

# Hydrophobic versus hydrophilic acrylic intraocular lens on posterior capsule opacification: a Meta-analysis

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## Abstract

• **AIM:** To conduct a Meta-analysis pooling randomized controlled trials (RCTs) to compare hydrophobic with hydrophilic acrylic intraocular lenses in terms of posterior capsule opacification (PCO) development.

• **METHODS:** Electronic databases including PubMed, Embase, and the Cochrane Library were queried from their starting till January 2020. RCTs investigating the impact of hydrophobic versus hydrophilic acrylic intraocular lenses on PCO were considered eligible in this study. The pooled effect estimates were calculated using the random-effects model.

• **RESULTS:** Thirteen RCTs comprising of 939 patients (1263 eyes) were covered in this study. Patients with hydrophobic acrylic intraocular lenses had a lower PCO score than those with a hydrophilic acrylic intraocular lenses [standard mean difference: -1.80; 95% confidence interval (CI): -2.62 to -0.98;  $P < 0.001$ ]. Moreover, the frequency of neodymium-doped yttrium aluminum garnet (Nd:YAG) capsulotomy in patients with hydrophobic acrylic intraocular lenses was significantly lower than patients with hydrophilic acrylic intraocular lenses (relative risk: 0.38; 95%CI: 0.20-0.71;  $P = 0.003$ ).

• **CONCLUSION:** These findings suggest that hydrophobic acrylic intraocular lenses are superior to hydrophilic acrylic intraocular lenses in patients after cataract surgery due to lower PCO score and reduced Nd:YAG capsulotomy. While similar studies are conducted by other researchers, the present study conducted subgroup analyses that show superior results with hydrophobic lenses in trials conducted in western countries.

• **KEYWORDS:** hydrophobic acrylic intraocular lens; hydrophilic acrylic intraocular lens; posterior cataract opacification; Nd:YAG capsulotomy; Meta-analysis

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## INTRODUCTION

Posterior capsule opacification (PCO) is regarded as the most frequent complication and serious hurdle following successful cataract surgery. It starts from the beginning of the extracapsular extraction with intraocular lens implantation and subsequently develops after a few years after undergoing the procedure, and its prevalence ranges from <5% up to 50%<sup>[1-3]</sup>. PCO involves the growth and proliferation of lens epithelial cells, causing lower visual acuity<sup>[4]</sup>. Although neodymium-doped yttrium aluminum garnet (Nd:YAG) laser capsulotomy was effective for treating PCO to date, it is associated with several complications<sup>[5]</sup>. Therefore, the identification of an effective strategy to prevent the progression of PCO in patients after cataract surgery is considered important.

The pathogenesis of PCO is multifactorial, and the incidence of PCO varies<sup>[6]</sup>. Several risk factors have already been identified for the progression of PCO, which include edge design, intraocular lens design, haptic design, and lens material<sup>[4,7]</sup>. Currently, there are several techniques introduced for preventing PCO, such as intraocular lens material, surgical techniques, and therapeutic agents<sup>[8-10]</sup>. Acrylic materials show a low ability to stimulate the proliferation of cells in the capsular bag<sup>[11]</sup> and intraocular lenses with sharp edge design might assist in inhibiting migration of lens epithelial cells<sup>[12]</sup>, showing an association with the low rate of PCO. Numerous long-term observational studies revealed the association of hydrophobic acrylic intraocular lenses with an extended period in patients who need Nd:YAG capsulotomy, lowering the risk or severity of PCO<sup>[13-15]</sup>. Still, inconsistent results were obtained from the published randomized controlled trials (RCTs). Thus, this systematic review and Meta-analysis was carried out to obtain valid evidence on the effects of hydrophobic and hydrophilic acrylic intraocular lenses on the progression of PCO and Nd:YAG capsulotomy. While similar studies were conducted by other researchers, the present study conducted subgroup analyses.

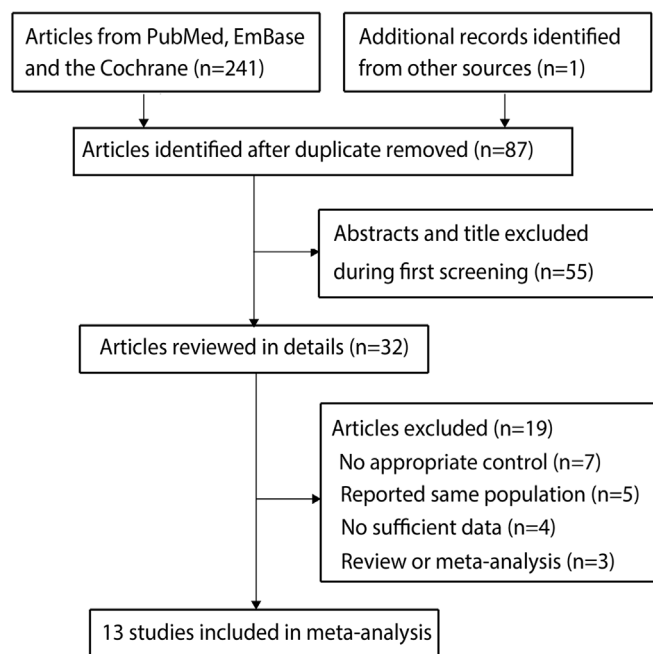
## MATERIALS AND METHODS

**Data Sources, Search Strategy, and Selection Criteria** The report of this systematic review and Meta-analysis followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement<sup>[16]</sup>. The studies that compared the effects of hydrophobic versus hydrophilic acrylic intraocular lenses on the progression of PCO and incidence of Nd:YAG capsulotomy in patients after undergoing cataract surgery were considered eligible in this study. Only English publications were considered. PubMed, Embase, and the Cochrane Library were systematically searched for relevant studies from the beginning of the databases till January 2020. The core search terms included “cataract” AND “intraocular lens” AND “posterior capsule opacification” AND “hydrophilic” AND “hydrophobic” AND “randomized controlled trials”. The complete trials that were not yet published were also checked in <http://clinicaltrials.gov/> (US NIH) and metaRegister of Controlled Trials. The references of the retrieved studies were also manually searched to obtain new eligible studies.

Two authors independently carried out the literature search and study selection, and any inconsistencies between them were resolved by mutual discussions. The inclusion criteria were as follows: 1) study design: studies with RCT design; 2) patients: patients after undergoing cataract surgery; 3) intervention: hydrophobic acrylic intraocular lens; 4) control: hydrophilic acrylic intraocular lens; 5) outcomes: PCO score and Nd:YAG capsulotomy; 6) publication language: studies published in English. The studies with high methodological quality were used when multiple studies reported data from similar populations.

**Data Collection and Quality Assessment** The titles, abstracts, and data were separately assessed by two authors, and any disagreement was settled by discussion. A third author was approached if the discussion did not reach any consensus. The extracted information was entered into a structured characteristics table, and data extracted included the first authors' surname, country, publication year, number of eyes and patients, mean age, male (%), bilateral/unilateral, piece number, optic material, optic edge, the details of hydrophobic and hydrophilic acrylic intraocular lenses, outcomes and follow-up period. Study quality was evaluated using the Jadad scale, which was scored by domains including randomization, blinding, allocation concealment, withdrawals and dropouts, and the application of intention-to-treat analysis<sup>[17]</sup>. A high-quality study had a Jadad score of 4 or 5.

**Statistical Analysis** The effect of hydrophobic or hydrophilic acrylic intraocular lenses on PCO was assigned as a continuous variable, and the incidence of Nd:YAG capsulotomy was used as a categorical variable. If the pooled effects were estimated



**Figure 1** The study selection process according to PRISMA flowchart.

by standard mean differences (SMDs) and relative risk (RR) with corresponding 95% confidence intervals (CIs), then the random-effects model was used<sup>[18-19]</sup>. The index of  $I^2$  and  $Q$  statistics were used for assessing heterogeneity across the included trials, and  $I^2 > 50.0\%$  or  $P < 0.10$  was considered to suggest significant heterogeneity<sup>[20-21]</sup>. Sensitivity analyses were conducted to evaluate the robustness of the pooled conclusions by sequentially excluding each trial<sup>[22]</sup>. The source of heterogeneity was assessed by subgroup analyses, and the differences between subgroups were assessed based on country, age, bilateral/unilateral, length of follow-up, and study quality<sup>[23]</sup>. Both qualitative and quantitative methods, including a funnel plot, Egger, and Begg tests, were used for evaluating publication bias<sup>[24-25]</sup>. The  $P$ -value for pooled results was two-sided, and a  $P$  value of less than 0.05 was regarded as statistically significant between hydrophobic and hydrophilic acrylic intraocular lenses. The STATA software (Version 10.0; StataCorp, Texas, USA) was used for conducting all statistical analyses.

## RESULTS

**Literature Search** A total of 241 articles were identified using the predefined search strategies, and 1 additional study was identified by reading through the reference lists of the articles. After removing the duplicates and irrelevant articles, the full-texts of 32 studies were evaluated. Of these, 19 studies were excluded due to being review or Meta-analysis ( $n=3$ ), no appropriate control ( $n=7$ ), studies that included similar populations ( $n=5$ ), and no sufficient data ( $n=4$ ). The remaining 13 eligible RCTs were finally selected for a Meta-analysis<sup>[26-38]</sup>. The detailed literature search process are displayed in Figure 1.

**Study Characteristics** Table 1 summarized the characteristics of the included studies<sup>[26-38]</sup>. A total of 939 patients, with 1263 eyes from 13 RCTs, were identified, and these were published from 2005-2018. Four trials were completed in eastern countries (India, Korea, and Japan), and the other 9 trials were conducted in western countries (UK, Sweden, and Austria). Seven trials focused on patients with bilateral PCO, and the remaining 6 trials enrolled patients with unilateral PCO. The follow-up duration of the studies ranged from 1.0-4.0y, and 6 studies had a quality score of 4, and 7 studies were scored 3.

**Posterior Capsule Opacification Score** A total of 11 RCTs reported the comparison of hydrophobic with hydrophilic acrylic intraocular lenses with regard to PCO score. The pooled results revealed that hydrophobic acrylic intraocular lenses were associated with a lower PCO score when compared with hydrophilic acrylic intraocular lenses (SMD: -1.80; 95%CI: -2.62 to -0.98;  $P < 0.001$ ; Figure 2). Moreover, substantial heterogeneity across studies was found ( $I^2 = 96.8\%$ ;  $P < 0.001$ ). Sensitivity analysis revealed that the conclusion was unchanged even after excluding any particular trial (Figure 3).

**Nd:YAG Capsulotomy** All included trials reported the incidence of Nd:YAG capsulotomy following wearing hydrophobic and hydrophilic acrylic intraocular lenses. After pooling all studies, the use of hydrophobic acrylic intraocular lenses significantly reduced Nd:YAG capsulotomy when comparing with hydrophilic acrylic intraocular lenses (RR: 0.38; 95%CI: 0.20-0.71;  $P = 0.003$ ; Figure 4), and significant heterogeneity was detected ( $I^2 = 60.6\%$ ;  $P = 0.002$ ). Sensitivity analysis revealed that the pooled conclusion was robust (Figure 5).

**Subgroup Analyses** Subgroup analyses for PCO score and incidence of Nd:YAG capsulotomy were also evaluated to minimize the potential heterogeneity and compare hydrophobic with hydrophilic acrylic intraocular lenses in specific subpopulations. Although a significant difference between hydrophobic and hydrophilic acrylic intraocular lenses on PCO score was observed in most of the subsets, no significant difference was observed on PCO score between hydrophobic and hydrophilic acrylic intraocular lenses when pooled trials were conducted in Western countries, the mean age of the patients was  $\geq 70.0y$ , patients with bilateral PCO, trials with long-term follow-up, and trials with a high-quality score. The differences between subgroups showed statistically significant association when stratified by age, bilateral/unilateral, and study quality (Table 2). In addition, hydrophobic acrylic intraocular lenses showed association with lower incidence of Nd:YAG capsulotomy when pooled trials were conducted in Western countries, the mean age of the patients was  $\geq 70.0y$ , patients with bilateral PCO, trials with long-term follow-up, and trials with a high-quality score. The differences between subgroups showed statistically significant association when stratified by age, bilateral/unilateral, and study quality (Table 2).

**Table 1 The characteristics of included studies**

Study	Country	Eyes/patients	Age (y)	Male (%)	Bilateral/unilateral	Piece number	Optic material	Optic edge	Hydrophobic	Hydrophilic	Length of follow-up	Study quality
Heatley 2005 <sup>[26]</sup>	UK	106/53	NA	NA	Bilateral	1/1	Acrylic	NA	Alcon AerySof SA60AT	Raynet Centerflex 570H	1.0	3
Kugelberg 2006 <sup>[27]</sup>	Sweden	116/116	72.5	NA	Unilateral	1/1	Acrylic	Square edge	Alcon AerySof SA60AT	BL27, Bausch & Lomb	1.0	4
Hancox 2007 <sup>[28]</sup>	UK	60/30	71.3	43.3	Bilateral	3/3	Acrylic	Square edge	AerySof MA30	ICU	2.0	3
Kang 2008 <sup>[29]</sup>	Korea	100/100	68.0	44.0	Unilateral	3/3	Acrylic	NA	Sensar <sup>®</sup> AR40e	BioVue3 <sup>®</sup>	1.0	3
Kugelberg 2008 <sup>[30]</sup>	Sweden	115/120	72.5	39.0	Unilateral	1/1	Acrylic	Square edge	Alcon AerySof SA60AT	BL27, Bausch & Lomb	1.0	4
Cleary 2009 <sup>[31]</sup>	UK	48/24	73.5	46.0	Bilateral	3/1	Acrylic	NA	Alcon AerySof MA60AC	HumanOpticsMC611MI microincision	2.0	4
Kang 2009 <sup>[32]</sup>	Korea	76/76	67.1	NA	Unilateral	3/1	Acrylic	Double square edge	Sensar AR40e	BioVue 3HSM	1.0	3
Iwase 2011 <sup>[33]</sup>	Japan	126/63	73.4	32.0	Bilateral	1/1	Acrylic	Double square edge	Aerysof SA60AT	Meridian HP60M	2.0	3
Vasavada 2011 <sup>[34]</sup>	India	128/64	66.5	67.2	Bilateral	1/1	Acrylic	Double square edge	Aerysof IQSN60WF	C-flex570C	3.0	4
Gangwani 2011 <sup>[35]</sup>	UK	70/35	72.0	NA	Bilateral	1/1	Acrylic	6.0 mm optic diameter	Aerysof SA60AT	Idea 613 XC	2.0	4
Schriefel 2015 <sup>[36]</sup>	Austria	120/60	75.0	32.0	Bilateral	3/1	Acrylic	Square edge	Y-60H	MI60	4.0	3
Chang 2017 <sup>[37]</sup>	Sweden	120/120	72.8	38.0	Unilateral	1/1	Acrylic	Square edge	Alcon AerySof SA60AT	BL27, Bausch & Lomb	2.0	4
Koshy 2018 <sup>[38]</sup>	UK	78/78	NA	50.0	Unilateral	1/1	Acrylic	Sharp optic edge	Alcon AerySof SA60AT	Superflex <sup>®</sup> intraocular lens	2.0	3

NA: Not applicable.

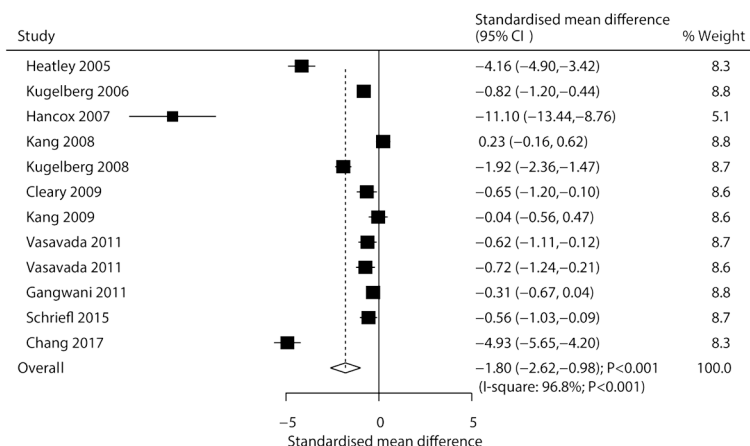


Figure 2 Hydrophobic versus hydrophilic acrylic intraocular lens on posterior capsular opacification score.

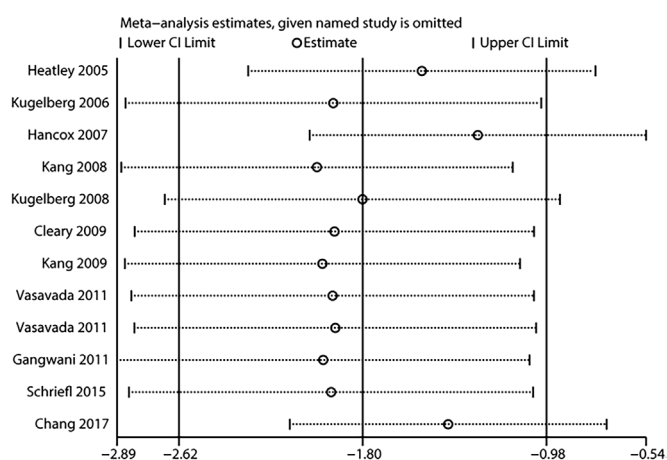


Figure 3 Sensitivity analysis for posterior capsular opacification score.

**Publication Bias** The publication biases for the PCO scores and Nd:YAG capsulotomy are presented in Figures 6 and 7. A significant publication bias for PCO score was found ( $P$ -value for Egger: 0.003;  $P$  value for Begg: 0.064), while no significant publication bias for Nd:YAG capsulotomy was shown ( $P$ -value for Egger: 0.294;  $P$  value for Begg: 0.951). Still, the conclusion of the PCO score was unaltered when adjusted using the trim and fill method<sup>[39]</sup>.

**DISCUSSION**

Currently, both hydrophobic and hydrophilic acrylic intraocular lenses are widely used in cataract surgeries. A study revealed that hydrophobic acrylic intraocular lenses consistently demonstrated a good PCO rate<sup>[40]</sup>. Still, hydrophilic acrylic intraocular lenses might be more applicable to implantation through smaller intraocular lens injection systems because of their mechanical properties<sup>[35]</sup>. The current study included 939 patients (1263 eyes) from 13 RCTs with varied patients' characteristics. This Meta-analysis revealed that hydrophobic acrylic intraocular lenses had a lower PCO score and reduced rate of Nd:YAG capsulotomy compared with hydrophilic acrylic intraocular lenses. Moreover, the effects of hydrophobic

acrylic intraocular lenses were affected by country, age, bilateral/unilateral, and study quality.

Several Meta-analyses already compared the effects of hydrophobic vs hydrophilic acrylic intraocular lenses on the progression of PCO in patients undergoing cataract surgery. A Meta-analysis on 9 RCTs conducted by Li *et al*<sup>[41]</sup> found that the hydrophobic acrylic intraocular lenses were linked with low rates of PCO and reduced rate of laser capsulotomy. Zhao *et al*<sup>[42]</sup> have conducted a Meta-analysis of 11 RCTs and found that the effects of hydrophobic acrylic intraocular lenses were superior to that of hydrophilic acrylic intraocular lenses after cataract surgery in lowering the PCO scores and reduced the rate of Nd:YAG capsulotomy. Nevertheless, two questions were raised from these two studies: 1) the data abstracted were not consistent with the results obtained from the original article, especially for Nd:YAG capsulotomy; 2) these studies just reported pooled effect estimates, and subgroup analyses stratified by study or patients' characteristics were not performed. Therefore, this study was conducted to address these questions and provided comprehensive results regarding the hydrophobic versus hydrophilic acrylic intraocular lenses on the progression of PCO in patients after undergoing cataract surgery.

This Meta-analysis revealed that the PCO score was significantly lower in patients wearing hydrophobic acrylic intraocular lenses, while 3 trials showed no significant differences between hydrophobic and hydrophilic acrylic intraocular lenses. Two trials conducted by Kang *et al*<sup>[29,32]</sup> showed no significant differences in the degree or severity of PCO between the heparin-surface-modified hydrophilic acrylic intraocular lens and hydrophobic acrylic intraocular lenses. They also pointed out that heparin might contribute to some of the preventive effects of PCO, while the degree of preventive effects did not exceed the hydrophobic acrylic intraocular lenses. Moreover, Gangwani *et al*<sup>[35]</sup> found that microincision cataract surgery and small-incision cataract surgery intraocular

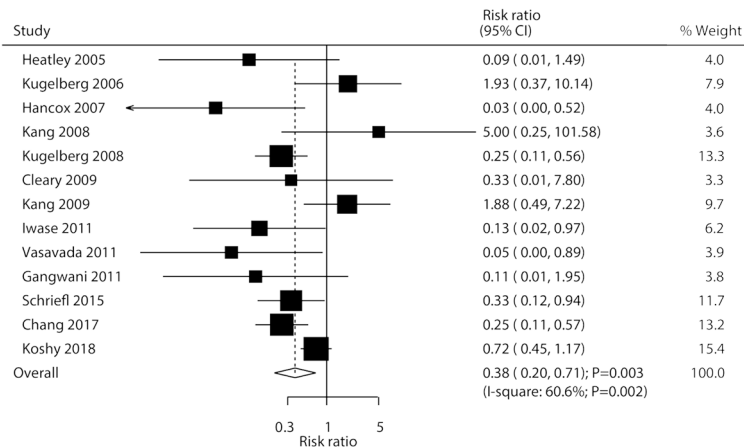


Figure 4 Hydrophobic versus hydrophilic acrylic intraocular lens on the incidence of Nd:YAG capsulotomy.

Table 2 Subgroup analysis for posterior capsular opacification and Nd:YAG capsulotomy rate

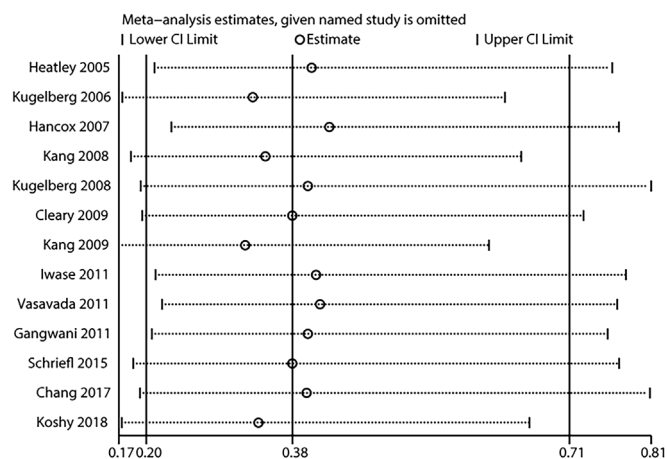
Outcomes	SMD or RR and 95%CI	P	Heterogeneity (%)	P value for heterogeneity	P value between subgroups
Posterior capsular opacification score					
Country					<0.001
Eastern	-0.27 (-0.74 to 0.20)	0.255	74.3	0.009	
Western	-2.69 (-3.87 to -1.51)	<0.001	97.5	<0.001	
Age (y)					<0.001
≥70.0	-2.43 (-3.60 to -1.26)	<0.001	97.3	<0.001	
<70.0	-1.03 (-2.23 to 0.17)	0.092	96.4	<0.001	
Bilateral/unilateral					0.420
Bilateral	-2.06 (-3.14 to -0.97)	<0.001	96.3	<0.001	
Unilateral	-1.47 (-2.87 to -0.07)	0.039	97.8	<0.001	
Follow-up (y)					0.869
1.0	-1.31 (-2.53 to -0.10)	0.035	97.1	<0.001	
2.0-4.0	-2.25 (-3.47 to -1.03)	<0.001	97.1	<0.001	
Study quality					0.009
High	-1.40 (-2.28 to -0.51)	0.002	96.0	<0.001	
Low	-2.69 (-4.50 to -0.88)	0.004	97.9	<0.001	
Nd:YAG capsulotomy rate					
Country					0.884
Eastern	0.52 (0.07 to 3.99)	0.526	71.2	0.015	
Western	0.34 (0.17 to 0.66)	0.002	60.1	0.010	
Age (y)					0.003
≥70.0	0.28 (0.16 to 0.49)	<0.001	23.2	0.244	
<70.0	0.85 (0.07 to 11.01)	0.903	71.8	0.029	
Bilateral/unilateral					0.002
Bilateral	0.18 (0.09 to 0.39)	<0.001	0.0	0.565	
Unilateral	0.66 (0.31 to 1.41)	0.281	69.2	0.006	
Follow-up (y)					1.000
1.0	0.79 (0.21 to 2.98)	0.731	68.8	0.012	
2.0-4.0	0.24 (0.10 to 0.56)	0.001	65.3	0.005	
Study quality					0.019
High	0.30 (0.14 to 0.61)	0.001	30.6	0.206	
Low	0.44 (0.17 to 1.17)	0.100	66.1	0.007	

Nd:YAG: Neodymium-doped yttrium aluminum garnet; SMD: Standard mean differences; RR: Relative risk; CI: Confidence interval.

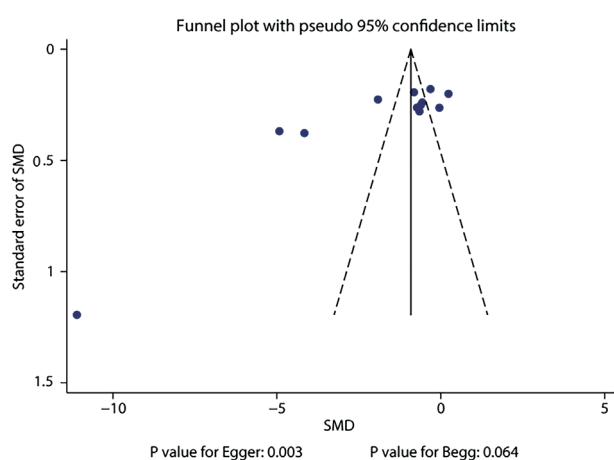
lenses demonstrated similar PCO rates. The potential reason for this could be that the microincision cataract surgery intraocular lenses had good capsular bag stability but a compromised PCO score when compared with small-incision cataract surgery intraocular lenses. Moreover, subgroup analyses revealed superior effects of hydrophobic acrylic intraocular lenses in trials conducted in western countries, mean age of patients

≥70.0y, and irrespective of bilateral/unilateral, long-term follow-up, and study quality.

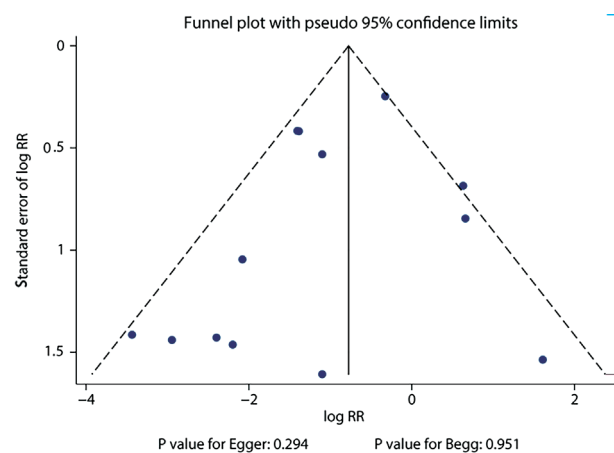
The hydrophobic versus hydrophilic acrylic intraocular lenses showed association with a lower rate of Nd:YAG capsulotomy. It could be because the hydrophobic acrylic intraocular lenses adhered to the collagen membrane, leading to increased attachment of the intraocular lenses to the posterior capsule.



**Figure 5** Sensitivity analysis for the incidence of Nd:YAG capsulotomy.



**Figure 6** Funnel plot for posterior capsular opacification score.



**Figure 7** Funnel plot for the incidence of Nd:YAG capsulotomy.

These results could result in pressure on the atrophy of lens epithelial cells, avoiding migration into the space between the intraocular lenses and posterior capsule<sup>[43]</sup>. Subgroup analyses found superior effects of hydrophobic acrylic intraocular lenses when trials were conducted in western countries, patients with a mean age of  $\geq 70.0y$ , bilateral cataract surgery, long-term follow-up, and high-quality studies. The potential reasons for these results are related to intraocular lens design, surgical techniques, therapeutic agents, and disease severity<sup>[4,9]</sup>.

There are several limitations in this study that should be noted. First, substantial heterogeneity was detected for pooled results, which could not be fully clarified by sensitivity analysis and subgroup analyses. Second, the PCO scores were observed by the degree or severity of the disease, but the WMD was not calculated. Third, publication bias was inevitable since only published articles were analyzed. Finally, there were inherent limitations of any traditional Meta-analysis, as the analysis was based on pooled data, restricting us from conducting more detailed analyses on individual patient data.

This study revealed that hydrophobic acrylic intraocular lenses were associated with lower PCO scores and rate of Nd:YAG capsulotomy when compared with hydrophilic acrylic intraocular lenses, especially for western populations, elderly patients, bilateral cataract surgery, and long-term follow-up. While similar studies were conducted by other researchers, the present study conducted subgroup analyses that showed superior results with hydrophobic lenses in trials conducted in western countries. Further prospective studies should be conducted to investigate other modifiable risk factors on the progression of PCO.

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**Authors' contributions:** Wu Q conceived and supervised the study; Li Y and Wu L analyzed data; Wu Q wrote the manuscript; Wang CY made manuscript revisions. All authors reviewed the results and approved the final version of the manuscript.

**Conflicts of Interest:** Wu Q, None; Li Y, None; Wu L, None; Wang CY, None.

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