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## Minimally invasive trabecular meshwork surgery for open-angle glaucoma (Protocol)

Hu K, Vemulapalli K, Gandhewar R, Shah A, Virgili G, Bunce C, Gazzard G

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[Intervention Protocol]

# Minimally invasive trabecular meshwork surgery for open-angle glaucoma

Kuang Hu<sup>1,2</sup>, Kalyan Vemulapalli<sup>3</sup>, Rishikesh Gandhewar<sup>3</sup>, Anupa Shah<sup>4</sup>, Gianni Virgili<sup>4,5</sup>, Catey Bunce<sup>6</sup>, Gus Gazzard<sup>1</sup>

<sup>1</sup>Glaucoma Service, Moorfields Eye Hospital NHS Foundation Trust, London, UK. <sup>2</sup>UCL Institute of Ophthalmology, London, UK. <sup>3</sup>Imperial College School of Medicine, Imperial College London, London, UK. <sup>4</sup>Cochrane Eyes and Vision, Centre for Public Health, Queen's University Belfast, Belfast, UK. <sup>5</sup>Department of Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence, Florence, Italy. <sup>6</sup>The Royal Marsden NHS Foundation Trust, London, UK

**Contact:** Kuang Hu, [kuang.hu1@nhs.net](mailto:kuang.hu1@nhs.net).

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## ABSTRACT

### Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of minimally invasive trabecular meshwork surgery in comparison to medical, laser, or surgical treatment (including other MIGS techniques) in people with open-angle glaucoma.

## BACKGROUND

### Description of the condition

Glaucoma is a chronic progressive optic neuropathy affecting 3.5% of people between the ages of 40 and 80. It is the leading cause of irreversible blindness, affecting 76 million people globally in 2014; this is expected to increase to 111.8 million people by 2040 (Tham 2014).

Open-angle glaucoma (OAG) is the most common type, with an estimated global prevalence of 2.4% that equates to an affected population of nearly 69 million people (Zhang 2021). In one large population cohort, one in six people with OAG became bilaterally blind (Peters 2013). The only proven way to prevent vision loss is to reduce the pressure inside the eye (intraocular pressure (IOP)) over the long term (AGIS 2000; CNTG Study Group 1998; Heijl 2002; Kass 2002). OAG may be classified as primary when there is no identifiable cause, or secondary when there is a known cause. Approaches to reducing IOP include medical therapy, laser treatments, and surgery.

As commercially available eye drop preparations have a short-lasting effect, medical therapy requires eye drops to be instilled one or more times daily for life. Adherence is very poor, even if use is monitored (Friedman 2009; Okeke 2009). Conventional surgical techniques such as trabeculectomy are associated with significant risks, with more than 40% of patients developing perioperative complications (Kirwan 2013; Lichter 2001). Between 7% and 18% of cases have been shown to require reoperation (Gedde 2012; Kirwan 2013), with one recent single centre study reporting a rate of 23% (Cardakli 2020). These techniques are, therefore, often reserved for disease that is progressing despite other treatments (King 2013). Other treatments such as selective laser trabeculoplasty (Gazzard 2019), and new minimally invasive surgical techniques, are alternatives to conventional surgery or eye drop preparations.

### Description of the intervention

A number of minimally invasive surgical techniques have been developed with the aim of achieving long-term reduction of IOP, with a better safety profile than conventional surgery (Francis 2011). Since the inception of our previous Cochrane Review on ab interno trabecular bypass surgery with Trabectome (Hu 2021), a new range of minimally invasive surgical techniques has emerged to lower IOP by acting on the trabecular meshwork, either directly or indirectly. In this review, we expand our scope to include all minimally invasive procedures that act on the trabecular meshwork in open-angle glaucoma.

Some of the procedures that we anticipate being included are:

- Trabectome: Trabectome uses a bipolar 550kHz electrode to ablate the trabecular meshwork over 180°. The device utilises ionisation and disintegration, allowing any heat dissipation to be well confined (Bussel 2015).
- Gonioscopy-assisted Transluminal Trabeculotomy (GATT): the GATT procedure is a modification of the traditional trabeculotomy that involves cannulating the entire Schlemm's canal, allowing access to the entire drainage system (Grover 2014).
- Kahook Dual Blade: this is designed to allow for a near-complete removal of the trabecular meshwork, compared to

other techniques where residual trabecular meshwork may remain. Minimising these residues may result in less fibrosis and therefore better long-term outcomes compared to other procedures (Seibold 2013).

- OMNI® Surgical System: this allows surgeons to perform an ab interno (from the inside) canaloplasty followed by a trabeculotomy using a single handheld surgical system, allowing for reduction in the intraocular pressure. Therefore, a single device can be used to address multiple points of resistance in the conventional outflow pathway (Vold 2021).
- iTrack: this combines catheterisation and pressurised viscodilation of Schlemm's canal, which separates compressed trabecular planes within the trabecular meshwork (Körber 2018).
- Other variations of ab interno trabecular bypass surgery: e.g. microhook ab interno trabeculotomy (Tanito 2018), needle trabecular meshwork incisions.

Some of these interventions are often combined with phacoemulsification (cataract surgery), a surgery where the natural lens of the eye is removed, due to clouding and subsequent deterioration of vision, and replaced by an artificial one. Phacoemulsification in itself is known to reduce IOP (Mansberger 2012). Therefore, we plan to specifically examine the evidence for each of the treatments in people who have had concomitant phacoemulsification compared to those who have not.

### How the intervention might work

One method to decrease the IOP would be to increase the outflow of aqueous humour (the clear fluid between the lens and cornea). Aqueous humour drains through several tissues, including the trabecular meshwork (which is where the largest resistance to flow occurs) and Schlemm's canal (Overby 2009).

As such, methods to increase the outflow can include bypassing the trabecular meshwork using ab interno trabecular bypass surgery. Dilating Schlemm's canal causes compressed trabecular planes within the trabecular meshwork to be separated, which may contribute to increased aqueous outflow. The procedures introduced in [Description of the intervention](#) are thought to work as follows:

- Trabectome: Trabectome is designed to selectively ablate a portion of the trabecular meshwork, enabling aqueous humour to have direct access to Schlemm's canal and thence the collector channels (Francis 2006). This is intended to promote aqueous outflow, thereby reducing IOP.
- GATT: after an incision through the trabecular meshwork via the cornea, Schlemm's canal is cannulated 360°. Schlemm's canal is unroofed, allowing the trabecular meshwork to be entirely bypassed (Grover 2014).
- Kahook Dual Blade: the Kahook Dual Blade is designed specifically for a more complete removal of the trabecular meshwork. It has a sharp tip to allow for entry of the blade through the trabecular meshwork to Schlemm's canal. The device has a ramp allowing for gentle stretching of the trabecular meshwork. As the blade advances, parallel incisions are made into the trabecular meshwork. This results in a strip of the trabecular meshwork being excised, allowing for a near-complete removal of the trabecular meshwork (Seibold 2013).

- OMNI surgical system: this allows for Schlemm's canal to be microcatheterised circumferentially from a single corneal incision. This can then be followed by a trabeculotomy using the same device (Vold 2021).
- iTrack: by catheterisation and pressurized viscodilation of Schlemm's canal, compressed trabecular planes within the trabecular meshwork are separated and any herniated inner wall tissue is caused to withdraw from the collector channels (Körber 2018).

### Why it is important to do this review

Consultation with people with sight loss or an eye condition and healthcare professionals has identified a need for better treatments for glaucoma (James Lind Alliance 2014). Minimally invasive glaucoma procedures may safely and effectively reduce IOP in the long term, offering another surgical option for people with open-angle glaucoma where medical therapy is ineffective, not tolerated, or not adhered to. A single treatment may also be more acceptable to people than daily and indefinite self-administration of eye drops.

Results of several of these different trabecular meshwork surgeries have been reported. Positive initial results of ab interno trabecular bypass surgery with Trabectome were reported in 2005 (Minckler 2005). There have been 4600 treatments performed between 2004 and 2013 at over 200 centres worldwide (Mosaed 2014; NeoMedix). Results from studies of the Kahook Dual blade (Berdahl 2018; Sieck 2018), the GATT procedure (Grover 2018; Rahmatnejad 2017), the OMNI surgical system (Vold 2021), and iTrack (Körber 2018) also show efficacy in reducing IOP, with positive surgical outcomes.

Therefore, due to the potential benefits of each of these procedures for people with open-angle glaucoma, it is important to evaluate the evidence to determine whether the treatment with each procedure is safe, with minimal complications, and efficacious.

This Cochrane Review supersedes and expands upon the published review on ab interno trabecular bypass surgery with Trabectome for open-angle glaucoma (Hu 2021). It is part of a suite of reviews on minimally invasive glaucoma surgery (MIGS) techniques and devices currently being undertaken by the Cochrane Eyes and Vision MIGS Consortium, which includes Hydrus Schlemm's canal Microstent (Ivantis Inc., Irvine, CA, USA) (Otarola 2017), endoscopic cytophotocoagulation (Endo Optiks, Waltham, MA, USA) (Tóth 2019), XEN Glaucoma Implant (AqueSys Implant, Aliso Viejo, CA, USA) (King 2018), iStent and iStent inject (Glaukos Corporation, Laguna Hills, CA, USA) (Le 2019), and supraciliary microstent surgery (Sandhu 2021).

### OBJECTIVES

To assess the effects of minimally invasive trabecular meshwork surgery in comparison to medical, laser, or surgical treatment (including other MIGS techniques) in people with open-angle glaucoma.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We will include randomised controlled trials (RCTs) only. We will include all study reports published in English (or which have been translated into English), irrespective of their publication status.

We will not include quasi-RCTs (in which allocation is decided by an approximation of randomisation such as allocation by patient ID number). We plan to exclude within-person studies because of the potential for comparator treatments (such as topical beta blockers) or surgical procedures used for one eye to influence the outcome in the other eye (Piltz 2000; Radcliffe 2010).

#### Types of participants

We will include RCTs where participants have open-angle glaucoma of any type, including primary and secondary open-angle glaucoma. We will exclude closed-angle glaucoma. The difference between open-angle and closed-angle glaucoma is that, while both are diseases of increased IOP, closed-angle glaucoma is often due to an obstruction to the outflow of aqueous as a result of a narrow or closed angle between the iris and the cornea. Open-angle glaucoma, on the other hand, is due to an increase in the resistance to flow in the drainage channels of the trabecular meshwork without a reduced angle between the iris and the cornea (Weinreb 2014).

As there are no universally accepted criteria by which glaucoma may be defined, we will permit studies to use their own definitions of glaucoma (provided these are clearly stated). We will also include participants with ocular hypertension, normal-tension glaucoma, or possible glaucoma (suspects for glaucoma). We will not apply restrictions regarding location, setting, or demographic factors. For studies that include only a subset of relevant participants that meet the inclusion criteria, we will include only those eligible participants. Otherwise, we will contact the individuals or organisations responsible for those studies to collect the specific information. If this is unsuccessful, we will exclude these studies.

#### Types of interventions

We will compare trabecular meshwork surgeries (including Trabectome, GATT, Kahook Dual blade, OMNI surgical system, iTrack) to the following:

- laser treatment (selective laser trabeculoplasty or argon laser trabeculoplasty);
- other trabecular meshwork MIGS techniques, such as those listed above;
- MIGS techniques that work on pathways other than the trabecular meshwork;
- conventional glaucoma surgery (trabeculectomy);
- medical therapy, such as IOP-lowering eye drops including prostaglandin analogues, beta-blockers, carbonic anhydrase inhibitors, and sympathomimetics, among others.

We will also include trials in which these devices are combined with phacoemulsification compared to phacoemulsification in combination with other glaucoma surgery or alone.

## Types of outcome measures

We do not plan to use the reporting of particular outcomes as a criterion for eligibility for this review. We will not exclude studies from this review solely on the grounds of an outcome of interest not being reported.

We will report outcomes in the short term (6 to 18 months), medium term (18 to 36 months), and long term (36 months or longer).

### Critical outcomes

- Proportion of participants who are medication-free (not using eye drops) at each time point (short term, medium term, and long term).

Several glaucoma outcome measures have been specified as primary outcomes in other Cochrane Reviews and protocols (Ismail 2015). A recent study classified IOP, visual field, safety, and anatomic outcomes as being highly important to glaucoma experts (Ismail 2016). A panel of patients from the Patient and Public Involvement Group of the National Institute for Health Research (NIHR) Biomedical Research Centre for Ophthalmology identified drop-free disease control as a highly valued outcome (PPIG 2014). We chose a patient-centred critical outcome. In assessing this effect measure, we planned to report how prescribing IOP-lowering eye drops was determined during follow-up. We plan to examine whether the people measuring IOP and those deciding on prescribing IOP-lowering eye drops were masked to the treatment group.

- Rate of visual field progression (decibels (dB)/time) or proportion of participants whose field loss progressed in the follow-up period.

### Important outcomes

- Mean change in IOP, measured using Goldmann applanation tonometry.
- Mean change in number of IOP-lowering drops taken per day.
- Proportion of participants who achieve an IOP of 21 mmHg or less.
- Proportion of participants who achieve an IOP of 17 mmHg or less.
- Proportion of participants who achieve an IOP of 14 mmHg or less.
- Proportion of participants who required further glaucoma surgery, including laser, as recorded by the investigators of the included trial.
- Mean change in health-related quality of life (HRQoL), measured using any scale.

### Adverse effects

Proportion of participants experiencing intra- and postoperative complications, including, but not restricted to, the following:

- loss of visual acuity (more than 2 Snellen lines or more than 0.3 logMAR, according to the method of recording visual acuity; or loss of light perception);
- bleeding, as recorded by the investigators;
- endophthalmitis, as recorded by the investigators;

- IOP spikes (postoperative rise in IOP, measured using Goldmann applanation tonometry, of more than 10 mmHg compared to the previous assessment, including measurements taken during the first postoperative month).

## Search methods for identification of studies

### Electronic searches

The Cochrane Eyes and Vision Information Specialist will conduct systematic searches in the following databases for randomised controlled trials and controlled clinical trials. There will be no restrictions to language or year of publication.

- Cochrane Central Register of Controlled Trials (which contains the Cochrane Eyes and Vision Trials Register) in the Cochrane Library (latest issue) (Appendix 1).
- MEDLINE Ovid (1946 to present) (Appendix 2).
- Embase Ovid (1980 to present) (Appendix 3).
- ISRCTN registry ([www.isrctn.com/editAdvancedSearch](http://www.isrctn.com/editAdvancedSearch)) (Appendix 4).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) (Appendix 5).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) ([www.who.int/ictrp](http://www.who.int/ictrp)) (Appendix 6).

### Searching other resources

We will search the reference lists of included studies for other possible studies, and we will contact any individuals or organisations we believe may have conducted or be conducting relevant RCTs. We will also search the websites of the various manufacturers for any information on forthcoming trials. This includes:

- Trabectome - NeoMedix Inc, Tustin, CA, USA; [www.trabectome.com](http://www.trabectome.com)
- OMNI Surgical Device - Sight Sciences Inc, Menlo Park, CA, USA; [www.sightsciences.com](http://www.sightsciences.com); [www.omnisurgical.com](http://www.omnisurgical.com)
- Kahook Dual Blade - New World Medical, Rancho Cucamonga, CA; [www.newworldmedical.com/kahook-dual-blade](http://www.newworldmedical.com/kahook-dual-blade)
- iTrack - Nova Eye Medical, Kent Town, SA, Australia; [nova-eye.com/physicians/itrack/](http://nova-eye.com/physicians/itrack/)

## Data collection and analysis

### Selection of studies

We will screen the search results in the systematic review software **Covidence**. Two review authors (KV, RG) will independently screen titles and abstracts; if abstracts are not available, we plan to screen full-text articles. Two review authors (KV, RG) will independently assess full-text reports of all potentially eligible studies. In case of disagreement regarding eligibility, a third review author (KH) will arbitrate. We will place any full-text reports that we reject at this stage in the excluded studies table and record a reason for exclusion.

### Data extraction and management

Two review authors (KV, RG) will independently extract study characteristics from reports of each study, as per [Appendix 7](#), and present these in the characteristics of included studies table in RevMan Web ([RevMan Web 2022](#)). Two authors (KV, RG) will

independently extract data for the analyses. The data extraction form in [Appendix 7](#) was previously used in the published Cochrane Review on ab interno trabecular bypass surgery with Trabectome for open-angle glaucoma ([Hu 2021](#)), which this review supersedes.

If data on included studies are missing or unclear, we will contact the individuals or organisations involved to obtain clarification. We intend to collect and use the most detailed numerical data available to facilitate analyses of included studies. We plan to obtain these data from individuals or organisations instead of using less precise methods, such as extracting numeric data from graphs. If this is necessary, two review authors (KV, RG) will independently extract the data.

In any cases where the two authors (KV, RG) are in disagreement with respect to any independent data extraction, a third author (KH) will arbitrate.

### Assessment of risk of bias in included studies

Two review authors (KV, RG) will independently assess the risk of bias in each included trial using the original risk of bias 1 tool in Chapter 8 of the *Cochrane Handbook for Systematic Review of Interventions* ([Higgins 2017](#)). We will assess risk of bias for the following domains: selection bias, performance bias, detection bias, attrition bias, reporting bias and other sources of bias.

Two review authors (KV, RG) will grade each domain as low risk of bias, unclear risk of bias or high risk of bias. If there are any disagreements between the two authors, a third author (KH) will arbitrate.

### Measures of treatment effect

We will report outcomes in the short term (6 to 18 months), medium term (18 to 36 months), and long term (36 months or longer) after randomisation.

There are two critical outcomes to this study. Firstly, for the proportion of participants who were medication-free, we will use the risk ratio (RR) as the treatment effect measure. Secondly, for the rate of visual field progression, the mean difference (MD) will be the treatment effect measure. Where studies report the proportion of participants whose field loss progressed in the follow-up period, we will use the odds ratio (OR) as the treatment effect measure.

We will report MD in IOP and MD in number of IOP-lowering drops taken per day. We will further report the proportion of participants achieving various target IOPs or requiring further glaucoma surgery using ORs as the treatment effect measure. We will also report HRQoL outcomes as differences in means or ORs for continuous and binary data, respectively. We will report secondary safety outcomes as ORs.

### Unit of analysis issues

We will note whether the studies included one or two eyes from each participant and whether randomisation had been conducted at the level of the participant or the eye. There is a potential for medical treatments, such as topical beta blockers, used for one eye to influence the outcome in the other eye ([Piltz 2000](#)). Surgery to lower IOP in one eye may also affect the IOP of the other eye ([Radcliffe 2010](#)). We therefore plan to exclude studies that adopted a paired-eye design.

If we identify a multiple-arm study, we may include it if the study design ensured that an independent analysis of each treatment group occurred.

### Dealing with missing data

We plan to minimise missing outcome data by contacting individuals and organisations to try to obtain them. If the data are unavailable, but the level of missing data in each group and reasons for missing data in each group are similar, we may simply analyse available case data if an intention-to-treat (ITT) analysis was not performed. If the authors conducted their own ITT analysis despite missing data, we plan to document whether they provided any justification for the method they used to deal with missing data, and whether they compared their ITT result with an available case result.

### Assessment of heterogeneity

We plan to assess heterogeneity between trials by careful examination of the study reports, assessing forest plots, and an examination of the  $I^2$  value with its 95% confidence interval. We will consider  $I^2$  values greater than 50% as indicating substantial heterogeneity.

### Assessment of reporting biases

We plan to use a funnel plot to assess the risk of publication bias if we include more than 10 trials in an analysis.

### Data synthesis

We plan to undertake a meta-analysis where data appear to be clinically, methodologically, and statistically homogeneous. We will check that participants, interventions, comparators, and outcomes are sufficiently similar to give a clinically meaningful result, and that our  $I^2$  value result indicated little inconsistency (that is,  $I^2 < 50%$ ).  $I^2$  values greater than 50% are indicative of substantial heterogeneity and are, therefore, suggestive that meta-analysis might not be wise. However, we would give consideration to the consistency of the effect estimates; if all estimates are in the same direction we may meta-analyse even where heterogeneity is evident, but will comment on this. We will use a random-effects model unless there are fewer than three eligible studies, in which case we will use a fixed-effect model. In the event that we cannot carry out a meta-analysis due to heterogeneity, we will perform a narrative summary of the data following guidance in Chapter 12 of the *Cochrane Handbook for Systematic Review of Interventions* ([McKenzie 2021](#)).

### Subgroup analysis and investigation of heterogeneity

We do not plan to conduct subgroup analysis.

### Sensitivity analysis

We plan to assess the impact of including studies at high risk of bias by removing these from the sensitivity analysis and comparing the result with the primary analysis.

### Summary of findings and assessment of the certainty of the evidence

We will prepare a table to summarise the findings of the review, including the assessment of the certainty of evidence for all outcomes using the GRADE approach outlined in Chapter 14 of

the *Cochrane Handbook for Systematic Review of Interventions* (Schünemann 2022). For this, two authors (KV and RG) will independently utilise the five GRADE considerations: risk of bias, consistency of effect, imprecision, indirectness and publication bias.

We will report on the following outcomes at short-term follow-up (6 to 18 months) in a summary of findings table for each comparison listed in the [Types of interventions](#):

- proportion of participants who were medication-free (not using eye drops);
- rate of visual field progression (dB/time) or, secondarily, proportion of participants whose field loss progressed in the follow-up period;
- mean change in IOP, measured using Goldmann applanation tonometry;
- mean change in number of IOP-lowering drops taken per day;

- proportion of participants who required further glaucoma surgery, including laser;
- mean change in HRQoL;
- proportion of participants experiencing intra- and postoperative complications (any time point).

We will pool the various types of trabecular meshwork surgery in a single summary of findings table. However, in the case that there is strong evidence, ideally in the form of a randomised control trial, to suggest that different types of trabecular meshwork surgery yield different results, we will have separate tables.

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**APPENDICES**
**Appendix 1. CENTRAL search strategy**

- #1 MeSH descriptor: [Glaucoma, Open-Angle] explode all trees
- #2 MeSH descriptor: [Intraocular Pressure] this term only
- #3 MeSH descriptor: [Ocular Hypertension] this term only
- #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 ab interno trabeculectomy or trabeculectomy ab interno
- #21 ab interno trabeculotomy or trabeculotomy ab interno
- #22 ab interno goniotrabeculotomy or goniotrabeculotomy ab interno
- #23 ab interno canaloplasty or canaloplasty ab interno
- #24 trabecular near/2 bypass\*

**Minimally invasive trabecular meshwork surgery for open-angle glaucoma (Protocol)**

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#25 trabectome  
 #26 goniotom\*  
 #27 trabecular near/3 (ablat\* or incis\* or excis\*)  
 #28 Kahook Dual Blade or KDB  
 #29 gonioscop\* near/2 assist\* near/2 transluminal or GATT  
 #30 OMNI or iTrack  
 #31 #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30  
 #32 #19 and #31

## Appendix 2. MEDLINE Ovid search strategy

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. 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. trabecular meshwork/
33. or/13-32
34. (Ab interno adj3 (trabeculectom\$ or trabeculotom\$ or canaloplast\$ or goniotrabeculotom\$)).tw.
35. (trabecular adj2 bypass\$).tw.
36. trabectome.tw.
37. goniotom\$.tw.
38. (trabecular adj3 (ablat\$ or incis\$ or excis\$)).tw.
39. (Kahook Dual Blade or KDB).tw.
40. (gonioscop\$ adj2 assist\$ adj2 transluminal).tw.
41. GATT.tw.
42. (OMNI or iTrack).tw.
43. or/34-42
44. 33 and 43
45. 12 and 44

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. trabeculotomy/
53. (Ab interno adj3 (trabeculectom\$ or trabeculotom\$ or canaloplast\$ or goniotrabeculotom\$)).tw.
54. (trabecular adj2 bypass\$).tw.
55. trabeculotome/
56. trabectome.tw.
57. goniotom\$.tw.
58. (trabecular adj3 (ablat\$ or incis\$ or excis\$)).tw.
59. (Kahook Dual Blade or KDB).tw.
60. (gonioscop\$ adj2 assist\$ adj2 transluminal).tw.
61. GATT.tw.
62. (OMNI or iTrack).tw.
63. or/52-62
64. 51 and 63

65. 32 and 64

#### Appendix 4. ISRCTN search strategy

(Open Angle Glaucoma OR intraocular pressure) AND (ab interno OR trabectome OR goniotomy OR Kahook OR KDB OR GATTOR OMNI OR iTRACK)

#### Appendix 5. ClinicalTrials.gov search strategy

ab interno OR trabectome OR goniotomy OR Kahook OR KDB OR GATT OR OMNI OR iTRACK | Open Angle Glaucoma OR intraocular pressure

#### Appendix 6. WHO ICTRP search strategy

Open Angle Glaucoma OR intraocular pressure = Condition

ab interno OR trabectome OR goniotomy OR Kahook OR KDB OR GATT OR OMNI OR iTRACK = Intervention

#### Appendix 7. Data on study characteristics

| Mandatory items                        |   | Optional items   |
|--|---|--|
| <b>Methods</b>                         |   |  |
| Study design                           | <ul style="list-style-type: none"> <li>• <b>Parallel-group RCT</b> <i>i.e. people randomised to treatment</i></li> <li>• <b>Within-person RCT</b> <i>i.e. eyes randomised to treatment</i></li> <li>• <b>Cluster RCT</b> <i>i.e. communities randomised to treatment</i></li> <li>• <b>Crossover RCT</b></li> <li>• Other, specify</li> </ul>   | Number of study arms<br>Method of randomisation<br>Exclusions after randomisation<br>Losses to follow-up                                     |
| Eyes                                   | <ul style="list-style-type: none"> <li>• <b>1 eye included in study</b>, <i>specify how eye selected</i></li> <li>• <b>2 eyes included in study, both eyes received same treatment</b>, <i>briefly specify how analysed (best/worst/average/both and adjusted for within-person correlation/both and not adjusted for within-person correlation) and specify if mixture of 1 eye and 2 eyes</i></li> <li>• <b>2 eyes included in study, eyes received different treatments</b>, <i>specify if correct pair-matched analysis done</i></li> </ul> | Number randomised/analysed<br>Method of masking<br>How were missing data handled?<br><i>e.g. available-case analysis, imputation methods</i> |
| Unit of randomisation/unit of analysis |   | Reported power calculation (Y/N), <i>if yes, sample size and power</i><br>Unusual study design/issues  |
| <b>Participants</b>                    |   |  |
| Country                                | -   | Setting  |
| Total number of participants           | <i>This information should be collected for total study population recruited into the study. If these data are reported for the people who were followed up only, please indicate</i>   | Ethnic group<br>Method of recruitment  |
| Number (%) of men and women            |   | Participation rate   |
| Average age and age range              |   | Equivalence of baseline characteristics (Y/N)<br>Diagnostic criteria   |
| Inclusion criteria                     | -   |  |
| Exclusion criteria                     | -   |  |

(Continued)

**Interventions**

|                    |  |  |
|--------------------|--|--|
| Intervention (n =) | <ul style="list-style-type: none"> <li>Number of people randomised to this group</li> </ul>  | Trabectome surgical parameters, e.g. degrees of meshwork ablated, electro-surgical power |
| Comparator (n =)   | <ul style="list-style-type: none"> <li>Intervention name</li> <li>Comparator name</li> <li>Specify whether phacoemulsification or other intervention performed at same time as intervention</li> </ul> | Comparator parameters, e.g. dosage of drugs  |

**Outcomes**

|  |  |                                    |
|--|--|------------------------------------|
| Primary and secondary outcomes as defined in study reports | <ul style="list-style-type: none"> <li>IOP at baseline</li> <li>IOP at follow-up</li> <li>Number of glaucoma medications at baseline</li> <li>Number of glaucoma medications at follow-up</li> <li>Intraoperative complications</li> <li>Postoperative complications or secondary surgery</li> <li>Duration of follow-up</li> <li>Loss to follow-up</li> <li>Intervals at which outcomes assessed</li> </ul> | Planned/actual length of follow-up |
|  | Adverse events reported (Y/N)  |                                    |

**Notes**

|                         |   |                                     |
|-------------------------|---|-------------------------------------|
| Trial registration      |   |                                     |
| Date conducted          | Specify dates of recruitment of participants mm/yr to mm/yr | Full study name: (if applicable)    |
| Sources of funding      | -   | Date of publication                 |
| Declaration of interest | -   | Reported subgroup analyses (Y/N)    |
|                         |   | Were trial investigators contacted? |

**CONTRIBUTIONS OF AUTHORS**

The protocol from the published review (Hu 2021) was used as the template for this protocol. KV, RG and KH updated the text to fit in with the scope of this review with help from AS and GV. All authors assisted in responding to peer review comments.

**DECLARATIONS OF INTEREST**

KH: none known

KV: none known

RG: none known

AS: is Managing Editor for Cochrane Eyes and Vision (CEV). All editorial decisions were made by another Editor.

GV: is Co-ordinating Editor for CEV. All editorial decisions and sign off were made by another Editor.

CB: none known

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