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Iridotomy to slow progression of visual field loss in angle-closure glaucoma (Review)

Rouse B, Le JT, Gazzard G

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[Intervention Review]

Iridotomy to slow progression of visual field loss in angle-closure glaucoma

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ABSTRACT

Background

Primary angle-closure glaucoma is a type of glaucoma associated with a physically obstructed anterior chamber angle. For example, contact between the iris and lens at the pupillary margin creates a pupillary block that increases resistance to aqueous outflow. Obstruction of the anterior chamber angle blocks drainage of fluids (aqueous humor) within the eye and may raise intraocular pressure (IOP). Elevated IOP is associated with glaucomatous optic nerve damage and visual field loss. Laser peripheral iridotomy ('iridotomy') is a procedure to eliminate pupillary block by allowing aqueous humor to pass directly from the posterior to anterior chamber, which is achieved by creating a hole in the iris using laser. Iridotomy is used to treat patients with primary angle-closure glaucoma, patients with primary angle-closure (narrow angles and no signs of glaucomatous optic neuropathy), and patients who are primary angle-closure suspects (patients with reversible obstruction). However, the effectiveness of iridotomy on slowing progression of visual field loss is uncertain.

Objectives

To assess the effects of iridotomy compared with no iridotomy for primary angle-closure glaucoma, primary angle-closure, and primary angle-closure suspect.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 10), which contains the Cochrane Eyes and Vision Trials Register; MEDLINE Ovid; Embase Ovid; PubMed; LILACS; ClinicalTrials.gov; and the WHO ICTRP. The date of the most recent search was 10 October 2021.

Selection criteria

Randomized or quasi-randomized controlled trials that compared iridotomy with no iridotomy in primary angle-closure suspects, people with primary angle-closure, or people with primary angle-closure glaucoma in one or both eyes were eligible.

Data collection and analysis

We used standard Cochrane methodology and assessed the certainty of the body of evidence for prespecified outcomes using the GRADE approach.

Main results

We identified four studies (3086 eyes of 1543 participants) that compared iridotomy with no iridotomy in participants (range of mean age 59.6 to 62.9 years) who were primary angle-closure suspects from China, Singapore, or the UK. Study investigators randomized one eye of each participant to iridotomy and the other to no iridotomy. Two studies provided long-term (five or more years) results. We judged the certainty of the evidence as moderate to low across the prespecified outcomes, downgrading for high risk of bias (e.g. performance and detection biases) and imprecision of results.

Meta-analyses of data from two studies suggest that iridotomy probably results in little to no difference in IOP compared with no iridotomy at one year (mean difference (MD) 0.04 mm Hg, 95% confidence interval (CI) −0.17 to 0.24; I^2 = 65%; 2598 eyes of 1299 participants; moderate certainty evidence) and five years (MD 0.12 mm Hg, 95% CI −0.11 to 0.35; I^2 = 0%; 2016 eyes of 1008 participants), and in best-corrected visual acuity measured as logMAR at one year (MD 0.00, 95% CI −0.01 to 0.01; I^2 = 69%; 2596 eyes of 1298 participants; moderate certainty evidence) and five years (MD 0.01, 95% CI −0.01 to 0.03; I^2 = 0%; 2002 eyes of 1001 participants). In terms of gonioscopic findings, eyes treated with iridotomy likely had wider angles in Shaffer grading scale (MD 4.93 units, 95% CI 4.73 to 5.12; I^2 = 59%; 2598 eyes of 1299 participants at one year; MD 5.07, 95% CI 4.78 to 5.36; I^2 = 97%; 2016 eyes of 1008 participants at five years; moderate certainty evidence) and experienced fewer peripheral anterior synechiae (PAS) than eyes that received no iridotomy at five years (risk ratio (RR) 0.41, 95% CI 0.24 to 0.67; I^2 = 28%; 2 studies, 2738 eyes of 1369 participants), but the evidence was less conclusive at one year (RR 0.62, 95% CI 0.25 to 1.54; I^2 = 57%; 3 studies, 2896 eyes of 1448 participants; low certainty evidence). No studies reported data on the proportion of participants with progressive visual field loss during follow-up (the primary outcome of this review), mean number of medications to control IOP, or quality of life outcomes. Low certainty evidence suggests that iridotomy may result in little to no difference in the incidence of acute angle-closure (RR 0.29, 95% CI 0.07 to 1.20; I^2 = 0%; 3 studies, 3006 eyes of 1503 participants). Other ocular adverse events (e.g. eye pain, dry eye, redness of eyes, and ocular discomfort), although rare, were more common in eyes treated with iridotomy than in eyes in the control group.

Authors' conclusions

We did not find sufficient evidence to draw any meaningful conclusions on the use of iridotomy for the purpose of slowing progression of visual field loss. No study reported on progressive visual field loss, the primary outcome of this review. Although there is moderate certainty evidence that iridotomy results in improved gonioscopic findings, in is unclear if these findings translate to clinically meaningful benefits.

PLAIN LANGUAGE SUMMARY

Iridotomy to slow progression of visual field loss in angle-closure glaucoma

What did we study in this review?

Glaucoma is a group of eye diseases that cause damage to the nerve in the eye. If left untreated, glaucoma can lead to blindness. Primary angle-closure glaucoma is a type of glaucoma that happens when the drainage canals ('angles') in the eyes get blocked, like a sink with something covering the drain. This blockage may lead to increased eye pressure, resulting in a decrease of the total area in which objects can be seen in side vision ('visual field').

Iridotomy involves using a laser to create a hole in the eye's iris, the colorful disc around the pupil. This opening allows fluid to flow again, which helps control eye pressure and may slow the progression of visual field loss.

What was the aim of this review?

The aim of this Cochrane Review was to find out whether iridotomy compared with no iridotomy can slow progression (or development) of visual field loss in (1) people with primary angle-closure glaucoma, (2) people with primary angle-closure, and (3) people who are suspected of having primary angle-closure.

What were the main results of this review?

We collected and analyzed all relevant clinical trials and identified four eligible trials (3086 eyes of 1543 participants) comparing iridotomy with no iridotomy that addressed our review question.

The four included trials recruited participants from China, Singapore, or the UK who were suspected of having primary angle-closure. One eye of each participant received iridotomy, and the other eye did not receive iridotomy.

Two large studies found that eyes treated with iridotomy likely had wider angles at one year and five years after the treatment, and had less scarring of the drainage channels, which may reduce outflow of aqueous humor (the clear liquid inside the front part of the eye), than eyes that received no iridotomy at five years. The evidence for the effect of iridotomy on drainage channels at one year was uncertain. Our confidence in the evidence for eye pressure and visual acuity is only moderate because of concerns about study design. Unwanted effects related to the treatment, although rare, appeared to be more common in iridotomy-treated eyes than in non-treated eyes.

No studies measured:

• how visual field was affected;

• the number of medications needed to control eye pressure; or

• people's well-being (quality of life).

Key messages

(1) Iridotomy probably changes the internal structure of the eyes (e.g. wider angles) of people with high risk of having primary angle-closure. However, the effects of iridotomy on eye pressure and vision are limited. There is no evidence on visual field change, as no included study reported this outcome.

(2) The included studies only looked at people who were suspected of having primary angle-closure. No evidence is available for other populations.

How up-to-date is the review?

We searched for studies published up to 10 October 2021.

Summary of findings 1. Iridotomy compared to no iridotomy for people with primary angle-closure suspect

Iridotomy compared to no iridotomy for people with primary angle-closure suspect

Patient or population: people with primary angle-closure suspect
Setting: hospital or outpatient
Intervention: iridotomy
Comparison: no iridotomy

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of eyes (studies)	Certainty of the evidence (GRADE)	Comments
		No iridotomy	Iridotomy				
Proportion of progressive visual field loss at 1 year		No data were available for this outcome.			-	-	
Mean change in IOP (mm Hg) at 1 year		The mean IOP across control groups from 14.11 to 14.81	The mean IOP in the intervention group was on average **0.04 higher** (95% CI −0.17 to 0.24).	-	2598 (2)	⊕⊕⊕⊖ MODERATE[1]	5 year (MD 0.12 mm Hg, 95% CI −0.11 to 0.35; 2 studies, 2016 eyes of 1008 participants)
Gonioscopic findings	Mean angle width (Shaffer grading scale**) at 1 year	The mean Shaffer grade across control groups from 2.53 to 4.53	The mean Shaffer grade in the iridotomy group was on average **4.93 units greater** (95% CI 4.73 to 5.12).	-	2598 (2)	⊕⊕⊕⊖ MODERATE[1]	5 year (MD 5.07, 95% CI 4.78 to 5.36; 2 studies, 2016 eyes of 1008 participants)
	Presence of PAS at 1 year	10 per 1000	6 per 1000 (3 to 15)	**RR 0.62** (95% CI 0.25 to 1.54)	2896 (3)	⊕⊕⊖⊖ LOW[1,2]	5 year (RR 0.41, 95% CI 0.24 to 0.67; 2 studies, 2738 eyes of 1369 participants)
Need for additional surgery: proportion of participants who received additional surgery to control IOP within 1 year***		4 per 1000	2 per 1000 (0 to 22)	**RR 0.50** (95% CI 0.05 to 5.50)	960 (1)	⊕⊕⊖⊖ LOW[1,2]	
Medications: mean number of medications used to control IOP at 1 year		No data were available for this outcome.			-	-	
Quality of life measures		No data were available for this outcome.			-	-	

Adverse events	IOP spike (≥ 30 mm Hg) at 1-hour postiridotomy	0 per 1000	4 per 1000 (0 to 38)	**RR 13.70** (95% CI 0.73 to 230.42)	1778 (1)	⊕⊕⊖⊖ LOW[1,2]	Deaths (9) and other serious AEs (27, 8 eye-specific) by 5 years (ANA-LIS); localized hyphema (257 eyes), localized corneal burns (1) by 72 months (ZAP)
	Acute angle closure	5 per 1000	2 per 1000 (0 to 6)	**RR 0.29** (95% CI 0.07 to 1.20)	3006 (3)	⊕⊕⊖⊖ LOW[1,2]	

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
**Measure is sum of Shaffer grading of all 4 quadrants (range 0 to 16, larger number indicates wider angle).

***Timing of additional surgery was unknown.

AE: adverse events;**CI**: confidence interval; **IOP**: intraocular pressure; **MD**: mean difference; **PAS**: peripheral anterior synechiae; **RR**: risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded by one level for risk of bias.
[2]Downgraded by one level for imprecision: confidence interval of the risk ratio between groups is wide.

BACKGROUND

Description of the condition

Glaucoma refers to a group of similar diseases defined by progressive damage to the optic nerve (optic neuropathy). This damage occurs in a characteristic pattern with associated structural and functional changes, including visual field loss (Foster 2002). Elevated intraocular pressure (IOP) is associated with glaucomatous optic nerve damage. IOP can rise when aqueous humor, a clear fluid that continuously flows through the anterior chamber to nourish and pressurize the eye, does not drain properly (AAO 2020; EGS 2014; Mapstone 1968). There are two broad subtypes of glaucoma, that is angle-closure and open-angle, in which the drainage pathway for aqueous humor is occluded or not, respectively (AAO 2020).

Primary angle-closure glaucoma, the focus of this review, involves appositional (reversible) or synechial (adhesional) closure of the anterior chamber angle (AAO 2020; Emanuel 2014). Two main mechanisms have been hypothesized to be responsible for angle-closure: (1) pupillary block; and (2) anterior displacement of the iris. In the former, contact between the iris and lens at the pupillary margin increases resistance to aqueous outflow, as the iris bows forward and comes into contact with the trabecular meshwork (iridotrabecular contact [ITC]) (AAO 2020). In the latter, a large or anteriorly positioned ciliary body pushes the peripheral iris forward, often leading to continued ITC (AAO 2020).

In this review, we have followed a recently proposed classification of angle-closure glaucoma (Table 1) (AAO 2020; Aung 2001; Foster 2000; Foster 2002; Ng 2012). This definition rests on the idea of describing an 'occludable' angle, using terms such as 'narrow' to specify the anatomical predisposition to angle-closure, further qualified by degrees of ITC, presence of IOP elevated above the population-based norm, and presence of peripheral anterior synechiae (PAS). The drainage angle is assessable by gonioscopy with a diagnostic contact prism. In brief:

- primary angle-closure suspects (PACS) are patients who have reversible ITC of 180° or more on gonioscopy; however, there is no evidence of permanent aqueous outflow obstruction, damage to the angle (i.e. no PAS), rise in IOP, or glaucomatous optic neuropathy;
- primary angle-closure (PAC) patients have ITC of 180° or more plus elevated IOP or PAS or both, but no signs of glaucomatous optic neuropathy; and
- primary angle-closure glaucoma (PACG) patients have ITC of 180° or more in the presence of glaucomatous optic nerve damage (with or without PAS or elevated IOP at the time of examination).

Epidemiology

Glaucoma is among the leading causes of blindness and, particularly due to the irreversible nature of the disease, a pressing public health challenge (Bourne 2013; Kingman 2004; Resnikoff 2004). The World Health Organization characterizes glaucoma as one of its priority eye diseases, and researchers have approximated that about five million people today are blind as a consequence of glaucoma (Osborne 2003; Quigley 2006). A recent systematic review found a global prevalence of glaucoma in the 40 to 80 years age group of 3.54%, and estimated that prevalence will reach 76 million by 2020 and 111.8 million by 2040 (Tham 2014).

Although angle-closure glaucoma is less common than open-angle glaucoma, it is often more severe and more likely to result in irreversible blindness if left untreated (AAO 2020). Among the 64.3 million people with glaucoma aged 40 to 80 years, 20.2 million were estimated to have PACG in 2013; in this subpopulation, 14.5 million were estimated to be living in Asia (Quigley 2006; Tham 2014). For example, the number of people in China with PACS, PAC, and PACG has been estimated as 28.2 million, 9.1 million, and 3.5 million, respectively (Foster 2001). Moreover, 91% of the 1.7 million cases of bilateral blindness in this population are attributable to PACG (Foster 2001). The risk of progression from PACS to PAC and from PAC to PACG has also been estimated as 22% and 29%, respectively, over five years (Thomas 2003; Thomas 2003a). PACG is less common among people of European descent, with the pooled prevalence of PACG for people aged 40 years or older estimated to be 0.4% (Day 2012). Other risk factors for angle-closure diseases include female sex, older age, and family history of angle-closure (AAO 2020; Bonomi 2002; Day 2012).

Treatment options

Treatments for angle-closure glaucoma include medical interventions and surgical interventions (with or without laser) that open the angle to remove blockage of the normal flow of aqueous humor, lower IOP, and equalize pressure across the anterior and posterior chambers of the eye. Medical options include miotics such as topical pilocarpine. Other agents, including beta-blockers, alpha2-agonists, carbonic anhydrase inhibitors, and prostaglandin analogs, can also lower IOP but do not remove the risk of disease progression from PACS to PAC and PACG (AAO 2020; See 2011). Surgical options include lens extraction, iridoplasty, iridectomy, iridotomy, and trabeculectomy (Azuara-Blanco 2016; See 2011). The current standard first-line treatment for angle-closure glaucoma includes iridotomy.

Description of the intervention

Laser peripheral iridotomy ('iridotomy') is an outpatient procedure in which an opening is created in the peripheral iris using a neodymium-doped yttrium aluminum garnet (Nd:YAG) or argon laser mounted on a slit lamp biomicroscope (AAO 2020; Nolan 2000). Iridotomy is based on the same principle as iridectomy, which involves surgical removal of part of the iris. Iridotomy has largely replaced iridectomy; for every iridectomy performed, there are approximately 51 iridotomies (Ramulu 2007).

Iridotomy has some limitations. Changes in aqueous pressure gradients and iris configuration after iridotomy may increase contact between the lens and the iris, theoretically leading to a risk of more rapid development of cataracts (Caronia 1996; Lim 2005). Other potential risks include the rare occurrence of corneal endothelial damage localized to the surgery site, dysphotopsias or stray light symptoms, and the development of posterior synechiae (Pollack 1981; Quigley 1981; Robin 1984). Posterior synechiae can limit vision in dimly lit environments and complicate later cataract surgery or other ocular procedures.

How the intervention might work

Iridotomy eliminates the pressure gradient caused by pupillary block by making an opening in the peripheral iris; this hole—

created with laser—allows free circulation of aqueous humor from posterior to anterior chambers even if the pupil is blocked (Fleck 1997; Friedman 2001; Ng 2012). By restoring a more posterior iris position, this opening may prevent progression of PAS and further IOP rise, minimize subsequent optic nerve damage, and slow progression of visual field loss. However, it is worth noting that PAS formation and IOP rise are not synonymous; later permanent IOP rise can occur without any (or more) PAS formation, and vice versa. In cases of suspected angle-closure, iridotomy is often used as a prophylactic measure to prevent further progression of angle-closure (AAO 2020).

Why it is important to do this review

This review is an update of a previous review (Le 2018). Glaucoma remains the leading cause of irreversible blindness worldwide. Iridotomy is a common procedure used to treat people with PACG. Iridotomy has also been used prophylactically in the contralateral eye of people who have previously been diagnosed with PAC or PACG in one eye (Ang 2000; Edwards 1982; Snow 1977). However, iridotomy does not directly correct the underlying anatomical defects related to angle-closure, and it is unclear if it is sufficient for achieving long-term control of IOP in people with PACG (See 2011). Additionally, a recent survey of glaucoma specialists to set priorities for comparative effectiveness research on the management of angle-closure disease identified that understanding the role of iridotomy for the prevention of angle-closure glaucoma is an important unmet evidence gap (Yu 2015). It is critical to evaluate interventions such as iridotomy on outcomes that are important to patients (Li 2020). A systematic review of the evidence is needed to evaluate the benefits and risks of iridotomy in people with PACS, PAC, and PACG.

OBJECTIVES

To assess the effects of iridotomy compared with no iridotomy for primary angle-closure glaucoma, primary angle-closure, and primary angle-closure suspect.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs). As we anticipated few RCTs on this intervention, we planned to also include quasi-randomized trials. We defined quasi-randomized trials as studies that employed a method of allocating patients to a treatment arm that is not strictly random (e.g. by date of birth, hospital record number, in alternation, etc.). We included studies irrespective of their publication status or language. We included reports of secondary analyses of included RCTs and grouped them with the RCT.

Types of participants

We included studies of participants with gonioscopically narrow angles, that is participants with PACS, PAC, or PACG in one or both eyes. We did not restrict by age, gender, or ethnicity.

Types of interventions

We included trials that compared iridotomy versus no iridotomy or sham treatment. We applied no restrictions with respect to IOP-lowering medications.

Types of outcome measures

Primary outcomes

Proportion of participants with any progression of visual field loss at one year. We planned to assess progression of visual field loss using criteria as defined in the included studies measured using any validated tool, such as automated Humphrey Field Analyzer, Heidelberg Edge Perimeter, or Oculus. We also planned to consider other time points during follow-up as reported in the included studies and to assess this outcome for studies involving participants with PAC or PACG.

Secondary outcomes

- Mean change in IOP from baseline to one year, measured by any method of applanation tonometry, e.g. Goldmann or Perkins.
- Gonioscopic findings in the participant, including angle width and presence of PAS, as reported by the investigators at one year.
- Need for additional surgery, defined as the proportion of participants who received additional surgery to control IOP within one year after iridotomy.
- Number of medications used to control IOP at one year.
- Mean best corrected visual acuity (BCVA) as measured by logMAR one year after iridotomy.
- Quality of life data, as recorded by the investigators.

To improve comparability and consistency, we adapted some of the above outcomes from previous Cochrane Reviews (Friedman 2006; Zhang 2015). In a post hoc decision, we also reported results for longer-term outcomes (i.e. five years). If trials did not report outcomes at one year or five years, we considered longer-term outcomes closest to one year or five years, respectively.

Adverse events

We reported adverse effects as recorded by the investigators.

Search methods for identification of studies

Electronic searches

The Cochrane Eyes and Vision Information Specialist conducted systematic searches for RCTs and quasi-randomized trials in the following databases. There were no language or publication year restrictions. The date of the search was 10 October 2021.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 10) (which contains the Cochrane Eyes and Vision Trials Register) in the Cochrane Library (searched 10 October 2021) (Appendix 1).
- MEDLINE Ovid (1946 to 10 October 2021) (Appendix 2).
- Embase.com (1980 to 10 October 2021) (Appendix 3).
- PubMed (1948 to 10 October 2021) (Appendix 4).
- LILACS (Latin American and Caribbean Health Science Information database) (1982 to 10 October 2021) (Appendix 5).

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 10 October 2021) (Appendix 6).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched 10 October 2021) (Appendix 7).

Searching other resources

We searched the references of included studies for information about further trials. We did not conduct manual searches of journals or conference proceedings for this review.

Data collection and analysis

Selection of studies

Two review authors independently screened the titles and abstracts identified in the electronic searches using Covidence (Covidence). We classified each title and abstract as 'Yes' (relevant), 'Maybe' (maybe relevant), or 'No' (not relevant). We retrieved the full-text articles for records classified as 'Yes' or 'Maybe' and reviewed them against our inclusion criteria. We contacted trial authors for any clarifications needed to permit a complete assessment of the relevance or design of a study. We documented the reasons for exclusion for any studies excluded after full-text review. Any discrepancies between review authors were resolved by discussion at each stage of the selection process.

Data extraction and management

Two review authors independently extracted data from the included studies onto a web-based, electronic data collection form using Covidence (Covidence). We extracted information on the study design (e.g. study setting, countries where recruitment took place, sample size, study duration and follow-up time, study design, analysis choice, sources of funding, and potential conflicts of interests); participant characteristics (e.g. inclusion/exclusion criteria, underlying disease conditions, and medical history, including visual acuity and other vision-related characteristics); interventions and comparators (e.g. type of laser, duration and timing); and outcomes (e.g. domain, specific measurement, specific metric, method of aggregation, and the time frame). Where 2 × 2 tables or means and standard deviations (SDs) (or standard errors) were not available, we would include effect estimates (e.g. odds ratios and regression coefficients), confidence intervals, test statistics, or P values. We relied on the information available in published reports.

The two review authors compared the extracted data, resolving any discrepancies by discussion. One review author completed data entry into RevMan Web (RevMan Web 2022), and a second review author verified the data entered.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias in the included studies following the guidance in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We considered the following risk of bias domains: random sequence generation and allocation concealment (selection bias); masking of participants and study personnel (performance bias); masking of outcome assessors (detection bias); missing data and intention-to-treat analysis (attrition bias); selective outcome reporting (reporting bias); and other potential sources of bias. We assigned each domain as having 'low risk,' 'high risk,' or, if the information provided was insufficient to make an assessment, 'unclear risk' according to the criteria in Chapter 8 of the *Cochrane Handbook* (Higgins 2011). We documented the reasons for our assessments.

Any discrepancies were resolved through discussion. We relied on the information available in published reports in our assessment of risk of bias.

Measures of treatment effect

We reported risk ratios (RR) with 95% confidence intervals (CIs) for any dichotomous outcomes (i.e. proportion of participants with any evidence of progression of visual field loss and proportion of participants who needed additional surgery to control IOP), and mean differences (MD) in change from baseline with 95% CIs for continuous outcomes (i.e. mean change in IOP, progressive field loss, number of medications used, and mean change in BCVA). We intended to conduct separate analyses for outcomes in the eyes of participants with PACG, PAC, and PACS. If any trials on eyes with narrow angles compared eyes within individuals (e.g. one eye was randomized to the treatment while the other was randomized to observation), we would note whether the study investigators included statistical methods accounting for the correlation between eyes belonging to the same individual.

Unit of analysis issues

We planned that our unit of analysis would be one study eye per individual participant, therefore accounting for non-independence of eyes would not be necessary. However, all of the included studies applied a paired-eye design in which one eye from each participant was randomized to the iridotomy group and the fellow eye to the no iridotomy group. We analyzed the data as reported without considering intraperson correlation of outcomes. This approach was conservative, as confidence intervals were wider than they would have been if the potential within-person correlation had been accounted for.

Dealing with missing data

We considered multiple imputation for missing data. In the event that the quality of the available data prevented any meaningful analysis, we would omit the study from the analysis and note this decision in the Results and Discussion.

Assessment of heterogeneity

We assessed clinical and methodological heterogeneity by examining participant characteristics, iridotomy procedures, and outcomes by carefully reviewing the available data and taking into consideration potential risk of bias. We assessed statistical heterogeneity by assessing forest plots and examining the I^2 statistic (Deeks 2011; Higgins 2003). The I^2 statistic describes the proportion of total variation across studies due to heterogeneity rather than chance (Higgins 2011). We considered I^2 values over 50% as indicative of substantial heterogeneity, but also considered Chi^2 P value. As this may have low power when the number of studies are few, we considered $P < 0.1$ to indicate statistical significance of the Chi^2 test. We also considered the magnitude and direction of effects (Deeks 2019).

Assessment of reporting biases

We examined selective outcome reporting as part of the risk of bias assessment, by comparing the outcomes reported in the included studies and the outcomes listed in study registration or study protocols (where available). We planned to examine funnel plots of intervention effect estimates for evidence of asymmetry in the case of a sufficient number of included studies (i.e. 10 or more). An asymmetrical funnel plot may imply possible publication bias or exaggeration of treatment effects in small, low-quality studies (Sterne 2001).

Data synthesis

We performed data analysis according to the guidance in Chapter 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2019). In the absence of substantial clinical and methodological heterogeneity, we would use a random-effects model to compute a quantitative synthesis. If the number of studies included in the quantitative synthesis was less than three with no evidence of substantial statistical heterogeneity, we would consider a fixed-effect meta-analysis. We provided a descriptive, qualitative synthesis of studies and their results, based on the available information.

Subgroup analysis and investigation of heterogeneity

We planned to consider the following prespecified subgroups: (1) with or without use of IOP-lowering medications; and (2) by ethnic or racial groups. The effect of iridotomy may vary based on the use of IOP-lowering medication, and ethnicity or race is a known risk factor for angle-closure glaucoma (AAO 2020).

Sensitivity analysis

We planned to conduct two sensitivity analyses to determine the effect of excluding studies at high risk of bias for incomplete outcome data (i.e. the amount or distribution of missing outcomes differ between treatment groups) (Higgins 2011), and the effect of excluding quasi-randomized trials. If appropriate, we would conduct additional sensitivity analyses to determine the impact of any post hoc decisions made during the review process.

Summary of findings and assessment of the certainty of the evidence

We prepared a summary of findings table (Summary of findings 1). We assessed the certainty of the evidence using the GRADE approach, employing GRADEpro GDT software (GRADEpro GDT). One review author (BR) did the initial assessment, which another review author (JL) checked. We considered risk of bias, inconsistency, indirectness, imprecision, and publication bias when assessing the certainty of the evidence. We included the following outcomes in the summary of findings table.

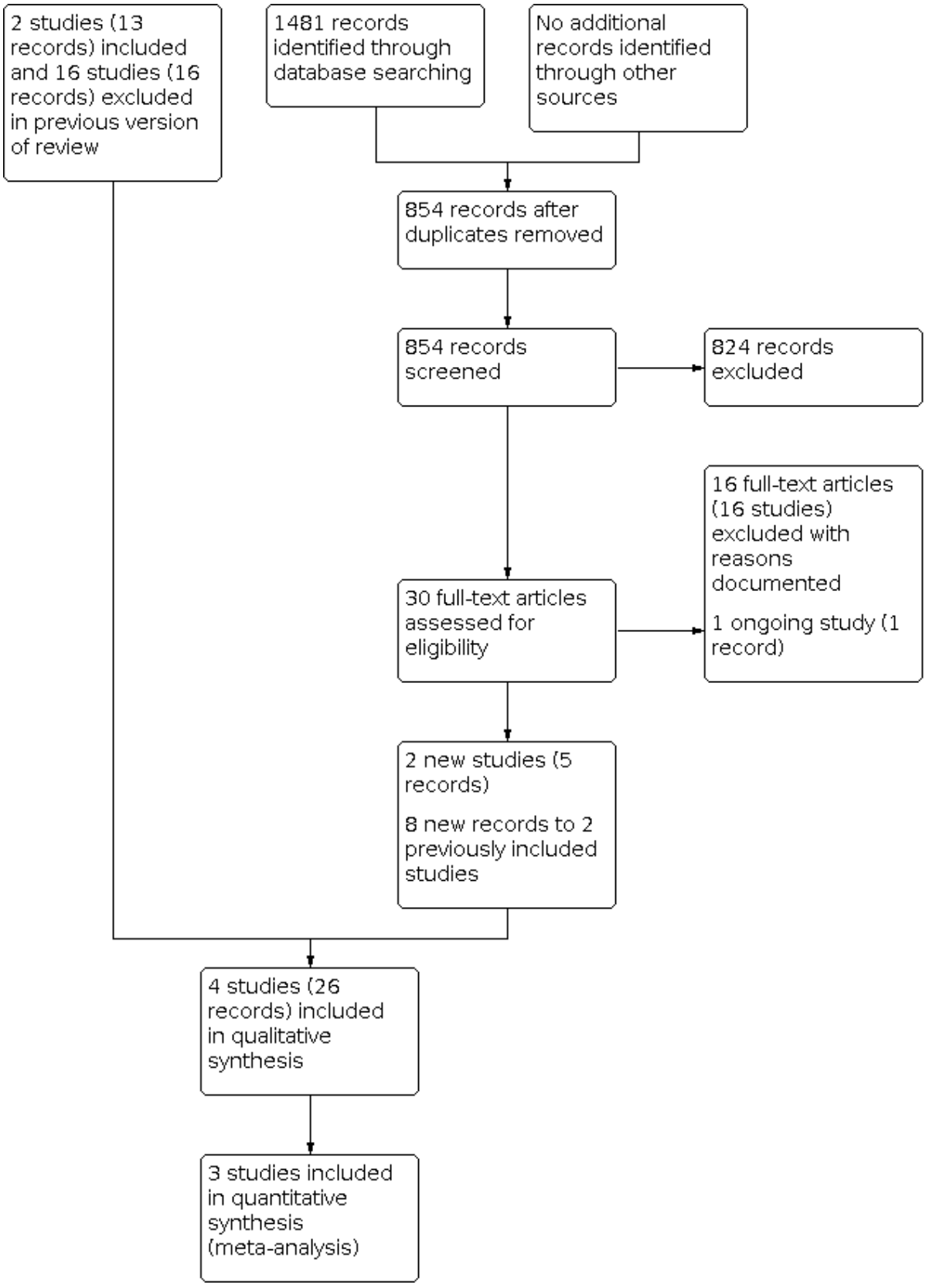
- Proportion of participants with progressive visual field loss at one year.
- Mean change in IOP from baseline to one year.
- Gonioscopic findings in the participant at one year.
- Need for additional surgery: proportion of participants who received additional surgery to control IOP within one year.
- Number of medications used to control IOP at one year.
- Quality of life measures.
- Adverse effects as documented.

RESULTS

Description of studies

A study flow diagram is shown in Figure 1.

Figure 1. Study flow diagram.



Results of the search

Detailed results of the searches in the original version of this review were published previously (Le 2018). Briefly, we included two studies (13 records) with outcomes partially reported, and excluded 16 studies (16 records) from 2573 unique records.

We performed updated database searches on 10 October 2021, which yielded 854 unique records. After title and abstract screening, we retrieved 30 full-text articles for further review. We excluded 16 studies (16 records), identified one ongoing study (one record) (CTRI/2021/03/032311), and included two new studies (five records) and eight new records pertaining to the two previously included studies (ANA-LIS; ZAP).

In total, we included four studies (26 records), excluded 32 studies (32 records), and identified one ongoing study (one record). The one ongoing study, which compares laser peripheral iridotomy with no iridotomy, started in April 2021 and plans to enroll 2400 participants with PACS in India (CTRI/2021/03/032311).

Included studies

We included four RCTs with 3086 eyes of 1543 participants (ANA-LIS; IMPACT; Mou 2021; ZAP), ranging from 40 participants, in IMPACT, to 889 participants, in ZAP. Details on each included study are described in Characteristics of included studies. All trials compared iridotomy with no iridotomy and used a paired-eye design, where one eye from each participant was randomized to the iridotomy group and the fellow eye to the no iridotomy group. The follow-up period ranged from 6 months, in IMPACT, to 10 years, in Mou 2021. One study reported that Tomey Corporation (Nagoya, Japan) loaned the instrument for the trial (IMPACT). The remaining three studies were not industry funded.

Types of participants

The trials included bilateral primary angle-closure suspects. The trials recruited participants from eye hospitals or glaucoma clinics in Singapore (ANA-LIS), China (Mou 2021; ZAP), or the UK (IMPACT).

Across trials, the majority of participants were female (range 67% to 87%), and the populations comprised older adults (range of mean age 59.6 to 62.9 years).

Types of interventions

Three trials specified using neodymium-doped yttrium–aluminum–garnet (Nd:YAG) laser iridotomy in the laser group (ANA-LIS; Mou 2021; ZAP). IMPACT reported that laser procedures were performed using the surgeon's standard technique with superior placement of the iridotomy in the treated eye.

Specifically, in ANA-LIS, investigators reported that laser peripheral iridotomy was performed in one randomly selected eye per participant by sequential argon and Nd:YAG laser after pre-treatment with 2% pilocarpine instilled into the eye (ANA-LIS). In this trial, argon settings of 500 mW to 1000 mW power with a spot size of 50 µm for a duration of 0.05 seconds and a yttrium–aluminum–garnet setting of 2 mJ to 5 mJ were used (ANA-LIS). In the ZAP trial, the trial authors reported specifically that participants also received one drop of brimonidine 0.15% and pilocarpine 2% in the intervention eye 15 minutes before treatment (ZAP). Iridotomy was performed using the YAG laser, starting at an initial setting of 1.5 mJ (ZAP). Mou 2021 reported that 1% pilocarpine eye drops were instilled 4 times prior to treatment, and laser power was set at 4 mJ and increased as necessary (up to 11 mJ) until achieving a patent iridotomy of approximately 0.2 mm. In IMPACT, the mean total power used to perform the iridotomy was 16.11 mJ (SD 10.8 mJ), and the mean number of shots was 13 (SD 8.6).

Types of outcomes

Proportion of participants with progressive visual field loss

No trial reported data on this outcome.

Of note, ANA-LIS described measuring visual field loss by automated perimetry, but presented these data as part of a composite outcome (i.e. presence of glaucomatous optic neuropathy with visual field loss compatible with glaucoma) and was thus not quantifiable.

Mean change in IOP

Both the ANA-LIS and ZAP trials reported measuring mean IOP to five years or longer. Mou 2021 reported mean IOP up to one year, but no precision measures were reported for the control group. IMPACT provided mean IOP results only up to six months.

Gonioscopic findings

ANA-LIS reported that static and dynamic gonioscopy was performed using both 2-mirror Goldmann-type gonioscope and Sussman (Ocular Instruments, Inc) gonioscope under standard dark illumination. The ZAP trial reported angle width as measured by a Goldmann-type, 1-mirror gonioscopic lens as well as development of PAS (≥ 1 o'clock position) after up to six years. Mou 2021 reported gonioscopic outcomes for up to one year based on examination with a Goldmann-type 1-mirror lens with low-ambient illumination. IMPACT reported gonioscopic findings for a subgroup of participants who did not require further treatment; we did not extract these data due to concerns about potential bias.

Need for additional surgery

ANA-LIS reported that some participants needed additional surgery (including additional laser peripheral iridotomy, cataract surgery, and penetrating keratoplasty) by five years. The other three studies did not specify need for additional surgery as an outcome.

Number of medications to control IOP

The included studies did not report measuring number of medications to control IOP as an outcome.

Mean change in BCVA

ANA-LIS and ZAP both reported mean visual acuity using logMAR after up to five years of follow-up or longer.

Quality of life

No trial reported this outcome.

Adverse events

ANA-LIS considered mortality, IOP spikes (defined as IOP ≥ 30 mm Hg at one week after treatment), acute angle-closure (AAC), eye pain, dry eyes, redness of eyes, and ocular discomfort as adverse events. ZAP reported adverse events in terms of IOP spikes (defined as IOP ≥ 30 mm Hg immediately after treatment), AAC, localized hyphema, localized corneal burn, endothelial cell density, cataract lens opacity, and occurrence of serious adverse

events. Mou 2021 reported on AAC. IMPACT did not report data on adverse events.

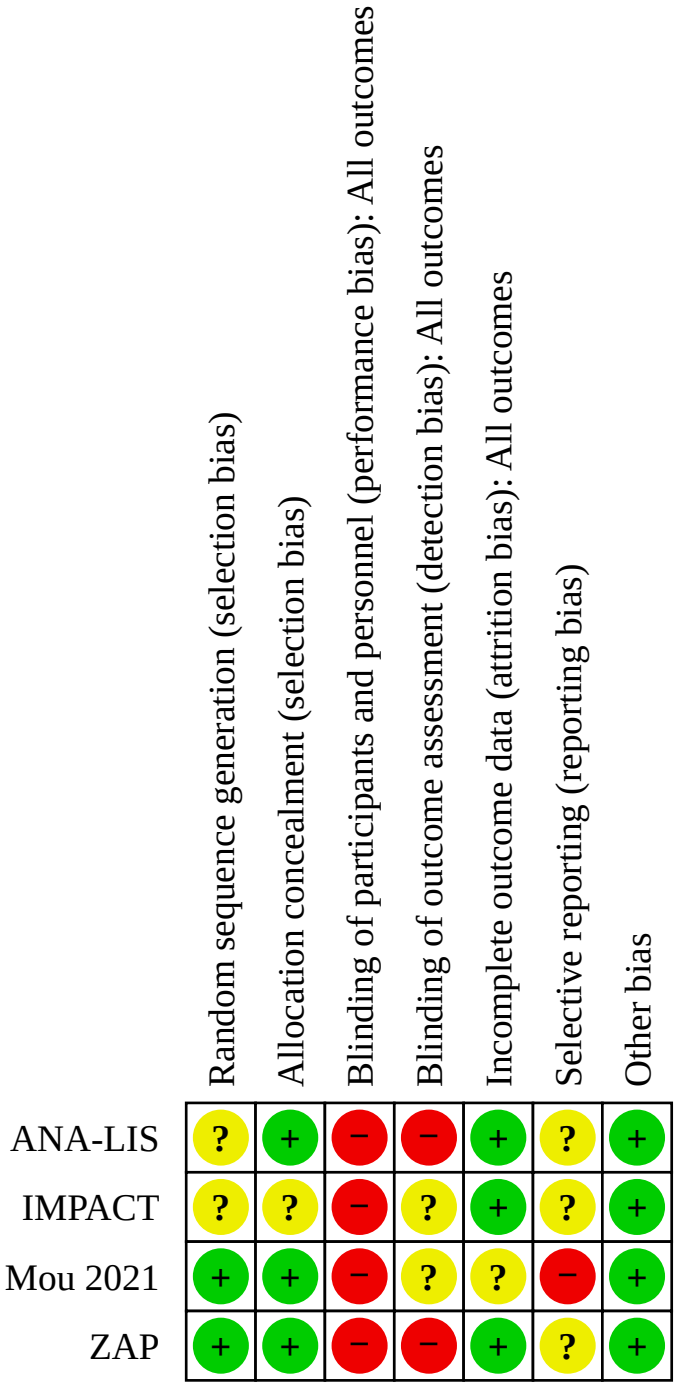
Excluded studies

We excluded 32 articles after full-text review (Figure 1). The reasons for exclusion of these studies are provided in Characteristics of excluded studies. In summary, 21 reports were not the study design of interest (e.g. not RCTs), and 11 reports were not the interventions or comparator of interest (e.g. iridoplasty).

Risk of bias in included studies

Our assessment of the risk of bias for the four included studies is described in Characteristics of included studies. A summary of risk of bias assessments for each trial is shown in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Two studies employed computer-generated random numbers (Mou 2021; ZAP), and were therefore judged as at low risk of bias for random sequence generation. We judged the remaining two studies as having an unclear risk of bias because the method of random sequence generation was not clearly described (ANA-LIS; IMPACT).

Based on the reported use of adequate procedures, we judged three studies as at low risk of bias for allocation concealment before assignment (ANA-LIS; Mou 2021; ZAP). We assessed the remaining study as at unclear risk of bias for this domain because it did not describe how allocation was concealed (IMPACT).

Blinding

Participants and study personnel could not be masked due to the nature of intervention (i.e. iridotomy versus no surgical treatment). We judged all four studies as having a high risk of performance bias.

The trial registry record for ANA-LIS describes this trial as "open-label," therefore we assessed this trial as having a high risk of performance and detection bias (ANA-LIS). The ZAP trial registry record describes the trial as "not masked" (ZAP). The research nurse who assessed IOP using Goldmann applanation tonometry in the ZAP trial “was unaware of the treatment status of each eye” (ZAP). Gonioscopy was performed by "an examiner who was masked to the findings collected at other visits" (ZAP). The study authors reported that due to the nature of the procedure, outcome examiners could not be masked. Accordingly, we assessed this trial as having a high risk of detection bias overall. In one study, gonioscopy was performed by one glaucoma specialist who was described as masked to treatment assignment (Mou 2021). We judged this study as at unclear risk of detection bias. We judged the remaining study as having an unclear risk of bias, as masking of outcome assessors was not described (IMPACT).

Incomplete outcome data

We judged three studies in which either intention-to-treat analysis was followed (ANA-LIS; ZAP), or nearly all (97.5%) randomized participants provided outcome data (IMPACT), as at low risk of attrition bias. In one study, data for 54 participants (40.3%) were missing in each group (Mou 2021). Given that loss to follow-up was reported at the individual level, it seems reasonable to infer that the reasons for loss to follow-up were balanced for both groups. We judged this study as at unclear risk of attrition bias.

Selective reporting

All of the included studies have a publicly available trial register, published protocol, or both. However, we could not access detailed information for one study, which we assessed as having an unclear risk of bias (IMPACT). In two large studies, not all outcomes specified in the trial registry were reported in the publication, but they may be reported in future publications. We judged these studies as at unclear risk of reporting bias (ANA-LIS; ZAP). We judged one study as having a high risk of bias because some relevant outcomes such as visual acuity were measured at follow-up based on the methods, but the results were not reported (Mou 2021).

Other potential sources of bias

We identified no other potential sources of bias in any of the included studies. We judged all studies as having a low risk of bias for this domain.

Effects of interventions

See: **Summary of findings 1** Iridotomy compared to no iridotomy for people with primary angle-closure suspect

See Summary of findings 1 for the comparison iridotomy versus no iridotomy for people with primary angle-closure suspect.

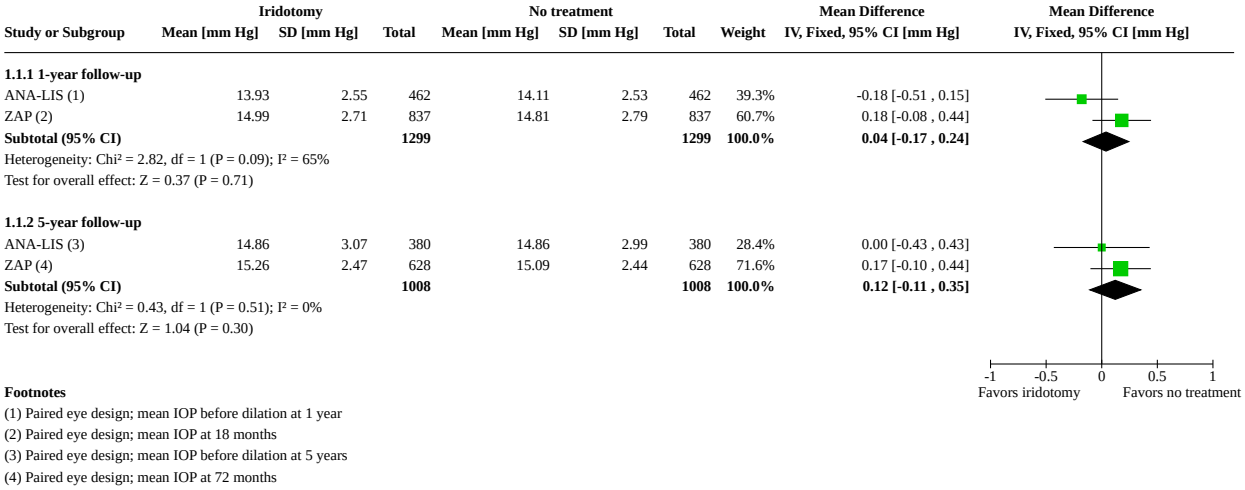
Proportion of participants with progressive visual field loss

No studies reported number of participants with progressive visual field loss.

Mean change in IOP

Meta-analyses of data from two studies showed no evidence of difference in mean IOP between iridotomy and no treatment at one year (mean difference (MD) 0.04 mm Hg, 95% confidence interval (CI) −0.17 to 0.24; I^2 = 65%; 2598 eyes of 1299 participants) and five years (MD 0.12 mm Hg, 95% CI −0.11 to 0.35; I^2 = 0%; 2016 eyes of 1008 participants) (Analysis 1.1; Figure 3). Mou 2021 did not contribute to the meta-analysis due to missing precision data, but findings at one year were consistent with the meta-analysis (iridotomy: mean 15.5 mm Hg, SD 2.9, 80 eyes; no treatment: mean 15.6 mm Hg, SD not reported, 80 eyes).

Figure 3. Forest plot of mean difference in intraocular pressure between iridotomy and no treatment at 1 and 5 years of follow-up.



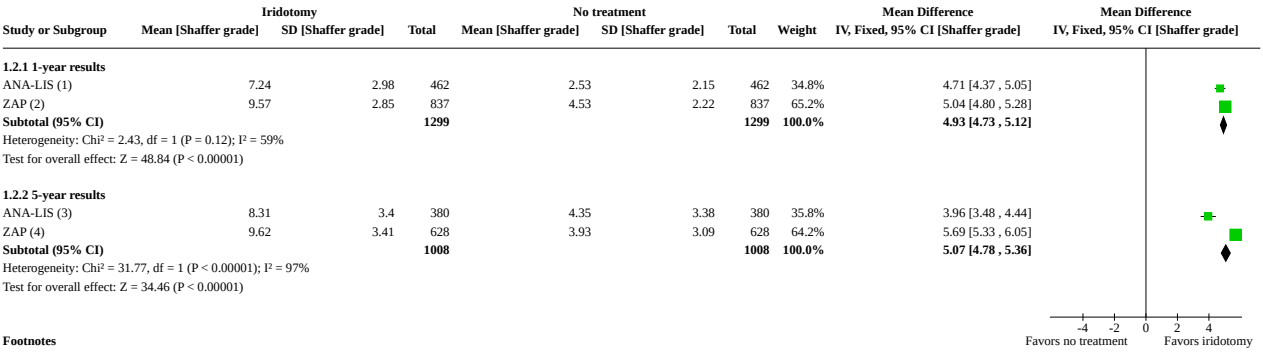
Footnotes
(1) Paired eye design; mean IOP before dilation at 1 year
(2) Paired eye design; mean IOP at 18 months
(3) Paired eye design; mean IOP before dilation at 5 years
(4) Paired eye design; mean IOP at 72 months

Using the GRADE approach, we assessed the certainty of the evidence at one year as moderate, downgrading one level due to high risk of bias.

Gonioscopic findings

Meta-analyses of data from two studies suggests that iridotomy probably improves angle width at one year (Shaffer grading scale, MD 4.93, 95% CI 4.73 to 5.12; I^2 = 59%; 2598 eyes of 1299 participants) and five years (Shaffer grading scale, MD 5.07, 95% CI 4.78 to 5.36; I^2 = 97%; 2016 eyes of 1008 participants) (Analysis 1.2; Figure 4). Although the I^2 statistic may represent substantial or considerable heterogeneity in the analyses, we have presented the pooled estimate because only two studies were included (i.e. low power), and the direction of effect is the same in the two studies.

Figure 4. Forest plot of mean difference in angle width between iridotomy and no treatment at 1 and 5 years of follow-up.

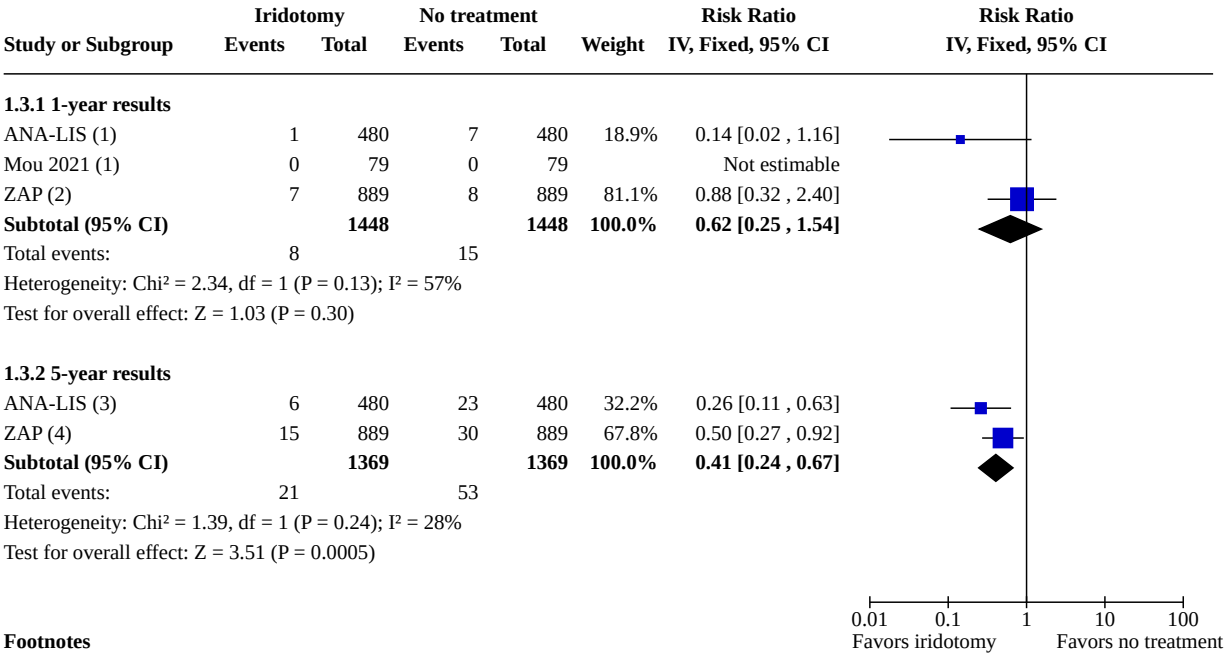


Footnotes
(1) Paired eye design; at 1 year; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(2) Paired eye design; at 1.5 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(3) Paired eye design; at 5 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(4) Paired eye design; at 6 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)

Using the GRADE approach, we assessed the certainty of the evidence for angle width at one year as moderate, downgrading one level for high risk of bias.

There were few occurrences of PAS at one year as reported by three studies (ANA-LIS; Mou 2021; ZAP). Meta-analysis suggests that iridotomy may have little to no effect on this outcome (risk ratio (RR) 0.62, 95% CI 0.25 to 1.54; I^2 = 57%; 3 studies, 2896 eyes of 1448 participants) (Analysis 1.3; Figure 5). At five years, meta-analysis of ANA-LIS and ZAP found that iridotomy reduced the occurrence of PAS (RR 0.41, 95% CI 0.24 to 0.67; I^2 = 28%; 2 studies, 2738 eyes of 1369 participants).

Figure 5. Forest plot of risk ratio of peripheral anterior synechiae between iridotomy and no treatment at 1 and 5 years of follow-up.



Footnotes

(1) Paired eye design; at 1 year
(2) Paired eye design; at 1.5 years
(3) Paired eye design; at 5 years
(4) Paired eye design; at 6 years

Using the GRADE approach, we assessed the certainty of the evidence for presence of PAS at one year as low, downgrading one level for high risk of bias and one level for imprecision.

Need for additional surgery

ANA-LIS reported that two participants (one iridotomy-treated eye in one participant and one control eye in another participant) experienced acute angle-closure (AAC) during follow-up which required standard management of AAC followed by iridotomy to recover vision completely (timing not reported). Additionally, one participant who had AAC in the control eye (at 2.5 years after enrollment) underwent cataract surgery and later required penetrating keratoplasty (RR 0.50, 95% CI 0.05 to 5.50; 1 study, 960 eyes of 480 participants) (Analysis 1.4).

Using the GRADE approach, we assessed the certainty of the evidence for this outcome as low, downgrading one level for risk of bias and one level for imprecision of results because rare events contributed to wide confidence intervals.

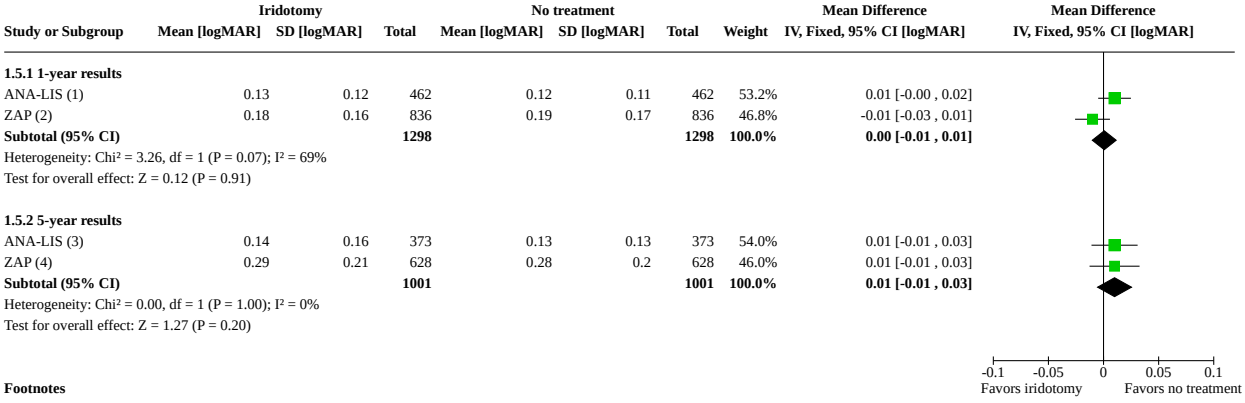
Number of medications used to control IOP

No trial reported on number of medications needed to control IOP.

Mean BCVA

Meta-analyses of data from two trials showed no evidence of an important difference in mean BCVA between iridotomy and no treatment at one year (logMAR, MD 0.00, 95% CI −0.01 to 0.01; I^2 = 69%; 2596 eyes of 1298 participants) and five years (logMAR, MD 0.01, 95% CI −0.01 to 0.03; I^2 = 0%; 2002 eyes of 1001 participants) (Analysis 1.5; Figure 6).

Figure 6. Forest plot of mean difference in best-corrected visual acuity between iridotomy and no treatment at 1 and 5 years of follow-up.



Footnotes
(1) Paired eye design; mean logMAR BCVA distance at 1 year
(2) Paired eye design; mean logMAR BCVA at 18 months
(3) Paired eye design; mean logMAR BCVA distance at 5 years
(4) Paired eye design; mean logMAR BCVA at 6 years

Using the GRADE approach, we assessed the certainty of the evidence for BCVA at one year as moderate, downgrading one level due to high risk of bias.

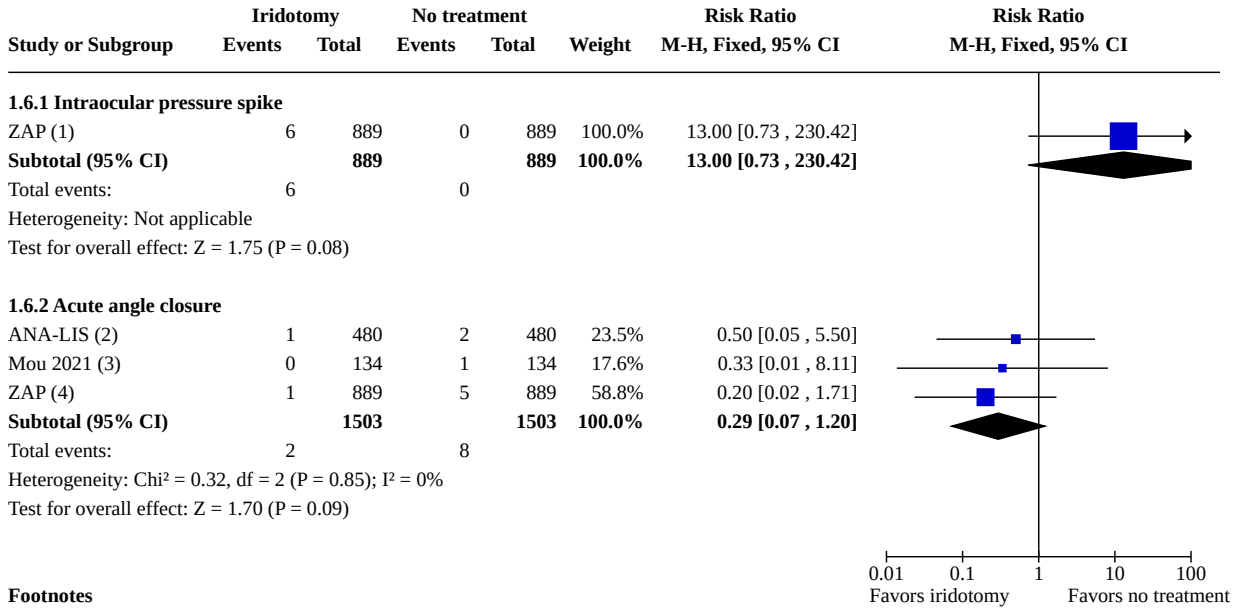
Quality of life

No trial reported on quality of life measures.

Adverse events

One study reported that six eyes (0.67%) experienced IOP spike, defined as ≥ 30 mm Hg at one-hour postiridotomy, in the iridotomy arm compared with zero cases in the no iridotomy arm (RR 13.00, 95% CI 0.73 to 230.42; 1778 eyes of 889 participants) (Analysis 1.6; Figure 7) (ZAP). Another study reported that no IOP spike, defined as ≥ 30 mm Hg at one-week postiridotomy, was observed in both arms (ANA-LIS). Since the risk ratio was not estimable, we did not include the data in the analysis.

Figure 7. Forest plot of risk ratio of adverse events (intraocular pressure spike and acute angle closure) between iridotomy and no treatment.



Footnotes
(1) IOP spike defined as >= 30 mmHg at one hour post-iridotomy
(2) Acute angle closure at 60 months
(3) Acute angle closure at 1 year
(4) Acute angle closure at 72 months

A meta-analysis of three trials suggests no evidence of difference in incidence of AAC between iridotomy and no treatment study arms during study follow-up (RR 0.29, 95% CI 0.07 to 1.20; I^2 = 0%; 3 studies, 3006 eyes of 1503 participants) (Analysis 1.6; Figure 7).

We have presented other adverse events as reported by the study investigators.

- ANA-LIS reported 9 deaths and 27 other serious adverse events, of which 8 were eye-specific (i.e. 3 AAC, 1 branch retinal artery occlusion, 1 rhegmatogenous retinal detachment, 1 posterior chorioretinitis, 1 acute anterior uveitis, and 1 macular branch retinal vein occlusion) by the 5-year follow-up. In addition, investigators noted that non-serious "eye-specific AEs [adverse events] such as eye pain, dry eyes, redness of eyes, and ocular discomfort were rare in both LPI [laser peripheral iridotomy]-treated eyes and control eyes, each occurring in less than 5% of eyes ... these were more common in LPI-treated eyes (22%) than in control eyes (14.5%; P < 0.001)."
- ZAP reported that immediately after iridotomy, 257 eyes experienced localized hyphema, and 1 eye experienced localized corneal burns. Investigators noted that "at the end of 72 months, the endothelial cell densities and lens grading were similar between the two groups."

IMPACT did not report data on adverse events or safety outcomes.

Using the GRADE approach, we assessed the certainty of the evidence for this outcome as low, downgrading one level for risk of bias and one level for imprecision of results.

DISCUSSION

Summary of main results

We identified two additional trials in this updated Cochrane Review, bringing the total number of included studies to four RCTs (3086 eyes of 1543 participants). We have summarized the key findings as follows.

- All four included RCTs relied on eligibility criteria that excluded people with PAC or PACG at baseline, thus the results summarized in this review are limited to patients who received a diagnosis of PACS at baseline. To our knowledge, there are no ongoing studies evaluating the effects of iridotomy versus no iridotomy on people with PAC or PACG at this time.
- No included RCTs reported visual field data as specified in the protocol of this review (Le 2018), nor did any report on number of additional medications to control IOP or quality of life outcomes.
- We conducted meta-analyses for three outcomes. We found no evidence of an important difference in change in IOP and in BCVA between eyes treated with iridotomy versus no iridotomy (at both one and five years). In terms of gonioscopic findings, eyes treated with iridotomy had wider angles (at both one and five years) and experienced fewer PAS than eyes that received no iridotomy (at five years), but evidence was less conclusive for PAS at one year.
- Ocular adverse events including eye pain, dry eye, redness of eyes, and ocular discomfort were more common in eyes treated with iridotomy than eyes in the control group, although such events were rare (i.e. incidence less than 5% of eyes).
- Three of the four included RCTs specified as their primary outcome incident primary angle-closure disease defined as a composite endpoint involving elevation of IOP, PAS, or AAC during follow-up. The investigators noted that "the vast majority of end points reached were the result of development of PAS" (ANA-LIS; ZAP). In this review, we analyzed the three component outcome domains individually as mean IOP, gonioscopic findings, and adverse events.

We recognize that gonioscopic findings such as PAS and angle-width may be of concern to patients and could indicate future difficulties with managing IOP (ANA-LIS); however, it remains that no differences were observed in terms of IOP or BCVA between treated and untreated eyes. And while development of AAC may be an important concern for patients, incidence was low overall. Of note, the investigators of the ZAP and ANA-LIS trials, the two largest included RCTs, both recommended against use of iridotomy in asymptomatic PACS. They caution that given "the low incidence rate of outcomes that have no immediate threat to vision, the benefit of prophylactic laser peripheral iridotomy is limited" (ZAP).

Overall completeness and applicability of evidence

Given the lack of inclusion of PAC and PACG patients, the findings of this review may only be applicable to people with PACS. The study population adequately reflects the real-world distribution of people who are at risk of developing PACG, although it was limited to China, Singapore, and the UK, comprised adults aged 50 years and older, and was majority female (Quigley 2006; Tham 2014).

Data were available for analysis for half of our prespecified outcomes: IOP, gonioscopic findings, need for additional surgery, BCVA, and adverse events. Two RCTs also published long-term (i.e. five years or longer) results. All data were derived from peer-reviewed, full-text articles.

In addition, we observed that most of the included RCTs assessed measures such as IOP and PAS, which are clinically meaningful in terms of managing glaucoma; however, it is critical to recognize that the ultimate goal of glaucoma management is to prevent damage to the optic nerve, minimize visual field loss, and improve quality of life (Le 2019; Le 2019a; Ong 2021).

Quality of the evidence

Using the GRADE approach, we assessed the certainty of the evidence as moderate to low across the specified outcomes. We downgraded the certainty of evidence for high risk of bias (e.g. performance and detection biases) and imprecision of results due to wide confidence intervals.

Potential biases in the review process

We followed standard Cochrane methodology in conducting this review update and Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards for the reporting of new Cochrane Intervention Reviews (editorial-unit.cochrane.org/mecir). We worked with a medical Information Specialist to conduct a highly sensitive search to identify trials meeting our prespecified eligibility criteria. We also searched trial registries, anticipating finding few or no RCTs on this topic. The review team involved three methodologists and a clinical expert. The team members worked in pairs to independently screen, review, and extract data to minimize

errors and reduce bias. None of the review authors has any financial conflicts of interest.

Agreements and disagreements with other studies or reviews

We found no other published systematic reviews evaluating the effectiveness of iridotomy versus no iridotomy for angle-closure.

Determining the effectiveness and safety of iridotomy is important, but there is growing interest in examining other modalities for treating PACG, such as removing pupillary block through extraction of the lens. The Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE) trial, which randomized 419 participants to surgical lens extraction or iridotomy, favored lens extraction for reducing IOP and improving quality of life (Azuara-Blanco 2016). Among participants randomized to iridotomy, the investigators observed that IOP decreased from 30.3 mm Hg (SD 8.1 mm Hg) to 18.4 mm Hg (SD 4.3 mm Hg) at one year, but required more medical treatment to achieve this. This RCT was included in the Cochrane Review 'Lens extraction for chronic angle-closure glaucoma,' which concluded that "moderate certainty evidence showed that lens extraction has an advantage over iridotomy in treating chronic PACG with clear crystalline lenses over three years of follow-up" (Ong 2021).

AUTHORS' CONCLUSIONS

Implications for practice

We summarize implications for practice as follows.

- There is currently no high certainty evidence on the use of iridotomy to prevent visual field loss.
- Moderate certainty evidence suggests that iridotomy has a modest prophylactic effect in terms of gonioscopic findings (e.g. angle width and peripheral anterior synechiae [PAS]) for people who are primary angle-closure suspects (PACS).
- Moderate certainty evidence indicates that iridotomy probably does not improve intraocular pressure (IOP) or visual acuity in people with PACS.
- There is no evidence showing substantial risks involved with iridotomy. We found no randomized controlled trials (RCTs) that evaluated iridotomy compared to no iridotomy in people with primary angle-closure (PAC) or primary angle-closure glaucoma (PACG).
- There is insufficient evidence to recommend for or against iridotomy in practice. People with PACS and physicians who use iridotomy should be aware that modest benefits in terms of gonioscopic outcomes may not translate to clinically meaningful improvements.

Implications for research

Although we identified one registry record for an ongoing study, its relevance is unclear, as the investigators refer to it as a natural history study of primary angle-closure disease. We are not aware of any further ongoing trials of iridotomy for PACS, PAC, or PACG.

If future trials are undertaken, investigators may need to prioritize recruitment of participants with PAC and PACG so that findings can be generalized to a broader patient population. For people with PACS, although clinical measures such as IOP, PAS, and angle-width are available, collecting and reporting data on patient-important outcomes like visual field and quality of life is needed to fully understand the effectiveness of iridotomy. Investigators of any future trials should mask outcome assessors where possible and continue to report findings following the CONSORT statement for RCTs.

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We also thank an anonymous reviewer for providing insightful comments for the protocol, review, and this review update.

This review update was managed by CEV@US and was signed off for publication by Tianjing Li and Gianni Virgili.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

ANA-LIS

Study characteristics	
Methods	**Study design**: randomized controlled trial **Study grouping**: paired-eye design **Number randomized (total and per group):** 960 eyes total (480 participants total) 480 eyes randomized to LPI and 480 contralateral eyes randomized to no treatment control **Unit of randomization:** eye (paired-eye design) **Exclusions and losses to follow-up (total and per group):** all eyes were included in intention-to-treat analysis. 3 did not receive allocated treatment, 2 withdrawn by investigator, 1 withdrawn on own accord. 456 (95.0%) censored at last visit, 354 (73.8%) censored at year 5 visit, 9 (1.9%) died, 32 (6.7%) received LPI due to progression in fellow eyes, 61 (12.7%) withdrawn or lost to follow-up, 10 before year 1, 16 before year 2, 10 before year 3, 15 before year 4, 10 before year 5 **Number analyzed (total and per group):** 960 eyes of 480 participants in total (intention-to-treat analysis) **Unit of analysis (individual or eye):** eye (paired-eye design) **Length of follow-up:** 5 years **How were missing data handled?:** not applicable **Reported sample size calculation (Y/N), if yes, sample size and power**: Y, "the required number of participants (i.e., pairs of eyes) was 435 for 90% power and 2-sided 5% type I error. This was increased to 480 participants to allow for a 10% dropout rate. This calculation ignored the within-participant correlation between eyes. Hence, the actual power was more than 90% with the assumed parameters."
Participants	**Country:** Singapore **Setting:** glaucoma clinics at Singapore eye centers (hospitals) **Baseline characteristics**: Overall • Age (year) (mean, SD): 62.8 (6.9) • Female sex (n, [%]): 364 (75.8) **Inclusion criteria:** patients 50 years of age or older with bilateral PACS (defined as having >= 2 quadrants of appositional angle-closure with non-visibility of the pigmented posterior trabecular meshwork on non-indentation gonioscopy) and capable of giving informed consent **Exclusion criteria:** IOP of more than 21 mm Hg at any previous visit, an IOP spike of more than 15 mm Hg after pupil dilation, presence of PAS (defined as at least one-half clock hour of iris adherent to posterior trabecular meshwork in any quadrant on indentation gonioscopy), (glaucomatous optic neuropathy [GON]) (defined as loss of neuroretinal rim [notch or erosion], a vertical cup-to-disc ratio of more than 0.7, nerve fiber layer defect attributable to glaucoma, or both), secondary angle-closure,

ANA-LIS *(Continued)*

	prior incisional or laser surgery or penetrating eye injury, corneal disorders such as corneal endothelial dystrophy or corneal opacity preventing LPI, prior episode of acute angle-closure (AAC; defined by the following criteria: (1) presence of at least 2 of the following symptoms: ocular or periocular pain; nausea, vomiting, or both; an antecedent history of intermittent blurring of vision with haloes; (2) IOP of more than 30 mm Hg; and (3) presence of at least 3 of the following signs: conjunctival injection, corneal epithelial edema, mid-dilated unreactive pupil, glaukomflecken, and shallow anterior chamber), significant cataract requiring surgery, best-corrected visual acuity less than 20/40, use of a contact lens, chronic use of topical or systemic steroids, retinal diseases requiring regular pupil dilatation, any other disease likely to cause visual field loss, or severe health problems resulting in a life expectancy of less than 1 year precluding follow-up
Interventions	**Intervention 1:** laser peripheral iridotomy was performed by sequential thermal laser (514 nm) and neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser (1064 nm). All iridotomies were performed using an Abraham lens (Ocular Instruments) after application of a coupling agent. After LPI, all participants received betamethasone 0.1% drops every 3 hours for the first day followed by 4 times daily for 1 week. • Use of IOP-lowering medications: none **Intervention 2:** no treatment
Outcomes	**Primary outcomes per trial register** • Peripheral anterior synechiae formation • IOP elevation > 21 mm Hg • Development of acute angle-closure event **Primary outcomes per Baskaran 2021** • Primary angle-closure, defined as the presence of: (1) more than one-half clock hour of PAS formation, or (2) IOP of more than 21 mm Hg verified on 2 separate days, or (3) development of an AAC event • Primary angle-closure glaucoma, defined as the presence of GON with visual field loss compatible with glaucoma **Secondary outcomes per trial register** • Changes in grading of Modified Schaffer Grading • Development of glaucomatous optic neuropathy • Development of corresponding visual field loss by automated perimetry • Change in Heidelberg Retina Tomography (HRT) optic disc parameters • Change in ultrasound biomicroscopy (UBM) angle parameters • Formation of disc pallor **Intervals at which outcomes assessed:** 1 year, 2 years, 3 years, 4 years, and 5 years
Notes	**Study date**: 2005 to 2015 (participants were randomized into the study between January 2005 and August 2010) **Funding source(s)**: National Medical Research Council (NMRC), Singapore (NMRC/1133/2007, NMRC/CIRG/1323/2012, and NMRC/STAR/0023/2014) **Conflicts of interest**: "The author(s) have no proprietary or commercial interest" **Publication language**: English **Trial register:** ClinicalTrials.gov NCT00347178

Risk of bias

Bias	Authors' judgement	Support for judgement

ANA-LIS *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation was not described. "After verifying eligibility and obtaining written informed consent, each participant was randomized by delegated site personnel with a password-secured account through the Singapore Clinical Research Institute randomization website and a trial number was assigned"
Allocation concealment (selection bias)	Low risk	"Each participant was randomized by delegated site personnel with a password-secured account through the Singapore Clinical Research Institute randomization website and a trial number was assigned. One eye was randomized to undergo LPI, whereas the other eye remained untreated."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Trial described as "Open-label" on ClinicalTrials.gov (NCT00347178).
Blinding of outcome assessment (detection bias) All outcomes	High risk	Trial described as "Open-label" on ClinicalTrials.gov (NCT00347178).
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomized participants were included in the intention-to-treat analysis. Authors reported that "Of the remaining participants who received LPI, 58 participants (12%) either withdrew or were lost to follow-up" and "Not all patients completed the 5 years of follow-up, with many dropping out of the study because of the need for cataract surgery".
Selective reporting (reporting bias)	Unclear risk	Not all outcomes specified in the trial registry were reported, but it is anticipated that they will be reported in future publications.
Other bias	Low risk	Authors acknowledged that "Using 1 eye for treatment and the contralateral eye as the control removes confounding for all but ocular factors, and these almost certainly are highly similar between the 2 eyes of a single individual".

IMPACT

Study characteristics	
Methods	**Study design**: randomized controlled trial **Study grouping**: paired-eye design **Number randomized (total and per group):** 80 eyes (40 consecutive patients newly referred to a hospital glaucoma service); 40 eyes (20 participants) randomized to LPI, 40 contralateral eyes (20 participants) acted as control **Unit of randomization:** eye (paired-eye design) **Exclusions and losses to follow-up (total and per group):** 2 eyes (from 1 participant) **Number analyzed (total and per group):** 78 eyes (39 participants) **Unit of analysis (individual or eye):** eye (paired-eye design) **Length of follow-up:** 6 months **How were missing data handled?:** not applicable **Reported sample size calculation (Y/N), if yes, sample size and power**: Y, "A sample size of 40 patients was chosen based on the minimal detectable difference for intraocular pressure with sample

IMPACT *(Continued)*

	power of 80% and an alpha error of 0.05 in order to achieve statistically significant difference in pressure change of 5%."
Participants	**Country:** UK **Setting:** hospital glaucoma service **Baseline characteristics**: Overall • Age (year) (mean, SD): 59.6 (SD not reported), range 25 to 77 years • Female sex (n, [%]): 26 (66.7%) **Inclusion criteria**: patients newly referred to a hospital glaucoma service with a gonioscopic diagnosis (less than 180 posterior pigmented trabecular meshwork visible on applanation gonioscopy) of bilateral PAC, PACS, or a combination of both conditions and no other ocular comorbidity **Exclusion criteria**: not reported
Interventions	**Intervention 1**: LPI procedures were performed using the surgeon's standard technique with superior placement of the iridotomy in a randomly allocated eye of each participant. • Use of IOP-lowering medications: not reported **Intervention 2**: no treatment
Outcomes	**Primary outcomes** • Angle opening distance (AOD), trabecular–iris angle (TIA), angle recess area (ARA), and trabecular–iris space area (TISA) at 500 and 750 µm from scleral spur **Secondary outcomes:** unclear **Adverse events:** not reported **Intervals at which outcomes assessed:** 1, 6, 12, and 26 weeks
Notes	**Study date**: not reported **Funding source(s)**: "This research was supported by Hinchingbrooke Hospital Ophthalmology Research Fund. Tomey Corporation (Nagoya, Japan) loaned the instrument for the purposes of the study." **Conflicts of interest**: none declared **Publication language**: English **Trial register:** not provided **Notes:** this study had twice randomization: initially, and the second randomization (where eyes with gonioscopically closed anterior chamber angles were randomized to argon laser peripheral iridoplasty or no further treatment), which took place 3 months post-LPI.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment before randomization was not described.

IMPACT *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking of participants and personnel could not be done due to the nature of the intervention.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Masking of outcome assessors was not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Of 40 participants recruited, 39 provided outcome data.
Selective reporting (reporting bias)	Unclear risk	This study was registered in National Institute for Health Research Clinical Research Network Portfolio, but we could not access the information.
Other bias	Low risk	None identified.

Mou 2021

Study characteristics	
Methods	**Study design**: randomized controlled trial **Study grouping**: paired-eye design **Number randomized (total and per group):** 134 participants total; 134 eyes iridotomy, 134 eyes control **Unit of randomization:** eye (paired-eye design) **Exclusions and losses to follow-up (total and per group):** 54 participants (40.3%) at 1 year (8 participants declined follow-up, 25 could not be contacted, 2 moved and could not be contacted, and 19 did not attend follow-up despite repeated requests) **Number analyzed (total and per group):** 80 participants total; 80 eyes iridotomy, 80 eyes control **Unit of analysis (individual or eye):** eye (paired-eye design) **Length of follow-up:** 10 years **How were missing data handled?:** available-case analysis **Reported sample size calculation (Y/N), if yes, sample size and power**: Y, "sample size of 116 patients was calculated to allow demonstration of superiority at the 5.0% significance level with a power of 80%. Anticipating a loss to follow up of 10% per year, the sample size was increased to 177"
Participants	**Country:** China **Setting:** Handan Eye Hospital **Baseline characteristics**: Overall • Age (year) (mean, SD): 60.5 (SD 8.0) • Female sex (n, [%]): 117 (87%) **Inclusion criteria**: 1) age ≥ 40 years; 2) non-visibility of the trabecular meshwork for ≥ 180° in both eyes; 3) no PAS; 4) IOP ≤ 21 mm Hg without any IOP-lowering medications; 5) normal optic disc appearance

Mou 2021 *(Continued)*

	(cup:disc ratio < 0.7, rim:disc ratio > 0.1); 6) normal visual field (VF) determined by a normal glaucoma hemifield test **Exclusion criteria**: 1) severe systemic disease such as heart or renal failure which could preclude eye examinations and follow-up; 2) any past ocular surgery; 3) history or signs of acute angle-closure attack; 4) need for frequent pupil dilation due to diabetes or other retinal disease; 5) plan to move out of Handan city within 5 years; 6) unwillingness to sign an informed consent; 7) those considered at high risk of AACG (an arbitrary IOP increase of ≥ 15 mm Hg following mydriasis or darkroom provocative testing)
Interventions	**Intervention 1**: "LPI was performed with an Abraham contact lens in the superior (10:00 to 2:00 o'clock) region of the iris by [a study investigator] using an Nd:YAG laser (YL-1600; NIDEK Co., LTD, Japan). The 1% pilocarpine eye drops (Freda Company, Shandong Province, China) were instilled 4 times at an interval of 5min prior to treatment. The laser power was initially set at 4-mJ and increased as necessary (up to 11 mJ) until a patent iridotomy of approximately 0.2 mm was achieved. Full-thickness perforation was confirmed by dispersion of pigment with flow of aqueous from the posterior to the anterior chamber and direct visualization of the posterior chamber." • Use of IOP-lowering medications: 1% pilocarpine drops 4 times at 5-minute intervals prior to surgery **Intervention 2**: no treatment
Outcomes	**Primary outcomes** • Incident event of acute angle-closure glaucoma or primary angle-closure (acute angle-closure was characterized by a combination of acute symptoms of pain, headache, blurred vision and haloes around lights with signs of ischemic iris changes, corneal edema, glaukomflecken, and elevated IOP above 30 mm Hg; primary angle closure was defined as primary angle-closure suspects with IOP > 21 mm Hg on 2 separate occasions or peripheral anterior synechia of 0.5 clock hours, or both) **Secondary outcomes:** • Intraocular pressure • Gonioscopic findings • Visual acuity • Spherical equivalent • Anterior chamber depth • Lens thickness • Axial length **Adverse events:** not reported **Intervals at which outcomes assessed:** 7 days, 1 month, 1 year
Notes	**Study date**: recruitment between October 2005 and January 2008 **Funding source(s)**: "Supported in part by the Ministry of Science and Technology of the National "Eleventh Five-Year" Science and Technology Program in China (No.2007BAI1 8B08); Beijijng Municipal Science and Technology Commission, Capital Characteristic Clinic Project (No.Z171100001017040)." **Conflicts of interest**: none declared **Publication language**: English **Trial register:** ChiCTR-TCH-10000820 **Notes:** study was initially designed to collect 10-year follow-up data, but because only 30% of participants could be contacted, the authors decided to only report results up to 1 year.
Risk of bias	

Mou 2021 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization: "The SPSS program generated a series of numbers to randomly select the right or left eye of the participants to be treated with LPI. "
Allocation concealment (selection bias)	Low risk	"Allocation concealment was achieved by involving a research nurse (Zhang CY) in the process: when a patient met the criteria for enrollment, the ophthalmologist (Fan SJ) involved in this study contacted the research nurse who communicated the allocation." Central allocation by telephone: "Allocation concealment was achieved by involving a research nurse ... in the process: when a patient met the criteria for enrollment, the ophthalmologist ... involved in this study contacted the research nurse who communicated the allocation"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking of participants does not appear to be feasible. Masking of personnel not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	"Gonioscopy was carried out by one glaucoma specialist (Fan SJ) who was blinded after assignment to the treatment prior to LPI, day 7, 1, and 12mo post LPI, using a Goldmanntype 1-mirror lens with low-ambient illumination that did not impinge on the pupil" It is unclear how gonioscopic outcome assessor could have been masked to treatment assignment given the nature of the procedure.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	40% of data were missing overall and in each group. Given that loss to follow-up was reported at the individual level, it seems reasonable to infer that when an individual was lost to follow-up, 1 eye in the treated group and 1 eye in the control group were lost to follow-up, and that the reasons for loss to follow-up were the same for both groups. In an analysis of baseline characteristics by loss to follow-up at 1 year, those who missed follow-up had a slightly lower IOP and better visual acuity than those who attended, but there were no meaningful differences between treated and untreated eyes.
Selective reporting (reporting bias)	High risk	Based on the methods, it appears that some relevant outcomes such as visual acuity were measured at follow-up but the results were not reported.
Other bias	Low risk	None identified.

ZAP

Study characteristics	
Methods	**Study design:** randomized controlled trial **Study grouping:** paired-eye design **Number randomized (total and per group):** 1778 eyes of 889 participants (paired-eye design) **Unit of randomization:** eye (paired-eye design) **Exclusions and losses to follow-up (total and per group):** 204 in LPI and 208 in observation control refused or were lost to follow-up before end of analysis

ZAP *(Continued)*

	Number analyzed (total and per group): 1778 eyes of 889 participants (889 eyes each group) in intention-to-treat analysis **Unit of analysis (individual or eye):** eye (paired-eye design) **Length of follow-up:** 72 months **How were missing data handled?:** not applicable **Reported sample size calculation (Y/N), if yes, sample size and power:** Y, "a final target of sample size of 700 individuals was established, which had 80% power with a two-sided error (α=0·05) to detect a difference of 30% in incidence of the study endpoint in 36 months of follow-up"
Participants	**Country:** China **Setting:** Zhongshan Ophthalmic Center, a tertiary specialised hospital in Guangzhou **Baseline characteristics:** Overall • Age (year) (mean, SD): 59.4 (5.0) • Female sex (n, [%]): 737, 83% **Inclusion criteria**: "Participants aged 50–70 years; bilateral primary angle-closure suspects defined as an individual with angle-closure (≥6 clock hours of angle circumference, in which the posterior, usually pigmented, trabecular meshwork was not visible under non-indentation gonioscopy) in the absence of primary angle-closure or primary angle-closure glaucoma. Eyes were eligible if vertical cup-to-disc ratio was less than 0·7, cup-to-disc asymmetry was no greater than 0·2, and neuroretinal rim width was greater than 0·1 vertical disc diameter with reference to standard photos." **Exclusion criteria**: severe health problems resulting in a life expectancy of less than 1 year, previous intraocular surgery or penetrating eye injury, media opacity preventing laser peripheral iridotomy, best-corrected visual acuity worse than 20/40, or an IOP increase greater than 15 mm Hg after dilation or after a 15-minute dark room prone provocative testing
Interventions	**Intervention 1**: "Laser peripheral iridotomy was done by a trained doctor, per a standard clinical protocol, with the use of an Abraham lens. 15 min after one drop of brimonidine 0·15% and pilocarpine 2%, a YAG laser machine was used to create an iridotomy starting with an initial setting of 1.5 mJ and titrating as needed to create a patent iridotomy of at least 200 µm in diameter. Wherever possible, the laser peripheral iridotomy was placed in a crypt or other area where the iris appeared thinnest and was positioned beneath the superior lid. All participants received dexamethasone 0.1% eye drops hourly for 24 hours and then four times daily for 1 weeks after the laser peripheral iridotomy" • Use of IOP-lowering medications: brimonidine 0.15% and pilocarpine 2%, 1 dose each 15 minutes before surgery **Intervention 2**: no treatment
Outcomes	**Primary outcomes** • Incidence of primary angle closure (composite of IOP measurements above 24 mm Hg on 2 separate occasions; development of at least 1 clock hour of peripheral anterior synechiae in any quadrant; or an episode of acute angle-closure) **Secondary outcomes** • Presenting visual acuity • IOP • Total angle width on gonioscopy • Limbal anterior chamber depth

ZAP *(Continued)*

	Intervals at which outcomes assessed: 2 weeks, 6 months, 18 months, 36 months, 54 months, 72 months
Notes	**Start date**: screening assessment between 19 June 2008 and 31 December 2008; recruitment was completed on 29 October 2010. The study was completed on 6 November 2016, which provided time for 72-month follow-up visits for all participants. **Funding source(s)**: this work is supported by the Fight for Sight (grant 1655; UK), the Sun Yat-sen University 5010 Project Fund (grant 2007033; China), the National Natural Science Foundation of China (grant 81420108008; China), Fundamental Research Funds of the State Key Laboratory in Ophthalmology (China)and Moorfields Eye Charity (previously Special Trustees of Moorfields Eye Hospital). MH receives support from the University of Melbourne Research at Melbourne Accelerator Program Professorship. The Centre for Eye Research Australia receives operational infrastructural support from the Victorian government. YJ and PJF are supported by a grant from the British Council for Prevention of Blindness. PJF received additional support from the National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital, London, UK (NIHR-BRC2 009; Moorfields/ UCL-IOO) and the Richard Desmond Charitable Foundation (via Fight for Sight UK). These funding sources did not play any role in the design and conduct of the study, the collection, management, analysis, or interpretation of the data, the preparation, review, or approval of the manuscript, or the decision to submit the manuscript for publication. **Conflicts of interest**: "We declare no competing interests" **Publication language**: English **Trial register:** ISRCTN45213099 **Notes:** an independent biostatistics and data monitoring centre was set up at the beginning of the study. The ZAP database was transferred to the data monitoring centre on a weekly basis. The data monitoring and safety committee met annually for a comprehensive review of the data and to provide recommendations. This study was extended from 36 months to 72 months and enrolled an additional 155 participants, given the much lower than predicted event rate. "Image acquisition using each instrument is carried out by a single, well-trained and qualified technician. Standard photos of excellent, good, fair, and poor images are posted alongside examination instruments as reference images for the technicians to determine if a repeated acquisition is indicated; Images of 10 participants are randomly selected once a month and reviewed by one of the principal investigators for quality" (from Jiang 2010)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"computer-generated list of random numbers was used to select the eye to be treated by LPI" (Jiang 2012 report) "A pregenerated list of random numbers was used to perform randomisation. Each eligible participant was assigned a number according to their sequence of entering the study. Randomisation numbers and their corresponding eye assignment were generated at the data monitoring centre at Wilmer Eye Institute (Baltimore, MD, USA)." Description is consistent with a random numbers table.
Allocation concealment (selection bias)	Low risk	"The random number was kept in a sealed envelope with the corresponding sequential number written on the cover and sent to the clinical data collection centre at Zhongshan Ophthalmic Center. The envelope was opened by a masked research nurse before laser peripheral iridotomy treatment." Envelopes were concealed and sequentially numbered, and it appears they were opened right before treatment, but it is unclear if they were opaque to minimize potential manipulation.

ZAP *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	"it was not possible to mask the participants and outcome examiners"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"... due to the nature of the laser peripheral iridotomy procedure, it was not possible to mask the participants and outcome examiners, which could have introduced observational bias."
Incomplete outcome data (attrition bias) All outcomes	Low risk	"All analyses were based on intentiontotreat principle and included all participants who randomly assigned. Participants who prematurely received laser peripheral iridotomy in the control eye but did not withdraw from the study were followed and analysed according to randomisation (n=24). Data from individuals who underwent cataract surgery were censored at the last visit before cataract surgery." Participants without missing data appear to have been analyzed based on the group to which they had been randomized. 23% of eyes were lost to follow-up in both groups. While the reasons for loss to follow-up are not reported, attrition rates for each group at each follow-up time point are provided. Given that the make-up of the 2 groups is different eyes of the same person, it is expected that the reasons are largely the same for both groups. This is consistent with the similarity of attrition between groups at each follow-up time point.
Selective reporting (reporting bias)	Unclear risk	The trial design publication (Jiang 2010) reports that visual field testing would be conducted at some follow-up visits; however, neither the trial record, which states that the trial was prospectively registered (ISRCTN45213099), nor the primary results publication (He 2019) indicates that this measure was performed at all.
Other bias	Low risk	None identified.

AACG: acute angle-closure glaucoma
IOP: intraocular pressure
LPI: laser peripheral iridotomy
PACG: primary angle-closure glaucoma
PACS: primary angle-closure suspect
PAS: peripheral anterior synechiae
RCT: randomized controlled trial
SD: standard deviation

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alberti 1988	Study design did not meet the eligibility criteria.
Baeteman 2007	Study design did not meet the eligibility criteria.
Bass 1979	Study design did not meet the eligibility criteria.
Bourne 2016	Intervention did not meet the eligibility criteria.
Chen 2017	Comparator did not meet the eligibility criteria.
ChiCTR2000040607	Study design did not meet the eligibility criteria.

Study	Reason for exclusion
ChiCTR-TRC-07000034	Comparator did not meet the eligibility criteria.
ChiCTR-TRC-09000645	Intervention did not meet the eligibility criteria.
ChiCTR-TRC-10000810	Comparator did not meet the eligibility criteria.
CTRI/2021/05/033352	Study design did not meet the eligibility criteria.
Defranco 1989	Study design did not meet the eligibility criteria.
Dimopoulos 1974	Study design did not meet the eligibility criteria.
Gupta 2019	Study design did not meet the eligibility criteria.
Harada 1989	Study design did not meet the eligibility criteria.
Harada 1990	Study design did not meet the eligibility criteria.
Haut 1983	Study design did not meet the eligibility criteria.
He 2007	Study design did not meet the eligibility criteria.
He 2007a	Study design did not meet the eligibility criteria.
Jain 2018	Study design did not meet the eligibility criteria.
Jin 1986	Study design did not meet the eligibility criteria.
Kavitha 2019	Comparator did not meet the eligibility criteria.
Leroy 1983	Study design did not meet the eligibility criteria.
Ling 2018	Study design did not meet the eligibility criteria.
NCT00980473	Comparator did not meet the eligibility criteria.
NCT04495491	Study design did not meet the eligibility criteria.
Pollack 1981	Study design did not meet the eligibility criteria.
Schrems 1987	Study design did not meet the eligibility criteria.
Tom 2020	Study design did not meet the eligibility criteria.
Trevino 2019	Comparator did not meet the eligibility criteria.
Yunard 2019	Comparator did not meet the eligibility criteria.
Zhai 2019	Comparator did not meet the eligibility criteria.
Zhekov 2016	Intervention did not meet the eligibility criteria.

Characteristics of ongoing studies *[ordered by study ID]*

CTRI/2021/03/032311

Study name	Risk of Progression In Incident Versus Prevalent Gonioscopic Angle Closure—IPAC
Methods	Randomized, parallel-group trial

Participants	**Inclusion criteria:** PACS ≥ 180 degrees of occludable drainage angles without visible posterior TM. Participants in the PACS group will need to meet criteria for PACS in both eyes; HROA individuals who have at least 1 eye open on gonioscopy (visible pigment TM ≥ 270) who meet 1 of the following criteria: first-degree relatives of individuals with PAC/PACG; hyperopic by at least +2 diopters and a cACD < 3 mm on optical biometry in at least 1 eye; found to have narrow angles/shallow anterior chamber (defined as a van Herick grade ≤ 2) and a cACD < 3 mm on optical biometry in at least 1 eye
	
	Exclusion criteria: people with PACS will be excluded if they meet the exclusion criteria in any eye. People with HROA will be excluded if they meet the exclusion criteria in the eye meeting HROA inclusion criteria.
	
	• Individuals < 40 years of age
	• Individuals without the capacity to consent/neurocognitive disorders
	• Presence of peripheral anterior synechia, localized hyperpigmentation or other findings suggesting obstruction of TM
	• IOP by Goldmann Applanation Tonometry ≥ 22 per Ocular Hypertension Treatment Study (OHTS) protocol. IOP will be measured at 2-month follow-up. The average of the baseline and 2-month follow-up IOP will be calculated. If the average is ≥ 22, the individual will be excluded.
	• Evidence of glaucomatous optic neuropathy on examination according to the ISGEO classification of glaucoma:
	  ○ Category 1 (structural and functional evidence): VCDR ≥ 0.7, VCDR asymmetry ≥ 0.2 or neuroretinal rim width ≤ 0.1 CDR and definite visual field (VF) defect. No alternative explanation for CDR or VF findings.
	  ○ Category 2 (advanced structural damaged with unproved field loss): VCDR ≥ 0.85, VCDR asymmetry ≥ 0.25 and incomplete VF. No alternative explanation for CDR findings
	  ○ Category 3 (optic disc not seen; field test impossible): IOP ≥ 22 mm Hg and 3/60 visual acuity or visual acuity < 3/60 and glaucoma surgery or documented history of glaucoma
	• Visually significant cataract
	• Pseudophakia
	• Previous glaucoma laser or incisional surgery
	• Signs or symptoms of acute angle-closure attack in any eye
	• Evidence of secondary glaucoma, other vision-threatening retinal pathology or systemic disease requiring frequent dilation, such as diabetic retinopathy and age-related macular degeneration
	• Visual acuity < 20/40

Interventions	**Intervention:** laser peripheral iridotomy **Control 1:** high risk open angles **Control 2:** PACS not undergoing laser peripheral iridotomy
Outcomes	**Primary outcomes:** progression to incident angle closure among high risk open angle eyes; progression to PAC/PACG among incident angle closure vs PACS eyes that have not undergone laser peripheral iridotomy; IOP changes from baseline for primary angle-closure suspects and high risk open angle eyes, calculated at specified time points **Secondary outcomes:** progression to PAC/PACG among PACS eyes with and without laser peripheral iridotomy; progression to PAC/PACG among PACS eyes post-laser peripheral iridotomy with and without persistent angle closure (defined as >= 180 degrees occludable drainage angles without visible posterior TM)

CTRI/2021/03/032311 *(Continued)*	**Measurement time point:** 2, 6, 12, 18, 24, 30, 36, 42, 48, 54, 60 months (planned)
Starting date	Not yet recruiting
Contact information	Dr S Kavitha, Aravind Eye Hospital Pondicherry; skavitha.shree@gmail.com
Notes	CTRI/2021/03/032311

cACD: corrected anterior chamber depth
CDR: cup:disc ratio
HROA: high risk open angles
IOP: intraocular pressure
ISGEO: International Society of Geographical and Epidemiological Ophthalmology
PAC: primary angle-closure
PACG: primary angle-closure glaucoma
PACS: primary angle-closure suspect
TM: trabecular meshwork
VCDR: vertical cup:disc ratio
VF: visual field

DATA AND ANALYSES

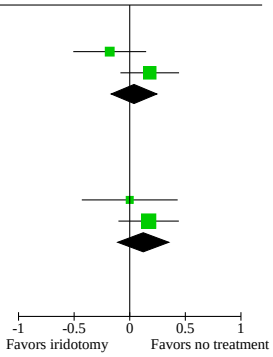
Comparison 1. Iridotomy versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Intraocular pressure	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1.1 1-year follow-up	2	2598	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.17, 0.24]
1.1.2 5-year follow-up	2	2016	Mean Difference (IV, Fixed, 95% CI)	0.12 [-0.11, 0.35]
1.2 Gonioscopic findings: angle width	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.2.1 1-year results	2	2598	Mean Difference (IV, Fixed, 95% CI)	4.93 [4.73, 5.12]
1.2.2 5-year results	2	2016	Mean Difference (IV, Fixed, 95% CI)	5.07 [4.78, 5.36]
1.3 Gonioscopic findings: presence of peripheral anterior synechiae	3		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
1.3.1 1-year results	3	2896	Risk Ratio (IV, Fixed, 95% CI)	0.62 [0.25, 1.54]
1.3.2 5-year results	2	2738	Risk Ratio (IV, Fixed, 95% CI)	0.41 [0.24, 0.67]
1.4 Need for additional surgery to control intraocular pressure	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
1.4.1 5-year follow-up	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.5 Best-corrected visual acuity	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.5.1 1-year results	2	2596	Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.01, 0.01]
1.5.2 5-year results	2	2002	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.01, 0.03]
1.6 Adverse events	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.6.1 Intraocular pressure spike	1	1778	Risk Ratio (M-H, Fixed, 95% CI)	13.00 [0.73, 230.42]
1.6.2 Acute angle closure	3	3006	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.07, 1.20]

Analysis 1.1. Comparison 1: Iridotomy versus no treatment, Outcome 1: Intraocular pressure

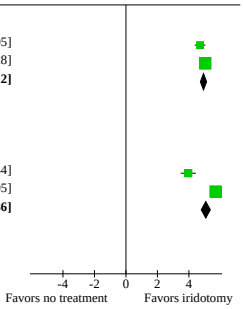
Study or Subgroup	Iridotomy Mean [mm Hg]	Iridotomy SD [mm Hg]	Iridotomy Total	No treatment Mean [mm Hg]	No treatment SD [mm Hg]	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI [mm Hg]
1.1.1 1-year follow-up								
ANA-LIS (1)	13.93	2.55	462	14.11	2.53	462	39.3%	-0.18 [-0.51 , 0.15]
ZAP (2)	14.99	2.71	837	14.81	2.79	837	60.7%	0.18 [-0.08 , 0.44]
Subtotal (95% CI)			**1299**			**1299**	**100.0%**	**0.04 [-0.17 , 0.24]**
Heterogeneity: Chi² = 2.82, df = 1 (P = 0.09); I² = 65%								
Test for overall effect: Z = 0.37 (P = 0.71)								
1.1.2 5-year follow-up								
ANA-LIS (3)	14.86	3.07	380	14.86	2.99	380	28.4%	0.00 [-0.43 , 0.43]
ZAP (4)	15.26	2.47	628	15.09	2.44	628	71.6%	0.17 [-0.10 , 0.44]
Subtotal (95% CI)			**1008**			**1008**	**100.0%**	**0.12 [-0.11 , 0.35]**
Heterogeneity: Chi² = 0.43, df = 1 (P = 0.51); I² = 0%								
Test for overall effect: Z = 1.04 (P = 0.30)								



Footnotes
(1) Paired eye design; mean IOP before dilation at 1 year
(2) Paired eye design; mean IOP at 18 months
(3) Paired eye design; mean IOP before dilation at 5 years
(4) Paired eye design; mean IOP at 72 months

Analysis 1.2. Comparison 1: Iridotomy versus no treatment, Outcome 2: Gonioscopic findings: angle width

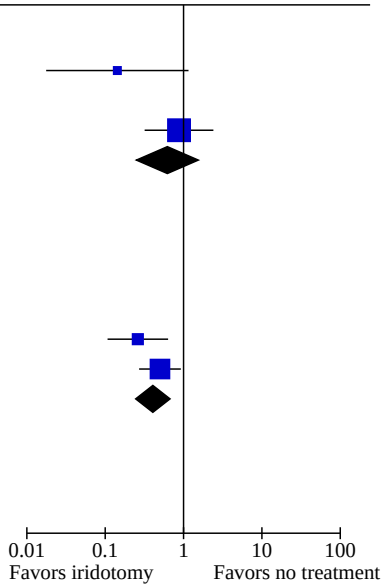
Study or Subgroup	Iridotomy Mean [Shaffer grade]	Iridotomy SD [Shaffer grade]	Iridotomy Total	No treatment Mean [Shaffer grade]	No treatment SD [Shaffer grade]	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI [Shaffer grade]
1.2.1 1-year results								
ANA-LIS (1)	7.24	2.98	462	2.53	2.15	462	34.8%	4.71 [4.37 , 5.05]
ZAP (2)	9.57	2.85	837	4.53	2.22	837	65.2%	5.04 [4.80 , 5.28]
Subtotal (95% CI)			**1299**			**1299**	**100.0%**	**4.93 [4.73 , 5.12]**
Heterogeneity: Chi² = 2.43, df = 1 (P = 0.12); I² = 59%								
Test for overall effect: Z = 48.84 (P < 0.00001)								
1.2.2 5-year results								
ANA-LIS (3)	8.31	3.4	380	4.35	3.38	380	35.8%	3.96 [3.48 , 4.44]
ZAP (4)	9.62	3.41	628	3.93	3.09	628	64.2%	5.69 [5.33 , 6.05]
Subtotal (95% CI)			**1008**			**1008**	**100.0%**	**5.07 [4.78 , 5.36]**
Heterogeneity: Chi² = 31.77, df = 1 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 34.46 (P < 0.00001)								



Footnotes
(1) Paired eye design; at 1 year; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(2) Paired eye design; at 1.5 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(3) Paired eye design; at 5 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)
(4) Paired eye design; at 6 years; measure is sum of Shaffer grading of all four quadrants (range from 0 to 16, larger number indicates wider angle)

Analysis 1.3. Comparison 1: Iridotomy versus no treatment, Outcome 3: Gonioscopic findings: presence of peripheral anterior synechiae

Study or Subgroup	Iridotomy Events	Iridotomy Total	No treatment Events	No treatment Total	Weight	Risk Ratio IV, Fixed, 95% CI
1.3.1 1-year results						
ANA-LIS (1)	1	480	7	480	18.9%	0.14 [0.02 , 1.16]
Mou 2021 (1)	0	79	0	79		Not estimable
ZAP (2)	7	889	8	889	81.1%	0.88 [0.32 , 2.40]
Subtotal (95% CI)		**1448**		**1448**	**100.0%**	**0.62 [0.25 , 1.54]**
Total events:	8		15			
Heterogeneity: Chi² = 2.34, df = 1 (P = 0.13); I² = 57%						
Test for overall effect: Z = 1.03 (P = 0.30)						
1.3.2 5-year results						
ANA-LIS (3)	6	480	23	480	32.2%	0.26 [0.11 , 0.63]
ZAP (4)	15	889	30	889	67.8%	0.50 [0.27 , 0.92]
Subtotal (95% CI)		**1369**		**1369**	**100.0%**	**0.41 [0.24 , 0.67]**
Total events:	21		53			
Heterogeneity: Chi² = 1.39, df = 1 (P = 0.24); I² = 28%						
Test for overall effect: Z = 3.51 (P = 0.0005)						

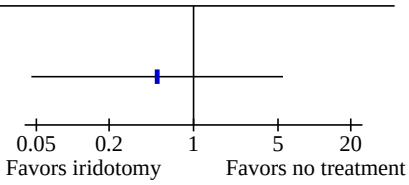


Footnotes

(1) Paired eye design; at 1 year
(2) Paired eye design; at 1.5 years
(3) Paired eye design; at 5 years
(4) Paired eye design; at 6 years

Analysis 1.4. Comparison 1: Iridotomy versus no treatment, Outcome 4: Need for additional surgery to control intraocular pressure

Study or Subgroup	Iridotomy Events	Iridotomy Total	No treatment Events	No treatment Total	Risk Ratio IV, Fixed, 95% CI
1.4.1 5-year follow-up					
ANA-LIS (1)	1	480	2	480	0.50 [0.05 , 5.50]

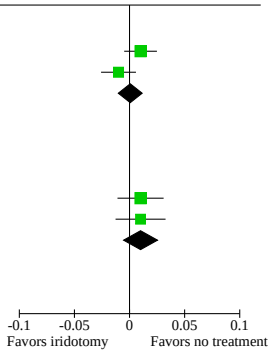


Footnotes

(1) Paired-eye design; at 5 years; one participant each group had acute angle closure and underwent LPI ;one participant in the control eye ha

Analysis 1.5. Comparison 1: Iridotomy versus no treatment, Outcome 5: Best-corrected visual acuity

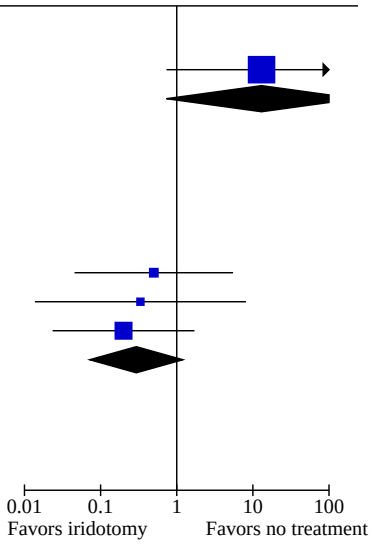
Study or Subgroup	Iridotomy Mean [logMAR]	Iridotomy SD [logMAR]	Iridotomy Total	No treatment Mean [logMAR]	No treatment SD [logMAR]	No treatment Total	Weight	Mean Difference IV, Fixed, 95% CI [logMAR]
1.5.1 1-year results								
ANA-LIS (1)	0.13	0.12	462	0.12	0.11	462	53.2%	0.01 [-0.00 , 0.02]
ZAP (2)	0.18	0.16	836	0.19	0.17	836	46.8%	-0.01 [-0.03 , 0.01]
Subtotal (95% CI)			**1298**			**1298**	**100.0%**	**0.00 [-0.01 , 0.01]**
Heterogeneity: Chi² = 3.26, df = 1 (P = 0.07); I² = 69%								
Test for overall effect: Z = 0.12 (P = 0.91)								
1.5.2 5-year results								
ANA-LIS (3)	0.14	0.16	373	0.13	0.13	373	54.0%	0.01 [-0.01 , 0.03]
ZAP (4)	0.29	0.21	628	0.28	0.2	628	46.0%	0.01 [-0.01 , 0.03]
Subtotal (95% CI)			**1001**			**1001**	**100.0%**	**0.01 [-0.01 , 0.03]**
Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%								
Test for overall effect: Z = 1.27 (P = 0.20)								



Footnotes
(1) Paired eye design; mean logMAR BCVA distance at 1 year
(2) Paired eye design; mean logMAR BCVA at 18 months
(3) Paired eye design; mean logMAR BCVA distance at 5 years
(4) Paired eye design; mean logMAR BCVA at 6 years

Analysis 1.6. Comparison 1: Iridotomy versus no treatment, Outcome 6: Adverse events

Study or Subgroup	Iridotomy Events	Iridotomy Total	No treatment Events	No treatment Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 Intraocular pressure spike						
ZAP (1)	6	889	0	889	100.0%	13.00 [0.73 , 230.42]
Subtotal (95% CI)		**889**		**889**	**100.0%**	**13.00 [0.73 , 230.42]**
Total events:	6		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
1.6.2 Acute angle closure						
ANA-LIS (2)	1	480	2	480	23.5%	0.50 [0.05 , 5.50]
Mou 2021 (3)	0	134	1	134	17.6%	0.33 [0.01 , 8.11]
ZAP (4)	1	889	5	889	58.8%	0.20 [0.02 , 1.71]
Subtotal (95% CI)		**1503**		**1503**	**100.0%**	**0.29 [0.07 , 1.20]**
Total events:	2		8			
Heterogeneity: Chi² = 0.32, df = 2 (P = 0.85); I² = 0%						
Test for overall effect: Z = 1.70 (P = 0.09)						



Footnotes
(1) IOP spike defined as >= 30 mmHg at one hour post-iridotomy
(2) Acute angle closure at 60 months
(3) Acute angle closure at 1 year
(4) Acute angle closure at 72 months

ADDITIONAL TABLES

Table 1. AAO summary of clinical findings defining angle-closure diseases

	Primary angle-closure suspect (PACS)	Primary angle-closure (PAC)	Primary angle-closure glaucoma (PACG)
Iridotrabecular contact greater than or equal to 180°	X	X	X

Table 1. AAO summary of clinical findings defining angle-closure diseases *(Continued)*

Elevated intraocular pressure OR peripheral anterior synechiae	X	X
Optic nerve damage		X

AAO: American Academy of Ophthalmology

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Glaucoma, Angle-Closure] explode all trees
#2 (angle* near/3 closure*)
#3 (angle* near/3 close*)
#4 (Uncompensat* near/2 glaucoma*)
#5 (Narrow* near/2 angle*)
#6 (occlude* near/3 angle*)
#7 Acute glaucoma*
#8 (APAC or AACG or PACG or PACS)
#9 pupillary block glaucoma*
#10 {or #1-#9}
#11 MeSH descriptor: [Laser Therapy] explode all trees
#12 MeSH descriptor: [Lasers] explode all trees
#13 Laser*
#14 (iridotom* or LPI)
#15 {or #11-#14}
#16 #10 AND #15

Appendix 2. MEDLINE (Ovid) search strategy

1. exp Glaucoma, Angle-Closure/
2. (angle* adj3 closure*).tw.
3. (angle* adj3 close*).tw.
4. (Uncompensat* adj2 glaucoma*).tw.
5. (Narrow* adj2 angle*).tw.
6. (occlude* adj3 angle*).tw.
7. Acute glaucoma*.tw.
8. (APAC or AACG or PACG or PACS).tw.
9. pupillary block glaucoma.tw.
10. or/1-9
11. exp Laser Therapy/
12. exp Lasers/
13. Laser*.tw.
14. (iridotom* or LPI).tw.
15. or/11-14
16. 10 and 15

Appendix 3. Embase.com search strategy

#1 'closed angle glaucoma'/exp
#2 (angle* NEAR/3 closure*):ab,ti
#3 (angle* NEAR/3 close*):ab,ti
#4 (uncompensat* NEAR/2 glaucoma*):ab,ti
#5 (narrow* NEAR/2 angle*):ab,ti
#6 (occlude* NEAR/3 angle*):ab,ti
#7 (acute NEAR/1 glaucoma*):ab,ti
#8 apac:ab,ti OR aacg:ab,ti OR pacg:ab,ti OR pacs:ab,ti
#9 ('pupillary block' NEAR/2 glaucoma):ab,ti
#10 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 'low level laser therapy'/exp

#12 'laser'/exp
#13 laser*:ab,ti
#14 'iridotomy'/exp
#15 iridotom*:ab,ti OR lpi:ab,ti
#16 #11 OR #12 OR #13 OR #14 OR #15
#17 #10 AND #16

Appendix 4. PubMed search strategy

1. (angle*[tw] AND closure*[tw]) NOT Medline[sb]
2. (angle*[tw] AND close*[tw]) NOT Medline[sb]
3. (Uncompensat*[tw] AND glaucoma*[tw]) NOT Medline[sb]
4. (Narrow*[tw] AND angle*[tw]) NOT Medline[sb]
5. (occlude*[tw] AND angle*[tw]) NOT Medline[sb]
6. Acute glaucoma*[tw] NOT Medline[sb]
7. (APAC[tw] or AACG[tw] or PACG[tw] or PACS[tw]) NOT Medline[sb]
8. pupillary block glaucoma[tw] NOT Medline[sb]
9. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
10. Laser*[tw] NOT Medline[sb]
11. (iridotom*[tw] OR LPI[tw]) NOT Medline[sb]
12. #10 OR #11
13. #9 AND #12

Appendix 5. LILACS search strategy

("Glaucoma de Ángulo Cerrado" OR "Glaucoma de Ângulo Fechado" OR MH:C11.525.381.056$ OR (angle$ AND (closure$ OR close$ OR narrow$ OR occlude$)) OR (Uncompensat$ glaucoma$) OR (Acute glaucoma$) OR (pupillary block glaucoma$) OR APAC OR AACG OR PACG OR PACS) AND (Laser$ OR iridotom$ or LPI OR MH:E02.594$ OR MH:E04.014.520$ OR MH:E07.632.490$ OR MH:E07.710.520$ OR MH:SP4.011.087.698.384.075.166.027$ OR MH:VS2.006.002.009$)

Appendix 6. ClinicalTrials.gov search strategy

Angle closure glaucoma OR Acute glaucoma OR pupillary block glaucoma

Appendix 7. WHO ICTRP search strategy

Angle closure glaucoma OR Acute glaucoma OR pupillary block glaucoma OR narrow-angle glaucoma OR uncompensated glaucoma OR uncompensative glaucoma

WHAT'S NEW

Date	Event	Description
30 June 2022	New citation required and conclusions have changed	Two studies were newly identified (IMPACT; Mou 2021). Two studies that were previously listed as ongoing studies were fully published (ANA-LIS; ZAP).
30 June 2022	New search has been performed	Conclusions have changed.

HISTORY

Protocol first published: Issue 6, 2016
Review first published: Issue 6, 2018

Date	Event	Description
10 October 2021	New search has been performed	Updated database searches were performed.

CONTRIBUTIONS OF AUTHORS

- Title and abstract screening and full-text review (BR, JL, Cochrane Eyes and Vision [CEV] methodologists)
- Data extraction (BR, JL, CEV methodologists)
- Risk of bias assessment (BR, JL, CEV methodologists)
- Drafting of the review (BR, JL, GG)
- Reviewing the review in detail and providing feedback (BR, JL, GG, CEV methodologists)
- Final approval of the review to be published (BR, JL, GG)

DECLARATIONS OF INTEREST

BR: none known.

JL: Dr Le reports that this research was conducted when he was a doctoral candidate and methodologist at the Johns Hopkins Bloomberg School of Public Health. The opinions expressed in this article are the author's own and do not reflect the view of the National Institutes of Health, the Department of Health and Human Services, or the United States government.

GG has received travel funding and both educational and unrestricted research funding from pharmaceutical and equipment manufacturers that are involved in the treatment of glaucoma; however, none of the funding is otherwise related to (or competing with) the subject of this review.

SOURCES OF SUPPORT

Internal sources

- None, Other

  No internal source of support.

External sources

- National Eye Institute, National Institutes of Health, USA

  Cochrane Eyes and Vision US Project supported by cooperative agreement 1 UG1 EY020522.
- National Institute on Aging, National Institutes of Health, USA

  JL was a doctoral candidate supported by the Epidemiology and Biostatistics of Aging Training Program (T32 AG000247).
- Queen's University Belfast, UK

  Gianni Virgili, Co-ordinating Editor for Cochrane Eyes and Vision's work is funded by the Centre for Public Health, Queen's University of Belfast, Northern Ireland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added methods for assessing the certainty of the evidence and presenting outcomes in a summary of findings table in accordance with revised Cochrane standards and GRADE. We revised the Background to be more concise and clarified that comparator (observation) refers to no iridotomy. For our secondary outcomes, we also considered data for longer-term follow-up closest to one year if trials did not report outcomes at one year. In the current update, we reported outcome results in the longer term (e.g. five years) as a post hoc decision to provide additional evidence for this time period. We reported mean best-corrected visual acuity as measured by logMAR at one year after iridotomy instead of mean change due to the sparsity of data reported.

Methods not implemented

We did not perform assessment of reporting biases, subgroup analyses, or sensitivity analyses due to lack of studies included.

INDEX TERMS

Medical Subject Headings (MeSH)

*Disease Progression; Glaucoma, Angle-Closure [complications] [*surgery]; Intraocular Pressure; Iris [*surgery]; Randomized Controlled Trials as Topic; Time Factors; Vision Disorders [*prevention & control]; Visual Fields

MeSH check words

Humans