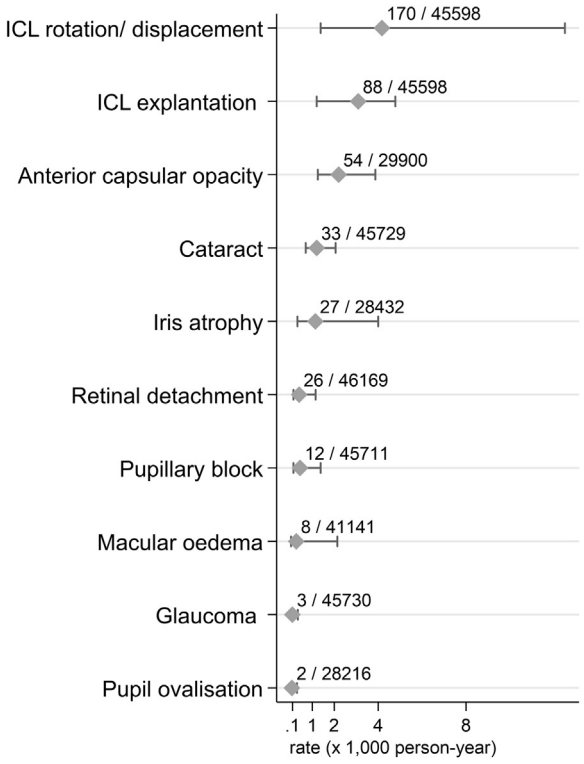

FIGURE 2. Harms incidence rates. Incidence rates (gray diamond) and 95% CIs (caps) for each harm with the raw sum of events and person-years based on a frequentist model excluding studies with missing data. The x-axis corresponds to rates per 1000 person-years.

Baseline characteristics for 45,027 eyes are reported in File 4, Supplementary materials.

• **ADVERSE EVENTS:** Across the 214 included studies, 29 studies (3297 eyes, 7.3%) did not mention harms or complications, 103 studies (8962 eyes, 19.9%) explicitly reported that no harms or complications occurred, and 82 studies (32,768 eyes, 72.8%) reported the specific harms or complications.

Figure 2 presents incidence rate for each harm with the raw sum of events and person-years based on a frequentist model excluding studies with missing data. Table 1 shows incidence rates (95% CI) in numerical form based on different assumptions on missing data and analytic framework (frequentist vs. Bayesian models). These data will be discussed in detail for each type of harm as follows. A projection of the expected number of cases at 5 years will be provided in a following paragraph by incorporating the effect of mean follow-up time in analyses.

TABLE 1. Incidence Rates of Complications After Posterior Chamber Phakic Intraocular Lens Implantation, Expressed As Events Per 1000 person-years

Variable	Events	Excluding Studies Not Stating That There Were No Adverse Events		Missing Events Imputed As Zero When No Mention	
		Studies Person-year	Incidence rate (per 1000 person-year)	Studies Person-year	Incidence rate (per 1000 person-year)
ICL rotation/ displacement	170	160 45,598	4.17 (1.38-12.5)	185 47,518	3.80 (2.23-6.47)
ICL explantation	88	170 45,598	3.09 (1.20- 4.78)	176 45,598	2.83 (1.83-4.36)
Anterior capsular opacity	54	157 29,900	2.20 (1.25-3.87)	157 30,633	2.02 (1.54-3.26)
Cataract	33	161 45,729	1.20 (0.70-2.06)	161 45,729	1.11(0.65-2.04)
Iris atrophy	27	158 28,432	1.14 (0.32-4.00)	186 30,353	1.05 (0.30-3.64)
Retinal detachment	26	157 46,169	0.40 (0.14-1.15)	186 48,089	0.37 (0.13-1.07)
Macular oedema	8	175 41,141	0.27 (0.03-2.14)	185 47,979	0.25 (0.03-1.94)
Pupillary block	12	160 45,711	0.44 (0.14-1.38)	185 47,631	0.41 (0.13-1.25)
Glaucoma	3	161 45,730	0.09 (0.02-0.34)	186 47,650	0.08 (0.02-0.32)
Pupil ovalisation	2	156 28,216	0.07 (0.02-0.30)	181 30,136	0.07 (0.02-0.29)
Infections	0				
Endothelial failure	0				
Iris cyst	0				

Primary estimates are obtained from frequentist negative binomial models (95% CIs). Models in which studies with no mention of complications were imputed as having zero events are presented as a sensitivity analyses.

TABLE 2. Meta-Regression of Complication Incidence After Posterior Chamber Phakic Intraocular Lens Implantation

Variable	Follow-Up (Per 1 Year)	Publication Year (Per 1 Year)	Non-Asian Studies (vs Asian)	Refractive Error (Per −1 D Only Myopes)
ICL rotation/ displacement	0.67 (0.53-0.83)*	1.11 (0.89-1.34)	2.56 (0.86-7.57)	0.89 (0.773-1.03)
ICL explantation	0.92 (0.74-1.13)	0.97 (0.86-1.10)	3.56 (1.45-8.74)*	0.79 (0.66-0.93)*
Anterior capsular opacity	1.19 (1.00-1.42)	0.84 (0.77-0.92)*	2.25 (0.69-7.32)	1.16 (0.99-1.37)
Cataract	1.22 (1.09-1.37)*	0.93 (0.83-1.04)	6.45 (1.97-21.1)*	1.23 (1.01-1.49)
Iris atrophy	1.47 (1.08-2.00)*	0.81 (0.68-0.95)*	13.5 (1.06-171)*	2.29 (1.40-3.74)*
Retinal detachment	0.86 (0.55-1.34)	1.55(0.73-3.28)	NE*	1.14 (0.85-1.53)

Incidence rate ratio (IRR, 95% CI) are reported to investigate covariate effects.
*The 95% CI does not include 1 or equality. NE: not estimable.

ICL rotation/displacement and explantation

The most frequent complication was ICL rotation or displacement, reported in 170 eyes, with a pooled incidence rate of 4.17 (95% CI, 1.38-12.50) per 1000 person-years (Table 1). In practical terms, this corresponds to an expected frequency of approximately 4 cases for every 100 eyes observed over a 10-year period, acknowledging that actual risks will vary across centers, surgical techniques, and patient characteristics. Estimates from the frequentist negative binomial meta-regression were similar to those from the corresponding Bayesian baseline model, although the latter yielded greater precision. When studies not mentioning this complication were assumed to have zero events, the rate slightly decreased to 3.80 to 3.85 per 1000 person-years.

ICL explantation occurred in 88 eyes, corresponding to an incidence rate of approximately 3 cases per 1000 person-years (3.09; 95% CI, 1.20-4.78). When missing data were imputed as zero events, the rate remained comparable (around 2.8 per 1000 person-years) (Table 1).

Sensitivity analyses using Bayesian negative binomial models yielded incidence estimates that were highly consistent with the frequentist models, with slightly narrower credible intervals and no clinically meaningful discrepancies (File 5, Supplementary Materials).

Meta-regression (Table 2) indicated that ICL rotation/displacement rates decreased significantly with longer follow-up (IRR, 0.67; 95% CrI, 0.53-0.83), with no association with publication year. Temporal trends for ICL explantation were inconclusive, but rates were lower for high myopes (0.79 per 1 diopter more myopic; 95% CI, 0.66-0.93)

To enhance clinical interpretability, Figure 3 illustrates the predicted absolute number of events per 1000 eyes at 5 years for Asian and Non-Asian cohorts, providing an at-a-glance comparison of the expected burden of each complication.

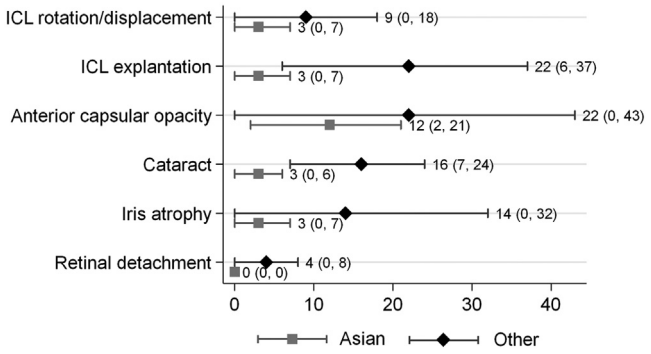

FIGURE 3. Predicted absolute number of complications per 1000 eyes at 5 years. Predicted cumulative numbers of selected complications per 1000 eyes over 5 years for Asian and Non-Asian cohorts, derived from negative binomial meta-analytic models. Complications shown include ICL rotation/displacement, ICL explantation, anterior capsular opacification, cataract, iris atrophy, and retinal detachment. (ICL = indicates implantable collamer lens).

Anterior segment adverse events

Anterior capsular opacification was reported in 54 eyes, with an incidence of about 2 cases per 1000 person-years (2.20; 95% CI, 1.25-3.87; Table 1), followed by cataract (about 1.2 cases) and iris atrophy (about 1.1 cases) per 1000 person-years (Table 1). Both cataract (IRR: 1.22, 1.09-1.37) and iris atrophy (1.47, 1.08-2.00) were more frequent with longer follow-up (Table 2). Rates of anterior capsular opacification and iris atrophy decreased with more recent publication year (Table 2). Bayesian sensitivity analyses produced comparable estimates, confirming the robustness of the findings (File 5, Supplementary Materials).

Pupillary block, glaucoma, pupil ovalisation were recorded in 0.1 to 0.4 cases per 1000 person-years (Table 1). No cases of infection, endothelial failure, or iris cyst were identified.

Posterior segment adverse events

Retinal detachment was documented in 26 eyes, with an incidence of about 0.4 per 1000 person-years (0.40; 95% CI, 0.14-1.15; Table 1) without evidence of temporal trends (Table 2). Macular oedema was observed in 8 eyes, with an incidence of about 0.3 per 1000 person-years (0.27; 95% CI, 0.03-2.14; Table 1), with too few cases for covariate analysis.

Other covariate effects

Compared to 132 Asian studies (188 ICL datasets), we found that 58 studies (71 ICL datasets) conducted elsewhere consistently reported higher complication rates, a pattern that persisted after adjusting for follow-up duration. (Table 2). Data were insufficient to cf complication rates between newer lens models (IPCL, Eyecryl) and the ICL. Finally, in 174 datasets including only myopes, we found ICL explantation decreased with increasing myopia, whereas iris atrophy increased (Table 2).

DISCUSSION

This systematic review and meta-analysis, encompassing over 45,000 eyes from 214 studies, provides the most comprehensive synthesis to date of the harms profile and complications associated with PCPIOL implantation.

Contemporary models, including the V4c ICL, Eyecryl, and IPCL, have evolved from earlier non-port designs to central-port versions that improve aqueous flow and reduce the risk of anterior subcapsular opacities. These innovations have enhanced both safety and surgical convenience, most notably by eliminating the need for peripheral iridotomy.[5,17–21]

Over two decades, research on PCPIOLs has progressed from small single-centre case series to larger multicentre cohorts and a few trials, establishing strong refractive effectiveness and generally low rates of serious complications. However, most available studies are observational, underpowered for rare events, and limited by heterogeneous outcome definitions and short follow-up (12 months), making long-term risk of harm difficult to quantify. Many reports do not describe how complications were detected, and geographic clustering (notably Chinese series) further limits generalizability.

The value of this analysis lies in providing incidence rates that are directly interpretable in everyday practice. The distinction between early mechanical issues (rotation, vault-related complications) and later anterior-segment changes (capsular opacification, cataract, iris atrophy) offers a clinically actionable framework for postoperative care and long-term surveillance. The absolute predicted numbers shown in Figure 2 further summarize these patterns, highlighting the low overall burden of serious complications.

The most frequent complication was rotation or displacement (~4/1000 person-years), usually related to sizing or vaulting errors. Explantation occurred at ~3/1000 person-years, lower than reported in previous reviews (2%-3%).[1,17,18] Early explantations were often linked to vaulting or pigment dispersion, while later cases reflected endothelial loss, cataract, or lens opacification. However, reasons for explantation were inconsistently reported across studies, and patient-reported symptoms such as glare or dysphotopsias, as well as sizing methods and vault parameters, were rarely described in sufficient detail to allow formal analysis. This heterogeneity in underlying causes may explain why our results showed a more evenly distributed pattern over time, despite overall rates remaining comparable to published data. Clinically, these data emphasize the need for early postoperative confirmation of centration, axis alignment in toric models, and appropriate vault, as most modifiable risks emerge in the initial postoperative period.

Anterior capsular opacification and cataract formation have been estimated at ~2/1000 and ~1.2/1000 person-years, respectively. Historically, anterior subcapsular cataract limited adoption of PCPIOLs, with rates exceeding 6% with 1.2% progressing to visually significant cataract, most often in older or highly myopic patients, using non-port designs.[5,1] In contrast, central-port ICLs show markedly lower rates (0.17%), supporting the role of lens design rather than surgical technique and intraoperative factors in cataractogenesis.[19] From a practical standpoint, cataract risk should still be discussed during counselling - particularly with older or highly myopic patients - but is markedly lower with current designs.

Posterior segment events were rare. Retinal detachment (~0.4/1000 person-years) and macular edema (~0.3/1000) were broadly comparable to background risks in high myopia, suggesting PCPIOL implantation does not substantially increase posterior segment risk. A recent 10-year retrospective study comparing RD incidence in high myopes with and without ICL implantation demonstrated that RD occurred in 1.71% of the ICL group and 1.25% of controls ($P = .773$), with survival analysis showing no significant difference ($P = .59$).[12] Notably, no cases of endophthalmitis were identified across our included reports, with this complication remaining confined to isolated anecdotal case reports. This provides reassurance that PCPIOL implantation does not appear to introduce additional posterior-segment risk beyond that intrinsic to high myopia itself. Nonetheless, failure to report endophthalmitis may be due to underreporting, given that over 45,000 eyes where included in our review.

While endothelial cell loss is a concern with any intraocular surgery, no cases of corneal decompensation or endothelial failure were reported in our cohort. This is reassuring given that previous studies have shown an initial postoperative endothelial cell density loss of ~6.5% in the first year after ICL implantation, followed by ~1.8% annually.[5] In previous reports, long-term data with other posterior chamber pIOLs, including Eyecryl and IPCL, suggest cumulative losses ranging from ~3% to 7% over 5 years.[20,21] Taken together, our absence of corneal decompensation supports the low-risk of central-port PCPIOLs, while underscoring the need for incorporating periodic specular microscopy into long-term follow-up, especially in older patients or those with borderline preoperative ECD.

Clear temporal patterns emerged. Mechanical events such as rotation or displacement, which were the most frequent complications in our synthesis, decreased with time, reflecting early instability that stabilizes postoperatively, whereas other anterior segment complications increased with longer follow-up. More recent studies reported lower anterior complication rates overall, consistent with advances in lens design, sizing methods (including increasing use of sulcus-based measurements), patient selection and surgical techniques. However, sizing methods (eg, UBM-based approaches and nomograms) and vault-related parameters were inconsistently reported across studies, precluding a formal quantitative assessment of whether these approaches reduce mechanical events and vault-related complications. This temporal profile reinforces a dual follow-up strategy: intensive early assessment to detect mechanical issues, and structured long-term review to identify late anterior-segment changes.

Geographic effects were evident from our analysis: studies conducted in Asia reported lower complication rates, even after adjusting for follow-up. This may reflect differences in ocular anatomy, ametropia prevalence, patient selection, surgeon experience, perioperative protocols, or reporting practices and should be interpreted with caution. Data were insufficient to draw firm, head-to-head comparisons among models (ICL, IPCL, Eyecryl), although the overall profile across models remained favorable.

The findings in this review has several limitations. Most included studies were observational, and 95% were judged at high risk of bias. Follow-up was generally short (median 12 months), and in 46% of eyes the duration could not be determined, likely leading to underestimation of late complications such as cataract or endothelial failure. Adverse event definitions were heterogeneous, and nearly one-fifth of studies simply reported "no complications" without describing detection methods. Publication bias is possible, particularly given the predominance of private-practice series. Finally, the evidence base is heavily weighted toward ICL V4c, with limited data for IPCL and Eyecryl, reducing the strength of model-level comparisons; nonetheless, ICL V4c is the most commonly used model in most settings.

Our findings support PCPIOLs as a low-risk refractive option for appropriately selected patients. From a clinical perspective, these findings support a structured two-phase follow-up model: an early phase focused on centration, vault and toric stability, and a long-term phase centered on endothelial monitoring and anterior-segment assessment. The use of central-port designs appears to lower the risk of anterior subcapsular opacities and eliminate the need for peripheral iridotomy, supporting their preferential adoption.

This meta-analysis provides the most comprehensive synthesis to date of PCPIOL harms, incorporating more than 45,000 eyes from both English- and Chinese-language studies. Despite our broad data collection, these estimates must be considered with caution, taking into account the uncertainty around some estimates, and the limited methodological quality of the studies for what concerns reporting of harms. Since most of the evidence was produced in Asia, the higher rate of adverse events in non-Asian studies is concerning, and studies are needed to rule out underreporting as compared to clinical differences in Asian studies. This reinforces the need for large studies that prospectively and actively collect Adverse Events of ICL

implantation and other refractive surgical techniques. Finally, we selected a statistical approach yielding marginal or population-average estimates, which may differ from random effects models; further guidance is necessary on model selection in meta-analyses of count data with several zero event studies (Supplemental file 2).

Acknowledging these uncertainties, these findings provide the most reliable basis currently available to support patient counseling and guide postoperative surveillance worldwide, while further underscoring the urgent need for standardized, high-quality multicenter registries to more definitively clarify long-term risks.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Maria Laura Passaro: Writing – original draft, Methodology, Data curation. **Matilde Buzzi:** Writing – original draft, Data curation. **Riaz Qureshi:** Supervision, Methodology. **Yuhao Zou:** Validation, Methodology. **Ving Fai Chan:** Validation, Supervision, Investigation. **Rita Mencucci:** Supervision. **Ersilia Lucenteforte:** Formal analysis. **Vito Romano:** Supervision, Conceptualization. **Gianni Virgili:** Supervision, Methodology, Formal analysis.

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