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Device-modified trabeculectomy for glaucoma (Review)

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[Intervention Review]

Device-modified trabeculectomy for glaucoma

Junghyun Park[1], Thanitsara Rittiphairoj[2], Xue Wang[3], Jian-Yu E[4], Amanda K Bicket[5]

[1]Department of Ophthalmology, Inje University Seoul Paik Hospital, Seoul, Korea, South. [2]Department of Ophthalmology, University of Colorado Denver Anschutz Medical Campus, Aurora, Colorado, USA. [3]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA. [4]Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. [5]Ophthalmology & Visual Sciences, University of Michigan, Ann Arbor, Michigan, USA

Contact: Amanda K Bicket, abicket@umich.edu.

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ABSTRACT

Background

Glaucoma is an optic neuropathy that leads to visual field defects and vision loss. It is the second leading cause of irreversible blindness in the world. Treatment for glaucoma aims to reduce intraocular pressure (IOP) to slow or prevent further vision loss. IOP can be lowered with medications, laser, or incisional surgery. Trabeculectomy is a surgical approach which lowers IOP by shunting aqueous humor to a subconjunctival bleb. Device-modified trabeculectomy techniques are intended to improve the durability and safety of this bleb-forming surgery. Trabeculectomy-modifying devices include the Ex-PRESS, the XEN Gel Stent, the PreserFlo MicroShunt, as well as antifibrotic materials such as Ologen, amniotic membrane, expanded polytetrafluoroethylene (ePTFE) membrane, Gelfilm and others. However, the comparative effectiveness and safety of these devices are uncertain.

Objectives

To evaluate the benefits and harms of different devices as adjuncts to trabeculectomy on IOP control in eyes with glaucoma compared to standard trabeculectomy.

Search methods

We used standard, extensive Cochrane search methods. The latest search was August 2021.

Selection criteria

We included randomized controlled trials in participants with glaucoma comparing device-modified trabeculectomy techniques with standard trabeculectomy. We included studies that used antimetabolites in either or both treatment groups.

Data collection and analysis

We used standard Cochrane methods. Our primary outcomes were 1. change in IOP and 2. mean postoperative IOP at one year. Our secondary outcomes were 3. mean change in IOP from baseline, 4. mean postoperative IOP at any time point, 5. mean best-corrected visual acuity (BCVA), 6. visual field change, 7. quality of life, 8. proportion of participants who are drop-free at one year, 9. mean number of IOP lowering medications at one year, and 10. proportion of participants with complications.

Main results

Eight studies met our inclusion criteria, of which seven were full-length journal articles and one was a conference abstract. The eight studies included 961 participants with glaucoma, and compared two types of devices implanted during trabeculectomy versus standard trabeculectomy. Seven studies (462 eyes, 434 participants) used the Ex-PRESS, and one study (527 eyes, 527 participants) used the

PreserFlo MicroShunt. No studies using the XEN Gel Stent implantation met our criteria. The studies were conducted in North America, Europe, and Africa. Planned follow-up periods ranged from six months to five years. The studies were reported poorly, which limited our ability to judge risk of bias for many domains. None of the studies explicitly masked outcome assessment. We rated seven studies at high risk of detection bias.

Low-certainty of evidence from five studies showed that using the Ex-PRESS plus trabeculectomy compared with standard trabeculectomy may be associated with a slightly lower IOP at one year (mean difference (MD) −1.76 mmHg, 95% confidence interval (CI) −2.81 to −0.70; 213 eyes). Moderate-certainty of evidence from one study showed that using the PreserFlo MicroShunt may be associated with a slightly higher IOP than standard trabeculectomy at one year (MD 3.20 mmHg, 95% CI 2.29 to 4.11). Participants who received standard trabeculectomy may have a higher risk of hypotony compared with those who received device-modified trabeculectomy, but the evidence is uncertain (RR 0.73, 95% CI 0.46 to 1.17; I^2 = 38%; P = 0.14). In the subgroup of participants who received the PreserFlo MicroShunt, there was a lower risk of developing hypotony or shallow anterior chamber compared with those receiving standard trabeculectomy (RR 0.44, 95% CI 0.25 to 0.79; 526 eyes). Device-modified trabeculectomy may lead to less subsequent cataract surgery within one year (RR 0.46, 95% CI 0.27 to 0.80; I^2 = 0%).

Authors' conclusions

Use of an Ex-PRESS plus trabeculectomy may produce greater IOP reduction at one-year follow-up than standard trabeculectomy; however, due to potential biases and imprecision in effect estimates, the certainty of evidence is low. PreserFlo MicroShunt may be inferior to standard trabeculectomy in lowering IOP. However, PreserFlo MicroShunt may prevent postoperative hypotony and bleb leakage. Overall, device-modified trabeculectomy appears associated with a lower risk of cataract surgery within five years compared with standard trabeculectomy. Due to various limitations in the design and conduct of the included studies, the applicability of this evidence synthesis to other populations or settings is uncertain. Further research is needed to determine the effectiveness and safety of other devices in subgroup populations, such as people with different types of glaucoma, of various races and ethnicity, and with different lens types (e.g. phakic, pseudophakic).

PLAIN LANGUAGE SUMMARY

Device-modified trabeculectomy for glaucoma

Review question

We reviewed the evidence about the effectiveness and safety of using devices modifying a standard surgery (trabeculectomy) for the treatment of glaucoma.

What is glaucoma and how is it treated?

Glaucoma is a disease of the optic nerve, which relays information from the eye to the brain to create images. Increasing pressure within the eye (increased intraocular pressure or IOP) damages the optic nerve leading to vision loss and blindness. It is the second leading cause of blindness worldwide in adults aged 50 years and over. Treatment for glaucoma aims to reduce pressure in the eye, which helps to slow down or prevent further vision loss. Eye pressure can be lowered with medicines, laser therapy, or surgery. Trabeculectomy is one of the most common standard surgical procedures for the treatment of glaucoma. It lowers IOP by creating a channel between the inside of the eye and the subconjunctival space (a fluid-filled space just under the surface of the eye), and it can be modified with implantable devices. Studies have reported using various devices such as the Ex-PRESS, the XEN Gel Stent, and the PreserFlo MicroShunt, along with materials such as Ologen, amniotic membrane, expanded polytetrafluoroethylene (ePTFE) membrane, Gelfilm, and others.

What did we do?

We searched medical databases for well-designed clinical studies in people with glaucoma comparing device-modified trabeculectomy techniques with standard trabeculectomy.

What did we find?

We found eight studies that met our inclusion criteria. These studies included 961 people with glaucoma and compared one of two types of device implanted during trabeculectomy versus standard trabeculectomy. Seven studies used the Ex-PRESS (434 participants), and one study used the PreserFlo MicroShunt (527 participants). These studies were conducted in North America, Europe, and Africa. Planned follow-up periods ranged from six months to five years. We found no studies using the XEN Gel Stent that met our criteria.

Main results

Five studies found that using the Ex-PRESS shunt during trabeculectomy may slightly reduce eye pressure by about 1.76 mmHg more than standard trabeculectomy. Another study showed that using the PreserFlo MicroShunt may be associated with a slightly higher eye pressure by 3.20 mmHg than standard trabeculectomy. Use of PreserFlo MicroShunt reduces the risk of developing abnormally low eye pressure by about 50% compared with standard trabeculectomy. Five studies found that the use of either device may lower the risk of subsequent cataract surgery (replacing a cloudy lens within the eye).

What are the limitations of the evidence?

The overall quality of the included studies varied by the type of device studied. Specifically, the quality was very low for studies using the Ex-PRESS, and low for studies using the PreserFlo MicroShunt study to flaws in study design and incomplete reporting. Therefore, the data need to be interpreted with caution.

How up to date is this evidence?

The evidence is current to 8 August 2021.

Summary of findings 1. Device-modified trabeculectomy compared with standard trabeculectomy for people with open-angle glaucoma

Device-modified trabeculectomy compared with standard trabeculectomy for people with open-angle glaucoma

Patient or population: people with glaucoma

Settings: ophthalmic clinic

Intervention: device-modified trabeculectomy (Ex-PRESS implanted during trabeculectomy or PreserFlo MicroShunt)

Comparison: standard trabeculectomy

Outcomes		Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of eyes (studies)	Certainty of the evidence (GRADE)	Comments
		Assumed risk	Corresponding risk				
		Standard trabeculectomy	Device-modified trabeculectomy				
Postoperative mean IOP at 1 year	**Ex-PRESS**	The mean IOP in the standard trabeculectomy group was **14.4 mmHg**, ranged from 13.5 mmHg to 15.4 mmHg	The mean IOP in the Ex-PRESS group was **12.6 mmHg**, ranged from 11.6 mmHg to 13.7 mmHg	**MD −1.76 mmHg** (95% CI −2.81 to −0.70)	213 (5 RCTs)	⊕⊕⊖⊖ **Low**[a]	—
	PreserFlo MicroShunt	The mean IOP in the standard trabeculectomy group was **11.1 mmHg**, ranged from 10.3 mmHg to 11.9 mmHg	The mean IOP in the PreserFlo group was **14.3 mmHg**, ranged from 13.4 mmHg to 15.2 mmHg	**MD 3.20 mmHg** (95% CI 2.29 to 4.11)	446 (1 RCT)	⊕⊕⊕⊖ **Moderate**[b]	—
Postoperative mean change in IOP from baseline to 1 year		Change in postoperative IOP in the Ex-PRESS group was on average 2.00 mmHg (95% CI −3.66 to 7.66) greater than in the standard trabeculectomy.		**MD 2.00 mmHg** (95% CI −3.66 to 7.66)	20 (1 RCT)	⊕⊖⊖⊖ **Very low**[a,c]	—
Postoperative mean logMAR BCVA at 1 year		The mean logMAR BCVA in the standard trabeculectomy group was **0.57**, ranged from 0.37 to 0.78	The mean logMAR BCVA in the Ex-PRESS group was **0.53**, ranged from 0.38 to 0.67	**MD −0.04** (95% CI −0.19 to 0.10)	110 (3 RCTs)	⊕⊕⊖⊖ **Low**[a]	—

Postoperative mean visual field change at 1 year		No studies measured this outcome.					
Quality of life at 1 year		No studies measured this outcome.					
Proportion of participants who were drop-free at 1 year	**Ex-PRESS**	**458 per 1000**	**934 per 1000** (192 to 1000)	**RR 2.04** (0.42 to 9.82)	48 (2 RCTs)	⊕⊖⊖⊖ **Very low**[a,c]	—
	PreserFlo MicroShunt	**848 per 1000**	**712 per 1000** (653 to 789)	**RR 0.84** (0.77 to 0.93)	509 (1 RCT)	⊕⊕⊕⊖ **Moderate**[b]	—
Proportion of participants with endophthalmitis **Follow-up: 2 years**		**16 per 1000**	**5 per 1000** (0 to 133)	**RR 0.34** (0.01 to 8.29)	120 (1 RCT)	⊕⊖⊖⊖ **Very low**[a,c]	Trial duration was 2 years.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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).
BCVA: best-corrected visual acuity; **CI:** confidence interval; **IOP:** intraocular pressure; **logMAR**: logarithm of the minimum angle of resolution; **MD:** mean difference; **RCT:** randomized controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[a]Downgraded two levels for limitations in the design and implementation of available studies, mainly due to unmasked outcome assessors, suggesting high likelihood of bias.
[b]Downgraded one level for risk of bias.
[c]Downgraded one level for imprecision.

BACKGROUND

Description of the condition

Glaucoma is an optic neuropathy that leads to vision loss and blindness (Foster 2002). Among the many known and unknown factors that contribute to the damage to the optic nerve, elevated intraocular pressure (IOP) is the only modifiable risk factor (Coleman 2012). Normally, IOP is balanced when the rate of aqueous production by the ciliary body is equal to the rate of its outflow from the posterior to the anterior chamber through the trabecular meshwork and the canal of Schlemm in the anterior chamber angle (Small 1986). When excess aqueous humor is produced or when part or all the drainage system of aqueous humor is blocked, the result is an increase in IOP, which has been shown to be associated with progressive glaucomatous optic nerve damage (Pan 2011; Turkoski 2012).

Epidemiology

Glaucoma is the second-leading cause of vision loss in the world (GBD 2021). The World Health Organization (WHO) estimated that 60.5 million people would have glaucoma worldwide by 2010 (Quigley 2006), and that number is estimated to increase globally to 111.8 million by 2040 (Tham 2014). There are several types of glaucoma, of which open-angle glaucoma (OAG) and angle-closure glaucoma (ACG) are two major types. The most common type of glaucoma is OAG, accounting for 74% of glaucoma cases worldwide. ACG is less common. Women comprise 55% of OAG cases, 70% of ACG cases, and 59% of all glaucoma cases. People of Asian origin represent 47% of people who have glaucoma and 87% of those with ACG (Quigley 2006).

Neovascular glaucoma (NVG) is a form of secondary glaucoma characterized by new vessels on the iris and angle of the anterior chamber. The most common etiologies include proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), and ocular ischemic syndrome (OIS).

Symptoms and diagnosis

OAG is often asymptomatic initially. There is no pain and those affected tend not to notice the loss of visual field until their central vision is affected in the later stage of the disease; by then optic nerve damage is already severe (Boland 2008; Quigley 2011; Small 1986). The symptoms of ACG vary. It may occur suddenly without warning or gradually with progressive deterioration; people may have signs and symptoms including severe pain and eye redness, decreased vision, nausea, vomiting, and bradycardia (Boland 2008; Douglas 1975; Small 1986). Clinical exams for diagnosing glaucoma include, but are not limited to, tonometry, gonioscopy, imaging of optic nerve head and retinal nerve fiber layer, visual acuity measurement, and visual field assessment.

Description of the intervention

Trabeculectomy, first introduced by John Cairns in 1968 and then modified by Watson in 1972, remains the gold standard incisional surgical procedure for the treatment of glaucoma (Cairns 1968; Watson 1972; Watson 1981). It includes lifting the conjunctiva and dissecting a partial thickness scleral flap, then making a perforating scleral entrance into the anterior chamber to allow aqueous humor drainage. Beneath the flap, part of the eye's trabecular meshwork and adjacent structures are removed before the flap is reapposed to surrounding sclera and the conjunctiva closed. This procedure lowers IOP by allowing aqueous fluid to percolate into the subconjunctival space through the scleral hole, forming a bleb (a blister-like collection of fluid of the conjunctiva). Over the years, trabeculectomy has been modified in various ways, including the use of antimetabolites such as 5-fluorouracil (5-FU) (Green 2014) and mitomycin C (MMC) (Wilkins 2005), the use of biodegradable materials to modify healing and maintain bleb space (e.g. Ologen or amniotic membrane), and creation of a fornix-based rather than the traditional limbus-based conjunctival flap. Most recently, the modifications have included the use of adjunctive devices with standard trabeculectomy. Surgeons may use a tube without a reservoir (e.g. Ex-PRESS, XEN Gel Stent, or PreserFlo MicroShunt) to enhance aqueous humor outflow and to promote continued drainage from the anterior chamber to the bleb without the sclerectomy or peripheral iridectomy of a standard trabeculectomy.

How the intervention might work

This review considers adjunctive devices used with trabeculectomy to lower IOP. The devices are intended to maintain drainage of aqueous humor from the anterior chamber into a filtering bleb formed in the subconjunctival space, and may be used with or without antimetabolites.

Ex-PRESS mini glaucoma implant

The Ex-PRESS implant is a 3 mm stainless steel shunt with an internal lumen 50 µm in diameter. Implantation of this device leads to the formation of a thin-walled filtration bleb, as is seen with standard trabeculectomy. It was originally developed for unguarded placement beneath the conjunctiva, but because this technique led to complications, the Ex-PRESS is now implanted under a partial thickness scleral flap. Investigators who have conducted retrospective studies and randomized controlled trials have reported that the Ex-PRESS provides IOP control that is similar to or better than that provided by standard trabeculectomy (Dahan 2012; De Jong 2009; Francis 2011; Gallego-Pinazo 2009; Maris 2007). They have also reported that the Ex-PRESS results in fewer complications, fewer postoperative surgical interventions, and less need for glaucoma medications (Chan 2015). The device is manufactured by Alcon (a Novartis company).

PreserFlo MicroShunt

The PreserFlo MicroShunt (formerly known as the InnFocus MicroShunt, Santen Inc) is made of a stable and flexible polymer 'SIBS' (poly[styrene-block-isobutylene-block-styrene]), which is already used for long-term implantation in the body in cardiac stents (Pinchuk 2008). The PreserFlo MicroShunt device has an overall length of 8.5 mm and a beveled tip. A 1-mm fin positioned 4.5 mm from the tip allows fixation and prevents peritubular leakage. Implantation of the PreserFlo MicroShunt facilitates aqueous humor outflow from the anterior chamber to a posterior bleb formed under the conjunctiva and Tenon's capsule. It has a lumen diameter of 70 µm and is implanted using an ab externo approach (Pinchuk 2017). The flow-limiting design is based on the Hagen–Poiseuille equation, supposedly limiting chronic hypotony, yet allowing postoperative hypotensive efficacy and safety (Batlle 2021). The ab-externo approach allows for hemostasis, precise placement, and exact verification of flow (Pillunat 2021).

XEN Gel Stent

The XEN Gel Stent is a hydrophilic tube composed of porcine gelatin cross-linked with glutaraldehyde, a material that has been used in a variety of medical devices due to its demonstrated biocompatibility (Fea 2020). It has a lumenal diameter of 45 µm, an outer diameter of 150 µm, and is 6 mm in length. Like the PreserFlo MicroShunt, the XEN Gel Stent lowers IOP by creating a permanent outflow pathway from the anterior chamber to the subconjunctival space through a scleral channel, and is designed to geometrically limit hypotony. In contrast to PreserFlo MicroShunt, however, the XEN Gel Stent can be placed ab interno, using its injector designed for this approach, without incising the conjunctiva.

Why it is important to do this review

The purpose of this review is to compare the effectiveness and safety of device-modified trabeculectomy procedures versus standard trabeculectomy, with or without the use of antimetabolites, in the surgical treatment of glaucoma. Device-modified trabeculectomy techniques are relatively new; many studies have not had sample sizes sufficiently large to provide reliable evidence to assess the effectiveness and safety of these procedures. Therefore, it is important to examine the evidence from multiple completed studies. When meta-analysis of outcomes is appropriate, pooling across studies should increase the power and yield valuable information. However comprehensive, rigorous systematic reviews in this area are warranted.

OBJECTIVES

To evaluate the benefits and harms of different devices as adjuncts to trabeculectomy on IOP control in eyes with glaucoma compared to standard trabeculectomy.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomized controlled trials in this review.

Types of participants

We included trials in which the participants were aged 18 years or older and had been diagnosed with glaucoma. We included trials in which participants had any type of glaucoma (e.g. primary open-angle glaucoma (POAG), ACG, pigmentary glaucoma, exfoliation glaucoma, and secondary glaucoma such as NVG), except pediatric and congenital glaucoma. There were no restrictions with regards to gender, ethnicity, comorbidity, use of adjunctive medication, lens status (phakic, aphakic, or pseudophakic), and the number of participants enrolled in an individual trial. We excluded studies that performed combined trabeculectomy and cataract surgery as this was outside the scope of the review. Another Cochrane Review evaluated surgical interventions for primary congenital glaucoma (Ghate 2015).

Types of interventions

We included trials that compared, with or without the use of antimetabolites, device-modified trabeculectomy versus standard trabeculectomy. The previous review assessed the following devices: the Ex-PRESS, silicone tube implant, and SOLX Gold Shunt, which could be deployed under a standard trabeculectomy flap, as well as antifibrotic materials including Ologen, amniotic membrane, expanded polytetrafluoroethylene (ePTFE), and Gelfilm.

In the current update of this review, we included the Ex-PRESS shunt, XEN Gel Stent, and PreserFlo MicroShunt, which are the major devices available to patients in the current US or EU market. We included Xen Gel Stent or PreserFlo MicroShunt versus standard trabeculectomy (with or without antimetabolites) in this review because these devices modify the implementing procedure of trabeculectomy, although they did not address the procedures as trabeculectomy plus devices. We excluded some devices assessed in the previous review, such as silicone tube and SOLX Gold Shunt, as they are no longer in wide use combined with trabeculectomy. We also excluded antifibrotic materials including Ologen, amniotic membrane, ePTFE and Gelfilm which are used as adjuvants in trabeculectomy, as they are not devices. We planned to make the following comparisons.

1. Trabeculectomy plus Ex-PRESS shunt versus standard trabeculectomy
2. Trabeculectomy with antimetabolites (MMC, 5-FU, or both) plus Ex-PRESS shunt versus trabeculectomy with antimetabolites
3. Xen Gel Stent or PreserFlo MicroShunt versus standard trabeculectomy or with antimetabolites

There are two comparisons that we did not plan to include, as these are already covered in other Cochrane Reviews.

1. MMC versus 5-FU on the outcome of standard trabeculectomy (Cabourne 2015)
2. Fornix-based (the modification) versus traditional limbus-based trabeculectomy (Al-Haddad 2015)

Types of outcome measures

Primary outcomes

1. Change in IOP, measured as a mean decrease from baseline (immediate preoperative IOP) at one year after the intervention when IOP had been measured using Goldmann tonometry, TonoPen, or another standard device. When the change in IOP was not available and baseline IOP distributions were similar in the two surgery groups, we would not compare postoperative IOP as a surrogate to estimate the effect of device-modified trabeculectomy as we had mean postoperative IOP as a separate outcome for our review.
2. Mean postoperative IOP at one year after the intervention when IOP had been measured using Goldmann tonometry, TonoPen, or another standard device.

Secondary outcomes

1. Mean change in IOP from baseline, measured at any time point less than one year and longer than one year. Within each timeframe, we chose the outcome measurement at the longest follow-up. When the change in IOP was not available and baseline IOP distributions were similar in the two surgery groups, we would not compare postoperative IOP as a surrogate to estimate the effect of device-modified trabeculectomy as we had mean postoperative IOP as a separate outcome for our review.

2. Mean postoperative IOP at any time point less than one year and longer than one year. Within each timeframe, we will choose the outcome measurement at the longest follow-up. IOP had to be measured using Goldmann tonometry, TonoPen, or another standard device.
3. Mean best-corrected visual acuity (BCVA) in logMAR, measured using a Snellen chart or Snellen equivalent and assessed at one year after the intervention. We analyzed BCVA data as a continuous outcome in the meta-analyses.
4. Visual field change, measured in units of mean deviation or mean defect (the mean point-wise difference between a given test result and the normal age-matched reference value) at one year after the intervention.
5. Quality of life, measured using the National Eye Institute Visual Function Questionnaire (NEI VFQ) or any other validated instrument at one year after the intervention.
6. Proportion of participants who were drop-free at one year after the intervention.
7. Mean number of IOP-lowering medications at one year after the intervention.
8. Proportion of participants with the following complications: loss of vision of more than two lines or loss of light perception, IOP less than 5 mmHg (hypotony) or shallow anterior chamber, bleb leakage, endophthalmitis, reoperations for glaucoma, endophthalmitis, cataract extraction (among phakic eyes), device migration, and device exposure.

Search methods for identification of studies

Electronic searches

We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (2014 Issue 12); Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (December 2014 to August 2021); Embase (December 2014 to August 2021); PubMed (December 2014 to August 2021); Latin American and Caribbean Literature on Health Sciences (LILACS) (December 2014 to August 2021); the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com); ClinicalTrials.gov (www.clinicaltrials.gov); and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not impose any date, language, or publication status restrictions in the electronic search for trials.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), Embase (Appendix 3), PubMed (Appendix 4), LILACS (Appendix 5), mRCT (Appendix 6), ClinicalTrials.gov (Appendix 7), and ICTRP (Appendix 8).

Searching other resources

We searched the references listed in reports from included studies to identify additional relevant studies, without restriction regarding language or date of publication.

Data collection and analysis

Selection of studies

Two review authors (from JP, TR, XW, JE) independently reviewed the titles and abstracts of all reports identified through the electronic and manual searches. We first classified all titles and abstracts as 'definitely relevant', 'unsure', or 'definitely not relevant'. We then adjudicated discrepancies through discussion and retrieved full-text reports for those classified as 'definitely relevant' or 'unsure' by both review authors. By review of full-text reports, we independently assessed eligibility and classified each study as 'include', 'unsure', or 'exclude'. For studies labeled as 'unsure' at this stage, we requested further information from study investigators. When they did not respond within two weeks, we used the information available. We resolved disagreements by discussion between the two review authors. When resolution was not possible, we consulted a third review author. All publications from studies that met the inclusion criteria then underwent assessment of risk of bias and data extraction. We recorded the reasons for exclusion of studies classified as 'exclude' in the Characteristics of excluded studies table. For reports not published in English or Chinese, we planned to use Google Translate to screen titles and abstracts and to ask translators to translate or assess reports for full-text screening. However, all reports relevant to this review were published in English or Chinese languages. We illustrated the study selection process in a PRISMA diagram (Figure 1).

Figure 1. Study flow diagram. [a]Altogether, 56 unique studies were excluded in this updated review.

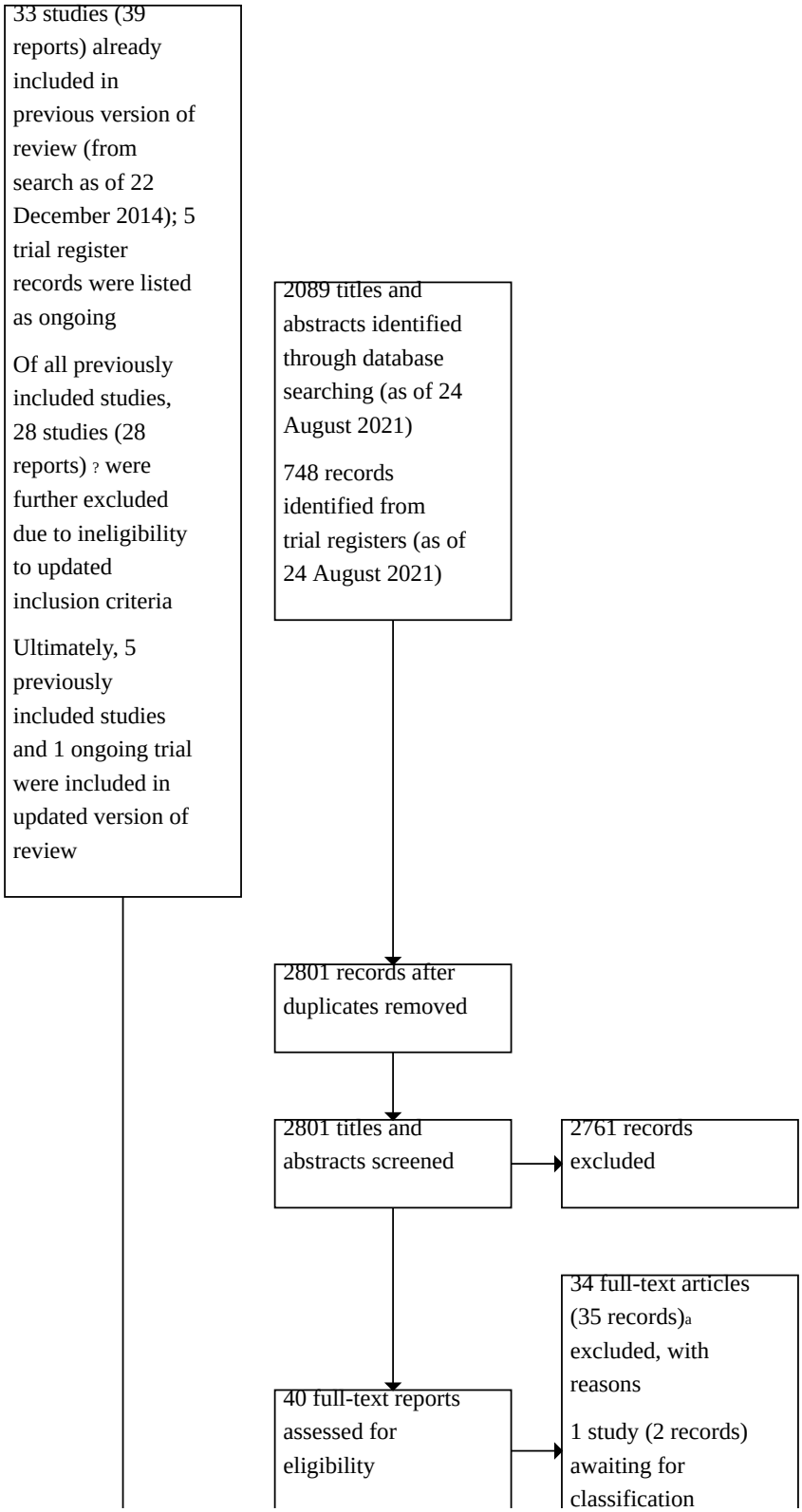
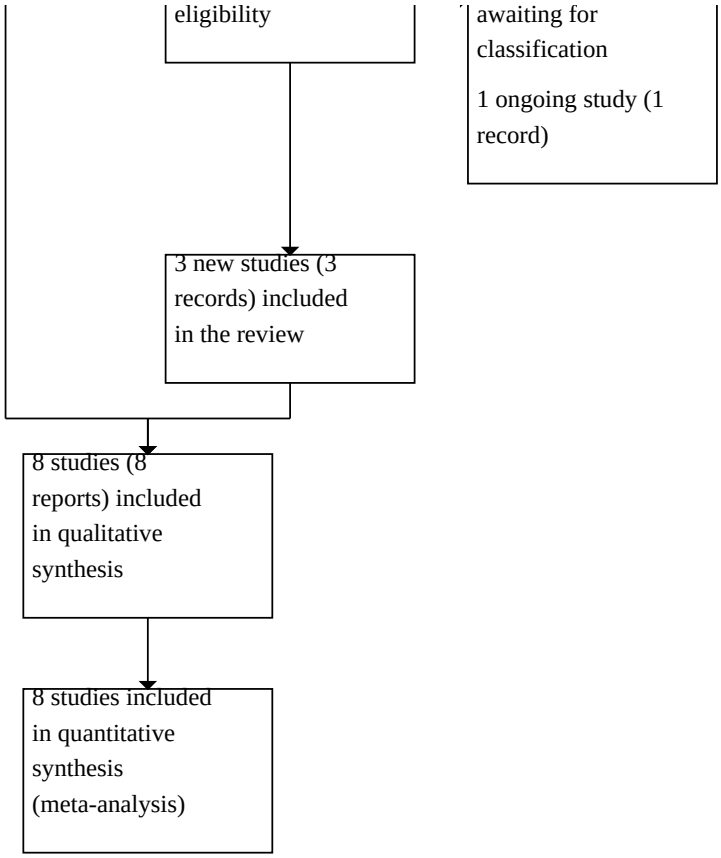


Figure 1. (Continued)



Data extraction and management

Two review authors (JP, TR) independently extracted data regarding study design and methods, participant characteristics, and the primary and secondary outcomes, and recorded the information onto paper data collection forms developed in collaboration with Cochrane Eyes and Vision. Whenever there were discrepancies between review authors, we reached consensus by discussion. When we could not reach a consensus, we consulted a third review author who made the final decision. We contacted study investigators to obtain missing information and to elucidate unclear reporting. When they did not respond within two weeks, we used the information available. One review author (TR) entered data into Review Manager 5 (Review Manager 2020), and a second review author (JP) verified the data entered.

Assessment of risk of bias in included studies

Two review authors (JP, TR) independently assessed each included study for risks of bias as part of the data extraction process. We based our judgments on the tools for assessing risk of bias set in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We judged each study with respect to the following risk of bias domains.

1. Selection bias (sequence generation and allocation concealment before randomization)
2. Performance bias (masking of participants and personnel)
3. Detection bias (masking of outcome assessors)
4. Attrition bias (incomplete outcome data)
5. Reporting bias (selective outcome reporting)
6. Other potential sources of bias (e.g. funding source)

We assessed each trial for each risk of bias criterion as being at high, low, or unclear risk of bias (lack of information or uncertainty over the potential for bias).

Measures of treatment effect

Dichotomous outcomes

We analyzed dichotomous outcomes, such as complications and proportion of participants who were drop-free, using summary risk ratios (RRs) with 95% confidence intervals (CIs).

Continuous outcomes

We estimated the difference between continuous outcomes, such as mean change (or mean) IOP, BCVA, mean number of IOP lowering medications, as the mean difference (MD) with 95% CIs. We planned to analyze IOP fluctuations, visual field changes, quality-of-life scores as continuous outcomes, but such data were not available.

Unit of analysis issues

The unit of analysis was the eye that had glaucoma surgery. We recorded whether studies used a parallel-group design or a paired-eye design, and whether the study used matched-analysis when a paired-eye design was used. When both eyes of all or some participants were allocated to the same intervention group, we recorded the information as available and did not estimate or impute intraperson correlations for individual outcomes.

All studies were parallel-group designs. Of the eight trials, four included only one eye per participant. Both eyes of some participants were included in another three parallel-group trials; a mean of 7% of participants across these three trials contributed both eyes to the analysis. One trial was a paired-eye design in which each participant had one eye in each intervention group. None of the studies that included more than one eye per participant accounted for intraperson correlation.

Dealing with missing data

We contacted study investigators to request missing data or to clarify unclearly reported data or information, including but not limited to information about study methods, effect estimates, and standard deviations of effect estimates. When study investigators did not respond within two weeks or after three attempts to contact them, we used the available information. We did not impute data for this review.

Assessment of heterogeneity

We assessed clinical and methodological heterogeneity among included trials by examining variations in the trial designs and methods, characteristics of the trial participants, variations in interventions, and lengths of follow-up. We assessed statistical heterogeneity among the reported treatment effect estimates of included trials by examining the overlap of the 95% CIs on estimates from individual trials in forest plots and I^2 values (Higgins 2003). We considered poor overlap in the 95% CIs and an I^2 above 50% as indications of substantial statistical heterogeneity.

Assessment of reporting biases

We investigated whether our review was subject to reporting biases. For selective reporting bias, we compared outcomes specified in trial protocols or trial register records with outcomes reported in published full-text articles. When no trial protocol or trial register record was available, we examined whether outcomes specified in the methods section were reported in the results section of the same published report. We did not use funnel plots to examine signs of asymmetry due to the limited number of studies included in the same meta-analysis.

Data synthesis

We determined whether data synthesis in meta-analyses was appropriate based on evidence of heterogeneity. When we considered that there was substantial heterogeneity, we presented results in a narrative summary. In the absence of clinical and methodological heterogeneity across studies, and when the I^2 statistic was less than 50% (indicating no substantial statistical heterogeneity), we combined study results using a random-effects meta-analysis model. Likewise, we applied a random-effects meta-analysis model when the I^2 statistic was greater than 50% but all studies favored the same intervention, or when the I^2 statistic was greater than 50% but no study showed a clinical difference between groups.

Subgroup analysis and investigation of heterogeneity

We compared a subgroup by the use of device within a single analysis for each outcome where information was available. We did not conduct subgroup analysis for comparisons of outcomes with use of adjuvant antimetabolites (e.g. MMC) because all studies used adjuvant MMC. Also, we were unable to carry out the following planned subgroup analyses as the included studies did not stratify participants based on 1. the status of the lens (i.e. eyes that possessed their natural lens (phakic), eyes without the crystalline lens (aphakic, cataract extraction), or eyes with an intraocular lens implanted that replaced the eye's natural lens (pseudophakic)); 2. ethnicity; 3. baseline IOP; or 4. type of glaucoma.

Sensitivity analysis

We were unable to conduct sensitivity analyses to assess the influence on effect estimates of excluding studies at high risk of reporting bias, as most studies had a low risk of reporting bias. We had also planned to conduct a sensitivity analysis after excluding industry-funded studies; however, funding information was not always available, so we did not have enough information to conduct such analyses.

Summary of findings and assessment of the certainty of the evidence

Two review authors (JP, TR) independently assessed the certainty of the evidence by outcome using the GRADE system (Guyatt 2011). We reported results in a Summary of findings 1.

Our prespecified outcome measures were:

1. change in IOP;
2. postoperative mean IOP at one year after the intervention;
3. mean BCVA in logMAR;
4. postoperative visual field change at one year after the intervention;
5. quality of life;
6. proportion of participants who were drop-free at one year after the intervention;
7. frequency of the following complication: proportion of participants with endophthalmitis at end of follow-up.

RESULTS

Description of studies

Results of the search

For the current update of the review, we amended intervention types in the prespecified inclusion criteria to include only Ex-PRESS, XEN Gel Stent, and PreserFlo MicroShunt. According to the electronic searches for the previous version of the review as of 22 December 2014, we previously included 39 reports from 33 studies and four ongoing trials. Per the updated inclusion criteria, which excluded antifibrotic materials and devices formerly combined with trabeculectomy but no longer in use assessed in the previous review, we further excluded 28 reports from 28 studies due to ineligible interventions, leaving five previously included studies, and one ongoing trial.

Through an updated search as of 24 August 2021, we retrieved and screened the titles and abstracts of 2801 records after duplicate removal and excluded 2761 of these records. We screened 40 full-text reports, excluded 34 studies (35 records) with reasons, and classified one study (two records) as awaiting classification. Altogether, we included eight studies (eight reports) and assessed one as ongoing and one as awaiting classification in this version of the review. The ongoing trial is being conducted in Japan and compares Ex-PRESS with standard trabeculectomy; result are not available yet. We did not identify any additional studies through searching reference lists of included trials.

A flow diagram describing the search and screening process is shown in Figure 1.

Included studies

We included eight trials. All trials were published in either English or Chinese. Details of each trial are presented in the Characteristics of included studies table. We summarized the basic trial characteristics in Table 1.

Types of participants

The eight trials included 989 eyes of 961 participants and had follow-up periods ranging from six months to five years after surgery. All trials included men and women. Seven trials included participants with OAG; El-Saied 2021 included participants with NVG. None of the trials stratified participants by type of glaucoma, race, or lens type. They were conducted in North America, Europe, and Africa.

Types of interventions

The eight trials assessed either the Ex-PRESS with standard trabeculectomy or the PreserFlo MicroShunt. None assessed XEN Gel Stent.

Seven trials assessed trabeculectomy with Ex-PRESS compared with standard trabeculectomy (Dahan 2012; De Jong 2005; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015). They enrolled 462 eyes of 395 participants. Six of the seven trials were two-arm studies that compared standard trabeculectomy versus trabeculectomy and Ex-PRESS, with MMC applied to both groups. The remaining trial was a three-arm trial; it compared Ex-PRESS implanted under a scleral flap with standard trabeculectomy, Ex-PRESS implanted under the conjunctiva (without creation of a standard trabeculectomy flap), and standard trabeculectomy (De Jong 2005).

One trial (527 eyes of 527 participants) was a two-arm study that compared PreserFlo MicroShunt with MMC with standard trabeculectomy with MMC (Baker 2021).

Types of outcomes

All trials considered IOP control as their main outcome; however, trials differed in how they reported IOP. One trial reported change of IOP from baseline (El-Saied 2021); the remaining trials did not report this. All trials reported postoperative IOP at certain time points, and one trial did not report any quantitative data but provided a descriptive summary only (De Jong 2005).

Seven trials reported visual acuity outcomes at different time points (Baker 2021; Dahan 2012; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015); one trial reported visual field outcome qualitatively (Wagdy 2021); and all studies reported postoperative complications either quantitatively or qualitatively. None of the studies reported IOP fluctuation or quality-of-life outcomes.

Funding sources

Seven trials reported the funding sources: industry funded five trials (Baker 2021; Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015); and two trials reported receiving no funding (El-Saied 2021; Wagdy 2021). De Jong 2005 did not disclose information about sources of funding.

Excluded studies

According to the updated inclusion criteria, we excluded 56 unique studies and listed the reasons for exclusion in the Characteristics of excluded studies table.

Studies awaiting classification

One study is awaiting classification (Konstantinidis 2021).

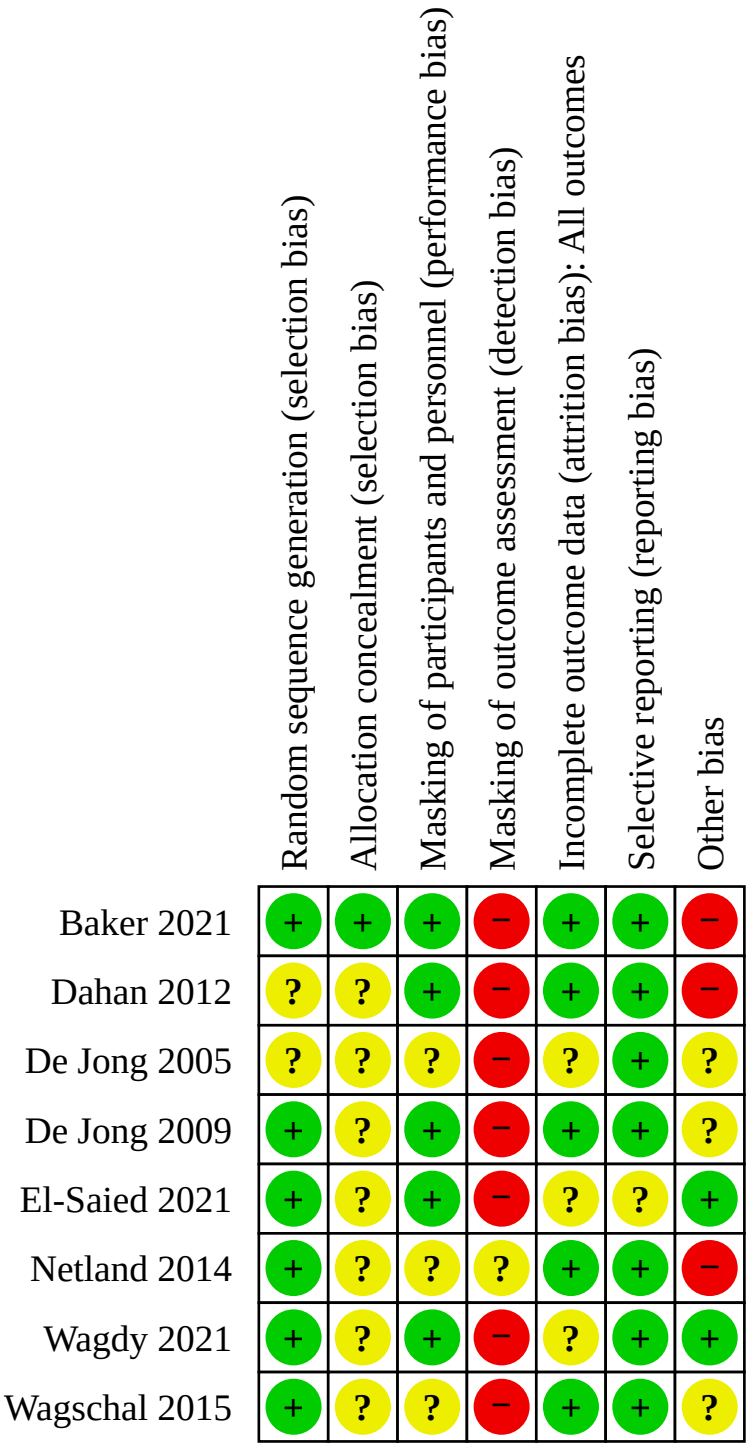
Ongoing studies

One study is ongoing (JPRN-UMIN000008981).

Risk of bias in included studies

Figure 2 shows a summary of the risk of bias assessments. Seven of the eight included trials had a high risk of detection bias. Most trials had either missing or inadequate information in trial reports to assess the risk of selection bias, especially in unclear allocation concealment. All but one trial had a low risk of reporting bias while less than half of included trials received funding from the manufacturer of the device, which was judged as high risk of bias. A description for each domain is summarized below.

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



Allocation

Of the eight trials, six specified adequate methods of randomization and were at low risk of bias (Baker 2021; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015): five out of seven trials for Ex-PRESS (De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015) and one study for the PreserFlo MicroShunt (Baker 2021). The remaining two trials did not specify methods for random sequence generation, so we judged them at unclear risk of bias (Dahan 2012; De Jong 2005).

Of the eight trials, only Baker 2021, which was a study for PreserFlo MicroShunt, performed proper allocation concealment and was at low risk of bias. The other seven trials did not specify the method for allocation concealment, so they were at unclear risk of bias.

Blinding

Masking (performance bias and detection bias)

Study authors from five trials noted masking of participants: four of seven trials for Ex-PRESS (Dahan 2012; De Jong 2009; El-Saied 2021; Wagdy 2021), and one trial for PreserFlo MicroShunt (Baker 2021). The remaining three trials did not report whether participants were masked and were at unclear risk of performance bias (De Jong 2005; Netland 2014; Wagschal 2015). As masking of surgeons is logistically difficult and trabeculectomy is a standardized procedure (all studies described the surgical procedures in detail), we did not consider the lack of masking of surgeons to be an important modifiable source of bias.

In terms of detection bias, only Netland 2014 used a special protocol to minimize bias, so we judged this trial at unclear risk of detection bias. Otherwise, none specified masking of outcome assessors. Due to the easy detection of devices when examining the eye, unmasked outcome assessors could tend to anticipate and thus report favorable changes in IOP among participants with the implant or alternatively, among participants who received the surgery the outcome assessor preferred; therefore, the remaining trials were at high risk of detection bias (Baker 2021; Dahan 2012; De Jong 2005; De Jong 2009; El-Saied 2021; Wagdy 2021; Wagschal 2015).

Incomplete outcome data

Investigators of five trials reported few or no losses to follow-up, resulting in our assessment of low risk of attrition bias: four of seven trials of Ex-PRESS (Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015), and one study for PreserFlo MicroShunt (Baker 2021). We assessed the remaining three trials at unclear risk of attrition bias as they did not report the number of losses to follow-up; all were Ex-PRESS trials (De Jong 2005; El-Saied 2021; Wagdy 2021).

Selective reporting

We judged seven trials at low risk of reporting bias as they had 1. clinical trial registry records and reported all outcomes listed in the registry (Baker 2021; Dahan 2012; Netland 2014; Wagdy 2021; Wagschal 2015), or 2. reported all outcome measures defined in their methods section of the full-text reports (De Jong 2005; De Jong 2009). These included six of seven studies for Ex-PRESS and one for PreserFlo MicroShunt. We judged El-Saied 2021 to have unclear risk of bias as no protocol or trial registration was publicly available.

Other potential sources of bias

We judged two trials at low risk of other potential sources of bias (El-Saied 2021; Wagdy 2021). Three trials were at high risk because they received funding from the manufacturer of the device (Baker 2021; Dahan 2012; Netland 2014). The remaining studies were at unclear risk of bias, as funding and methodological details were reported insufficiently to render a judgment of low or high risk of bias (De Jong 2005; De Jong 2009; Wagschal 2015).

Effects of interventions

See: **Summary of findings 1** Device-modified trabeculectomy compared with standard trabeculectomy for people with open-angle glaucoma

Device-modified trabeculectomy versus trabeculectomy

Seven trials assessed the use of Ex-PRESS (Dahan 2012; De Jong 2005; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015), and one trial assessed the use of PreserFlo MicroShunt (Baker 2021). Six of eight trials reported a sample size calculation: Dahan 2012 had a power of 96% to detect a 2.0 mmHg IOP difference between groups; De Jong 2009 had a power of 80% to detect a 32% between-group difference in IOP; and both Netland 2014 and Wagschal 2015 had power of 80% to detect a 2.0 mmHg IOP difference between groups. Baker 2021 had a power of 90% to detect 15% margin of non-inferiority, which is a lowering of 2.5 mmHg IOP. Wagdy 2021 performed a post-hoc power analysis with a post-hoc power estimation of 0.83. De Jong 2005 and El-Saied 2021 did not report a power or sample size calculation.

Intraocular pressure

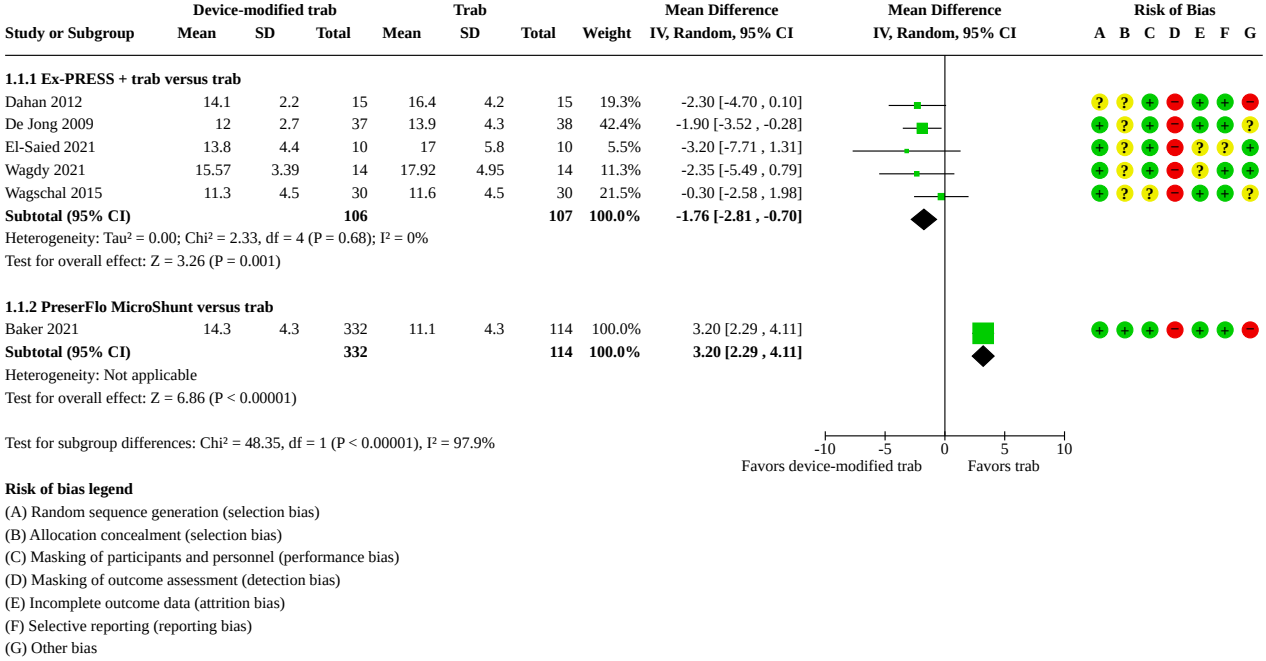
Six trials comparing trabeculectomy plus Ex-PRESS versus standard trabeculectomy reported postoperative IOP (Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015; El-Saied 2021; Wagdy 2021). One trial comparing PreserFlo MicroShunt versus trabeculectomy reported postoperative IOP (Baker 2021).

Dahan 2012 reported IOP data at the last follow-up time point and presented a figure with IOP reduction over time. The trial encompassed 30 eyes of 15 participants at one year, 20 eyes of 10 participants at two years, and 14 eyes of seven participants at 30 months (last follow-up). Upon our request, the study investigators shared their original data, so we were able to calculate the mean change in IOP from baseline to one-year follow-up and postoperative IOP at various follow-up time points (months six, 12, and 24). We did not combine trials of Ex-PRESS and PreserFlo MicroShunt due to substantial statistical and clinical heterogeneity. We instead performed meta-analyses for this outcome by the device.

Our primary time frame was at one year, in the subgroup comparing trabeculectomy plus Ex-PRESS versus trabeculectomy, five trials comprising 213 eyes reported mean IOP (Dahan 2012; De Jong 2009; Wagschal 2015; El-Saied 2021; Wagdy 2021). The use of Ex-PRESS may lead to a slightly improved IOP reduction at one year compared to standard trabeculectomy (MD −1.76 mmHg, 95% CI −2.81 to −0.70; I^2 = 0%; Analysis 1.1; Figure 3). Netland 2014 did not provide quantitative data, but reported that there was no between-group difference in IOP reduction at one year. We rated the certainty of evidence as low, downgrading for risk of bias and limitations in the design. The trial comparing PreserFlo MicroShunt versus trabeculectomy reported a mean IOP of 446 eyes at one year (Baker

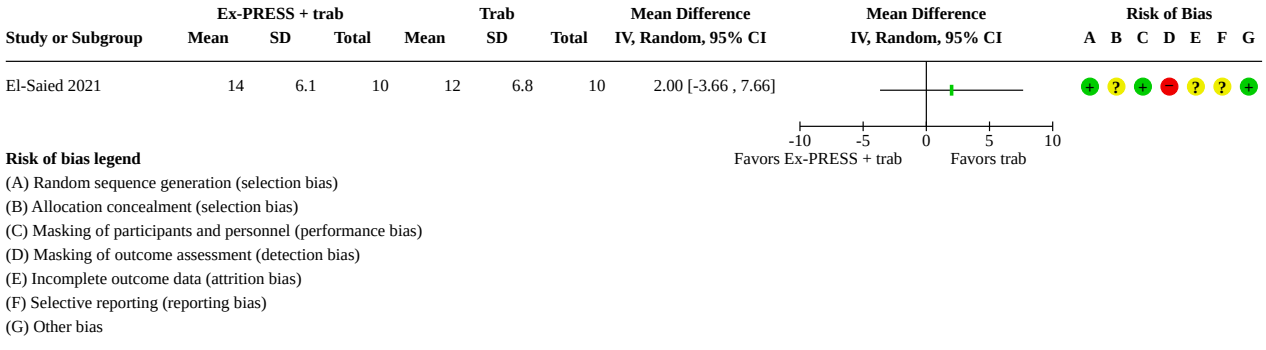
2021). We found that the PreserFlo MicroShunt group had a higher IOP than the trabeculectomy group (MD 3.20 mmHg, 95% CI 2.29 to 4.11). We rated the certainty of evidence as moderate, downgrading one level for risk of bias. There was evidence of a difference in mean IOP at one year between the Ex-PRESS and PreserFlo MicroShunt groups when tested using the Cochrane test (P < 0.001).

Figure 3. Forest plot of comparison: 2 Trabeculectomy + Ex-PRESS versus trabeculectomy, outcome: postoperative intraocular pressure at one year.



Only El-Saied 2021 provided data, so we could calculate the mean change in IOP from baseline to one-year follow-up. It is uncertain whether the Ex-PRESS led to improved IOP reduction at one year compared to standard trabeculectomy (MD 2.00, 95% CI −3.66 to 7.66; P = 0.49; Analysis 1.2; Figure 4). We rated the certainty of evidence as very low, downgrading two levels for risk of bias due to limitations in the design and implementation of available studies and one level for imprecision.

Figure 4. Forest plot of comparison: Trabeculectomy (Trab) + Ex-PRESS versus trabeculectomy (Trab), outcome: change of intraocular pressure from baseline at one year.



At six months, in the subgroup comparing trabeculectomy plus Ex-PRESS versus trabeculectomy, five trials comprising 253 eyes reported mean IOP (Dahan 2012; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015). It was unclear whether the use of Ex-PRESS leads to IOP reduction at six months compared to standard trabeculectomy (MD −0.10 mmHg, 95% CI −1.40 to 1.20; I^2 = 54%; Analysis 1.3). The study comparing PreserFlo MicroShunt versus trabeculectomy suggested that the conventional trabeculectomy led to a further reduction of IOP at six months (MD 3.00 mmHg, 95% CI 1.62 to 4.38; Analysis 1.3).

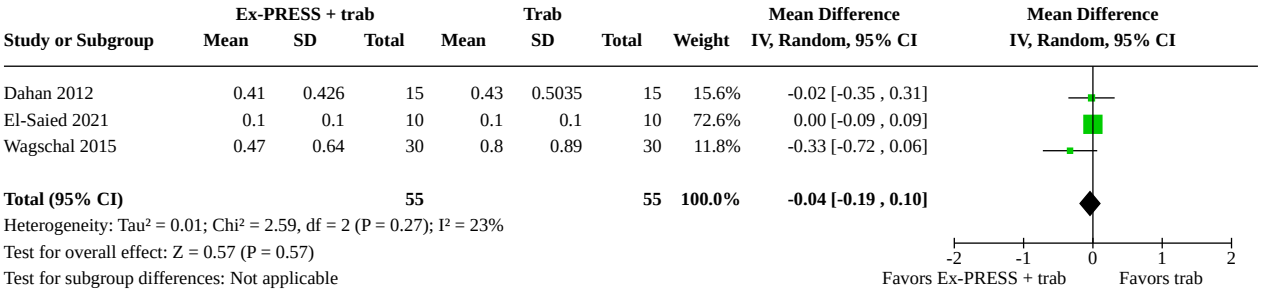
At six months, only El-Saied 2021 reported the mean change in IOP from baseline. It was unclear whether the use of Ex-PRESS improved the IOP reduction at six months compared to standard trabeculectomy (MD 0.20, 95% CI −5.46 to 5.86; Analysis 1.5).

At two years, three trials of Ex-PRESS comprising 212 eyes reported mean IOP outcome (Dahan 2012; De Jong 2009; Netland 2014). Overall estimate suggested that Ex-PRESS may slightly improve IOP reduction at two years compared to standard trabeculectomy (MD −1.38 mmHg, 95% CI −2.66 to −0.09; I^2 = 21%; Analysis 1.4).

Postoperative mean best-corrected visual acuity at one year

Three studies reported logMAR BCVA at one year (Dahan 2012; El-Saied 2021; Wagschal 2015). It is uncertain whether Ex-PRESS prevents loss in BCVA compared to standard trabeculectomy (MD −0.04, 95% CI −0.19 to 0.10; I^2= 23%; 110 eyes; Analysis 1.6; Figure 5).

Figure 5. Forest plot of comparison: 1 Trabeculectomy (Trab) + Ex-PRESS versus trabeculectomy (Trab), outcome: postoperative logMAR best-corrected visual acuity at one year.



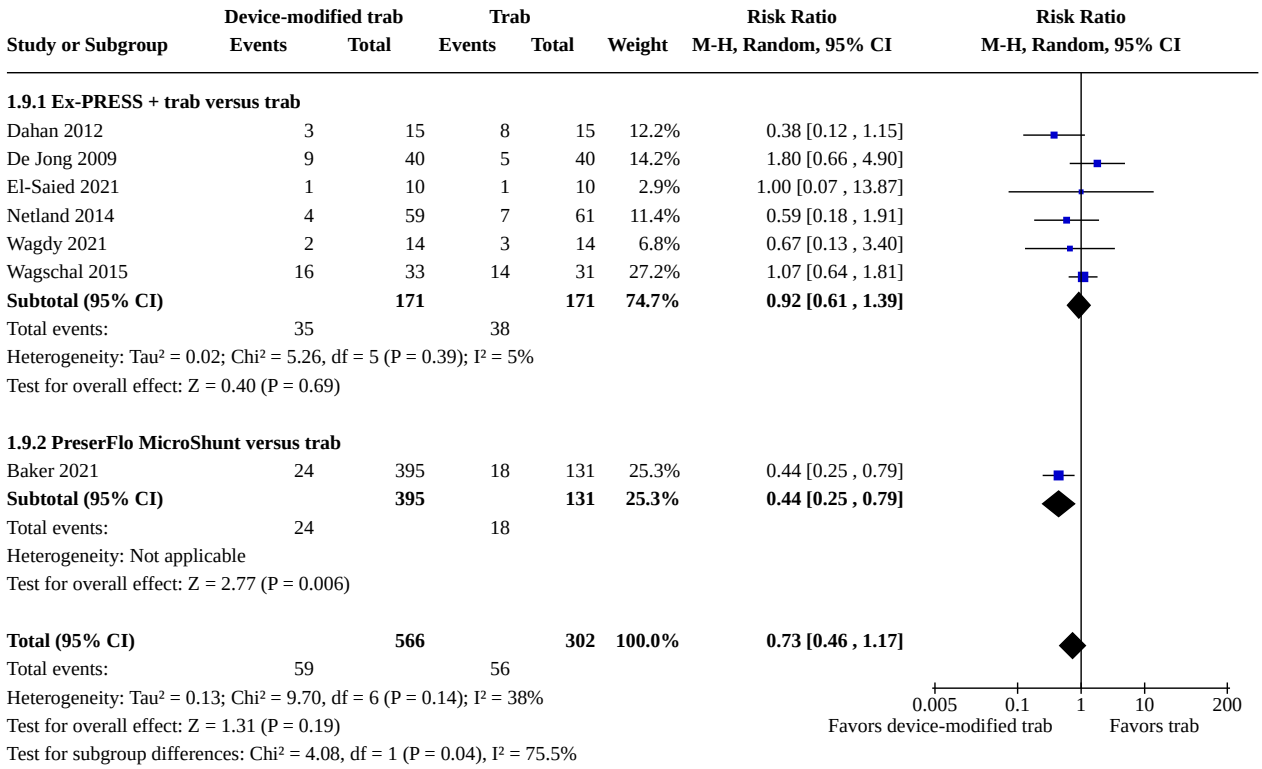
Wagschal 2015 and El-Saied 2021 reported logMAR BCVA at one year, but Dahan 2012 did not publish quantitative data for this outcome. The authors of Dahan 2012 provided us with original data from which we calculated the postoperative mean logMAR BCVA to be mean 0.41 (standard error [SE] 0.11) for the Ex-PRESS plus trabeculectomy group and 0.43 (SE 1.33) for the standard trabeculectomy group at one year.

Although De Jong 2009 also assessed visual acuity preoperatively and at each follow-up visit, quantitative data were not reported. They reported that visual acuity remained equivalent in most participants, with no difference between the groups at one year. Wagdy 2021 did not report quantitative data on visual acuity. They reported one case of visual deterioration in the trabeculectomy group. We rated the certainty of evidence as low, downgrading two levels for high risk of bias due to limitations in the design and implementation of available studies.

Proportion of participants who were drop-free at one year

Two trials (48 participants) reported the proportion of participants who were drop-free at one year; both used the Ex-PRESS (El-Saied 2021; Wagdy 2021). The effect of Ex-PRESS on the proportion of participants who were drop-free at one year compared with standard trabeculectomy was uncertain (RR 2.04, 95% CI 0.42 to 9.82; P = 0.09; I^2 = 64%; Analysis 1.7; Figure 6). We rated the certainty of evidence as very low, downgrading two levels for high risk of bias and one level for imprecision. The use of the PreserFlo MicroShunt may lead to a lower chance of drop-free at one year (RR 0.84, 95% CI 0.77 to 0.93; 509 eyes). We rated the certainty of evidence as moderate, downgrading one level for risk of bias. There was no evidence of a difference between the Ex-PRESS groups and the PreserFlo MicroShunt group when tested using the Cochrane test (P = 0.27). We did not combine trials of Ex-PRESS and PreserFlo MicroShunt due to substantial statistical and clinical heterogeneity.

Figure 6. Forest plot of comparison: 1 Trabeculectomy (Trab) + Ex-PRESS versus trabeculectomy (Trab), outcome: 1.5 Complications.



Mean number of intraocular pressure-lowering medications at one year

Three trials (170 participants) reported the mean number of IOP-lowering medications at one year; all used the Ex-PRESS (Dahan 2012; De Jong 2009; Wagschal 2015). Ex-PRESS may lead to using a lower number of IOP-lowering medications at one year compared to standard trabeculectomy (MD −0.34, 95% CI −0.62 to −0.07; I^2 = 0%; Analysis 1.8). In contrast, the trial of PreserFlo MicroShunt (509 participants) reported a non-significant effect in the number of IOP-lowering medications at one year in both groups (MD 0.30, 95% CI 0.11 to 0.49; Analysis 1.8) (Baker 2021).

Postoperative mean visual field change at one year

No studies reported postoperative mean visual field change at one year.

Quality of life at one year

No studies reported quality of life at one year.

Complications

Eight trials reported complications in 868 eyes during their respective follow-up visits (Baker 2021; Dahan 2012; De Jong 2005; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015). We conducted a meta-analysis using the proportion of participants with each complication in each group (Analysis 1.9; Analysis 1.10; Analysis 1.11; Analysis 1.12; Analysis 1.13; Analysis 1.14; Figure 6). De Jong 2005 did not report any complications.

Intraocular pressure less than 5 mmHg (hypotony) or shallow anterior chamber

Seven trials reported either hypotony or shallow anterior chamber, six using the Ex-PRESS (Dahan 2012; De Jong 2009; El-Saied 2021; Netland 2014; Wagdy 2021; Wagschal 2015), and one using the PreserFlo MicroShunt (Baker 2021). Overall, we found that participants who received device-modified trabeculectomy may have a lower risk of hypotony, but the evidence was uncertain (RR 0.73, 95% CI 0.46 to 1.17; I^2 = 38%; P = 0.14; Analysis 1.9).

In the subgroup of Ex-PRESS trials comprising 342 eyes, there was no evidence of a difference in the risk of developing hypotony or shallow anterior chamber between the two groups (RR 0.92, 95% CI 0.61 to 1.39; I^2 = 5%). In contrast, in the subgroup of a PreserFlo MicroShunt trial comprising 526 eyes, there was a lower risk of hypotony or shallow anterior chamber with PreserFlo MicroShunt compared with trabeculectomy (RR 0.44, 95% CI 0.25 to 0.79; Analysis 1.9).

Bleb leakage

Six trials reported bleb leakage, five using the Ex-PRESS (Dahan 2012; De Jong 2009; El-Saied 2021; Netland 2014; Wagschal 2015), and one using the PreserFlo MicroShunt (Baker 2021). Overall, participants who received device-modified trabeculectomy may have a higher risk of bleb leakage than the standard trabeculectomy but the evidence was uncertain (RR 0.63, 95% CI 0.40 to 1.02; P = 0.71; I^2 = 0%; Analysis 1.9).

In the subgroup of Ex-PRESS trials comprising 314 eyes, it is unclear whether Ex-PRESS prevents bleb leakage compared to standard

trabeculectomy (RR 0.99, 95% CI 0.45 to 2.16; I^2 = 0%; Analysis 1.10). In contrast, in the subgroup of a PreserFlo MicroShunt trial comprising 526 eyes, participants who received PreserFlo MicroShunt had a lower risk of bleb leakage compared with participants with trabeculectomy (RR 0.51, 95% CI 0.28 to 0.90; P = 0.02; Analysis 1.10).

Reoperations for glaucoma

Five trials reported reoperations for glaucoma, four using the Ex-PRESS (Dahan 2012; De Jong 2009; El-Saied 2021; Wagschal 2015), and one using the PreserFlo MicroShunt (Baker 2021). Overall, there was no difference in the risk of reoperation for glaucoma between device-modified trabeculectomy and trabeculectomy (RR 0.69, 95% CI 0.24 to 1.98; P = 0.20; I^2 = 33%). In the subgroup of Ex-PRESS trials comprising 194 eyes, there was no difference in risk of reoperation for glaucoma between groups (RR 0.34, 95% CI 0.09 to 1.26; I^2 = 0%; Analysis 1.11). In the subgroup of a PreserFlo MicroShunt trial comprising 526 eyes, there was no difference in risk of reoperations for glaucoma between groups (RR 1.30, 95% CI 0.77 to 2.22; Analysis 1.11).

Device migration or exposure

Two trials of Ex-PRESS comprising 144 eyes reported this complication (De Jong 2009; Wagschal 2015). Obviously, device migration or exposure occurred only in the device-modified trabeculectomy group. De Jong 2005 found that 1/40 participants (2.5%) reported device migration or exposure and Wagschal 2015 reported that 2/33 participants (6%) reported device migration or exposure. We did not perform a meta-analysis on this outcome as device migration or exposure cannot occur with standard trabeculectomy.

Cataract surgery

Five trials reported subsequent requirement for cataract surgery after glaucoma surgery, four using the Ex-PRESS (Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015), and one trial using the PreserFlo MicroShunt (Baker 2021). Overall, device-modified trabeculectomy was associated with less frequent subsequent cataract surgery (RR 0.46, 95% CI 0.27 to 0.80; I^2 = 0%). Subgroup analysis in the Ex-PRESS group comprising 294 eyes showed that Ex-PRESS may lead to a lower risk of subsequent cataract surgery than standard trabeculectomy (RR 0.34, 95% CI 0.14 to 0.80; I^2 = 0%; only 3 studies included in meta-analysis as 1 study had no events in either group). In the subgroup of a PreserFlo MicroShunt trial comprising 526 eyes, it was unclear whether the use of PreserFlo MicroShunt reduced subsequent cataract surgery (RR 0.57, 95% CI 0.28 to 1.17; P = 0.13; Analysis 1.12).

Endophthalmitis

Only Netland 2014 reported endophthalmitis. The trial found that only one participant who underwent a standard trabeculectomy developed endophthalmitis, and there was no difference on risk of endophthalmitis between the Ex-PRESS plus trabeculectomy group and standard trabeculectomy (RR 0.34, 95% CI 0.01 to 8.29; Analysis 1.13). We rated the certainty of evidence for this complication as very low, downgrading two levels for high risk of bias, and one level for imprecision.

Loss of vision of more than two lines or loss of light perception

Only Baker 2021 reported the proportion of participants with loss of vision of more than two lines, or loss of light perception. PreserFlo MicroShunt appears to be associated with less vision loss, but the evidence was uncertain (RR 0.57, 95% CI 0.30 to 1.07; P = 0.08; Analysis 1.14). Dahan 2012 reported no cases with loss of vision of more than two lines in either group.

DISCUSSION

Summary of main results

The addition of an Ex-PRESS to trabeculectomy may result in lower IOP than standard trabeculectomy, based on data from five trials comprising 213 eyes (Dahan 2012; De Jong 2009; El-Saied 2021; Wagdy 2021; Wagschal 2015). PreserFlo MicroShunt may not lower IOP as well as standard trabeculectomy. Data from three studies comprising 55 eyes found no difference in CVA between device-modified and standard trabeculectomy groups at one year (Dahan 2012; El-Saied 2021; Wagschal 2015). There was no difference in the number of IOP-lowering medications at one year between groups. PreserFlo MicroShunt may prevent postoperative hypotony and bleb leakage compared with trabeculectomy. Other complications such as reoperations for glaucoma, device migration, endophthalmitis, or loss of vision were similar between the two groups. Device-modified trabeculectomy appears to have a lower risk of subsequent cataract surgery.

Overall completeness and applicability of evidence

For Ex-PRESS, of the seven included trials, five were powered to detect between-group differences (Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015; Wagdy 2021). These trials were conducted in China, South Africa, the Netherlands, the USA, Canada, and Egypt. They included a mix of white, African American, Asian, and Indian participants. In four trials, the mean age was around 65 years (Dahan 2012; De Jong 2009; Netland 2014; Wagschal 2015), whereas Wagdy 2021 included participants aged between 42 and 55 years. Since six trials included participants with OAG, the Ex-PRESS results are most applicable to people with OAG (Dahan 2012; De Jong 2005; De Jong 2009; Netland 2014; Wagdy 2021; Wagschal 2015). Wagdy 2021 included participants with failed trabeculectomy previously.

For the PreserFlo MicroShunt, one study comparing PreserFlo MicroShunt with trabeculectomy was conducted in the US and Europe (Baker 2021). This study included a mix of white, Black/African American, and Asian participants, with a mean age of around 65 years. There was a higher proportion of Black/African American participants in the PreserFlo MicroShunt group compared with the trabeculectomy group. This study included participants with POAG and excluded participants with secondary OAG or ACG. Thus, the effectiveness and safety in people with other types of glaucoma remain uncertain for both devices.

We found no eligible trials assessing the XEN Gel Stent.

Quality of the evidence

Overall, the agreement in absolute IOP measurements at one year across the included studies was high within each device. The widths of the 95% CI for MD in IOP measurement between device-modified and standard trabeculectomy were small, ranging from −2.81 mmHg to −0.7 mmHg for the Ex-PRESS and from 2.29 mmHg to 4.11 mmHg for the PreserFlo MicroShunt. Only one small study of Ex-PRESS reported mean change in IOP, finding it varied, with a large 95% CI ranging from −3.66 mmHg to 7.66 mmHg.

Most of the trials were at high risk of detection bias for lack of masking outcome assessors. Most trials had either missing or inadequate information in trial reports to assess the risk of selection bias, especially in unclear allocation concealment. Furthermore, some Ex-PRESS and PreserFlo MicroShunt studies had potential conflicts of interest due to receiving funding support from the device manufacturer, which may suggest high likelihood of bias in the study design and implementation of available studies. Overall, we graded the certainty of the evidence as low or very low for most outcomes due to potential high risks of detection bias and imprecision.

Potential biases in the review process

We conducted comprehensive electronic searches for studies with no imposed date or language restrictions to minimize potential biases in the study selection process. We followed standard Cochrane Review methodology.

Agreements and disagreements with other studies or reviews

Ex-PRESS plus trabeculectomy versus trabeculectomy

Our meta-analyses of five trials (at one year) and three trials (at two years) found that the use of Ex-PRESS plus trabeculectomy may lead to greater IOP reduction compared with standard trabeculectomy, while it was uncertain whether the risk of complications, such as hypotony, bleb leakage, operations, device migration, and endophthalmitis differed between the groups. The proportion of participants requiring subsequent cataract extraction was lower in the device-modified trabeculectomy group than in the trabeculectomy group.

One retrospective comparative series by Maris 2007 of 100 eyes, Good 2011 of 70 eyes, Moisseiev 2015 of 200 eyes, and Bustros 2017 of 56 eyes found no difference between Ex-PRESS plus trabeculectomy and trabeculectomy in lowering IOP. One retrospective review of 153 eyes showed a lower risk of postoperative hypotony with Ex-PRESS plus trabeculectomy compared with trabeculectomy, but no difference in lowering IOP (Marzette 2011).

One systematic review concluded that Ex-PRESS has the same effectiveness in IOP reduction compared with standard trabeculectomy, with a lower frequency of hypotony and hyphema compared with standard trabeculectomy (Wang 2013a). However, these pooled results were from a mix of randomized controlled trials, prospective non-randomized controlled trials, and retrospective studies, which limits the reliability of their inference.

One meta-analysis found no reduction in IOP between Ex-PRESS plus trabeculectomy and standard trabeculectomy, and a lower frequency of hyphema with Ex-PRESS plus trabeculectomy (Chen 2014). The other complications, such as hypotony, shallow or flat anterior chamber, choroidal effusion, and encapsulated bleb were no different between groups. However, this review was flawed in that it mixed the different follow-up periods from different studies for IOP control (e.g. six months and one year) in one meta-analysis. Also, one included study was a subset of another (both were references from Wagschal 2015), and its meta-analyses of complications included both studies, thereby double-counting the data.

One meta-analysis reported that Ex-PRESS implantation achieved better outcomes in terms of long-term IOP control, complete success rate, and lower numbers of IOP lowering medications (Zhang 2022). However, this review included trials with short follow-up periods and mixed the different follow-up periods for IOP. Also, this review compared Ex-PRESS, trabeculectomy, and Ahmed glaucoma valve implant together, including more participants with secondary glaucoma compared with studies included in our review.

Some of the reviews, including the one presented here, reported that Ex-PRESS plus trabeculectomy may lead to greater IOP reduction compared with standard trabeculectomy, whereas some other reviews reported there was no difference in reduction of IOP between Ex-PRESS and trabeculectomy. Some reviews reported that Ex-PRESS showed a lower rate of complications, such as hypotony and hyphema. Only our review reported that the risk of subsequent cataract extraction was lower in Ex-PRESS plus trabeculectomy group than the standard trabeculectomy group.

PreserFlo MicroShunt versus trabeculectomy

Baker 2021 is the only study in our meta-analysis that compared PreserFlo MicroShunt versus trabeculectomy. This study found that the PreserFlo MicroShunt was inferior in IOP-lowering effect compared with conventional trabeculectomy, but produced smaller proportions of participants with hypotony and bleb leakage compared with the trabeculectomy group. One non-randomized study of 52 eyes that were treated with PreserFlo MicroShunt or trabeculectomy found no differences in the reduction of IOP (Pillunat 2021). The incidence of early (within four weeks) hypotony was higher in the PreserFlo MicroShunt group compared with the trabeculectomy group, but the incidences of hypotony requiring anterior chamber formation, hypotony leading to choroidal effusion, hypotony maculopathy, or prolonged hypotony were not different between groups. We found no previous meta-analysis of PreserFlo MicroShunt versus standard trabeculectomy.

AUTHORS' CONCLUSIONS

Implications for practice

Our findings suggest that the use of Ex-PRESS plus trabeculectomy may lead to slightly greater intraocular pressure (IOP) reduction at one-year follow-up than standard trabeculectomy. The PreserFlo MicroShunt was inferior to trabeculectomy with respect to mean IOP at one-year follow-up but it may be effective in preventing postoperative hypotony. Overall complication rates were not different between the two groups, but device-modified trabeculectomy is associated with less frequent need for cataract extraction after trabeculectomy. Conclusions for each type of device are limited due to methodological concerns for bias and poor reporting of outcomes. Currently, these devices increase costs for insurance companies and patients compared with those incurred for a standard trabeculectomy. Whether the greater IOP reduction or improved safety that can be achieved with these devices is sufficient to outweigh these additional costs will need to be determined on a case-by-case basis. As it has been reported that a 1 mmHg reduction in IOP can be associated with a 10% decrease in the risk of glaucomatous progression, the additional IOP reduction that may be obtained at one-year follow-up may be valuable in selected populations (Heijl 2002). As these devices are also intended to reduce surgical risk and simplify postoperative

management, their benefits and harms need to be considered for each individual patient.

Implications for research

Because the certainty in evidence of this review is low, better-quality trials with higher-certainty evidence are warranted to determine the comparative effectiveness of all devices included in this review. These studies are limited and the applicability of the evidence to other populations or settings remains unclear. Therefore, more research is needed to generate evidence for or against the use of devices such as Ex-PRESS, PreserFlo MicroShunt, and XEN Gel Stent.

In the absence of definitive evidence, we need more trials of better quality for most comparisons and outcomes. These should account for losses to follow-up at each follow-up time point measured and for the correlation of outcomes between two eyes when applicable. They also need to consider the appropriate use of adjunctive agents, such as mitomycin C, in both groups to ensure comparability. It would be helpful for future trials to specify the types of glaucoma, and also to consider stratifying participants by type of glaucoma, race, and perhaps lens status. Data reporting needs to be improved by reporting differences between groups to allow more robust inferences when applicable. Future trials should also report the elements of trial quality identified above and ensure consistency between protocols and published studies.

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- Sign-off Editors (final editorial decision): Dr Tianjing Li (University of Colorado Anschutz Medical Campus) and Dr Gianni Virgilli (Queen's University Belfast)
- Managing Editor and Assistant Managing Editors (selected peer reviewers, collated peer-reviewer comments): Anupa Shah (Queen's University Belfast); Louis Leslie (University of Colorado Anschutz Medical Campus), and Genie Han (Johns Hopkins University)
- Methodologist (provided methodological and editorial guidance to authors, edited the article): Sueko Ng and Alison Su-Hsun Liu (University of Colorado Anschutz Medical Campus)
- Information Specialist: Lori Rosman (CEV)
- Copy Editor: Anne Lawson (Central Production Service, Cochrane)
- Peer reviewers: Renee Bovelle (Howard University), Anthony King (Nottingham University)

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Baker 2021

Study characteristics	
Methods	**Study design:** multicenter, parallel-group, randomized controlled trial
	Country: the US, France, Italy, the Netherlands, Spain, the UK

Baker 2021 *(Continued)*

	Number randomized: 527 eyes of 527 participants total; 395 for PreserFlo MicroShunt + MMC and 132 for trabeculectomy + MMC **Exclusions after randomization:** none reported **Losses to follow-up**: 21 for total; 14 for PreserFlo MicroShunt + MMC and 7 for trabeculectomy + MMC **Unit of analysis:** eye **Number analyzed:** 527 eyes of 527 participants total; 395 for PreserFlo MicroShunt + MMC and 132 for trabeculectomy + MMC **How were missing data handled?** imputed **Power calculation:** (quote) "sample size calculations were based on a Z-test with normal distribution approximation and assuming an annual dropout rate of 6%."
Participants	**Mean age:** none reported for overall; 66.4 (SD 9.3) years for PreserFlo MicroShunt + MMC group; 67.8 (SD 9.3) years for trabeculectomy + MMC group **Gender** 181/395 (45.8%) men and 214/395 (54.2%) women in PreserFlo MicroShunt + MMC group; 59/132 (44.7%) men and 73/132 (55.3%) women in trabeculectomy + MMC group **Inclusion criteria:** aged 40–85 years with mild-to-severe POAG inadequately controlled on maximum tolerated medical therapy, with IOP > 15 mmHg and < 40 mmHg and a visual field mean deviation of ≤ −3.00 dB **Exclusion criteria:** secondary OAG such as post-trauma, pseudoexfoliative, or pigment dispersion (pigmentary glaucoma); ACG; aphakia; vision level of no light perception; previous incisional ophthalmic surgery involving the conjunctiva; prior clear corneal cataract, angle, or trabecular meshwork surgery conducted within the past 6 months; ocular steroid use in the planned study eye or systemic steroid use any time within 3 months of the procedure; BCVA < 20/80 in the non-study eye; and laser surgery within 90 days of enrollment **Equivalence of baseline characteristics:** yes, apart from a higher proportion of Black/African American people (18.0% in the PreserFlo MicroShunt group vs 8.3% in the trabeculectomy group; P < 0.01).
Interventions	**Intervention 1:** PreserFlo MicroShunt + MMC **Intervention 2:** trabeculectomy + MMC **Length of follow-up** Planned: 1 years Actual: 1 years
Outcomes	**Primary outcomes, as defined:** ≥ 20% reduction in mean diurnal IOP from baseline at 1 year follow-up visit without increasing the number of glaucoma medications. **Secondary outcomes, as defined:** mean diurnal IOP change from baseline at 1 year; requirement for postoperative intervention by 1 year; number of glaucoma medications per participant at each follow-up visit; incidence of adverse events; presence of cataract in phakic eyes; time for postoperative BCVA to return to baseline; change in endothelial cell density **Intervals at which outcomes assessed:** 1 day; 1 and 4 weeks; 3, 6, 12, 18, and 24 months
Notes	**Publication type:** published article

Baker 2021 *(Continued)*

Funding sources: InnFocus Inc, a Santen Pharmaceutical Co Ltd Company and Santen Inc (quote: "the sponsor participated in the design and conduct of the study, data collection, and management. This analysis was also sponsored by Santen Inc., which participated in the data analysis, interpretation of the data, and preparation, review, and approval of the manuscript").

Disclosures of interest: "N.D.B.: Consultant/Advisor: Molteno Ophthalmic, Santen; Investigator: Santen.

H.S.B.: Consultant/Advisor: Santen; Lecture fees Aerie, Bausch & Lomb.

M.R.M.: Consultant/Advisor: Aerie, Alcon, Allergan, Qura, Santen; Lecture fees: Aerie, Alcon, Allergan, Bausch & Lomb, Iridex, MedEdicus, Novartis; Grant support: Aerie, Alcon, Allergan, Bausch & Lomb, Glaukos, InnFocus, Iridex, Santen; Equity/Owner: Qura.

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S.D.V.: Consultant/Advisor: Aerie, Alcon, Allergan, Bausch & Lomb, Carl Zeiss Meditec, Glaukos, Iridex, iSTAR Medical, Ivantis, New World Medical, Sight Sciences, Volk Optical; Grant support: Aerie, Alcon, Allergan, Bausch & Lomb, Carl Zeiss Meditec, Glaukos, Ivantis, RxSight, Santen, Sight Sciences; Equity/Owner: Alphaeon, Ivantis, O3 Optix; Patents/Royalty: Iridex, Volk Optical.

A.K.K.: Consultant/Advisor: Gore Inc, Ivantis, Reliance/Haag-Streit; Lecture fees: Aerie, Ivantis; Grant support: Glaukos, InnFocus, Santen.

B.E.F.: Consultant/Advisor: Alcon, Bausch & Lomb, Eyenovia, Glaukos, InnFocus, iSTAR Medical, Ivantis, New World Medical, l, Sight Sciences; Grant support: Eyenovia, Glaukos, InnFocus, iSTAR Medical, Ivantis, Santen, Sight Sciences.

D.S.G.: Consultant/Advisor: Allergan, MicroOptx, New World Medical, Reichert Instruments, Santen; Lecture fees: Aerie, Allergan, Bausch & Lomb, New World Medical, Reichert Instruments; Grant support: Allergan.

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J.F.P.: Consultant/Advisor: Aerie, Allergan, Cornea Gen, Glaukos, New World Medical, Santen; Grant support: Allergan."

Trial registry: NCT01881425

Study period: December 2015 to November 2017

Subgroup analyses: (quote) "Prespecified subgroup analyses in patients with baseline mean diurnal IOP<18, 18–20, and >21 mmHg were conducted."

Publication language: English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Study authors clearly reported that randomization was performed in a 3:1 ratio, which was stratified by investigational site and within site by lens status. The baseline characteristics in both groups were similar, suggesting effective randomization.
Allocation concealment (selection bias)	Low risk	Allocation concealment was performed using envelopes containing the randomization assignments.

Baker 2021 *(Continued)*

Masking of participants and personnel (performance bias)	Low risk	Participants were masked to the assignment, and it is unlikely that they were aware of their group assignment after the operation given the similar possible complications.
Masking of outcome assessment (detection bias)	High risk	Outcome assessors were not masked to the participant's group assignment. The study authors did not explicitly specify the method used to measure IOP. However, as some methods of IOP measurement, e.g. using Goldmann applanation, could be subjective, it is likely that the unmasking of outcome assessors would affect the outcome.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 3–5% of each group were lost to follow-up. This missingness was unlikely related to worsening participants' health status due to device or procedure.
Selective reporting (reporting bias)	Low risk	The trial was analyzed according to the prespecified plan in terms of outcome measurements (e.g. definition, scales, and time points) within each outcome.
Other bias	High risk	This study was sponsored by the InnFocus company and many of the authors had industrial support.

Dahan 2012

Study characteristics	
Methods	**Study design:** paired-eye randomized controlled trial **Country:** South Africa **Number randomized:** 30 eyes of 15 participants total; each participant had 1 eye in each intervention group **Exclusions after randomization:** none reported **Losses to follow-up:** 0 up to 1 year after surgery; 1 participant died at 13 months and 2 were subsequently lost to follow-up **Unit of analysis:** eye **Number analyzed:** 30 eyes of 15 participants total; each participant had 1 eye in each intervention group **How were missing data handled?** no missing data at 1 year **Power calculation:** a power of 96% to detect a 2 mmHg IOP difference between groups
Participants	**Mean age:** 65 years; not reported by intervention group **Gender:** 10/15 (67%) men and 5/15 (33%) women; not reported by intervention group **Inclusion criteria:** aged ≥ 18 years and presented with medically uncontrolled POAG requiring bilateral incisional surgery for IOP reduction. Patients with prior cataract operation or failed filtration surgery in either eye were eligible if surgery took place ≥ 3 months prior to enrolment **Exclusion criteria:** any form of glaucoma other than POAG; history of active uveitis; any ocular abnormality that would preclude accurate IOP assessment **Equivalence of baseline characteristics:** yes
Interventions	**Intervention 1:** trabeculectomy + MMC + Ex-PRESS X200

Dahan 2012 *(Continued)*

	Intervention 2: trabeculectomy + MMC **Length of follow-up** Planned: ≥ 1 year Actual: all participants followed ≥ 1 year; the longest follow-up visit for a participant was 30 months
Outcomes	Primary and secondary outcomes not distinguished **Outcomes, as reported:** IOP, visual acuity, number of medicines for IOP control, complications **Intervals at which outcomes assessed:** 1 and 7 days; 1, 3, 6, 9, 12, 18, 24, and 30 months after surgery
Notes	**Publication type:** published article **Funding sources:** (quote) "the study was supported by a financial grant from Alcon Laboratories." **Disclosures of interest:** "E Dahan is a paid consultant in Alcon Laboratories. GJ Ben Simon and A Lafuma has no financial or proprietary interest in any of the drugs or materials mentioned in this study. A Lafuma is employed by CEMKAEVAL, a company that provides services in statistical analyses and epidemiology." **Trial registry:** NCT00698438 **Study period:** not reported **Subgroup analyses:** none reported **Publication language:** English Study authors contacted and outcome data shared (IOP reduction, number of medications, and mean IOP at 1 and 7 days; and 1, 3, 6, 12, 18, 24, and 30 months after surgery)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomisation of contralateral operations was achieved by opening an envelope in which the procedure (trabeculectomy or Ex-PRESS implantation) that would be applied to the first eye was stated, thereby determining the procedure in the other eye." Comment: the method of randomization was not described and thus its adequacy could not be judged.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.
Masking of participants and personnel (performance bias)	Low risk	Because trabeculectomy is a surgical procedure with informed consent, masking of the participants and personnel becomes impossible. However, given that (quote) "after sub-tenonian local anaesthesia, surgery was performed by one experienced surgeon (ED), for consistency, using a standardized technique for both procedures," the risk of performance bias was comparably low for a surgical procedure.
Masking of outcome assessment (detection bias)	High risk	The study mentioned: (quote) "It was not possible to mask the surgical technique as trabeculectomy is easily differentiated from Ex-PRESS implantation during postoperative follow-ups. However, this limitation is overcome by the fact that all patients were followed up concurrently by their referring ophthalmologists from the first month postoperatively till completion of the study."

Dahan 2012 *(Continued)*

		Comment: although it was not possible to mask outcome assessors, devices could be easily seen during exam of the eye.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 15 patients were followed-up for 12 months after surgery. One patient died 13 months after surgery and two patients were subsequently lost to follow-up. All data available for these patients (i.e., up to 1 year) are included in the analyses."
Selective reporting (reporting bias)	Low risk	The study was registered at www.ClinicalTrials.gov. All defined outcomes in www.ClinicalTrials.gov were reported in full text. Complete and qualified success was reported and defined using IOP.
Other bias	High risk	Received industry monetary support from device manufacturer; (quotes) "ED is a paid consultant to Alcon Laboratories." "The study was supported by a financial grant from Alcon Laboratories." To consider intraperson correlation between eyes, the analysis used Wilcoxon matched-pairs t-test to compare preoperative and final IOP values. No other sources of bias identified.

De Jong 2005

Study characteristics	
Methods	**Study design:** parallel-group randomized controlled trial (11 participants both eyes included) **Country:** the Netherlands **Number randomized:** 120 eyes of 109 participants; not reported by intervention group **Exclusions after randomization:** not reported **Losses to follow-up:** not reported **Unit of analysis:** eye **Number analyzed:** not reported **How were missing data handled?** not reported **Power calculation:** not reported
Participants	**Mean age:** overall not reported 61.8 years for trabeculectomy + Ex-PRESS R50 implanted under a scleral flap group; 61.8 years for trabeculectomy + Ex-PRESS R50 implanted under the conjunctiva group; 68.7 years for trabeculectomy group **Gender:** not reported **Inclusion criteria:** OAG; medical treatment failure, indicated for glaucoma surgery **Exclusion criteria:** not reported **Equivalence of baseline characteristics:** yes
Interventions	**Intervention 1:** trabeculectomy + Ex-PRESS R50 implanted under a scleral flap

De Jong 2005 *(Continued)*

	Intervention 2: trabeculectomy + Ex-PRESS R50 implanted under the conjunctiva **Intervention 3:** trabeculectomy **Length of follow-up** Planned: not reported Actual: 6 months
Outcomes	Primary and secondary outcomes not distinguished **Outcomes, as reported:** success rate (defined as % IOP reduction and medication reduction), IOP, and use of IOP-lowering medications **Intervals at which outcomes assessed:** 6 months after surgery
Notes	**Publication type:** published abstract **Funding sources:** not reported **Disclosures of interest:** not reported **Trial registry:** not registered **Study period:** not reported **Subgroup analyses:** none reported **Publication language:** English Attempted to contact author, but unable to find contact information in abstract.

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.
Masking of participants and personnel (performance bias)	Unclear risk	Not reported.
Masking of outcome assessment (detection bias)	High risk	It is not possible to mask outcome assessors, as devices can be easily seen during eye exam.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported.
Selective reporting (reporting bias)	Low risk	Protocol was not available. All defined outcomes were reported.
Other bias	Unclear risk	Did not report source of support or conflict of interest. Insufficient information from the abstract.

De Jong 2009

Study characteristics	
Methods	**Study design:** parallel-group randomized controlled trial (2 participants both eyes included) **Number randomized:** 80 eyes of 78 participants total; 40 eyes in each group **Exclusions after randomization:** none reported **Losses to follow-up:** 5 eyes total at 1 year; 3 eyes in trabeculectomy + MMC + Ex-PRESS group; 2 eyes in trabeculectomy + MMC group **Unit of analysis:** eye **Number analyzed:** 75 eyes total; 37 eyes in trabeculectomy + MMC + Ex-PRESS group; 38 eyes in trabeculectomy + MMC group **How were missing data handled?** 5 eyes with missing data excluded from analysis **Power calculation:** a power of 80% to detect 32% between-group difference in IOP
Participants	**Country:** the Netherlands **Mean age:** 66 years; 62.3 years for trabeculectomy + MMC + Ex-PRESS group 68.9 years for trabeculectomy + MMC group **Gender:** 46/80 (58%) men and 34/80 (42%) women 19/40 (48%) men and 21/40 (52%) women in trabeculectomy + MMC + Ex-PRESS group; 27/40 (68%) men and 13/40 (32%) women in trabeculectomy + MMC group **Inclusion criteria:** aged > 18 years with a diagnosis of OAG that could not be controlled with maximal-tolerated medical therapy **Exclusion criteria:** any other ocular disease or previous ocular surgery other than cataract extraction **Equivalence of baseline characteristics:** not reported
Interventions	**Intervention 1:** trabeculectomy + Ex-PRESS **Intervention 2:** trabeculectomy **Length of follow-up** Planned: 5 years Actual: mean 262 weeks for Ex-PRESS group and 266 weeks for trabeculectomy group
Outcomes	**Primary outcome, as defined:** complete success (final IOP > 4 mmHg and ≤ 18 mmHg without antiglaucoma medication) and overall success (final IOP > 4 mmHg and ≤ 18 mmHg with or without medications) **Secondary outcomes, as defined:** IOP, postoperative medication use, surgical failure (IOP > 18 mmHg or the requirement for further glaucoma surgery), stringent target (final IOP > 4 mmHg and ≤ 15 mmHg), complications, and visual acuity

De Jong 2009 *(Continued)*

	Intervals at which outcomes assessed: 1 day; 1 week; 1, 3, and 6 months; and 1, 2, 3, 4, and 5 years after surgery **Length of follow-up** Planned: not reported Actual: 60-month follow-up
Notes	**Publication type:** published article **Funding sources:** Alcon Management SA, Geneva, Switzerland **Disclosures of interest:** (quote) "L. de J. has no proprietary interest in any of the products mentioned here." **Trial registry:** not registered **Study period:** October 2003 to November 2004 **Subgroup analyses:** none reported **Publication language:** English Authors contacted to retrieve number of participants lost to follow-up at 2–5 years, but no response received

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quotes: "The participants were assigned randomly to receive either Ex-PRESS implantation under a scleral flap (Group A), or trabeculectomy (Group B) in the study eye, according to a computer-generated randomization list." "Randomization was determined before surgery according to a block randomization sequence prepared by SAS (version 9.1; SAS Institute Inc., Cary, NC, USA)."
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.
Masking of participants and personnel (performance bias)	Low risk	Because trabeculectomy is a surgical procedure with informed consent, masking of the participants and personnel becomes impossible. However, given that a strict and standardized surgical protocol was followed and differences in the surgical protocol of the 2 groups were minimized, the risk of performance bias is comparably low for a surgical procedure.
Masking of outcome assessment (detection bias)	High risk	Quote: "Secondly, the evaluator was not blinded to the procedure used in each case; however, it is difficult to carry out truly blinded evaluation as the type of surgery used is usually visible to the assessor." Comment: but how they controlled the risk was not specified.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There are 2 articles related to this study, as reported in 2009, the number analyzed was 40 eyes per treatment group (no loss to follow-up); however, as reported in 2011, the number analyzed was 38 eyes per treatment group.
Selective reporting (reporting bias)	Low risk	Protocol was not available. All defined outcomes were reported.
Other bias	Unclear risk	Total industry support but no other source of potential bias identified.

De Jong 2009 *(Continued)*

	Quote: "There were no significant differences between the two groups except for age; the Ex-PRESS group (Group A) included significantly younger patients compared with the trabeculectomy group (Group B)."
	Comment: age-adjusted values are reported in de Jong 2011 and do not significantly change the results.

El-Saied 2021

Study characteristics	
Methods	**Study design:** parallel-group randomized controlled trial (2 participants both eyes included)
	Country: Egypt
	Number randomized: 20 eyes of 20 participants total; 10 eyes in each group
	Exclusions after randomization: not reported
	Losses to follow-up: not reported
	Unit of analysis: eye
	Number analyzed: 20 eyes total;
	10 eyes in trabeculectomy + Ex-PRESS mini shunt + MMC group;
	10 eyes in trabeculectomy + MMC group
	How were missing data handled? not reported
	Power calculation: the sample size was calculated using MedCalc 10.2.0.0, by referring to success rates of glaucoma surgeries for NVG from literature. The power and alpha were not reported.
Participants	**Mean age:** 55.7(SD 5.6) years
	55.4 (SD 5.8) years for trabeculectomy + Ex-PRESS mini shunt group
	56 (SD 5.3) years for trabeculectomy group
	Gender
	5/10 (50%) men and 5/10 (50%) women in trabeculectomy + Ex-PRESS mini shunt group;
	4/10 (40%) men and 6/10 (60%) women in trabeculectomy group
	Inclusion criteria: IOP > 21 mmHg on maximum tolerated topical antiglaucoma medication (medication score 3 for all the eyes); had secondary angle-closure NVG, as confirmed by gonioscopy.
	Exclusion criteria: not reported
	Equivalence of baseline characteristics: yes
Interventions	**Intervention 1:** trabeculectomy + Ex-PRESS mini shunt
	Intervention 2: trabeculectomy
	Length of follow-up
	Planned: 1 year
	Actual: 1 year

El-Saied 2021 *(Continued)*

Outcomes	**Primary outcomes, as defined:** IOP, BCVA, central foveal thickness, intraoperative bleeding, postoperative complications, and secondary intervention: needling or diode-cyclo photocoagulation **Secondary outcomes, as defined:** postoperative hypotony, surgical success rate **Intervals at which outcomes assessed:** 1 day; 1 week; 1, 3, and 6 months; 1 year
Notes	**Publication type:** published article **Funding sources:** none **Disclosures of interest:** authors declared that they had no conflict of interest **Trial registry:** not reported **Study period:** October 2016 to November 2017 **Subgroup analyses:** none reported **Publication language:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Study authors clearly reported that randomization was performed using computer-generated numbers. Baseline characteristics in both groups were similar, suggesting effective randomization.
Allocation concealment (selection bias)	Unclear risk	Study authors did not mention how the allocation concealment was performed.
Masking of participants and personnel (performance bias)	Low risk	There was no description about masking study participants and personnel. However, as the IOP was an objective measurement for participants and personnel, it was unlikely that the unmasking of participants and personnel would affect the outcome.
Masking of outcome assessment (detection bias)	High risk	Outcome assessors were not masked to the participant's group assignment. As the IOP measurement using Goldmann applanation could be subjective, there were some possibilities that the unmasking of outcome assessors would affect the outcome.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study authors did not explicitly report the number of losses to follow-up.
Selective reporting (reporting bias)	Unclear risk	No statistical analysis plan was available, so it was unclear if the reported approach to analyzing this outcome was prespecified or influenced by the results.
Other bias	Low risk	Study authors had no financial or proprietary interest in this paper.

Netland 2014

Study characteristics

Methods	**Study design:** parallel-group randomized controlled trial

Netland 2014 *(Continued)*

	Country: USA **Number randomized:** 120 eyes of 120 participants total; 59 participants in trabeculectomy + MMC + Ex-PRESS group; 61 participants in trabeculectomy + MMC group **Exclusions after randomization:** 1 participant randomized to receive treatment but was withdrawn prior to surgery because of thin sclera **Losses to follow-up:** 6 participants total; 2 participants in trabeculectomy + MMC + Ex-PRESS group; 4 participants in the trabeculectomy + MMC group **Unit of analysis:** individual (1 eye per participant) **Number analyzed:** 114 participants total; 57 participants in trabeculectomy + MMC + Ex-PRESS group; 57 participants in trabeculectomy + MMC group **How were missing data handled?** 6 participants excluded from analysis **Power calculation:** a power of 80% to detect a 2 mmHg IOP difference between groups with a sample size of 60 participants in each group
Participants	**Mean age:** 69 years 69.4 years for trabeculectomy + MMC + Ex-PRESS group 67.8 years for trabeculectomy + MMC group **Gender** 32/59 (54%) men and 27/59 (46%) women in trabeculectomy + MMC + Ex-PRESS group 33/61 (54%) men and 28/61 (46%) women in trabeculectomy + MMC group **Inclusion criteria:** aged > 18 years; diagnosed with OAG (including POAG, PEXG, and pigmentary glaucoma); previously treated with ocular hypotensive medications; candidate for glaucoma surgery with intraoperative MMC; IOP ≥ 18 mmHg **Exclusion criteria:** ACG, normal tension glaucoma, or NVG; previous incisional glaucoma surgery, penetrating keratoplasty, extracapsular cataract extraction; visually significant cataract planned for extraction at time of filtering surgery or within 12 months thereafter; any significant ocular disease or history in the operated eye other than glaucoma and cataract; ocular pathology that could interfere with accurate IOP measurements; vitreous present in the anterior chamber for which vitrectomy is anticipated; participation in any other concurrent ophthalmic clinical trial **Equivalence of baseline characteristics:** yes
Interventions	**Intervention 1:** trabeculectomy + MMC + Ex-PRESS (Alco Laboratories, Fort Worth, Texas, USA) **Intervention 2:** trabeculectomy + MMC **Length of follow-up** Planned: 2 years Actual: 2 years

Netland 2014 *(Continued)*

Outcomes	**Primary outcomes, as defined:** IOP, medication reduction, and surgical success (5 mmHg ≤ IOP ≤ 18 mmHg) **Secondary outcomes, as defined:** visual acuity, complications, and IOP at 2 weeks' follow-up **Intervals at which outcomes assessed:** 1 and 7 days; 1, 3, 6, 12, 18, and 24 months
Notes	**Publication type:** published article **Funding sources:** (quote) "research support for this investigator-initiated trial was obtained from Optonol Ltd. (Neve Ilan, Israel) and Alcon Laboratories, Inc. (Fort Worth, TX)." **Disclosures of interest:** several co-authors received research support, consulting fees, and speaker honoraria from industries, but no company wrote or influenced the writing of the manuscript **Trial registry:** NCT00444080 **Study period:** not reported **Subgroup analyses:** none reported **Publication language:** English Authors contacted for 1-year IOP and visual acuity data, but no response received.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed separately for each study site. Each subject was assigned a 3-digit identifying number, and all subjects were randomized using a computer-based random-number generator to undergo treatment with EX-PRESS glaucoma filtration implant under scleral flap or trabeculectomy."
Allocation concealment (selection bias)	Unclear risk	Not reported.
Masking of participants and personnel (performance bias)	Unclear risk	No-one was masked in this study. We are uncertain whether this has introduced bias.
Masking of outcome assessment (detection bias)	Unclear risk	The outcome assessors were not masked. However, the authors mentioned that (quote) "we did provide standardized methods for measurement of IOP and documentation of other clinical findings, which may reduce, to some degree, the potential for bias."
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study had 6/120 participants lost to follow-up and with approximately even numbers of participants lost in the 2 groups.
Selective reporting (reporting bias)	Low risk	The study was registered at www.ClinicalTrials.gov. All defined outcomes in www.ClinicalTrials.gov were reported in full text.
Other bias	High risk	Received funding from manufacturer of device. No other sources of bias identified.

Wagdy 2021

Study characteristics	
Methods	**Study design:** parallel-group randomized controlled trial **Country:** Egypt **Number randomized:** 28 eyes of 28 participants total; 14 participants in trabeculectomy + MMC + Ex-PRESS implant group; 14 participants in trabeculectomy + MMC group **Exclusions after randomization:** none reported **Losses to follow-up:** none reported **Unit of analysis:** individual (1 eye per participant) **Number analyzed:** 28 participants total; 14 participants in each group **How were missing data handled?** none reported **Power calculation:** (quote) "The effect size for this study was 2.28, considered to be large using Cohen's (1988) criteria, with an alpha=0.05 and sample size=28 distributed as 14 for group I and 14 for group II."
Participants	**Mean age:** overall 42–55 years; not reported by intervention group **Gender:** 11/28 (39.3%) men and 17/28 (60.7%) women overall; not reported by intervention group **Inclusion criteria:** OAG, despite maximally tolerated medication and previous subscleral trabeculectomy with a fibrotic bleb for > 4 months **Exclusion criteria:** other types of glaucoma; complained of any diseases that interfered with wound healing such as diabetes and other vascular or autoimmune disorders; subscleral trabeculectomy failure other than fibrotic bleb; followed < 4 months after the first surgery or < 12 months after the second surgery **Equivalence of baseline characteristics:** yes; baseline age and IOP were comparable
Interventions	**Intervention 1:** trabeculectomy + MMC + Ex-PRESS implant group **Intervention 2:** trabeculectomy + MMC group **Length of follow-up** Planned: 1 year Actual: 1 year
Outcomes	**Primary outcome, as defined:** reduction of IOP throughout 1-year follow-up **Secondary outcomes, as defined:** complete success (defined as an IOP < 21 mmHg without treatment), postoperative changes in visual acuity, postoperative changes in visual field, bleb-related complications throughout 1-year follow-up **Intervals at which outcomes assessed:** 1 day; 1 and 6 months; and 1 year after surgery
Notes	**Publication type:** published article **Funding sources:** none reported **Disclosures of interest:** (quote) "the authors reported no conflict of interest."

Wagdy 2021 *(Continued)*

Trial registry: NCT04417920

Study period: July 2017 to May 2019

Subgroup analyses: none reported

Publication language: English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization performed using computer-generated random number table.
Allocation concealment (selection bias)	Unclear risk	No comment about concealment of allocation.
Masking of participants and personnel (performance bias)	Low risk	No description about masking study participants and personnel. However, as the IOP was an objective measurement for participants and personnel, it was unlikely that the unmasking of participants and personnel would affect the outcome.
Masking of outcome assessment (detection bias)	High risk	Outcome assessors were not masked to the participant's group assignment. As the IOP measurement using Goldmann applanation could be subjective, it was likely that the unmasking of outcome assessors would affect the outcome.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Study authors did not report the number of losses to follow-up.
Selective reporting (reporting bias)	Low risk	Trial was analyzed according to the prespecified plan in terms of outcome measurements (e.g. definition, scales, and time points) within each outcome.
Other bias	Low risk	Study did not receive any additional funding. Study authors reported no conflict of interest.

Wagschal 2015

Study characteristics

Methods

Study design: parallel-group randomized controlled trial

Country: Canada

Number randomized: 64 eyes of 64 participants total

33 participants in trabeculectomy + MMC + Ex-PRESS P50 group

31 participants in trabeculectomy + MMC group

Exclusions after randomization: none reported

Losses to follow-up: 4 participants total at 1 year

3 participants in trabeculectomy + MMC + Ex-PRESS P50 group

1 participant in trabeculectomy + MMC group

Wagschal 2015 *(Continued)*

	Unit of analysis: individual (1 eye per participant)
	Number analyzed: 60 participants total; 30 participants in each group
	How were missing data handled? 4 participants excluded from analysis
	Power calculation: a power of 80% to detect a 2 mmHg IOP difference with a sample size of 52 eyes
Participants	**Mean age:** overall not reported
	61.9 years for trabeculectomy + MMC + Ex-PRESS P50 group
	65.9 years for trabeculectomy + MMC group
	Gender: 41/64 (64%) men and 23/64 (36%) women overall; not reported by intervention group
	Inclusion criteria: aged 18–85 years with OAG and uncontrolled IOP on maximum tolerated medication and trabeculectomy as the planned surgical procedure
	Exclusion criteria: previous ocular incisional surgery (except for clear cornea cataract surgery or 1 trabeculectomy), history of uveitis, unwilling or unable to give consent, unwilling to accept randomization, or unable to return for scheduled protocol visits
	Equivalence of baseline characteristics: yes; baseline IOP and visual acuity were comparable
Interventions	**Intervention 1:** trabeculectomy + MMC + Ex-PRESS P50
	Intervention 2: trabeculectomy + MMC
	Length of follow-up
	Planned: 1 year
	Actual: 1 year
Outcomes	**Primary outcome, as defined:** IOP, complete success ("IOP between 5 and 18 mmHg and a 20% reduction from baseline without medication and qualified success was defined as above with hypotensive medications"), failure ("reoperation for glaucoma or loss of light perception")
	Secondary outcomes, as defined: visual acuity, surgery time, glaucoma medication usage, IOP, bleb morphology, Seidel test, additional procedures, complications, and potential risk factors for vision loss
	Intervals at which outcomes assessed: 1 day; 1 and 2 weeks; and 1, 2, 3, and 6 months after surgery
Notes	**Publication type:** published article
	Funding sources: (quote) "some Ex-PRESS shunts were provided at no cost by Imed and Alcon Canada"
	Disclosures of interest: (quote) "Y.M.B. has received speaking honoraria from Alcon Canada. The remaining authors declare no conflict of interest."
	Trial registry: NCT01263561
	Study period: May 2009 to July 2011
	Subgroup analyses: subgroup of 43 participants randomly chosen for cost-effectiveness analysis
	Publication language: English
	Authors contacted for randomization method, reasons for lost to follow-up, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement

Wagschal 2015 *(Continued)*

Random sequence generation (selection bias)	Low risk	As this was not provided in the published report, we contacted the study investigator, and received the following response: (quote) "randomization was done by drawing a piece of paper with procedure name from a bag."
Allocation concealment (selection bias)	Unclear risk	Not reported.
Masking of participants and personnel (performance bias)	Unclear risk	By contacting the study investigators, we found participants were not masked, but whether this would introduce bias was uncertain as current evidence did not show 1 procedure significantly better than the other.
Masking of outcome assessment (detection bias)	High risk	By contacting the study investigators, we found the outcome assessors were not masked. Although it is not possible to mask outcome assessors, devices can be easily seen during exam of the eye.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study had 4/64 participants lost to follow-up, and little difference in numbers in the 2 groups (lost 3 versus 1). Also, exclusions were due to death (3 participants) and 1 participant not adhering to the assigned procedure.
Selective reporting (reporting bias)	Low risk	Study registered in www.ClinicalTrials.gov. All defined outcomes in www.ClinicalTrials.gov were reported in full text.
Other bias	Unclear risk	Partial industry support and other source(s) of potential bias.

ACG: angle-closure glaucoma; BCVA: best-corrected visual acuity; dB: decibel; IOP: intraocular pressure; MMC: mitomycin C; NVG: neovascular glaucoma; OAG: open-angle glaucoma; PEXG: pseudoexfoliation glaucoma; POAG: primary open-angle glaucoma; SD: standard deviation.

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

Study	Reason for exclusion
Birt 1998	Not the intervention of interest
Bruno 2008	Not the intervention of interest
Cai 2012	Not the intervention of interest
ChiCTR-IPC-17011900	Not the intervention of interest
Cho 2013	Not the intervention of interest
Cillino 2008	Not the intervention of interest
Cillino 2011	Not the intervention of interest
CTRI/2011/06/001836	Not the intervention of interest
CTRI/2016/12/007595	Not a randomized controlled trial
Dhalla 2016	Combined phacoemulsification
Donoso 1998	Not the intervention of interest
El 2019	Not the intervention of interest

Study	Reason for exclusion
Eldaly 2017	Not the intervention of interest
Eliezer 2006	Not the intervention of interest
EUCTR2013-000395-15-GB	Not the comparator of interest
Fang 2019	Not the intervention of interest
Huang 2007	Not the intervention of interest
IRCT201212284166N	Not the intervention of interest
IRCT2015020620979N	Not the intervention of interest
Ji 2013	Not the intervention of interest
JPRN-UMIN000008391	Early termination
JPRN-UMIN000011069	Not a randomized controlled trial
Khairy 2015	Not the intervention of interest
Li 2010	Not the intervention of interest
Lia 2016	Not the intervention of interest
Liu 2009	Not the intervention of interest
Maheshwari 2012	Not the intervention of interest
Marey 2013	Not the intervention of interest
Mitra 2012	Not the intervention of interest
Mohamed 2018	Pediatric population
NCT00449098	Not the intervention of interest
NCT00472810	Not the intervention of interest
NCT00524758	Not the intervention of interest
NCT00538590	Not the intervention of interest
NCT01440751	Not the intervention of interest
NCT01753492	Not a randomized controlled trial
NCT01912638	Not the intervention of interest
NCT02121171	Pediatric population
NCT03541551	Not the population of interest
Papaconstantinou 2010	Not the intervention of interest

Study	Reason for exclusion
Ren 2009	Not the intervention of interest
Rosentreter 2010	Not the intervention of interest
Rosentreter 2014	Not the intervention of interest
Sarker 2019	Not the intervention of interest
Sen 2018	Not the intervention of interest
Senthil 2013	Not the intervention of interest
Sheha 2008	Not the intervention of interest
Stavrakas 2012	Not the intervention of interest
Wang 2008	Not the intervention of interest
Wang 2009	Not the intervention of interest
Yadava 2017	Not the intervention of interest
Yan 2004	Not the intervention of interest
Yang 2004	Not the intervention of interest
Yu 2017	Not the intervention of interest
Zhang 2009	Not the intervention of interest
Zheng 2005	Not the intervention of interest

IOP: intraocular pressure; MMC: mitomycin C.

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

Konstantinidis 2021

Methods	**Study design:** prospective comparative study (unclear randomization), single center **Country:** Greece **Number analyzed:** 30 eyes of 30 participants total; 19 for in trabeculectomy + Ex-PRESS mini shunt group and 11 for trabeculectomy group **Losses to follow-up:** 0 eyes of 0 participants total; 0 for in trabeculectomy + Ex-PRESS mini shunt group and 0 for trabeculectomy group **Unit of analysis:** eye **How were missing data handled?** not reported **Power calculation:** "The power of all statistical tests used was greater than 0.8, suggesting that the size of our sample was sufficient (G*Power 3.1.9.2, University of Dusseldorf, Dusseldorf, Germany)"
Participants	**Age**

Konstantinidis 2021 *(Continued)*	
	Range 16–81 (mean 62.4) years for trabeculectomy + Ex-PRESS mini shunt group; Range 60–78 (mean 67.2) years for trabeculectomy group **Gender** 10/19 (53%) men and 9/19 (47%) women in trabeculectomy + Ex-PRESS mini shunt group; 6/11 (55%) men and 5/11 (54%) women in trabeculectomy group **Inclusion criteria:** not reported **Exclusion criteria:** previous ocular trauma, ocular surgery other than phacoemulsification, previous disease of the ocular surface, and congenital glaucoma **Equivalence of baseline characteristics:** yes
Interventions	**Intervention 1:** trabeculectomy + Ex-PRESS mini shunt **Intervention 2:** trabeculectomy **Length of follow-up** Planned: 1, 6, and 12 months Actual: 1, 6, and 12 months
Outcomes	**Primary outcomes, as defined:** corneal resistance factor and corneal hysteresis measured using the Ocular Response Analyzer **Secondary outcomes, as defined:** IOP measured with the Goldmann Applanation Tonometry **Intervals at which outcomes assessed:** 1, 6, and 12 months
Notes	**Publication type:** published article **Funding sources:** none **Disclosures of interest:** authors declared that they had no conflicts of interest **Trial registry:** not reported **Study period:** July 2013 to May 2016 **Subgroup analyses:** none reported **Publication language:** English

IOP: intraocular pressure.

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

JPRN-UMIN000008981

Study name	Prospective comparative study of the Ex-PRESS mini glaucoma shunt with standard trabeculectomy
Methods	**Study design:** interventional, randomized, parallel, open label clinical trial **Number randomized:** 200 participants (number of eyes not reported) total; not reported by intervention group **Unit of analysis:** not reported

JPRN-UMIN000008981 *(Continued)*	**Power calculation:** not reported
Participants	**Country:** Japan **Inclusion criteria:** aged ≥ 20 years with open-angle glaucoma **Exclusion criteria:** angle-closure glaucoma; uveitis
Interventions	**Intervention 1:** trabeculectomy + Ex-PRESS mini shunt implantation **Intervention 2:** trabeculectomy **Length of follow-up:** planned: not reported
Outcomes	**Primary outcome, as defined in study reports:** IOP reduction **Secondary outcomes, as defined in study reports:** not reported **Adverse events reported:** not reported **Intervals at which outcomes assessed:** not reported
Starting date	1 October 2012
Contact information	Hideki Mochizuki: mochizuki-h@hiroshima-u.ac.jp 1-2-3 Kasumi Minamiku Hiroshima, Japan Hiroshima University Department of Ophthalmology
Notes	**Funding source:** self-funding **Last updated:** 3 June 2014 This study is completed but no results published.

IOP: intraocular pressure.

DATA AND ANALYSES

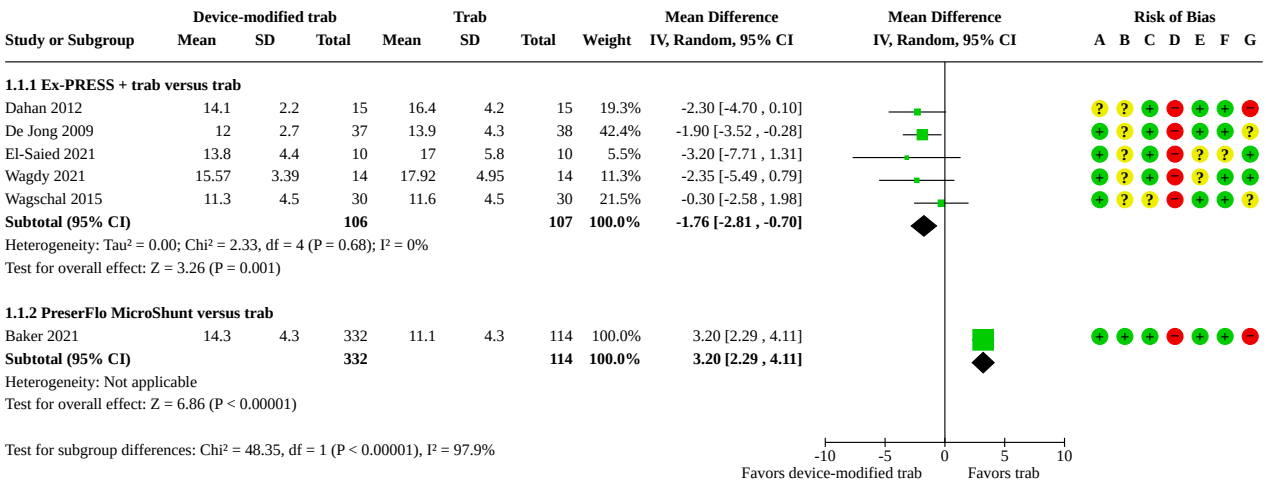
Comparison 1. Device-modified trabeculectomy (trab) versus trabeculectomy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Postoperative intraocular pressure (IOP) at 1 year by device type	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 Ex-PRESS + trab versus trab	5	213	Mean Difference (IV, Random, 95% CI)	-1.76 [-2.81, -0.70]
1.1.2 PreserFlo MicroShunt versus trab	1	446	Mean Difference (IV, Random, 95% CI)	3.20 [2.29, 4.11]
1.2 Change in IOP from baseline at 1 year	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 Postoperative IOP at 6 months by device type	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.3.1 Ex-PRESS + trab versus trab	5	253	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.40, 1.20]
1.3.2 PreserFlo MicroShunt versus trab	1	446	Mean Difference (IV, Random, 95% CI)	3.00 [1.62, 4.38]
1.4 Postoperative IOP at 2 years	3	212	Mean Difference (IV, Random, 95% CI)	-1.38 [-2.66, -0.09]
1.5 Change in IOP from baseline at 6 months	1	20	Mean Difference (IV, Random, 95% CI)	0.20 [-5.46, 5.86]
1.6 Postoperative logMAR best-corrected visual acuity at 1 year	3	110	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.19, 0.10]
1.7 Proportion of participants who are drop-free at 1 year by device type	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.7.1 Ex-PRESS + trab versus trab	2	48	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.42, 9.82]
1.7.2 PreserFlo MicroShunt versus trab	1	509	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.77, 0.93]
1.8 Mean number of IOP lowering medications at 1 year by device type	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.8.1 Ex-PRESS + trab versus trab	3	170	Mean Difference (IV, Random, 95% CI)	-0.34 [-0.62, -0.07]
1.8.2 PreserFlo MicroShunt versus trab	1	509	Mean Difference (IV, Random, 95% CI)	0.30 [0.11, 0.49]
1.9 Proportion of participants with IOP less than 5 mmHg (hypotony) or shallow anterior chamber by device type	7	868	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.46, 1.17]
1.9.1 Ex-PRESS + trab versus trab	6	342	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.61, 1.39]
1.9.2 PreserFlo MicroShunt versus trab	1	526	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.25, 0.79]
1.10 Proportion of participants with bleb leakage by device type	6	840	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.40, 1.02]
1.10.1 Ex-PRESS + trab versus trab	5	314	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.45, 2.16]
1.10.2 PreserFlo MicroShunt versus trab	1	526	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.28, 0.90]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.11 Proportion of participants with re-operations for glaucoma by device type	5	720	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.24, 1.98]
1.11.1 Ex-PRESS + trab versus trab	4	194	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.09, 1.26]
1.11.2 PreserFlo MicroShunt versus trab	1	526	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.77, 2.22]
1.12 Proportion of participants with cataract extraction by device type	5	820	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.27, 0.80]
1.12.1 Ex-PRESS + trab versus trab	4	294	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.14, 0.80]
1.12.2 PreserFlo MicroShunt versus trab	1	526	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.28, 1.17]
1.13 Proportion of participants with endophthalmitis	1	120	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.29]
1.14 Proportion of participants with loss of vision of > 2 lines or loss of light perception	1	526	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.30, 1.07]

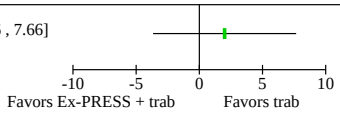
Analysis 1.1. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 1: Postoperative intraocular pressure (IOP) at 1 year by device type



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

Analysis 1.2. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 2: Change in IOP from baseline at 1 year

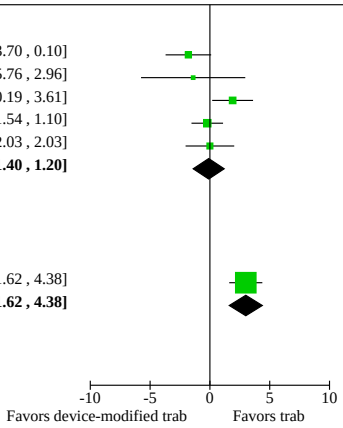
Study or Subgroup	Ex-PRESS + trab Mean	SD	Total	Trab Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
El-Saied 2021	14	6.1	10	12	6.8	10	2.00 [-3.66 , 7.66]		+ ? + − ? ? +



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

Analysis 1.3. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 3: Postoperative IOP at 6 months by device type

Study or Subgroup	Device-modified trab Mean	SD	Total	Trab Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.3.1 Ex-PRESS + trab versus trab										
Dahan 2012	13.1	2.4	15	14.9	2.9	15	21.3%	-1.80 [-3.70 , 0.10]		? ? + − + + −
El-Saied 2021	15	5.4	10	16.4	4.5	10	7.2%	-1.40 [-5.76 , 2.96]		+ ? + − ? ? +
Netland 2014	13.8	4.7	57	11.9	4.6	57	23.4%	1.90 [0.19 , 3.61]		+ ? ? ? + + −
Wagdy 2021	14.35	1.39	14	14.57	2.1	14	28.0%	-0.22 [-1.54 , 1.10]		+ ? + − ? + +
Wagschal 2015	10.2	4.1	30	10.2	4	31	20.0%	0.00 [-2.03 , 2.03]		+ ? ? − + + ?
Subtotal (95% CI)			**126**			**127**	**100.0%**	**-0.10 [-1.40 , 1.20]**		
Heterogeneity: Tau² = 1.11; Chi² = 8.69, df = 4 (P = 0.07); I² = 54%										
Test for overall effect: Z = 0.15 (P = 0.88)										
1.3.2 PreserFlo MicroShunt versus trab										
Baker 2021	14.3	6.5	332	11.3	6.5	114	100.0%	3.00 [1.62 , 4.38]		+ + + − + + −
Subtotal (95% CI)			**332**			**114**	**100.0%**	**3.00 [1.62 , 4.38]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 4.25 (P < 0.0001)										
Test for subgroup differences: Chi² = 10.27, df = 1 (P = 0.001), I² = 90.3%										

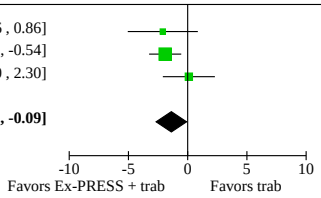


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.4. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 4: Postoperative IOP at 2 years

Study or Subgroup	Ex-PRESS + trab Mean	SD	Total	Trab Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Dahan 2012	15	2.44949	10	17.1	4.094712	10	16.7%	-2.10 [-5.06 , 0.86]	? ? + − + + −
De Jong 2009	11.9	2.9	39	13.8	3.2	39	55.6%	-1.90 [-3.26 , -0.54]	+ ? + − + + ?
Netland 2014	14.7	4.6	57	14.6	7.1	57	27.7%	0.10 [-2.10 , 2.30]	+ ? ? ? + + −
Total (95% CI)			**106**			**106**	**100.0%**	**-1.38 [-2.66 , -0.09]**	

Heterogeneity: Tau² = 0.30; Chi² = 2.52, df = 2 (P = 0.28); I² = 21%
Test for overall effect: Z = 2.10 (P = 0.04)
Test for subgroup differences: Not applicable

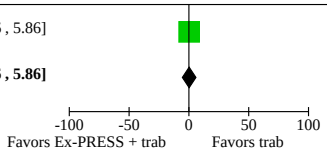


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.5. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 5: Change in IOP from baseline at 6 months

Study or Subgroup	Ex-PRESS + trab Mean	SD	Total	Trab Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
El-Saied 2021	12.8	6.8	10	12.6	6.1	10	100.0%	0.20 [-5.46 , 5.86]	+ ? + − ? ? +
Total (95% CI)			**10**			**10**	**100.0%**	**0.20 [-5.46 , 5.86]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.94)
Test for subgroup differences: Not applicable

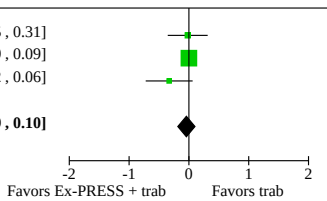


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.6. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 6: Postoperative logMAR best-corrected visual acuity at 1 year

Study or Subgroup	Ex-PRESS + trab Mean	SD	Total	Trab Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Dahan 2012	0.41	0.426	15	0.43	0.5035	15	15.6%	-0.02 [-0.35 , 0.31]	? ? + − + + −
El-Saied 2021	0.1	0.1	10	0.1	0.1	10	72.6%	0.00 [-0.09 , 0.09]	+ ? + − ? ? +
Wagschal 2015	0.47	0.64	30	0.8	0.89	30	11.8%	-0.33 [-0.72 , 0.06]	+ ? ? − + + ?
Total (95% CI)			**55**			**55**	**100.0%**	**-0.04 [-0.19 , 0.10]**	

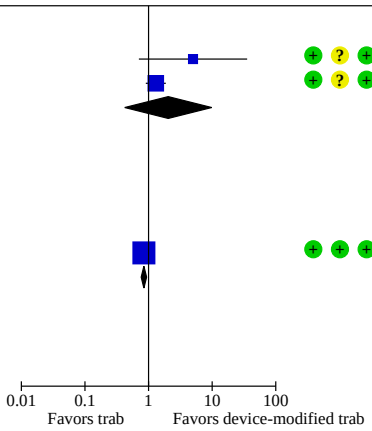
Heterogeneity: Tau² = 0.01; Chi² = 2.59, df = 2 (P = 0.27); I² = 23%
Test for overall effect: Z = 0.57 (P = 0.57)
Test for subgroup differences: Not applicable

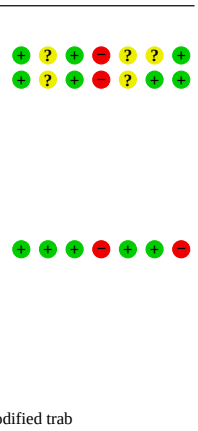


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.7. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 7: Proportion of participants who are drop-free at 1 year by device type

Study or Subgroup	Device-modified trab Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Ex-PRESS + trab versus trab						
El-Saied 2021	5	10	1	10	33.3%	5.00 [0.70 , 35.50]
Wagdy 2021	13	14	10	14	66.7%	1.30 [0.91 , 1.87]
Subtotal (95% CI)		**24**		**24**	**100.0%**	**2.04 [0.42 , 9.82]**
Total events:	18		11			
Heterogeneity: Tau² = 0.93; Chi² = 2.80, df = 1 (P = 0.09); I² = 64%						
Test for overall effect: Z = 0.89 (P = 0.38)						
1.7.2 PreserFlo MicroShunt versus trab						
Baker 2021	275	384	106	125	100.0%	0.84 [0.77 , 0.93]
Subtotal (95% CI)		**384**		**125**	**100.0%**	**0.84 [0.77 , 0.93]**
Total events:	275		106			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.40 (P = 0.0007)						
Test for subgroup differences: Chi² = 1.20, df = 1 (P = 0.27), I² = 16.6%						

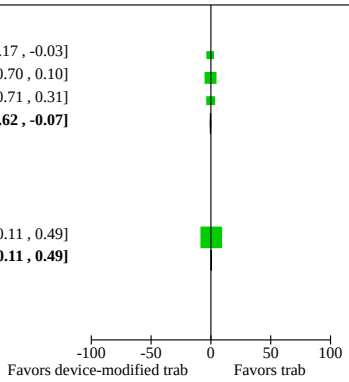


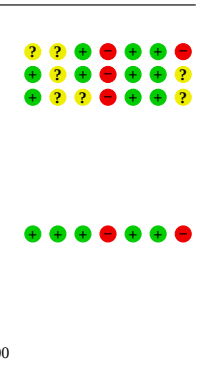


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.8. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 8: Mean number of IOP lowering medications at 1 year by device type

Study or Subgroup	Device-modified trab Mean	SD	Total	Trab Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.8.1 Ex-PRESS + trab versus trab								
Dahan 2012	0.3	0.5	15	0.9	1	15	23.7%	-0.60 [-1.17 , -0.03]
De Jong 2009	0.3	0.7	40	0.6	1.1	40	46.6%	-0.30 [-0.70 , 0.10]
Wagschal 2015	0.4	1	30	0.6	1	30	29.7%	-0.20 [-0.71 , 0.31]
Subtotal (95% CI)			**85**			**85**	**100.0%**	**-0.34 [-0.62 , -0.07]**
Heterogeneity: Tau² = 0.00; Chi² = 1.14, df = 2 (P = 0.56); I² = 0%								
Test for overall effect: Z = 2.43 (P = 0.02)								
1.8.2 PreserFlo MicroShunt versus trab								
Baker 2021	0.6	1.1	384	0.3	0.9	125	100.0%	0.30 [0.11 , 0.49]
Subtotal (95% CI)			**384**			**125**	**100.0%**	**0.30 [0.11 , 0.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.06 (P = 0.002)								
Test for subgroup differences: Chi² = 13.99, df = 1 (P = 0.0002), I² = 92.9%								

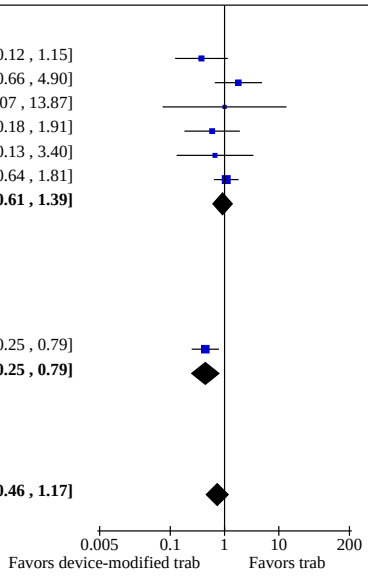


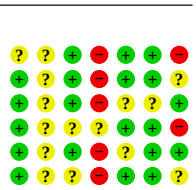


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Masking of participants and personnel (performance bias)
(D) Masking of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Analysis 1.9. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 9: Proportion of participants with IOP less than 5 mmHg (hypotony) or shallow anterior chamber by device type

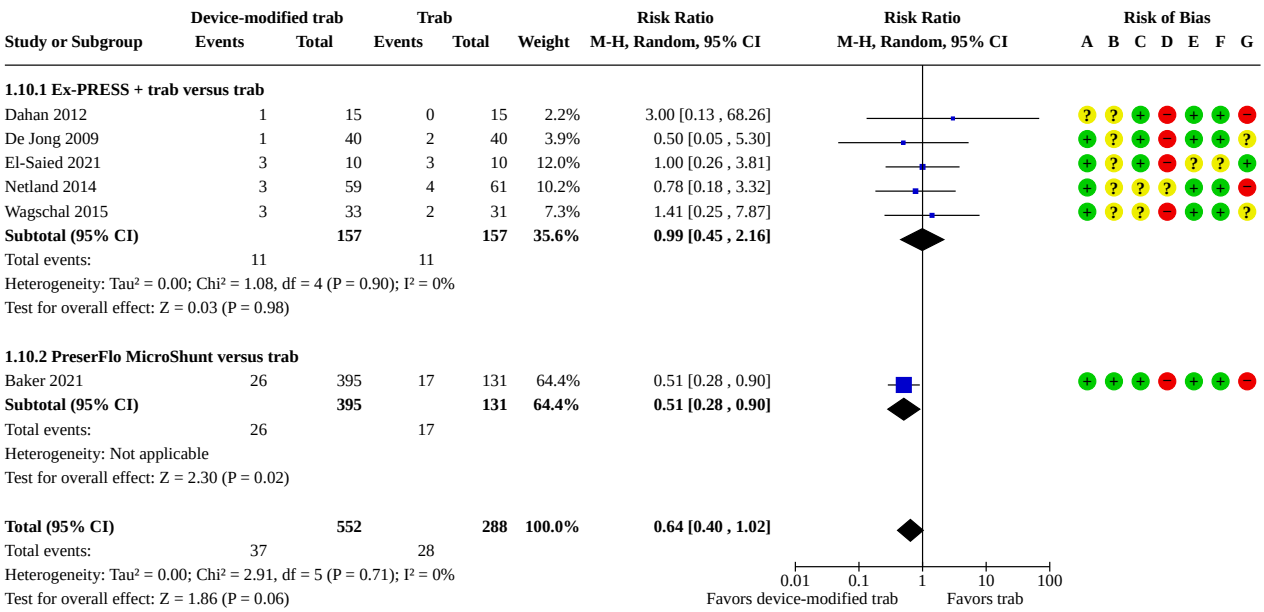
Study or Subgroup	Device-modified trab Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 Ex-PRESS + trab versus trab						
Dahan 2012	3	15	8	15	12.2%	0.38 [0.12 , 1.15]
De Jong 2009	9	40	5	40	14.2%	1.80 [0.66 , 4.90]
El-Saied 2021	1	10	1	10	2.9%	1.00 [0.07 , 13.87]
Netland 2014	4	59	7	61	11.4%	0.59 [0.18 , 1.91]
Wagdy 2021	2	14	3	14	6.8%	0.67 [0.13 , 3.40]
Wagschal 2015	16	33	14	31	27.2%	1.07 [0.64 , 1.81]
Subtotal (95% CI)		**171**		**171**	**74.7%**	**0.92 [0.61 , 1.39]**
Total events:	35		38			
Heterogeneity: Tau² = 0.02; Chi² = 5.26, df = 5 (P = 0.39); I² = 5%						
Test for overall effect: Z = 0.40 (P = 0.69)						
1.9.2 PreserFlo MicroShunt versus trab						
Baker 2021	24	395	18	131	25.3%	0.44 [0.25 , 0.79]
Subtotal (95% CI)		**395**		**131**	**25.3%**	**0.44 [0.25 , 0.79]**
Total events:	24		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.77 (P = 0.006)						
Total (95% CI)		**566**		**302**	**100.0%**	**0.73 [0.46 , 1.17]**
Total events:	59		56			
Heterogeneity: Tau² = 0.13; Chi² = 9.70, df = 6 (P = 0.14); I² = 38%						
Test for overall effect: Z = 1.31 (P = 0.19)						
Test for subgroup differences: Chi² = 4.08, df = 1 (P = 0.04), I² = 75.5%						





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

Analysis 1.10. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 10: Proportion of participants with bleb leakage by device type

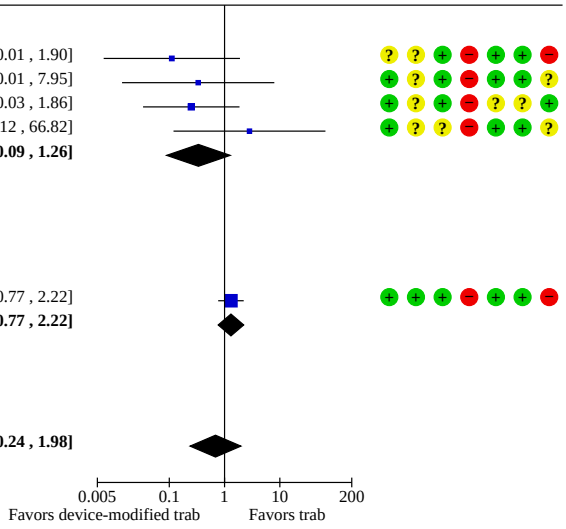


Risk of bias legend

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

Analysis 1.11. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 11: Proportion of participants with reoperations for glaucoma by device type

Study or Subgroup	Device-modified trab Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.11.1 Ex-PRESS + trab versus trab						
Dahan 2012	0	15	4	15	11.2%	0.11 [0.01 , 1.90]
De Jong 2009	0	40	1	40	9.4%	0.33 [0.01 , 7.95]
El-Saied 2021	1	10	4	10	18.9%	0.25 [0.03 , 1.86]
Wagschal 2015	1	33	0	31	9.4%	2.82 [0.12 , 66.82]
Subtotal (95% CI)		**98**		**96**	**48.9%**	**0.34 [0.09 , 1.26]**
Total events:	2		9			
Heterogeneity: Tau² = 0.00; Chi² = 2.41, df = 3 (P = 0.49); I² = 0%						
Test for overall effect: Z = 1.61 (P = 0.11)						
1.11.2 PreserFlo MicroShunt versus trab						
Baker 2021	59	395	15	131	51.1%	1.30 [0.77 , 2.22]
Subtotal (95% CI)		**395**		**131**	**51.1%**	**1.30 [0.77 , 2.22]**
Total events:	59		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.98 (P = 0.33)						
Total (95% CI)		**493**		**227**	**100.0%**	**0.69 [0.24 , 1.98]**
Total events:	61		24			
Heterogeneity: Tau² = 0.50; Chi² = 5.98, df = 4 (P = 0.20); I² = 33%						
Test for overall effect: Z = 0.70 (P = 0.48)						
Test for subgroup differences: Chi² = 3.47, df = 1 (P = 0.06), I² = 71.2%						

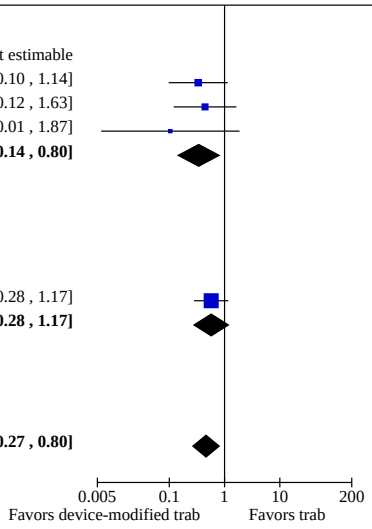


Risk of bias legend

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

Analysis 1.12. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 12: Proportion of participants with cataract extraction by device type

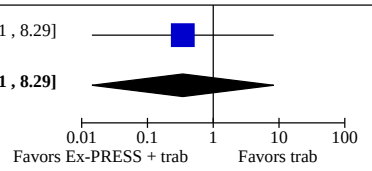
Study or Subgroup	Device-modified trab Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
1.12.1 Ex-PRESS + trab versus trab							
Dahan 2012	0	15	0	15		Not estimable	? ? + − + + −
De Jong 2009	3	40	9	40	19.9%	0.33 [0.10 , 1.14]	+ ? + − + + ?
Netland 2014	3	59	7	61	17.7%	0.44 [0.12 , 1.63]	+ ? ? ? + + −
Wagschal 2015	0	33	4	31	3.6%	0.10 [0.01 , 1.87]	+ ? ? − + + ?
Subtotal (95% CI)		**147**		**147**	**41.2%**	**0.34 [0.14 , 0.80]**	
Total events:	6		20				
Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 2 (P = 0.66); I² = 0%							
Test for overall effect: Z = 2.47 (P = 0.01)							
1.12.2 PreserFlo MicroShunt versus trab							
Baker 2021	19	395	11	131	58.8%	0.57 [0.28 , 1.17]	+ + + − + + −
Subtotal (95% CI)		**395**		**131**	**58.8%**	**0.57 [0.28 , 1.17]**	
Total events:	19		11				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.53 (P = 0.13)							
Total (95% CI)		**542**		**278**	**100.0%**	**0.46 [0.27 , 0.80]**	
Total events:	25		31				
Heterogeneity: Tau² = 0.00; Chi² = 1.70, df = 3 (P = 0.64); I² = 0%							
Test for overall effect: Z = 2.76 (P = 0.006)							
Test for subgroup differences: Chi² = 0.84, df = 1 (P = 0.36), I² = 0%							



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

Analysis 1.13. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 13: Proportion of participants with endophthalmitis

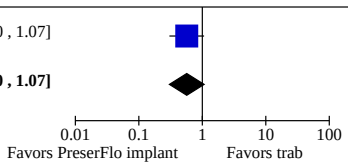
Study or Subgroup	Ex-PRESS + trab Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Netland 2014	0	59	1	61	100.0%	0.34 [0.01 , 8.29]	+ ? ? ? + + −
Total (95% CI)		**59**		**61**	**100.0%**	**0.34 [0.01 , 8.29]**	
Total events:	0		1				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.66 (P = 0.51)							
Test for subgroup differences: Not applicable							



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

Analysis 1.14. Comparison 1: Device-modified trabeculectomy (trab) versus trabeculectomy, Outcome 14: Proportion of participants with loss of vision of > 2 lines or loss of light perception

Study or Subgroup	PreserFlo Microshunt Events	Total	Trab Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Baker 2021	24	395	14	131	100.0%	0.57 [0.30 , 1.07]		+ + + − + + −
Total (95% CI)		**395**		**131**	**100.0%**	**0.57 [0.30 , 1.07]**		
Total events:	24		14					



Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)
Test for subgroup differences: Not applicable

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

ADDITIONAL TABLES

Table 1. Summary of included studies

Device	Study ID	Study design	Country	Participant diagnosis	Interventions	Total number of participants randomized	Total number of eyes randomized	Total number of eyes analyzed	Longest follow-up period (months)
Ex-PRESS	Dahan 2012	RCT, paired-eye design	South Africa	POAG	1. Trab + MMC 2. Trab + MMC + Ex-PRESS	15	30	30	12
	De Jong 2005 (abstract)	RCT, parallel-group design	The Netherlands	OAG	1. Trab + Ex-PRESS under a scleral flap 2. Trab + Ex-PRESS under conjunctiva 3. Trab	109	120	N/A	6
	De Jong 2009	RCT, parallel-group design	The Netherlands	OAG	1. Trab 2. Trab + Ex-PRESS	78	78	78	60
	El-Saied 2021	RCT, parallel-group design	Egypt	Secondary angle-closure neovascular glaucoma	1. Trab 2. Trab + Ex-PRESS	20	20	20	12
	Netland 2014	RCT, parallel-group design	USA	OAG	1. Trab + MMC 2. Trab + MMC + Ex-PRESS	120	120	114	24
	Wagdy 2021	RCT, parallel-group design	Egypt	OAG	1. Trab + MMC 2. Trab + MMC + Ex-PRESS	28	28	28	12
	Wagschal 2015	RCT, parallel-group design	Canada	OAG, uncontrolled IOP	1. Trab + MMC 2. Trab + MMC + Ex-PRESS	64	64	60	12
	Subtotal for Ex-PRESS					**434**	**460**	**N/A**	**Range 6–60 months**

Table 1. Summary of included studies *(Continued)*

PreserFlo MicroShunt	Baker 2021	RCT, parallel-group design	USA, France, Italy, the Netherlands, Spain, the UK	Mild-to-severe POAG	1. MicroShunt + MMC 2. Trab + MMC	527	527	527	12
Subtotal for PreserFlo MicroShunt						**527**	**527**	**527**	**12**
Total for all included studies						**961**	**987**	**N/A**	**Range 6–60 months**

ACG: angle-closure glaucoma; MMC: mitomycin C; N/A: not applicable; OAG: open-angle glaucoma; POAG: primary open-angle glaucoma; RCT: randomized controlled trial; trab: trabeculectomy.

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Trabeculectomy] explode all trees
#2 MeSH descriptor: [Glaucoma] explode all trees and with qualifiers: [Surgery - SU]
#3 MeSH descriptor: [Trabecular Meshwork] explode all trees and with qualifiers: [Surgery - SU]
#4 MeSH descriptor: [Filtering Surgery] explode all trees
#5 Trabeculectom* or Trabeculoplast* or Trabeculotom* or Goniotom* or Microtrabeculectom*
#6 (Glaucoma* near/5 (surg* or filter* or filtrate*))
#7 #1 or #2 or #3 or #4 or #5 or #6
#8 MeSH descriptor: [Glaucoma Drainage Implants] explode all trees
#9 (modif* near/5 (Trabeculectom* or Trabeculoplast* or Trabeculotom* or Goniotom* or Microtrabeculectom*))
#10 MeSH descriptor: [Polytetrafluoroethylene] explode all trees
#11 (Polytef or Politef or "E PTFE" or EPTFE or PTFE or TFE or FEP or SOLX or polytetrafluoroethylen* or polytetrafluorethylen* or polytetrafluoroethen* or Fluoroflex or Fluoroplast or Ftoroplast or Halon or Polyfene or Tetron or Tarflen or "GORE TEX" or Goretex or gortex or Teflon or Fluon or Ex-press or ologen or Baerveldt or Krupin or Ahmed or Molteno or ExPress or collagen matrix or collagen-GAG or collagen-glycosaminoglycan copolymer matrix)
#12 Device* or implant* or shunt* or valve* or tube*
#13 #8 or #9 or #10 or #11 or #12
#14 MeSH descriptor: [Fluorouracil] explode all trees
#15 5FU or 5-FU or Fluorouracil* or Fluoruracil* or 5-HU or Adrucil or Carac or Efudix or Fluoro Uracile or Fluoro-Uracile or Efudex or Fluoroplex or Flurodex or Fluracedyl or Haemato-fu or Neofluor or Onkofluor or Ribofluor or 5-Fluorouracil
#16 MeSH descriptor: [Mitomycin] explode all trees
#17 Mitomycin* or NSC-26980 or NSC 26980 or NSC26980 or Mutamycin or Ametycine or Mitocin-C or MitocinC or mytomycin* or mitomicin* or mytomicin* or MMC
#18 MeSH descriptor: [Mitomycins] explode all trees
#19 #18 from 1966 to 1991
#20 MeSH descriptor: [Antimetabolites] explode all trees
#21 MeSH descriptor: [Antimetabolites, Antineoplastic] explode all trees
#22 MeSH descriptor: [Nucleic Acid Synthesis Inhibitors] explode all trees
#23 Antimetabolite* or anti-metabolite*
#24 Antifibrotic* or anti-fibrotic*
#25 #14 or #15 or #16 or #17 or #19 or #20 or #21 or #22 or #23 or #24
#26 #7 and (#13 or #25)

Appendix 2. MEDLINE (OvidSP) search strategy

1. Randomized Controlled Trial.pt.
2. Controlled Clinical Trial.pt.
3. (randomized or randomised).ab,ti.
4. placebo.ab,ti.
5. drug therapy.fs.
6. randomly.ab,ti.
7. trial.ab,ti.
8. groups.ab,ti.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp animals/ not humans.sh.
11. 9 not 10
12. exp Trabeculectomy/
13. exp Glaucoma/su [Surgery]
14. exp Trabecular Meshwork/su [Surgery]
15. (Trabeculectom* or Trabeculoplast* or Trabeculotom* or Goniotom* or Microtrabeculectomy).tw.
16. (Glaucoma$ adj5 (surg$ or filter$ or filtrat$)).tw.
17. exp filtering surgery/
18. 12 or 13 or 14 or 15 or 16 or 17
19. exp Glaucoma Drainage Implants/
20. (modif* adj5 (Trabeculectom* or Trabeculoplast* or Trabeculotom* or Goniotom* or Microtrabeculectomy)).tw.
21. exp Polytetrafluoroethylene/
22. (Polytef or Politef or "E PTFE" or EPTFE or PTFE or TFE or FEP or SOLX or polytetrafluoroethylen* or polytetrafluorethylen* or polytetrafluoroethen* or Fluoroflex or Fluoroplast or Ftoroplast or Halon or Polyfene or Tetron or Tarflen or "GORE TEX" or Goretex or

gortex or Teflon or Fluon or Ex-press or ologen or Baerveldt or Krupin or Ahmed or Molteno or ExPress or collagen matrix or collagen-GAG or collagen-glycosaminoglycan copolymer matrix).tw.
23. (Device* or implant* or shunt* or valve* or tube*).tw.
24. 19 or 20 or 21 or 22 or 23
25. exp Fluorouracil/
26. (5FU or 5-FU or Fluorouracil* or Fluoruracil* or 5-HU or Adrucil or Carac or Efudix or Fluoro Uracile or Fluoro-Uracile or Efudex or Fluoroplex or Flurodex or Fluracedyl or Haemato-fu or Neofluor or Onkofluor or Ribofluor or 5-Fluorouracil).tw.
27. exp Mitomycin/
28. (Mitomycin* or NSC-26980 or NSC 26980 or NSC26980 or Mutamycin or Ametycine or Mitocin-C or MitocinC or mytomycin* or mitomicin* or mytomicin* or MMC).tw.
29. exp Mitomycins/
30. limit 29 to yr="1966 - 1991"
31. antimetabolites/
32. Antimetabolites, Antineoplastic/
33. Nucleic Acid Synthesis Inhibitors/
34. (Antimetabolite* or anti-metabolite*).tw.
35. (Antifibrotic* or anti-fibrotic*).tw.
36. 25 or 26 or 27 or 28 or 30 or 31 or 32 or 33 or 34 or 35
37. 11 and 18 and (24 or 36)

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

Appendix 3. Embase search strategy

1. 'randomized controlled trial'/exp
2. 'randomization'/exp
3. 'double blind procedure'/exp
4. 'single blind procedure'/exp
5. random*:ab,ti
6. 1 OR 2 OR 3 OR 4 OR 5
7. 'animal'/exp OR 'animal experiment'/exp
8. 'human'/exp
9. 7 AND 8
10. 7 NOT 9
11. 6 NOT 10
12. 'clinical trial'/exp
13. (clin* NEAR/3 trial*):ab,ti
14. ((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)):ab,ti
15. 'placebo'/exp
16. placebo*:ab,ti
17. random*:ab,ti
18. 'experimental design'/exp
19. 'crossover procedure'/exp
20. 'control group'/exp
21. 'latin square design'/exp
22. 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21
23. 22 NOT 10
24. 23 NOT 11
25. 'comparative study'/exp
26. 'evaluation'/exp
27. 'prospective study'/exp
28. control*:ab,ti OR prospectiv*:ab,ti OR volunteer*:ab,ti
29. 25 OR 26 OR 27 OR 28
30. 29 NOT 10
31. 30 NOT (11 OR 23)
32. 11 OR 24 OR 31
33. 'trabeculectomy'/exp
34. 'trabeculoplasty'/exp
35. 'trabeculotomy'/exp
36. trabeculectom*:ab,ti OR trabeculoplast*:ab,ti OR trabeculotom*:ab,ti OR goniotom*:ab,ti OR microtrabeculectom*:ab,ti
37. 'glaucoma surgery'/de
38. 'trabecular meshwork'/exp

39. (glaucoma* NEAR/5 (surg* OR filter* OR filtrate*)):ab,ti
40. 'filtering operation'/de
41. 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40
42. 'glaucoma drainage implant'/exp
43. (modif* NEAR/5 (trabeculectom* OR trabeculoplast* OR trabeculotom* OR goniotom* OR microtrabeculectom*)):ab,ti
44. 'politef'/exp
45. (Polytef or Politef or 'E PTFE' or EPTFE or PTFE or TFE or FEP or SOLX or polytetrafluoroethylen* or polytetrafluorethylen* or polytetrafluoroethen* or Fluoroflex or Fluoroplast or Ftoroplast or Halon or Polyfene or Tetron or Tarflen or 'GORE TEX' or Goretex or gortex or Teflon or Fluon or Ex-press or ologen or Baerveldt or Krupin or Ahmed or Molteno or ExPress or 'collagen matrix' or 'collagen-GAG' or 'collagen-glycosaminoglycan copolymer matrix'):ab,ti
46. device*:ab,ti OR implant*:ab,ti OR shunt*:ab,ti OR valve*:ab,ti OR tube*:ab,ti
47. 42 OR 43 OR 44 OR 45
48. 'fluorouracil'/exp
49. 5fu:ab,ti OR '5 fu':ab,ti OR fluorouracil*:ab,ti OR fluoruracil*:ab,ti OR '5 hu':ab,ti OR adrucil:ab,ti OR carac:ab,ti OR efudix:ab,ti OR fluoro:ab,ti AND uracile:ab,ti OR 'fluoro uracile':ab,ti OR efudex:ab,ti OR fluoroplex:ab,ti OR flurodex:ab,ti OR fluracedyl:ab,ti OR 'haemato fu':ab,ti OR neofluor:ab,ti OR onkofluor:ab,ti OR ribofluor:ab,ti OR '5 fluorouracil':ab,ti OR '5 fluoro 2':ab,ti OR '4 pyrimidinedione':ab,ti OR '5 fu':ab,ti OR accusite:ab,ti OR 'actino hermal':ab,ti OR effluderm:ab,ti OR efurix:ab,ti OR f6627:ab,ti OR fivoflu:ab,ti OR fluoroblastin:ab,ti OR fluouracil:ab,ti OR fluoxan:ab,ti OR fluracil:ab,ti OR fluracilium:ab,ti OR fluril:ab,ti OR 'fluro uracil':ab,ti OR fluroblastin:ab,ti OR ifacil:ab,ti OR 'nsc 18913':ab,ti OR 'nsc 19893':ab,ti OR 'nsc18913':ab,ti OR nsc19893:ab,ti OR 'oncofu':ab,ti OR 'ro 2-9757':ab,ti OR 'ro 2 9757':ab,ti OR 'ro2-9757':ab,ti OR 'ro2 9757':ab,ti OR uflahex:ab,ti OR utoral:ab,ti OR verrumal:ab,ti OR '51 21 8':ab,ti
50. 'mitomycin'/exp
51. mitomycin*:ab,ti OR 'nsc 26980':ab,ti OR nsc:ab,ti AND 26980:ab,ti OR nsc26980:ab,ti OR mutamycin:ab,ti OR ametycine:ab,ti OR 'mitocin c':ab,ti OR mitocinc:ab,ti OR mytomycin*:ab,ti OR mitomicin*:ab,ti OR mytomicin*:ab,ti OR mmc:ab,ti OR datisan:ab,ti OR metomit:ab,ti OR mitocyna:ab,ti OR mitosol:ab,ti OR mixandex:ab,ti OR mytocine:ab,ti OR mytozytrex:ab,ti OR vetio:ab,ti OR '1404 00 8':ab,ti
52. 'antimetabolite'/de
53. 'antineoplastic antimetabolite'/de
54. 'nucleic acid synthesis inhibitor'/de
55. antimetabolite*:ab,ti OR (anti NEAR/1 metabolite*):ab,ti
56. antifibrotic*:ab,ti OR (anti NEAR/1 fibrotic*):ab,ti
57. 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56
58. 32 AND 41 AND (47 OR 57)

Appendix 4. PubMed search strategy

#1 ((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomised[tiab] OR randomized[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh])
#2 (Trabeculectom*[tiab] OR Trabeculoplast*[tiab] OR Trabeculotom*[tiab] OR Goniotom*[tiab] OR Microtrabeculectomy[tiab]) NOT MEDLINE[sb]
#3 (Glaucoma*[tiab] AND (surge*[tiab] OR surgi*[tiab] OR filter*[tiab] OR filtrate*[tiab])) NOT MEDLINE[sb]
#4 #2 OR #3
#5 (modif*[tiab] AND (Trabeculectom*[tiab] OR Trabeculoplast*[tiab] OR Trabeculotom*[tiab] OR Goniotom*[tiab] OR Microtrabeculectomy[tiab])) NOT MEDLINE[sb]
#6 (Polytef[tiab] OR Politef[tiab] OR "E PTFE"[tiab] OR EPTFE[tiab] OR PTFE[tiab] OR TFE[tiab] OR FEP[tiab] OR SOLX[tiab] OR polytetrafluoroethylen*[tiab] OR polytetrafluorethylen*[tiab] OR polytetrafluoroethen*[tiab] OR Fluoroflex[tiab] OR Fluoroplast[tiab] OR Ftoroplast[tiab] OR Halon[tiab] OR Polyfene[tiab] OR Tetron[tiab] OR Tarflen[tiab] OR "GORE TEX"[tiab] OR Goretex[tiab] OR gortex[tiab] OR Teflon[tiab] OR Fluon[tiab] OR Ex-press[tiab] OR ologen[tiab] OR Baerveldt[tiab] OR Krupin[tiab] OR Ahmed[tiab] OR Molteno[tiab] OR ExPress[tiab] OR collagen matrix[tiab] OR collagen-GAG[tiab] OR collagen-glycosaminoglycan copolymer matrix[tiab]) NOT MEDLINE[sb]
#7 (Device*[tiab] OR implant*[tiab] OR shunt*[tiab] OR valve*[tiab] OR tube[tiab] OR tubes[tiab]) NOT MEDLINE[sb]
#8 (5FU[tiab] OR 5-FU[tiab] OR Fluorouracil*[tiab] OR Fluoruracil*[tiab] OR 5-HU[tiab] OR Adrucil[tiab] OR Carac[tiab] OR Efudix[tiab] OR Fluoro Uracile[tiab] OR Fluoro-Uracile[tiab] OR Efudex[tiab] OR Fluoroplex[tiab] OR Flurodex[tiab] OR Fluracedyl[tiab] OR Haemato-fu[tiab] OR Neofluor[tiab] OR Onkofluor[tiab] OR Ribofluor[tiab] OR 5-Fluorouracil[tiab]) NOT MEDLINE[sb]
#9 (Mitomycin*[tiab] OR NSC-26980[tiab] OR NSC 26980[tiab] OR NSC26980[tiab] OR Mutamycin[tiab] OR Ametycine[tiab] OR Mitocin-C[tiab] OR MitocinC[tiab] OR mytomycin*[tiab] OR mitomicin*[tiab] OR mytomicin*[tiab] OR MMC[tiab]) NOT MEDLINE[sb]
#10 (Antimetabolite*[tiab] OR anti-metabolite*[tiab]) NOT MEDLINE[sb]
#11 (Antifibrotic*[tiab] OR anti-fibrotic*[tiab]) NOT MEDLINE[sb]
#12 #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13 #1 AND #4 AND #12

Appendix 5. LILACS Controlled Trials search strategy

(Trabeculectom$ or Trabeculoplast$ or Trabeculotom$ or Goniotom$ or Microtrabeculectom$ or **"**trabecular meshwork**"** or **"**filtering surgery**"** or glaucoma$)

AND
(Polytef or Politef or "E PTFE"or EPTFE or PTFE or TFE or FEP or SOLX or polytetrafluoroethylen$ or polytetrafluorethylen$ or polytetrafluoroethen$ or Fluoroflex or Fluoroplast or Ftoroplast or Halon or Polyfene or Tetron or Tarflen or "GORE TEX" or Goretex or gortex or Teflon or Fluon or Ex-press or ologen or Baerveldt or Krupin or Ahmed or Molteno or ExPress or "collagen matrix" or "collagen-GAG" or "collagen-glycosaminoglycan copolymer matrix" or Device$ or implant$ or shunt$ or valve$ or tube$ or (modif$ and Trabeculectom$ or Trabeculoplast$ or Trabeculotom$ or Goniotom$ or Microtrabeculectom$) or Fluorouracil$ or 5FU or 5-FU or Fluoruracil$ or 5-HU or Adrucil or Carac or Efudix or Fluoro Uracile or Fluoro-Uracile or Efudex or Fluoroplex or Flurodex or Fluracedyl or Haemato-fu or Neofluor or Onkofluor or Ribofluor or 5-Fluorouracil or Mitomycin$ or NSC-26980 or NSC 26980 or NSC26980 or Mutamycin or Ametycine or Mitocin-C or MitocinC or mytomycin$ or mitomicin$ or mytomicin$ or MMC or Antimetabolite$ or anti-metabolite$ or Antifibrotic$ or anti-fibrotic$)

Appendix 6. metaRegister of Controlled Trials search strategy

(Trabeculectomy OR (glaucoma surgery)) AND (device OR implant OR implants OR shunt OR valve OR tube OR 5FU OR 5-FU OR Fluorouracil OR Fluoruracil OR Fluoro Uracile OR 5-Fluorouracil OR Mitomycin OR MMC OR Antimetabolite OR Antimetabolites OR Antifibrotic)

Appendix 7. ClinicalTrials.gov search strategy

(search terms) Trabeculectomy OR Trabeculoplasty OR Trabeculotomy OR Goniotomy OR Microtrabeculectomy OR glaucoma

(intervention) Device OR implant OR implants OR shunt OR valve OR tube OR Fluorouracil OR 5- Fluorouracil OR 5-FU OR Fluoruracil OR Mitomycin OR mytomycin OR mitomicin OR mytomicin OR MMC OR Antimetabolite OR Antifibrotic

Appendix 8. ICTRP search strategy

(condition) Trabeculectomy OR Trabeculoplasty OR Trabeculotomy OR Goniotomy OR Microtrabeculectomy OR Goniotomy OR Microtrabeculectomy OR glaucoma
(intervention) Device OR implant OR implants OR shunt OR valve OR tube OR Fluorouracil OR 5- Fluorouracil OR 5-FU OR Fluoruracil OR Mitomycin OR mytomycin OR mitomicin OR mytomicin OR MMC OR Antimetabolite OR Antifibrotic

WHAT'S NEW

Date	Event	Description
13 March 2023	New search has been performed	Updated search on studies comparing three devices only: Ex-PRESS shunts, XEN GelStent, and PreserFlo MicroShunt.
13 March 2023	New citation required and conclusions have changed	Inclusion criteria for the update revised, not affecting search strategies. In the current updates of this review, we included the Ex-PRESS shunt, XEN GelStent, and PreserFlo MicroShunt, which are the major devices available to patients in the current US or EU market. We excluded some devices assessed in the previous review (i.e. silicone tube implant, SOLX Gold Shunt, Ologen, amniotic membrane, expanded polytetrafluoroethylene (ePTFE), and Gelfilms) as they are no longer in current use combined with trabeculectomy or they are adjuvant materials rather than devices.

HISTORY

Protocol first published: Issue 4, 2013
Review first published: Issue 12, 2015

CONTRIBUTIONS OF AUTHORS

Conceiving the review: JP, TR, XW, JE, AKB

Designing the review: JP, TR, XW, JE, AKB

Co-ordinating the review: TR

Screening search results: JP, TR, XW, JE

Organizing retrieval of papers: TR

Screening retrieved papers against inclusion criteria: JP, TR

Appraising quality of papers: JP, TR

Extracting data from papers: JP, TR

Writing to authors of papers for additional information: TR

Providing additional data about papers: TR

Obtaining and screening data on unpublished studies: TR

Data management for the review: TR

Entering data into Review Manager: TR

Analysis of data: TR

Interpretation of data: JP, TR, AKB

Writing the review: JP, TR, AKB

Critical revision: JP, TR, XW, JE, AKB

Performing previous work that was the foundation of current study: XW, RK (Rabeea Khan), AC (Anne Coleman)

DECLARATIONS OF INTEREST

JP: none.

TR: none.

XW: none.

JE: none.

AB reports a consulting relationship with W.L. Gore & Associates, Inc. developing a novel glaucoma drainage implant. This device is currently in preclinical testing and is not intended for use with trabeculectomy.

SOURCES OF SUPPORT

Internal sources

- None, Other

  No internal source of support.

External sources

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- Queen's University Belfast, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following change from our review protocol (Wang 2013b).

We performed all meta-analyses using a random-effects model regardless of the number of pooled studies.

For complications reported for each study, the time of measurement may be different. We combined them in the analyses, based on the assumption that most complications occur within a short time after the surgery. These data should be interpreted with caution.

INDEX TERMS

Medical Subject Headings (MeSH)

*Cataract; *Glaucoma [surgery]; Intraocular Pressure; Quality of Life; Randomized Controlled Trials as Topic; *Trabeculectomy [methods]

MeSH check words

Humans