Laser trabeculoplasty for open-angle glaucoma and ocular hypertension

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[Intervention Review]

Laser trabeculoplasty for open-angle glaucoma and ocular hypertension

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ABSTRACT

Background

Open-angle glaucoma (OAG) is an important cause of blindness worldwide. Laser trabeculoplasty, a treatment modality, still does not have a clear position in the treatment sequence.

Objectives

To assess the effects of laser trabeculoplasty for treating OAG and ocular hypertension (OHT) when compared to medication, glaucoma surgery or no intervention. We also wished to compare the effectiveness of different laser trabeculoplasty technologies for treating OAG and OHT.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2021, Issue 10); Ovid MEDLINE; Ovid Embase; the ISRCTN registry; LILACS, ClinicalTrials.gov and the WHO ICTRP. The date of the search was 28 October 2021. We also contacted researchers in the field.

Selection criteria

We included randomised controlled trials (RCTs) comparing laser trabeculoplasty with no intervention, with medical treatment, or with surgery in people with OAG or OHT. We also included trials comparing different types of laser trabeculoplasty technologies.

Data collection and analysis

We used standard methods expected by Cochrane. Two authors screened search results and extracted data independently. We considered the following outcomes at 24 months: failure to control intraocular pressure (IOP), failure to stabilise visual field progression, failure to stabilise optic neuropathy progression, adverse effects, quality of life, and costs. We graded the 'certainty' of the evidence using GRADE.

Main results

We included 40 studies (5613 eyes of 4028 people) in this review. The majority of the studies were conducted in Europe and in the USA. Most of the studies were at risk of performance and/or detection bias as they were unmasked. None of the studies were judged as having low risk of bias for all domains. We did not identify any studies of laser trabeculoplasty alone versus no intervention.

Laser trabeculoplasty versus medication

Fourteen studies compared laser trabeculoplasty with medication in either people with primary OAG (7 studies) or primary or secondary OAG (7 studies); five of the 14 studies also included participants with OHT. Six studies used argon laser trabeculoplasty and eight studies used selective laser trabeculoplasty. There was considerable clinical and methodological diversity in these studies leading to statistical heterogeneity in results for the primary outcome "failure to control IOP" at 24 months. Risk ratios (RRs) ranged from 0.43 in favour of laser trabeculoplasty to 1.87 in favour of medication (5 studies, I^2 = 89%). Studies of argon laser compared with medication were more likely to show a beneficial effect compared with studies of selective laser (test for interaction P = 0.0001) but the argon laser studies were older and the medication comparator group in those studies may have been less effective. We considered this to be low-certainty evidence because the trials were at risk of bias (they were not masked) and there was unexplained heterogeneity. There was evidence from two studies (624 eyes) that argon laser treatment was associated with less failure to stabilise visual field progression compared with medication (7% versus 11%, RR 0.70, 95% CI 0.42 to 1.16) at 24 months and one further large recent study of selective laser also reported a reduced risk of failure at 48 months (17% versus 26%) RR 0.65, 95% CI 0.52 to 0.81, 1178 eyes). We judged this outcome as moderate-certainty evidence, downgrading for risk of bias. There was only very low-certainty evidence on optic neuropathy progression. Adverse effects were more commonly seen in the laser trabeculoplasty group including peripheral anterior synechiae (PAS) associated with argon laser (32% versus 26%, RR 11.74, 95% CI 5.94 to 23.22; 624 eyes; 2 RCTs; low-certainty evidence); 5% of participants treated with laser in three studies of selective laser group had early IOP spikes (moderate-certainty evidence). One UK-based study provided moderate-certainty evidence that laser trabeculoplasty was more cost-effective.

Laser trabeculoplasty versus trabeculectomy

Three studies compared laser trabeculoplasty with trabeculectomy. All three studies enrolled participants with OAG (primary or secondary) and used argon laser. People receiving laser trabeculoplasty may have a higher risk of uncontrolled IOP at 24 months compared with people receiving trabeculectomy (16% versus 8%, RR 2.12, 95% CI 1.44 to 3.11; 901 eyes; 2 RCTs). We judged this to be low-certainty evidence because of risk of bias (trials were not masked) and there was inconsistency between the two trials (I^2 = 68%). There was limited evidence on visual field progression suggesting a higher risk of failure with laser trabeculoplasty. There was no information on optic neuropathy progression, quality of life or costs. PAS formation and IOP spikes were not reported but in one study trabeculectomy was associated with an increased risk of cataract (RR 1.78, 95% CI 1.46 to 2.16) (very low-certainty evidence).

Authors' conclusions

Laser trabeculoplasty may work better than topical medication in slowing down the progression of open-angle glaucoma (rate of visual field loss) and may be similar to modern eye drops in controlling eye pressure at a lower cost. It is not associated with serious unwanted effects, particularly for the newer types of trabeculoplasty, such as selective laser trabeculoplasty.

PLAIN LANGUAGE SUMMARY

Laser trabeculoplasty for open-angle glaucoma

Key messages

- Laser trabeculoplasty may work better than topical medication (eye drops) in slowing down the progression of open-angle glaucoma (rate of visual field loss i.e. vision loss at the edges of vision) and may be similar to modern eye drops in controlling eye pressure at a lower cost. It is not associated with any serious unwanted effects, particularly for the newer types of trabeculoplasty, such as selective laser trabeculoplasty.

- Laser trabeculoplasty appears to work less well than trabeculectomy (surgery for glaucoma).

What is open-angle glaucoma?

Glaucoma is an eye disease where the nerve that connects the eye to the brain (optic nerve) is damaged. Usually, this happens because the pressure inside the eye (intraocular pressure) is too high, probably because the drainage channels in the eye have become blocked.

How is open-angle glaucoma treated?

The aim of treatment for glaucoma is to reduce the pressure in the eye to protect the optic nerve from more damage. Reducing the pressure in the eye can be done by eye drops, laser treatment, or surgery. Laser trabeculoplasty involves opening up the blocked drainage channels in the eye.

What did we want to find out?

The aim of this Cochrane Review is to find out how well laser trabeculoplasty works as a treatment for open-angle glaucoma.

What did we do?

This review compared laser treatment (laser trabeculoplasty) with topical medication (eye drops) and surgery (trabeculectomy). Cochrane researchers collected and analysed all relevant studies to answer this question.

What did we find?
Cochrane researchers found 40 studies. These studies were mainly from Europe and the USA.

The results were as follows:

• Different studies found different effects on eye pressure when comparing laser trabeculoplasty with eye drops. Older studies were more likely to show a benefit of laser trabeculoplasty which may be because the eye drops in these older studies did not work as well as modern eye drops (low-certainty evidence). Three studies showed a benefit of trabeculoplasty over eye drops for avoiding visual field progression at 24 months (argon) and 48 months (selective) (moderate-certainty evidence, downgraded for risk bias).

• Harmful effects were more common in the laser trabeculoplasty group and included more cases where the iris was stuck to the edge of the drainage mechanism inside the eye (peripheral anterior synaechiae) but this was seen only with older types of laser (argon) trabeculoplasty (low-certainty evidence).

• People receiving laser trabeculoplasty may be more likely to have pressure in the eye that is too high compared with people who had surgery (trabeculectomy) (low-certainty evidence).

• Surgery (trabeculectomy) may increase the risk of cataract compared with laser (very low-certainty evidence).

• A number of studies compared different types of laser (argon, selective, diode, excimer, pattern scanning, titanium-sapphire, and micropulse) but with inconclusive results.

What are the limitations of the evidence?

Some of the studies were not masked and were not large enough to provide a reliable answer to the question. There have been changes over time in both laser and eye drops which meant that, for some outcomes, there were different effects in different studies.

How up-to-date is this evidence?
Cochrane Review authors searched for studies that had been published up to 28 October 2021.

SUMMARY OF FINDINGS

Summary of findings 1. Laser trabeculoplasty versus medication

Laser trabeculoplasty versus medication

Patient or population: people with open-angle glaucoma
Setting: eye hospital
Intervention: laser trabeculoplasty
Comparison: medication

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of eyes (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with medication	Risk with laser trabeculoplasty				
Failure to control IOP (as defined by study investigators) follow-up: 24 months	Considerable clinical and methodological diversity leading to statistical heterogeneity (I^2 = 89%). Risk ratios ranged from 0.43 in favour of laser trabeculoplasty to 1.87 in favour of medication. Studies of argon laser compared with medication were more likely to show a beneficial effect compared with studies of selective laser (test for interaction P = 0.0001) but the argon laser studies were older and the medication comparator group in those studies may have been less effective.			408 (5 RCTs)	⊕⊕⊖⊖ LOW [1,2]	
Failure to stabilise visual field progression (as defined by study investigators) follow-up: 24 months	105 per 1000	74 per 1000 (44 to 122)	RR 0.70 (0.42 to 1.16)	624 (2 RCTs)	⊕⊕⊕⊖ MODERATE[1,3]	Both studies of argon laser. One further study found RR 0.65 (0.52 to 0.81) in favour of selective laser at 48 months.
Failure to stabilise optic neuropathy progression (as defined by study investigators) follow-up: 24 months	100 per 1000	73 per 1000 (44 to 120)	RR 0.73 (0.44 to 1.20)	624 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[1,2,5]	Both studies of argon laser. One- further study found RR of 0.68 (0.11 to 4.08) in favour of selective laser at 36 months (5 events only).
Quality of life measures	One study reported little difference in scores on 12 domains of the GOAT (Glaucoma Outcomes Assessment Tool) at 24 months with the exception of 'social well-being'			819 people (2 RCTs)	⊕⊕⊕⊖ MODERATE [1]	

follow-up: 24 months	whereby participants treated with selective laser reported a greater improvement (MD 0.28, 95% CI 0.03 to 0.53) but it was unclear if this difference was important to patients. One study reported quality of life as measured using EuroQol EQ-5D 5 Levels was similar comparing selective laser and medication groups at 36 months (MD 0.01, 95% CI −0.01 to 0.03; P = 0·23).					
Adverse effects: PAS formation follow-up: any time point	25 per 1000	294 per 1000 (149 to 580)	RR 11.74 (5.94 to 23.22)	624 (2 RCTs)	⊕⊕⊖⊖ LOW [1,4]	Both these studies were argon laser. No PAS events observed in three studies of selective laser.
Adverse effects: IOP spikes follow-up: any time point	21/429 (5%) of participants in the laser group had early IOP spikes			429 (3 RCTs)	⊕⊕⊕⊖ MODERATE[1]	All three studies were selective laser.
Costs	One UK-based study considered ophthalmology costs and used a willingness-to-pay cut-point of £20,000 per quality-adjusted life-year gained. There was a strong probability (97%) that selective laser (as first-line treatment) was more cost-effective than topical medication (as first-line treatment).			1235 (1 RCT)	⊕⊕⊕⊖ MODERATE[6]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI). The assumed risk in the comparison group is the median risk across the included studies.
CI: Confidence interval;**IOP:** intraocular pressure; **PAS**: peripheral anterior synechiae; **RR:** Risk ratio; **OR:** Odds 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 effect, but there is a possibility that it is substantially different

Low-certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different

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 for risk of bias (-1): the trials were not masked.
[2]Downgraded for inconsistency (-1): unexplained heterogeneity with study results ranging from 0.43 to 1.87 (for outcome, failure to control IOP) and between 0.5 and 1.0 (for outcome, failure to stablise optic neuropathy progression).

[3]We did not downgrade for imprecision because an additional study at 48 months found a statistically significant effect of a similar order of magnitude.
[4]Downgraded for inconsistency (-1): PAS events only seen in studies of argon laser
[5]Downgraded for imprecision (-1): confidence intervals included risk ratios compatible with benefit or harm.
[6]Downgraded for indirectness (-1): results may not generalise globally.

Summary of findings 2. Laser trabeculoplasty versus trabeculectomy

Laser trabeculoplasty versus trabeculectomy

Patient or population: people with open-angle glaucoma
Setting: eye hospital
Intervention: laser trabeculoplasty
Comparison: trabeculectomy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of eyes (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with trabeculectomy	Risk with laser trabeculoplasty				
Failure to control IOP (as defined by study investigators) follow-up: 24 months	80 per 1000	170 per 1000 (115 to 249)	RR 2.12 (1.44 to 3.11)	901 (2 RCTs)	⊕⊕⊖⊖[1,2] LOW	I^2 = 68%
Failure to stabilise visual field progression (as defined by study investigators) follow-up: 24 months	Limited data from follow-up in one study suggested evidence of greater deterioration in the (argon) laser group compared with trabeculectomy at 5 years follow-up.			112 (1 RCT)	⊕⊕⊖⊖[1,3] LOW	
Failure to stabilise optic neuropathy progression (as defined by study investigators) follow-up: 24 months	This outcome was not reported in the included trials.					
Quality of life follow-up: 24 months	This outcome was not reported in the included trials.					
Adverse effects PAS formation follow-up: any time point	PAS formation and IOP spikes not reported, but in one study trabeculectomy was associated with an increased risk of cataract (RR 1.78, 95% CI 1.46 to 2.16).			789 (1 RCT)	⊕⊖⊖⊖[1,4] VERY LOW	
Adverse effects: IOP spikes						

follow-up: any time point

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI). The assumed risk in the comparison group is the median risk across the included studies.

** No events were observed with medication. We have assumed a low risk for illustrative purposes.
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds 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 effect, but there is a possibility that it is substantially different

Low-certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different

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 for risk of bias (-1): none of the studies were masked and one study was at high risk of attrition bias.
[2]Downgraded for inconsistency (-1): I^2 = 68%
[3]Downgraded for imprecision (-1): wide confidence intervention crossed the line of no effect.
[4]Downgraded for imprecision (-2): sparse data.

BACKGROUND

Description of the condition

Projections estimate that the number of people with glaucoma worldwide (aged 40 to 80 years old) will increase from 64.3 million in 2013 to 111.8 million in 2040 and 11.1 million will become blind because of glaucoma. Prevalence of glaucoma in Europe and North America is estimated at 2.93% and 3.55% respectively (Tham 2014). Several studies suggest that people of African origin have three times higher rates of primary open-angle glaucoma (POAG) compared with people of European or Asian origin.

Glaucoma is described as a group of disorders with a common denominator; a characteristic optic neuropathy. Various risk factors are associated with glaucoma but increased intraocular pressure (IOP) is consistently one of the most important (Shields 2005). Primary open-angle glaucoma has these characteristics, but also an open, normal-appearing anterior chamber angle with no ocular or systemic abnormality that might account for the elevated IOP, that is consistently above 21 mmHg, at least in one eye (Shields 2005). Normal tension glaucoma has similar characteristics but IOP is not the most influential causative factor (Shields 2005). However, it is now widely accepted that dichotomising the disease into normal tension and POAG around an IOP of 21 mmHg or any other statistically derived figure is arbitrary and that there is a continuity or gradation of risk with increasing IOP which reflects the extent to which the disease is determined by elevated pressure. At lower levels of IOP, other mechanisms are believed to influence progression of the disease. Ocular hypertension (OH) is a condition in which eyes with normal angles, have IOP above 21 mmHg, but no detected lesion in optic nerve or visual field. The risk of conversion to POAG is already well established in the literature in some of these cases and IOP reduction is the only treatment known to avoid the progression in high-risk cases (Kass 2002).

Glaucoma secondary to pigment dispersion syndrome (pigmentary glaucoma) is a form of glaucoma where, although the anterior chamber angle is open, there is an unusually heavy dispersion of pigment, which may be significantly involved in the pathogenesis of elevated IOP. Pseudoexfoliation glaucoma or capsular glaucoma is another form of glaucoma with an open anterior chamber angle, but it is associated with a deposition of a proteinaceous material in the anterior segment of the eye. All these four entities are included in a group called open-angle glaucoma (OAG). Glaucomatous neuropathy leads to visual field loss, initially in an arcuate or paracentral pattern extending to the periphery and ultimately to loss of central vision.

Description of the intervention

Reduction of IOP is still the goal of OAG treatment and it has been shown in a couple of systematic reviews to be important in preventing visual field deterioration (Maier 2005; Vass 2007). Medical therapy is usually the first-line therapy and there are currently many combinations of hypotensive topical medicines that can lead to a satisfactory IOP reduction (Li 2016; Realini 2002). Surgical approaches are usually reserved for cases in which good IOP control is not achieved with medication (Shields 2005) because of the risks of surgical complications. Laser trabeculoplasty is a non-invasive technique that has been employed as first-line or adjunctive therapy, or in order to avoid or delay surgical procedures.

Treating the trabecular meshwork with laser in human eyes was first described by Krasnov 1973. He believed the ruby laser caused a 'puncture' of the meshwork and thus an improvement in aqueous filtration. Later, Worthen 1974 described a series of uncontrolled OAG patients treated with argon laser, calling the procedure a laser trabeculotomy. Wise 1979 followed a series of 56 cases submitted to trabecular argon laser treatment for 18 months and considered this to be an effective alternative to filtration surgery. With a longer follow-up, Schwartz 1985 observed a decreasing success rate over time and poorer IOP control in black people. Some authors observed an improvement in visual fields, most likely related to laser trabeculoplasty-induced IOP reduction (Traverso 1986), but this finding was not reproduced in other studies (AGIS 2001; GLT 1990). Peripheral anterior synechiae (PAS) and IOP spikes were frequently described complications of argon laser trabeculoplasty (ALT) (GLT 1990).

In 1995, Latina and Park were the first to conduct selective laser treatment of pigment-containing trabecular meshwork tissue. They demonstrated that by using a Q-switched frequency-doubled 532-nm Nd:YAG laser for a short duration (3ns) and power range of 0.2 to 2 mJ, they could selectively target the pigment-containing trabecular meshwork with minimal thermal diffusion to non-pigmented cells, potentially a major safety advantage compared to argon laser. This technique was subsequently named selective laser trabeculoplasty (SLT); many studies have assessed its safety and efficacy. In a randomised clinical trial, a success rate of over 70% was demonstrated in people who received SLT up to 30 months following treatment (Lai 2004). A new modality of ALT has been developed recently, using low radiance, to reduce IOP and minimise trabecular tissue damage. It is called Micropulse laser trabeculoplasty (Detry-Morel 2008).

How the intervention might work

During the development of the technology, authors proposed laser trabeculoplasty for managing OAG as an effective alternative to filtration surgery, but currently laser trabeculoplasty is being considered as a first-line alternative to medical treatment and could delay the need for medical or surgical intervention (Katz 2012; McIlraith 2006; Melamed 2003; Nagar 2005) for IOP reduction. The exact mechanism of action of ALT/SLT is still speculative but it is not due to perforation of the meshwork. One theory is that it causes circumferential contraction of the meshwork, thereby opening spaces between the meshwork beams. For SLT, there is thought to be a rejuvenative stimulus to the meshwork endothelium.

Why it is important to do this review

Although studies suggest a positive effect of laser trabeculoplasty for controlling IOP in OAG and OH, there is no consensus on the role of laser trabeculoplasty in the treatment pathway for these diseases and its use varies widely in practice in different parts of the world. This reflects underlying uncertainty of its effectiveness and, hence, there is a need for a systematic review of all the best evidence of the effectiveness of this intervention.

OBJECTIVES

To assess the effects of laser trabeculoplasty for treating OAG and OH when compared to medication, glaucoma surgery or no intervention. We also wished to compare the effectiveness of

different laser trabeculoplasty technologies for treating OAG and OH.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) only. We included both parallel-group designs, whereby people were randomly allocated to treatment, and within-person studies i.e. 'split-body' designs where eyes were randomly allocated to treatment.

Types of participants

Participants in the trials were people with any diagnosis of OAG (this included primary, secondary pigment dispersion, corticosteroid-induced glaucoma and exfoliation or pseudoexfoliation syndromes) and OH. Gender, age and nationality were not used as exclusion criteria. We excluded studies where people were previously treated with laser.

Types of interventions

We included trials where any laser trabeculoplasty technique was compared with one or more of the following:

- no intervention (untreated control groups);
- medical ocular hypotensive therapy;
- laser trabeculoplasty combined with medical ocular hypotensive therapy;
- glaucoma drainage surgery;
- alternative laser trabeculoplasty techniques.

We included studies where laser trabeculoplasty was combined with medication where this was compared with medication alone, but we excluded studies where laser trabeculoplasty was combined with medication and compared to no treatment.

Types of outcome measures

We considered the following outcomes measure. Reporting of these outcome measures was not a criterion for inclusion however we excluded studies where it was clear that none of these outcomes were measured .

Primary outcomes

- failure to control IOP (as defined by study investigators);
- failure to stabilise visual field progression (as defined by study investigators);
- failure to stabilise optic neuropathy progression (as defined by study investigators).

Secondary outcomes

- quality of life measures as available in the trial reports;
- economic data as available in the trial reports.

A minimum six months follow-up was required; trials with less than six months of follow-up were excluded.

We also collected outcomes at 12 and 24 months, when possible.

Adverse effects

Adverse effects (severe, minor) including: IOP spikes; uveitis; cyclitis; hyphema; PAS formation; corneal oedema; persistent IOP elevation; loss of vision (central island); bronchospasm; corneal endothelial cell loss

Search methods for identification of studies

Electronic searches

The Cochrane Eyes and Vision Information Specialist conducted systematic searches in the following electronic databases for RCTs and controlled clinical trials. There were no language or publication year restrictions. The date of the search was 28 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 28 October 2021 (Appendix 1).
- MEDLINE Ovid (1946 to 28 October 2021) (Appendix 2).
- Embase Ovid (1980 to 28 October 2021) (Appendix 3).
- LILACS (Latin American and Caribbean Health Science Information Database (1982 to 28 October 2021). (Appendix 4).
- ISRCTN registry (www.isrctn.com/editAdvancedSearch; searched 28 October 2021) (Appendix 5).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 28 October 2021) (Appendix 6).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched 28 October 2021) (Appendix 7).

Searching other resources

The authors of the included studies and experts in the field were contacted to find out if they knew of any published or unpublished RCTs of laser trabeculoplasty for OAG which had not been identified. We used the Science Citation Index to search for reports that cited the studies included in this review. We also searched the reference lists of included study reports to check for details of further relevant trials.

Data collection and analysis

Selection of studies

Two authors working independently (AP/CRM, DB/ML or CRM/JE), screened the abstracts of all publications that were found by the searches. Full-text reports of all potentially relevant studies were obtained and were assessed against the inclusion criteria. Disagreements were discussed and final decisions were adopted after discussion, including a third author as necessary (RW). For the current update, results of searches were entered into internet-based review management software (Covidence).

Excluded studies were documented in the Characteristics of excluded studies.

Data extraction and management

In the first version of the review, two authors extracted data independently (CRM, AP); in the current update, two authors (DB/ML or CRM/JE) also extracted data independently. We discussed any disagreements and the decisions were documented. Where

necessary, the authors of the studies were contacted to help resolve the issue.

Where means or standard deviations were not available, we tried to calculate these values based on extracting data from graphics.

Assessment of risk of bias in included studies

Two authors (AP/CRM, CRM/JE) independently assessed risk of bias in the included studies using Cochrane's tool for assessing risk of bias, disagreements were discussed, and conciliation was achieved.

We graded risk of bias as: low risk of bias, high risk of bias or unclear using the criteria as listed in Appendix 8. Attempts to contact the authors of the trials which were graded as unclear were made for further information.

Measures of treatment effect

Dichotomous outcomes were analysed by calculating the risk ratio for each trial with 95% confidence intervals.

Continuous outcomes were analysed according to the difference in mean treatment effects (mean difference) with 95% confidence intervals.

Unit of analysis issues

There were three types of studies included in this review with different implications for unit of analysis:

1. Parallel-group studies: in these studies, people were randomly allocated to intervention or comparator and one eye selected as the 'study eye'. In this case, there was no unit of analysis issue as the unit of analysis was the same as the unit of randomisation. We documented how the selection of the study eye was done.
2. Clustered studies: in these studies, people were randomly allocated to intervention or comparator and results for both eyes were reported. This means that the data can be considered to be 'clustered' and ideally effect estimates and 95% confidence intervals should be adjusted for the extra variation introduced by the cluster design.
3. Within-person studies: in these studies, eyes were randomly allocated to intervention or comparator with a paired or 'split-body' design; one eye receiving the intervention and the other eye receiving the comparator. Ideally, any analysis of these data should report a paired analysis.

For the designs with a potential unit of analysis issue (2 and 3), we checked whether a correct analysis was reported taking into account the unit of analysis issue specific to that study design. If a correct analysis was reported, we used these correct estimates and variance, entering the effect estimate and adjusted standard error using the generic inverse variance approach in Revman. If a correct analysis was not reported, we used the data on eyes as reported.

For analyses that contributed to the summary of findings tables (Summary of findings 1; Summary of findings 2), we performed a sensitivity analysis to check how robust the findings were under reasonable assumptions of within-person correlation and following methods outlined in chapter 23 of the Cochrane Handbook (Higgins 2020). These methods were:

- For clustered data, we multiplied the standard error of the effect estimate for the study (if clustering had been ignored) by the square root of the design effect. We calculated the design effect using the formula 1 - (M - 1) * ICC where M = average cluster size and ICC is the intra-cluster correlation coefficient. We assumed an ICC of 0.05.
- For within-person studies not reporting a correct analysis, we used the Becker-Balagtas method for dichotomous outcomes (Stedman 2011).

Dealing with missing data

We used data as reported by included studies, which was largely complete case analysis.

Assessment of heterogeneity

We assessed clinical and methodological diversity by careful perusal of the study reports and statistical heterogeneity in the results of the trials by inspection of graphical presentations and by performing a Chi^2 test and an I^2 test. Following the guidance in the Cochrane Handbook, we considered an I^2 value of 50% or greater to represent substantial heterogeneity but also took into account the Chi^2 test ($P < 0.1$) and direction of effects when making this judgement (Deeks 2022).

Assessment of reporting biases

There were not enough trials/data on any single comparison to evaluate formally the possibility of publication bias with funnel plots.

Data synthesis

The risk ratios from the individual trials were combined through meta-analysis. We used a random-effects model unless there were fewer than three trials in a comparison when we used a fixed-effect model. We did not pool studies if we judged that there was substantial heterogeneity (I^2 of 50% or greater with a Chi^2 test P value less than 0.1 or different direction of effects).

Subgroup analysis and investigation of heterogeneity

We undertook subgroup analyses of the different technologies used - argon laser, selective laser. Other planned subgroup analyses were not done because of lack of data (Differences between protocol and review).

Sensitivity analysis

In modification to our protocol (Differences between protocol and review), we performed a sensitivity analysis to check how robust the findings were given that some data were reported without correct adjustment for within-person correlation (clustered studies where one or both eyes were included in the analysis) and some within-person studies were not reported in accordance with their paired design.

Summary of findings and assessment of the certainty of the evidence

We included a summary of findings table summarising absolute and relative effects. We considered the following comparisons: laser trabeculoplasty versus medication and laser trabeculoplasty versus trabeculectomy.

We included the following outcomes:

- failure to control IOP (as defined by study investigators);
- failure to stabilise visual field progression (as defined by study investigators);
- failure to stabilise optic neuropathy progression (as defined by study investigators);
- quality of life measures, as available in the trial reports;
- adverse effects: PAS formation;
- adverse effects: IOP spikes;
- costs.

We included data reported at the 24-month time point, where possible. If those data were not available, we reported data at the nearest time point.

Two authors (CRM and JE working together) graded the certainty of the evidence for each outcome using the GRADE approach (GRADEpro GDT).

RESULTS

Description of studies

Results of the search

The previous edition of this review (published in 2007) included 19 studies.

The original scope of this review has since changed to include participants with ocular hypertension; see Differences between protocol and review. Therefore, the searches were edited and re-run on all databases for all years, and two previously excluded studies were included (Lai 2004; Nagar 2005).

The searches were last updated on 28 October 2021. The re-run of the searches generated a total of 4257 records (Figure 1). After the removal of 2110 duplicates, the Cochrane Information Specialist screened the remaining 2147 records and removed 1350 references that were not relevant to the scope of the review. We screened the remaining 794 references and obtained 86 full-text reports for further assessment. We included 31 reports of 20 new studies and have identified 10 ongoing studies and will assess these for potential inclusion when data become available. See Characteristics of ongoing studies for details. There are also six studies that are awaiting classification, see Characteristics of studies awaiting classification for details of follow-up with the authors of these studies.

Figure 1. Prisma flow diagram

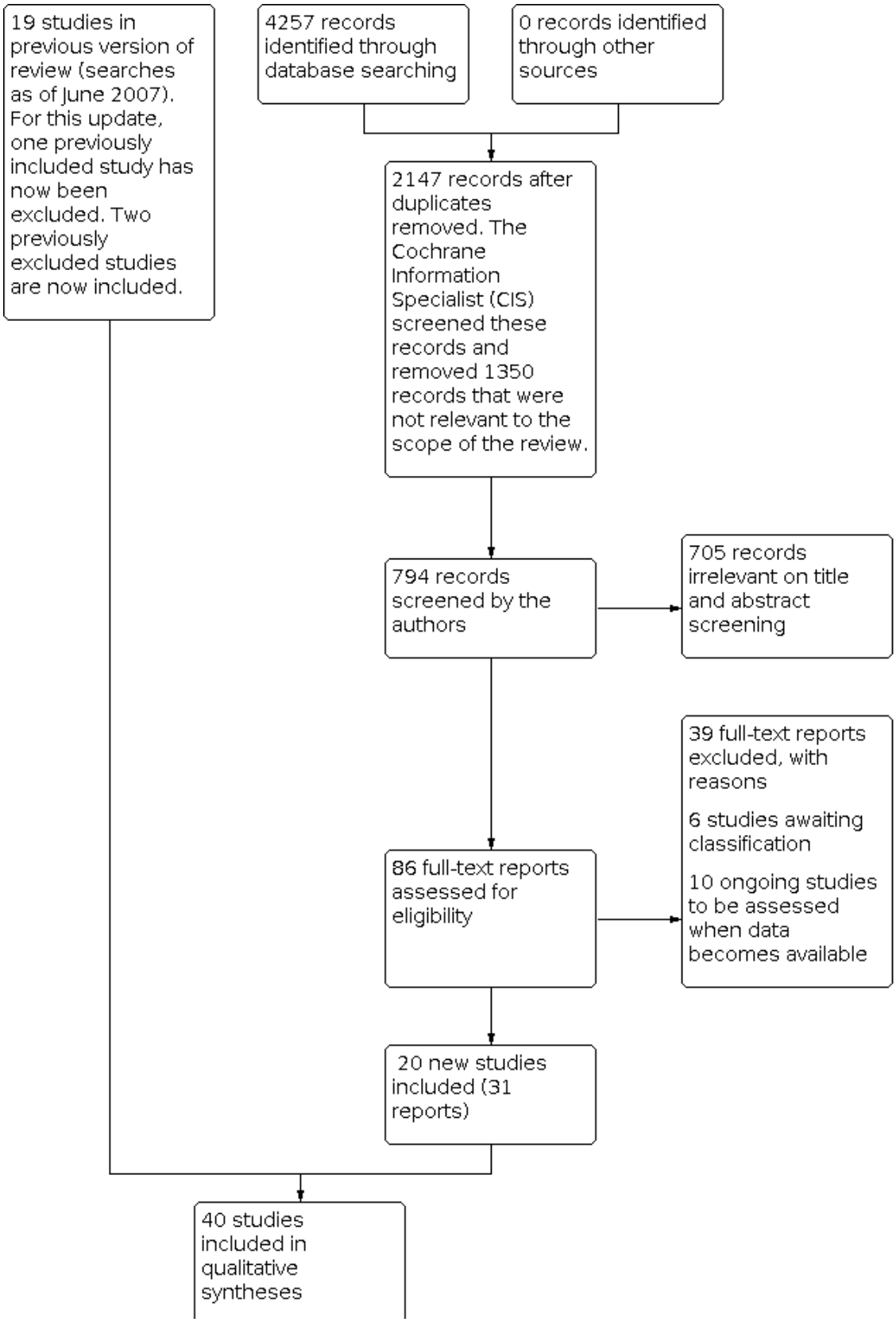
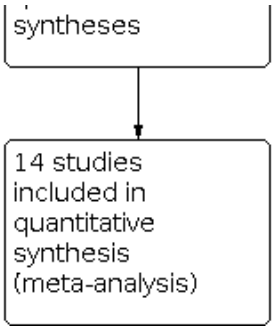


Figure 1. (Continued)



In total, this review now contains 40 included studies and 59 excluded studies.

We excluded EMGT 1999 which was included in the previous edition of this review: we considered the comparison not eligible for inclusion because laser trabeculoplasty was combined with medication and compared to no treatment.

Included studies

Types of participants

The 40 studies randomised 5613 eyes of 4028 participants (Table 1). These studies were conducted in the European region (19 studies), region of the Americas (13 studies), Western Pacific Region (6 studies) and African region (1 study, Tanzania). One further study was conducted in 15 sites in Australia, New Zealand, Singapore, and UK.

The average age of participants in the included studies ranged from 45 years to 75 years and the median average age was 67 years. In the individual studies, participants ranged in age from 18 to 92 years. The percentage of female participants ranged from 13% to 70% with a median value of 52%. Thirteen studies reported the ethnicity of participants and the percentage of people who were black or of African heritage ranged from 0% (Bergea 1992; Brancato 1991; Lai 2004; Smith 1984) to 100% (KiGIG 2021; Moriarty 1988). Five studies were from China (Lai 2004; Tang 2011; Wong 2021; Zhang 2015; Zhang 2016).

All of the participants had OAG or OHT. The majority of participants in these trials had POAG but some had pseudoexfoliation (PXF) glaucoma or pigment dispersion. There were two major groups of participants: people who were newly diagnosed as glaucomatous or having OHT who needed initial therapy; and people who already had glaucoma or OHT diagnosed but showed signs of progression even with the use of maximal antihypertensive medical therapy.

Types of interventions

Argon laser trabeculoplasty was mainly performed with blue-green (488 and 514 nm) continuous *wave argon laser*, with a 50 micron spot size, 50 to 100 burns, with 0.8 to 2.0 watts, and 0.1 second exposure. Selective laser trabeculoplasty was mainly performed with a Nd:Yag laser, applied in non-overlapping shots of a preset 3 nanoseconds duration and a preset 400 µm spot size with the laser energy varying from 0.3 mJ to 1.4 mJ by the clinician using any laser gonioscopy lens. The desired endpoint was the production of a few fine 'champagne bubbles'.

Laser trabeculoplasty was compared with medication in 14 studies (Table 2) and with trabeculectomy in three studies (Table 3). Thirteen studies compared different lasers (Table 4). A further 10 studies compared different modifications of the laser technique (Table 5).

Types of outcomes

All included trials reported success rates with a minimum six-month follow-up. The exact definition of success varied across trials, but IOP at or below 21 mmHg with or without medication was an inclusive definition. Others used a 20% decrease from initial IOP as the primary outcome (Babighian 2010; Damji 2006; Kaplovitz 2016; Mansouri 2016; Nagar 2005; Zhang 2015) or 15% decrease (Geffen 2017). Some studies considered the need for filtering surgery as failure criteria (Elsas 1989; Grayson 1993; Watson 1984). In addition, glaucoma progression defined as progression of visual field parameters, optic disk deterioration, and visual acuity decay was considered as failure criteria for some trials (Glaucoma Initial Treatment Study 2020; GLT 1990; LIGHT 2019; Ozen 2020; Wong 2021). Peripheral anterior synechiae formation was a complication that defined failure of the procedure in one of the trials (Rouhiainen 1988). Some trials (Blyth 1999; Damji 2006; Hugkulstone 1990; Katz 2012; Watson 1984) reported the final mean and standard deviation of the IOP and others (Damji 2006; GLT 1990) reported the mean change and the standard deviation of the IOP from entry. The higher the change from entry, the better the result was. Intraocular pressure spikes in the initial hours after laser trabeculoplasty (Damji 2006; Elsas 1989; Hugkulstone 1990), uveitis after laser treatment (Damji 2006), systemic adverse events and ocular adverse events (Gandolfi 2005), such as the need for cataract surgery, trabeculectomy or self-reported eye conditions (reduction of visual acuity, floaters and conjunctivitis) were adverse events reported in some studies.

Indexes of quality of life were also considered outcomes in some trials (Glaucoma Initial Treatment Study 2020; LIGHT 2019; KiGIG 2021; Yong 2020).

Corneal endothelial cell counting decrease was recently used as a secondary outcome in two studies (Ozen 2020; Wong 2021).

Study design

Nineteen studies enrolled one eye of each participant in the study, although only a minority of these studies indicated how the eye was selected: the worse eye (Bergea 1992; Glaucoma Initial Treatment Study 2020; Moorfields PTT 1994; Nagar 2005; Yong 2020), the right eye (Kaplovitz 2016), the first eye treated (Liu 2012), or alternate

right/left eyes (Wong 2021). Seven studies were within-person RCTs with one eye randomly allocated to treatment and the other to control (or other treatment) (Gandolfi 2005; Hugkulstone 1990; Lai 2004; Mansouri 2016; Ozen 2020; Sherwood 1987; Zhang 2016). The remaining studies enrolled one or both eyes per person. Some studies randomised eyes to treatment (Chung 1998; Grayson 1993; Watson 1984); some studies randomised people to treatment but, for participants with two eyes eligible, used a within-person study approach (Elsas 1989; Grayson 1994; Moriarty 1988); some studies randomised people to treatment and both eyes received the same treatment (Katz 2012; KiGIG 2021) and, in some studies, it was not clear how they allocated people/eyes (Damji 2006; Gandolfi 2005; Rouhiainen 1988; Zhang 2015).

In Damji 2006, the analysis was done with and without adjusting for within-person correlation and results were similar. None of the other studies took into account the study design when doing the analysis: within-person studies did not do a matched analysis and studies that randomly allocated eyes to treatment independently of the person did not take into account within-person correlation.

Excluded studies

See Characteristics of excluded studies for further details. We excluded 59 studies for the following reasons:

- not a randomised controlled trial (24 studies)
- reported follow-up was less than six months (14 studies)
- comparison not relevant for this review (9 studies)
- review outcome not measured (3 studies)
- study probably not done, or terminated early (6 studies)
- participants previously treated with laser (2 studies)
- primary angle-closure glaucoma (1 study)

Risk of bias in included studies

The following authors assessed risk of bias independently in pairs or checked the risk of bias assessments, or both (AP, DB, JE, ML, CRM). See Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

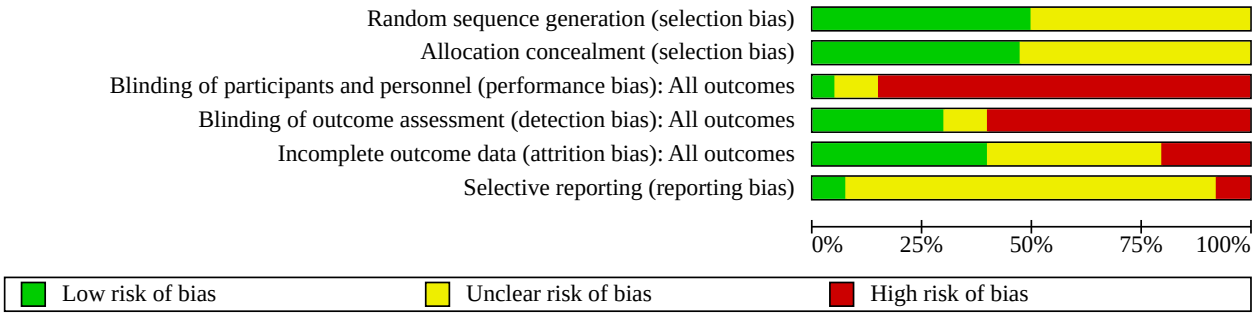


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

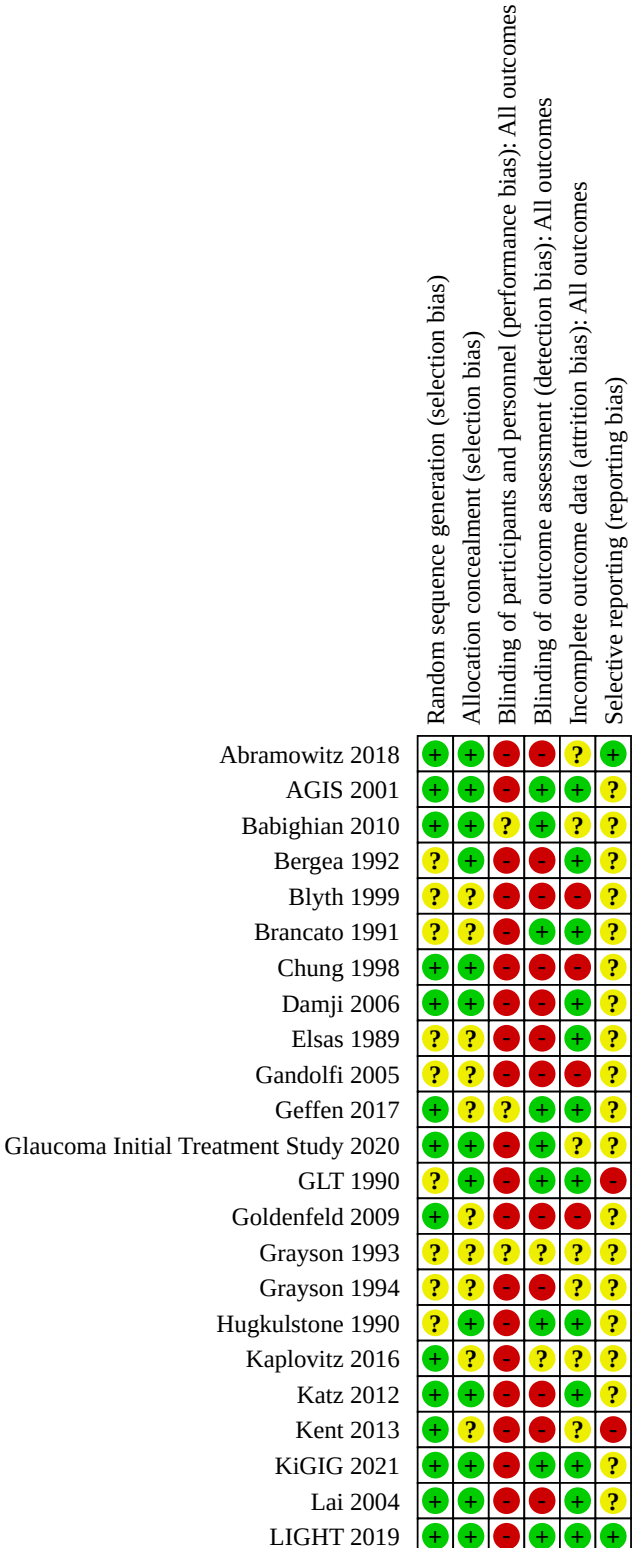
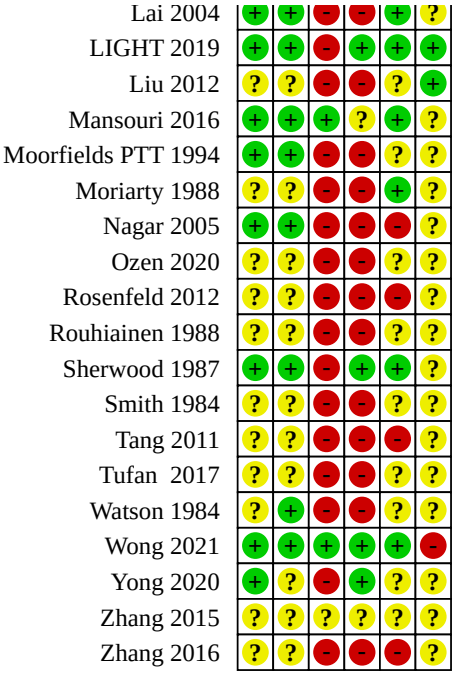


Figure 3. (Continued)



Allocation

We judged 15 studies to be at low risk of selection bias (see Figure 3). In these studies, we considered that adequate methods were used to generate an unpredictable (random) sequence that was adequately concealed from people recruiting participants. The other included studies did not provide enough information to judge one or both of these domains properly.

Blinding

We judged only two studies at low risk of performance bias (Mansouri 2016; Wong 2021). Participants were randomly allocated to two types of laser and the study authors reported specifically that the participants were masked to treatment allocation.

Twelve studies reported masking observers and we judged these studies likely to be low risk of detection bias (see Figure 3).

The remaining studies were largely judged at high risk of performance and detection bias although some studies did not report enough information to make this judgement.

Incomplete outcome data

We judged eight studies to be at high risk of attrition bias, largely due to high or uneven loss to follow-up between groups, or both (see Figure 3) and, in one study, people who developed IOP greater than 22 mmHg during follow-up were excluded (Gandolfi 2005). In the remaining studies, often follow-up was not clearly described. Only 16 studies had convincing descriptions of high follow-up balanced between groups.

Selective reporting

Selective reporting was difficult to judge for most studies due to lack of availability of either a protocol or clinical trials registry entry. The majority of RCTs were assessed as unclear for reporting bias, since the initial protocol was not clearly prespecified. There was some evidence of selective reporting from GLT 1990 and Wong 2021 and, in three studies where it was clear, all prespecified outcomes had been reported (Abramowitz 2018; LIGHT 2019; Liu 2012),

Other potential sources of bias

None noted.

Effects of interventions

See: **Summary of findings 1** Laser trabeculoplasty versus medication; **Summary of findings 2** Laser trabeculoplasty versus trabeculectomy

Laser trabeculoplasty versus medication

Fourteen studies addressed this comparison. The studies are summarised in Table 2. Results at 24 months are presented in Summary of findings 1, including GRADE assessment for that time point.

Eight of these 14 studies included participants with primary open-angle glaucoma and six studies included participants with primary or secondary open-angle glaucoma. Five of the studies also included people with ocular hypertension. In most studies, the glaucoma was newly diagnosed, or probably newly diagnosed, but three studies enrolled people whose IOP was uncontrolled on maximum medication and one study enrolled people who were either newly diagnosed or already controlled on medical therapy.

Six studies considered argon laser and eight studies considered selective laser trabeculoplasty. In two studies, the laser was combined with medication. The medication used in the comparator group of these studies was heterogeneous including pilocarpine,

timolol, and latanoprost. Several studies specified a stepped regimen. In one study, the medication used was not specified clearly but was the maximum that could be tolerated (Sherwood 1987). In one study, various medications were used: β-blocker, pilocarpine, dorzolamide, and latanoprost either as monotherapy or in combination (Lai 2004). The LIGHT 2019 study investigated laser first followed by topical medication compared with topical medication first.

Failure to control IOP

Studies reported failure to control IOP at:

- six months: Bergea 1992; GLT 1990; Katz 2012; Yong 2020 (mean IOP only);
- 12 months: Bergea 1992; Glaucoma Initial Treatment Study 2020; GLT 1990; Katz 2012; KiGIG 2021; LIGHT 2019; Moorfields PTT 1994; Moriarty 1988; Nagar 2005; Sherwood 1987;
- 24 months: Bergea 1992; Glaucoma Initial Treatment Study 2020; GLT 1990; Moorfields PTT 1994;
- 36 months Gandolfi 2005; LIGHT 2019;
- five years Lai 2004; Moorfields PTT 1994.

Different definitions of failure to control IOP were used:

- Cut-point: 22 mmHg or greater: Gandolfi 2005; GLT 1990; Lai 2004; Moorfields PTT 1994; Moriarty 1988;
- Relative to baseline IOP: less than 20% fall in IOP from baseline: Nagar 2005; 25% or less fall in IOP: Glaucoma Initial Treatment Study 2020;
- Combination of relative to baseline IOP and cut-point: less than 20% fall or IOP 22 mmHg or greater: Sherwood 1987:
- Cut-point or visual field loss: 26 mmHg or greater or 'visual field decay': Bergea 1992;
- Target IOP defined on the basis of baseline IOP and visual field score: Katz 2012, or severity: KiGIG 2021:
- Mean IOP only reported Yong 2020.

Six months: Different results were seen for the three studies reporting outcomes around six months (Analysis 1.1, I^2 = 97%). The studies of argon laser showed a reduction in risk of failure to control IOP when compared with medication (RR 0.57, 95% CI 0.25 to 1.27 (Bergea 1992) and RR 0.08, 95% CI 0.04 to 0.16) (GLT 1990). The study of selective trabeculoplasty (Katz 2012) reported a similar risk of failure in people with OAG or OHT treated with selective laser compared with a stepped medical regimen (RR 1.04, 95% CI 0.74 to 1.47). Katz 2012 reported data for right and left eyes separately. We have used these data for both eyes as reported and have not adjusted for within-person correlation. This means that the confidence interval will be narrower than it should be. Yong 2020 reported mean IOP at six months in a small sample of 17 patients only. Quote "Mean reduction of IOP was 4.30 ± 1.64 mmHg in the SLT group and 2.71 ± 2.56 mmHg in the MED group at six months which was not statistically significant (P = 0.14) between two groups."

12 months: There was considerable heterogeneity with effects ranging from an RR of 0.19 (Sherwood 1987) to 1.77 (Nagar 2005) (Analysis 1.2). Overall I^2 was 90%, suggesting that much of the observed variation was not due to chance effects. As for six months follow-up, the effect with argon laser appeared to be stronger (RR 0.37, 95% CI 0.22 to 0.61; participants/eyes = 788; studies = 5) than with selective laser which showed comparable effects to medication (RR 1.15, 95% CI 0.67 to 1.97; participants/eyes = 1882; studies = 5) and the test for subgroup differences showed a difference between groups (P = 0.002).

24 months: Three studies of argon laser and two studies of selective laser reported failure to control IOP at 24 months (Analysis 1.3). Again, there was considerable heterogeneity of effect. Risk ratios ranged from 0.43 in favour of laser trabeculoplasty to 1.87 in favour of medication. Studies of argon laser compared with medication were more likely to show a beneficial effect compared with studies of selective laser (test for interaction, P = 0.0001). We judged this to be low-certainty evidence, downgrading for risk of bias as the studies were not masked and there was inconsistency due to unexplained heterogeneity.

36 months: In the LIGHT 2019 study, fewer eyes were not at target IOP at 36 months in the selective laser group compared with the medication group (Analysis 1.4) (RR 0.73, 95% CI 0.45 to 1.18; eyes = 1072). A different result was seen in Gandolfi 2005 (argon laser) but the study was very small with only 21 participants so the effect was imprecisely measured (RR 1.32, 95% CI 0.58 to 3).

Five years: The follow-up in Moorfields PTT 1994 (argon laser) was extended for five years and, at this time point, the risk of uncontrolled IOP was greater in the laser trabeculoplasty group (RR 1.83) but the confidence interval ranged from 0.93 to 3.61, i.e. including no effect (Analysis 1.5). A different direction of effect was seen in Lai 2004 but again with wide confidence intervals compatible with both benefit and harm (selective laser, RR 0.63, 95% CI 0.24 to 1.64).

Failure to stabilise visual field progression

Four studies reported visual field progression at:

- 12 months: Bergea 1992; GLT 1990;
- 24 months: Bergea 1992; GLT 1990;
- 48 months: LIGHT 2019;
- five years: Moorfields PTT 1994.

With regard to the visual field assessment methods, Bergea 1992 used Goldman manual perimetry and the field plots were evaluated in a masked fashion by two independent observers. In Moorfields PTT 1994, the visual field was tested with a Friedman Mark II tangent screen initially but was replaced after two years with the Humphrey field analyser using a threshold 24-2 testing strategy. In GLT 1990, an Octopus automated perimeter, models 201 or 2000 were used. in LIGHT 2019, visual fields were measured using standard automated perimetry and a global progression rate was calculated for each eye; fast and moderate progression were considered failure to stabilise visual field progression.

12 months: Different results were seen in the two studies of argon laser reporting this outcome at 12 months (Analysis 1.6). In Bergea 1992, there was a reduced risk of failure to stabilise visual field progression (RR 0.44, 95% CI 0.20 to 0.94) and, in GLT 1990, laser trabeculoplasty and medication had similar results (RR 0.96, 95% CI 0.59 to 1.59).

24 months: There was a reduced risk of visual field progression at two years of follow-up (RR 0.70, 95% CI 0.42 to 1.16) in two studies but the confidence interval ranged from 0.42 to 1.16, i.e. including

no effect (Bergea 1992; GLT 1990) (Analysis 1.7). We judged this to be moderate-certainty evidence. We downgraded for risk of bias as the studies were not masked but we did not downgrade for imprecision partly because of additional confirmatory evidence from the LIGHT 2019 study at 48 months (see below).

48 months: In LIGHT 2019 (selective laser), there was a reduced chance of visual field progression in the laser group (RR 0.65. 95% CI 0.52 to 0.81) (Analysis 1.8).

Five years: In Moorfields PTT 1994), there was no precisely reported dichotomous outcome indicating the relative risk of visual field deterioration in each group. But there was a statement that, in the medicine-treated group, there was a greater risk of visual field deterioration when compared with participants in the argon laser-treated group.

Failure to stabilise optic neuropathy progression

Three studies reported optic neuropathy progression, two argon laser studies at 24 months (Bergea 1992; GLT 1990) and one selective laser study at 36 months (LIGHT 2019).

24 months: There was no evidence of a difference in the risk of progression of optic neuropathy at 24 months in GLT 1990 (RR 1.00, 95% 0.47 to 2.12) but, in Bergea 1992, there was a reduced risk (RR 0.53, 95% CI 0.27 to 1.03). The pooled RR was 0.73 (95% CI 0.44 to 1.20, I^2 =37%) (Analysis 1.9). We judged this to be very low-certainty evidence because of risk of bias, imprecision, and inconsistency.

36 months: In the LIGHT 2019 study, 2/605 eyes treated with selective laser had evidence of optic neuropathy progression at 36 months, compared with 3/621 eyes in the medication group (RR 0.68, 95% CI 0.11 to 4.08).

Quality of life measures

The Glaucoma Initial Treatment Study 2020 reported health-related and glaucoma-specific quality of life scores at 12 months and 24 months. There was little difference in scores on 12 domains of the GOAT (Glaucoma Outcomes Assessment Tool) with the exception of 'social well-being' where SLT patients reported a greater improvement at 24 months (mean difference (MD) 0.28, 95% CI 0.03 to 0.53) but it was unclear if this difference was important to patients.

LIGHT 2019 measured quality of life using EuroQol (EQ-5D) 5 levels. At 36 months, average EQ-5D score was 0.89 (standard deviation (SD) 0.18) in the selective laser trabeculoplasty group versus 0.90 (SD 0.16) in the medication group (MD 0.01, 95% CI −0.01 to 0.03; P = 0·23). Similar findings were seen at other time points.

We judged this to be moderate-certainty evidence, downgrading for risk of bias only.

Economic data

LIGHT 2019 did an economic analysis over 36 months. The UK study considered ophthalmology costs and used a willingness-to-pay cut-point of £20,000 per quality-adjusted-life-year gained. There was a strong probability (97%) that selective laser (as first-line treatment) was more cost-effective than topical medication (as first-line treatment). In a small study of 17 participants in Malaysia, the cost per 1mmHg reduction in IOP was 165% higher in SLT compared with medication groups.

Adverse effects

Peripheral anterior synechiae (PAS) formation

Bergea 1992 and GLT 1990 (argon laser) described this outcome. The risk of PAS formation was greater in the laser trabeculoplasty group (RR 11.74, 95% CI 5.94 to 23.22) (Analysis 1.10). Both studies used argon laser. Three studies of selective laser (Katz 2012; Lai 2004; LIGHT 2019) reported no PAS.

We judged this to be low-certainty evidence downgrading for risk of bias and inconsistency.

IOP spikes

Five percent of eyes randomised to SLT (21/429) developed early IOP spikes and, obviously, there was no IOP spike reported in the medication group (430 eyes) (RR 14.31, CI 95% 2.75 to 74.33). Three studies contributed data; all used selective laser trabeculoplasty (Analysis 1.11).

We judged this to be low-certainty evidence downgrading for risk of bias and indirectness.

Other adverse effects

Systemic adverse effects

An example is a decrease of 20% or more in the forced expiratory volume after a metacholine test. Gandolfi 2005 presented the results of a trial in which a subclinical bronchial reactivity after treatment of glaucomatous participants with laser trabeculoplasty or timolol eye drops was analysed. At both periods, three and four years, there was a tendency of a reduced risk ratio in bronchial reactivity in the trabeculoplasty group, but the estimate was imprecise and compatible with no difference in risk except at three years when the difference was statistically significant.

Laser trabeculoplasty versus trabeculectomy

Three trials compared the effectiveness of laser trabeculoplasty with trabeculectomy. The details of these trials are summarised in Table 3 (AGIS 2001, Moorfields PTT 1994; Watson 1984). All three studies enrolled participants with open-angle glaucoma (primary or secondary) and used argon laser compared with trabeculectomy. Results at 24 months are presented in Summary of findings 1, including GRADE assessment for that time point.

Failure to control IOP

Since AGIS had a cross-over design, we included the first intervention comparisons of AGIS 2001 and considered failure when the participant met the criteria for re-intervention because of uncontrolled IOP. This information was received after personal contact with the study coordinator. Moorfields PTT 1994 defined failure to control IOP as a value of 22 mmHg or greater. Watson 1984 only reported IOP as a continuous variable and so was not included in these analyses.

Six months: Failure to control IOP was more frequently observed in the laser trabeculoplasty group when compared with trabeculectomy at six months (RR 3.33, 95% CI 1.72 to 6.42) but this finding largely reflected the results from AGIS which provided over 95% of the evidence (Analysis 2.1).

24 months: Failure to control IOP was more frequently observed in the laser trabeculoplasty group when compared with

trabeculectomy at two years (RR 2.12, 95% CI 1.44 to 3.11) (Analysis 2.2). There was heterogeneity in the comparison (I^2 = 68%) but both estimates of effect were in the same direction. We judged this to be low-certainty evidence downgrading for risk of bias and inconsistency.

Failure to stabilise visual field progression

Moorfields PTT 1994 reported the number of absolute defects detected in the visual fields obtained by Friedmann and Humphrey fields after five years of follow-up. But these findings were not reported as failure criteria. Mean deterioration in field score (number of spots) was greater in the laser group (approximately 2.3 (SD 3.7), approximate data extracted from graphs) compared with reduction of an average of 0.8 spots (SD 3.8) in the surgery group (and assuming error bars were correctly labelled as standard errors of the mean). Regression analysis, however, suggested that this difference was not statistically significant.

Failure to stabilise optic neuropathy progression

Although the optic disc was photographed yearly in Moorfields PTT 1994 and after six months in Watson 1984, optic disc progression of structural damage was not reported and was not considered a failure criterion in these two studies.

Adverse effects

These were not consistently reported by these three studies. In AGIS 2001, trabeculectomy was associated with an increased risk of cataract (RR 1.78, 95% CI 1.46 to 2.16).

Outcomes not reported

- quality of life;
- economic data.

Different types of laser trabeculoplasty compared with each other

Thirteen studies compared different types of laser (Table 4). Nine of the studies recruited people whose glaucoma was not controlled on topical medication; two studies did not specify this as an inclusion criterion (Babighian 2010; Kaplovitz 2016). One study enrolled people with primary OAG or OH (Kaplovitz 2016), three studies enrolled people with primary OAG only (Babighian 2010; Blyth 1999; Brancato 1991), three studies included people with primary or secondary glaucoma (Chung 1998; Damji 2006; Liu 2012; Mansouri 2016), one study enrolled patients with pseudoexfoliation syndrome only (Kent 2013), and two studies did not specify type of participants (Abramowitz 2018; Goldenfeld 2009).

Four studies compared selective laser with argon laser (Damji 2006; Kent 2013; Liu 2012; Rosenfeld 2012) and three studies compared diode laser with argon laser (Blyth 1999; Brancato 1991; Chung 1998). The remaining six studies compared different lasers to selective laser: these were excimer laser (Babighian 2010), pattern scanning laser (Mansouri 2016, Wong 2021), titanium-sapphire (Kaplovitz 2016; Goldenfeld 2009), and micropulse (Abramowitz 2018).

Failure to control IOP

Different definitions of failure to control IOP were used.

- less than 20% IOP decrease from initial values (Abramowitz 2018; Damji 2006; Liu 2012; Mansouri 2016; Wong 2021);
- less than 20% IOP decrease from initial values or needing to increase the number of glaucoma medications (Babighian 2010; Brancato 1991);
- 22 mmHg or more (Blyth 1999);
- need for trabeculectomy (Chung 1998);
- IOP 22 mmHg or less than 20% decrease from baseline (Kaplovitz 2016);
- IOP 18 mmHg or more or less than 30% IOP decrease from baseline (Goldenfeld 2009);
- Less than 3 mmHg reduction (Abramowitz 2018).

Table 6 shows the results of these studies with respect to failure to control IOP. There was no consistent pattern to suggest any particular laser was better than any other with respect to control of IOP. However, there were few studies available for each comparison and the studies were underpowered.

Adverse effects

Table 7 shows the adverse effects in these studies.

Outcomes not reported

None of the twelve studies reported any of the following outcomes:

- failure to stabilise visual field progression;
- failure to stabilise optic neuropathy progression;
- quality of life;
- economic data.

Wong 2021 reported that visual field mean deviation, average retinal nerve fibre layer (RNFL) thickness, corneal endothelial cell counts and visual acuity were similar between the treatment groups (pattern scanning laser trabeculoplasty (PLT) and SLT) at 12 months.

Modifications of laser trabeculoplasty technique or regimens

Ten studies compared different techniques of laser trabeculoplasty (Table 5), six using argon laser trabeculoplasty (Elsas 1989; Grayson 1993; Grayson 1994; Hugkulstone 1990; Rouhiainen 1988; Smith 1984) and four using selective laser trabeculoplasty (Geffen 2017; Ozen 2020; Tang 2011; Zhang 2015).

Monochromatic wavelength trabeculoplasty versus bichromatic wavelength trabeculoplasty

Smith 1984 examined the effect of trabeculoplasty using a continuous-wave laser (green) compared to the standard technology performed with the blue-green continuous-wave laser.

Failure to control IOP

Failure was defined as IOP at a level requiring any additional intervention to prevent glaucoma progression. There was no clear difference in the risk ratio of uncontrolled IOP between groups (RR 0.57, 95% CI 0.18 to 1.83).

Adverse effects: PAS formation

There was no clear difference in the risk ratio of PAS formation between the two groups (RR 1.30, 95% CI 0.63 to 2.68).

Outcomes not reported

- Failure to control visual field progression;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

Two-stage trabeculoplasty versus one-stage trabeculoplasty

Elsas 1989 analysed the effectiveness of laser trabeculoplasty performed in one session (one stage), treating 360 degrees of the angle and in two sessions, four weeks apart, treating 180 degrees of the angle in each session and reported risk of field progression and IOP spikes as outcomes. Grayson 1993 stratified eyes in three groups: group one was randomised to receive 100 burns over 360 degrees over the trabecular meshwork, group two received 50 burns over 180 degrees in two sessions and group three received 50 burns over 360 degrees also in two sessions. The primary outcome was the need for further intervention, an outcome not included in this review. At seven years follow-up, there did appear to be a significant benefit of a two-stage procedure.

Failure to stabilise visual field progression

In Elsas 1989, the relative risk of progression between the two groups was based on a few events making the estimate very imprecise (RR 3.3, 95% CI 0.14 to 76.46).

Adverse effects: IOP spikes

We defined spikes as IOP elevations above 22 mmHg. In Elsas 1989, six eyes in the two stages group developed IOP elevation, while 11 eyes in the one-stage group showed this increase. The confidence limit of the relative risk between these two groups (RR 0.60, 95% CI 0.28 to 1.31) was compatible with no difference.

Outcomes not reported

- Failure to control IOP;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

Superior trabeculoplasty versus inferior trabeculoplasty

In Grayson 1994, the primary outcome was the need for further glaucoma surgery, which was not included as an outcome in this review. There was no difference at two years of follow-up in the need for further surgery between the group in which the meshwork was treated superiorly (18/40) and the group treated inferiorly (23/53).

Argon laser trabeculoplasty applied at different power levels

Rouhiainen 1988 is the only trial that compared different power levels for laser trabeculoplasty. Four groups were randomised to receive laser at 500 mW, 600 mW, 700 mW and 800 mW. We used 500 mW as the standard technique and compared the other three power levels with the first. The authors described an adverse effect as outcome (PAS formation). Effectiveness in controlling IOP, visual field decay, and optic nerve progression were unpublished data and no additional information was obtained from the authors.

Adverse effects: PAS formation

Two eyes of 29 randomised to 500 mW developed PAS formation at six months of follow-up compared to eyes treated with 600 mW, in which 7/30 developed PAS (RR 3.38; 95% CI 0.77 to 14.96). When compared to eyes treated with 700 mW, of which 5/30 developed PAS, no significant difference was again observed (RR 2.42, 95% CI 0.51 to 11.48). But when eyes treated with 500 mW were compared to those treated with 800 mW, there was an increased risk of synechiae formation in the latter (12/30 developed PAS) (RR 5.80, 95% CI 1.42 to 23.69).

Outcomes not reported

- Failure to control IOP;
- Failure to control visual field progression;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

Argon laser trabeculoplasty using 0.1 seconds versus 0.2 seconds

Time of exposure, a parameter used during laser trabeculoplasty, was analysed in Hugkulstone 1990. The study used 0.1 seconds versus 0.2 seconds time exposure laser in a within-person design. Outcomes described were mean IOP at six, 12 and 18 months (outcomes not included in this review), and the presence of IOP spikes at one hour. Intraocular pressures were marginally but not significantly lower in the participants with longer treatment duration.

Adverse effects: Intraocular pressure spikes at one hour

At one hour of follow-up, 7/33 eyes treated with energy delivered at 0.1 seconds and 10/33 eyes treated with 0.2 seconds developed an increase of 10 mmHg or more. The confidence limits around the estimated difference in risk (RR 0.70, 95% CI 0.30 to 1.62) are compatible with no difference.

Outcomes not reported

- Failure to control IOP;
- Failure to control visual field progression;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

Low energy selective laser trabeculoplasty versus normal energy laser trabeculoplasty

Failure to control IOP

Two trials described this outcome (Tang 2011; Zhang 2015). In Tang 2011, at 12 months of follow-up 20/39 eyes that received low energy trabeculoplasty developed uncontrolled IOP at 24 months of follow-up and 18/35 eyes that were submitted to normal energy laser trabeculoplasty had uncontrolled IOP, suggesting no difference but with a wide confidence interval. In Zhang 2015 at 12 months, 6/26 eyes randomised to conventional SLT had uncontrolled IOP, while 5/26 of the eyes that received low energy SLT, had the same outcome.

Adverse effects: IOP spikes

IOP spikes were significantly more frequent in the normal energy group (10/39 eyes in low energy and 24/35 eyes in normal energy group (RR 0.37 95% CI 0.21 to 0.67) in Tang 2011.

Outcomes not reported

- Failure to control visual field progression
- Failure to control optic neuropathy progression
- Health-related quality of life
- Economic data

Trans-scleral laser trabeculoplasty without a goniolens versus conventional SLT

Failure to control IOP

Geffen 2017 noted that 2/14 participants in the new technique failed in the 6th postoperative period (14.3%), while 5/14 (35.7%) did the same in the conventional SLT technique at this follow-up period.

Adverse effects: IOP spikes

IOP spikes were found in 1/14 eyes in trans-scleral SLT and 4/14 eyes in conventional SLT.

Outcomes not reported

- Failure to control visual field progression;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

180° selective laser trabeculoplasty versus 360° selective trabeculoplasty

Failure to control IOP

Ozen 2020 described at six months, a failure rate in decreasing IOP 20% or more in 27% of eyes that received 180° SLT and in 23% of eyes receiving 360° SLT.

Adverse effects: IOP spikes

Two eyes of the same participant developed a non-persistent 3 mmHg IOP increase when receiving 180° in one eye and 360° in the other eye.

Outcomes not reported

- Failure to control visual field progression;
- Failure to control optic neuropathy progression;
- Health-related quality of life;
- Economic data.

DISCUSSION

Summary of main results

We included 40 studies (5613 eyes of 4028 people) in this review. The majority of the studies were conducted in Europe and in the USA. Most of the studies were at risk of performance and/or detection bias as they were unmasked. None of the studies were judged as having low risk of bias for all domains. We did not identify any studies of laser trabeculoplasty alone versus no intervention.

Laser trabeculoplasty versus medication

Fourteen studies compared laser trabeculoplasty with medication in either people with primary OAG (7 studies), or primary or secondary OAG (7 studies); five of the 14 studies also included participants with OHT. Six studies used argon laser trabeculoplasty and eight studies used selective laser trabeculoplasty. There was considerable clinical and methodological diversity in these studies leading to statistical heterogeneity in results for the primary outcome "failure to control IOP" at 24 months. Risk ratios (RR) ranged from 0.43 in favour of laser trabeculoplasty to 1.87 in favour of medication (5 studies, I^2 = 89%). Studies of argon laser compared with medication were more likely to show a beneficial effect compared with studies of selective laser (test for interaction P = 0.0001) but the argon laser studies were older and the medication comparator group in those studies may have been less effective. We considered this to be low-certainty evidence because the trials were at risk of bias (they were not masked) and there was unexplained heterogeneity. There was evidence from two studies (624 eyes) that argon laser treatment was associated with less failure to stabilise visual field progression compared with medication (RR 0.70, 95% CI 0.42 to 1.16) at 24 months and one further study of selective laser also reported a reduced risk at 48 months (RR 0.65, 95% CI 0.52 to 0.81, 1178 eyes). We judged this moderate-certainty evidence downgrading for risk of bias. There was only very low-certainty evidence on optic neuropathy progression. Adverse effects were more commonly seen in the laser trabeculoplasty group including peripheral anterior synechiae (PAS) associated with argon laser (RR 11.15, 95% CI 5.63 to 22.09; 624 eyes; 2 RCTs; low-certainty evidence); 5% of participants treated with laser in three studies of selective laser group had early IOP spikes (moderate-certainty evidence). One UK-based study provided moderate-certainty evidence that laser trabeculoplasty was more cost-effective.

Laser trabeculoplasty versus trabeculectomy

Three studies compared laser trabeculoplasty with trabeculectomy. All three studies enrolled participants with OAG (primary or secondary) and used argon laser. People receiving laser trabeculoplasty may have a higher risk of uncontrolled IOP at 24 months compared with people receiving trabeculectomy (RR 2.12, 95% CI 1.44 to 3.11; 901 eyes; 2 RCTs). We judged this to be low-certainty evidence because of risk of bias (trials were not masked) and there was inconsistency between the two trials (I^2 = 68%). There was limited evidence on visual field progression suggesting a higher risk of failure with laser trabeculoplasty. There was no information on optic neuropathy progression, quality of life, or costs. PAS formation and IOP spikes were not reported but in one study trabeculectomy was associated with an increased risk of cataract (RR 1.78, 95% CI 1.46 to 2.16) (very low-certainty evidence).

Comparison of different laser trabeculoplasty technologies

Thirteen studies compared different types of laser; six of these studies recruited patients whose glaucoma was not controlled on topical medication. Participants had primary OAG (6 studies) or primary or secondary OAG (4 studies). Three of these studies included people with OHT. The following comparisons were made: selective versus argon laser (4 studies); diode versus argon laser (3 studies); pattern scanning (2 studies), excimer (1 study), micropulse (1 study) or titanium-sapphire (1 study) versus selective laser and titanium-sapphire versus argon laser (1 study). There was no

consistent pattern to suggest any particular laser was better than any other with respect to control of IOP. However, there were few studies available for each comparison and the studies were underpowered. Ten studies compared different protocols of laser trabeculoplasty and, in general, there were no clear differences observed. Again, the studies were underpowered. Power levels above 800 mW in ALT seemed to have an increased risk of PAS at six months of follow-up compared to eyes that received 500 mW ALT (RR 5.80, 95% CI 1.42 to 23.69, 30 eyes, 1 RCT).

Overall completeness and applicability of evidence

Laser trabeculoplasty and its role in OAG and OHT management is still controversial and there is much variation in practice. This review included evidence of the effects of laser trabeculoplasty as a first intervention and in participants already using maximal medical tolerated therapy. It included trials published in the last 30 years during which period there have been numerous developments in glaucoma management. Topical carbonic anhydrase inhibitors, alpha-agonists, and prostaglandin analogues were introduced after 1990. The trials comparing medication and ALT were usually designed before this decade (Bergea 1992; GLT 1990; Moorfields PTT 1994; Moriarty 1988; Sherwood 1987). Incisional surgery has also changed in the past few decades. There is evidence showing that antimetabolites are useful in achieving consistent low intraocular pressure in filtering surgery for glaucoma (Cabourne 2015). Trials comparing trabeculoplasty and trabeculectomy were designed before the 1990s and antimetabolites were not used in these studies (Moorfields PTT 1994; Watson 1984). In AGIS 2001, 205 eyes of 378 treated initially with trabeculectomy were operated on after 1990 and probably augmented with 5-fluorouracil or mitomycin C.

In the current update (2021), we have included trials that compared the effects of SLT and medication (Glaucoma Initial Treatment Study 2020; Katz 2012; KiGIG 2021; Lai 2004; LIGHT 2019; Nagar 2005; Tufan 2017; Yong 2020). SLT has been largely used to control IOP in OAG and OHT in the last decade, and many papers have been published since this technique was described. More recently, SLT is being recommended as first-line therapy for OAG and OHT and, with these new studies, some conclusions could have been drawn to analyse the position of SLT in the glaucoma treatment scale.

The main outcomes in this review were uncontrolled IOP and glaucoma progression, detected by progressive visual field damage and progressive optic neuropathy. Unfortunately, few trials had documented the latter two outcomes, and some of them had such a short follow-up (six months) that it would probably not be possible to detect progression. Trials with shorter follow-up and without detection of glaucomatous neuropathy progression were included, not only because they met the inclusion criteria but also because maintaining IOP control even in the short term may result in less discomfort, inconvenience, and costs for patients. The concept of target IOP, which defines failure in IOP control, has also evolved over this period. AGIS 2001 was one of the trials that concluded that a group of glaucomatous participants had an increased risk of progression when their IOP was consistently over 18 mmHg. In the majority of trials, uncontrolled IOP was considered to be consistently greater than 22 mmHg (Blyth 1999; Elsas 1989; GLT 1990; Moorfields PTT 1994; Moriarty 1988; Sherwood 1987). Even in AGIS 2001, failure was determined when IOP was higher than 22 mmHg for certain groups. Bergea 1992 considered failure as daily curves of IOP that had measurements over 26 mmHg. Other trials defined failure as the need for further surgical intervention (which was usually linked to uncontrolled IOP) (Grayson 1993; Smith 1984; Watson 1984)) or reducing IOP to less than 20% of initial values (Brancato 1991; Damji 2006).

Visual field testing has also changed in the past few decades. Because of this and inherent long-term fluctuation in test performance, it was difficult to standardise visual field progression as an outcome. In the current update, more consistent information regarding visual field progression has been described, especially in the LIGHT 2019 trial.

It is interesting that in GLT 1990 there was an improvement in the results of visual field after randomisation in both groups, suggesting a learning effect common in this kind of psychophysical analysis, but which could also lead to erroneous conclusions. Another consideration is that there is much heterogeneity in the instruments for visual field analysis. In Bergea 1992, Goldman manual perimetry was used and the plotted charts were evaluated in a masked fashion by two independent observers. In Moorfields PTT 1994, visual field was tested with a Friedman Mark III analyser initially and after two years, a Humphrey field analyser was used. In GLT 1990, the Octopus automated perimeter models 201 or 2000, were used.

Health-related quality of life is also an important outcome; EMGT 1999 was one of the studies that potentially attempted to estimate it, but it was excluded in this version (Differences between protocol and review). LIGHT 2019; KiGIG 2021; Glaucoma Initial Treatment Study 2020; and Yong 2020 used quality of life as one of the main outcomes of the trials. There were no significant differences between different questionnaires in the two groups, except for Glaucoma Assessment Tools (assessed in one trial), in which the trabeculoplasty group seemed to have a better result than medication.

There was limited evidence on cost-effectiveness and this was in a high-income setting (UK), as reported in LIGHT 2019.

Secondary outcomes were related to adverse effects and were: PAS formation, early IOP spikes, especially when different laser trabeculoplasty techniques were compared (Blyth 1999; Brancato 1991; Chung 1998; Damji 2006; Elsas 1989; Hugkulstone 1990; Rouhiainen 1988; Smith 1984), uveitis (Damji 2006), and ocular and general side effects (Gandolfi 2004). In the update, it was observed that decrease in endothelial cell count was a secondary outcome described in Ozen 2020 and Wong 2021, and also central corneal thickness was an outcome described in Ozen 2020.

In terms of complications, not surprisingly ALT caused a higher risk of PAS formation when compared to medication. PAS formation is not a relevant adverse event observed in trials developed with SLT. Considering systemic side effects, the risk of topical beta-blocker-induced bronchospasm after a metacholine test, when compared to laser trabeculoplasty in asymptomatic participants, was not statistically significant except at three years (Gandolfi 2005). Although this study was considered of good methodological quality, it was the only trial to examine this outcome and was small and probably lacked power to detect small risk effects.

Moriarty 1988 and Sherwood 1987 evaluated outcomes in participants already on maximally tolerated medical anti-glaucoma therapy. Argon laser trabeculoplasty decreased the risk of

uncontrolled IOP but there was considerable heterogeneity between the two trials. Racial differences and severity of glaucoma could explain the observed heterogeneity. We did not include these trials in the analysis, because the design of the studies was clearly different. They included uncontrolled participants on maximal medical therapy and randomised half of the participants to ALT, keeping the other participants on observation, despite being out of control. We did not include these studies because of lack of external validity.

We also studied trials that included SLT compared to medication in participants with OAG or OHT. With regard to the effectiveness of SLT when compared to medication, we did not observe differences in risk of uncontrolled IOP (low-certainty) in people on SLT compared with those on medication (Lai 2004, Nagar 2005), and a stepped regimen in (Katz 2012; Nagar 2005), nor in naive subjects as seen in Glaucoma Initial Treatment Study 2020; KiGIG 2021; LIGHT 2019. Data were available at 12, 24 and 36 months follow-up and significant heterogeneity between the comparisons was seen. With a moderate degree of certainty, it was observed that SLT decreased the risk of visual field progression at 15 years of follow-up (LIGHT 2019). Health-related quality of life was reported in some trials (Glaucoma Initial Treatment Study 2020; KiGIG 2021; LIGHT 2019 and Yong 2020). There were no significant differences in relative risks between different questionnaires, in the two groups, except for Glaucoma Assessment Tools (assessed in one trial), in which the trabeculoplasty group seemed to have a better result than medication.

AGIS 2001, Moorfields PTT 1994 and Watson 1984 all compared laser trabeculoplasty with trabeculectomy. At six months, there was a reduced relative risk of uncontrolled IOP for trabeculectomy (only in a few cases, mitomycin-augmented) compared to laser trabeculoplasty. If this result was to be extrapolated to current glaucoma management, the difference in the risk of uncontrolled IOP would probably be more pronounced because antimetabolites are now used more often and achieve a greater reduction in IOP. We could not detect a difference between groups at 24 months because, in combining the studies for this comparison, heterogeneity was too high (we used both the random-effects and fixed-effect models).

Considering different techniques for ALT, treating 360 degrees in one session or 180 degrees in two sessions did not affect the risk of progression of visual field loss after six months and did not increase the risk of postoperative IOP spikes (Elsas 1989). The sample size in this trial was small and further studies might help to confirm or refute these findings. The only factor that seemed to increase the risk of PAS formation was using higher power settings, such as 800 mW (Rouhiainen 1988).

In terms of comparison of different laser technology, SLT was evaluated in one trial which did demonstrate similar efficacy when compared to ALT (Damji 2006). Brancato 1991 and Blyth 1999 showed that the chance of uncontrolled IOP was similar in participants treated with ALT or diode at six months and one year and two years. The risk of early IOP spikes and PAS formation were also similar in both groups. Finally, a monochromatic wave laser, manufactured by MIRA, was compared with the traditional bichromatic wavelength. There was no difference in the risk of uncontrolled IOP or of PAS formation. This laser was not approved by the Food and Drug Administration (FDA) and consequently not used in USA.

Emerging technologies have been developed to be applied to people with OAG and OHT, and some trials compare their efficacy to SLT which is increasingly considered to be the standard form of trabeculoplasty. Babighian 2010 with excimer laser trabeculoplasty (ELT), Kaplovitz 2016 with titanium laser trabeculoplasty (TLT), Abramowitz 2018 with micropulse diode laser trabeculoplasty (MLT) and Mansouri 2016 and Wong 2021 with PLT showed that, when compared to standard SLT, failure rates were very similar at six and 12 months of follow-up, with similar adverse effects (rare IOP spikes).

Also, variations in technique were studied with RCTs, such as applying SLT without a goniolens (Geffen 2017), only 180 degrees (Ozen 2020; Tufan 2017) and decreasing the amount of energy (Tang 2011; Zhang 2015). These techniques were compared to standard SLT. Once again, no major differences were observed in terms of uncontrolled IOP or adverse effects (IOP spikes) at six and 12 months of follow-up but power to detect clinically relevant differences may have been limited.

Quality of the evidence

With regard to methodological quality, nine trials were considered of good quality in all criteria measured (AGIS 2001; Bergea 1992; GLT 1990; Katz 2012; KiGIG 2021; Lai 2004; LIGHT 2019; Sherwood 1987; Wong 2021).

The most important comparisons in this review were between laser trabeculoplasty and medication. Bergea 1992, GLT 1990 and Moorfields PTT 1994 were trials that described the effect of ALT compared with medication in newly diagnosed participants. Evidence showing that, at 24 months, argon laser decreased the risk of uncontrolled IOP compared to medication was graded low-certainty (downgraded for risk of bias) because trials were not masked and one trial was at risk of selective outcome reporting. In addition, the medical treatments used in these trials are not currently considered first-line medication (downgraded for indirectness).

From these trials based on very low grade of evidence, we concluded that there was no difference in the risk of decay of either visual field or optic disc when ALT was compared to medication in people with OAG at 24 months of follow-up. Evidence was downgraded because trials were not masked and one trial was at risk of selective outcome reporting (downgraded for risk of bias). As before, because the medical treatment used in these trials was not contemporary, evidence was downgraded for indirectness and there were wide confidence intervals compatible with both benefit and harm for ALT compared to medication (downgraded for imprecision).

When SLT and medication were compared for OAG and OHT (Glaucoma Initial Treatment Study 2020; Katz 2012; KiGIG 2021; Lai 2004; LIGHT 2019; Nagar 2005), we concluded that there was low-grade evidence that both laser and current medical treatment to reduce IOP in OAG and OHT are similarly effective. Evidence was downgraded because none of the studies were masked, one study was at high risk of attrition bias (downgraded for risk of bias), there were wide confidence intervals compatible with both benefit and harm for SLT compared to medication (downgraded for imprecision), and there was also significant heterogeneity in the studies comparisons. On the other hand, there was moderate-certainty evidence, provided by one trial, that the risk of visual field

progression could be reduced by initiating treatment with SLT in OAG and OH. This effect was observed at five years of follow-up. Depending on the health system, initiating treatment with SLT can be cost-effective.

Potential biases in the review process

The main source of bias in this review is likely to be publication bias. There were insufficient studies in any single intervention comparison to allow for funnel plots and many studies may have been conducted before trial registration was a requirement or even since that time because many trials in ophthalmology still go unregistered. Different stages of OAG and different inclusion criteria (naive or medicated subjects) could also introduce a bias in comparisons in SLT trials.

Some of the methods in the current update of the review were introduced since the last review: in particular, summary of findings tables. The choice of comparisons and outcomes for these tables therefore has the potential to be data-driven as they were not prespecified in the protocol. Where possible, we have focussed on time points - 24 months - and outcomes relevant to patients. In fact, we were able to include most of our outcomes in the summary of findings table including a selection of adverse events. In the current update, it was possible to introduce relevant outcomes, such as quality of life results and economic evaluation data, that were not available in previous publications.

Agreements and disagreements with other studies or reviews

Two recent systematic reviews on laser trabeculoplasty have been published.

Zhou 2021 compared the efficacy of laser trabeculoplasty with different modalities of treatment for OAG and OHT, but limited the search from 2000 to 2019. There were some differences in inclusion criteria to the current review - they included people previously treated with laser and outcomes were restricted to IOP control at six and 12 months of follow-up. The conclusions were similar to those obtained in the current review, but the grade of evidence was not clearly described.

Chi 2020 focussed on selective laser trabeculoplasty. The authors included eight studies, five of which were also included in the current review. The three studies not included in the current review were either out of scope for the current review (laser trabeculoplasty as an adjunctive treatment Lee 2014), reflected two publications considered in this review to be the same study (Nagar 2005) and one study was excluded from this review as being non-random (De Keyser 2017). The current review included three additional studies of selective laser trabeculoplasty published since Chi 2020 was published (Glaucoma Initial Treatment Study 2020; KiGIG 2021; Yong 2020). The focus of the Chi 2020 review on selective laser trabeculoplasty only and the fact that more recent studies such as KiGIG 2021 were not included meant there was less heterogeneity observed compared with the current review, however, overall the conclusions were similar.

AUTHORS' CONCLUSIONS

Implications for practice

Currently, moderate-certainty evidence is available to guide clinical decision-making in the use of laser trabeculoplasty. It may provide some advantages in control over topical medication, especially at 24 months of follow-up without serious adverse effects. It probably reduces the risk of visual field progression when treatment is done with selective laser trabeculoplasty in naive primary open-angle glaucoma and ocular hypertension patients. In a specific health system, laser trabeculoplasty was more cost-effective as initial treatment than medication.

However, it appears to work less well than trabeculectomy.

Diode laser and selective trabeculoplasty had similar side effects when compared to ALT. Micropulse laser trabeculoplasty and pattern scanning laser trabeculoplasty had similar effects when compared to SLT and different protocols of laser trabeculoplasty have similar risks of uncontrolled IOP, but higher power levels such as 800 mW in conventional ALT seemed to increase the risk of PAS formation in ALT.

The findings suggest that laser trabeculoplasty might be a useful initial treatment in people with early glaucoma when the availability of medicines or their cost or both might reduce the likelihood of compliance in the real world. This might be of particular relevance in lower-income countries but the concern will remain about the duration of effect and there may be issues regarding the maintenance of equipment.

There is no doubt that laser trabeculoplasty can have an effect on IOP control. A treatment delivered at a single sitting that is not invasive and has minimal side effects and is relatively cheap is probably worth looking at again very closely.

Implications for research

Further RCTs are necessary for different populations, particularly in lower-income settings. Laser trabeculoplasty should be compared to medication and trabeculectomy, to determine if there is actually a difference in response to laser in different contexts and stages of the disease.

Much can be done to improve the quality of RCTs addressing this important question. Trialists have assumed that masking of participants is not possible but, since such a large placebo effect was demonstrated in the European Glaucoma Prevention Study, it has become all the more important to provide single- if not double-masking. Double-masking might be achievable with the use of a specially devised pair of gonioscopy lenses, one of which absorbs laser energy. In such a circumstance, a standard laser power would have to be used and some degree of unmasking may occur if the operator notes blanching of trabecular pigment or bubbling but this is still probably better than no masking. In any event, masking of intervention status by those determining outcome should always be employed.

The other vitally important question is whether we can gain a better understanding of the determinants of responsiveness to laser trabeculoplasty; who responds and who does not and why? Related to this is discovering what determines the duration of effect and whether there is any way this can be predicted.

And, finally, the choice of studying relevant outcomes, such as quality of life, visual field decay and cost-effectiveness should be the goal of further RCTs.

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Gianni Virgili, Co-ordinating Editor for CEV signed the review off for publication.

REFERENCES

References to studies included in this review

Abramowitz 2018 *{published data only}*

Abramowitz B, Chadha N, Kouchouk A, Alhabshan R, Belyea DA, Lamba T. Selective laser trabeculoplasty vs micropulse laser trabeculoplasty in open-angle glaucoma. *Clinical Ophthalmology* 2018;**12**:1599-1604.

AGIS 2001 *{published and unpublished data}*

AGIS (Advanced Glaucoma Intervention Study) Investigators. The advanced glaucoma intervention study, 8: Risk of cataract formation after trabeculectomy. *Archives of Ophthalmology* 2001;**119**(12):1771-9.

AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within treatment groups. *American Journal of Ophthalmology* 2001;**132**(3):311-20.

Anonymous. The Advanced Glaucoma Intervention Study (AGIS): 3. Baseline characteristics of black and white patients. *Ophthalmology* 1998;**105**(7):1137-45.

Anonymous. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes within race. Seven-year results. *Ophthalmology* 1998;**105**(7):1146-64.

Caprioli J, Coleman A. Intraocular pressure fluctuation a risk factor for visual field progression at low intraocular pressures in the Advanced Glaucoma Intervention study. *Ophthalmology* 2008;**115**(7):1123-9.

Ederer F, Gaasterland DA, Dally LG, Kim J, VanVeldhuisen PC, Blackwell B, et al. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race. Ten-year results. *Ophthalmology* 2004;**111**(4):651-64.

Gaasterland DE, Blackwell B, Dally LG, Caprioli J, Katz LJ, Ederer F, et al. The Advanced Glaucoma Intervention Study (AGIS): 10. Variability among academic glaucoma subspecialists in assessing optic disc notching. *Transactions of the American Ophthalmological Society* 2001;**99**:177-85.

Schwartz AL, VanVeldhuisen PC, Gaasterland DE, Ederer F, Sullivan EK, Cyrlin MN, et al. The Advanced Glaucoma Intervention Study (AGIS): 5. Encapsulated bleb after initial trabeculectomy. *American Journal of Ophthalmology* 1999;**127**(1):8-19.

The AGIS Investigators. Advanced Glaucoma Intervention Study (AGIS): 2. Visual field: method of scoring and reliability. *Ophthalmology* 1994;**101**(8):1445-55.

The AGIS Investigators. The Advanced Glaucoma Intervention Study, 6: effect of cataract on visual field and visual acuity. *Archives of Ophthalmology* 2000;**118**(12):1639-52.

The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 1. Study design and methods, and baseline characteristics of study patients. *Controlled Clinical Trials* 1994;**15**(4):299-325.

* The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 11. Risk factors for failure of trabeculectomy and argon laser trabeculoplasty. *American Journal of Ophthalmology* 2002;**134**(4):481-93.

The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 12. Baseline risk factors for sustained loss of visual field and visual acuity in patients with advanced glaucoma. *American Journal of Ophthalmology* 2002;**134**(4):499-512.

The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *American Journal of Ophthalmology* 2000;**130**(4):429-40.

Babighian 2010 *{published data only}*

Babighian S, Caretti L, Tavolato M, Cian R, Galan A. Excimer laser trabeculotomy vs 180 degrees selective laser trabeculoplasty in primary open-angle glaucoma. A 2-year randomized, controlled trial. *Eye* 2010;**24**(4):632-8. [DOI: 10.1038/eye.2009.172]

Bergea 1992 *{published data only}*

Bergea B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine. II: Long-term effects on intraocular pressure and facility of outflow. Study design and additional therapy. *Acta Ophthalmologica* 1994;**72**(2):145-54.

Bergea B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine. III. Long-term effects on visual fields. *Acta Ophthalmologica Scandinavica* 1995;**73**(3):207-15.

Bergea B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine IV. Long-term effects on optic nerve head. *Acta Ophthalmologica Scandinavica* 1995;**73**(3):216-21.

* Bergea B, Svedbergh B. Primary argon laser trabeculoplasty vs. pilocarpine. Short-term effects. *Acta Ophthalmologica* 1992;**70**(4):454-60.

Svedbergh B, Bodin L, Bergea B. Primary argon laser trabeculoplasty versus pilocarpine. *Investigative Ophthalmology and Visual Science* 1994;**35**:ARVO E-abstract 3762.

Blyth 1999 *{published data only}*

* Blyth CPJ, Moriarty AP, McHugh JDA. Diode laser trabeculoplasty versus argon laser trabeculoplasty in the control of primary open angle glaucoma. *Lasers in Medical Science* 1999;**14**(2):105-8.

Moriarty AP, McHugh JD, Ffytche TJ, Marshall JM, Spalton DJ, Moriarty BJ. Diode laser trabeculoplasty (DLT) versus argon laser trabeculoplasty (ALT) in primary open angle glaucoma. In: American Academy of Ophthalmology; 1994. Vol. 107. 1994.

Brancato 1991 *{published data only}*

* Brancato R, Carassa R, Trabucchi G. Diode laser compared with argon laser for trabeculoplasty. *American Journal of Ophthalmology* 1991;**112**(1):50-5.

Chung 1998 *{published data only}*

Chung PY, Schuman JS, Netland PA, Lloyd-Muhammad RA, Jacobs DS. Five-year results of a randomized, prospective, clinical trial of diode vs argon laser trabeculoplasty for open-angle glaucoma. *American Journal of Ophthalmology* 1998;**126**(2):185-90.

Damji 2006 *{published data only}*

Bovell AM, Damji KF, Hodge WG, Rock WJ, Buhrmann RR, Pan YI. Long term effects on the lowering of intraocular pressure: selective laser or argon laser trabeculoplasty? *Canadian Journal of Ophthalmology* 2011;**46**(5):408-13. [DOI: 10.1016/j.jcjo.2011.01.016]

* Damji KF, Bovell AM, Hodge WG, Rock W, Shah K, Buhrman R, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty: results from a 1-year randomised clinical trial trabeculoplasty: results from a 1-year randomised clinical trial. *British Journal of Ophthalmology* 2006;**90**(12):1490–4.

Damji KF, Shah KC, Rock WJ, Bains HS, Hodge WG. Selective laser trabeculoplasty v argon laser trabeculoplasty: a prospective randomised clinical trial. *British Journal of Ophthalmology* 1999;**83**(6):718-22.

Hodge W, Damji KF, Bovell A, Buhrmann RR. Highly successful SLT is independent of glaucoma type, previous surgery, medical therapy, or glaucoma risk factors. In: American Academy of Ophthalmology; 2002. Vol. 257 (abstract). 2002.

Hodge WG, Bovell A, Rock W, Damji KF. Selective laser trabeculoplasty vs argon laser trabeculoplasty - a prospective randomized clinical trial. *Investigative Ophthalmology and Visual Science* 2001;**42**:ARVO E-abstract 2912.

Hodge WG, Damji KF, Rock W, Buhrmann R, Bovell AM, Pan Y. Baseline IOP predicts selective laser trabeculoplasty success at 1 year post-treatment: results from a randomised clinical trial. *British Journal of Ophthalmology* 2005;**89**(9):1157-60.

Elsas 1989 *{published data only}*

Elsas T, Johnsen H, Brevik TA. The immediate pressure response to primary laser trabeculoplasty - a comparison of one- and two-stage treatment. *Acta Ophthalmologica* 1989;**67**(6):664-8.

Gandolfi 2005 *{published data only}***NCT00466479**

Gandolfi S, Chetta A, Cimino K, Mora P, Sangermani C, Tardini G. Bronchial reactivity in healthy individuals undergoing long-term treatment with beta-blockers. *Archives of Ophthalmology* 2005;**123**(1):35-8.

Geffen 2017 *{published data only}*

Belkin M, Geffen N, Ofir S, Messas AK, Barkana Y, Belkin A, et al. Direct Trans-scleral Selective laser Trabeculoplasty (SLT) without a gonioscopy lens. *Investigative Ophthalmology and Visual Science* 2014;**55**(13):ARVO E-abstract 819.

* Geffen N, Ofir S, Belkin A, Segev F, Barkana Y, Messas AK, et al. Transscleral selective laser trabeculoplasty without gonioscopy lens. *Journal of Glaucoma* 2017;**26**(3):201-7.

Glaucoma Initial Treatment Study 2020 *{published data only}***12611000720910**

* Ang GS, Fenwick EK, Constantinou M, Gan ATL, Man REK, Casson RJ, et al. Selective laser trabeculoplasty versus topical medication as initial glaucoma treatment: the Glaucoma Initial Treatment study randomised clinical trial. *British Journal of Ophthalmology* 2020;**104**(6):813-21. [DOI: 10.1136/bjophthalmol-2018-313396]

Lamoureux EL, Mcintosh R, Constantinou M, Fenwick EK, Xie J, Casson R, et al. Comparing the effectiveness of selective laser trabeculoplasty with topical medication as initial treatment (the Glaucoma Initial Treatment Study): study protocol for a randomised controlled trial. *Trials* 2015;**11**(16):406. [DOI: 10.1186/s13063-015-0924-6]

GLT 1990 *{published data only}*

Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial: 4. Contralateral effects of timolol on the intraocular pressure of eyes treated with ALT. *Ophthalmic Surgery* 1991;**22**(6):324-9.

Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT): 3. Design and methods. *Controlled Clinical Trials* 1991;**12**(4):504-24.

Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT): 5. Subgroup differences at enrollment. *Ophthalmic Surgery* 1993;**24**(4):232-40.

Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT): 6. Treatment group differences in visual field changes. *American Journal of Ophthalmology* 1995;**120**(1):10-22.

* Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. *Ophthalmology* 1990;**97**(11):1403-13.

Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT) and glaucoma laser trial follow-up study: 7. Results. *American Journal of Ophthalmology* 1995;**120**(6):718-31.

Kiri A, Spaeth G, Beckman H, Sternberg A, GLT Research Group. Optic disc characteristics of blacks and whites in the glaucoma laser trial (GLT). *Investigative Ophthalmology and Visual Science* 1994;**35**:ARVO E-abstract 1187.

Sternberg A, Kiri A, Beckman H, Spaeth G, GLT Research Group. Quantitative optic disk characteristics in hypertensive POAG, and diabetic POAG patients in the glaucoma laser trial. *Investigative Ophthalmology and Visual Science* 1994;**35**:ARVO E-abstract 394.

Wilensky JT, Beckman H, Meiner CL, Ritch R, Sternberg AL, Glaucoma Laser Trabeculoplasty Study Group. Contribution of each treatment session to IOP reduction resulting from split therapy ALT in the Glaucoma Laser Trial (GLT). *Investigative Ophthalmology and Visual Science* 1994;**35**:ARVO E-abstract 3761.

Goldenfeld 2009 *{published data only}*

Goldenfeld M, Melamed S, Simon G, Simon GJB. Titanium: sapphire laser trabeculoplasty versus argon laser

trabeculoplasty in patients with open angle glaucoma. *Ophthalmic Surgery, Laser and Imaging* 2009;**40**(3):264-9.

Grayson 1993 *{published data only}*

* Grayson D, Ritch R, Camras C, Lustgarten J, Podos S. Influence of treatment protocol on the long-term efficacy of argon laser trabeculoplasty. *Journal of Glaucoma* 1993;**2**(7):7-12.

Lustgarten J, Podos SM, Ritch R, Fischer R, Stetz D, Zborowski L, et al. Laser trabeculoplasty. A prospective study of treatment variables. *Archives of Ophthalmology* 1984;**102**(4):517-9.

Grayson 1994 *{published data only}*

Grayson D, Chi T, Liebmann J, Ritch R. Initial argon laser trabeculoplasty to the inferior vs superior half of trabecular meshwork. *Archives of Ophthalmology* 1994;**112**(4):446-7.

Hugkulstone 1990 *{published data only}*

* Hugkulstone CE. Argon laser trabeculoplasty with standard and long duration. *Acta Ophthalmologica* 1990;**68**(5):579-81.

Hugkulstone CE. Two-year follow-up of intra-ocular pressure control with long duration argon laser trabeculoplasty. *Ophthalmologica* 1993;**71**(3):327-31.

Kaplovitz 2016 *{published data only}*

Kaplowitz K, Wang S, Bilonick R, Oatts J, Grippo T, Loewen N. Randomized controlled comparison of Titanium-Saphire versus standard Q-Switched Nd:Yag laser trabeculoplasty. *Journal of Glaucoma* 2016;**25**:e663-e7.

Katz 2012 *{published data only}*

Katz LJ, Steinmann WC, Kabir A, Molineaux J, Wizov SS, Marcellino G, et al. Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: a prospective, randomized trial. *Journal of Glaucoma* 2012;**21**(7):460-8. [DOI: 10.1097/IJG.0b013e318218287f]

Kent 2013 *{published data only}*

Kent SS, Hutnik CM, Birt CM, Damji KF, Harasymowycz P, Si F, et al. A randomized clinical trial of selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with pseudoexfoliation. *Journal of Glaucoma* 2015;**24**(5):344-7.

KiGIG 2021 *{published data only}***201508001235339**

Philippin H, Matayan E, Knoll KM, Macha E, Mbishi S, Makupa A, et al. Selective laser trabeculoplasty versus 0.5% timolol eye drops for the treatment of glaucoma in Tanzania: a randomised controlled trial. *Lancet Global Health* 2021;**9**(11):e1589-e99. [DOI: 10.1016/S2214-109X(21)00348-X]

Lai 2004 *{published data only}*

Lai JS, Chua JK, Tham CC, Lam DS. Five-year follow up of selective laser trabeculoplasty in Chinese eyes. *Clinical Experimental Ophthalmology* 2004;**32**(4):368-72.

LIGHT 2019 *{unpublished data only}***27208571**

Garg A, Vickerstaff V, Nathwani N, Garway-Heath D, Konstantakopoulou E, Ambler G, et al. Primary selective laser trabeculoplasty for open-angle glaucoma and ocular hypertension: clinical outcomes, predictors of success, and safety from the laser in glaucoma and ocular hypertension trial. *Ophthalmology* 2019;**126**(9):1238-48.

Garg A, Vickerstaff V, Nathwani N, Garway-Heath D, Konstantakopoulou E, Ambler G, et al. Efficacy of repeat selective laser trabeculoplasty in medication-naive open-angle glaucoma and ocular hypertension during the LiGHT Trial. *Ophthalmology* 2020;**127**(4):467-76.

Garg A, Vickerstaff V, Nathwani N, Konstantakopoulou E, Dowse E, Gazzard G. Primary selective laser trabeculoplasty for primary open angle glaucoma & ocular hypertension: early clinical outcomes from a prospective, multi-centre randomised controlled UK trial. *Investigative Ophthalmology and Visual Science* 2018;**59**(9):ARVO E-abstract 6091.

Gazzard G, Konstantakopoulou E, Garway-Heath D, Barton K, Wormald R, Morris S, et al. Laser in Glaucoma and ocular Hypertension (LiGHT) Trial. A multicentre, randomised controlled trial: design and methodology. *British Journal of Ophthalmology* 2018;**102**(5):593-8.

* Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al. Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. *Health Technology Assessesment* 2019;**23**(31):1-102.

Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet* 2019;**393**(10180):1505-16.

Konstantakopoulou E, Gazzard G, Vickerstaff V, Jiang Y, Nathwani N, Hunter R, et al. The Laser in Glaucoma and ocular Hypertension (LiGHT) Trial. A multicentre randomised controlled trial: baseline patient characteristics. *British Journal of Ophthalmology* 2018;**102**(5):599-603.

Vickerstaff V, Ambler G, Bunce C, Xing W, Gazzard G, LiGHT Trial Study Group. Statistical analysis plan for the Laser-1st versus Drops-1st for Glaucoma and Ocular Hypertension Trial (LiGHT): a multi-centre randomised controlled trial. *Trials* 2015;**16**:517.

Liu 2012 *{published data only}*

Liu Y, Birt CM. Argon versus selective laser trabeculoplasty in younger patients: 2-year results. *Journal of Glaucoma* 2012;**21**(2):112-5. [DOI: 10.1097/IJG.0b013e318202791c]

Mansouri 2016 *{published data only}*

Mansouri K, Shaarawy T. Comparing pattern scanning laser trabeculoplasty to selective laser trabeculoplasty: a randomized controlled trial. *Acta Ophthalmologica* 2016;**95**(5):e361-5.

Moorfields PTT 1994 *{published data only}*

Hitchings R, Migdal C, Fitzke F. Intraocular pressure: does it protect the visual fields? In: Glaucoma Update IV. Berlin; Heidelberg: Springer-Verlag, 1991.

Hitchings R, Migdal C, Gregory W, Poinooswamy D, Fitzke F. The use of Humphrey Perimeter to identify visual loss. In: Annual Congress of Royal College of Ophthalmologists; May 1993. 1993.

Hitchings R, Migdal C, Wormald R, Poinooswamy D, Fitzke F. The primary treatment trial: changes in the visual field analysis by computerised-assisted perimetry. *Eye* 1994;**8**(Pt 1):117-20.

McHam M, Migdal C, Netland P. Early trabeculectomy in the management of primary open angle glaucoma. *International Ophthalmology Clinics* 1994;**34**(3):163-72.

Migdal C, Clark P, Hitchings C. Glaucomatous field changes related to the method and the degree of intraocular pressure control. *Documenta Ophthalmologica* 1987;**49**:371-6.

* Migdal C, Gregory W, Hitchings R. Long-term functional outcome after early surgery compared with laser and medicine in open-angle glaucoma. *Ophthalmology* 1994;**101**(10):1651-6.

Migdal C, Hitchings R, Gregory M. Effect of mean IOP levels on visual field preservation in treated glaucoma patients. In: Annual Congress of Royal College of Ophthalmologists; May 1993. 1993.

Migdal C, Hitchings R. Control of chronic simple glaucoma with primary medical, surgical and laser treatment. *Transactions of the Ophthalmological Societies of the United Kingdom* 1986;**105**(Pt 6):653-6.

Migdal C, Hitchings R. Primary therapy for chronic simple glaucoma: the role of argon laser trabeculoplasty. *Transactions of the Ophthalmological Societies of the United Kingdom* 1984;**104**(Pt 1):62-6.

Migdal C, Hitchings R. The role of early surgery for open angle glaucoma. *Ophthalmology Clinics of North America* 1991;**4**(4):853-9.

Migdal C. What is the appropriate treatment for patients with primary open angle glaucoma: medicine, laser or primary surgery. *Ophthalmic Surgery* 1995;**26**(2):108-9.

Moriarty 1988 *{published data only}*

Moriarty BJ, Char JN, Acheson RW, Dunn DT. Argon laser trabeculoplasty in primary open-angle glaucoma - results in black Jamaican population. *International Ophthalmology* 1988;**12**(4):217-21.

Nagar 2005 *{published data only}***ISRCTN77145641**

Nagar M, Howes FW. Selective laser trabeculoplasty: a randomized controlled trial. In: American Academy of Ophthalmology; 2003. 2003:135-6.

Nagar M, Luhishi E, Shah N. Intraocular pressure control and fluctuation: the effect of treatment with selective laser trabeculoplasty. *British Journal of Ophthalmology* 2009;**93**(4):497-501.

* Nagar M, Ogunyomade A, O'Brart DP, Howes F, Marshall J. A randomised, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. *British Journal of Ophthalmology* 2005;**89**(11):1413-7.

Ozen 2020 *{published data only}*

* Özen B, Öztürk H, Yüce B. Comparison of the effects of 180° and 360° applications of selective laser trabeculoplasty on intraocular pressure and cornea. *International Ophthalmology* 2020;**40**(5):1103-10. [DOI: 10.1007/s10792-019-01275-6]

Rosenfeld 2012 *{published data only}*

* Rosenfeld E, Shemesh G, Kurtz S. The efficacy of selective laser trabeculoplasty versus argon laser trabeculoplasty in pseudophakic glaucoma patients. *Clinical Ophthalmology* 2012;**6**:1935-40. [DOI: 10.2147/OPTH.S34193]

Rouhiainen 1988 *{published data only}*

Rouhiainen HJ, Terasvirta ME, Tuovinen EJ. Peripheral anterior synechiae formation after trabeculoplasty. *Archives of Ophthalmology* 1988;**106**(2):189-91.

Rouhiainen HJ, Terasvirta ME, Tuovinen EJ. The effect of some treatment variables on the results of trabeculoplasty. *Archives of Ophthalmology* 1988;**106**(5):611-3.

Sherwood 1987 *{published data only}*

Sherwood MB, Lattimer J, Hitchings RA. Laser trabeculoplasty as supplementary treatment for primary open angle glaucoma. *British Journal of Ophthalmology* 1987;**71**(3):188-91.

Smith 1984 *{published data only}*

Smith J. Argon laser trabeculoplasty: comparison of bichromatic and monochromatic wavelengths. *Ophthalmology* 1984;**91**(4):355-60.

Tang 2011 *{published data only}*

* Tang M, Fu Y, Fu MS, Fan Y, Zou HD, Sun XD, et al. The efficacy of low-energy selective laser trabeculoplasty. *Ophthalmic Surgery, Lasers and Imaging* 2011;**42**(1):59-63. [DOI: http://dx.doi.org/10.3928/15428877-20101124-07]

Tang M, Fu Y, Ma Y, Fu M, Fan Y, Sun X, et al. The efficacy of low-energy selective laser trabeculoplasty. *Chinese Journal of Ophthalmology* 2011;**47**(10):887-92.

Tufan 2017 *{published data only}*

Tufan AK, Onur IU, Yiğit FU, Ağaçhan A, Naca SA. Selective laser trabeculoplasty vs. fixed combinations with timolol in practice: a replacement study in primary open angle glaucoma. *Turkish Journal of Ophthalmology* 2017;**47**:198-204.

Watson 1984 *{published data only}*

Watson PG, Allen ED, Graham CM, Porter GP, Pickering MS. Argon laser trabeculoplasty or trabeculectomy: a prospective randomised block study. *Transactions of the Ophthalmological Societies of the United Kingdom* 1984;**104**(Pt 1):55-61.

Wong 2021 *{published data only}*

Wong MOM, Wai Lai IS, Chan PP, Chan CY, Leung CK. A randomized controlled trial (RCT) comparing the efficacy and safety of pattern laser trabeculoplasty (PLT) and selective laser trabeculoplasty (SLT). *Investigative Ophthalmology and Visual Science* 2018;**59**(9):ARVO E-abstract 6098.

* Wong MOM, Lai IS, Chan PP, Chan NC, Chan AY, Lai GW, et al. Efficacy and safety of selective laser trabeculoplasty and

pattern scanning laser trabeculoplasty: a randomised clinical trial. *British Journal Ophthalmology* 2021;**105**(4):514–20. [DOI: 10.1136/bjophthalmol-2020-316178]

Yong 2020 *{published data only}*

* Yong MH, Che Hamzah J. Selective laser trabeculoplasty vs. topical medications for step-up treatment in primary open angle glaucoma: comparing clinical effectiveness, quality of life and cost-effectiveness. *Medical Journal of Malaysia* 2020;**75**(4):342-8.

Zhang 2015 *{published data only}*

* Zhang H, Yang Y, Xu J, Yu M. A prospective randomized study of selective laser trabeculoplasty (SLT) as a replacement for medial therapy in primary open angle glaucoma. *Zhonghua Yan Ke Za Zhi* 2015;**51**(2):109-14.

Zhang HY, Qin YJ, Yang YF, Xu JG, Yu MB. Intraocular pressure-lowering potential of subthreshold selctive laser trabeculoplasty in primary patients with primary open-angle glaucoma. *Journal of Ophthalmology* 2016;**2016**:Article ID 2153723. [DOI: 10.1155/2016/2153723]

Zhang 2016 *{published data only}*

Zhang HY, Qin YJ, Yang YF, Xu JG, Yu MB. Intraocular pressure-lowering potential of subthreshold selective laser trabeculoplasty in patients with primary open-angle glaucoma. *Journal of Ophthalmology* 2016;**2016**:Article ID 2153723.

References to studies excluded from this review

Agarwal 2006 *{published data only}*

* Agarwal HC, Poovali S, Sihota R, Dada T. Comparative evaluation of diode laser trabeculoplasty vs frequency doubled Nd:YAG laser trabeculoplasty in primary open angle glaucoma. *Eye* 2006;**20**:1352–6.

Ayala 2011 *{published data only}*

Ayala M, Chen E. Comparison of selective laser trabeculoplasty (SLT) in primary open angle glaucoma and pseudoexfoliation glaucoma. *Clinical Ophthalmology* 2011;**5**(1):1469-73.

Ayala 2014 *{published data only}***67927615**

Ayala M. Intraocular pressure reduction after initial failure of selective laser trabeculoplasty (SLT). *Graefe's Archive for Clinical and Experimental Ophthalmology* 2014;**252**(2):315-20.

Bozić 2011 *{published data only}*

Bozić M, Hentova-Senćić P, Kontić D, Marković V, Marjanović I. Prevention of intraocular pressure elevation after argon laser trabeculoplasty in primary open angle glaucoma. *Srpski Arhiv za Celokupno Lekarstvo* 2011;**139**(1-2):12-7.

Brancato 1988 *{published data only}*

Brancato R, Menchini U, Pece A, Bandello F, Serini P, Fantaguzzi S. Laser trabeculoplasty: argon laser or krypton laser? [Trabeculoplastie au laser: laser a l'argon ou laser au krypton?]. *Ophtalmologie* 1988;**2**(3):221-2.

Brooks 1993 *{published data only}*

Brooks AM, Gillies WE. Laser trabeculoplasty - argon or diode? . *Australian and New Zealand Journal of Ophthalmology* 1993;**21**(3):161-4.

Canadian Laser Study Trial Network 2019 *{published data only}*

Hodge W, Hutnik CML, Crichton AC, Ford B, Birt CM, Nicolela MT, et al. A randomized clinical trial of SLT vs ALT in patients who have already received 360 degrees of SLT - the Canadian laser study trial network. *Investigative Ophthalmology and Visual Science* 2018;**59**(9):ARVO E-abstract 3461.

* Hutnik C, Crichton A, Ford B, Nicolela M, Shuba, Birt C, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty in glaucoma patients treated previously with 360 selective laser trabeculoplasty. *Ophthalmology* 2019;**126**(2):223-32.

Chudoba 2014 *{published data only}*

Chudoba T, Sempinska-Szewczyk J, Filipak E, Malukiewca G, Shein A. Micropulse 577 nm laser trabeculoplasty - a prospective pilot study. *Klinic Oczna* 2014;**116**(3):174-9.

De Keyser 2017 *{published data only}*

De Keyser M, De Belder M, De Belder J, Groot V. Selective laser trabeculoplasty as replacement therapy in medically controlled glaucoma patients. *Acta Ophthalmologica* 2018;**96**(5):e577-e81.

* De Keyser M, De Belder M, De Groot V. Quality of life in glaucoma patients after selective laser trabeculoplasty. *International Journal of Ophthalmology* 2017;**10**(5):742-8.

Demailly 1989 *{published data only}*

Demailly P, Lehrer M, Kretz G. Argon laser trabeculoretraction in chronic open-angle glaucoma with normal pressure. A prospective study on the tonometric and perimetric effect [Trabéculorétraction au laser à l'argon dans le glaucome chronique à angle ouvert à pression normale. Une étude prospective sur l'effet tonométrique et périmétrique]. *Journal Francais d'Ophtalmologie* 1989;**12**(3):183-9.

Detry-Morel 2008 *{published data only}*

Detry-Morel M, Muschart F, Pourjavan S. Micropulse diode laser (810 nm) versus argon laser trabeculoplasty in the treatment of open-angle glaucoma: comparative short-term safety and efficacy profile. *Bulletin de la Societe Belge d'Ophtalmologie* 2008;**308**:21-8.

Douglas 1987 *{published data only}*

Douglas GR, Wijsman K. Effects of laser trabeculoplasty on intraocular pressure in the medically untreated eye. *Canadian Journal of Ophthalmology* 1987;**22**(3):157-60.

EMGT 1999 *{published data only}*

Bengtsson B, Leske MC, Yang Z, Heijl A, EMGT Group. Disc hemorrhages and treatment in the early manifest glaucoma trial. *Ophthalmology* 2008;**115**(11):2044-8.

Heijl A, Leske MC, Bengtsson B, Bengtsson B, Hussein M, Early Manifest Glaucoma Trial Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. *Acta Ophthalmologica Scandinavia* 2003;**81**(3):286-93.

Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M, Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression - results from Early Manifest Glaucoma Trial. *Archives of Ophthalmology* 2002;**120**(10):1268-79.

Hyman L, Komaroff E, Heijl A, Bengtsson B, Leske MC, Early Manifest Glaucoma Trial Group. Treatment and vision-related quality of life in Early Manifest Glaucoma Trial. *Ophthalmology* 2005;**112**(9):1505-13.

Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E, et al. Factors for glaucoma progression and the effect of treatment - the Early Manifest Glaucoma Trial. *Archives of Ophthalmology* 2003;**121**(1):48-56.

Leske MC, Heijl A, Hyman L, Bengtsson B, Komaroff E. Factors for progression and glaucoma treatment: the Early Manifest Glaucoma Trial. *Current Opinion in Ophthalmology* 2004;**15**(2):102-6.

* Leske MC, Heijl A, Hyman L, Bengtsson B. Early Manifest Glaucoma Trial: design and baseline data. *Ophthalmology* 1999;**106**(11):2144-53.

Englert 1997 *{published data only}*

Englert JA, Cox TA, Allingham RR, Shields MB. Argon vs diode laser trabeculoplasty. *American Journal of Ophthalmology* 1997;**124**(5):627-31.

Fea 2017 *{published data only}*

Fea A, Ahmed I, Lavia C, Mittica C, Consolandi G, Motolese I, et al. Hydrus microstent compared to selective laser trabeculoplasty in primary open angle glaucoma: one year results. *Clinical and Experimental Ophthalmology* 2017;**45**(2):120-7.

Fink 1988 *{published data only}*

Fink AI, Jordan AJ, Lao PN, Fong DA. Therapeutic limitations of argon laser trabeculoplasty. *British Journal of Ophthalmology* 1988;**72**(4):263-9.

Francis 2011 *{published data only}*

Francis BA, Winarko J. Laser trabeculoplasty in the treatment of open-angle glaucoma. *International Ophthalmology Clinics* 2011;**51**(3):165-77.

Frenkel 1997 *{published data only}*

Frenkel RE, Shin DH, Epstein DL, Hertzmark E, Bohn JL, Hong YJ. Laser trabeculoplasty: how little is enough. *Ophthalmic Surgery and Lasers* 1997;**28**(11):900-4.

Gandolfi 2004 *{published data only}*

Gandolfi SA, Sangermani C, Cimino L, Ungaro N, Tardini, Viswanathan A, et al. Is there a non IOP related effect of brimonidine on visual field progression in human glaucoma? *Investigative Ophthalmology and Visual Science* 2004;**45**(13):ARVO E-abstract 2298.

Germano 2021 *{published data only}*

Germano RA, Hatanaka M, Garcia AS, Germano FAS, Germano CS, Cid FB, et al. Comparison of the hypotensor effect between latanoprost versus selective laser trabeculoplasty obtained with the water drinking test. *Arquivos Brasileiros de Oftalmologia* 2021;**84**(4):361-6.

Glaucoma Intensive Treatment Study 2018 *{published and unpublished data}***10.1186/s13063-015-0924-6**

Bengtsson B, Heijl A, Johannesson G, Andersson-Geimer S, Aspberg J, Linden C. The Glaucoma Intensive Treatment Study (GITS), a randomized clinical trial: design, methodology and baseline data. *Acta Ophthalmologica* 2018;**96**(6):557-66.

* Lindén C, Heijl A, Jóhannesson G, Aspberg J, Andersson Geimer S, Bengtsson B. Initial intraocular pressure reduction by mono- versus multi-therapy in patients with open-angle glaucoma: results from the Glaucoma Intensive Treatment Study. *Acta Ophthalmologica* 2018;**96**(6):567-72.

Goyal 2010 *{published data only}***ISRCTN65144700**

Goyal S, Beltran-Agullo L, Rashid S, Shah SP, Nath R, Obi A, et al. Effect of primary selective laser trabeculoplasty on tonographic outflow facility: a randomised clinical trial. *British Journal of Ophthalmology* 2010;**94**(11):1443-7.

Heijl 1984 *{published data only}*

Heijl A. One- and two-session laser trabeculoplasty. A randomized, prospective study. *Acta Ophthalmologica* 1984;**62**(5):715-24.

Hollo 1996 *{published data only}*

Hollo G. Argon and low energy, pulsed Nd:YAG laser trabeculoplasty. A prospective, comparative clinical and morphological study. *Acta Ophthalmologica Scandinavica* 1996;**74**(2):126-31.

Hua 2014 *{published data only}*

Hua PY, Xu WH, Zhang YQ. Effect of phacoemulsification with selective laser trabeculoplasty on primary open angle glaucoma. *International Eye Science* 2014;**14**(3):496-8.

Huk 1991 *{published data only}*

Huk B, Garus HJ, Bleckmann H. Anti-inflammatory treatment after argon laser trabeculoplasty. *Ophthalmologica* 1991;**203**(1):24-9.

ISRCTN17339574 *{published data only}***ISRCTN17339574**

ISRCTN17339574. Effect of selective laser trabeculoplasty and standard medical treatment on day tension curve and intra-ocular pressure. www.isrctn.com/ISRCTN17339574 (first received 1 July 2005).

ISRCTN27208571 *{unpublished data only}*

ISRCTN27208571. Laser compared to topical medicine as primary treatment for glaucoma in Africa. www.isrctn.com/ISRCTN27208571 (first received 13 December 2015). [DOI: https://doi.org/10.1186/ISRCTN27208571]

ISRCTN42557387 *{published data only}***42557387**

ISRCTN42557387. Selective laser trabeculoplasty for primary angle-closure glaucoma: a pilot case study. www.isrctn.com/ISRCTN42557387 (first received 5 May 2006).

ISRCTN66330584 *{published data only}***ISRCTN66330584**

ISRCTN66330584. A randomized prospective study investigating the optimum power settings for selective laser trabeculoplasty (SLT) in ocular hypertension (OHT) and primary open angle glaucoma (POAG). www.isrctn.com/ISRCTN66330584 (first received 28 September 2007).

Jinapriya 2014 *{published data only}*

Jinapriya D, D'Souza M, Hollands H, El-Defrawy SR, Irrcher I, Smallman D, et al. Anti-inflammatory therapy after selective laser trabeculoplasty: a randomized, double-masked, placebo-controlled clinical trial. *Ophthalmology* 2014;**121**(12):2356-61.

Kara 2011 *{published data only}*

Kara N, Altan C, Satana B, Altinkaynak H, Bozkurt E, Demirok A, et al. Comparison of selective laser trabeculoplasty success in patients treated with either prostaglandin or timolol/dorzolamide fixed combination. *Journal of Ocular Pharmacology and Therapeutics* 2011;**27**(4):339-42.

Kiddee 2017 *{published data only}*

Kiddee W, Atthavuttisilp S. The effects of selective laser trabeculoplasty and travoprost on circadian intraocular pressure fluctuations (NCT02105311). *Medicine* 2017;**96**(6):1-7.

Kocabora 2013 *{published data only}*

Kocabora MS, Ozsutcu M, Kandemir N, Gocmez E, Fazil K, Gulkilik G. Efficacy and safety of pneumatic trabeculoplasty versus timolol added to latanoprost in primary open angle glaucoma. *Clinica Terapeutica* 2013;**164**(Suppl 4):e259-62.

Krasnov 1982 *{published data only}*

Krasnov MM, Akopian VS, Il'ina TS, Kazakova EL. Laser treatment of primary open-angle glaucoma. Randomized comparative studies. Cyclotrabeculospasis and trabeculoplasty. *Vestnik Oftalmologii* 1982;**5**:18-22.

McWherter 2021 *{published data only}***30070325**

McWherter I, Lanham M, Peplinski L, Zagorianos N, Steele A, Slayden K, et al. Selective laser trabeculoplasty versus brimonidine tartrate 0.2%/timolol maleate 0.5% as adjunct therapy in primary open angle glaucoma: a randomized prospective pilot study. HSOA Journal of Ophthalmology and Clinical Research (accessed 7 January 2021). [DOI: 10.24966/OCR-8887/100075]

Mermoud 1992 *{published data only}*

Mermoud A, Herbort C, Schnyder C, Pittet N. Comparison of argon and Nd-YAG laser trabeculoplasty. *Investigative Ophthalmology and Visual Science* 1992;**33**(4):ARVO E-abstract 2339.

* Mermoud A, Herbort CP, Schnyder CC, Pittet N. Comparison of the effects of trabeculoplasty using the Nd-YAG laser and the argon laser [Comparaison des effets de la trabéculoplastie effectuée avec le laser Nd-YAG et le laser argon]. *Klinische Monatsblätter für Augenheilkunde* 1992;**200**(5):404-6.

Moriarty 1993 *{published data only}*

Moriarty AP, McHugh JD, Spalton DJ, Ffytche TJ, Shah SM, Marshall J. Comparison of the anterior chamber inflammatory response to diode and argon laser trabeculoplasty using a laser flare meter. *Ophthalmology* 1993;**100**(8):1263-7.

NCT00000149 *{published data only}*

NCT00000149. Collaborative Initial Glaucoma Treatment Study (CIGTS). clinicaltrials.gov/ct2/show/NCT00000149 (first received 24 September 1999).

NCT00551395 *{published data only}*

NCT00551395. Timing of treatment completion in staged selective laser trabeculoplasty (SLT): early vs. late completion. clinicaltrials.gov/ct2/show/NCT00551395 (first received 31 October 2007).

NCT02774811 *{published data only}*

NCT02774811. Primary glaucoma treatment trial in Kenya and South Africa - SLT vs. medication (SLT/med). clinicaltrials.gov/ct2/show/NCT02774811 (first received 17 May 2016).

NCT02928289 *{unpublished data only}*

NCT02928289. Randomized study of the safety and effectiveness of the Sight Sciences VISCO™360 viscosurgical system versus SLT in primary open angle glaucoma (VISCO360 Study). clinicaltrials.gov/ct2/show/NCT02928289 (first received 10 October 2016).

NCT03648229 *{published data only}***NCT03648229**

NCT03648229. African glaucoma laser trial (AGLT). clinicaltrials.gov/ct2/show/NCT03648229 (first received 27 August 27 2018).

Popiela 2000 *{published data only}*

Popiela G, Muzyka M, Szelepin L, Cwirko M, Nizankowska MH. Use of YAG-Selecta laser and argon laser in the treatment of open angle glaucoma [Zastosowanie lasera YAG-Selecta i lasera argonowego w leczeniu jaskry otwartego kata]. *Klinica Oczna* 2000;**102**(2):129-33.

Realini 2010 *{published data only}*

Realini T, Charlton J, Hettlinger M. The impact of anti-inflammatory therapy on intraocular pressure reduction following selective laser trabeculoplasty. *Ophthalmic Surgery, Lasers and Imaging* 2010;**41**(1):100-3.

Russo 2009 *{published data only}*

Russo V, Barone A, Cosma A, Stella A, Noci N. Selective laser trabeculoplasty versus argon laser trabeculoplasty in patients with uncontrolled open-angle glaucoma. *European Journal of Ophthalmology* 2009;**19**(3):3429-34.

Schrems 1988 *{published data only}*

Schrems W, Hofmann G, Krieglstein GK. Therapy of open-angle glaucoma with the argon and neodymium laser. *Fortschritte der Ophthalmologie* 1988;**85**(1):119-23.

Shin 1996 *{published data only}*

Shin DH, Frenkel RE, David R, Cheetham JK. Effect of topical anti-inflammatory treatment on the outcome of laser trabeculoplasty. The Fluorometholone-Laser Trabeculoplasty Study Group. *American Journal of Ophthalmology* 1996;**122**(3):349-54.

Stunf Pukl 2018 *{published data only}*

Stunf Pukl S, Drnovšek-Olup B. Impact of laser pulse duration on the reduction of intraocular pressure during selective laser trabeculoplasty. *International Ophthalmology* 2018;**38**(1):83-91.

Tabak 1998 *{published data only}*

Tabak S, De Waard PWT, Lemij HG, Remeijer L. Selective laser trabeculoplasty in glaucoma. *Investigative Ophthalmology and Visual Science* 1998;**39**:ARVO E-Abstract 2160.

Tardif 2014 *{published data only}*

Tardif A, Bonnin N, Borel A, Viennet A, Pereira B, Chiambaretta F. Selective laser trabeculoplasty: results after a first and a second session, overall comparison and results for three indications [Trabéculoplastie au laser sélective: résultats après première et deuxième séances, comparaison globale puis dans trois indications]. *Journal Français d'Ophtalmologie* 2014;**37**(5):353-7.

Traverso 1984 *{published data only}*

Traverso CE, Greenidge KC, Spaeth GL. Formation of peripheral anterior synechiae following argon laser trabeculoplasty. A prospective study to determine relationship to position of laser burns. *Archives of Ophthalmology* 1984;**102**(6):861-3.

Tuulonen 1989 *{published data only}*

Tuulonen A, Koponen J, Alanko HI, Airaksinen PJ. Laser trabeculoplasty versus medication treatment as primary therapy for glaucoma. *Acta Ophthalmologica* 1989;**67**(3):275-80.

Uva 2010 *{published data only}*

Uva MG, Longo A, Reibaldi M. Pneumatic trabeculoplasty versus argon laser trabeculoplasty in primary open-angle glaucoma. *Ophthalmologica* 2010;**224**(1):10-5.

Vaidergorn *{published data only}*

Vaidergorn PG . Study of the effects of trabeculoplasty on the reduction of ocular hypotensive medicines in glaucoma patients [Estudo do efeito da trabeculoplastia na redução de medicamentos hipotensores oculares utilizados em pacientes glaucomatosos]. pesquisa.bvsalud.org/portal/resource/pt/lil-408993?src=similardocs (accessed 7 January 2021).

Veljko 2011 *{published data only}*

Veljko A, Miljković A, Babić N. Diode laser trabeculoplasty in open angle glaucoma: 50 micron vs. 100 micron spot size. *Medicinski Pregled* 2011;**64**(3-4):211-4.

Weinreb 1983a *{published data only}*

Weinreb RN, Ruderman J, Juster R, Zweig K. Immediate intraocular pressure response to argon laser trabeculoplasty. *American Journal of Ophthalmology* 1983;**95**(3):279-86.

Weinreb 1983b *{published data only}*

Weinreb RN, Ruderman J, Juster R, Wilensky JT. Influence of the number of laser burns administered on the early results of argon laser trabeculoplasty. *American Journal of Ophthalmology* 1983;**95**(3):287-92.

WIGLS 2017 *{published data only}*

* Realini T, Shillingford-Ricketts H, Burt D, Balasubramani GK. West Indies Glaucoma Laser Study (WIGLS): 1. 12-month efficacy of selective laser trabeculoplasty in Afro-Caribbeans with glaucoma. *American Journal of Ophthalmology* 2017;**184**:28-33. [DOI: 10.1016/j.ajo.2017.09.022]

Realini T, Shillingford-Ricketts H, Burt D, Balasubramani GK. Crystalline lens changes after selective laser trabeculoplasty in Afro-Caribbean patients with open-angle glaucoma; report 4 of the West Indies Glaucoma Laser Study (WIGLS). *Journal of Cataract and Refractive Surgery* 2019;**45**(10):1458-62.

References to studies awaiting assessment

NCT00145535 *{published data only}*

NCT00145535. SOLX titanium sapphire laser for trabeculoplasty. clinicaltrials.gov/ct2/show/NCT00145535 (first received 5 September 2005).

NCT01639807 *{published data only}*

NCT01639807. Clinical evaluation of efficacy of SLT to topical medication in lowering IOP. clinicaltrials.gov/ct2/show/NCT01639807 (first received 13 July 2012).

NCT01704989 *{published data only}*

NCT01704989. The laser in pseudoexfoliation (LIP) study (LIP). clinicaltrials.gov/ct2/show/NCT01704989 (first received 12 October 2012).

NCT01788319 *{published data only}*

NCT01788319. Micropulse laser trabeculoplasty (532 nm) versus conventional laser trabeculoplasty (532 nm). clinicaltrials.gov/ct2/show/NCT01788319 (first received 11 February 2013).

Sreckovic 2011 *{published data only}*

Srećković S, Petrović MJ, Petrović N, Vukosavljević M. Comparison of primary medicament therapy effects and primary argon laser trabeculoplasty on regulation of intraocular pressure and stability of perimetry findings in open angle glaucoma [Poređenje efekata primarne medikamentne terapije i primarne argonlaser trabekuloplastike na regulaciju intraokularnog pritiska i stabilnost perimetrijskog nalaza kod glaukoma otvorenog ugla]. *Vojnosanitetski Pregled* 2011;**68**(3):225-30.

Tawfique 2018 *{published data only}*

Tawfique K, Khademi P, Querat L, Khadamy J, Chen E. Comparison between 90-degree and 360-degree selective laser trabeculoplasty (SLT): a 2-year follow-up. *Acta Ophthalmologica* 2018;**97**(4):427-9.

References to ongoing studies

EudraCT 2015-003631-34 *{published data only}*

EudraCT 2015-003631-34. A comparison of bimatoprost SR to selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension. clinicaltrialsregister.eu/ctr-search/trial/2015-003631-34/DK (first received 26 April 2018).

GLAUrious *{unpublished data only}*

Congdon N, Azuara-Blanco A, Solberg Y, Traverso CE, Lester M, Cutolo CA, et al. Direct selective laser trabeculoplasty in open angle glaucoma study design: a multicentre, randomised, controlled, investigator-masked trial (GLAUrious). *British Journal of Ophthalmology* 2021 Aug 25 [epub ahead of print]. [DOI: 10.1136/bjophthalmol-2021-319379]

LIGHT China trial *{unpublished data only}*

Yang Y, Jiang Y, Lin M, Liu X, Fan Y, Nathwani N, et al. Laser in glaucoma and ocular hypertension trial (LIGHT) in China - an unmasked, pragmatic randomized controlled trial: design and baseline characteristics. *Investigative Ophthalmology and Visual Science* 2019;**60**(9):ARVO E-abstract 694.

Yang Y, Jiang Y, Huang S, Zhang X, Nathwani N, Lin M, et al. Laser in glaucoma and ocular hypertension trial (LIGHT) in China - a randomized controlled trial: design and baseline characteristics. *American Journal of Ophthalmology* 2021;**230**:143-50. [DOI: 10.1016/j.ajo.2021.04.020]

NCT01444105 *{published data only}*

NCT01444105. Open-angle glaucoma subjects on one ocular hypotensive medication randomized to treatment with two trabecular micro-bypass stents or selective laser trabeculoplasty. clinicaltrials.gov/ct2/show/NCT01444105 (first received 30 September 2011).

NCT01886456 *{published data only}*

NCT01886456. IOP lowering effect of PLT versus SLT in naive OAG patients. clinicaltrials.gov/ct2/show/NCT01886456 (first received 25 June 2013).

NCT02327312 *{published data only}*

NCT02327312. Multicenter investigation of trabecular micro-bypass stents vs. laser trabeculoplasty. clinicaltrials.gov/ct2/show/NCT02327312 (first received 30 December 2014).

NCT02636946/NCT02507687 *{unpublished data only}*

NCT02507687. Comparison of bimatoprost SR to selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension. clinicaltrials.gov/ct2/show/NCT02507687 (first received 24 July 2015).

NCT02636946. A comparison of bimatoprost SR to selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension. clinicaltrials.gov/ct2/show/NCT02636946 (first received 22 December 2015).

NCT02955849 *{unpublished data only}*

NCT02955849. A trial of China laser and surgery study glaucoma in rural China. clinicaltrials.gov/ct2/show/NCT02955849 (first received 4 November 2016).

NCT03529591 *{published data only}*

NCT03529591. Is the reduction in IOP after treatment of 180 degrees equivalent to treatment of 360 degrees with SLT? (SLT). clinicaltrials.gov/ct2/show/NCT03529591 (first received 18 May 2018).

NCT03798223 *{published data only}*

NCT03798223. Optimal treatment protocol for selective laser trabeculoplasty (OSLT). clinicaltrials.gov/ct2/show/NCT03798223 (first received 9 January 2019).

Additional references

Cabourne 2015

Cabourne E, Clarke JC, Schlottmann PG, Evans JR. Mitomycin C versus 5-fluorouracil for wound healing in glaucoma surgery. *Cochrane Database of Systematic Reviews* 2015 , Issue 11. Art. No: CD006259. [DOI: 10.1002/14651858.CD006259.pub2]

Chi 2020

Chi SC, Kang YN, Hwang DK, Liu CJ. Selective laser trabeculoplasty versus medication for open-angle glaucoma: systematic review and meta-analysis of randomised clinical trials. *British Journal of Ophthalmology* 2020;**104**(11):1500-7.

Covidence [Computer program]

Veritas Health Innovation Covidence. Melbourne, Australia: Veritas Health Innovation, (accessed 10 January 2022). Available at covidence.org.

Deeks 2022

Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 10: Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane 2022. Available from www.training.cochrane.org/handbook.

Glanville 2006

Glanville JM, Lefebvre C, Miles JN, Camosso-Stefinovic J. How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association* 2006;**94**(2):130-6.

GRADEpro GDT [Computer program]

McMasters University (developed by Evidence Prime) GRADEpro GDT. Version accessed 28 March 2022. Hamilton (ON): McMasters University (developed by Evidence Prime). Available at gradepro.org.

Higgins 2020

Higgins JPT, Eldridge S, Li T. Chapter 23: Including variants on randomized trials. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020), Cochrane 2020. Available from training.cochrane.org/handbook/archive/v6.1.

Kass 2002

Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Archives of Ophthalmology* 2002;**120**(6):701-13.

Krasnov 1973

Krasnov MM. Laseropuncture of anterior chamber angle in glaucoma. *American Journal of Ophthalmology* 1973;**75**(4):674-8.

Lee 2014

Lee JW, Chan CW, Wong MO, Chan JCh, Li Q, Lai JS. A randomized control trial to evaluate the effect of adjuvant selective laser trabeculoplasty versus medication alone in primary open-angle glaucoma: preliminary results. *Clinical Ophthalmology* 2014;**8**:1987-92. [DOI: 10.2147/OPTH.S70903]

Li 2016

Li T, Lindsley K, Rouse B, Hong H, Shi Q, Friedman DS, et al. Comparative effectiveness of first-line medications for primary open-angle glaucoma: a systematic review and network meta-analysis. *Ophthalmology* 2016;**123**(1):129-40.

Maier 2005

Maier PC, Funk J, Schwarzer G, Antes G, Fal k-Ytter YT. Treatment of ocular hypertension and open angle glaucoma: meta-analysis of randomised controlled trials. *BMJ* 2005;**331**(7509):134-9.

McIlraith 2006

McIlraith I, Strasfeld M, Colev G, Hutnik CM. Selective laser trabeculoplasty as initial and adjunctive treatment for open-angle glaucoma. *Journal of Glaucoma* 2006;**15**(2):124-30.

Melamed 2003

Melamed S, Ben Simon GJ, Levkovitch-Verbin H. Selective laser trabeculoplasty as primary treatment for open-angle glaucoma: a prospective, nonrandomized pilot study. *Archives of Ophthalmology* 2003;**121**(17):957-60.

Realini 2002

Realini T, Fechtner RD. 56,000 ways to treat glaucoma. *Ophthalmology* 2002;**109**(11):1955-6.

Schwartz 1985

Schwartz AL, Love DC, Schwartz MA. Long-term follow-up of argon laser trabeculoplasty for uncontrolled open-angle glaucoma. *Archives of Ophthalmology* 1985;**103**(10):1482-4.

Shields 2005

Allingham RR, Damji KF, Freedman S, Moroi SE, Shafranov G, Shields MB. Shields' Textbook of Glaucoma. 5th edition. Philadelphia: Lippincott Williams & Wilkins, 2005.

Stedman 2011

Stedman MR, Curtin F, Elbourne DR, Kesselheim AS, Brookhart MA. Meta-analyses involving cross-over trials: methodological issues. *International Journal of Epidemiology* 2011;**40**(6):1732-4.

Tham 2014

Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 2014;**121**(11):2081-90.

Traverso 1986

Traverso CE, Spaeth GL, Starita RJ, Fellman RL, Greenidge KC, Poryzees E. Factors affecting the results of argon laser trabeculoplasty in open-angle glaucoma. *Ophthalmic Surgery* 1986;**17**(9):554-9.

Vass 2007

Vass C, Hirn C, Sycha T, Findl O, Bauer P, Schmetterer L. Medical interventions for primary open angle glaucoma and ocular hypertension. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No: CD003167. [DOI: 10.1002/14651858.CD003167.pub2]

Wise 1979

Wise JB, Witter SL. Argon laser therapy for open-angle glaucoma. A pilot study. *Archives of Ophthalmology* 1979;**97**(2):319-22.

Worthen 1974

Worthen DM, Wickham MG. Argon laser trabeculotomy. *Transactions of the American Academy of Ophthalmology* 1974;**78**:371-5.

Zhou 2021

Zhou R, Sun Y, Chen H, Sha S, He M, Wang W. Laser trabeculoplasty for open-angle glaucoma: a systematic review and network meta-analysis. *American Journal of Ophthalmology* 2021;**229**:301-13. [DOI: 10.1016/j.ajo.2020.07.046]

References to other published versions of this review

Rolim de Moura 2002

Rolim de Moura C, Paranhos Jr A, Paranhos A. Laser trabeculoplasty for open angle glaucoma . *Cochrane Database of Systematic Reviews* 2002, Issue 4. Art. No: CD003919. [DOI: 10.1002/14651858.CD003919]

Rolim de Moura 2007

Rolim de Moura C, Paranhos A Jr, Wormald R. Laser trabeculoplasty for open angle glaucoma. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No: CD003919. [DOI: 10.1002/14651858.CD003919.pub2]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Abramowitz 2018

Study characteristics	
Methods	Parallel-group RCT One eye per person, unclear how selected
Participants	Country: USA Participants: 69 participants (69 eyes) Average age: 67 years Gender: 49% male, 51% female Race: NR Inclusion criteria: • uncontrolled OAG Exclusion criteria: • end-stage, neovascular, uveitic, or angle-closure glaucoma
Interventions	Intervention: MLT (n = 38 eyes, 38 participants) Comparator: SLT (n = 31 eyes, 31 participants)
Outcomes	IOP, inflammation, pain, IOP spikes Follow-up: 52 weeks
Notes	Date study conducted: August 2013 to July 2017 (from trials register entry) Funding: Quote: "We would like to acknowledge Dr Mansour Armaly and Family Glaucoma Research Fund for helping with the funding for this work." Conflict of interest: Quote "The authors report no conflicts of interest in this work." Trial registration ID: NCT01956942

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "In all, 38 patients were randomized to MLT and 31 patients to SLT via a random number generator protocol approved for up to 100 patients".
Allocation concealment (selection bias)	Low risk	Quote: "Patients were allocated to each group without any stratification based on prior characteristics via sealed numbers in a set sequence."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients, physicians, and researchers were not blinded to the different laser treatments."
Blinding of outcome assessment (detection bias)	High risk	Quote: "Patients, physicians, and researchers were not blinded to the different laser treatments."

Abramowitz 2018 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: follow-up not reported
Selective reporting (reporting bias)	Low risk	Judgement comment: outcomes on trials register were published.

AGIS 2001

Study characteristics	
Methods	Parallel-group RCT One or two eyes included, depending on eligibility
Participants	Country: USA (11 centres) Participants: 591 participants (789 eyes) Age: Average age 67 years (median) range 35 to 80 years Gender: 46% male; 54% female Race: 42% white, 56% black, 2% other History: hereditary 38% (first degree), hypertension 50%, vascular disorder 20%, diabetes 20% Inclusion criteria: • POAG in a phakic eye • OAG in a phakic eye four weeks or more after laser iridotomy, provided the eye is not inflamed, steroid medication has not been used for a week, and less than one-twelfth of the trabecular meshwork circumference is blocked by PAS • study eye on maximal medical therapy tolerated • at least 1 visual field test before the eligibility test • study eye meets at least 1 of the 9 combinations of criteria for consistent elevated IOP, glaucomatous visual field defect and optic disk rim deterioration specified in the study • visual acuity of 20/80 or better (Snellen) • visual field score at least 1 and not more than 16 • study eye treatable either with trabeculoplasty or trabeculectomy • patients able to cooperate • patients sign consent form Exclusion criteria: • Discernible congenital anomaly of the anterior chamber angle • Eyes with secondary glaucoma (pigment dispersion syndrome, exfoliation of the lens capsule) • Concurrent active disease in the study eye that may affect the IOP • Patient on kidney dialysis • History of laser or incisional surgery in the eye considered in the study, except laser iridotomy; laser retinal treatment anterior to the vortex vein ampullae, or local retinal cryotherapy, involving less than two quadrants for retinal holes • Eyes that have undergone gonioplasty in more than 180 degrees • Eyes with proliferative or severe non-proliferative retinopathy • Eyes with dilated pupil less than 2 mm

AGIS 2001 *(Continued)*

	• Eyes with field loss attributed to nonglaucomatous condition • Fellow eye enrolled in the study • Likelihood that the patient would not be able to meet the study long-term visit schedules
Interventions	Intervention 1: Consisted of a sequence of interventions, as the patient was considered a failure in each step • Argon laser trabeculoplasty + trabeculectomy + trabeculectomy (n = 404 eyes) Intervention 2: Consisted of a sequence of interventions, as the patient was considered a failure in each step • Trabeculectomy + argon laser trabeculoplasty + trabeculectomy (n = 385 eyes)
Outcomes	Early failure (6 weeks): IOP > initial levels, SVFD Late failure (more than 6 weeks): when met again, the eligibility criteria with maximal medical therapy (eligibility criteria are explicit in the AGIS protocol and combine visual field severity with IOP levels) Follow-up: 5 years
Notes	Considering this study had three interventions in each group, we considered the results just of the first intervention, which were obtained by personal contact. Date study conducted: 1988 to 2001 Funding: National Eye Institute and the Office of Research on Minority Health Conflict of interest: NR Trial registration ID: NCT00000148

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Data coordinator, from a stratified list generated by a formal randomization procedure assigned the eye to one of the two surgical sequences of surgical procedures."
Allocation concealment (selection bias)	Low risk	"Data coordinator, from a stratified list generated by a formal randomization procedure assigned the eye to one of the two surgical sequences of surgical procedures."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Treatments were different and masking not reported.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"An attempt has been made to mask information on treatment of study eyes from examiners, who performed the visual acu*ity,* visual field, and IOP tests." Although this may not have always been successful, standardised methods were used and described in detail for outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Eight eyes were randomised but did not received the interventions. Two eyes received the intervention but were lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	No access to protocol and outcomes not reported on the trials registry entry

Babighian 2010

Study characteristics	
Methods	Parallel-group randomised clinical trial One eye included, unclear how selected.
Participants	Country: Italy (1 centre) Participants: 30 participants (30 eyes) Age: average age 65.5 (mean) range 58 to 73 Gender: 42% male, 58% female Race: History: Inclusion criteria: POAG • IOP 22 mmHg or higher • glaucomatous optic disc abnormalities (stereo photographs) associated with glaucomatous retinal nerve-fibre layer defects (StratusOCT, software version 3.0, 3.4 mm scanning circle protocol, Carl Zeiss Ophthalmic System Inc., Dublin, CA, USA) • And/or glaucomatous visual field (VF) alterations (30-2 threshold programme, statpac 2 software, single field analysis, Humphrey–Zeiss, San Leandro, CA, USA) • Maximum tolerated medical therapy or non-compliance with medical therapy Exclusion criteria: • Narrow anterior chamber angle (Shaffer I-II) • Neovascularisation of the iris • Corneal diseases precluding an adequate view of the TM • Advanced VF defects with scotoma within 10 degrees of fixation; and split fixation • Patients in systemic steroid therapy were also excluded.
Interventions	Intervention 1: • Excimer laser trabeculoplasty (n = 15 eyes) Intervention 2: • Selective laser trabeculoplasty (n = 15 eyes)
Outcomes	Primary outcome: Failure: IOP less than 20% compared with baseline values or needing to increase the number of glaucoma medications from pretreatment levels Follow-up: 24 months
Notes	Date study conducted: February 2006 to September 2006 Funding: NR Conflict of interest: No conflict Trial registration ID: NR

Babighian 2010 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomization schedule and sequential numbering was generated using SAS version 8.2 (SAS Institute, Cary, NC, USA) program and stored in a locked cabinet."
Allocation concealment (selection bias)	Low risk	"The randomization schedule and sequential numbering was generated using SAS version 8.2 (SAS Institute, Cary, NC, USA) program and stored in a locked cabinet."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Although it is difficult to mask when using two different lasers, there was no mention of whether masking was attempted.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Authors evaluating the patients at each follow-up were blinded to whether the patient had undergone ELT or SLT."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"For randomization we adopted the intent-to-treat analysis, which also includes the patients who dropped out." But the extent of dropouts was not reported.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry.

Bergea 1992

Study characteristics

Methods	Parallel-group RCT One eye included per person (worse eye). Both eyes received the same treatment.
Participants	Country: Sweden (2 centres) Participants: 82 participants (82 eyes) Age: 71 years (range not specified) Gender: NR Race: 100% Caucasian History: no description of concomitant pathologies Inclusion criteria: • Newly diagnosed simple or capsular glaucoma • Untreated mean daytime IOP between 25 and 50 mmHg • Trabecular meshwork visible at least 3/4 at gonioscopy • Reproducible visual field defect at automated perimetry (Competer 350, threshold program 30 degrees) or Goldmann perimetry Exclusion criteria:

Bergea 1992 *(Continued)*

- Participants with other causes of visual field loss
- Participants that could not cooperate with a reliable visual field examination, gonioscopy or fundus examination
- Severe visual field in one eye (PV less than 100)
- Visual acuity less than 0.3 at Snellen's fraction
- Refractive errors greater than + - 5.00, aphakia or pseudophakia
- Ocular inflammation
- Corneal disease
- Age below 50 years

Interventions	Intervention: • ALT (n = 40 eyes, 40 participants). 2 sessions 1 month apart (randomly assigned superiorly or inferiorly). 50 spots, 50 micra, 0.1 seconds. No postoperative steroids were used. Comparator: • Ocular hypotensive medication (pilocarpine 4%, 3 times daily) (n = 42 eyes, 42 participants). Extra medications were not mentioned in the first publication. Stepped medication described in 1992: 1. beta-blocker; 2. oral acetazolamide; 3. ALT; 4. surgery
Outcomes	Failure: 1. 2 daily IOP curves > 26 mmHg 1 week apart 2. IOP reduction < 4 mmHg on 2 following IOP curves (1 week apart) 3. Clinically evident visual field decay 4. Adverse reaction that necessitates change in medication Success: no indication for additional therapy Continuous data of pressure for superior or inferior trabeculoplasty Optic nerve progression (documented with stereo photographs analysed by a 2 masked examiners, projected simultaneously) Follow-up: 24 months
Notes	1 participant deceased after 10 months of treatment Date study conducted: 1984 to 1989 Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Randomization was carried out by an independent person, utilising a randomization table with subclasses of six elements." There was not quite enough information to judge how the sequence was generated.
Allocation concealment (selection bias)	Low risk	"Randomization was carried out by an independent person, utilising a randomization table with subclasses of six elements. The outcome was printed on a paper, then folded in a brown envelope for total masking."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different

Bergea 1992 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Low risk	Three patients were excluded because they needed extra medication; two withdrawn from follow-up; and one died
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Blyth 1999

Study characteristics	
Methods	Parallel-group RCT One eye included per person, unclear how selected.
Participants	Country: United Kingdom (1 centre) Participants: 40 participants (40 eyes) Average age: 67 years Gender: NR Race: NR History: NR Inclusion criteria: • POAG for which maximum medical therapy had failed to control IOP at less than 22 mmHg. Maximum therapy for this study was topical timolol 0.25% twice daily and pilocarpine 2% 4 times a day. • No evidence of pseudoexfoliation or pigment dispersion syndrome • Absence of corneal opacities which might preclude view of the trabecular meshwork • No previous surgery or trabecular photocoagulation • Participant should be willing and capable of giving informed consent to the treatment and able to complete follow-up visits. Exclusion criteria: NR
Interventions	Intervention 1: • DLT (n = 20 eyes) Intervention 2: • ALT (n = 20 eyes)
Outcomes	Failure: 1. IOP > or equal to 22 mmHg 2. PAS formation 3. Continuous IOP data Follow-up: 14 months
Notes	Date study conducted: NR

Blyth 1999 *(Continued)*

	Funding: NR Conflict of interest: No conflict Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	16/20 (80%) eyes in the ALT group and 18/20 (90%) eyes in the DLT group completed 2-year review.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Brancato 1991

Study characteristics

Methods	Parallel-group RCT One eye included per person, unclear how selected.
Participants	Country: Italy (1 centre) Participants: 20 participants (20 eyes) Average age: 71 years (range not specified) Gender: 65% male, 35% female Race: 100% white History: NR Inclusion criteria: • Phakic eye • Primary open-angle glaucoma • On maximum tolerated medical therapy • Wide open angle with a visible ciliary body or scleral spur

Brancato 1991 *(Continued)*

	Exclusion criteria: • Closed angles • Aphakic or pseudophakic, no previously surgical or laser treatment • Juvenile glaucoma • Myopia over 3 diopters
Interventions	Intervention: • DLT (n = 10 eyes) Comparator: • ALT (n = 10 eyes)
Outcomes	Failure: 1. Less than 20% IOP reduction 2. Need for change in medication Follow-up: 12 months (7 to 20)
Notes	Date study conducted: NR Funding: NR Conflict of interest: No conflict Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All patients underwent complete ophthalmic examination by one of the authors who did not know which laser had been used for trabeculoplasty.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only one person lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Chung 1998

Study characteristics	
Methods	Parallel-group RCT Both eyes included, randomised independently
Participants	Country: USA (1 centre) Participants: 46 participants (50 eyes) Average age: 73 years (range not specified) Gender: 54% male, 46% female Race: NR History: 6 eyes in group 1 had intraocular surgeries before DLT and 5 eyes in group 2 (ALT) had previously intraocular surgeries. Diagnosis: 62% POAG; 12% mixed mechanisms; 8% exfoliation; 8% pigmentary; 10% NTG Inclusion criteria: • OAG with maximally tolerated medical therapy • Informed consent obtained Exclusion criteria: • Previous laser trabeculoplasty
Interventions	Intervention: • DLT (n = 22 eyes) Comparator: • ALT (n = 28 eyes)
Outcomes	Failure: Primary: Need for trabeculectomy Secondary: Side effects: discomfort, PAS formation, inflammation Follow-up: 5 years (1 to 68 months)
Notes	Date study conducted: January 1990 to April 1991 Funding: NR Conflict of interest: No conflict Trial registration ID: NR

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Patients were assigned to treatment with either the argon or diode laser using a random numbers table."
Allocation concealment (selection bias)	Low risk	"Only the study coordinator nurse had access to the random numbers table. The doctor was given the assigned number only after the patient consented to participate."

Chung 1998 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	Follow-up: DLT 1 year 16/22 (73%) 2 years 12/22 (55%) 5 years 9/22 (41%) ALT 1 year 21/28 (75%) 2 years 14/28 (50%) 5 years 9/28 (32%)
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry.

Damji 2006

Study characteristics	
Methods	Parallel-group RCT Both eyes included, randomised independently. Correlation between eyes was accounted for.
Participants	Country: Canada (1 centre) Participants: 152 participants (176 eyes) Average age: 70 years (range not specified). Gender: 41% male, 59% female Race: NR History: 6 eyes in group 1 received intraocular surgeries before DLT and 5 eyes in group 2 (ALT) received previously intraocular surgeries. Diagnosis: 58 % POAG; 29.5% exfoliation; 6.8% pigmentary; 2.3% mixed mechanisms; 2.8% others(?) Inclusion criteria: OAG • Uncontrolled IOP > 16 mmHg on maximal medical therapy or failed previous ALT (180/360, more than 6 months previously) • Had 2 sighted eyes • Age > 18 years old Exclusion criteria: • Advanced visual field defect (10 degrees central) • Previous glaucoma surgery • Corneal disease • Use of systemic steroids during the study
Interventions	Intervention 1: • SLT (n = 89 eyes) Intervention 2:

Damji 2006 *(Continued)*

	• ALT (n = 87 eyes)
Outcomes	Primary outcome: less than 20% IOP reduction from initial values at 6 months and one year. Secondary: anterior chamber reaction, IOP spikes at one hour post-laser and PAS formation. Follow-up: 12 months
Notes	Date study conducted: NR Funding: Lumenis Conflict of interest: No conflict Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was carried out in blocks of six to force reasonably equal numbers in each arm, using a computer-generated random number list to receive either ALT or SLT. A sequential opaque envelope technique was used."
Allocation concealment (selection bias)	Low risk	"Randomisation was carried out in blocks of six to force reasonably equal numbers in each arm, using a computer-generated random number list to receive either ALT or SLT. A sequential opaque envelope technique was used."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"The clinicians (KFD,WJR) who administered the laser were not masked as to the treatment allocation." It was not reported what patients were told.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Low risk	75/87 (86%) follow-up in ALT group and 78/89 (88%) follow-up in SLT group
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Elsas 1989

Study characteristics

Methods	Parallel-group RCT People were randomly allocated to treatment but for participants with two eyes eligible investigators used a within-person study approach.
Participants	Country: Norway (1 centre)

Elsas 1989 *(Continued)*

	Participants: 34 participants (40 eyes) Average age: 71 years (range from 54 to 89) Gender: NR Race: NR History: NR Inclusion criteria: • IOP equal or greater than 25 mmHg in a pre-laser curve • POAG or capsular glaucoma • Glaucomatous cupping of the optic disc • Glaucomatous visual field defect • No earlier glaucoma treatment
Interventions	Intervention 1: • ALT in 2 stages. Treatment of 180 degrees of trabecular meshwork in each stage (n = 19 eyes) Intervention 2: • ALT in 1 stage. Treatment of 360 degrees of trabecular meshwork (n = 21 eyes) Treatment protocol: 50 micra spot size, 0.1 seconds, 0.8 to 2.0 W
Outcomes	Failure: 1. IOP > 22 mmHg with hypotensive medication 2. Visual field deterioration (confirmed with manual perimetry) 3. Optic disc deterioration (detected by biomicroscopy) Follow-up: 6 months
Notes	Date study conducted: NR Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different

Elsas 1989 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Gandolfi 2005

Study characteristics	
Methods	Parallel-group RCT People randomly allocated to treatment; unclear how they dealt with eyes
Participants	Country: Italy (1 centre) Participants: 32 participants (? eyes) Average age: not reported (range 44 to 67 years) Gender: 47% male, 53% female Race: NR History: NR Inclusion criteria: • IOP greater than 22 mmHg in both eyes (mean of the 2 highest readings of the daily phasing) • Glaucomatous visual field defects in at least 1 eye as assessed by a computer-assisted static perimetry (Octopus G1) • In case of a unilateral field defect, the fellow eye had to show optic disc cupping consistent with glaucomatous optic neuropathy. Exclusion criteria: • Previous anti-glaucoma treatment • Smoking, history of allergic and respiratory disease, including asthma and atopy assessed by skin prick testing
Interventions	Intervention: • ALT (n = 16 participants, 32 eyes) Comparator: • 0.5% timolol twice daily (n = 16 participants, 32 eyes) No other treatment was administered to these participants during the follow-up. If the IOP reached 22 mmHg or more, the participant was excluded.
Outcomes	Primary: change in the provocative concentration that reduced at least 20% of the forced expiratory volume (PC20), presented in a logarithmic transformed value Follow-up: 4 years
Notes	Date study conducted: NR Funding: Ministero dell'Università e Ricerca Scientifica e Tecnologia, Roma

Gandolfi 2005 *(Continued)*

	Conflict of interest: None
	Trial registration ID: NCT00466479

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	Participants who developed IOP of 22 mmHg or greater during follow-up were excluded from the study: 5/16 people in timolol group and 6/16 people in the laser-treated group
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Geffen 2017

Study characteristics

Methods	Parallel-group randomised clinical trial One eye included; unclear how selected
Participants	Country: Israel (1 centre) Participants: 30 participants (30 eyes) Age: average age 67 (mean) range 40 to 80 Gender: 50% male, 50% female Race: Not stated History: Inclusion criteria: > 40 years POAG • uncontrolled IOP despite maximal tolerated medical therapy, or noncompliance, or intolerability to topical hypotensive treatment • glaucomatous optic disc abnormalities • reliable and reproducible evidence of visual field defects typical of glaucoma

Geffen 2017 *(Continued)*

	• pigmented open angles Exclusion criteria: • previous laser trabeculoplasty • uveitis, trauma or use of steroids within 3 months and ocular surgery within 6 months • corneal diseases precluding an adequate view of the TM • VA <= 20/200 • severe systemic disease or, disabling conditions, pregnancy or nursing women
Interventions	Intervention 1: • Experimental transscleral SLT (n = 14 eyes) Intervention 2: • Selective laser trabeculoplasty (n = 14 eyes)
Outcomes	Primary outcome: Failure: IOP less than 15% compared with baseline values and needing to increase the number of glaucoma medications or interventions Follow-up: 6 months
Notes	Date study conducted: December 2011 to September 2013 Funding: Grant from Clair and Ameedee Martier Institute for the Study of Blindness and Visual Disorders, Tel Aviv, Israel Conflict of interest: Author is actively pursuing commercial development of transscleral LTP. Trial registration ID: NCT01384149

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	All suitable subjects signed an informed consent form upon enrolment, received a serial number, and were randomised to either the study or control group according to a pre-prepared randomisation chart.
Allocation concealment (selection bias)	Unclear risk	Received a serial number
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	There was no mentioning of any attempt at masking.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Postoperative examinations were performed in the morning hours (at 08:00 to 10:00 AM) by a masked observer.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two subjects from the study group withdrew their consent before they were treated and all their data were excluded. All the remaining 30 treated subjects were included in the safety analysis. Two subjects from the control group were subsequently excluded from the performance analysis due to an insufficient follow- up period.

Geffen 2017 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Glaucoma Initial Treatment Study 2020

Study characteristics	
Methods	Parallel-group RCT One eye per person. Quote "If both eyes met the inclusion criteria, they received the same treatment but the one with higher IOP was selected for the study. If both eyes had the same IOP, the study eye was selected at the investigator's discretion."
Participants	Country: Australia, New Zealand, Singapore, UK (15 sites) Participants: 167 participants (167 eyes) Age: average age 64 years (mean) range not reported Gender: 52% male, 48% female Race: 77% Caucasian 20% Asian 3% other Inclusion criteria: • 35 years of age and above; • previously untreated patients with either POAG or PXF that warranted IOP-lowering treatment; • visual field - mean deviation values between 0 and -12 dB at baseline in the study eye on the Humphrey Visual Field Analyser; • optic disc changes consistent with glaucoma including rim loss, nerve fibre layer defects, and disc haemorrhages. Exclusion criteria: • history or evidence of glaucoma other than POAG or PXF; • advanced glaucomatous field loss with mean deviation values > -12 dB; • history of use of topical or systemic ocular hypotensive medication(s); • previous intraocular surgery (including glaucoma laser or glaucoma surgery), with the exception of uncomplicated phacoemulsification cataract surgery; • iridotrabecular drainage angle anomalies; • evidence of moderate non-proliferative diabetic retinopathy or worse, neovascularisation or rubeosis iridis; • current use of a systemic corticosteroid, epinephrine, or clonidine; • high risk of suffering symptomatic vision loss and/or may require glaucoma surgery within the 2-year follow-up to the study; • pregnant or currently breastfeeding and/or planning to become pregnant within the study period; • participants have a condition or are in a situation which may put them at significant risk or may interfere significantly with participation in the study.
Interventions	Intervention: SLT (n = 83 eyes, 83 participants) Comparator: Topical medication (n = 84 eyes, 84 participants)

Glaucoma Initial Treatment Study 2020 *(Continued)*

Outcomes	IOP reduction (defined as > 25 % fall in IOP from baseline), changes in the visual field and optic disc Follow-up: 24 months
Notes	Date study conducted: January 2013 onwards (end date not reported but in protocol it was stated it expected to finish December 2016) Funding: Quote "This Randomised Controlled Trial was funded by a Project Grant from the Australian National Health and Medical Research Council (NHMRC #1009844-EL as PI). CERA receives operational infrastructure support from the Victorian Government. Last and corresponding author ELL was funded by a NHMRC Research Fellowship (#1045280) and co-last author JGC was funded by an NHMRC Practitioner Fellowship (#529915) and by the Dorothy Adele Edols Charitable Trust. Co-main author EKF was funded by an NHMRC Early Career Fellowship (#1072987)." Conflict of interest: Quote "IG has the following conflicts of interest to declare: Advisory Board member for Allergan, Novartis, Mundipharma; Speaker Bureau for Allergan, Novartis; travel support from Pfizer KM has the following conflicts of interest to declare: Consultant to Allergan, Novartis, Quethera, Sensimed." Trial registration ID: ACTRN12611000720910 (https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=343165&isReview=true)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Randomisation schedules developed by the Centre for Eye Research Australia (CERA) Melbourne, (Co-ordinating Centre), using a list of computer-generated pseudo-random numbers are designed to yield an assignment ratio of 1:1. Randomisation, per person, will be stratified by clinical centre and type of glaucoma. The randomisation number will be assigned to a patient sequentially according to the order of enrolment within the stratum".
Allocation concealment (selection bias)	Low risk	Quote "Each study site will receive a block of sequentially numbered, sealed, and opaque envelopes containing treatment allocation for either 'SLT' or 'Drops'. Opaque envelopes will be opened in order of sequence per site. A unique study code will be assigned to each patient at randomisation, consisting of a three-digit randomisation number along with the patient's initials."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "Treating investigators and patients are not masked to treatment allocation due to the nature of the treatments."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Treating investigators and patients are not masked to treatment allocation due to the nature of the treatments; however, the QoL questionnaire administrators are masked to treatment allocation."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: Slightly lower follow-up in medication group 90% SLT versus 83% medication
Selective reporting (reporting bias)	Unclear risk	Judgement comment: Some differences with protocol e.g. 3 QoL scales specified in protocol but only two reported in final paper

GLT 1990

Study characteristics	
Methods	Within-person RCT
Participants	Country: USA (Centres: 8 clinical, 1 co-ordinating, 1 photography reading centre, 1 visual field reading centre) Participants: 271 participants (542 eyes) Age: median 61 years (range not specified) Gender: NR Race: 45% white, 43% black History: 15% diabetes; 12% coronary disease, 10% peripheral vascular disease, 37% hypertension, 7% anaemia, 4% using alfa-blocker, 6% using beta-blocker Inclusion criteria: • Age > or = 35 years • IOP in both eyes > or = 22 mmHg on 2 consecutive visits, IOP ratio between 0.67 and 1.5 inclusive • Glaucomatous field defect in at least 1 eye or disc abnormality in the presence of extremely elevated IOP • Best corrected visual acuity 20/70 or better in both eyes • Informed consent Exclusion criteria: • History of glaucoma other than POAG • Usage of topical or systemic antihypertensive medication within the last 6 months • Severe paracentral or central field defect • Contraindication for use of trial medication • Previous eye surgery • Goniosynechiae more than 10 degrees • Evidence of diabetic retinopathy • Current use of corticosteroids, epinephrine, or clonidine
Interventions	Intervention: • ALT first followed by topical medication if needed (n = 271 eyes, 271 participants) Comparator: • Medication first, applied according a stepped regimen (n = 271 eyes, 271 participants)
Outcomes	Failure criteria: 1. Primary: prescription of more than first-line medication Reduction of IOP was considered inadequate if the measurements were of 22 mmHg or more at 2 consecutive visits 2 weeks apart or above 80% of the reference IOP. The reference IOP could change if there was a visual field decay. 2. Secondary: deterioration of visual field. Visual fields were examined using Program 32 on the Octopus 201 or 2000 automated perimeter. 3. Deterioration of optic disc (subjective assessment) 4. Change in IOP 5. Deterioration of visual acuity 6. Need of further glaucoma intervention 7. Intraocular spikes observed at 4 hours of the first application (data used) 8. PAS formation at 3 months of follow-up Follow-up: the study was controlled for 2 years, but there was a follow-up until 9 years on an observational basis (no managed treatment).

GLT 1990 *(Continued)*

Notes	Date study conducted: February 1984 to April 1987 Funding: National Eye Institute Conflict of interest: None Trial registration ID: NCT00000144

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Low risk	The randomisation schedule for the trial was composed of 16 strata. Each stratum was constructed using a pseudo-random number generator and consisted of pairs of assignments designating LF for one eye and MF for the other eye for each patient enrolled.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The nature of the treatments precluded their administration in a masked fashion.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The duties of the lasering ophthalmologist and following ophthalmologist were separated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Until 2 years of follow-up, 18 people dropped out, however, the within-person study loss to follow-up was equal between the two groups.
Selective reporting (reporting bias)	High risk	271 people were enrolled, but the results of only 244 people were described at 2 years of follow-up.

Goldenfeld 2009

Study characteristics

Methods	Parallel-group RCT One eye per person; unclear how selected
Participants	Country: Israel Participants: 38 participants (38 eyes) Average age: 68 years (40 to 91) Sex: 41% male, 59% female Race: NR Inclusion criteria: People with OAG and a minimum IOP of 24 mmHg (measured twice) Exclusion criteria:

Goldenfeld 2009 *(Continued)*

	People with follow-up of less than 3 months were excluded from the study.
Interventions	Intervention: Titanium: Sapphire LT (n = 18 eyes, 18 participants) Comparator: ALT (n = 17 eyes, 17 participants)
Outcomes	IOP
Notes	Date study conducted: NR Funding: NR Conflict of interest: Quote: "The authors have no financial or proprietary interest in the materials presented herein." Trial registration ID: NCT00470964

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed based on a numbers list."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: study was not masked.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: study was not masked.
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: participants not followed up were excluded and these people were not included in the study report.
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no access to protocol and trial was not registered.

Grayson 1993

Study characteristics

Methods	Parallel-group RCT Both eyes included; eyes randomised to treatment
Participants	Country: USA (1 centre) Participants: 36 participants (45 eyes)

Grayson 1993 *(Continued)*

	Average age: 75 years (range 57 to 92) Gender: 50% male; 50% female Race: 75% white and 15% black History: NR Inclusion criteria: • POAG and exfoliation syndrome • No previous ocular surgery • Age 50 years or older • Current treatment with maximally tolerated ocular hypotensive medication
Interventions	Intervention 1: • ALT (100 burns, applied 360 degrees over the meshwork) (n = 15 eyes) Intervention 2: • ALT (50 burns, applied over 180 degrees of the meshwork) (n = 15 eyes) Intervention 3: • ALT (50 burns, applied over 360 degrees of the meshwork) (n = 15 eyes)
Outcomes	Failure criteria: further intervention required (after completion of 100 burns of ALT) Follow-up: 90 months
Notes	Date study conducted: NR Funding: National Institutes of Health, grant from Research to Prevent Blindness, Glaucoma Foundation Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not mentioned

Grayson 1993 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Grayson 1994

Study characteristics

Methods	Parallel-group RCT One or both eyes. For participants with two eyes eligible, investigators used a within-person study approach.
Participants	Country: USA (1 centre) Participants: 80 participants (102 eyes) Age: NR Gender: NR Race: NR History: NR Inclusion criteria: • POAG and exfoliative glaucoma requiring initial ALT
Interventions	Intervention `: • ALT receiving 50 burns to the superior 180 degrees of the trabecular meshwork (n = 49 eyes) Intervention 2: • ALT receiving 50 burns to the inferior 180 degrees of the trabecular meshwork (n = 53 eyes)
Outcomes	Failure criteria: further intervention required (either completion of ALT or filtration surgery) Follow-up: 24 months
Notes	Date study conducted: NR Funding: Glaucoma Foundation Conflict of interest: None Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias)	High risk	Masking not mentioned and interventions different

Grayson 1994 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Hugkulstone 1990

Study characteristics	
Methods	Within-person RCT
Participants	Country: United Kingdom (1 centre) Participants: 33 participants (66 eyes) Average age: 73 years (range not reported) Gender: 30% male, 70% female Race: NR History: NR Inclusion criteria: • POAG on topical hypotensive medication who had IOP of 21 mmHg or more and/or who showed deteriorating visual fields, using a suprathreshold static visual field analyser (Friedmann) Exclusion criteria: • Exfoliation, pigment dispersion syndrome and other secondary glaucomas
Interventions	Intervention 1: • ALT with duration of 0.1 sec in OD and with 0.3 seconds each spot in OS (n = 17 participants, 24 eyes) Intervention 2: • ALT with duration of 0.2 sec in OD and with 0.1 seconds each spot in OS (n = 16, 22 eyes). All eyes received a 50 micra spot size, applied to all 360 degrees of the trabecular meshwork in one or two sessions. The power setting was started at 0.9 W.
Outcomes	Failure criteria: Adverse effects: IOP spikes after one hour of laser application Follow-up: 6 months and posteriorly a new analysis with 24 months of follow-up
Notes	Date study conducted: NR Funding: NR Conflict of interest: None

Hugkulstone 1990 *(Continued)*

Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Low risk	Not reported but within-person study so all patients received both treatments
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Attempt was made to mask outcome assessment - ALT details were not recorded in patients charts to achieve a single-masked protocol.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient lost to follow-up, 5 were excluded and 3 patients died.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Kaplovitz 2016

Study characteristics

Methods	Parallel-group RCT One eye (right)
Participants	Country: USA (1 centre) Participants: 37 participants (37 eyes) Average age: 70 years (range not reported) Gender: 35% male, 65% female Race: 67% white, 28% black, 6% Hispanic Inclusion criteria: • 18 years of age or older • primary open-angle glaucoma or ocular hypertension with pre-glaucoma with an indication to lower IOP by laser trabeculoplasty. The indication for laser trabeculoplasty was determined by the clinician when the IOP was elevated to the threshold where progression was likely Exclusion criteria: • Non mentioned
Interventions	Intervention:

Kaplovitz 2016 *(Continued)*

	• Titanium-Sapphire laser trabeculoplasty (n = 18 eyes) Comparator: • Selective laser trabeculoplasty (n = 19 eyes)
Outcomes	Primary outcome: IOP < 21 mmHg with > 20% decrease in IOP as compared with baseline without the need for further glaucoma procedures Follow-up: 24 months
Notes	Date study conducted: NR Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"[U]sing a random number generator (Quick Random Number Generator, CWE Software LLC, Volo, IL)"
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	The clinicians were not masked to treatment arm.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The retention rate was 70%, with 26 patients (12 TLT, 14 SLT patients) reaching the 24-month follow-up period. This may have introduced bias but uncertain because details of characteristics of persons lost to follow-up not available.
Selective reporting (reporting bias)	Unclear risk	Not mentioned

Katz 2012

Study characteristics

Methods	Parallel-group RCT Randomised people to treatment and both eyes received the same treatment.
Participants	Country: USA (1 centre) Participants: 69 participants (127 eyes) Age: NR

Katz 2012 *(Continued)*

	Gender: 41% male, 59% female Race: NR Inclusion criteria: • Patients between 25 and 82 years of age • IOP > or equal to 24 and inferior to 31 (higher eye) and IOP > or equal to 20 (lower eye) • Diagnosis of primary OAG, pseudoexfoliation glaucoma, or mixed mechanism OAG with a narrow angle (if laser peripheral iridotomy was performed > 3 mo ago) • Diagnosis of ocular hypertension if central corneal thickness was < 600 microns • Adequate visualisation of angle structures (i.e. clear media and cooperative patient) • No previous intraocular surgery • No glaucoma medications in both eyes for more than 4 weeks • No systemic medications known to increase IOP (corticosteroids) • Visual acuity of 20/70 or better in both eyes Exclusion criteria: • On > 2 glaucoma medications (fixed combination products are considered 2 drugs) • On any eye drops for glaucoma 4 weeks before baseline I visit • Had a CIGTS visual field score that exceeded 16 in either eye • Evidence of ocular disease other than glaucoma or ocular hypertension, which might affect IOP measurements, assessment of visual function or visual field testing • Dagnosis of pigmentary OAG or proliferative diabetic retinopathy • Undergone ophthalmic laser (other than laser peripheral iridotomy > 3 mo ago) • Refractive, conjunctival, or intraocular surgery in either eye • Would likely require cataract surgery within 6 months of randomisation • Current or expected use of corticosteroids • Patient was pregnant or planning to become pregnant within the next year
Interventions	Intervention: • SLT (n = 67 eyes, 38 participants) Comparator: • Medical treatment (n = 60 eyes, 31 participants) Medical Treatment regimen included: Step 1: Start with ocular prostaglandin analog: latanoprost, bimatoprost, or travoprost; Step 2: If target IOP not met but initial medication deemed effective, add b-blocker (or substitute, if first drug used was ineffective or not tolerated); Step 3: Brimonidine: Step 4: High-dose pilocarpine, four times a day; Step 5: 0.5% timolol, twice a day with high-dose pilocarpine, four times a day; Step 6: 0.1% dipivefrin, twice a day with high-dose pilocarpine, four times a day; Step 7: Release from stepped regimen; treatment at discretion of GLT ophthalmologist
Outcomes	Primary outcome: IOP reduction Secondary: number of steps

Katz 2012 *(Continued)*

	Follow-up: 12 months
Notes	Date study conducted: NR Funding: Lumenis Inc. Conflict of interest: Jay Katz, MD, received research funds and speaker honoraria from Lumenis Inc. William C. Steinmann, MD, received research funds from Lumenis Inc. No other authors have any financial interest in any product mentioned in this article. George Marcellino, PhD, was a consultant/advisor for Lumenis Inc. Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Treatment assignment was determined by the Co-ordinating Center, after verifying eligibility. Target IOP and visual field scores were then generated. The Co-ordinating Center assigned the patient to either treatment arm based on an odd/even designation from a random numbers table masked to all clinical criteria except center designation."
Allocation concealment (selection bias)	Low risk	"Treatment assignment was determined by the Co-ordinating Center, after verifying eligibility. Target IOP and visual field scores were then generated. The Co-ordinating Center assigned the patient to either treatment arm based on an odd/even designation from a random numbers table masked to all clinical criteria except center designation."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Low risk	52/67 (78%) eyes followed up in SLT group and 48/60 (80%) eyes in medicine group followed up to 12 months
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Kent 2013

Study characteristics

Methods	Parallel-group RCT One or both eyes included
Participants	Country: Canada Participants: 60 participants (76 eyes) Average age: 73 years (range NR)

Kent 2013 *(Continued)*

	Gender: 34% male, 66% female Race: NR Inclusion criteria: • PXF • IOP that was not controlled on maximal medical management • open angles • at least one IOP reading > 24mm Hg Exclusion criteria: • prior laser trabeculoplasty or glaucoma surgery • ocular surgery within 6 months • advanced visual field defect • monocular vision • concurrent systemic or topical steroids
Interventions	Intervention: SLT Comparator: ALT
Outcomes	IOP, change in number of glaucoma medications, adverse events Follow-up: 6 months
Notes	Date study conducted: September 2006 to September 2009 (from trials register) Funding: NR Conflict of interest: Quote "The authors declare no conflict of interest." Trial registration ID: NCT01126203

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Eyes were randomized to receive SLT or ALT by a non blocked randomization schedule stratified by center."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not enough information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Neither patients nor physicians were masked as laser is essentially a surgical procedure."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Neither patients nor physicians were masked as laser is essentially a surgical procedure."
Incomplete outcome data (attrition bias)	Unclear risk	Judgement comment: follow-up was 83% but this was not reported separately by intervention/comparator group.

Kent 2013 *(Continued)*
All outcomes

Selective reporting (reporting bias)	High risk	Judgement comment: clinical trials registry entry specified IOP over 12 months but only 6 months reported

KiGIG 2021

Study characteristics	
Methods	Parallel-group RCT Quote "One or both eyes were enrolled, depending on eligibility, and were treated identically."
Participants	Country: Tanzania Participants: 201 participants (382 eyes) Age: average age 66 years (mean), range not reported Gender: 59% male, 41% female Race: 100% Black African: different ethnic groups in Tanzania Inclusion criteria: • chronic high-pressure OAG, defined as an IOP of more than 21 mmHg and a combination of structural and functional changes • IOP > 25 mmHg with structural changes only • IOP > 32 mmHg with no structural or functional changes Exclusion criteria: • younger than 18 years • opaque cornea • narrow angle (< 2 on the Shaffer scale in two quadrants) • absolute blindness (no perception of light) • history of previous uveitis • any previous glaucoma surgery or laser treatment • neovascular or traumatic glaucoma • history of asthma or bradycardia
Interventions	Intervention: SLT (191 eyes, 101 participants) Comparator: Timolol 0.5% (191 eyes, 100 participants)
Outcomes	"[T]reatment success" (i.e. achieved target IOP according to glaucoma severity), safety, acceptance, vision-related quality of life, adherence, preservation of visual acuity and visual fields, other glaucoma-related functional or structural changes, other IOP-related outcomes, analyses of focus group discussions, cost, and treatment affordability Follow-up: 12 months
Notes	Date study conducted: August 2015 to May 2017 Funding: Christian Blind Mission, Seeing is Believing Innovation Fund, and the Wellcome Trust

KiGIG 2021 *(Continued)*

Conflict of interest: Quote "GG reports personal fees from Alcon, Allergan, Belkin, Equinox, Genentech–Roche, Glaukos, Ivantis, Reichert, Sight Sciences, and from Thea; grants from Belkin, Santen, and from Thea; and non-financial involvement with the patient advocacy group GlaucomaUK, outside the submitted work; he is also a co-investigator on three other major SLT trials (LIGHT, COAST, and Belkin laser). All other authors declare no competing interests".

Trial registration ID: PACTR201508001235339 (https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=1235)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "The randomisation sequence was generated by an independent statistician with a variable block size between 4 and 8."
Allocation concealment (selection bias)	Low risk	Quote "Sequentially numbered and sealed opaque envelopes contained the allocation of participants to either the SLT or the timolol group (1:1)."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "Due to the nature of the interventions, participants, principal investigators, and healthcare staff administering treatments could not be masked to treatment allocation; however, the clinicians who examined IOP were masked to the trial arm, the individual IOP threshold, and previous IOP measurements of the participant, and were not involved in any other aspect of the trial."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Due to the nature of the interventions, participants, principal investigators, and healthcare staff administering treatments could not be masked to treatment allocation; however, the clinicians who examined IOP were masked to the trial arm, the individual IOP threshold, and previous IOP measurements of the participant, and were not involved in any other aspect of the trial."
Incomplete outcome data (attrition bias) All outcomes	Low risk	85% of SLT group and 91% of timolol group followed up
Selective reporting (reporting bias)	Unclear risk	Visual field not reported but principal investigator confirmed separate publication on this in progress.

Lai 2004

Study characteristics

Methods	Within-person RCT
Participants	Country: China (1 centre) Participants: 32 participants (64 eyes), 3 participants defaulted follow-up Average age: 52 years (range not reported) Gender: 45% male; 55% female Race: All Chinese with brown iris History: Not mentioned Inclusion criteria: • Newly diagnosed POAG and OHT patients

Lai 2004 *(Continued)*

	• IOP > 21 mmHG both eyes without anti-glaucoma medications • those with OAG demonstrated optic disc changes and/or visual field changes typical of glaucomatous damage Exclusion criteria: • Previous laser trabeculoplasty • Previous intraocular surgery disturbing the aqueous humor outflow • Active ocular inflammation • Poor visualisation of the trabecular meshwork • Single eye • Pregnancy
Interventions	Intervention: • SLT (n = 32 participants, 32 eyes) Comparator: • Medical treatment: β-blocker, pilocarpine, dorzolamide and latanoprost were started either as monotherapy or in combination (n = 32 participants, 32 eyes).
Outcomes	Primary outcome: failure IOP > 21 mmHG on maximal medical therapy Follow-up: 5 years
Notes	Date study conducted: randomisation March to June 1998 Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated allocation
Allocation concealment (selection bias)	Low risk	Not reported but within-person study so all patients received both treatments. To minimise cross-over medical effect, patients were instructed to apply digital lacrimal punctual pressure for five minutes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Low risk	Eleven patients lost follow-up during 5 years

Lai 2004 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry.

LIGHT 2019

Study characteristics	
Methods	Parallel-group RCT One or both eyes included, depending on eligibility. Unit of analysis person, based on worse eye
Participants	Country: UK (6 collaborating centres) Participants: 718 (1235 eyes) Average age: 63 years (range not reported) Gender: 55% male, 45% female Race: 70% white, 20% black, 10% other Inclusion criteria: • Newly diagnosed OAG or OHT in one or both eyes • A decision to treat had been made by a glaucoma specialist consultant ophthalmologist. • Patients were aged > 18 years and were able to provide informed consent. • Patients were able to complete QoL, disease-specific symptoms and cost questionnaires in English • It was possible to perform a VF test in the study eye(s) with < 15% false positives. Exclusion criteria: • advanced glaucoma in the potentially eligible eye • secondary glaucoma or any angle closure • any contraindication to SLT • an inability to use topical medical therapy • previous treatment for OAG or OHT • congenital or early childhood glaucoma • visually significant cataract in symptomatic patients who want to undergo cataract surgery • any current, active treatment for another ophthalmic condition in the hospital eye service • any history of retinal ischaemia, macular oedema or diabetic retinopathy • age-related macular degeneration with neovascularisation in either eye or geographic atrophy • visual acuity (VA) worse than 6/36 in a study eye; non-progressive VA loss better than 6/36 owing to any comorbidity was permitted provided that it did not affect the response to treatment or later surgical choices and that it was not under active follow-up. • any previous intraocular surgery, except uncomplicated phacoemulsification, at least 1 year before recruitment • pregnancy at the time of recruitment or intention to become pregnant within the duration of the trial • medical unsuitability for completion of the trial • recent involvement in another interventional research study (within 3 months) of any topic
Interventions	Intervention: Primary SLT followed by topical medications as required (Laser-1st) (n = 613 eyes, 356 participants) Comparator:

LIGHT 2019 *(Continued)*

	Topical IOP-lowering medication (Medicine-1st) (n = 622 eyes, 362 participants)
Outcomes	Health-related quality of life at 3 years Cost IOP over the course of the study Visual function at three years Patient toleration Follow-up: 36 months
Notes	Date study conducted: October 2012 to October 2014 (recruitment) Funding: National Institute for Health Research (UK) Conflict of interest: Quote "Gus Gazzard, David Garway-Heath, Rachael Hunter, Gareth Ambler, Catey Bunce, Richard Wormald, Keith Barton, Gary Rubin and Marta Buszewicz have received a grant from the National Institute for Health Research (NIHR) for the submitted work. Gus Gazzard reports grants from Lumenis (Borehamwood, UK) during the conduct of the study; grants from Ellex Medical Lasers (Adelaide, SA, Australia), Ivantis, Inc. (Irvine, CA, USA) and Thea Pharmaceuticals (Keele, UK) outside the submitted work; and personal fees from Allergan (Dublin, Ireland), Alcon (Fort Worth, TX, USA), Glaukos Corporation (San Clemente, CA, USA), Santen Pharmaceutical Co., Ltd (Osaka, Japan) and Thea Pharmaceuticals outside the submitted work. David Garway-Heath reports personal fees from Aerie Pharmaceuticals, Inc. (Durham, NC, USA), Alcon, Allergan, Bausch + Lomb (Rochester, NY, USA), Quark Pharmaceuticals, Inc. (Ness Ziona, Israel), Quethera Limited and Roche (Basel, Switzerland); grants from the Alcon Research Institute; and grants and personal fees from Pfizer (New York, NY, USA) and Santen Pharmaceutical Co., Ltd, outside the submitted work. In addition, David Garway-Heath was a member of the Health Technology Assessment (HTA) Clinical Trials Board from 2014 to 2017. Keith Barton received a grant from NIHR for the Treatment of Advanced Glaucoma Study during the conduct of the study. In addition, Keith Barton reports grants from Johnson & Johnson Vision (Santa Ana, CA, USA), New World Medical (Rancho Cucamonga, CA, USA), Alcon, Merck & Co. (Kenilworth, NJ, USA), Allergan and Refocus Group (Dallas, TX, USA); that he has had other financial relationships with Alcon, Merck & Co., Allergan, Refocus, AqueSys Inc. (Taipei, Taiwan), Ivantis, Carl Zeiss Meditec AG (Jena, Germany), Kowa Europe GmbH (Düsseldorf, Germany), Santen Pharmaceutical Co., Ltd, Transcend Medical (Scottsboro, AL, USA), Glaukos (San Clemente, CA, USA), Amakem NV (Diepenbeek, Belgium), Thea Pharmaceuticals, Alimera Sciences (Alpharette, GA, USA), Pfizer, Advanced Ophthalmic Implants Pte Ltd (Singapore), Vision Futures (UK) Ltd (London, UK), London Claremont Clinic Ltd (London, UK) and Vision Medical Events Ltd (London, UK), outside the submitted work; and that he has a patent with Ophthalmic Implants (PTE) Ltd. Stephen Morris was a member of NIHR Health Services and Delivery Research (HSDR) Research Funding Board (2014–19), the NIHR HSDR Commissioned Board (2014–16), the NIHR HSDR Evidence Synthesis Sub Board (2016), the NIHR HTA Clinical Evaluation and Trials Board (2007–10), the NIHR HTA Commissioning Board (2009–13), the NIHR Public Health Research Funding Board (2011–17) and the NIHR Programme Grants for Applied Research expert subpanel (2017–present). Marta Buszewicz was a member of the HTA Mental Health Panel from January to May 2018. In September 2018, this panel was amalgamated into the HTA Prioritisation Committee C (mental health, women and children's health), of which Marta Buszewicz was also a member. Marta Buszewicz has also been a member of the NIHR Research for Patient Benefit, London, funding panel since May 2017." Trial registration ID: ISRCTN32038223, NCT03395535

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was undertaken online on the same day by the clinical staff who obtained informed consent, using a web-based randomisation service (Sealed Envelope, London, UK) and achieving full allocation concealment."

LIGHT 2019 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was undertaken online on the same day by the clinical staff who obtained informed consent, using a web-based randomisation service (Sealed Envelope, London, UK) and achieving full allocation concealment."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Following randomisation, the details of the treatment and specific arrangements and instructions were communicated to the patients by a member of the trial team. Owing to the pragmatic design of this trial, the patients and clinicians were unmasked to the treatment arm; however, all clinical measurements (IOP, VF, HRT) were carried out by masked observers and treatment decisions were masked by the use of a computerised evidence-based decision support algorithm".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Following randomisation, the details of the treatment and specific arrangements and instructions were communicated to the patients by a member of the trial team. Owing to the pragmatic design of this trial, the patients and clinicians were unmasked to the treatment arm; however, all clinical measurements (IOP, VF, HRT) were carried out by masked observers and treatment decisions were masked by the use of a computerised evidence-based decision support algorithm".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: follow-up was high and equal between both groups (329/356 (92%) vs 323/362 (89%)).
Selective reporting (reporting bias)	Low risk	Judgement comment: protocol and statistical analysis plan published

Liu 2012

Study characteristics	
Methods	Parallel-group RCT One eye included per person (the first eye treated)
Participants	Country: Canada (1 centre) Participants: 42 participants (42 eyes) Average age: 50 years (range from 29 to 60) Gender: 69% male; 31% female Race: NR History: NR Inclusion criteria: • Young patients (age 60 or younger) who had never received laser trabeculoplasty or trabeculectomy • Topical medication did not lower IOP sufficiently according to their clinically-based target pressure level. Maximum tolerable medical therapy was not necessarily reached before laser was recommended, and visual field progression could result in a reassessment of the target IOP. Exclusion criteria: NR
Interventions	Intervention 1:

Liu 2012 *(Continued)*

	• SLT (n = 20 participants, 20 eyes) Intervention 2: • ALT (n = 22 participants, 22 eyes)
Outcomes	IOP measurement Follow-up: 2 years
Notes	Date study conducted: NR Funding: Neurosciences Research Program Summer Studentship award Conflict of interest: None Trial registration ID: NCT01087684

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	In trial registration, sample size was determined and primary outcomes

Mansouri 2016

Study characteristics

Methods	Within-person RCT
Participants	Country: Switzerland (1 centre) Participants: 29 participants (58 eyes) Average age: 54 years (range from 23 to 73) Gender: 72% male; 28% female Race: 72% white, 14% black, 14% Asian

Mansouri 2016 *(Continued)*

	History: NR Inclusion criteria: • > 18 years • primary or secondary OAG (repeatable abnormal standard automated perimetry test results (Octopus, Haag-Streit) in the presence of abnormal appearance of optic disc (presence of neuroretinal rim thinning or localised or diffuse retinal nerve fibre layer defects indicating glaucoma) by slit lamp or SD-OCT • gonioscopically open angle • medically uncontrolled IOP and/or intolerance to medical IOP treatment • topical medication did not lower IOP sufficiently according to their clinically-based target pressure level. Maximum tolerable medical therapy was not necessarily reached before laser was recommended, and visual field progression could result in a reassessment of the target IOP. Exclusion criteria: • previous laser trabeculoplasty or iridoplasty • previous glaucoma incisional surgery
Interventions	Intervention 1: • pattern scanning laser trabeculoplasty (n = 29 participants, 29 eyes) Intervention 2: • SLT (n = 29 participants, 29 eyes)
Outcomes	Primary outcome: >= 20% decrease in IOP without medication Follow-up: 6 months
Notes	NCT02231515

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed using sequentially numbered sealed envelopes
Allocation concealment (selection bias)	Low risk	[S]ealed envelopes, prepared by a study co-ordinator who was not involved in other aspects of the study, to assign each eye to PSLT or SLT
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients were masked as to the treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Intraocular pressure measurements were performed by experienced residents who were not masked to the laser procedure but were uninvolved in the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All eyes that were randomised were analysed in an intent-to-treat analysis.
Selective reporting (reporting bias)	Unclear risk	Not mentioned

Moorfields PTT 1994

Study characteristics	
Methods	Parallel-group RCT One eye included per person (if there was asymmetry between the eyes, the worse eye was included in the trial. If the eyes were equivalent then the eye to be included in the trial was selected randomly).
Participants	Country: United Kingdom (1 centre) Participants: 168 participants (168 eyes) Average age: 63 years (range not reported) Gender: NR History: NR Race: NR Inclusion criteria: • IOP equal or greater 24 mmHg on 2 different occasions • Cup to disc ratio equal or greater than 0.6 and/or notching, and/or pallor of the neuroretinal rim • Glaucomatous visual field loss using the Friedmann Field Analyser
Interventions	Intervention: • ALT (plus pilocarpine if IOP not controlled) (n = 55 eyes). It was performed in 2 sessions 2 weeks apart, 50 burns over 180 degrees each session, 50 micra spot size, 0.1 seconds, 0.5-1.0 W. 0.3% prednisolone was used 4 times a day for 4 days and pilocarpine if necessary. Pilocarpine was used 2% four times a day 1 week prior the laser treatment. Comparator 1: • Medical treatment (pilocarpine and/or sympathomimetics and/or timolol and/or carbonic anhydrase inhibitor (n = 56 eyes) Comparator 2: • Surgical treatment (trabeculectomy) (n = 57 eyes)
Outcomes	Failure criteria: 1. IOP equal or greater than 22 mmHg after 3 months of treatment or visual field loss greater than 2% per annum If failure occurred, the second-line treatment was undertaken and again randomly allocated. Success: 6 months: surgery = 100%; med = 87%; laser = 86%; 3 years: surgery = 99.9%; med = 89.2%; laser = 85% The visual field deterioration is determined by a mean score, but is shown in Table 4 (1994). There is no absolute number. Follow-up: 60 months
Notes	Date study conducted: NR Funding: Frost Foundation Conflict of interest: NR Trial registration ID: NR

Moorfields PTT 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence allocation
Allocation concealment (selection bias)	Low risk	The patients were randomly allocated using a computer selection.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Described failures but did not describe dropouts
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Moriarty 1988

Study characteristics	
Methods	Parallel-group RCT Randomised people to treatment but, for participants with two eyes eligible, investigators used a within-person study approach (right eyes were randomised and left eye received the alternative intervention).
Participants	Country: Jamaica (1 centre) Participants: 30 participants (48 eyes) Average age: 62 years (range from 27 to 77) Gender: 53% male, 47% female Race: 100% black History: NR Inclusion criteria: • Phakic POAG • IOP of 22 mmHg or greater despite maximal medical therapy • Glaucomatous optic disc cupping • Glaucomatous visual field changes on Goldmann perimetry Exclusion criteria: Developmental, aphakic, inflammatory, haemolytic and pseudo-exfoliative types of glaucoma

Moriarty 1988 *(Continued)*

Interventions	Intervention: • ALT (n = 25 eyes): Technique: 50 micra in the anterior portion of the trabecular meshwork, 0.1 sec of duration, power was adjusted to 800 to 1000 mW. 50 burns placed over nasal 180 degrees at first application. If, after 3 months, the IOP remained high, the procedure was repeated at 180 degrees temporally. Eyes received prednisolone acetate 1% if there was uveitis. Comparator: • Full tolerable anti-glaucoma medical treatment (n = 23 eyes) - pilocarpine 4% and acetazolamide orally. 4 participants also used timolol.
Outcomes	Success criteria: successful control: IOP < 22 mmHg Improvement: reduction in IOP of 5 mmHg but keeping levels of more than 22 mmHg No improvement: reduction in IOP of 4 mmHg or less but keeping levels of 22 mmHg or greater Deterioration: rise in IOP of 5 mmHg or more Follow-up: 12 months
Notes	Date study conducted: NR Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Low risk	48 eyes enrolled, one eye needed surgery and was excluded. 47 completed one year of follow-up.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Nagar 2005

Study characteristics

Methods	Parallel-group RCT

Nagar 2005 *(Continued)*

	Both eyes were treated with the same treatment, but only the eye with the higher IOP at baseline was enrolled in the study. If the IOP was the same in both eyes, the right eye was enrolled
Participants	Country: United Kingdom (2 centres) Participants: 167 participants (167 eyes) Average age: 63 years (range from 22 to 90) Gender: 46% male; 64% female Race: 22% African or Afro-Carribean origin; 78% white History: NR Inclusion criteria: • Ocular hypertension, primary or secondary open-angle glaucoma, either newly diagnosed or controlled on medical therapy Exclusion criteria: • Congenital glaucoma • Angle-closure glaucoma • Eyes with previous laser or surgical glaucoma intervention • Previous anterior segment pathology, such as uveitis, etc.
Interventions	Intervention 1: • 90° SLT (n = 35 participants, 35 eyes) Intervention 2: • 180° SLT (n = 49 participants, 49 eyes) Intervention 3: • 360° SLT (n = 44 participants, 44 eyes) Comparator: • Latanoprost (n = 39 participants, 39 eyes)
Outcomes	Primary success: 20% IOP reduction from baseline IOP and a 30% reduction from baseline with no additional anti-glaucomatous interventions Secondary outcomes: Transient adverse events during the first week Follow-up: 12 months
Notes	Date study conducted: Randomisation from January 2002 to 2003 Funding: Lumenis Inc. (Coherent Medical Group, Palo Alto, CA) Conflict of interest: The authors have no proprietary interest in Selectra. Trial registration ID: ISRCTN77145641 (retrospectively registered)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed using a sealed, shuffled envelope system, in which allocated treatment was written on treatment cards. These cards were

Nagar 2005 *(Continued)*

		placed into identical sealed envelopes, which were then shuffled several times and sequentially numbered.
Allocation concealment (selection bias)	Low risk	No participants' identifiers were used in this process. None of the individuals involved in generating the randomisation took any further part in the study. The sealed envelopes were kept in locked drawers, which were unlocked before treatment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	Mean follow-up was 10.3 months, but range from 1 to 12 months. There was no precise description of losses to follow-up nor number of participants at each time point of the follow-up.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Ozen 2020

Study characteristics	
Methods	Within-person study Quote "A single session of SLT 180 degrees to one randomly selected eye (Group 1, n = 26) and 360 degrees to the other eye (Group 2, n = 26) was applied on the same days as adjunctive treatment in these cases."
Participants	Country: Turkey Participants: 26 participants (52 eyes) Age: average age: 62 years (mean) range not reported Gender: 46% male, 54% female Race: Not reported Inclusion criteria: • bilateral POAG with high IOP despite anti-glaucoma drug treatment; • hospital visits regularly for at least 6 months; • both eyes receiving the maximum tolerable drug therapy. Exclusion criteria: • previous histories of ocular trauma or glaucoma surgery; • corneal pathologies; • receipt of more than one SLT treatment.
Interventions	Intervention: SLT 180 degrees (n = 26 eyes, 26 participants)

Ozen 2020 *(Continued)*

	Comparator: SLT 360 degrees (n = 26 eyes, 26 participants)
Outcomes	Iridocorneal angle, IOP, optic nerve and retinal exam, central corneal thickness, endothelial cell count Follow-up: 6 months
Notes	Date study conducted: Not reported Funding: Not reported Conflict of interest: Quote "The authors declare no conflict of interest." Trial registration ID: Not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "A single session of SLT 180 degrees to one randomly selected eye (Group 1, n = 26) and 360 degrees to the other eye (Group 2, n = 26) was applied on the same days as adjunctive treatment in these cases."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: Within-person study so both eyes followed up but unclear if people dropped out of study - inclusion criteria mentioned dropouts.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol and study not registered

Rosenfeld 2012

Study characteristics

Methods	Parallel-group RCT One eye per person; unclear how eye selected
Participants	Country: Israel Participants: 52 participants (52 eyes) Age: average age 72 years (mean range not reported) Gender: 48% male, 52% female Race: Not reported

Rosenfeld 2012 *(Continued)*

	Inclusion criteria: • older than 18 years of age; • history of glaucoma with subtypes POAG, PXF, pigmentary glaucoma, or OHT; • successful phacoemulsification-assisted cataract surgery with intracapsular lens implantation; • laser treatment (SLT or ALT) not less then 3 months and not more then 6 months following the cataract surgery. Exclusion criteria: • complicated cataract surgery; • intraocular lens implantation other than an intracapsular lens; • advanced visual field defect within 10° of fixation; • previous glaucoma surgery (except for peripheral iridotomy or ALT); • previous SLT; • severe corneal disease that resulted in inaccurate applanation measurements, or that inhibited the adequate visibility of the TM on gonioscopy; • systemic steroids; • endophthalmitis or uveitic glaucoma.
Interventions	Intervention: SLT (22 eyes, 22 participants) Comparator: ALT (30 eyes, 30 participants)
Outcomes	IOP-lowering effect; failure decrease < 15% in IOP Follow-up: 12 months
Notes	Date study conducted: Not reported Funding: None Quote "The authors have not received any grant support or research funding, and do not have any proprietary interests in the materials described in the article." Conflict of interest: Quote "The authors report no conflicts of interest in this work." Trial registration ID: Not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "Each patient was randomly assigned to receive either the SLT or ALT treatment according to a note that was written, which specified the name of the designated treatment, and which was placed in an unmarked and closed envelope."
Allocation concealment (selection bias)	Unclear risk	Quote: "Each patient was randomly assigned to receive either the SLT or ALT treatment according to a note that was written, which specified the name of the designated treatment, and which was placed in an unmarked and closed envelope."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not reported and interventions different

Rosenfeld 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: not reported and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: 73% of SLT group followed up compared with 57% of the ALT group
Selective reporting (reporting bias)	Unclear risk	Not possible to assess

Rouhiainen 1988

Study characteristics	
Methods	Parallel-group RCT Unclear how people/eyes were randomly allocated
Participants	Country: Finland (1 centre) Participants: 100 participants (120 eyes) Average age: 71 years (range from 51 to 87) Gender: 41% male; 59% female Race: NR History: NR Diagnosis: 50% POAG and 50% capsular glaucoma Inclusion criteria: • OAG; • On maximal tolerated anti-glaucoma medication insufficient to control the glaucoma. Exclusion criteria: NR
Interventions	Intervention 1: • ALT 50 micra, 0.1 sec, power level 500 mW (n = 30 eyes) Intervention 2: • ALT, 50 micra, 0.1 sec, power level 600 mW (n = 30 eyes) Intervention 3: • ALT, 50 micra, 0.1 sec, power level 700 mW (n = 30 eyes) Intervention 4: • ALT, 50 micra, 0.1 sec, power level 800 mW (n = 30 eyes) . Medication was kept unchanged. No anti-inflammatory drugs were used.
Outcomes	Failure criteria: 1. PAS formation 2. IOP > or = 21 mmHg or no decrease of IOP < 3 mmHg Follow-up: 12 months

Rouhiainen 1988 *(Continued)*

Notes	Date study conducted: Operations were done in 1986. Funding: Finish Eye Foundation, Helsinki Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Randomisation was done by "picking from a hat" (personal communication).
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded (personal communication)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded (personal communication)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Sherwood 1987

Study characteristics

Methods	Within-person RCT
Participants	Country: United Kingdom (1 centre) Participants: 25 participants (50 eyes) Average age: 73 years (range from 56 to 90) Gender; NR Race: NR History: NR Inclusion: • Bilateral POAG; • IOP above 21 mmHg; • Glaucomatous disc change; • Visual field loss; • No previous eye surgery; • No evidence of other eye disease;

Sherwood 1987 *(Continued)*

	• Patients taking in both eyes the maximum anti-glaucoma medication that could be tolerated; • Despite treatment, IOP was consistently exceeding 21 mmHg and considered to be inadequately controlled. Exclusion criteria: NR
Interventions	Intervention: • ALT (n = 25 eyes) (360 degrees, 100 burns, 0.1 seconds, 150 to 350 micra size spots) continued with maximal medical therapy. The participants received topical prednisolone 1% 4 times a day for one week after the treatment. Comparator: • MMT (n = 25 eyes)
Outcomes	Success criteria: IOP decrease of 20% or more from the baseline examination; no IOP readings above 21 mmHg; stable visual fields by Goldmann perimetry Follow-up: 35 months (30 to 40)
Notes	Date study conducted: NR Funding: GMC Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence generation by computer
Allocation concealment (selection bias)	Low risk	Not reported but within-person study so all patients received both treatments
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Post-laser tonometry readings were checked by two independent observers, who had no knowledge which eye had received the laser
Incomplete outcome data (attrition bias) All outcomes	Low risk	One patient died and one got dementia, so it was impossible to obtain accurate visual fields, but IOP was checked.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Smith 1984

Study characteristics

Smith 1984 *(Continued)*

Methods	Parallel-group RCT One eye included per person; unclear how selected
Participants	Country: USA (1 centre) Participants: 100 participants (100 eyes) Average age: 67 years (range not reported) Gender: NR Race: 89% white, 11% black History: NR Inclusion criteria: • COAG; • Phakic eyes; • Visual field and/or optic nerve damage (not specified by which methods); • Uncontrolled with maximum tolerated medical therapy. Exclusion criteria: NR
Interventions	Intervention 1: • Bichromatic wavelength (blue-green) ALT, performed with 80 burns over 360 degrees of the anterior portion of the trabecular meshwork (n = 50 eyes) Intervention 2: • Monochromatic wavelength (green) ALT applied with the same technique (n = 50 eyes) Maximum tolerated medical therapy was continued in both groups.
Outcomes	Failure: need for filtering surgery Follow-up: 2 to 14 months (9.5 months)
Notes	Date study conducted: NR Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different

Smith 1984 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Tang 2011

Study characteristics	
Methods	Parallel-group RCT Apparently one eye included per person, but it was not clear how the eye was selected.
Participants	Country: China (1 centre) Participants: 74 participants (74 eyes) Average age: 53 years (range from 32 to 79) Gender: 43% male; 57% female Race: NR Inclusion criteria: • Ocular hypertension (OHT), suspected glaucoma, or primary open-angle glaucoma (POAG); • OHT was defined by an IOP greater than 21 mm Hg without glaucomatous optic nerve head or nerve fibre changes; • Suspected glaucoma was defined by suspicious but not definite optic nerve head, nerve fibre layer, or visual field abnormalities suggesting glaucoma; • POAG was defined by definitely glaucomatous optic nerve head or nerve fibre layer abnormalities, with or without visual field defects; • None had received any related treatment; • Baseline IOP ranged from 21 to 30 mm Hg. Exclusion criteria: NR
Interventions	Intervention 1: • Low-energy SLT (half of the energy used in the control group, ranging from 0.3 to 0.5 mJ) Intervention 2: • Conventional-energy SLT (conventional energy used in laser, ranging from 0.6 to 1.0 mJ)
Outcomes	IOP outcome
Notes	Date study conducted: May 2007 to November 2008 Funding: NR Conflict of interest: NR

Tang 2011 *(Continued)*

	Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated as randomised but unclear how the allocation schedule was generated
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	High risk	29/39 (74%) eyes in low-energy group and 28/35 (80%) in conventional-energy group completed 1-year follow-up.
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Tufan 2017

Study characteristics

Methods	Within-person study and parallel-group RCT One eye randomly selected for laser treatment; contralateral continued with medication. Laser-treated eyes randomised to SLT 180 degrees or SLT 360 degrees
Participants	Country: Turkey Participants: 40 participants, 80 eyes Average age: 54 years (range not reported) Gender: 48% male, 52% female Race: NR Inclusion criteria: • presence of bilateral POAG; • both eyes receiving the same anti-glaucoma medications; • IOP of both eyes ≤ 23 mmHg (average of the last 3 measurements) and equal (difference between IOP of both eyes ≤ 2 mmHg in the last 3 measurements). Exclusion criteria: • previous intraocular operations or laser procedures;

Tufan 2017 *(Continued)*

	• pseudoexfoliation or pigmentary glaucoma or advanced glaucoma (vertical cup/disc ratio > 0.8); • signs of corneal and/or lens abnormalities that might preclude precise tonometry or visualisation of the cup and optic disc.
Interventions	Intervention: • SLT (40 eyes) divided into 360 (22 eyes) or 180 degrees (18 eyes) Comparator: • Medication (40 eyes)
Outcomes	IOP, complications Follow-up: 6 months
Notes	Date study conducted: December 2012 to June 2013 Funding: "The authors declared that this study received no financial support." Conflict of interest: Quote: "No conflict of interest was declared by the authors". Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: not reported
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: study was not masked
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: study was not masked
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: not reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no access to protocol or trials registry entry

Watson 1984

Study characteristics

Methods	Parallel-group randomised controlled clinical trial (RCT). If a participant required a second eye to be treated, this was subjected to the same randomisation procedure as the first.
Participants	Country: United Kingdom (2 centres)

Watson 1984 *(Continued)*

	Participants: 61 participants (95 eyes). There was some inconsistency in the description of the number of people enrolled and the number included in the analysis and follow-up. We considered 94 eyes. Average age: 70 years (range 38 to 86) Gender: 43% male, 57% female Race: NR History: NR Inclusion criteria: • OAG classified as severe or with evidence of progression of disease or not responding to medical treatment.
Interventions	Intervention: • ALT (n = 46 eyes). Blue/green laser source, applied 180 degrees of the trabecular meshwork, 50 burns, 50 micra spot Comparator: • Trabeculectomy (n = 48 eyes). Standard technique with a fornix-based flap
Outcomes	Continuous data; need for medication; need for filtering surgery Follow-up: 6 months
Notes	Date study conducted: December 1982 to October 1983 Funding: NR Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Low risk	Patients were allocated in a strictly randomised manner by a lay third party not involved in the study to have one of the treatments.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not mentioned and interventions different
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not mentioned and interventions different
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trial registration entry

Wong 2021

Study characteristics	
Methods	Parallel-group RCT One eye per person; quote "If both eyes of a patient were eligible for inclusion, only one eye would be assigned for randomisation according to an alternate right and left sequence except for patients with visual field defects detected in only one eye — the eye with visual field defects was randomised."
Participants	Country: China (Hong Kong) Participants: 132 participants (132 eyes) Age: average age: 62 years (mean) range not reported Gender: 51% male, 49% female Race: Chinese Inclusion criteria: • older than 18 years of age; • diagnosis of POAG or OHT with trabecular meshwork visible for 360 degrees; • IOP ≤ 35 mm Hg (after washout). Exclusion criteria: • visual acuity worse than 20/40; • history of uveitis; • previous laser trabeculoplasty; • previous glaucoma surgery; • systemic or topical use of steroid within 3 months of study entry; • using more than one class of IOP-lowering medication.
Interventions	Intervention: PSLT (65 eyes, 65 participants) Comparator: SLT (67 eyes, 67 participants)
Outcomes	IOP reduction >= 20%, mean IOP, visual fields, retinal nerve fibre layer thickness, visual acuity, corneal endothelial cell counts, complications Follow-up: 12 months
Notes	Date study conducted: January 2015 to December 2016 Funding: Quote "This study was funded by Hong Kong Food and Health Bureau Health and Medical Research Fund (02130446)." Conflict of interest: quote "CK-SL has received research support in the form of an instrument (Cirrus HD-OCT) from Carl Zeiss Meditec, and in the form of a research grant, speaker honorarium and instrument (Triton OCT) from Topcon." Trial registration ID: Clinical Trials Registry, the Chinese University of Hong Kong CUHK_CCT00407 (https://www2.ccrb.cuhk.edu.hk/registry/public/246)
Risk of bias	

Wong 2021 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation (1:1) to PSLT or SLT was carried out based on an odd/even designation generated from a random number table masked to the investigators except the technician (GL) responsible for the randomisation".
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation (1:1) to PSLT or SLT was carried out based on an odd/even designation generated from a random number table masked to the investigators except the technician (GL) responsible for the randomisation".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The patients, but not the ophthalmologists, were masked to treatment allocation. PSLT/SLT was performed by five trained ophthalmol*ogists* (MW, IL, PC, NC and CL)."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Intraocular pressure was measured at the baseline, and then at 1 day, 1 week, 1, 3, 6, 9 and 12 months after PSLT or SLT, using a calibrated Goldmann applanation tonometer by trained ophthalmologists masked to the clinical information."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: Follow-up high: 100% in SLT group and 95% in PSLT group
Selective reporting (reporting bias)	High risk	Judgement comment: Some modifications to outcome measures compared with trial registry e.g. primary outcome trials register: "The proportion of eyes with ≥ 20% reduction of IOP from baseline at 12 months following PLT/SLT" and primary outcome paper: "The primary outcome measure was the proportion of patients with ≥ 20% IOP reduction at 12 months without IOP-lowering medications (complete success)."

Yong 2020

Study characteristics	
Methods	Parallel-group RCT One eye per person; quote: "If both eyes require treatment, both eyes received the same treatment but only the eye with highest IOP was used for analysis. In the case where the IOP was same in both eyes, the worse eye with more severe MD [mean deviation] from HFA [Humphrey Field Analyser] was used."
Participants	Country: Malaysia Participants: 17 participants (17 eyes) Age: average age: 68 years, range 54 to 81 Gender: 53% male, 47% female Race: 70% Chinese, 30% Malay Inclusion criteria: • diagnosed with POAG with suboptimal IOP control despite pre-existing topical anti-glaucoma medications; • 18 years and above; • POAG with typical glaucomatous optic nerve head and retinal nerve fibre layer damage with corresponding visual field damage, open anterior chamber angle, and no signs of any secondary glaucoma;

Yong 2020 *(Continued)*

- using three or fewer topical anti-glaucoma medications;
- mean deviation values between 0 and -12 dB at baseline in the study eye on Humphrey Field Analyser;
- glaucoma progression that warranted step-up treatment;
- able to sign written informed consent.

Exclusion criteria:

- presence of history or evidence of glaucoma other than POAG;
- advanced glaucomatous field loss with mean deviation >-12dB;
- previous history of intraocular surgery (including glaucoma surgery), with the exception of uncomplicated phacoemulsification that did not require additional intervention for complications;
- iridotrabecular drainage angle anomalies;
- severe non-proliferative diabetic retinopathy or worse;
- neovascularisation or rubeosis iridis;
- current use of a systemic corticosteroid, epinephrine or clonidine;
- any conditions precluding or presumed to preclude reliable VFs and disc photography;
- unable to come for six months of follow-up.

Interventions	Intervention: SLT (10 eyes, 10 participants) Comparator: Topical medication (7 eyes, 7 participants))
Outcomes	IOP, health-related QoL, side effects, costs Follow-up: 6 months
Notes	Date study conducted: February 2016 to October 2017 Funding: Quote "We would like to acknowledge Universiti Kebangsaan Malaysia for providing study grant Dana Fundamental (study code FF-2016-046) for this project." Conflict of interest: not reported Trial registration ID: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were then randomised to one of the two treatment groups: adding SLT treatment (SLT group) or stepping-up topical anti-glaucoma medication (MED group) using a list of computer generated pseudo-random numbers designed to yield expected assignment ratio of 1:1. The randomisation number was assigned to patients sequentially according to the order of enrolment within the strata."
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "All other personnel were masked to the randomisation of patients except the study investigators (YMH and JCH). It was not possible to mask the patients."

Yong 2020 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "All other personnel were masked to the randomisation of patients except the study investigators (YMH and JCH). It was not possible to mask the patients."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Judgement comment: Groups rather small; 9/10 (90%) followed up in SLT and 5/7 (70%) in medical group
Selective reporting (reporting bias)	Unclear risk	Not possible to assess

Zhang 2015

Study characteristics	
Methods	Parallel-group RCT Only one eye; unclear how selected
Participants	Country: China (1 centre) Participants: 45 participants (67 eyes) Average age: 45 years (range 18 to 72) Gender: 87% male, 13% female Race: 100% Chinese Inclusion criteria: • primary open-angle glaucoma (POAG); • IOP greater than 21 mm Hg; • glaucomatous optic nerve head or nerve fibre abnormalities, with or without visual field defect. Suspected glaucoma was defined by suspicious but not definite changes in optic nerve head, nerve fibre layer, or visual field abnormalities suggesting glaucoma; • newly diagnosed or with 4 weeks medication washout. Exclusion criteria: • secondary open-angle glaucoma; • cup-to-disc ratio larger than 0.9; • remaining 5-10 central degrees or only preserved temporal island; • one eye patient; • patients on topical or systemic corticosteroid.
Interventions	Intervention: • Subthreshold SLT (n = 26 eyes) Comparator: • Standard SLT (n = 26 eyes)
Outcomes	Failure: IOP decrease >= 20% Follow-up:12 months

Zhang 2015 *(Continued)*

Notes	Date study conducted: NR Funding: Medical Scientific Research Foundation of Guangdong Province (A2014043, Guangzhou, China) (to Hong Yang Zhang) and the Key Clinical Program of the Ministry of Health ([2010]439-176, China) (to Min Bin Yu) Conflict of interest: NR Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not referred

Zhang 2016

Study characteristics

Methods	Parallel-group RCT One eye per person; unclear how selected
Participants	Country: China Participants: 52 participants, 52 eyes Average age: 45 years Gender: NR Inclusion criteria: • POAG i.e. glaucomatous optic nerve head or nerve fibre abnormalities, with or without visual field defects (International Society of Geographical and Epidemiological Ophthalmology (ISGEO) criteria); • IOP > 21 mmHg.

Zhang 2016 *(Continued)*

	Exclusion criteria: • secondary OAG; • cup to disc ratio larger than 0.9; • remaining of only 5°–10° of central visual field or having only a preserved temporal island; • one-eyed patients; • patients on topical or systemic corticosteroid.
Interventions	Intervention: Subthreshold SLT (number not reported) Comparator: Conventional SLT (number not reported)
Outcomes	Follow-up: 12 months
Notes	Date study conducted: NR Funding: Quote: "The work was supported by a grant from the Medical Scientific Research Foundation of Guangdong Province (A2014043, Guangzhou, China) (to Hong Yang Zhang) and the Key Clinical Program of the Ministry of Health ([2010]439-176, China) (to Min Bin Yu)." Conflict of interest: Quote: "The authors declare that there are no competing interests regarding the publication of this paper." Trial registration ID: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: not reported
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: follow-up not reported and numbers in each group not reported
Selective reporting (reporting bias)	Unclear risk	Judgement comment: no access to protocol or trial registry entry

AGIS: Advanced Glaucoma Intervention Study
ALT: argon laser trabeculoplasty
CIGTS: Collaborative Initial Glaucoma Treatment Study

COAG: chronic open-angle glaucoma
DLT: diode laser trabeculoplasty
ELT: excimer laser trabeculoplasty
GLT: Glaucoma Laser Trial
HRT: Heidelberg Retina Tomograph
ID: identification
IOP: intraocular pressure
ISGEO: International Society of Geographical and Epidemiological Ophthalmology
ITT: intention-to-treat
LF: laser first
MF: medication first
MLT: micropulse laser trabeculoplasty
mo: months
MMT: maximal medical therapy
NR: not reported
NTG: normal-tension glaucoma
OAG: open-angle glaucoma
OD: oculus dexter (right eye)
OHT: ocular hypertension
OS: oculus sinister (left eye)
PAS: peripheral anterior synechiae
PC20: provocative concentration that reduced at least 20% of the forced expiratory volume
POAG: primary open-angle glaucoma
PSLT: pattern scanning laser trabeculoplasty
PV: performance value
PXF: pseudoexfoliation syndrome
QoL: quality of life
RCT: randomised controlled trial
SD-OCT: spectral Domain Optical Coherence Tomography
SLT: selective laser trabeculoplasty
SVFD: sustained visual field defect
TM: trabecular meshwork
VA: visual acuity
VF: visual field
W: watts

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

Study	Reason for exclusion
Agarwal 2006	Not a randomised controlled trial (i.e. non random allocation to treatment)
Ayala 2011	Not a randomised controlled trial (i.e. non random allocation to treatment)
Ayala 2014	Participants had been previously treated with laser.
Bozić 2011	Comparison not eligible for inclusion: brimonidine versus apraclonidine for IOP spike prevention after ALT
Brancato 1988	Study did not measure any of the review outcomes.
Brooks 1993	Not a randomised controlled trial (i.e. non random allocation to treatment)
Canadian Laser Study Trial Network 2019	Participants had been previously treated with laser.
Chudoba 2014	Not a randomised controlled trial (i.e. non random allocation to treatment)

Study	Reason for exclusion
De Keyser 2017	Participants were initially randomly allocated but patients who refused SLT were allocated to the control group.
Demailly 1989	Comparison not eligible for inclusion: argon laser trabeculoplasty versus vascular medication
Detry-Morel 2008	Not a randomised controlled trial (i.e. non random allocation to treatment)
Douglas 1987	Follow-up less than 6 months (6 weeks)
EMGT 1999	Comparison not eligible for inclusion: laser trabeculoplasty combined with medication versus no treatment which was not one of the prespecified comparisons of the review.
Englert 1997	Follow-up less than 6 months (3 months)
Fea 2017	Not a randomised controlled trial (i.e. non random allocation to treatment)
Fink 1988	Not a randomised controlled trial (i.e. non random allocation to treatment)
Francis 2011	Not a randomised controlled trial (i.e. non random allocation to treatment)
Frenkel 1997	Study did not measure any of the review outcomes.
Gandolfi 2004	Study did not measure any of the review outcomes.
Germano 2021	Not a randomised controlled trial (i.e. non random allocation to treatment)
Glaucoma Intensive Treatment Study 2018	Comparison of multi-therapy versus mono-therapy in people with OAG
Goyal 2010	Follow-up less than 6 months (one month)
Heijl 1984	Not a randomised controlled trial (i.e. non random allocation to treatment)
Hollo 1996	Not a randomised controlled trial (i.e. non random allocation to treatment); right eye of each participant received argon laser trabeculoplasty and left eye received Q-switched Nd:Yag laser trabeculoplasty (non-randomised)
Hua 2014	Not a randomised controlled trial (i.e. non random allocation to treatment)
Huk 1991	Follow-up less than 6 months (24 hours)
ISRCTN17339574	Follow-up less than 6 months
ISRCTN27208571	Study stopped because of logistical problems (personal communication from principal investigator)
ISRCTN42557387	Primary angle-closure glaucoma.
ISRCTN66330584	Study was probably not done (personal communication)
Jinapriya 2014	Wrong intervention - anti-inflammatory approaches after SLT
Kara 2011	Not a randomised controlled trial (i.e. non random allocation to treatment)
Kiddee 2017	Follow-up less than 6 months (2 weeks)

Study	Reason for exclusion
Kocabora 2013	Comparison not eligible for inclusion: pneumatic trabeculoplasty plus latanoprost versus timolol added to latanoprost
Krasnov 1982	Not a randomised controlled trial (i.e. non random allocation to treatment)
McWherter 2021	Follow-up less than 6 months.
Mermoud 1992	Not a randomised controlled trial (i.e. non random allocation to treatment)
Moriarty 1993	Follow-up less than 6 months (8 weeks)
NCT00000149	Laser trabeculoplasty combined with trabeculectomy
NCT00551395	Principal investigator confirmed by email that the study (identified on www.clinicaltrials.gov) was not conducted.
NCT02774811	Study terminated after 15 participants enrolled. Quote from clinical trials registry entry: "Terminated (unable to maintain a functional laser in the environment)"
NCT02928289	Terminated (poor enrolment)
NCT03648229	Withdrawn because funding not available
Popiela 2000	Follow-up less than 6 months (3 months)
Realini 2010	Comparison not eligible for inclusion: prednisolone acetate 1% versus no treatment in eyes that received SLT
Russo 2009	Not a randomised controlled trial (i.e. non random allocation to treatment)
Schrems 1988	Not a randomised controlled trial (i.e. non random allocation to treatment)
Shin 1996	Follow-up less than 6 months (35 days)
Stunf Pukl 2018	Not a randomised controlled trial (i.e. non random allocation to treatment)
Tabak 1998	Follow-up less than 6 months
Tardif 2014	Not a randomised controlled trial (i.e. non random allocation to treatment)
Traverso 1984	Follow-up less than 6 months (16 weeks)
Tuulonen 1989	Not a randomised controlled trial (i.e. non-random allocation to treatment, participants born in even years received medication and participants born in odd years received argon laser trabeculoplasty)
Uva 2010	Comparison not eligible for inclusion: pneumatic versus argon laser trabeculoplasty
Vaidergorn	Not a randomised controlled trial (i.e. non random allocation to treatment)
Veljko 2011	Not a randomised controlled trial (i.e. non random allocation to treatment)
Weinreb 1983a	Follow-up less than 6 months (24 hours)
Weinreb 1983b	Follow-up less than 6 months (2 months)

Study	Reason for exclusion
WIGLS 2017	Not a randomised controlled trial

OAG: open-angle glaucoma
SLT: selective laser trabeculoplasty

Characteristics of studies awaiting classification *[ordered by study ID]*

NCT00145535

Methods	Randomised controlled trial
Participants	120 people with uncontrolled POAG
Interventions	Titanium sapphire laser versus ALT
Outcomes	Primary outcome measures : 1. Intraocular pressure (IOP) [time frame: 1 year] Secondary outcome measures : 1. Adverse event frequency [time frame: 1 year]
Notes	Title: SOLX titanium sapphire laser for trabeculoplasty Date study conducted: May 2004 to June 2009 Trial registration ID: NCT00145535 Contact with study investigators: Contact email: 'Nilay Shah' <nshah@emmes.com>. Emailed 13th September 2018, no reply. Follow-up email 14th November 2019

NCT01639807

Methods	Parallel-group RCT
Participants	600 participants
Interventions	SLT versus latanoprost
Outcomes	From clinical trials register Primary outcome measures : To assess the mean and percentage reduction of intraocular pressure 1. Intraocular pressure [time frame: 24 months] Secondary outcome measures : To assess the visual function and quality of life 1. Quality of life [time frame: 24 months]
Notes	Title: Clinical evaluation of efficacy of SLT to topical medication in lowering IOP Date study conducted: October 2011 to October 2013

NCT01639807 *(Continued)*

	Trial registration ID: NCT01639807 Contact with study investigators: Dr Puthuran Aravind. Emailed 13th September no reply. Emailed again November 12th 2019

NCT01704989

Methods	Parallel-group RCT
Participants	110 participants with pseudoexfoliation
Interventions	SLT versus prostaglandin
Outcomes	From clinical trials register entry Primary outcome measures: Proportion of patients in whom SLT (or mono-medical therapy) alone achieved target IOP 1. Number of drops (and surgical interventions) needed to reach target IOP [time frame: change in IOP at 6 months, 12 months and 2 years (from baseline)] 2. Percentage success [time frame: at 6 months, 12 months and 2 years] Secondary outcome measures: 1. Correlation of angle pigment grade with IOP reduction from SLT [time frame: 6 months, 12 months, 2 years] 2. Comparison of percentage success and number of drops in current study with the equivalent results of patients with POAG in the LiGHT study [time frame: 1 year and 2 years] 3. Number of progressing patients in each study arm (SLT or medical therapy) in terms of visual field loss and HRT [time frame: 2 years]
Notes	Title: A randomised controlled trial to compare the clinical effectiveness of selective laser trabeculoplasty (SLT) versus topical therapy in the treatment of pseudoexfoliative glaucoma. The Laser in Pseudoexfoliation (LIP) study Date study conducted: October 2012 to December 2015 (from trials register) Trial registration ID: NCT01704989 Contact with study investigators: Contact email: nicolela@dal.ca. Emailed 13th September 2018 no reply. Emailed 12th November 2019

NCT01788319

Methods	Unclear
Participants	30 people
Interventions	Micropulse laser trabeculoplasty (532 nm) versus conventional laser trabeculoplasty (532 nm)
Outcomes	Primary outcome measures: 1. to compare the intraocular pressure reduction with the micropulse laser trabeculoplasty (532 nm) versus the conventional laser trabeculoplasty (532 nm) [time frame: one year of follow-up] Secondary outcome measures:

NCT01788319 *(Continued)*

	1. the complication rate between the two techniques [time frame: one year of follow-up]
Notes	Title: Micropulse laser trabeculoplasty (532 nm) versus conventional laser trabeculoplasty (532 nm) in open-angle glaucoma patients Date study conducted: February 2013 to June 2015 Trial registration ID: NCT01788319 Contact with study investigators: Contact email: Evelien Vandewalle evelien.vandewalle@kuleuven.be. Response: "We performed the study but the results showed no difference so we decided not to publish the data." Further email sent 21/11/2019 requesting data

Sreckovic 2011

Methods	Comparative study; unclear if randomised
Participants	50 eyes of 35 glaucoma patients
Interventions	Argon laser trabeculoplasty versus timolol versus dorzolamide versus latanoprost
Outcomes	IOP control and visual field stabilisation
Notes	Date study conducted: NR Contact with investigators: Contact email: sunshinekg@sbb.rs. We emailed the authors on 16th May 2018 with no response. This email was sent again on 4th November 2019.

Tawfique 2018

Methods	Parallel-group RCT
Participants	People with glaucoma and OHT; 67
Interventions	90-degree and 360 degree SLT
Outcomes	IOP at 2 years
Notes	

ALT: argon laser trabeculoplasty
HRT: Heidelberg Retina Tomograph
ID: identification
IOP: intraocular pressure
OHT: ocular hypertension
POAG: primary open-angle glaucoma
RCT: randomised controlled trial
SLT: selective laser trabeculoplasty

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

EudraCT 2015-003631-34

Study name	A comparison of bimatoprost SR to selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension
Methods	Within-person study
Participants	People with OAG or OHT n = 100
Interventions	Bimatoprost versus SLT
Outcomes	Change in IOP, follow-up 24 weeks
Starting date	Unclear. Ethics approval June 2018, status ongoing
Contact information	ml-ctrg@allergan.com
Notes	https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-003631-34/DK

GLAUrious

Study name	Direct selective laser trabeculoplasty in open-angle glaucoma: a randomized controlled trial (GLAUrious)
Methods	Randomized controlled trial
Participants	Country: Israel, Italy, and UK People with open-angle glaucoma Target number of participants: 192
Interventions	Direct selective laser trabeculoplasty versus selective laser trabeculoplasty
Outcomes	Change in IOP between baseline and 6 months Safety endpoints Adverse events Percentage reduction in IOP at 3, 6, and 12 months Number of medications at 12 months
Starting date	Recruitment start date: October 2018 Estimated study completion date: November 2022
Contact information	Professor Nathan Congdon: ncongdon1@gmail.com
Notes	Trial registration ID: NCT03750201 and ISRCTN14033075

LIGHT China trial

Study name	Light China trial

LIGHT China trial *(Continued)*

Methods	Randomised controlled trial
Participants	Country: China People with primary open-angle glaucoma or ocular hypertension Number of participants: 771
Interventions	Selective laser trabeculoplasty first (followed by medication then surgery when required) versus conventional medical therapy first (followed by surgery when required)
Outcomes	Health-related quality of life Treatment pathway cost and cost-effectiveness Glaucoma-specific treatment-related quality of life: Glaucoma Utility Index (GUI) Patient-reported disease and treatment-related symptoms: Glaucoma Symptom Scale (GSS) Patient-reported visual function: Glaucoma Quality of Life-15 (GQL-15) Objective measures of pathway effectiveness and visual function Objective measures of the safety profiles of each pathway Concordance/compliance
Starting date	Recruitment: March 2015 to January 2019
Contact information	Gus Gazzard e-mail: g.gazzard@nhs.net Minbin Yu: yuminbin@mail.sysu.edu.cn
Notes	

NCT01444105

Study name	Open-angle glaucoma subjects on one ocular hypotensive medication randomized to treatment with two trabecular micro-bypass stents or selective laser trabeculoplasty
Methods	Parallel-group RCT
Participants	80
Interventions	iStent versus SLT
Outcomes	From clinical trials registry entry: Primary outcome measures 1. Change from baseline in mean diurnal IOP (mmHg) at the month 12 visit [time frame: 12 months]
Starting date	September 2011 End date: December 2018
Contact information	Lilit A Voskanyan, MD, PhD S.V. Malayan Ophthalmological Center, Yerevan, Armenia: lilit.voskanyan@yahoo.com

NCT01444105 *(Continued)*

Notes	Emailed Dr Voskanyan on 30th September 2021

NCT01886456

Study name	IOP lowering effect of PLT versus SLT in naive OAG patients
Methods	Parallel-group RCT
Participants	210
Interventions	Patterned laser trabeculoplasty versus SLT
Outcomes	From clinical trials registry entry: Primary outcome measures: Intraocular pressure 6 months after Intervention [time frame: 6 months]
Starting date	February 2013 Estimated study completion date: February 2017
Contact information	gregor.jaggi@usz.ch: christoph.kniestedt@usz.ch
Notes	Emailed Professor Kniestedt on 30th September 2021

NCT02327312

Study name	Multicentre investigation of trabecular micro-bypass stents vs. laser trabeculoplasty
Methods	Parallel-group RCT
Participants	1200
Interventions	Micro-bypass stents versus laser trabeculoplasty
Outcomes	From clinical trials registry entry: Primary outcome measures • IOP reduction [time frame: up to 24 months] Secondary outcome measures • % IOP reduction [time frame: up to 24 months]
Starting date	November 2014 Estimated study completion date: May 2024
Contact information	ssitaraman@glaukos.com jwells@glaukos.com

NCT02327312 *(Continued)*

Notes	

NCT02636946/NCT02507687

Study name	A comparison of bimatoprost SR to selective laser trabeculoplasty in patients with open-angle glaucoma or ocular hypertension
Methods	Randomised controlled trial
Participants	Country: USA, Europe, Thailand (NCT02636946 - 66 study locations; NCT02507687- 86 study locations) People with open-angle glaucoma or ocular hypertension Target number of participants: 160 (NCT02636946) and 210 (NCT02507687)
Interventions	Selective laser trabeculoplasty versus bimatoprost SR
Outcomes	Change from baseline in IOP at week 24 Change from baseline in IOP at week 4 Change from baseline in IOP at week 12 IOP at each visit
Starting date	Recruitment start date: February 2016 Recruitment end date: November 2018 Estimated study completion date: May 2023
Contact information	Chery Barcelon, Allergan
Notes	

NCT02955849

Study name	The China laser and surgery study: a mixed methods study with a random control trial comparing outcomes from selective laser trabeculoplasty versus surgical treatment (trabeculectomy) for glaucoma in rural China
Methods	Randomized controlled trial
Participants	Country: China People with glaucoma Target number of participants: 200
Interventions	Selective laser trabeculoplasty versus trabeculectomy versus topical timolol 0.5%
Outcomes	IOP at 12 months Visual quality of life at 12 months (NEI-VFQ 25)

NCT02955849 *(Continued)*

	Satisfaction score at 12 months Cataract surgery at 12 months Allocated treatment (acceptance questionnaire) at 12 months
Starting date	Recruitment start date: September 2016 Recruitment end date: October 2018 Estimated study completion date: February 2019
Contact information	Nathan G. Congdon
Notes	Emailed Nathan Congdon on 27th September

NCT03529591

Study name	Is the reduction in IOP after treatment of 180 degrees equivalent to treatment of 360 degrees with SLT?
Methods	Within-person RCT
Participants	48
Interventions	180 degrees SLT versus 360 degrees SLT
Outcomes	From registry entry: Primary outcome measures: • Intraocular pressure response (physiological parameter) [time frame: Six months] Secondary outcome measures: • The number of participants with treatment-related adverse events assessed by CTCAE v4.0. [time frame: six months] • The adverse events/complications in eyes treated with 180 degrees SLT compared to 360 degrees SLT
Starting date	May 2018 Estimated completion date: November 2018
Contact information	Tony.Lin@sjhc.london.on.ca
Notes	Emailed Tony Lin on 27th September

NCT03798223

Study name	Optimal treatment protocol for selective laser trabeculoplasty
Methods	Randomised controlled trial
Participants	400

NCT03798223 *(Continued)*

Interventions	4 different commonly used protocols
Outcomes	Primary outcome measures: The IOP is measured with a Goldmann Applanation Tonometer (GAT) three times before SLT and then at regular intervals after the procedure. The reduction is registered and analysed in absolute (mmHg) and relative (percent of the IOP before SLT) measures. Measurement of IOP is planned 1, 3, 6, and 12 months post-SLT, and thereafter every six months for 3 years after SLT. The study is conducted in a regular clinical setting and the above mentioned times might be delayed. If target pressure is not achieved, measurements will be planned at shorter intervals, according to a specified algorithm, due to safety reasons. See outcome 1. Analysis of differences between the study arms will also be conducted measuring the proportion of eyes achieving 20% reduction in IOP or more at different time points in each group. Kaplan-Meier survival analysis will be conducted, measuring the proportion of eyes that stay in the study groups but do not receive any further IOP-lowering intervention (medical, surgical or laser). 1. Change in intraocular pressure (IOP) [time frame: before SLT and thereafter regularly for 3 years] 2. Achievement of 20% reduction in IOP [time frame: for 3 years] 3. Survival (no additional intervention) [time frame: for 3 years] Secondary outcome measures: See outcome 3. Kaplan-Meier survival analysis is performed the same way, but additional SLT treatment will not be judged as failure. See outcome 3. Kaplan-Meier survival analysis is performed the same way, but additional SLT treatment or change in medical treatment will not be judged as failure. The patient will grade perioperative pain on an arbitrary scale between 0 (no pain) and 4 (maximum pain) on a written protocol. The patient will grade postoperative pain on an arbitrary scale between 0 (no pain) and 4 (maximum pain) on a written protocol, also stating the duration of pain. The patient will grade postoperative sensitivity to light on an arbitrary scale between 0 (no difference) and 4 (very intense sensitivity to light) on a written protocol, also stating the duration of light sensitivity. The patient will grade postoperative impairment of vision on an arbitrary scale between 0 (no difference) and 4 (cannot see one's own hand) on a written protocol, also stating the duration of vision impairment. The patient will grade postoperative redness of the eye on an arbitrary scale between 0 (no difference) and 4 (very intense redness) on a written protocol, also stating the duration of redness. 15 participants from each treatment arm (60 in total, randomised in a separate block after informed consent) will undergo measurement with a laser flare metre. The type and frequency of adverse events will be recorded and analysed in each of the study arms. 1. Survival (SLT allowed) [time frame: for 3 years] 2. Survival (no surgery) [time frame: for 3 years] 3. Pain perioperatively: on a scale [time frame: immediately after treatment] 4. Pain postoperatively: on a scale [time frame: during the first month] 5. Light sensitivity postoperatively [time frame: during the first month] 6. Impairment of vision postoperatively [time frame: during the first month] 7. Redness postoperatively [time frame: during the first month]

NCT03798223 *(Continued)*	8. Flare (inflammation measurement of the anterior chamber) [time frame: preoperatively and then one day, one week and one month postoperatively] 9. Adverse events [time frame: 3 years (although adverse events, if any, are anticipated to emerge in the first postoperative days or weeks)]
Starting date	Jan 2013. Study completion date Jan 2025
Contact information	https://clinicaltrials.gov/ct2/show/NCT03798223
Notes	Trial registration ID: NCT03798223

CTCAE: Common Terminology Criteria for Adverse Events
GAT: Goldmann Applanation Tonometer
GQL-15: Glaucoma Quality of Life - 15
GSS: Glaucoma Symptom Scale
GUI: Glaucoma Utility Index
ID: identification
NEI-VFQ 25: National Eye Institute Visual Function Questionnaire 25
OAG: open-angle glaucoma
OHT: ocular hypertension
PLT: pattern-scanning laser trabeculoplasty
RCT: randomised controlled trial
SLT: selective laser trabeculoplasty

DATA AND ANALYSES

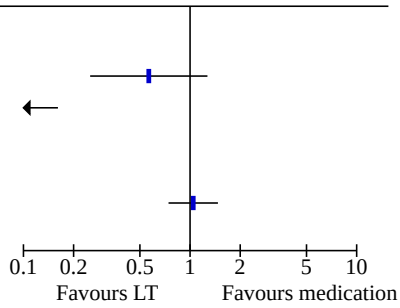
Comparison 1. Laser trabeculoplasty versus medication

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Failure to control IOP at 6 months	3		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1.1 Argon laser	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1.2 Selective laser	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.2 Failure to control IOP at 12 months	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.2.1 Argon laser	5	788	Risk Ratio (M-H, Random, 95% CI)	0.37 [0.22, 0.61]
1.2.2 Selective laser	5	1882	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.67, 1.97]
1.3 Failure to control IOP at 24 months	5		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.3.1 Argon laser	3		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3.2 Selective laser	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.4 Failure to control IOP at 36 months	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.5 Failure to control IOP at 5 years	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.6 Failure to stabilise visual field progression at 12 months	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.7 Failure to stabilise visual field progression at 24 months	2	624	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.42, 1.16]
1.8 Failure to stabilise visual field progression at 48 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.9 Failure to stabilise optic neuropathy progression at 24 months	2	624	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.44, 1.20]
1.10 Adverse effects: PAS formation	2	624	Risk Ratio (M-H, Fixed, 95% CI)	11.74 [5.94, 23.22]
1.11 Adverse effects: early IOP spikes	3	859	Risk Ratio (M-H, Fixed, 95% CI)	14.31 [2.75, 74.33]

Analysis 1.1. Comparison 1: Laser trabeculoplasty versus medication, Outcome 1: Failure to control IOP at 6 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Argon laser					
Bergea 1992 (1)	7	40	13	42	0.57 [0.25 , 1.27]
GLT 1990 (2)	8	264	100	264	0.08 [0.04 , 0.16]
1.1.2 Selective laser					
Katz 2012 (3)	35	67	30	60	1.04 [0.74 , 1.47]



Footnotes

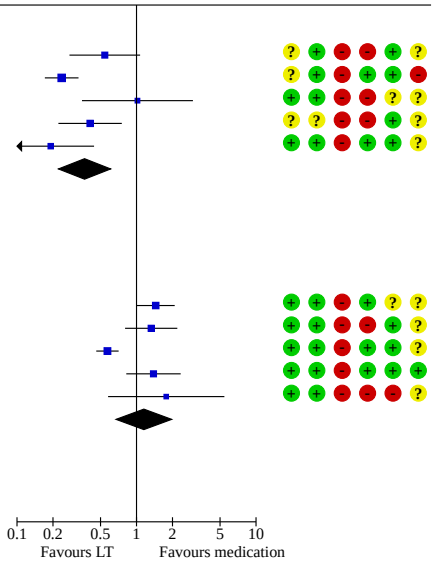
(1) Parallel group: one eye per person

(2) Within-person study. Outcome measured at 3 months.

(3) Clustered data: both eyes included (69 people, 127 eyes)

Analysis 1.2. Comparison 1: Laser trabeculoplasty versus medication, Outcome 2: Failure to control IOP at 12 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Argon laser						
Bergea 1992 (1)	9	40	17	41	20.1%	0.54 [0.27 , 1.07]
GLT 1990 (2)	35	251	148	251	28.2%	0.24 [0.17 , 0.33]
Moorfields PTT 1994 (1)	6	55	6	56	13.1%	1.02 [0.35 , 2.96]
Moriarty 1988 (3)	8	25	18	23	21.7%	0.41 [0.22 , 0.75]
Sherwood 1987 (4)	4	23	23	23	17.0%	0.19 [0.08 , 0.44]
Subtotal (95% CI)		**394**		**394**	**100.0%**	**0.37 [0.22 , 0.61]**
Total events:	62		212			
Heterogeneity: Tau² = 0.21; Chi² = 12.20, df = 4 (P = 0.02); I² = 67%						
Test for overall effect: Z = 3.90 (P < 0.0001)						
1.2.2 Selective laser						
Glaucoma Initial Treatment Study 2020 (1)	42	77	26	69	22.6%	1.45 [1.00 , 2.09]
Katz 2012 (5)	23	52	16	48	20.7%	1.33 [0.80 , 2.19]
KiGIG 2021 (5)	64	163	121	176	24.3%	0.57 [0.46 , 0.71]
LIGHT 2019 (5)	32	608	23	606	20.4%	1.39 [0.82 , 2.34]
Nagar 2005 (1)	8	44	4	39	12.0%	1.77 [0.58 , 5.43]
Subtotal (95% CI)		**944**		**938**	**100.0%**	**1.15 [0.67 , 1.97]**
Total events:	169		190			
Heterogeneity: Tau² = 0.30; Chi² = 29.80, df = 4 (P < 0.00001); I² = 87%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Test for subgroup differences: Chi² = 9.29, df = 1 (P = 0.002), I² = 89.2%						



Footnotes

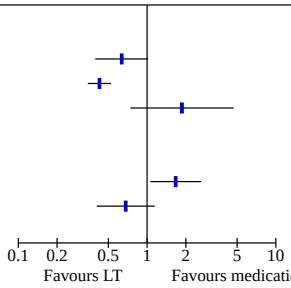
(1) Parallel group: one eye per person
(2) Within-person study
(3) Parallel group and within-person (30 people, 48 eyes): control group participants were on maximum medication
(4) Within-person study: control group on maximum medication
(5) Clustered data: both eyes included

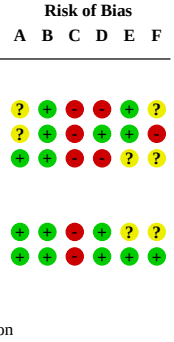
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)

Analysis 1.3. Comparison 1: Laser trabeculoplasty versus medication, Outcome 3: Failure to control IOP at 24 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Argon laser					
Bergea 1992 (1)	15	39	23	38	0.64 [0.40 , 1.02]
GLT 1990 (2)	73	244	171	244	0.43 [0.35 , 0.53]
Moorfields PTT 1994 (1)	11	55	6	56	1.87 [0.74 , 4.70]
1.3.2 Selective laser					
Glaucoma Initial Treatment Study 2020 (3)	34	73	19	68	1.67 [1.06 , 2.62]
LIGHT 2019 (4)	23	576	33	564	0.68 [0.41 , 1.15]





Footnotes

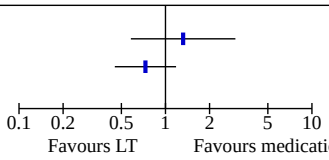
(1) Parallel group: one eye per person
(2) Within-person study
(3) Parallel group RCT: one eye per person. Worse than 25% reduction in IOP
(4) Clustered data: both eyes included. Eyes at target IOP

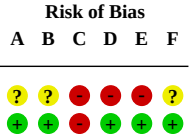
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)

Analysis 1.4. Comparison 1: Laser trabeculoplasty versus medication, Outcome 4: Failure to control IOP at 36 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
Gandolfi 2005 (1)	6	10	5	11	1.32 [0.58 , 3.00]
LIGHT 2019 (2)	27	536	37	536	0.73 [0.45 , 1.18]





Footnotes

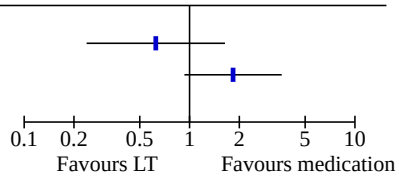
(1) Parallel group: measured per person
(2) Clustered data: both eyes included. Eyes at target intraocular pressure

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)

Analysis 1.5. Comparison 1: Laser trabeculoplasty versus medication, Outcome 5: Failure to control IOP at 5 years

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
Lai 2004 (1)	5	24	8	24	0.63 [0.24 , 1.64]
Moorfields PTT 1994 (2)	18	55	10	56	1.83 [0.93 , 3.61]



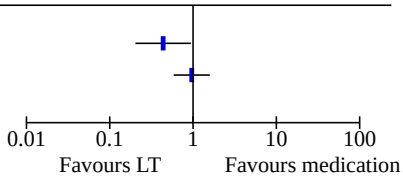
Footnotes

(1) Within-person study: IOP > 21 mmHg despite maximal medication

(2) Clustered data: both eyes included (718 people, 1235 eyes)

Analysis 1.6. Comparison 1: Laser trabeculoplasty versus medication, Outcome 6: Failure to stabilise visual field progression at 12 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
Bergea 1992 (1)	7	38	16	38	0.44 [0.20 , 0.94]
GLT 1990 (2)	27	249	28	249	0.96 [0.59 , 1.59]



Footnotes

(1) Parallel group: one eye per person: Argon laser. Goldman perimetry prgoression points -2.0 or worse

(2) Within-person study: argon laser. "Confirmed visual field deterioration from enrolment".

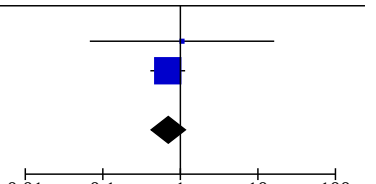
Analysis 1.7. Comparison 1: Laser trabeculoplasty versus medication, Outcome 7: Failure to stabilise visual field progression at 24 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bergea 1992 (1)	1	40	1	42	3.0%	1.05 [0.07 , 16.23]
GLT 1990 (2)	22	271	32	271	97.0%	0.69 [0.41 , 1.15]
Total (95% CI)		**311**		**313**	**100.0%**	**0.70 [0.42 , 1.16]**
Total events:	23		33			

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%

Test for overall effect: Z = 1.39 (P = 0.16)

Test for subgroup differences: Not applicable



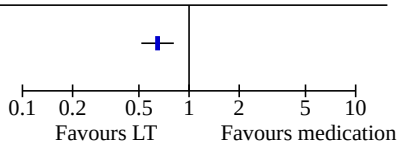
Footnotes

(1) Parallel group: one eye per person: argon laser

(2) Within-person study: argon laser

Analysis 1.8. Comparison 1: Laser trabeculoplasty versus medication, Outcome 8: Failure to stabilise visual field progression at 48 months

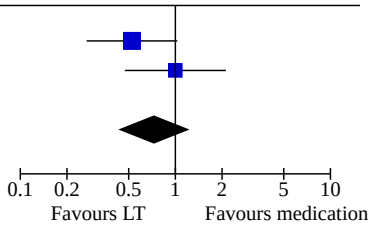
Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Risk Ratio M-H, Fixed, 95% CI
LIGHT 2019	100	590	154	588	0.65 [0.52 , 0.81]



Analysis 1.9. Comparison 1: Laser trabeculoplasty versus medication, Outcome 9: Failure to stabilise optic neuropathy progression at 24 months

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bergea 1992 (1)	9	40	18	42	57.5%	0.53 [0.27 , 1.03]
GLT 1990 (2)	13	271	13	271	42.5%	1.00 [0.47 , 2.12]
Total (95% CI)		**311**		**313**	**100.0%**	**0.73 [0.44 , 1.20]**
Total events:	22		31			

Heterogeneity: Chi² = 1.59, df = 1 (P = 0.21); I² = 37%
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable

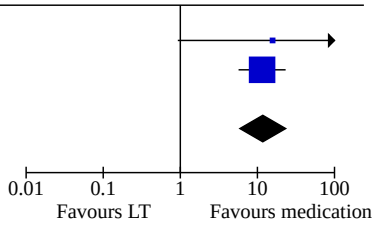


Footnotes
(1) Parallel group: one eye per person: argon laser
(2) Within-person study: argon laser

Analysis 1.10. Comparison 1: Laser trabeculoplasty versus medication, Outcome 10: Adverse effects: PAS formation

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bergea 1992 (1)	7	40	0	42	5.8%	15.73 [0.93 , 266.73]
GLT 1990 (1)	92	271	8	271	94.2%	11.50 [5.70 , 23.22]
Total (95% CI)		**311**		**313**	**100.0%**	**11.74 [5.94 , 23.22]**
Total events:	99		8			

Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 7.08 (P < 0.00001)
Test for subgroup differences: Not applicable

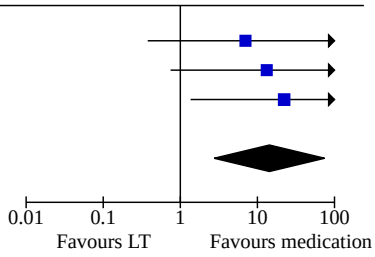


Footnotes
(1) Argon laser

Analysis 1.11. Comparison 1: Laser trabeculoplasty versus medication, Outcome 11: Adverse effects: early IOP spikes

Study or Subgroup	LT Events	LT Total	Medication Events	Medication Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lai 2004 (1)	3	29	0	29	32.8%	7.00 [0.38 , 129.74]
LIGHT 2019 (2)	6	356	0	362	32.5%	13.22 [0.75 , 233.77]
Nagar 2005 (3)	12	44	0	39	34.7%	22.22 [1.36 , 363.41]
Total (95% CI)		**429**		**430**	**100.0%**	**14.31 [2.75 , 74.33]**
Total events:	21		0			

Heterogeneity: Chi² = 0.33, df = 2 (P = 0.85); I² = 0%
Test for overall effect: Z = 3.16 (P = 0.002)
Test for subgroup differences: Not applicable



Footnotes
(1) Within-person study: selective laser
(2) Clustered data: both eyes included (718 people, 1235 eyes): selective laser
(3) Parallel group: one eye per person: selective laser

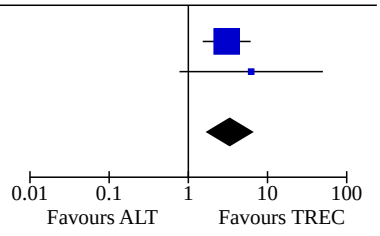
Comparison 2. Laser trabeculoplasty versus trabeculectomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Failure to control IOP at 6 months	2	901	Risk Ratio (M-H, Fixed, 95% CI)	3.33 [1.72, 6.42]
2.2 Failure to control IOP at 24 months	2	901	Risk Ratio (M-H, Fixed, 95% CI)	2.12 [1.44, 3.11]

Analysis 2.1. Comparison 2: Laser trabeculoplasty versus trabeculectomy, Outcome 1: Failure to control IOP at 6 months

Study or Subgroup	ALT Events	ALT Total	TREC Events	TREC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AGIS 2001 (1)	32	404	10	385	91.2%	3.05 [1.52 , 6.12]
Moorfields PTT 1994 (2)	6	55	1	57	8.8%	6.22 [0.77 , 49.99]
Total (95% CI)		**459**		**442**	**100.0%**	**3.33 [1.72 , 6.42]**
Total events:	38		11			

Heterogeneity: Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 3.58 (P = 0.0003)
Test for subgroup differences: Not applicable

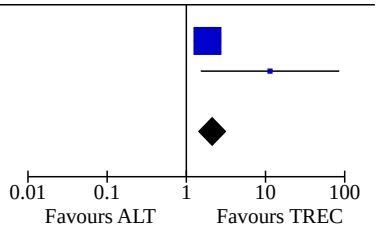


Footnotes
(1) Parallel group (one eye per person) and within-person (if two eyes eligible)
(2) Parallel group: one eye per person

Analysis 2.2. Comparison 2: Laser trabeculoplasty versus trabeculectomy, Outcome 2: Failure to control IOP at 24 months

Study or Subgroup	ALT Events	ALT Total	TREC Events	TREC Total	Weight	Risk Ratio M-H, Fixed, 95% CI
AGIS 2001 (1)	64	404	33	385	97.2%	1.85 [1.24 , 2.75]
Moorfields PTT 1994 (2)	11	55	1	57	2.8%	11.40 [1.52 , 85.36]
Total (95% CI)		**459**		**442**	**100.0%**	**2.12 [1.44 , 3.11]**
Total events:	75		34			

Heterogeneity: Chi² = 3.14, df = 1 (P = 0.08); I² = 68%
Test for overall effect: Z = 3.84 (P = 0.0001)
Test for subgroup differences: Not applicable



Footnotes

(1) Parallel group (one eye per person) and within-person (if two eyes eligible)
(2) Parallel group: one eye per person

ADDITIONAL TABLES

Table 1. Included studies

	Study	Country	People	Eyes	Average age (years)	Age range	% female	% black	Clustered (one or two eyes) or paired (within-person) design
1	Abramowitz 2018	USA	69	69	67	-	51	-	One eye per person
2	AGIS 2001	USA	591	789	67	35 to 80	54	56	Clustered
3	Babighian 2010	Italy	30	30	66	58 to 73	58	-	One eye per person
4	Bergea 1992	Sweden	82	82	71	-	-	0	One eye per person
5	Blyth 1999	UK	40	40	67	-	-	-	One eye per person
6	Brancato 1991	Italy	20	20	71	-	35	0	One eye per person
7	Chung 1998	USA	46	50	73	-	46	-	Clustered
8	Damji 2006	Canada	152	176	70	-	59	-	Clustered
9	Elsas 1989	Norway	34	40	71	54 to 89	-	-	Clustered
10	Gandolfi 2005	Italy	32	32	-	44 to 67	53	-	One eye per person
11	Geffen 2017	Israel	30	30	67	40 to 80	50	-	One eye per person
12	Glaucoma Initial Treatment Study 2020	Australia, New Zealand, Singapore, UK (15 sites)	167	167	64	-	48	77% Caucasian 20% Asian 3% other	One eye per person
13	GLT 1990	USA	271	542	61	-	-	43	Within-person
14	Goldenfeld 2009	Israel	38	38	68	40 to 91	59	-	One eye per person
15	Grayson 1993	USA	36	45	75	57 to 92	50	15	Clustered
16	Grayson 1994	USA	80	102	-	-	-	-	Clustered

Table 1. Included studies *(Continued)*

17	Hugkulstone 1990	UK	33	66	73	-	70	-	Within-person
18	Kaplovitz 2016	USA	37	37	70	-	65	28	One eye per person
19	Katz 2012	USA	69	127	-	-	59	-	Clustered
20	Kent 2013	Canada	60	76	73	-	66	-	Clustered
21	KiGIG 2021	Tanzania	201	382	66	-	41	100%	Clustered
22	LIGHT 2019	UK	718	1235	63	-	45	20	Clustered
23	Lai 2004	China	32	64	52	-	55	0	Within-person
24	Liu 2012	Canada	42	42	50	29 to 60	31	-	One eye per person
25	Mansouri 2016	Switzerland	29	58	54	23 to 73	28	14	Within-person
26	Moorfields PTT 1994	UK	168	168	63	-	-	-	One eye per person
27	Moriarty 1988	Jamaica	30	48	62	27 to 77	47	100	Clustered
28	Nagar 2005	UK	167	167	63	22 to 90	64	22	One eye per person
29	Ozen 2020	Turkey	26	52	62	-	54	-	Within-person
30	Rosenfeld 2012	Israel	52	52	72	-	52	-	One eye per person
31	Rouhiainen 1988	Finland	100	120	71	51 to 87	59	-	Clustered

Table 1. Included studies *(Continued)*

32	Sherwood 1987	UK	25	50	73	56 to 90	-	-	Within-person
33	Smith 1984	USA	100	100	67	-	-	11	One eye per person
34	Tang 2011	China	74	74	53	32 to 79	57	-	One eye per person
35	Tufan 2017	Turkey	40	80	54	-	52	-	Within-person
36	Watson 1984	UK	61	95	70	38 to 86	57	-	Clustered
37	Wong 2021	China (Hong Kong)	132	132	62	-	49		One eye per person
38	Yong 2020	Malaysia	17	17	68	54 to 81	47	70% Chinese, 30% Malay	One eye per person
39	Zhang 2015	China	45	67	45	18 to 72	13	0	Clustered
40	Zhang 2016	China	52	52	45	-	-	-	One eye per person
Total			4028	5613	Median: 67 Min: 45 Max: 75	Overall range: 18 to 92 years	Median: 52 Min: 13 Max: 70		

Table 2. Studies comparing laser trabeculoplasty with medication

	Study name	Participants	Type of laser	Comparison	Definition of uncontrolled IOP
1	Bergea 1992	OAG, newly diagnosed	ALT	Pilocarpine 4%	IOP > 26 mmHg or clinically evident visual field decay
2	Gandolfi 2005	POAG, newly diagnosed	ALT	Timolol 0.5%	22 mmHg or greater
3	Glaucoma Initial Treatment Study 2020	POAG or PXF, newly diagnosed	SLT	Prostaglandin analogue eye drop (latanoprost 0.005%, travoprost 0.004%, bimatoprost 0.03% or tafluprost 0.0015%). If the IOP was not sufficiently well-controlled, a stepped regimen of topical medications was followed which included the addition of beta-adrenergic antagonists, alpha agonists and carbonic anhydrase inhibitors	Less than or equal to 10% IOP reduction since baseline
4	GLT 1990	POAG, newly diagnosed	ALT	Timolol 0.5% Step 1: 0.5% timolol, twice a day Step 2: 0.1% dipivefrin, twice a day Step 3: Low-dose pilocarpine, four times a day Step 4: High-dose pilocarpine, four times a day Step 5: 0.5% timolol, twice a day with high dose pilocarpine, four times a day Step 6: 0.1% dipivefrin, twice a day with high dose pilocarpine, four times a day Step 7: Release from stepped regimen; treatment at discretion of GLT ophthalmologist	22 mmHg or more
5	Katz 2012	OAG or OHT, newly diagnosed	SLT	timolol or betaxolol Step 3: Brimonidine Step 4: Dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol	Target IOP was determined using the Collaborative Initial Glaucoma Treatment Study formula.
6	KiGIG 2021	OAG or OHT	SLT	Timolol 0.5%	IOP below or equal to target pressure according to glaucoma severity

Table 2. Studies comparing laser trabeculoplasty with medication *(Continued)*

7	Lai 2004	POAG or OHT, newly diagnosed	SLT	β-blocker, pilocarpine, dorzolamide and latanoprost either as monotherapy or in combination	> 21 mmHg on maximal therapy
8	LIGHT 2019	OAG or OHT, newly diagnosed	SLT followed by topical medication as required	Mainstream topical IOP-lowering medication Medication classes for first-, second- or third-line treatment as per NICE1 European Glaucoma Society guidance: first-line: prostaglandin analogue second-line: beta-blocker (alone or in combination with prostaglandin analogue combination) third- or fourth-line: topical carbonic anhydrase inhibitor or alpha-adrenoceptor agonist.	Not defined
9	Moorfields PTT 1994	OAG but unclear if newly diagnosed	ALT	Pilocarpine and/or a sympathomimetic and/or timolol as initial therapy, increasing to maximum-tolerated medical therapy which could require up to three topical medications and a carbonic anhydrase inhibitor	22 mmHg or greater
10	Moriarty 1988	POAG, on maximum medication	ALT and medication	Pilocarpine 4% and acetazolamide 250mg four times a day. Four participants used timolol 0.5%.	22 mmHg or greater
11	Nagar 2005	OAG or OHT newly diagnosed or controlled on medical therapy	SLT	Latanaprost	Not defined
12	Sherwood 1987	POAG, on maximum medication	ALT	Maximum medical therapy (not specified)	Drop of IOP of less than 20% or IOP reading 22mmHg or greater
13	Tufan 2017	POAG	SLT	Fixed combinations: timolol maleate 0.5%, bimatoprost 0.03%, travoprost 0.004%, and latanoprost 0.005%, or timolol maleate 0.5%, dorzolamide hydrochloride 2%, brinzolamide 1%, and brimonidine tartrate 0.2%	Not defined
14	Yong 2020	POAG, uncontrolled	SLT	Current medications. Quote "Patients in the MED group were advised to step-up their topical anti-glaucoma medications by adding another topical anti-glaucoma medication group until achieving target IOP. The step-up regimen was following the sequence of adding first prostaglandin group, followed by β-blocker, α2-agonist, and carbonic anhydrase inhibitor."	Not defined

ALT: argon laser trabeculoplasty
GLT: Glaucoma Laser Trial
IOP: intraocular pressure
MED: medication
OAG: primary or secondary open-angle glaucoma
OHT: ocular hypertension
POAG: primary open-angle glaucoma
PXF: pseudoexfoliation glaucoma
SLT: selective laser trabeculoplasty

Table 3. Studies comparing laser trabeculoplasty with trabeculectomy

	Study name	Participants	Type of laser	Trabeculectomy	Definition of uncontrolled IOP
1	AGIS 2001	OAG	Argon	Trabeculectomy	Participant met criteria for a further glaucoma intervention.
2	Moorfields PTT 1994	OAG but unclear if newly diagnosed	Argon	Trabeculectomy	22 mmHg or more
3	Watson 1984	OAG	Argon	Standard technique with a fornix based flap	Continuous IOP only

IOP: intraocular pressure
OAG: primary or secondary open-angle glaucoma
POAG: primary open-angle glaucoma

Table 4. Studies comparing different lasers

	Study name	Participants	Type of laser	Type of laser	Definition of uncontrolled IOP
1	Abramowitz 2018	uncontrolled OAG	MLT	SLT	On maximally tolerated medical therapy with the need for additional IOP lowering. Proportion success defined as >= 3 mmHg IOP decrease or >= 20.0% IOP decrease from baseline
2	Babighian 2010	POAG	Excimer	SLT	IOP less than 20% compared with baseline values or needing to increase the number of glaucoma medications from pretreatment level
3	Blyth 1999	POAG, uncontrolled on maximum medical dose	Diode	ALT	22 mmHg or more
4	Brancato 1991	POAG, on maximum tolerated medical therapy	Diode	ALT	IOP less than 20% compared with baseline values or needing to increase the number of glaucoma medications from pretreatment level

Table 4. Studies comparing different lasers *(Continued)*

5	Chung 1998	OAG, on maximum tolerated medical therapy	Diode	ALT	Need for trabeculectomy
6	Damji 2006	OAG, uncontrolled on maximum medical therapy	SLT	ALT	Less than 20% IOP reduction
7	Goldenfeld 2009	OAG, uncontrolled IOP	Titanium-sapphire	ALT	Success: reduction in IOP to 18 mm Hg or less, or by 30%
8	Kaplovitz 2016	Primary OAG or OHT	Titanium-sapphire	SLT	Success: IOP < 21 mm Hg with > 20% decrease in IOP as compared with baseline without the need for further glaucoma procedures
9	Kent 2013	OAG or OHT due to pseudoexfoliation syndrome, medically uncontrolled IOP	SLT	ALT	Success/failure not defined
10	Liu 2012	OAG uncontrolled on topical medication	SLT	ALT	"A complete success was defined as sustaining an IOP decrease from a baseline of more than 20% or of 3 mm Hg or greater, without undergoing further laser or surgery."
11	Mansouri 2016	OAG, uncontrolled on topical medication	Pattern scanning	SLT	< 20% decrease in IOP
12	Rosenfeld 2012	POAG, pseudoexfoliation glaucoma, pigmentary glaucoma, or ocular hypertension (OHT), uncontrolled on topical medication	SLT	ALT	decrease of < 15% in IOP from baseline
13	Wong 2021	POAG and OHT recently diagnosed	Pattern scanning	SLT	< 20% decrease in IOP

ALT: argon laser trabeculoplasty
IOP: intraocular pressure
MLT: micropulse laser trabeculoplasty
OAG: primary or secondary open-angle glaucoma
OHT: ocular hypertension
POAG: primary open-angle glaucoma
SLT: selective laser trabeculoplasty

Table 5. Studies comparing modifications of laser trabeculoplasty technique or regimens

	Study	Type of laser	Technique	Participants	Definition of uncontrolled IOP
1	Elsas 1989	ALT	180° x 360°	Newly diagnosed OAG	IOP < 21 mmHg, VF deterioration

Table 5. Studies comparing modifications of laser trabeculoplasty technique or regimens *(Continued)*

2	Geffen 2017	SLT	Transcleral x conventional	POAG and exfoliation uncontrolled on medication	IOP decrease < 15%
3	Grayson 1993	ALT	180° x 360°	POAG and exfoliation uncontrolled on medication	Need of further intervention
4	Grayson 1994	ALT	superior x inferior	POAG and exfoliation uncontrolled on medication	Need of further intervention
5	Hugkulstone 1990	ALT	0.1 sec x 0.2 sec	POAG, pigmentary glaucoma and exfoliation uncontrolled on medication	Continuous IOP
6	Ozen 2020	SLT	180° x 360°	Bilateral POAG uncontrolled on medication	IOP decrease < 20%
7	Rouhiainen 1988	ALT	Different power levels (500 mW x 800 mW)	POAG and exfoliation uncontrolled on medication	IOP ≥ 21 mmHg
8	Smith 1984	ALT	Continuous-wave laser (green) x blue-green continuous-wave laser	POAG uncontrolled on medication	Need of further intervention
9	Tang 2011	SLT	Low energy x normal energy		
10	Zhang 2015	SLT	Low energy x normal energy	POAG uncontrolled on medication	IOP changes, changes in types of medication use, intervention success, daytime IOP fluctuation and complications

ALT: argon laser trabeculoplasty
IOP: intraocular pressure
mW: milliwatts
OAG: primary or secondary open-angle glaucoma
OHT: ocular hypertension
POAG: primary open-angle glaucoma
SLT: selective laser trabeculoplasty
VF: visual field

Table 6. Studies comparing different lasers: failure to control IOP

RR (95% CI)	Intervention						
	Diode (3 studies)	**Selective (4 studies)**	**Titani-um-sapphire (1 study)**	**Excimer (1 study)**	**Pattern scanning (2 studies)**	**Titanium-sapphire (1 study)**	**Micropulse (1 study)**
	Comparator: argon				**Comparator: selective**		
6 months	0.85 (0.16 to 4.64) (1 study, n=50) Chung 1998	1.00 (0.44 to 2.29) (1 study, n=63) Kent 2013			63% of the eyes were considered failures in PLT group and 74% in SLT group (p=0.09) (n=58) Mansouri 2016.		Proportion success de-fined as >= 3 mmHg IOP decrease or >= 20.0% IOP decrease from baseline: MLT 29.6% vs SLT 36.0% (P = 0.77). (n=38) Abramowitz 2018
12 months	0.73 (0.26 to 2.11) (2 studies, n=70) Brancato 1991; Chung 1998	1.25 (0.84 to 1.84) (1 study, n = 153) Damji 2006 0.39 (0.15 to 0.97) (1 study, n=33) Rosenfeld 2012	There was a reduction of 8.3 mmHg (SD 2.7) in TLT group (n = 18) and 6.5 mmHg (SD 4.3) in the ALT group (n = 17). Goldenfeld 2009		Failure rate of 74.6% in SLT group and 84.6% in PLT group (p=0.155) (n=132) Wong 2021	Failure rates of 56% in TLT group and 39% in SLT group (p=0.11) (n=37). Kaplovitz 2016	
24 months	0.82 (0.35 to 1.94) (2 studies, n=90) Blyth 1999; Chung 1998	1.01 (0.76 to 1.33) (2 studies, n=97) Damji 2006; Liu 2012		The cumula-tive proba-bility of com-plete success was 53% for excimer laser vs 40% for SLT (p=0.35) (n=30)		In Kaplovitz 2016, at two years, rates in-creased to 78% in TLT and 54% in SLT (p=0.11) (n=37) Kaplovitz 2016	Proportion success at 12 months: MLT 37.0%, SLT 36.0% (P = 1.0) (n=38) Abramowitz 2018

Table 6. Studies comparing different lasers: failure to control IOP *(Continued)*

Babighian 2010	

ALT: argon laser trabeculoplasty
IOP: intraocular pressure
MLT: micropulse laser trabeculoplasty
NR: not reported
PLT: pattern-scanning laser trabeculoplasty
SD: standard deviation
SLT: selective laser trabeculoplasty
TLT: titanium-sapphire laser trabeculoplasty

Table 7. Studies comparing different lasers: adverse effects

	Study name	Argon laser	Selective laser	Other lasers	
1	Abramowitz 2018		*	Micropulse	"The MLT patients on average experienced less pain both during and after the treatment (P = 0.005)." "An IOP spike was defined as an elevation of.5 mmHg from the pre-treatment mean. Incidence of post-procedure spikes were 5.3% and 12.9% in the MLT and SLT groups, respectively, but this difference was not statistically significant (P = 0.4)."
2	Babighian 2010		*	Excimer	There was no difference in IOP spikes between the two groups of treatment (2/15 eyes in ELT versus 3/15 eyes in SLT group (RR 0.67, 95% CI 0.13 to 3.44).
3	Blyth 1999	*		Diode	IOP spikes: two eyes in each group had an increase of more than 5 mmHg after two hours postoperatively. PAS formation: Four eyes of the argon group developed PAS (RR 0.54; 95% CI 0.17 to 1.76).
4	Brancato 1991	*		Diode	IOP spikes: IOP after trabeculoplasty within two hours postoperatively and did not observe any IOP elevation greater than 5 mmHg in either group. PAS formation: no goniosynechiae formation was observed.
5	Chung 1998	*		Diode	IOP spikes: an increase in IOP from baseline of 2 to 6 mmHg in the first hour postoperatively in two eyes of the diode group and five eyes in the argon laser group. After 24 hours from the laser procedures in both groups, no eye experienced elevated IOP greater than 3 mmHg from baseline. PAS formation: Chung 1998: some eyes presented at three months with synechiae.
6	Damji 2006;	*	*		Clinical examination for flare and cells was assessed one hour post-laser and graded on a scale from 0 (no reaction) to 4 (very marked reaction). There was no difference observed in mean score of flare in anterior chamber between the eyes treated with SLT (1.00, SD 0.6) and eyes treated with laser trabeculoplasty (0.8 SD 0.6).
7	Goldenfeld 2009	*		Titanium-sapphire	Two patients (1 in each group) had trabeculectomy. Three cases of peripheral anterior synechiae in the ALT group but none in the TLT group.

Table 7. Studies comparing different lasers: adverse effects *(Continued)*

8	Kaplovitz 2016		*	Titanium-sapphire	IOP spikes: Three participants in each group experienced spikes > 10 mmHg, but two participants (11%) in TLT maintained an uncontrolled IOP and needed filtering surgeries.
9	Kent 2013	*	*		No IOP spikes in either group (pressure difference of 6 or more after 1 hour)
10	Liu 2012	*	*		None reported
11	Mansouri 2016		*	Pattern scanning	IOP spikes: One patient in SLT group, had a spike of 15 mmHG, and needed a filtering surgery.
12	Rosenfeld 2012	*	*		
13	Wong 2021		*	Pattern scanning	One patient in PLT group developed a protracted uveitis, that resolved with topical steroids after 6 months. One subject in SLT and one in PLT group had IOP spike in the first day (> 20% IOP). One patient in PLT developed cataracts and one in SLT developed angle closure, and needed an iridotomy.

ALT: argon laser trabeculoplasty
ELT: excimer laser trabeculoplasty
IOP: intraocular pressure
MLT: micropulse laser trabeculoplasty
OAG: primary or secondary open-angle glaucoma
OHT: ocular hypertension
PLT: pattern scanning laser trabeculoplasty
POAG primary open-angle glaucoma
SD: standard deviation
SLT: selective laser trabeculoplasty
TLT: titanium-sapphire laser trabeculoplasty

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Glaucoma, Open-Angle] explode all trees
#2 MeSH descriptor: [Intraocular Pressure] explode all trees
#3 MeSH descriptor: [Ocular Hypertension] explode all trees
#4 OAG or POAG or IOP or OHT
#5 simple near/3 glaucoma*
#6 open near/2 angle near/2 glaucoma*
#7 chronic near/2 glaucoma*
#8 secondary near/2 glaucoma*
#9 low near/2 tension near/2 glaucoma*
#10 low near/2 pressure near/2 glaucoma*
#11 normal near/2 tension near/2 glaucoma*
#12 normal near/2 pressure near/2 glaucoma*
#13 pigment near/2 glaucoma*
#14 MeSH descriptor: [Exfoliation Syndrome] this term only
#15 exfoliat* near/2 syndrome*

#16 exfoliat* near/2 glaucoma*
#17 pseudoexfoliat* near/2 syndrome*
#18 pseudoexfoliat* near/2 glaucoma*
#19 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18
#20 MeSH descriptor: [Trabeculectomy] explode all trees
#21 argon laser* or ALT
#22 trabeculoplast*
#23 SLT or PNT or DLT
#24 #20 or #21 or #22 or #23
#25#19 and #24

Appendix 2. MEDLINE Ovid search

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. exp glaucoma open angle/
14. exp intraocular pressure/
15. ocular hypertension/
16. (OAG or POAG or IOP or OHT).tw.
17. (simple$ adj3 glaucoma$).tw.
18. (open adj2 angle adj2 glaucoma$).tw.
19. (primary adj2 glaucoma$).tw.
20. (chronic adj2 glaucoma$).tw.
21. (secondary adj2 glaucoma$).tw.
22. (low adj2 tension adj2 glaucoma$).tw.
23. (low adj2 pressure adj2 glaucoma$).tw.
24. (normal adj2 tension adj2 glaucoma$).tw.
25. (normal adj2 pressure adj2 glaucoma$).tw.
26. (pigment$ adj2 glaucoma$).tw.
27. exfoliation syndrome/
28. (exfoliat$ adj2 syndrome$).tw.
29. (exfoliat$ adj2 glaucoma$).tw.
30. (pseudoexfoliat$ adj2 syndrome$).tw.
31. (pseudoexfoliat$ adj2 glaucoma$).tw.
32. or/13-31
33. exp trabeculectomy/
34. (argon laser$ or ALT).tw.
35. trabeculoplast$.tw.
36. (SLT or PNT or DLT).tw.
37. or/33-36
38. 32 and 37
39. 12 and 38

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville 2006.

Appendix 3. Embase Ovid search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5

7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin$ adj3 trial$).tw.
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. open angle glaucoma/
34. intraocular pressure/
35. intraocular hypertension/
36. (OAG or POAG or IOP or OHT).tw.
37. (open adj2 angle adj2 glaucoma$).tw.
38. (primary adj2 glaucoma$).tw.
39. (chronic adj2 glaucoma$).tw.
40. (secondary adj2 glaucoma$).tw.
41. (low adj2 tension adj2 glaucoma$).tw.
42. (low adj2 pressure adj2 glaucoma$).tw.
43. (normal adj2 tension adj2 glaucoma$).tw.
44. (normal adj2 pressure adj2 glaucoma$).tw.
45. (pigment$ adj2 glaucoma$).tw.
46. exfoliation syndrome/
47. (exfoliat$ adj2 syndrome$).tw.
48. (exfoliat$ adj2 glaucoma$).tw.
49. (pseudoexfoliat$ adj2 syndrome$).tw.
50. (pseudoexfoliat$ adj2 glaucoma$).tw.
51. or/33-50
52. trabeculoplasty/
53. (argon laser$ or ALT).tw.
54. trabeculoplast$.tw.
55. (SLT or PNT or DLT).tw.
56. or/52-55
57. 51 and 56
58. 32 and 57

Appendix 4. LILACS search strategy

(tw:(glaucoma OR "ocular hypertension" OR "intraocular pressure" OR IOP)) AND (tw:(trabeculoplasty or ALT or SLT or PNT or DLT or Argon laser))

Appendix 5. ISRCTN search strategy

(glaucoma OR "ocular hypertension" OR "intraocular pressure" OR IOP) AND (trabeculoplasty OR ALT OR SLT OR PNT OR DLT OR Argon laser)

Appendix 6. ClinicalTrials.gov search strategy

(glaucoma OR ocular hypertension OR intraocular pressure OR IOP) AND (trabeculoplasty OR ALT OR SLT OR PNT OR DLT OR Argon laser)

Appendix 7. WHO ICTRP search strategy

(glaucoma OR ocular hypertension OR intraocular pressure OR IOP) = Condition AND (trabeculoplasty OR ALT OR SLT OR PNT OR DLT OR Argon laser) = Intervention

Appendix 8. Risk of bias assessments

Sequence generation (selection bias)

- **Low risk of bias:** computer-generated, random number table
- **Unclear risk of bias:** not clearly described or not reported
- **High risk of bias:** non-random process e.g. alternation (these trials were excluded)

Allocation concealment (selection bias)

- **Low risk of bias**: data co-ordination center, opaque sealed envelope
- **Unclear risk of bias:** low-risk (random) sequence generation but not described clearly how this was assigned/stored
- **High risk of bias:** investigator was involved in sequence generation and/or assignment

Masking (blinding) of participants and study personnel (performance bias)

- **Low risk of bias:** masking reported
- **Unclear risk of bias:** masking not reported or not reported clearly (e.g. "double blinded" without explicit description of masking) but treatments similar
- **High risk of bias**: no masking or masking not reported clearly (e.g. "double blinded" without explicit description of masking) and treatments different (e.g. intervention versus observation)

Masking of outcome assessors (detection bias)

- **Low risk of bias:** masking of outcome assessors reported
- **Unclear risk of bias**: masking of outcome assessors not reported or not reported clearly (e.g. "double blinded" without explicit description of masking) but treatments similar
- **High risk of bias**: no masking of outcome assessors or masking not reported clearly (e.g. "double blinded" without explicit description of masking) and treatments different (eg intervention versus observation)

Incomplete outcome data (attrition bias)

- **Low risk of bias:** missing data less than 20% and no obvious reason why loss to follow-up should be related to outcome
- **Unclear risk of bias**: not reported or ≥20% loss to follow-up but follow-up similar in both groups
- **High risk of bias**: loss to follow-up different in different groups or follow-up clearly related to outcome

Selective outcome reporting (reporting bias)

- **Low risk of bias**: all outcomes reported as per protocol or trial registry entry
- **Unclear risk of bias**: protocol and trial registry not available for comparison
- **High risk of bias**: reported primary/secondary outcomes different from protocol/trial registry or outcomes mentioned in methods section not reported in results

WHAT'S NEW

Date	Event	Description
30 May 2022	New search has been performed	Searches update and new studies added
30 May 2022	New citation required but conclusions have not changed	Cochrane methods updated, risk of bias tables completed and Summary of findings tables generated

HISTORY

Protocol first published: Issue 4, 2002
Review first published: Issue 4, 2007

Date	Event	Description
5 February 2010	New search has been performed	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Coordinating the review: CRM
Data collection for the review: CRM
Screening search results: DB, ML
Screening retrieved papers against inclusion criteria: CRM, AP, DB, ML, JE
Appraising quality of papers: CRM, AP, DB, ML, JE
Extracting data from papers: CRM, AP, DB, ML
Writing to authors of papers for additional information: CRM
Data management for the review: CRM
Entering data into RevMan: CRM, JE
Writing the review: CRM, ML, RW, JE

DECLARATIONS OF INTEREST

None known.

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External sources

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- Queen's University Belfast, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We updated the methods for the current update including risk of bias tables and summary of fIndings tables.

We included people with ocular hypertension in the review (excluded in the protocol and earlier versions of this review) because laser trabeculoplasty is now used in people with ocular hypertension. We excluded people previously treated with laser as we felt that the effects of laser treatment may be different in this group and it would be better addressed in a different review.

We did not consider the outcome "Necessity of adding or changing the medical therapeutic regimen in consequence of uncontrolled IOP and visual field or optic disc damage progression" as planned in our protocol.

We planned to do the following subgroup analyses but only there were only data for the first analysis.

- different technologies used in the intervention (argon laser, Nd:YAG laser, etc);
- where laser treatment was provided in conjunction with ocular hypotensive drugs;
- ethnic characteristics of people participating in the trials.

Due to few studies contributing data to each comparison, we used a fixed-effect model and did not do planned sensitivity analyses comparing fixed- and random-effects models. We also did not assess the impact of studies at high risk of bias, again due to few studies contributing data to each comparison.

INDEX TERMS

Medical Subject Headings (MeSH)

Argon [therapeutic use]; *Glaucoma [surgery]; *Glaucoma, Open-Angle [drug therapy] [surgery]; *Ocular Hypertension [etiology] [surgery]; *Optic Nerve Diseases [etiology] [surgery]; *Trabeculectomy [adverse effects] [methods]

MeSH check words

Humans