

Glaucoma: diagnosis and management

[A] Evidence reviews for selective laser trabeculoplasty in ocular hypertension or chronic open-angle glaucoma adult patients

NICE guideline NG81

Evidence reviews underpinning recommendations x to y and research recommendations in the NICE guideline

October 2021

Draft for Consultation

*These evidence reviews were developed
by Guideline Updates Team*

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Selective laser trabeculoplasty (SLT) in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients

1.1 Review question

What is the effectiveness and cost-effectiveness of selective laser trabeculoplasty (SLT) as a first line treatment compared to intraocular pressure-lowering eyedrops in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients?

1.1.1 Introduction

The NICE guideline on glaucoma: diagnosis and management (NICE guideline NG81) was reviewed in 2019 as part of NICE's surveillance programme. New evidence was identified that could affect recommendations following the publication of a Health Technology Assessment (HTA) report on selective laser trabeculoplasty versus eye drops for newly diagnosed ocular hypertension and glaucoma: the Laser in Glaucoma and Ocular Hypertension (LiGHT) trial (Gazzard et al. 2019). No additional evidence published since the NICE guideline launched in November 2017 was considered by the surveillance program because this was an exceptional review after the publication of the HTA report. The authors of the LiGHT trial concluded that SLT 'is an efficient, safe and cheaper alternative to eye drops' and should be considered as a first-line treatment for COAG and OHT in need of intraocular pressure (IOP) reduction. As a result, the decision was made to update this part of the guideline.

The interventions under consideration in this guideline are SLT and eye drops. SLT is performed as an outpatient procedure. Depending on the patient's ability to tolerate the procedure, both eyes may be treated at a single sitting. The procedure involves a single, painless outpatient application of laser to 90°, 180° or 360° of the trabecular meshwork using a contact lens. There are 5 main classes of eye drops available to lower IOP: prostaglandin analogues, beta-blockers (beta receptor antagonists), carbonic anhydrase inhibitors, sympathomimetics (alpha receptor agonists), and miotics (cholinergic agonists). Tablets of the oral carbonic anhydrase inhibitor acetazolamide are only rarely used to treat COAG (because of systemic side effects). Although SLT can be applied to 90°, 180° or 360° of the trabecular meshwork, 360° is the preferred option as it is expected to be more effective compared to the other applications.

The aim of this review is to compare the effectiveness and cost-effectiveness as a first line treatment between SLT and intraocular pressure-lowering eyedrops in OHT or COAG adult patients. This review identified randomised controlled trials that fulfilled the conditions specified in [Table 1](#). See [Appendix A](#) for full details of the review protocol.

1.1.2 Summary of the protocol

Table 1: PICO table for SLT compared to intraocular pressure-lowering eyedrops in OHT or COAG adult patients

Population	Inclusion
	<ul style="list-style-type: none"> Adults (18 and over) with OHT Adults (18 and over) with COAG

	Exclusion <ul style="list-style-type: none"> • People who have received first line treatment for OHT or COAG, • People with secondary glaucoma, for example, neovascular or uveitic glaucoma • People with, or at risk of, primary or secondary angle closure glaucoma • People with primary congenital, infantile or childhood glaucoma • People with angle closure
Intervention	<ul style="list-style-type: none"> • Selective laser trabeculoplasty
Comparator	<ul style="list-style-type: none"> • Intraocular pressure-lowering eyedrops alone
Outcome (s)	Critical outcomes <ul style="list-style-type: none"> • IOP (intraocular pressure) level/outcomes • Glaucomatous visual field loss ^(a) • Normal visual field to visual field defect ^(a) • Progression of glaucomatous visual field defect ^(a) • Vision loss • Health-related quality of life • Adverse events Important outcomes <ul style="list-style-type: none"> • Optic nerve head damage • Progression of optic nerve head damage • Normal or suspicious-to- abnormal optic nerve head • Treatment adherence • Treatment discontinuation

1 (a) Follow up for outcomes related to visual field should be restricted to those 6 months or greater.

2 1.1.3 Methods and process

3 This evidence review was developed using the methods and process described in
4 [Developing NICE guidelines: the manual](#). Methods specific to this review question are
5 described in the review protocol in [Appendix A](#) and the methods section in [Appendix L](#).

6 Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

7 1.1.4 Effectiveness evidence

8 1.1.4.1 Included studies

9 A systematic search was carried out to identify randomised controlled trials (RCTs) and
10 systematic reviews of RCTs, which found 1,320 references (see [Appendix L](#) for the literature
11 search strategy). Evidence from the original guideline (1 RCT) and evidence identified from
12 systematic reviews (1 RCT) was also reviewed. In total, 1,322 references were identified for
13 screening at title and abstract level with 1,298 excluded at this level. Full texts were ordered
14 to be screened for 24 references.

15 In total 5 RCTs were included based on their relevance to the review protocol ([Appendix A](#)).
16 The LiGHT trial was reported in 2 references, therefore 6 references were included in total.
17 The clinical evidence study selection is presented as a PRISMA diagram in [Appendix C](#).

18 See section [1.1.13 References – included studies](#) for a list of included references.

19 1.1.4.2 Excluded studies

20 See [Appendix J](#) for a list of excluded studies with reasons for exclusion.

1 **1.1.5 Summary of studies included in the effectiveness evidence**2 **Table 2: Summary of studies for SLT compared to intraocular pressure-lowering eyedrops in OHT or COAG adult patients**

Study	Intervention	Comparator	Follow-up	Outcomes
Gazzard, 2019 Study location: UK	<ul style="list-style-type: none"> • 360° SLT (n=356 participants; n=613 eyes) <p>Next treatment escalation was medical therapy. One re-treatment with 360° SLT was allowed.</p>	<ul style="list-style-type: none"> • Eye drops (n=362 participants; n=622 eyes) <p>Treatment escalation included:</p> <ul style="list-style-type: none"> • First line: prostaglandin analogues • Second line: β blockers • Third or fourth line: topical carbonic anhydrase inhibitors or α agonists 	<ul style="list-style-type: none"> • 36 months 	<ul style="list-style-type: none"> • Intraocular pressure <ul style="list-style-type: none"> ○ IOP target for OHT <ul style="list-style-type: none"> - <25 mmHg and >20% reduction ○ IOP target for primary open-angle glaucoma (POAG) <ul style="list-style-type: none"> - Mild disease: <21 mmHg and >20% reduction - Moderate disease: <18 mmHg and >30% reduction - Severe disease: <15 mmHg and >30% reduction • Health-related quality of life • Adverse events • Treatment adherence • Visual field progression • Optic disc progression
Katz, 2012 Study location: US	<ul style="list-style-type: none"> • 360° SLT (n=38 participants) <p>Sequence of steps:</p> <ul style="list-style-type: none"> • Step 1: 360° SLT • Step 2: If target IOP not maintained in 1 or both eyes within 4 to 6 weeks, SLT over nasal 180° with 50 applications • Step 3: If target IOP not attained or maintained in 1 or both eyes within 4 to 6 weeks, SLT over temporal 180° with 50 applications 	<ul style="list-style-type: none"> • Eye drops (n=31 participants) <p>Sequence of steps:</p> <ul style="list-style-type: none"> • Step 1: Start with ocular prostaglandin analogue • Step 2: If target IOP not met but initial medication deemed effective, add β blocker • Step 3: Brimonidine • Step 4: Dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol 	<ul style="list-style-type: none"> • 12 months 	<ul style="list-style-type: none"> • Intraocular pressure <ul style="list-style-type: none"> ○ Mean differences of IOP from baseline to follow-up ○ Target IOP was established based on the patient's reference IOP (ie, the mean of 6 separate IOP measurements taken in the course of 2 baseline visits) and their reference visual field score (ie, the mean of visual field scores from at least 2 Humphrey 24-2 visual fields taken during baseline visits before randomization). The formula for target IOP calculations was as follows: target IOP = $[1-(\text{reference IOP} + \text{visual field score}/100)] \times \text{reference IOP}$. Therefore, if the reference IOP=28mm Hg and the reference visual field score=5, then target IOP= $[1-(28+5)/100] \times 28 = (1-0.33) \times 28 = 0.67 \times 28 = 19\text{mm Hg}$.

Study	Intervention	Comparator	Follow-up	Outcomes
	<ul style="list-style-type: none"> Step 4: Treating clinician choice of next therapy for intervention failure 			
Lai, 2004 Study location: China	<ul style="list-style-type: none"> 360° SLT (n=29 eyes) 	<ul style="list-style-type: none"> Eye drops (n=29 eyes) <p>Eye drops included: β blocker, pilocarpine, dorzolamide and latanoprost</p>	<ul style="list-style-type: none"> 5 years 	<ul style="list-style-type: none"> Intraocular pressure <ul style="list-style-type: none"> Mean IOP reduction at follow-up
Nagar, 2005 Study location: UK	<ul style="list-style-type: none"> 360° SLT (n=44 participants; n=44 eyes) 180° SLT (n=49 participants; n=49 eyes) 360° SLT (n=35 participants; n=35 eyes) 	<ul style="list-style-type: none"> Latanoprost (n=39 participants; n=39 eyes) 	<ul style="list-style-type: none"> 12 months 	<ul style="list-style-type: none"> Intraocular pressure <ul style="list-style-type: none"> Success was defined both as a 20% or more reduction in IOP from baseline measurements and also as a 30% or greater IOP reduction from baseline with no additional antiglaucomatous interventions Adverse events
Nagar, 2009 Study location: UK	<ul style="list-style-type: none"> SLT (n=20 participants) 	<ul style="list-style-type: none"> Latanoprost (n=20 participants) 	<ul style="list-style-type: none"> 6 months 	<ul style="list-style-type: none"> Intraocular pressure <ul style="list-style-type: none"> Treatment success for IOP control was defined as at least a 20% reduction from baseline measurement

1 See [Appendix D](#) for full evidence tables.

1 **1.1.6 Summary of the effectiveness evidence**2 **Comparison: 360°SLT vs eye drops**3 **Table 3: Outcome: Intraocular pressure**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Eyes at target IOP at 12 months (RR greater than 1 favours 360°SLT)				
Gazzard 2019	1214	RR 0.98 (0.96, 1.01)	High	No meaningful difference
Eyes at target IOP at 24 months (RR greater than 1 favours 360°SLT)				
Gazzard 2019	1140	RR 1.02 (0.99, 1.05)	High	No meaningful difference
Eyes at target IOP at 36 months (RR greater than 1 favours 360°SLT)				
Gazzard 2019	1072	RR 1.02 (0.99, 1.05)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 12 months – OHT (RR greater than 1 favours 360°SLT)				
Gazzard 2019	362	RR 0.98 (0.94, 1.02)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 12 months – Mild OAG (open angle-glaucoma) (RR greater than 1 favours 360°SLT)				
Gazzard 2019	647	RR 0.99 (0.96, 1.02)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 12 months – Moderate OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	111	RR 0.94 (0.85, 1.04)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 12 months – Severe OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	93	RR 1.00 (0.88, 1.14)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 24 months – OHT (RR greater than 1 favours 360°SLT)				
Gazzard 2019	327	RR 1.06 (1.01, 1.11)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 24 months – Mild OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	604	RR 1.01 (0.98, 1.05)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 24 months – Moderate OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	133	RR 1.00 (0.93, 1.08)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 24 months – Severe OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	78	RR 0.98 (0.83, 1.15)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 36 months – OHT (RR greater than 1 favours 360°SLT)				
Gazzard 2019	296	RR 1.04 (0.98, 1.10)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 36 months – Mild OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	545	RR 1.02 (0.98, 1.06)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 36 months – Moderate OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	130	RR 1.02 (0.95, 1.10)	High	No meaningful difference
Eyes at target IOP by type of glaucoma at 36 months – Severe OAG (RR greater than 1 favours 360°SLT)				
Gazzard 2019	101	RR 0.99 (0.84, 1.16)	High	No meaningful difference

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Right and left eyes at target IOP – Right eye at 6 months (RR greater than 1 favours 360°SLT)				
Katz 2012	66	RR 0.83 (0.52, 1.33)	Very low	Could not differentiate
Right and left eyes at target IOP – Right eye at 12 months (RR greater than 1 favours 360°SLT)				
Katz 2012	52	RR 0.81 (0.53, 1.22)	Very low	Could not differentiate
Right and left eyes at target IOP – Left eye at 6 months (RR greater than 1 favours 360°SLT)				
Katz 2012	61	RR 1.12 (0.65, 1.93)	Very low	Could not differentiate
Right and left eyes at target IOP – Left eye at 12 months (RR greater than 1 favours 360°SLT)				
Katz 2012	48	RR 0.87 (0.54, 1.40)	Very low	Could not differentiate
Mean IOP reduction at 6 months (MD greater than 0 favours 360°SLT)				
Katz 2012	69	MD -0.60 (-1.99, 0.79)	Very low	Could not differentiate
Mean IOP reduction at 12 months (MD greater than 0 favours 360°SLT)				
Katz 2012	54	MD -0.70 (-1.91, 0.51)	Very low	Could not differentiate
Mean IOP reduction at 5 years – (MD greater than 0 favours 360°SLT)				
Lai 2004	58	MD -0.10 (-3.52, 3.32)	Very low	Could not differentiate

1 a) No meaningful difference: 95% CI completely between MID's and crossing line of no effect; Could not
2 differentiate: 95% CI are not completely between MID's and crossing line of no effect
3 RR: relative risk; MD: mean difference

4 **Table 4: Outcomes: Visual field progression; optic disc progression**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Eyes with visual field progression at 36 months (RR less than 1 favours 360°SLT)				
Gazzard 2019	1072	RR 0.67 (0.37, 1.20)	Moderate	Could not differentiate
Eyes with optic disc progression at 36 months (RR less than 1 favours 360°SLT)				
Gazzard 2019	1072	RR 0.67 (0.11, 3.97)	Low	Could not differentiate

5 a) Could not differentiate: 95% CI are not completely between MID's and crossing line of no effect

6 **Table 5: Outcome: Quality of life**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
EQ-5D at 6 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	662	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
EQ-5D at 12 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	654	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
EQ-5D at 18 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	654	MD 0.00 (-0.02, 0.02)	High	No meaningful difference
EQ-5D at 24 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	652	MD 0.00 (-0.02, 0.02)	High	No meaningful difference
EQ-5D at 30 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	637	MD 0.00 (-0.02, 0.02)	High	No meaningful difference
EQ-5D at 36 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	673	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
GUI at 6 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	659	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
GUI at 12 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	635	MD 0.01 (-0.01, 0.03)	High	No meaningful difference

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
GUI at 18 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	608	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
GUI at 24 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	603	MD 0.02 (0.00, 0.04)	High	No meaningful difference
GUI at 30 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	590	MD 0.02 (0.00, 0.04)	High	No meaningful difference
GUI at 36 months (MD greater than 0 favours 360°SLT)				
Gazzard 2019	602	MD 0.01 (-0.01, 0.03)	High	No meaningful difference
GQL-15 at 6 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	647	MD -0.80 (-1.60, 0.00)	High	No meaningful difference
GQL-15 at 12 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	632	MD -0.50 (-1.34, 0.34)	High	No meaningful difference
GQL-15 at 18 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	600	MD -0.60 (-1.40, 0.20)	High	No meaningful difference
GQL-15 at 24 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	587	MD -0.50 (-1.34, 0.34)	High	No meaningful difference
GQL-15 at 30 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	580	MD -0.30 (-1.10, 0.50)	High	No meaningful difference
GQL-15 at 36 months (MD less than 0 favours 360°SLT)				
Gazzard 2019	601	MD -0.40 (-1.34, 0.54)	High	No meaningful difference

1 a) No meaningful difference: 95% CI completely between MDs and crossing line of no effect

2 Table 6: Outcome: Adverse events

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Total adverse events (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.02 (0.93, 1.12)	High	No meaningful difference
Ocular adverse events: Aesthetic side effects of medication (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.13 (0.06, 0.28)	High	Favours 360°SLT
Ocular adverse events: Ophthalmic allergic reactions (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.78 (0.38, 1.58)	Low	Could not differentiate
Ocular adverse events: Reactivation of herpes simplex keratitis (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.02 (0.06, 16.19)	Low	Could not differentiate
Ocular adverse events: Uveitis (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 2.03 (0.19, 22.33)	Low	Could not differentiate
Ocular adverse events: Other (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.86 (0.75, 0.97)	Moderate	Favours 360°SLT
SLT-related ocular adverse events: Inflammation after SLT (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 3.05 (0.12, 74.63)	Low	Could not differentiate
SLT-related ocular adverse events: IOP spike after SLT (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 13.22 (0.75, 233.77)	Low	Could not differentiate
SLT-related ocular adverse events: Other transient events (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 124.06 (17.43, 882.95)	High	Favours eye drops

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
SLT-related ocular adverse events: Participants with an adverse event during SLT procedure (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 29.49 (1.77, 492.44)	High	Favours eye drops
Systemic adverse events: Pulmonary problems (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.87 (0.41, 1.86)	Low	Could not differentiate
Systemic adverse events: Cardiac events (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.02 (0.30, 3.48)	Low	Could not differentiate
Systemic adverse events: Drug-related events (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.45 (0.28, 0.72)	High	Favours 360°SLT
Systemic adverse events: Other (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.97 (0.74, 1.27)	Low	Could not differentiate
Serious adverse events: Total (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.96 (0.70, 1.30)	Low	Could not differentiate
Serious adverse events: Ocular (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.36 (0.48, 3.87)	Low	Could not differentiate
Serious adverse events: Pulmonary problems (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.68 (0.11, 4.03)	Low	Could not differentiate
Serious adverse events: Cerebrovascular accidents (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 2.03 (0.19, 22.33)	Low	Could not differentiate
Serious adverse events: Cardiac events (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.16 (0.43, 3.17)	Low	Could not differentiate
Serious adverse events: Cancer (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.65 (0.69, 3.94)	Low	Could not differentiate
Serious adverse events: Death (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 4.07 (0.87, 19.02)	Moderate	Could not differentiate
Serious adverse events: Other systemic (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 0.87 (0.60, 1.28)	Low	Could not differentiate

1 a) No meaningful difference: 95% CI completely between MIDs and crossing line of no effect; Could not
2 differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Favours: statistically
3 significant

4 Table 7: Outcome: Treatment adherence

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Treatment adherence (self-reported concordance at 36 months) (RR greater than 1 favours 360°SLT)				
Gazzard 2019	626	RR 1.00 (0.98, 1.02)	High	No meaningful difference

5 a) No meaningful difference: 95% CI completely between MIDs and crossing line of no effect

6 Table 8: Outcome: Treatment discontinuation

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Treatment discontinuation (RR less than 1 favours 360°SLT)				
Gazzard 2019	718	RR 1.81 (0.81, 4.04)	Moderate	Could not differentiate

7 a) Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect

1 **Comparison: 360°SLT vs latanoprost**2 **Table 9: Outcomes: Intraocular pressure; adverse events**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Eyes at target IOP at 12 months – >20% IOP reduction (RR greater than 1 favours 360°SLT)				
Nagar 2005	57	RR 0.79 (0.62, 1.00)	Very low	Could not differentiate
Eyes at target IOP at 12 months – >30% IOP reduction (RR greater than 1 favours 360°SLT)				
Nagar 2005	57	RR 0.62 (0.40, 0.95)	Very low	Favours latanoprost
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 360°SLT)				
Nagar 2005	57	RR 10.89 (0.70, 169.72)	Very low	Could not differentiate
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 360°SLT)				
Nagar 2005	57	RR 14.00 (0.91, 216.28)	Very low	Could not differentiate
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 360°SLT)				
Nagar 2005	57	RR 7.78 (0.49, 123.17)	Very low	Could not differentiate

3 a) *Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Favours:*
4 *statistically significant*

5 **Comparison: 180°SLT vs latanoprost**6 **Table 10: Outcomes: Intraocular pressure; adverse events**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Eyes at target IOP at 12 months – >20% IOP reduction (RR greater than 1 favours 180°SLT)				
Nagar 2005	62	RR 0.71 (0.55, 0.92)	Very low	Favours latanoprost
Eyes at target IOP at 12 months – >30% IOP reduction (RR greater than 1 favours 180°SLT)				
Nagar 2005	62	RR 0.56 (0.36, 0.86)	Very low	Favours latanoprost
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 180°SLT)				
Nagar 2005	62	RR 5.88 (0.37, 94.25)	Very low	Could not differentiate
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 180°SLT)				
Nagar 2005	62	RR 11.48 (0.74, 178.16)	Very low	Could not differentiate
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 180°SLT)				
Nagar 2005	62	RR 4.76 (0.29, 77.49)	Very low	Could not differentiate

7 a) *Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Favours:*
8 *statistically significant*

9 **Comparison: 90°SLT vs latanoprost**10 **Table 11: Outcomes: Intraocular pressure; adverse events**

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Eyes at target IOP at 12 months – >20% IOP reduction (RR greater than 1 favours 90°SLT)				
Nagar 2005	48	RR 0.37 (0.23, 0.60)	Very low	Favours latanoprost
Eyes at target IOP at 12 months – >30% IOP reduction (RR greater than 1 favours 90°SLT)				
Nagar 2005	48	RR 0.15 (0.06, 0.39)	Very low	Favours latanoprost
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 90°SLT)				
Nagar 2005	48	RR 1.94 (0.10, 38.01)	Very low	Could not differentiate

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 90°SLT)				
Nagar 2005	48	RR 8.94 (0.56, 141.79)	Very low	Could not differentiate
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 90°SLT)				
Nagar 2005	48	RR 2.72 (0.15, 49.38)	Very low	Could not differentiate

1 a) *Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Favours:*
2 *statistically significant*

3 Comparison: SLT (degrees not specified) vs latanoprost

4 Table 12: Outcome: Intraocular pressure

No. of studies	Sample size	Effect estimate (95% CI)	Quality	Interpretation of effect ^a
Mean IOP reduction at day 3 (MD greater than 0 favours SLT)				
Nagar 2009	40	MD 0.00 (-1.94, 1.94)	Very low	Could not differentiate
Mean IOP reduction at week 1 (MD greater than 0 favours SLT)				
Nagar 2009	40	MD -1.70 (-3.78, 0.38)	Low	Could not differentiate
Mean IOP reduction at month 1 (MD greater than 0 favours SLT)				
Nagar 2009	40	MD -3.80 (-5.88, -1.72)	Moderate	Favours latanoprost
Mean IOP reduction at month 6 (MD greater than 0 favours SLT)				
Nagar 2009	40	MD -1.60 (-3.82, 0.62)	Low	Could not differentiate
Eyes at target IOP at day 3 (RR greater than 1 favours SLT)				
Nagar 2009	40	RR 1.14 (0.75, 1.73)	Very low	Could not differentiate
Eyes at target IOP at week 1 (RR greater than 1 favours SLT)				
Nagar 2009	40	RR 0.65 (0.40, 1.04)	Low	Could not differentiate
Eyes at target IOP at month 1 (RR greater than 1 favours SLT)				
Nagar 2009	40	RR 0.35 (0.16, 0.80)	Low	Favours latanoprost
Eyes at target IOP at month 6 (RR greater than 1 favours SLT)				
Nagar 2009	40	RR 0.86 (0.65, 1.14)	Low	Could not differentiate

5 a) *Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Favours:*
6 *statistically significant*

7 See [Appendix F](#) for full GRADE tables.

8 1.1.7 Economic evidence

9 1.1.7.1 Included studies

10 A single search was performed to identify published economic evidence (see Appendix B).
11 The search retrieved 597 studies. Based on title and abstract screening, 578 of the studies
12 could confidently be excluded. Eighteen studies were excluded following the full-text review.
13 There was also a Health Technology Assessment (HTA) identified from citation searching
14 that was linked to the included study from the review. Thus, two studies were included from
15 the existing literature, both reporting different results from the same original study.

16 1.1.7.2 Excluded studies

17 See Appendix J for a list of references for excluded studies, with reasons for exclusion.

1.1.8 Summary of included economic evidence

The two included studies are summarised below, with full evidence tables and quality assessments given in Appendix H. Both analyses are based on the LiGHT trial, one a between trial analysis and the other a lifetime Markov model, and both found SLT to dominate (cost less and provide more QALYs than) first-line treatment with eye drops.

Table 13: Economic evidence profile [for body of evidence review]

Study	Applicability	Limitations	Other comments	Incremental			Uncertainty
				Cost ¹ (£)	Effects (QALYs)	ICER (£/QALY)	
Gazzard et al. 2019	Directly applicable ²	Minor limitations ³	3-year time horizon (within-trial analysis of the LiGHT RCT)	Eye drops - £4,228 SLT ⁴ - £4,119	Eye drops – 2.62 SLT – 2.65	SLT dominates	Probabilistic sensitivity analysis: There is a 97% probability that SLT is cost effective at a £20,000 willingness-to-pay threshold and a 93% probability that SLT is cost effective at a £30,000 willingness-to-pay threshold.
Gazzard et al. 2019 (HTA ⁵)	Directly applicable ⁶	Minor limitations ⁷	HTA report based on the evidence from Gazzard et al. 2019 but over a lifetime time horizon, using a Markov model	Eye drops - £21,248 SLT - £18,239	Eye drops – 12.3 SLT – 12.5	SLT dominates	Probabilistic sensitivity analysis: There is a 90% probability that SLT is cost effective compared with eye drops at a 20,000 willingness-to-pay threshold

¹ Costs updated to 2021 costs using <https://eppi.ioe.ac.uk/costconversion/default.aspx> ² QALYs assessed using EQ-5D-5L rather than EQ-5D-3L

³ Time horizon 3 years, financial conflicts of interests declared but model appears robust

⁴ Selective laser trabeculoplasty

⁵ Health Technology Assessment

⁶ QALYs assessed using EQ-5D-5L rather than EQ-5D-3L

⁷ Lifetime time horizon, financial conflicts of interests declared but model appears robust

1 **1.1.9 Economic model**

2 The two cost-utility analyses reported above are based on clinical data from the LiGHT RCT.
3 The effectiveness review conducted for this guideline did not find any further data that would
4 affect the model (no studies other than the LiGHT RCT reported data on outcomes used in
5 the modelling) and therefore no updates were felt necessary to make to the analyses
6 reported in the published papers. Thus, no original economic modelling was completed for
7 this review question.

8 **1.1.10 Evidence statement**

9 Two economic studies were included in the evidence. Both studies were based on the LiGHT
10 RCT, one had a three-year time horizon and the other had a lifetime time horizon. Both of the
11 studies were directly applicable and had minor limitations.

12 **1.1.11 The committee's discussion and interpretation of the evidence**

13 **1.1.11.1. The outcomes that matter most**

14 The committee agreed that the key outcome for adults with OHT or COAG was visual field
15 progression which, in the long-term, could affect people's vision. Intraocular pressure was
16 considered to be a relevant surrogate outcome because lowering intraocular pressure could
17 prevent the risk of optic nerve damage and vision loss. This means that if the IOP is high
18 (≥ 24 mmHg) and left untreated, the high IOP is likely to damage the optic nerve and it could
19 also cause vision loss. Other relevant outcomes were health-related quality of life, adverse
20 events, optic disc progression, treatment adherence and treatment discontinuation. The
21 committee discussed that the number of eye drop treatments might have an effect on
22 people's quality of life and on their treatment adherence which was taken into account when
23 developing recommendations while this was not an outcome in the protocol it was
24 considered important. Most of the outcomes listed in the review protocol were reported by
25 the included studies apart from glaucomatous visual field loss, normal visual field to visual
26 field defect, vision loss, optic nerve head damage, and normal or suspicious-to- abnormal
27 optic nerve head.

28 **1.1.11.2 The quality of the evidence**

29 Overall, the quality of the evidence was from high to very low with the main reasons for
30 downgrading being due to imprecision of the evidence, risk of bias, and indirectness. In some
31 of the evidence, imprecision was considered to be serious or very serious with the 95%
32 confidence intervals crossing one or two ends of the defined minimally important differences
33 (MIDs) thresholds. Risk of bias for some of the included RCTs was due to lack of information
34 on allocation concealment, lack of reporting on statistical methods to estimate treatment
35 effect (intention-to-treat analysis or per-protocol analysis), and lack of reporting that protocols
36 were pre-registered where the pre-specific analysis plan would be reported. There were
37 differences in comparators and follow-up times between included RCTs which prevented
38 meta-analysis to be carried out.

39 The review protocol states that studies including people who have previously received first
40 line treatment for OHT or COAG would be excluded. One study (Katz 2012) was identified
41 which included people who were not treatment naïve and it was unclear if participants were
42 treatment naïve in another study (Nagar 2005). The committee highlighted that these studies
43 provide context but that they should be downgraded for indirectness.

44 Three studies included in this review were conducted in the UK (Gazzard 2019, Nagar 2005
45 and Nagar 2009), 1 study was conducted in the US (Katz 2012) and 1 study was conducted
46 in China (Lai 2004). Authors of Lai 2004 highlighted that Asian eyes have more pigmented

1 trabecular meshwork. This means that the laser energy required and the clinical response
2 might be different from eyes with lightly pigmented trabecular meshwork. The committee
3 highlighted that this study is relevant to a subset of the UK population, but it's not directly
4 applicable to the UK general population.

5 RCTs were the main study designs included in this review. The committee noted that while
6 RCTs are useful, these trials often include people who are highly motivated and who are
7 provided extensive support, resulting in high adherence to treatment. The committee
8 highlighted that in practice, it can be difficult to get patients to adhere to eye drops. Patient
9 adherence to eye drops may have been overestimated in the included studies as this
10 outcome was self-reported.

11 The committee highlighted that there was a lack of long-term evidence on progression of
12 glaucomatous visual field defect and progression of optic nerve head damage (only 1 RCT
13 reported both outcomes at 36 months follow-up). They also noted that patients care more
14 about vision outcomes compared to other outcomes such as IOP. The committee discussed
15 the importance of investigating these outcomes at longer follow-up times (5 and 10 years) to
16 know how effective SLT is at long-term. This evidence could help to target interventions
17 which could prevent progression. Therefore, a research recommendation was developed to
18 cover this gap in the evidence.

19 **1.1.11.3 Benefits and harms**

20 High quality evidence showed that there was no meaningful difference between SLT, and
21 eye drops in achieving the target IOP (either 20% or 30% IOP reduction), no meaningful
22 difference in the change of health-related quality of life overtime, no meaningful difference in
23 the risk of total adverse events, and no meaningful difference in treatment adherence.

24 Further evidence was identified from the LiGHT trial that showed people who were given eye
25 drops as first line treatment, used more eye drops and required the use of more than 1 eye
26 drop medication at 12 months, compared to people who were given SLT as first line
27 treatment (see Table 18 in Appendix M). Cost effectiveness evidence further showed that
28 first-line treatment with 360° SLT was more effective and less costly compared with eye
29 drops. This evidence also showed that SLT resulted in a longer period without eye drops, or
30 with fewer eyedrops, and slightly slower estimated progression rates for glaucoma, which
31 improved quality of life. Based on this evidence (see section [1.1.11.4 Cost effectiveness and
32 resource use](#) for further details), the committee agreed that 360° SLT could be a treatment
33 option for OHT and COAG.

34 However, evidence did show that that there were transient adverse events associated with
35 SLT such as transient discomfort, blurred vision, photophobia and hyperaemia. Based on
36 their clinical expertise, the committee noted that some people with OHT or COAG might
37 choose to have SLT to be free of having eye drops and that it was important to clarify that
38 they might need to receive eye drops in the future if IOP is not successfully reduced after the
39 SLT procedure. Additionally, people might also need further SLT if the effect of the first SLT
40 procedure reduces over time, which is an important factor to take into consideration when
41 choosing treatment options.

42 Furthermore, evidence was mainly identified for newly diagnosed OHT or newly diagnosed
43 primary open-angle glaucoma (POAG) which is defined in the 2017 version of the guideline
44 as COAG in the absence of any other ocular, systemic or pharmacological cause and
45 accompanied by elevated intraocular pressure. In the evidence, people with secondary
46 glaucoma associated with pigment dispersion syndrome were excluded from the LiGHT trial
47 (Gazzard 2019 HTA).

48 The committee agreed that SLT is an appropriate treatment option for people with OHT and
49 COAG but in practice people can be newly diagnosed but have pigment dispersion
50 syndrome. In this population, SLT would not be appropriate. There was no evidence on the

1 use of SLT in people with pigment dispersion syndrome and the committee agreed that eye
2 drop treatment is more suitable for people with pigment dispersion syndrome. Based on the
3 evidence and clinical understanding, the committee noted that SLT as first line treatment was
4 not appropriate for people with pigment dispersion syndrome.

5 Based on the new evidence, the committee agreed that 360° SLT should be offered as first-
6 line treatment to people with newly diagnosed OHT (and if they are at risk of visual
7 impairment within their lifetime) or COAG, however this should exclude cases associated
8 with pigment dispersion syndrome.

9 To aid decision making, the committee further stated that information should be provided on
10 the possibility of needing eye drops treatment after SLT, the time that SLT takes to improve
11 IOP, the SLT specific side effects including the type and duration, and that they might need
12 further SLT treatment at a later date.

13 Based on the LiGHT trial, a further recommendation was added to clarify that a second 360°
14 SLT could be needed if the initial SLT was successful, but the IOP was above target
15 intraocular pressure (24 mmHg or more). It was also noted that a study (Katz 2012) used
16 180° SLT if a second or third SLT was needed but this study included people who were not
17 treatment naïve. Katz 2012 did not meet one of the exclusion criteria in our review protocol
18 and was downgraded for indirectness (see section 1.1.11.2 for more details). Based on their
19 clinical understanding, the committee noted that the success of treatment is judged by
20 individual clinicians but generally, the treatment to reduce IOP had to work for at least 6
21 months to be considered successful. Based on their clinical experience, the committee noted
22 that any effect from SLT might be reduced after repeating the procedure more than 2 or 3
23 times.

24 The committee agreed that some people might prefer not to have SLT or that this procedure
25 might not be suitable for some people. The 2017 guideline recommended prostaglandin
26 analogue (PGA) eye drops for OHT or COAG. Therefore, they amended this to reflect the
27 new 2022 recommendations on using SLT. The amended recommendation offers a generic
28 PGA to these people as an alternative first-line option instead of SLT. As previously noted, in
29 people with pigment dispersion syndrome, SLT was not considered to be an appropriate
30 treatment. Therefore, eye drops were recommended as first line treatment for this population.

31 The committee noted that the first line use of SLT to treat OHT or COAG might lead to a
32 significant change in practice that requires different organisation of care. They also
33 discussed the safety of the SLT procedure and agreed that healthcare professionals should
34 discuss with the responsible consultant ophthalmologist the decision to offer SLT and how it
35 will be performed.. This means that healthcare professionals such as associate specialists,
36 specialist nurses, optometrists and allied health professionals can perform SLT with support
37 from a consultant ophthalmologist.

38 The committee also noted that healthcare professionals who provide SLT should be given
39 support and have relevant training on the suitability and safety of the procedure, including the
40 benefits and risks. They should also be trained on discussing these points and patient
41 consent with patients and their family members or carers. A similar approach was taken in
42 the LiGHT trial where training was given to all treating surgeons before recruitment and at
43 least 1 laser treatment was observed by the chief investigator, who was a consultant
44 ophthalmic surgeon. Based on these discussions new recommendations were added to
45 provide further clarification on organisation of care.

46 **1.1.11.4 Cost effectiveness and resource use**

47 The committee discussed the published cost-utility evidence relating to selective laser
48 trabeculoplasty (SLT) compared with pharmacological treatment (eyedrops) in ocular
49 hypertension and open-angle glaucoma. This included a published study and a health
50 technology appraisal (HTA) that were both based on the same clinical trial (LiGHT) and both

1 these studies were assessed to be directly relevant to the review question. The difference
2 between the study and the HTA was the time horizon; the study had a three-year time
3 horizon (to match that of the LiGHT trial) whereas the HTA had a lifetime time horizon and
4 extrapolated the data beyond the time horizon of the trial.

5 The evidence from both analyses showed that SLT dominates eye drops for both a 3-year
6 time horizon and a lifetime time horizon (that is, SLT is associated with both lower costs and
7 better outcomes). The committee noted that the pathway modelled as the comparator
8 (multiple lines of eye drops followed by surgery if needed) was not current treatment within
9 the NHS, as SLT is an option later in the eye drops pathway in the previous NICE guidance.
10 However, the committee felt this was not a significant limitation and the comparison of SLT
11 and eye drops as a first-line treatment was valid, and therefore that the study and HTA still
12 showed that it would be cost effective to move SLT to the beginning of the treatment
13 pathway. They also noted the LiGHT trial found no meaningful differences in the
14 effectiveness of SLT between people with ocular hypertension and people with open-angle
15 glaucoma, and were therefore confident the findings applied to both populations, as long as
16 they met the inclusion criteria for the LiGHT trial.

17 The committee noted that there was only a small difference in the quality of life between the
18 two comparators and therefore the main reason that SLT was the dominant option was
19 because the SLT arm was less costly. These lower costs were primarily driven by the finding
20 that using SLT means people are likely to need to use significantly fewer eye drops, which
21 reduces costs both of the medicines themselves, and also appointments to monitor and
22 modify treatment. The committee noted that SLT may need to be repeated and that was
23 included in the analyses (with approximately 15% of people in the SLT arm having a second
24 procedure within the first year) and therefore that gave the committee more confidence in the
25 result, as it reflected their expectations of how the treatment would be used in practice.

26 The committee acknowledged that there are some patients who may prefer using eye drops
27 because it feels like they are actively doing something to improve their eyes and may make
28 them feel more in control of their condition. However, the committee felt that more patients
29 would prefer to not have to use eye drops. The committee also felt that it was important to be
30 aware of patients who find eye drops difficult to use, for example if the patient also has
31 dementia or arthritis, this can affect adherence and therefore effect the improvements the
32 patients are able to achieve. The committee felt that in these cases some patients would
33 require a carer to come in to administer the eye drops that would increase the cost of the eye
34 drops arm. Therefore, this group are likely to benefit even more from SLT.

35 The sensitivity analyses from both the study and the HTA varied the parameters of the
36 analysis and for each analysis the probability of SLT being cost effective was over 90%. The
37 committee felt that this was strong evidence in support of SLT as a first line treatment. The
38 committee discussed having SLT or eye drops as equal options as first line treatment.
39 However, the committee felt that given the cost-effectiveness evidence, and their expectation
40 that a significant majority of patients would prefer SLT if it were available, it was important to
41 rank SLT higher than eye drops and therefore SLT should be the first line treatment. The
42 committee felt that using SLT is becoming more common in practice and with the clinical and
43 cost effectiveness data there was strong evidence to move SLT to become the first line
44 treatment for glaucoma.

45 **1.1.11.5 Other factors the committee took into account**

46 The 2017 update of the guideline included recommendations for people with suspected
47 COAG. The recommendation stated that generic PGA should be offered to people with
48 suspected COAG and IOP of 24 mmHg or more. The committee flagged that this
49 recommendation could cause confusion amongst clinicians as the IOP level stated is the
50 same as the level recommended to treat OHT. The committee further stated that people with
51 suspected glaucoma would not be treated unless there were clear clinical grounds, for

1 example, if they developed OHT or COAG. Therefore, the committee agreed to remove that
2 recommendation from the guideline.

3 Additionally, in the 2017 update, recommendations on treatment for people with COAG,
4 primarily focused on laser trabeculoplasty. As the evidence identified in the current review
5 focused specifically on SLT, the committee noted it was important that all recommendations
6 in the guideline are in line with the evidence and new recommendations. Therefore, SLT is
7 now a treatment option for people in whom adherence and eye drop instillation technique are
8 satisfactory.

9 The 2017 update included a recommendation which stated that clinicians could consider
10 offering people with COAG who cannot tolerate treatment either a drug from another
11 therapeutic class or preservative eye drops. After trying drugs from 2 therapeutic classes, it
12 was recommended to consider surgery with pharmacological augmentation (MMC) as
13 indicated or laser trabeculoplasty. The committee amended this recommendation to add
14 further clarity by stating that a drug from another therapeutic class or preservative-free
15 eyedrops should be offered to people with COAG who cannot tolerate pharmacological
16 treatment. The committee further added that SLT or surgery should be considered after
17 trying drugs from 2 therapeutic classes, in order to be consistent with the new
18 recommendations.

19 The 2017 update also included recommendations for people with COAG who have
20 undergone surgery, but IOP has not reduced sufficiently to prevent the risk of progression to
21 sight loss. Laser trabeculoplasty or cyclodiode treatment were a suggested treatment option
22 for the group. The recommendation was previously based on committee consensus. The
23 new evidence in the current update, excluded people with a previous intraocular surgery and
24 the committee highlighted that they were not aware of any other evidence for the use of SLT
25 after surgery. Due to the lack of evidence in this population, the option of having laser
26 trabeculoplasty after surgery was removed from the recommendation.

27 No evidence was identified in people with advanced COAG as the LIGHT trial excluded
28 people with advanced COAG. Therefore, no specific recommendations were developed.
29 However, the 2017 update, included a recommendation that stated in people with advanced
30 COAG surgery could be offered with pharmacological augmentation. The committee noted
31 that there are instances where surgery might not be suitable (for example due to systemic
32 comorbidities). The 2017 update also included a recommendation stating that for people with
33 COAG who prefer not to have surgery or for whom surgery is not suitable pharmacological
34 treatment, laser trabeculoplasty or cyclodiode laser treatment could be offered. The
35 committee amended this recommendation to state that SLT can be a treatment option
36 instead of laser trabeculoplasty. SLT is the type of laser trabeculoplasty currently used in
37 clinical practice.

38 Recommendations for people with OHT have been amended to be in line with the new
39 recommendation which offers SLT as first-line treatment. In particular, SLT was added to the
40 recommendation to refer people whose IOP cannot be reduced sufficiently with
41 pharmacological treatment to a consultant ophthalmologist.

42 The committee identified older people (aged over 70 years) as an important subgroup. Older
43 people, including people with cognitive or physical impairment, people with learning
44 disabilities and people with dementia might find it difficult to administer eye drops or may
45 require assistance from carers in receiving IOP-lowering eye drops to manage their OHT or
46 COAG. In these populations, adherence to medication is a concern. It was also highlighted
47 that IOP-lowering eye drops might not be the preferred treatment to manage OHT or COAG
48 during pregnancy or breastfeeding because of the side effects that these treatments could
49 have on women and their children (manufacturers advise to avoid use during pregnancy and
50 breastfeeding).

1 The new recommendations allow SLT to be considered as a treatment option in these
2 groups. This can be beneficial for older people, people with cognitive or physical impairment,
3 people with learning disabilities and people with dementia as this can lead to people needing
4 to use significantly fewer eyedrops. Polypharmacy is also a concern, especially in older
5 people therefore a reduction in the need for eyedrops can potentially result in fewer
6 medications being used in this population.

7 The committee acknowledged that late presentation of glaucoma (usually in the form of
8 advanced glaucoma) might be associated with people who are of black African or black
9 Caribbean descent and with greater individual and area level deprivation. Late presentation
10 of glaucoma might be driven by clinical variation and by variations in healthcare seeking
11 behaviours and healthcare inequalities in referrals or diagnosis. Evidence included in the
12 review, excluded people with advanced glaucoma, therefore specific recommendations could
13 not be drafted for this population. However, the committee agreed that new
14 recommendations were unlikely to have an impact on late presentation of glaucoma because
15 surgery is the main treatment option for advanced glaucoma and this is stated in existing
16 recommendations.

17 **1.1.12 Recommendations supported by this evidence review**

18 This evidence review supports recommendations 1.4.4 and 1.4.5, 1.4.13 and 1.4.14, 1.4.19
19 and 1.4.21 to 1.4.23 and the research recommendation on long-term effectiveness of SLT.

20 **1.1.13 References – included studies**

21 **1.1.13.1 Effectiveness evidence**

22 Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective
23 laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and
24 glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet* (London, England)
25 393(10180): 1505-1516

26 Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019 HTA)
27 Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and
28 glaucoma: the LiGHT RCT. *Health technology assessment* (Winchester, England) 23(31): 1-
29 102

30 Katz, L Jay, Steinmann, William C, Kabir, Azad et al. (2012) Selective laser trabeculoplasty
31 versus medical therapy as initial treatment of glaucoma: a prospective, randomized trial.
32 *Journal of glaucoma* 21(7): 460-8

33 Lai JS, Chua JK, Tham CC et al. (2004) Five-year follow up of selective laser trabeculoplasty
34 in Chinese eyes. *Clinical & experimental ophthalmology* 32(4): 368-372

35 Nagar M, Ogunyomade A, O'Brart DP et al. (2005) A randomised, prospective study
36 comparing selective laser trabeculoplasty with latanoprost for the control of intraocular
37 pressure in ocular hypertension and open angle glaucoma. *The British journal of*
38 *ophthalmology* 89(11): 1413-1417

39 Nagar, M; Luhishi, E; Shah, N (2009) Intraocular pressure control and fluctuation: the effect
40 of treatment with selective laser trabeculoplasty. *The British journal of ophthalmology* 93(4):
41 497-501

42 **1.1.13.2 Economic**

43 Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty
44 versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a

- 1 multicentre randomised controlled trial Lancet. 2019;393(10180):1505-1516.
- 2 doi:10.1016/S0140-6736(18)32213-X
- 3
- 4 Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.
- 5 Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and
- 6 glaucoma: the LiGHT RCT. Health Technol Assess 2019;23(31).

7

1 Appendices

2 Appendix A – Review protocols

3 Review protocol for selective laser trabeculoplasty (SLT) in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients. 4

ID	Field	Content
0.	PROSPERO registration number	
1.	Review title	Effectiveness and cost-effectiveness of selective laser trabeculoplasty (SLT) as a first line treatment compared to intraocular pressure-lowering eyedrops in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients.
2.	Review question	1.1 What is the effectiveness and cost-effectiveness of selective laser trabeculoplasty (SLT) as a first line treatment compared to intraocular pressure-lowering eyedrops in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients?
3.	Objective	To establish whether SLT should be offered as a first line treatment in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients.

<p>4.</p>	<p>Searches</p>	<p>The following databases will be searched:</p> <ul style="list-style-type: none"> • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • August 2008 onwards • English language • Human studies <p>Other searches:</p> <ul style="list-style-type: none"> • Reference searching • Citation searching • Inclusion lists of systematic reviews • Websites <p>The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion.</p> <p>The full search strategies for MEDLINE database will be published in the final review.</p>
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5.	Condition or domain being studied	Ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) in adult patients.
6.	Population	<p>Inclusion:</p> <ul style="list-style-type: none"> • Adults (18 and over) with OHT • Adults (18 and over) with COAG <p>Exclusion:</p> <ul style="list-style-type: none"> • People who have received first line treatment for OHT or COAG, • People with secondary glaucoma, for example, neovascular or uveitic glaucoma • People with, or at risk of, primary or secondary angle closure glaucoma • People with primary congenital, infantile or childhood glaucoma • People with angle closure
7.	Intervention/Exposure/ Test	<ul style="list-style-type: none"> • Selective laser trabeculoplasty
8.	Comparator/Reference standard/Confounding factors	<ul style="list-style-type: none"> • Intraocular pressure-lowering eyedrops alone

9.	Types of study to be included	<ul style="list-style-type: none"> • Systematic Review of RCTs • RCTs
10.	Other exclusion criteria	<ul style="list-style-type: none"> • Other study types • RCTs with a crossover study design.
11.	Context	An exceptional surveillance review was completed on glaucoma management following the publication of a HTA report on selective laser trabeculoplasty for ocular hypertension and glaucoma. This relates to the current recommendations on treatment for people with OHT and treatment for people with COAG in NICE guideline NG81, glaucoma: diagnosis and management. This review concluded that the new evidence could impact on these recommendations, so this section of the guideline is being updated.
12.	Primary outcomes (critical outcomes)	<p>Critical outcomes:</p> <ul style="list-style-type: none"> • IOP (intraocular pressure) level/outcomes • Glaucomatous visual field loss* • Normal visual field to visual field defect* • Progression of glaucomatous visual field defect* • Vision loss • Health-related quality of life • Adverse events <p>*Follow up for outcomes related to visual field should be restricted to those 6 months or greater.</p>

13.	Secondary outcomes (important outcomes)	<p>Important outcomes:</p> <ul style="list-style-type: none"> • Optic nerve head damage • Progression of optic nerve head damage • Normal or suspicious-to- abnormal optic nerve head • Treatment adherence • Treatment discontinuation
14.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.2).</p>
15.	Risk of bias (quality) assessment	<p>Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.</p>
16.	Strategy for data synthesis	<p>Where possible, data will be meta-analysed. Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) to combine the data given in all studies for each of the</p>

		<p>outcomes stated above. A fixed effect meta-analysis, with weighted mean differences for continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome.</p> <p>Heterogeneity between the studies in effect measures will be assessed using the I² statistic and visually inspected.</p> <p>Where data is available sensitivity analyses will be conducted using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented using random-effects.</p> <p>GRADE pro will be used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results.</p> <p>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</p> <p>Network meta-analysis is not planned for this review.</p>
17.	Analysis of sub-groups	<p>Possible sub-groups include;</p> <ul style="list-style-type: none"> • Older people (over 70 years) • Younger adults with chronic open angle glaucoma or ocular hypertension (under 50 years) • Different ranges of trabecular meshwork treated (90, 180 or 360 degrees) • Different laser application end points (sub-threshold / threshold / supra-threshold) • Patients undergoing early repeat SLT treatment (i.e. within 6 or 12 months of the initial SLT treatment)
18.	Type and method of review	<p style="text-align: center;"><input checked="" type="checkbox"/></p> <p style="text-align: center;"><input type="checkbox"/></p> <p style="text-align: right;">Diagnostic</p>

		<input type="checkbox"/> Prognostic <input type="checkbox"/> Qualitative <input type="checkbox"/> Epidemiologic <input type="checkbox"/> Service Delivery <input type="checkbox"/> Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	26/08/2021		
22.	Anticipated completion date	26/01/2022		
23.	Stage of review at time of this submission	Review stage		
		Preliminary searches	<input type="checkbox"/>	<input type="checkbox"/>

		Piloting of the study selection process	<input type="checkbox"/>	<input type="checkbox"/>
		Formal screening of search results against eligibility criteria	<input type="checkbox"/>	<input type="checkbox"/>
		Data extraction	<input type="checkbox"/>	<input type="checkbox"/>
		Risk of bias (quality) assessment	<input type="checkbox"/>	<input type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input type="checkbox"/>
24.	Named contact	<p>5a. Named contact NICE Guideline Updates Team</p> <p>5b Named contact e-mail [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address]</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and NICE Guideline Updates Team</p>		

25.	Review team members	<p>[Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.]</p> <p>From the [Insert Development centre]:</p> <ul style="list-style-type: none"> • [Tech lead] • [Tech analyst] • [Health economist] • [Information specialist] • [Others]
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Updates Team which receives funding from NICE.
27.	Conflicts of interest	<p>All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.</p>
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of <u>Developing NICE</u>

		<u>guidelines: the manual</u> . Members of the guideline committee are available on the NICE website: [NICE guideline webpage].
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	First line treatment, chronic open angle glaucoma, ocular hypertension, selective laser trabeculoplasty (SLT), intraocular pressure-lowering eyedrops
33.	Details of existing review of same topic by same authors	This is a new review question that will update the treatment section in the NICE Guideline: Glaucoma: diagnosis and management (2017) NICE guideline NG81.
34.		☒

	Current review status	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
35..	Additional information	This review will be used to update the treatment section in the current NICE guideline NG81 Glaucoma: diagnosis and management.
36.	Details of final publication	www.nice.org.uk

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Appendix B – Literature search strategies

Search design and peer review

A NICE information specialist conducted the literature searches for the evidence review. The searches were run between the 25th to 26th of August 2021. This search report is compliant with the reporting requirements of [PRISMA-S](#).

The MEDLINE strategy below was quality assured (QA) by a trained NICE information specialist. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the [2016 PRESS Checklist](#).

The principal search strategy was developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

The terms for 'glaucoma' are based on those used for the previous NICE guideline, NG81 Glaucoma: diagnosis and management (2017). However, amendments were made to the search strategy as appropriate for this specific evidence review topic. For instance, search terms for 'ocular hypotension' from the original NG81 search strategy were not added to the update search strategy because the new review question specified 'hypertension'. In addition, the original NG81 search strategy was changed by adding truncation where relevant. On line 4, 'hypertension' was changed to 'hypertens*' to also find references with the term 'hypertensive'. In addition, the following terms were added to line 4 of the update strategy to provide synonyms for 'ocular adj hypertension' from line 5 of the original NG81 'population' search strategy: 'intraocular', 'eye*', and 'tension'.

Limits and restrictions

English language limits were applied in adherence to standard NICE practice and the review protocol.

Limits to exclude books, chapters, conference abstracts, conference papers, "conference reviews", letters, notes, and tombstones were applied to the Embase (Ovid) search. Limits for conference abstracts and trial registry data were also applied in the Cochrane Central Register of Controlled Trials - CENTRAL (Wiley). These limits were applied in adherence to standard NICE practice and the review

protocol. The search was limited from 2008 to the present day as defined in the review protocol.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from: Dickersin, K., Scherer, R., & Lefebvre, C. (1994). [Systematic Reviews: Identifying relevant studies for systematic reviews](#). *BMJ*, 309(6964), 1286.

Search filters

Clinical/public health searches Systematic reviews

The MEDLINE SR filter was “Health-evidence.ca Systematic review search filter” from Lee et al. (2012).

The standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.

The Embase SR filter was “Health-evidence.ca Systematic review search filter” from Lee et al. (2012).

The standard NICE modifications were used: pubmed.tw added to line medline.tw.

- Lee, E. et al. (2012) [An optimal search filter for retrieving systematic reviews and meta-analyses](#). *BMC Medical Research Methodology*, 12(1), 51.

RCTs

The MEDLINE RCT filter was [McMaster Therapy – Medline - “best balance of sensitivity and specificity” version](#).

The standard NICE modifications were used: randomized.mp changed to randomi?ed.mp.

- Haynes RB et al. (2005) [Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey](#). *BMJ*, 330, 1179-1183.

The Embase RCT filter was [McMaster Therapy – Embase “best balance of sensitivity and specificity” version](#).

- Wong SSL et al. (2006) [Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE](#). *Journal of the Medical Library Association*, 94(1), 41-47.

Cost effectiveness searches

The following search filter was applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

- Glanville J et al. (2009) [Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE](#). Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)

Several modifications have been made to these filters over the years that are standard NICE practice.

Clinical/public health searches

Main search - Databases

Database	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	25th Aug 2021	Wiley	Issue 8 of 12, August 2021	741
Cochrane Database of Systematic Reviews (CDSR)	25th Aug 2021	Wiley	Issue 8 of 12, August 2021	43
Embase	25th Aug 2021	Ovid	Embase <1974 to 2021 August 24>	1010
MEDLINE	26th Aug 2021	Ovid	Ovid MEDLINE(R) <1946 to August 25, 2021>	558
MEDLINE-in-Process	25th Aug 2021	Ovid	Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to August 24, 2021>	28
MEDLINE Epub Ahead-of-Print	25th Aug 2021	Ovid	Ovid MEDLINE(R) Epub Ahead of Print <August 24, 2021>	22
CRD	25th Aug 2021	DARE	Up to 2015	18

Search strategy history

Database name: MEDLINE

- 1 exp Ocular Hypertension/ (57729)
- 2 Intraocular Pressure/ (39811)
- 3 (glaucom* or coag).tw. (55708)
- 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (39644)
- 5 or/1-4 (89862)
- 6 Trabeculectomy/ (5905)
- 7 (trabecul* or slt or surgical* or surgeon*).tw. (1717046)
- 8 6 or 7 (1717754)
- 9 exp Prostaglandins/ (101690)
- 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepulin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (179854)
- 11 exp Adrenergic beta-Antagonists/ (85400)
- 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (72785)
- 13 exp Carbonic Anhydrase Inhibitors/ (10850)
- 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (3063)
- 15 exp Sympathomimetics/ or Brimonidine Tartrate/ (261489)
- 16 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphanagan* or bromoxidine* or mirvaso*).tw. (6484)
- 17 exp Miotics/ (32550)
- 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen).tw. (7689)
- 19 exp Ophthalmic Solutions/ (16532)
- 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (1540311)
- 21 or/9-20 (2080041)
- 22 8 and 21 (117813)
- 23 5 and 22 (6260)
- 24 limit 23 to english language (5468)
- 25 animals/ not humans/ (4844801)
- 26 24 not 25 (5183)
- 27 (MEDLINE or pubmed).tw. (198262)
- 28 systematic review.tw. (153596)
- 29 systematic review.pt. (163468)
- 30 meta-analysis.pt. (140255)
- 31 intervention\$.ti. (140028)
- 32 or/27-31 (446528)
- 33 randomized controlled trial.pt. (541466)
- 34 randomi?ed.mp. (863018)
- 35 placebo.mp. (206660)
- 36 or/33-35 (916788)

- 37 32 or 36 (1237523)
 38 26 and 37 (997)
 39 limit 38 to yr="2008 -Current" (558)

Database name: MEDLINE in Process

- 1 exp Ocular Hypertension/ (0)
 2 Intraocular Pressure/ (0)
 3 (glaucom* or coag).tw. (1104)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (784)
 5 or/1-4 (1415)
 6 Trabeculectomy/ (0)
 7 (trabecul* or slt or surgical* or surger*).tw. (27541)
 8 6 or 7 (27541)
 9 exp Prostaglandins/ (0)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepulin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (1990)
 11 exp Adrenergic beta-Antagonists/ (0)
 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (597)
 13 exp Carbonic Anhydrase Inhibitors/ (0)
 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*).tw. (54)
 15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
 16 (sympathomimetic* or apraclonidine* or lopicine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (35)
 17 exp Miotics/ (0)
 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (86)
 19 exp Ophthalmic Solutions/ (0)
 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (34192)
 21 or/9-20 (36431)
 22 8 and 21 (2247)
 23 5 and 22 (168)
 24 limit 23 to english language (167)
 25 animals/ not humans/ (0)
 26 24 not 25 (167)
 27 (MEDLINE or pubmed).tw. (8848)
 28 systematic review.tw. (8308)
 29 systematic review.pt. (260)
 30 meta-analysis.pt. (64)
 31 intervention\$.ti. (4322)

- 32 or/27-31 (15852)
 33 randomized controlled trial.pt. (0)
 34 randomi?ed.mp. (14660)
 35 placebo.mp. (3388)
 36 or/33-35 (15678)
 37 32 or 36 (27864)
 38 26 and 37 (28)

Database name: MEDLINE ePubs

- 1 exp Ocular Hypertension/ (0)
 2 Intraocular Pressure/ (0)
 3 (glaucom* or coag).tw. (1014)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (798)
 5 or/1-4 (1373)
 6 Trabeculectomy/ (0)
 7 (trabecul* or slt or surgical* or surger*).tw. (34706)
 8 6 or 7 (34706)
 9 exp Prostaglandins/ (0)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepelin* or xalatan* or xalmono* or xaloptic* or xalost* or xelox* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (1505)
 11 exp Adrenergic beta-Antagonists/ (0)
 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (551)
 13 exp Carbonic Anhydrase Inhibitors/ (0)
 14 (carbon* anhydraz* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*).tw. (46)
 15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
 16 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (83)
 17 exp Miotics/ (0)
 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (57)
 19 exp Ophthalmic Solutions/ (0)
 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (32519)
 21 or/9-20 (34301)
 22 8 and 21 (2850)
 23 5 and 22 (169)
 24 limit 23 to english language (166)
 25 animals/ not humans/ (0)
 26 24 not 25 (166)
 27 (MEDLINE or pubmed).tw. (9814)

- 28 systematic review.tw. (9866)
 29 systematic review.pt. (126)
 30 meta-analysis.pt. (116)
 31 intervention\$.ti. (4370)
 32 or/27-31 (17843)
 33 randomized controlled trial.pt. (1)
 34 randomi?ed.mp. (14976)
 35 placebo.mp. (3125)
 36 or/33-35 (15981)
 37 32 or 36 (29784)
 38 26 and 37 (22)

Database name: Embase

- 1 exp glaucoma/ (87790)
 2 intraocular pressure/ (59452)
 3 (glaucom* or coag).tw. (75059)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (65775)
 5 or/1-4 (141889)
 6 trabeculectomy/ or trabeculoplasty/ or trabeculotome/ or trabeculotomy/ or trabeculotomy probe/ (11255)
 7 (trabecul* or slt or surgical* or surger*).tw. (2655737)
 8 6 or 7 (2657584)
 9 exp prostaglandin/ (159880)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepulin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (265129)
 11 exp beta adrenergic receptor blocking agent/ (304185)
 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (104588)
 13 exp carbonate dehydratase inhibitor/ (27024)
 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*).tw. (4276)
 15 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (8042)
 16 miotic agent/ (669)
 17 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (10063)
 18 exp agents acting on the eye/ (602000)
 19 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (2735190)
 20 or/9-19 (3711711)
 21 8 and 20 (264098)

- 22 5 and 21 (13473)
 23 limit 22 to english language (12014)
 24 nonhuman/ not human/ (4840847)
 25 23 not 24 (11573)
 26 (MEDLINE or pubmed).tw. (310383)
 27 exp systematic review/ or systematic review.tw. (370567)
 28 meta-analysis/ (223214)
 29 intervention\$.ti. (222618)
 30 or/26-29 (762859)
 31 random:.tw. (1696406)
 32 placebo:.mp. (479182)
 33 double-blind:.tw. (222469)
 34 or/31-33 (1958865)
 35 30 or 34 (2483360)
 36 25 and 35 (1737)
 37 limit 36 to (books or chapter or conference abstract or conference paper or "conference review" or letter or note or tombstone) (212)
 38 36 not 37 (1525)
 39 limit 38 to yr="2008 -Current" (1010)

Database name: Cochrane Library

- #1 MeSH descriptor: [Ocular Hypertension] explode all trees 3641
 #2 MeSH descriptor: [Intraocular Pressure] this term only 3438
 #3 (glaucom* or coag):ti,ab,kw 8232
 #4 ((ocular* or intraocular* or intra-ocular* or eye*) near/3 (hypertensi* or tension* or pressur*)):ti,ab,kw or (oht or iop):ti,ab,kw 10838
 #5 #1 or #2 or #3 or #4 12949
 #6 MeSH descriptor: [Trabeculectomy] this term only 592
 #7 (trabecul* or slt or surgical* or surger*):ti,ab,kw 259639
 #8 #6 or #7 259639
 #9 MeSH descriptor: [Prostaglandins] explode all trees 6123
 #10 (prostaglandin* or "pg" or "pga" or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or "latan-ophtal*" or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepelin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*):ti,ab,kw 21467
 #11 MeSH descriptor: [Adrenergic beta-Antagonists] explode all trees 4595
 #12 ("beta-blocker*" or "beta-antagon*" or "beta-adren*" or betaxolol* or betoptica* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*):ti,ab,kw 3083
 #13 MeSH descriptor: [Carbonic Anhydrase Inhibitors] explode all trees 326
 #14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*):ti,ab,kw 1122

- #15 MeSH descriptor: [Sympathomimetics] explode all trees 298
 #16 MeSH descriptor: [Brimonidine Tartrate] explode all trees 350
 #17 (sympathomimetic* or apraclonidine* or lopicidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*):ti,ab,kw 1940
 #18 MeSH descriptor: [Miotics] explode all trees 51
 #19 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen):ti,ab,kw 830
 #20 MeSH descriptor: [Ophthalmic Solutions] explode all trees 3557
 #21 (eyedrop* or drop* or medicat* or medici* or pharm*):ti,ab,kw 391578
 #22 {or #9-#21} 411540
 #23 #8 and #22 49802
 #24 #5 and #23 2367
 #25 "conference":pt or (clinicaltrials or trialsearch):so 559928
 #26 #24 not #25 with Cochrane Library publication date Between Jan 2008 and Aug 2021, in Cochrane Reviews 43
 #27 #24 not #25 with Publication Year from 2008 to 2021, in Trials 741
 #28 #26 or #27 784

Database name: CRD databases

1	(MeSH DESCRIPTOR Ocular Hypertension EXPLODE ALL TREES)	212
2	(MeSH DESCRIPTOR Intraocular Pressure)	115
3	((glaucom* or coag))	294
4	((ocular* or intraocular* or intra-ocular* or eye*) near3 (hypertensi* or tension* or pressur*)) or (oht or iop))	221
5	#1 OR #2 OR #3 OR #4	340
6	((trabecul* or slt or surgical* or surger*))	17240
7	(MeSH DESCRIPTOR Trabeculectomy)	39
8	#6 OR #7	17240
9	(MeSH DESCRIPTOR Prostaglandins EXPLODE ALL TREES)	227
10	((prostaglandin* or "pg" or "pga" or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or laticris* or latadin* or latalux* or "latan-ophtal*" or latanelb* or lanatiston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepolin* or xalatan* or xalmono* or xaloptic* or xalost* or xelol* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*))	569
11	(MeSH DESCRIPTOR Adrenergic beta-Antagonists EXPLODE ALL TREES)	349
12	((("beta-blocker*" or "beta-antagon*" or "beta-adren*" or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or	581

	fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyezeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*))	
13	(MeSH DESCRIPTOR Carbonic Anhydrase Inhibitors EXPLODE ALL TREES)	13
14	((carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*))	37
15	(MeSH DESCRIPTOR Sympathomimetics EXPLODE ALL TREES)	196
16	(MeSH DESCRIPTOR Brimonidine Tartrate EXPLODE ALL TREES)	14
17	((sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*))	49
18	(MeSH DESCRIPTOR Miotics EXPLODE ALL TREES)	8
19	((miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen))	12
20	(MeSH DESCRIPTOR Ophthalmic Solutions EXPLODE ALL TREES)	35
21	((eyedrop* or drop* or medicat* or medici* or pharm*))	22490
22	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)	23247
23	(#8 AND #22)	4050
24	(#5 AND #23)	74
25	(#5 AND #23) FROM 2008 TO 2021	44

Cost-effectiveness searches

Main search - Databases

Database	Date searched	Database Platform	Database segment or version	No. of results downloaded
EconLit	26th Aug 2021	OVID	Econlit <1886 to August 19, 2021>	0
EED	25th Aug 2021	CRD	Up to 2015	15
Embase	26th Aug 2021	Ovid	Embase <1974 to 2021 August 25>	550
HTA	25th Aug 2021	CRD	Up to 2018	11
INAHTA	26th Aug 2021	INAHTA	Searched 26th Aug 2021	11
MEDLINE	26th Aug 2021	Ovid	Ovid MEDLINE(R) <1946 to August 25, 2021>	215
MEDLINE-in-Process	26th Aug 2021	Ovid	Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to August 25, 2021>	14

Search strategy history

Database name: MEDLINE

- 1 exp Ocular Hypertension/ (57729)
- 2 Intraocular Pressure/ (39811)
- 3 (glaucom* or coag).tw. (55708)
- 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (39644)
- 5 or/1-4 (89862)
- 6 Trabeculectomy/ (5905)
- 7 (trabecul* or slt or surgical* or surger*).tw. (1717046)
- 8 6 or 7 (1717754)
- 9 exp Prostaglandins/ (101690)
- 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar * or tafluprost* or vlepolin* or xalatan* or

xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (179854)

11 exp Adrenergic beta-Antagonists/ (85400)

12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (72785)

13 exp Carbonic Anhydrase Inhibitors/ (10850)

14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (3063)

15 exp Sympathomimetics/ or Brimonidine Tartrate/ (261489)

16 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphanagan* or bromoxidine* or mirvaso*).tw. (6484)

17 exp Miotics/ (32550)

18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (7689)

19 exp Ophthalmic Solutions/ (16532)

20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (1540311)

21 or/9-20 (2080041)

22 8 and 21 (117813)

23 5 and 22 (6260)

24 limit 23 to english language (5468)

25 animals/ not humans/ (4844801)

26 24 not 25 (5183)

27 Economics/ (27361)

28 exp "Costs and Cost Analysis"/ (248565)

29 Economics, Dental/ (1919)

30 exp Economics, Hospital/ (25275)

31 exp Economics, Medical/ (14278)

32 Economics, Nursing/ (4006)

33 Economics, Pharmaceutical/ (3014)

34 Budgets/ (11476)

35 exp Models, Economic/ (15766)

36 Markov Chains/ (15204)

37 Monte Carlo Method/ (30047)

38 Decision Trees/ (11626)

39 econom\$.tw. (266638)

40 cba.tw. (10052)

41 cea.tw. (21661)

42 cua.tw. (1051)

43 markov\$.tw. (19796)

44 (monte adj carlo).tw. (32318)

45 (decision adj3 (tree\$ or analys\$)).tw. (15793)

46 (cost or costs or costing\$ or costly or costed).tw. (505917)

47 (price\$ or pricing\$).tw. (36499)

48 budget\$.tw. (25406)

49 expenditure\$.tw. (53387)

50 (value adj3 (money or monetary)).tw. (2311)

51 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw. (3635)

52 or/27-51 (1007274)

53 "Quality of Life"/ (219677)
 54 quality of life.tw. (258440)
 55 "Value of Life"/ (5757)
 56 Quality-Adjusted Life Years/ (13634)
 57 quality adjusted life.tw. (12330)
 58 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (10131)
 59 disability adjusted life.tw. (3258)
 60 daly\$.tw. (2913)
 61 Health Status Indicators/ (23885)
 62 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (24224)
 63 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1428)
 64 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (5547)
 65 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (31)
 66 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (394)
 67 (euroqol or euro qol or eq5d or eq 5d).tw. (10777)
 68 (qol or hql or hqol or hrqol).tw. (50162)
 69 (hye or hyes).tw. (63)
 70 health\$ year\$ equivalent\$.tw. (38)
 71 utilit\$.tw. (189065)
 72 (hui or hui1 or hui2 or hui3).tw. (1437)
 73 disutilit\$.tw. (436)
 74 rosser.tw. (97)
 75 quality of wellbeing.tw. (22)
 76 quality of well-being.tw. (402)
 77 qwb.tw. (194)
 78 willingness to pay.tw. (5309)
 79 standard gamble\$.tw. (808)
 80 time trade off.tw. (1105)
 81 time tradeoff.tw. (245)
 82 tto.tw. (987)
 83 or/53-82 (544379)
 84 Cost-Benefit Analysis/ (86015)
 85 Quality-Adjusted Life Years/ (13634)
 86 Markov Chains/ (15204)
 87 exp Models, Economic/ (15766)
 88 cost*.ti. (111936)
 89 (cost* adj2 utilit*).tw. (5366)
 90 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (192211)
 91 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (32187)
 92 (qualit* adj2 adjust* adj2 life*).tw. (12610)
 93 QALY*.tw. (10014)
 94 (incremental* adj2 cost*).tw. (12257)
 95 ICER.tw. (3834)

- 96 utilities.tw. (6487)
 97 markov*.tw. (19796)
 98 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (41432)
 99 ((utility or effective*) adj2 analys*).tw. (17563)
 100 (willing* adj2 pay*).tw. (6146)
 101 (EQ5D* or EQ-5D*).tw. (8407)
 102 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (2132)
 103 (european* adj2 quality adj3 ("5" or five)).tw. (417)
 104 or/84-103 (362603)
 105 52 or 83 or 104 (1502207)
 106 26 and 105 (287)
 107 limit 106 to yr="2008 -Current" (215)

Database name: MEDLINE in Process

- 1 exp Ocular Hypertension/ (0)
 2 Intraocular Pressure/ (0)
 3 (glaucom* or coag).tw. (1102)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (781)
 5 or/1-4 (1412)
 6 Trabeculectomy/ (0)
 7 (trabecul* or slt or surgical* or surger*).tw. (27419)
 8 6 or 7 (27419)
 9 exp Prostaglandins/ (0)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepolin* or xalatan* or xalmono* or xaloptic* or xalost* or xelox* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (1983)
 11 exp Adrenergic beta-Antagonists/ (0)
 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyezeeta* or ganfort* or tiopep* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (597)
 13 exp Carbonic Anhydrase Inhibitors/ (0)
 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (53)
 15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
 16 (sympathomimetic* or apraclonidine* or lopicidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (35)
 17 exp Miotics/ (0)
 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (85)
 19 exp Ophthalmic Solutions/ (0)
 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (34081)

-
- 21 or/9-20 (36311)
 22 8 and 21 (2235)
 23 5 and 22 (167)
 24 limit 23 to english language (166)
 25 animals/ not humans/ (0)
 26 24 not 25 (166)
 27 Economics/ (0)
 28 exp "Costs and Cost Analysis"/ (0)
 29 Economics, Dental/ (0)
 30 exp Economics, Hospital/ (0)
 31 exp Economics, Medical/ (0)
 32 Economics, Nursing/ (0)
 33 Economics, Pharmaceutical/ (0)
 34 Budgets/ (0)
 35 exp Models, Economic/ (0)
 36 Markov Chains/ (0)
 37 Monte Carlo Method/ (0)
 38 Decision Trees/ (0)
 39 econom\$.tw. (6160)
 40 cba.tw. (75)
 41 cea.tw. (336)
 42 cua.tw. (18)
 43 markov\$.tw. (521)
 44 (monte adj carlo).tw. (583)
 45 (decision adj3 (tree\$ or analys\$)).tw. (660)
 46 (cost or costs or costing\$ or costly or costed).tw. (11377)
 47 (price\$ or pricing\$).tw. (779)
 48 budget\$.tw. (439)
 49 expenditure\$.tw. (1123)
 50 (value adj3 (money or monetary)).tw. (80)
 51 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw. (53)
 52 or/27-51 (18997)
 53 "Quality of Life"/ (0)
 54 quality of life.tw. (7643)
 55 "Value of Life"/ (0)
 56 Quality-Adjusted Life Years/ (0)
 57 quality adjusted life.tw. (473)
 58 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (354)
 59 disability adjusted life.tw. (146)
 60 daly\$.tw. (116)
 61 Health Status Indicators/ (0)
 62 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (396)
 63 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (19)
 64 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (134)
 65 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (0)

- 66 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (5)
- 67 (euroqol or euro qol or eq5d or eq 5d).tw. (404)
- 68 (qol or hql or hqol or hrqol).tw. (1574)
- 69 (hye or hyes).tw. (0)
- 70 health\$ year\$ equivalent\$.tw. (0)
- 71 utilit\$.tw. (5596)
- 72 (hui or hui1 or hui2 or hui3).tw. (19)
- 73 disutili\$.tw. (18)
- 74 rosser.tw. (0)
- 75 quality of wellbeing.tw. (2)
- 76 quality of well-being.tw. (6)
- 77 qwb.tw. (1)
- 78 willingness to pay.tw. (248)
- 79 standard gamble\$.tw. (8)
- 80 time trade off.tw. (18)
- 81 time tradeoff.tw. (1)
- 82 tto.tw. (18)
- 83 or/53-82 (13490)
- 84 Cost-Benefit Analysis/ (0)
- 85 Quality-Adjusted Life Years/ (0)
- 86 Markov Chains/ (0)
- 87 exp Models, Economic/ (0)
- 88 cost*.ti. (1875)
- 89 (cost* adj2 utilit*).tw. (187)
- 90 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (4256)
- 91 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (842)
- 92 (qualit* adj2 adjust* adj2 life*).tw. (477)
- 93 QALY*.tw. (352)
- 94 (incremental* adj2 cost*).tw. (440)
- 95 ICER.tw. (187)
- 96 utilities.tw. (193)
- 97 markov*.tw. (521)
- 98 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (739)
- 99 ((utility or effective*) adj2 analys*).tw. (476)
- 100 (willing* adj2 pay*).tw. (266)
- 101 (EQ5D* or EQ-5D*).tw. (318)
- 102 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (122)
- 103 (european* adj2 quality adj3 ("5" or five)).tw. (14)
- 104 or/84-103 (6820)
- 105 52 or 83 or 104 (31097)
- 106 26 and 105 (14)

Database name: MEDLINE ePubs

- 1 exp Ocular Hypertension/ (0)
- 2 Intraocular Pressure/ (0)

-
- 3 (glaucom* or coag).tw. (1016)
 - 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (795)
 - 5 or/1-4 (1374)
 - 6 Trabeculectomy/ (0)
 - 7 (trabecul* or slt or surgical* or surger*).tw. (34730)
 - 8 6 or 7 (34730)
 - 9 exp Prostaglandins/ (0)
 - 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepolin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflostan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (1505)
 - 11 exp Adrenergic beta-Antagonists/ (0)
 - 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (553)
 - 13 exp Carbonic Anhydrase Inhibitors/ (0)
 - 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*).tw. (46)
 - 15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
 - 16 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (83)
 - 17 exp Miotics/ (0)
 - 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (57)
 - 19 exp Ophthalmic Solutions/ (0)
 - 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (32560)
 - 21 or/9-20 (34344)
 - 22 8 and 21 (2843)
 - 23 5 and 22 (169)
 - 24 limit 23 to english language (166)
 - 25 animals/ not humans/ (0)
 - 26 24 not 25 (166)
 - 27 Economics/ (0)
 - 28 exp "Costs and Cost Analysis"/ (0)
 - 29 Economics, Dental/ (0)
 - 30 exp Economics, Hospital/ (0)
 - 31 exp Economics, Medical/ (0)
 - 32 Economics, Nursing/ (0)
 - 33 Economics, Pharmaceutical/ (0)
 - 34 Budgets/ (0)
 - 35 exp Models, Economic/ (0)
 - 36 Markov Chains/ (0)
 - 37 Monte Carlo Method/ (0)
 - 38 Decision Trees/ (0)

39 econom\$.tw. (8574)
40 cba.tw. (58)
41 cea.tw. (280)
42 cua.tw. (14)
43 markov\$.tw. (665)
44 (monte adj carlo).tw. (1008)
45 (decision adj3 (tree\$ or analys\$)).tw. (612)
46 (cost or costs or costing\$ or costly or costed).tw. (14127)
47 (price\$ or pricing\$).tw. (1163)
48 budget\$.tw. (606)
49 expenditure\$.tw. (1220)
50 (value adj3 (money or monetary)).tw. (89)
51 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw. (46)
52 or/27-51 (24318)
53 "Quality of Life"/ (0)
54 quality of life.tw. (8604)
55 "Value of Life"/ (0)
56 Quality-Adjusted Life Years/ (0)
57 quality adjusted life.tw. (463)
58 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (395)
59 disability adjusted life.tw. (113)
60 daly\$.tw. (93)
61 Health Status Indicators/ (0)
62 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (485)
63 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (43)
64 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (185)
65 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (0)
66 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (4)
67 (euroqol or euro qol or eq5d or eq 5d).tw. (485)
68 (qol or hql or hqol or hrqol).tw. (1744)
69 (hye or hyes).tw. (1)
70 health\$ year\$ equivalent\$.tw. (0)
71 utilit\$.tw. (5081)
72 (hui or hui1 or hui2 or hui3).tw. (48)
73 disutili\$.tw. (16)
74 rosser.tw. (0)
75 quality of wellbeing.tw. (2)
76 quality of well-being.tw. (9)
77 qwb.tw. (2)
78 willingness to pay.tw. (242)
79 standard gamble\$.tw. (8)
80 time trade off.tw. (19)
81 time tradeoff.tw. (3)
82 tto.tw. (30)
83 or/53-82 (14112)

- 84 Cost-Benefit Analysis/ (0)
 85 Quality-Adjusted Life Years/ (0)
 86 Markov Chains/ (0)
 87 exp Models, Economic/ (0)
 88 cost*.ti. (2055)
 89 (cost* adj2 utilit*).tw. (236)
 90 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*).tw. (5481)
 91 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*).tw. (1056)
 92 (qualit* adj2 adjust* adj2 life*).tw. (469)
 93 QALY*.tw. (394)
 94 (incremental* adj2 cost*).tw. (400)
 95 ICER.tw. (163)
 96 utilities.tw. (168)
 97 markov*.tw. (665)
 98 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (907)
 99 ((utility or effective*) adj2 analys*).tw. (623)
 100 (willing* adj2 pay*).tw. (265)
 101 (EQ5D* or EQ-5D*).tw. (398)
 102 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (96)
 103 (european* adj2 quality adj3 ("5" or five)).tw. (21)
 104 or/84-103 (8701)
 105 52 or 83 or 104 (36873)
 106 26 and 105 (18)

Database name: Embase

- 1 exp glaucoma/ (87807)
 2 intraocular pressure/ (59459)
 3 (glaucom* or coag).tw. (75077)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (65787)
 5 or/1-4 (141910)
 6 trabeculectomy/ or trabeculoplasty/ or trabeculotomy/ or trabeculotomy/ or trabeculotomy probe/ (11256)
 7 (trabecul* or slt or surgical* or surgeon*).tw. (2656254)
 8 6 or 7 (2658101)
 9 exp prostaglandin/ (159890)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepulin* or xalatan* or xalmono* or xaloptic* or xalost* or xelol* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (265164)
 11 exp beta adrenergic receptor blocking agent/ (304192)

- 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (104597)
- 13 exp carbonate dehydratase inhibitor/ (27024)
- 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (4276)
- 15 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphan* or bromoxidine* or mirvaso*).tw. (8042)
- 16 miotic agent/ (669)
- 17 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (10064)
- 18 exp agents acting on the eye/ (602043)
- 19 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (2735773)
- 20 or/9-19 (3712362)
- 21 8 and 20 (264138)
- 22 5 and 21 (13475)
- 23 limit 22 to english language (12016)
- 24 nonhuman/ not human/ (4841740)
- 25 23 not 24 (11575)
- 26 exp Health Economics/ (895913)
- 27 exp "Health Care Cost"/ (306659)
- 28 exp Pharmacoeconomics/ (212140)
- 29 Monte Carlo Method/ (43946)
- 30 Decision Tree/ (15489)
- 31 econom\$.tw. (412178)
- 32 cba.tw. (13210)
- 33 cea.tw. (36978)
- 34 cua.tw. (1628)
- 35 markov\$.tw. (33663)
- 36 (monte adj carlo).tw. (52966)
- 37 (decision adj3 (tree\$ or analys\$)).tw. (27681)
- 38 (cost or costs or costing\$ or costly or costed).tw. (848436)
- 39 (price\$ or pricing\$).tw. (62817)
- 40 budget\$.tw. (41649)
- 41 expenditure\$.tw. (80375)
- 42 (value adj3 (money or monetary)).tw. (3752)
- 43 (pharmacoeconomic\$ or (pharmaco adj economic\$)).tw. (9013)
- 44 or/26-43 (1914629)
- 45 "Quality of Life"/ (519606)
- 46 Quality Adjusted Life Year/ (29620)
- 47 Quality of Life Index/ (2912)
- 48 Short Form 36/ (32566)
- 49 Health Status/ (135586)
- 50 quality of life.tw. (490720)
- 51 quality adjusted life.tw. (22086)
- 52 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (22485)
- 53 disability adjusted life.tw. (4735)
- 54 daly\$.tw. (4579)

- 55 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (44628)
- 56 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2584)
- 57 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (10444)
- 58 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (64)
- 59 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (475)
- 60 (euroqol or euro qol or eq5d or eq 5d).tw. (24008)
- 61 (qol or hql or hqol or hrqol).tw. (108666)
- 62 (hye or hyes).tw. (144)
- 63 health\$ year\$ equivalent\$.tw. (41)
- 64 utilit\$.tw. (319219)
- 65 (hui or hui1 or hui2 or hui3).tw. (2602)
- 66 disutili\$.tw. (1031)
- 67 rosser.tw. (130)
- 68 quality of wellbeing.tw. (57)
- 69 quality of well-being.tw. (523)
- 70 qwb.tw. (258)
- 71 willingness to pay.tw. (10187)
- 72 standard gamble\$.tw. (1139)
- 73 time trade off.tw. (1812)
- 74 time tradeoff.tw. (302)
- 75 tto.tw. (1852)
- 76 or/45-75 (1091861)
- 77 cost utility analysis/ (10570)
- 78 quality adjusted life year/ (29620)
- 79 cost*.ti. (172119)
- 80 (cost* adj2 utilit*).tw. (10675)
- 81 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (327854)
- 82 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (55489)
- 83 (qualit* adj2 adjust* adj2 life*).tw. (22644)
- 84 QALY*.tw. (22247)
- 85 (incremental* adj2 cost*).tw. (23878)
- 86 ICER.tw. (10462)
- 87 utilities.tw. (12797)
- 88 markov*.tw. (33663)
- 89 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (61780)
- 90 ((utility or effective*) adj2 analys*).tw. (31584)
- 91 (willing* adj2 pay*).tw. (11595)
- 92 (EQ5D* or EQ-5D*).tw. (20190)
- 93 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (3792)
- 94 (european* adj2 quality adj3 ("5" or five)).tw. (722)
- 95 or/77-94 (540768)

- 96 44 or 76 or 95 (2873313)
 97 25 and 96 (896)
 98 limit 97 to yr="2008 -Current" (718)
 99 limit 98 to (books or chapter or conference abstract or conference paper or "conference review" or letter or note or tombstone) (168)
 100 98 not 99 (550)

Database name: EconLit

- 1 [exp Ocular Hypertension/] (0)
 2 [Intraocular Pressure/] (0)
 3 (glaucom* or coag).tw. (28)
 4 (((ocular* or intraocular* or intra-ocular* or eye*) adj3 (hypertensi* or tension* or pressur*)) or (oht or iop)).tw. (20)
 5 or/1-4 (46)
 6 [Trabeculectomy/] (0)
 7 (trabecul* or slt or surgical* or surger*).tw. (916)
 8 6 or 7 (916)
 9 [exp Prostaglandins/] (0)
 10 (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepolin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*).tw. (133)
 11 [exp Adrenergic beta-Antagonists/] (0)
 12 (beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*).tw. (25)
 13 [exp Carbonic Anhydrase Inhibitors/] (0)
 14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (0)
 15 [exp Sympathomimetics/ or Brimonidine Tartrate/] (0)
 16 (sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*).tw. (1)
 17 [exp Miotics/] (0)
 18 (miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocuser* or salagen).tw. (1)
 19 [exp Ophthalmic Solutions/] (0)
 20 (eyedrop* or drop* or medicat* or medici* or pharm*).tw. (16044)
 21 or/9-20 (16192)
 22 8 and 21 (100)
 23 5 and 22 (0)

Database name: CRD databases

1	(MeSH DESCRIPTOR Ocular	212	Delete
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	Hypertension EXPLODE ALL TREES)		
2	(MeSH DESCRIPTOR Intraocular Pressure)		115
3	((glaucom* or coag))		294
4	((ocular* or intraocular* or intra-ocular* or eye*) near3 (hypertensi* or tension* or pressur*)) or (oht or iop))		221
5	#1 OR #2 OR #3 OR #4		340
6	((trabecul* or slt or surgical* or surger*))		17240
7	(MeSH DESCRIPTOR Trabeculectomy)		39
8	#6 OR #7		17240
9	(MeSH DESCRIPTOR Prostaglandins EXPLODE ALL TREES)		227
10	((prostaglandin* or "pg" or "pga" or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or latacris* or latadin* or latalux* or "latan-ophtal*" or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or oculusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepelin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse*))		569
11	(MeSH DESCRIPTOR Adrenergic beta-Antagonists EXPLODE ALL TREES)		349
12	((("beta-blocker*" or "beta-antagon*" or "beta-adren*" or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyezeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar*))		581
13	(MeSH DESCRIPTOR Carbonic Anhydrase Inhibitors EXPLODE ALL TREES)		13
14	((carbon* anhydraz* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eyedelto* or trusopt* or vizidor*))		37
15	(MeSH DESCRIPTOR Sympathomimetics EXPLODE ALL TREES)		196
16	(MeSH DESCRIPTOR Brimonidine Tartrate EXPLODE ALL TREES)		14
17	((sympathomimetic* or apraclonidine* or lopicidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso*))		49
18	(MeSH DESCRIPTOR Miotics EXPLODE ALL TREES)		8

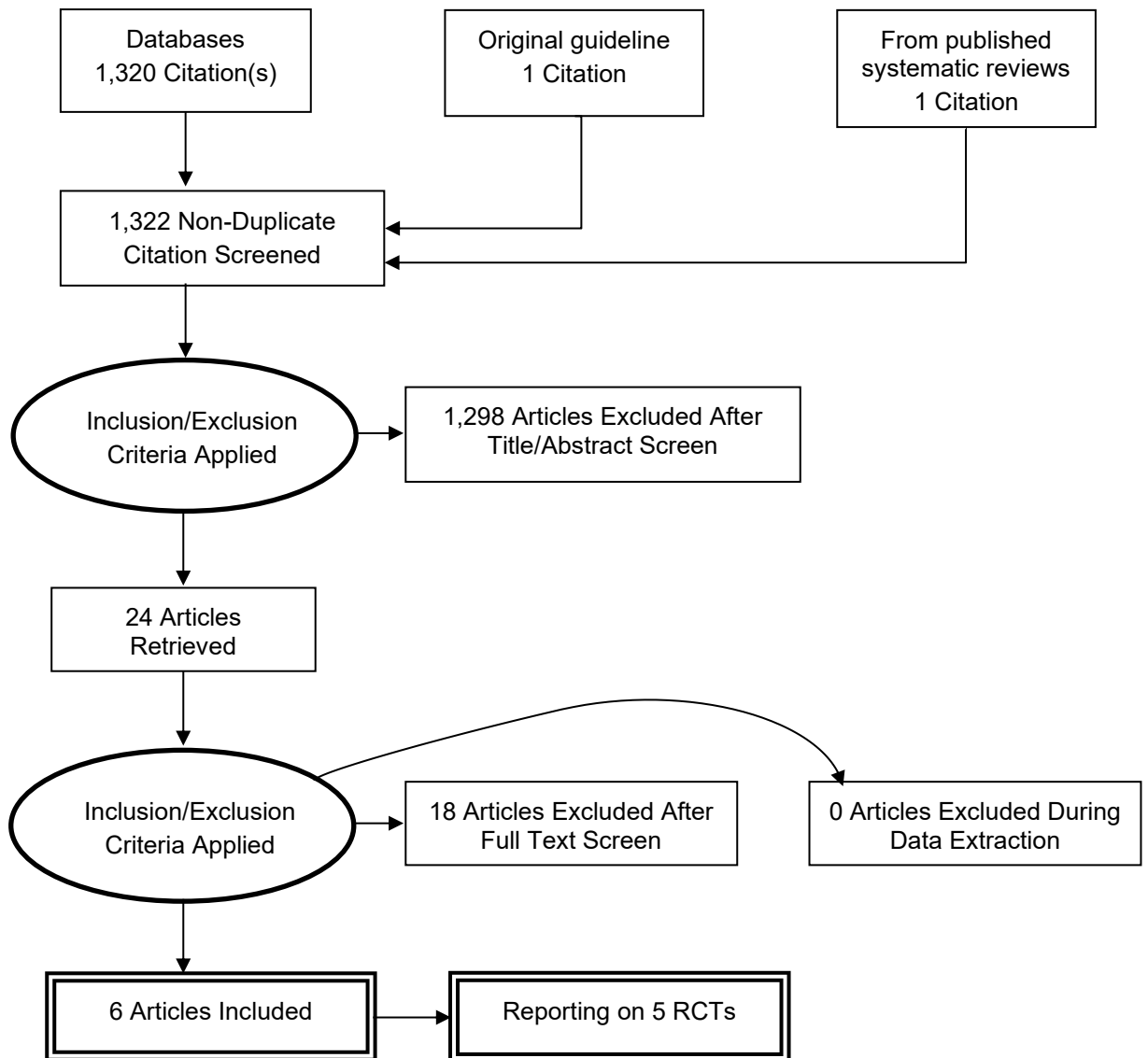
19	((((miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen)))	12
20	(MeSH DESCRIPTOR Ophthalmic Solutions EXPLODE ALL TREES)	35
21	((((eyedrop* or drop* or medicat* or medici* or pharm*)))	22490
22	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)	23247
23	(#8 AND #22)	4050
24	(#5 AND #23)	74
25	(#5 AND #23) FROM 2008 TO 2021	44

Database name: INAHTA databases

(glaucom* or coag or (((ocular* or intraocular* or intra-ocular* or eye*) and (hypertensi* or tension* or pressur*)) or (oht or iop))) AND (trabecul* or slt or surgical* or surger*) AND (prostaglandin* or pg or pga or latanoprost* or akistan* or arulatan* or catioprost* or droplatan* or droxal* or eylasol* or gisolom* or glaukodoc* or iopize* or jaskroptic* or lanotan* or laticris* or latadin* or latalux* or latan-ophtal* or latanelb* or lataniston* or latano* or latapres* or latizolil* or latop* or louten* or medizol* or microprost* or monopost* or monoprost* or ocusynt* or oftastad* or optopress* or pharmaprost* or pharmecol* or polat* or polprost* or proxal* or rozaprost* or sifitan* or tonlit* or xalatan* or visobar* or tafluprost* or vlepelin* or xalatan* or xalmono* or xaloptic* or xalost* or xelor* or xelpros* or zakoprost* or saflutan* or taflotan* or travoprost* or travatan* or bimatoprost* or eyreida* or lumigan* or latisse* or beta-blocker* or beta-antagon* or beta-adren* or betaxolol* or betoptic* or betoptima* or kerlon* or oxadol* or levobunolol* or novolevobunolol* or pmslevobunolol* or betagan* or akbeta* or ultracortenol* or vistagan* or timolol* or fixapost* or medox* or xalacom* or combigan* or duotrav* or azarga* or taptiqom* or eyzeeta* or ganfort* or tiopex* or eysano* or cosopt* or eylamdo* or blocadren* or optimol* or timacar* or carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor* or sympathomimetic* or apraclonidine* or lopidine* or brimonidine* or simbrinza* or brymont* or alphagan* or bromoxidine* or mirvaso* or miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen* or eyedrop* or drop* or medicat* or medici* or pharm*) 11 hits

Limits - Date: 2008-2021, English language

Appendix C – Effectiveness evidence study selection



Appendix D – Effectiveness evidence

Gazzard, 2019

Bibliographic Reference Gazzard, Gus; Konstantakopoulou, Evgenia; Garway-Heath, David; Garg, Anurag; Vickerstaff, Victoria; Hunter, Rachael; Ambler, Gareth; Bunce, Catey; Wormald, Richard; Nathwani, Neil; Barton, Keith; Rubin, Gary; Buszewicz, Marta; LiGHT Trial Study, Group; Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial.; Lancet (London, England); 2019; vol. 393 (no. 10180); 1505-1516

Study details

Other publications associated with this study included in review	<p>Anonymous. (2019) Erratum: Department of Error (The Lancet (2019) 393(10180) (1505-1516), (S014067361832213X), (10.1016/S0140-6736(18)32213-X)). The Lancet 394(10192): e1</p> <p>Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2018) Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre, randomised controlled trial: design and methodology. The British journal of ophthalmology 102(5): 593-598</p> <p>Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. Health technology assessment (Winchester, England) 23(31): 1-102</p>
Trial registration number and/or trial name	ISRCTN32038223 / LiGHT trial
Study type	Randomised controlled trial (RCT)
Study location	UK

Study setting	Hospitals
Study dates	Participants were recruited between Oct 10, 2012, and Oct 27, 2014
Sources of funding	National Institute for Health Research, Health and Technology Assessment Programme
Inclusion criteria	<p>Newly diagnosed, untreated OAG or ocular hypertension in one or both eyes</p> <p>Qualified for treatment according to NICE guidelines</p> <p>Those with OAG, had visual field loss with mean deviation not worse than -12 decibels (dB) in the better eye or -15 dB in the worse eye and corresponding damage to the optic nerve</p> <p>Able to read and understand English</p> <p>Visual acuity of 6/36 or better in the eyes to be treated</p> <p>No previous intraocular surgery, except uncomplicated phacoemulsification at least 1 year before randomisation</p> <p>A decision to treat had been made by a glaucoma specialist consultant ophthalmologist</p> <p>Aged >18 years and able to provide informed consent</p> <p>Able to complete QoL, disease-specific symptom and cost questionnaires in English (physical help with completion and assistance with reading was permitted, as long as an interpreter was not required)</p> <p>It was possible to perform a VF test in the study eye(s) with $<15\%$ false positives</p>
Exclusion criteria	<p>Contraindications to selective laser trabeculoplasty (e.g. unable to sit at the slit lamp mounted laser, past history of uveitis, neovascular glaucoma, inadequate view of trabecular meshwork)</p> <p>A visually significant cataract in symptomatic patients who want to undergo cataract surgery</p>

Any current, active treatment for another ophthalmic condition in the hospital eye service (this applied to both eyes, even if one was not in the trial, as the fellow eye might affect the patient's visit frequency)

Advanced glaucoma in the potentially eligible eye as determined by Early Manifest Glaucoma Trial (EMGT I) criteria (77 VF loss mean deviation worse than -12 decibels (dB) in the better eye or -15 dB in the worse eye)

Secondary glaucoma (e.g. pigment dispersion syndrome, rubeosis, trauma, etc.) or any angle closure

Inability to use topical medical therapy because of, for example, physical infirmity and a lack of carers able to administer daily eyedrops

A previous treatment for OAG or OHT

Congenital or early childhood glaucoma

Any history of retinal ischaemia, macular oedema or diabetic retinopathy

Age-related macular degeneration with neovascularisation in either eye or geographic atrophy

Visual acuity (VA) worse than 6/36 in a study eye; non-progressive VA loss better than 6/36 owing to any comorbidity was permitted provided that it did not affect the response to treatment or later surgical choices and that it was not under active follow-up (e.g. an old, isolated retinal scar no longer under review or amblyopia)

Any previous intraocular surgery, except uncomplicated phacoemulsification, at least 1 year before recruitment (this applied to both eyes, even if one was not in the trial, as it could affect the required treatment intensity and visit frequency for any glaucoma in the fellow eye)

Pregnancy at the time of recruitment or intention to become pregnant within the duration of the trial

Medical unsuitability for completion of the trial (e.g. suffering from a terminal illness or too unwell to be able to attend hospital clinic visits)

	Recent involvement in another interventional research study (within 3 months) of any topic
Intervention(s)	<p>SLT</p> <p>Selective laser trabeculoplasty was delivered to 360° of the trabecular meshwork. 100 non-overlapping shots (25 per quadrant) were used, with the laser energy varied from 0.3 to 1.4 mJ by the clinician, using an appropriate laser gonioscopy lens. One re-treatment with selective laser trabeculoplasty was allowed, provided there had been a reduction in intraocular pressure after the initial treatment; the next escalation was medical therapy.</p>
Comparator	<p>Eye drops</p> <p>First line drug class was prostaglandin analogues, second line was β blockers, third or fourth line was topical carbonic anhydrase inhibitors or α agonists. Fixed combination drops were allowed. Systemic carbonic anhydrase inhibitors were only permitted while awaiting surgery. Maximum tolerated medical therapy was defined by the treating clinician as the most intensive combination of drops an individual could reasonably, reliably, and safely use and thus varied between patients. A need for treatment escalation beyond maximum tolerated medical therapy triggered an offer of surgery.</p>
Outcome measures	<p>Intraocular pressure</p> <p>Proportion of visits at target intraocular pressure.</p> <p>The target was eye specific and was objectively defined and adjusted by the computerised decision algorithm to avoid bias from unmasked treating clinicians. The lowest permitted target was 8 mmHg for OAG and 18 mmHg for OHT.</p> <p>IOP target for OHT</p> <ul style="list-style-type: none"> • <25 mmHg and >20% reduction <p>IOP target for POAG</p> <ul style="list-style-type: none"> • Mild disease: <21 mmHg and >20% reduction • Moderate disease: <18 mmHg and >30% reduction • Severe disease: <15 mmHg and >30% reduction

Health-related quality of life

EuroQol EQ-5D 5 Levels (EQ-5D-5L) utility scores at 36 months.

Glaucoma-specific treatment related quality of life assessed with the Glaucoma Utility Index (GUI).

Patient-reported visual function assessed using the Glaucoma Quality of Life-15 questionnaire (GQL-15).

Adverse events

Treatment adherence

Compliance/concordance was assessed by two questions shown to predict the probability of non-concordance.

Visual field progression

"Worsening of VF loss was defined as 'likely' or 'possible' in the absence of any identifiable retinal or neurological cause. The 'minimum data set' to determine VF progression was two reliable baseline VF measurements followed by three follow-up VF tests. 'Likely VF progression' was defined as ≥ 3 points on the Humphrey Visual Field (HVF) GPA software (Carl Zeiss Meditec, Dublin, CA, USA) at $p < 0.05$ for change on three consecutive occasions. 'Possible VF progression' was ≥ 3 points on Humphrey Visual Field GPA software at $p < 0.05$ for change on two consecutive occasions. VF series were independently assessed for progression using the automated algorithm software at each visit. Any treatment escalation triggered by worsening VF loss had to be agreed by a senior clinician after excluding retinal or neurological causes." (Gazzard 2019 HTA report)

Optic disc progression

"Worsening of disc damage was defined as a rate of neuroretinal rim loss exceeding 1% of baseline rim area per year on a minimum of five repeat HRT images. This slope value was selected as approximately double that of age-related rim area loss and gave a similar specificity to VF trend analyses." (Gazzard 2019 HTA report)

	Treatment discontinuation
Duration of follow-up	36 months
Additional comments	For all quality of life outcomes, mean differences were adjusted for baseline score, severity, centre, baseline intraocular pressure, and number of eyes affected at baseline.

Study arms

Eye drops (N = 362)

Number of participants	n=362 participants (one or both eyes eligible and treated identically) n=622 eyes
Loss to follow-up	39 participants

Topical medication to lower intraocular pressure.

SLT (N = 356)

Number of participants	n=356 participants (one or both eyes eligible and treated identically) n=613 eyes
Loss to follow-up	27 participants

Primary selective laser trabeculoplasty followed by topical medications as required.

Characteristics

Arm-level characteristics

Characteristic	Eye drops (N = 362)	SLT (N = 356)
Female		
Sample size	n = 165 ; % = 45.6	n = 156 ; % = 43.8
Age (years)		
Mean (SD)	62.7 (11.6)	63.4 (12)
Ethnicity		
Asian		
Sample size	n = 28 ; % = 7.7	n = 23 ; % = 6.5
Black		
Sample size	n = 69 ; % = 19.1	n = 77 ; % = 21.6
White		
Sample size	n = 258 ; % = 71.3	n = 243 ; % = 68.3
Other		
Sample size	n = 7 ; % = 1.9	n = 13 ; % = 3.7
Diagnosis by participant		
Primary open angle glaucoma		
Sample size	n = 282 ; % = 77.9	n = 273 ; % = 76.7

Characteristic	Eye drops (N = 362)	SLT (N = 356)
Ocular hypertension		
Sample size	n = 80 ; % = 22.1	n = 83 ; % = 23.3
Other health conditions		
Asthma		
Sample size	n = 45 ; % = 12.4	n = 48 ; % = 13.5
Hypertension		
Sample size	n = 119 ; % = 32.9	n = 132 ; % = 37.1
Diabetes		
Sample size	n = 40 ; % = 11.1	n = 42 ; % = 11.8
Angina		
Sample size	n = 11 ; % = 3	n = 10 ; % = 2.8
Cardiac arrhythmia		
Sample size	n = 20 ; % = 5.5	n = 17 ; % = 4.8
Medications		
Statins		
Sample size	n = 92 ; % = 25.4	n = 104 ; % = 29.2
Systemic beta blockers		
Sample size	n = 12 ; % = 3.3	n = 22 ; % = 6.2

Characteristic	Eye drops (N = 362)	SLT (N = 356)
Calcium channel blockers		
Sample size	n = 60 ; % = 16.6	n = 56 ; % = 15.7
ACE inhibitors		
Sample size	n = 43 ; % = 11.9	n = 57 ; % = 16
corticosteroids		
Sample size	n = 20 ; % = 29.6	n = 22 ; % = 6.2
Family history of glaucoma In a first degree relative		
Sample size	n = 107 ; % = 29.6	n = 107 ; % = 30.1
Diagnosis by eyes Eye drops (n=622 eyes); SLT (n=613 eyes)		
OHT		
Sample size	n = 185 ; % = 29.7	n = 195 ; % = 31.8
Mild OAG		
Sample size	n = 325 ; % = 52.3	n = 311 ; % = 50.7
Moderate OAG		
Sample size	n = 77 ; % = 12.4	n = 67 ; % = 10.9
Severe OAG		
Sample size	n = 35 ; % = 5.6	n = 40 ; % = 6.5

Characteristic	Eye drops (N = 362)	SLT (N = 356)
Visual acuity Eye drops (n=622 eyes); SLT (n=613 eyes) Mean (SD)	0.1 (0.1)	0.1 (0.2)
Visual field mean deviation (Decibels (dB)) Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant Mean (SD)	-3 (3.6)	-3 (3.4)
HRT rim area (mm²) Eye drops (n=622 eyes); SLT (n=613 eyes); no data for 62 participants Mean (SD)	1.1 (0.4)	1.2 (0.4)
Intraocular pressure (mmHg) Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant Mean (SD)	24.4 (5)	24.5 (5.2)
Central corneal thickness (μm) Eye drops (n=622 eyes); SLT (n=613 eyes); no data for 3 participants Mean (SD)	551.6 (36.2)	550.7 (38.1)
Pseudo-exfoliation Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant Sample size	n = 12 ; % = 1.9	n = 5 ; % = 0.8
Pseudophakia Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant Sample size	n = 33 ; % = 5.3	n = 39 ; % = 6.4

Characteristic	Eye drops (N = 362)	SLT (N = 356)
EQ-5D n=716 participants Mean (SD)	0.92 (0.13)	0.91 (0.13)
Glaucoma Utility Index (Higher scores indicate better health-related quality of life) n=716 participants Mean (SD)	0.89 (0.11)	0.89 (0.12)
Glaucoma Quality of Life-15 (Higher scores indicate worse health-related quality of life) Mean (SD)	18.7 (5.6)	18.9 (6.6)
Central subscale Mean (SD)	2.5 (1)	2.5 (1)
Peripheral subscale Mean (SD)	8.4 (2.9)	8.5 (3.4)
Dark subscale Mean (SD)	7.9 (2.8)	7.9 (3)
Outdoor subscale Mean (SD)	1.1 (0.4)	1.1 (0.4)

Critical appraisal - GUT Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low <i>(There were protocol deviations but unlikely to have an effect on outcomes.)</i>
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	<i>Not applicable</i>
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Low <i>(There were protocol deviations but unlikely to have an effect on outcomes.)</i>
Overall bias and Directness	Overall Directness	Directly applicable

Gazzard, 2019 HTA

Bibliographic Reference Gazzard, Gus; Konstantakopoulou, Evgenia; Garway-Heath, David; Garg, Anurag; Vickerstaff, Victoria; Hunter, Rachael; Ambler, Gareth; Bunce, Catey; Wormald, Richard; Nathwani, Neil; Barton, Keith; Rubin, Gary; Morris, Stephen; Buszewicz, Marta; Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT.; Health technology assessment (Winchester, England); 2019; vol. 23 (no. 31); 1-102

Study details

Secondary publication of another included study- see primary study for details	Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. Lancet (London, England) 393(10180): 1505-1516
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Katz, 2012

Bibliographic Reference Katz, L Jay; Steinmann, William C; Kabir, Azad; Molineaux, Jeanne; Wizov, Sheryl S; Marcellino, George; SLT/Med Study, Group; Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: a prospective, randomized trial.; Journal of glaucoma; 2012; vol. 21 (no. 7); 460-8

Study details

Trial registration number and/or trial name	SLT/MED study
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Study type	Randomised controlled trial (RCT)
Study location	US
Study setting	Study centres
Study dates	Not reported
Sources of funding	Supported by a research grant from Lumenis Inc., Santa Clara, CA.
Inclusion criteria	<p>25 to 82 years of age</p> <p>IOP ≥ 24 and ≤ 31 (higher eye) and IOP ≥ 20 (lower eye)</p> <p>Diagnosis of primary OAG, pseudoexfoliation glaucoma, or mixed mechanism OAG with a narrow angle (if laser peripheral iridotomy was performed >3mo ago)</p> <p>Diagnosis of ocular hypertension if central corneal thickness was <600 microns</p> <p>Adequate visualisation of angle structures (that is clear media and cooperative patient)</p> <p>No previous intraocular surgery</p> <p>No glaucoma medications in both eyes for ≥ 4 weeks</p> <p>No systemic medications known to increase IOP (corticosteroids)</p> <p>Visual acuity of 20/70 or better in both eyes</p>
Exclusion criteria	<p>>2 glaucoma medications (fixed combination products are considered 2 drugs)</p> <p>Any eye drops for glaucoma 4 weeks before baseline I visit</p>

	<p>Collaborative Initial Glaucoma Treatment Study (CIGTS) visual field score that exceeded 16 in either eye</p> <p>Evidence of ocular disease other than glaucoma or ocular hypertension, which might affect IOP measurements, assessment of visual function or visual field testing</p> <p>Diagnosis of pigmentary OAG or proliferative diabetic retinopathy</p> <p>Undergone ophthalmic laser (other than laser peripheral iridotomy >3mo ago) or had refractive, conjunctival, or intraocular surgery in either eye</p> <p>Likely to require cataract surgery within 6 months of randomisation</p> <p>Current or expected use of corticosteroids</p> <p>Pregnant or planning to become pregnant within the next year</p>
Intervention(s)	<p>SLT</p> <p>Participants' study eyes received 360° SLT within 14 days of randomisation. If further treatment was required, repeat 180° SLT was the next step, followed by another 180° SLT.</p> <ul style="list-style-type: none"> • Step 1: Each eye treated within 2 weeks if both eyes were eligible. Treatment parameters: Number of Applications=100; Extent of angle=360°; Starting Power=If pigmentation grade is 1 or 2, started with 0.8 mJ (titrated according to target tissue response of blanching of trabecular meshwork and cavitation bubbles). Power adjusted by 0.1 mJ steps until visible response. If pigment grade was 3 or 4, power start at 0.4 mJ. Depending on tissue response and pigment in angle, energy was increased or decreased by 0.1 mJ increments to a maximum of 1.2 mJ and a minimum of 0.2 mJ. • Step 2: If target IOP not maintained in 1 or both eyes within 4 to 6 weeks, SLT over nasal 180° with 50 applications. • Step 3: If target IOP not attained or maintained in 1 or both eyes within 4 to 6 weeks, SLT over temporal 180° with 50 applications. • Step 4: Treating clinician choice of next therapy for intervention failure.
Comparator	Eye drops

	<p>The treatment regimen was not rigidly standardised but the following treatment regimen was recommended:</p> <ul style="list-style-type: none"> • Step 1: Start with ocular prostaglandin analogue: latanoprost, bimatoprost, or travoprost • Step 2: If target IOP not met but initial medication deemed effective, add b-blocker (or substitute, if first drug used was ineffective or not tolerated): timolol or betaxolol • Step 3: Brimonidine • Step 4: Dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol
Outcome measures	<p>Intraocular pressure</p> <p>Mean differences of IOP from baseline to follow-up 4 to 6 months, and to follow-up 9 to 12 months.</p> <p>Percentage of participants who met \leqtarget IOP.</p> <p>Target IOP was established based on the patient's reference IOP (ie, the mean of 6 separate IOP measurements taken in the course of 2 baseline visits) and their reference visual field score (ie, the mean of visual field scores from at least 2 Humphrey 24-2 visual fields taken during baseline visits before randomization). The formula for target IOP calculations was as follows: target IOP = $[1-(\text{reference IOP} + \text{visual field score}/100)] \times \text{reference IOP}$. Therefore, if the reference IOP=28mm Hg and the reference visual field score=5, then target IOP= $[1-(28+5)/100] \times 28 = (1-0.33) \times 28 = 0.67 \times 28 = 19\text{mm Hg}$.</p>
Duration of follow-up	12 months

Study arms

Eye drops (N = 31)

Number of participants	Eye drops (n=38 participants; n=67 eyes [one or both eyes eligible])
Loss to follow-up	6 participants were lost to follow-up after 4 to 6 months

Eye drops included ocular prostaglandin analogue, beta blockers, brimonidine, dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol depending on the recommended regimen.

SLT (N = 38)

Number of participants	SLT (n=31 participants; n=60 eyes [one or both eyes eligible])
Loss to follow-up	9 participants were lost to follow-up after 4 to 6 months

360° SLT within 14 days of randomisation. If further treatment was required, repeat 180° SLT was the next step, followed by another 180° SLT.

Characteristics

Arm-level characteristics

Characteristic	Eye drops (N = 31)	SLT (N = 38)
Female		
Sample size	n = 19 ; % = 61.3	n = 22 ; % = 57.9
Age		
Less than 60 years		
Sample size	n = 14 ; % = 45.2	n = 14 ; % = 36.8
60 years or more		
Sample size	n = 17 ; % = 54.8	n = 24 ; % = 63.2

Characteristic	Eye drops (N = 31)	SLT (N = 38)
Race		
White	n = 23 ; % = 74.2	n = 27 ; % = 71.1
Sample size		
Non-white	n = 8 ; % = 25.8	n = 11 ; % = 28.9
Sample size		
Glaucoma in immediate family		
No or uncertain	n = 18 ; % = 58.1	n = 20 ; % = 52.6
Sample size		
Yes	n = 13 ; % = 41.9	n = 18 ; % = 47.4
Sample size		
Hypertension		
No	n = 20 ; % = 64.5	n = 26 ; % = 68.4
Sample size		
Yes	n = 11 ; % = 35.5	n = 12 ; % = 31.6
Sample size		
Diabetes		
No	n = 25 ; % = 80.7	n = 30 ; % = 78.9
Sample size		

Characteristic	Eye drops (N = 31)	SLT (N = 38)
Yes	n = 6 ; % = 19.4	n = 8 ; % = 21.1
Sample size		

Critical appraisal - GUT Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low <i>(Two participants crossed over to the alternative treatment (one from each arm) but both were analysed under the intention to treat approach.)</i>
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Low <i>(Two participants crossed over to the alternative treatment (one from each arm) but both were analysed under the intention to treat approach.)</i>
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns <i>(No reasons were given for participants lost to 9 to 12 months follow-up)</i>
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low

Section	Question	Answer
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns (No information on whether the trial was analysed in accordance with a pre-specified plan.)
Overall bias and Directness	Risk of bias judgement	Moderate
Overall bias and Directness	Overall Directness	Partially applicable (Participants were not treatment naïve. One of the inclusion criteria was "on no glaucoma medications in both eyes for ≥ 4 weeks")

Lai, 2004

Bibliographic Reference

Lai JS; Chua JK; Tham CC; Lam DS; Five-year follow up of selective laser trabeculoplasty in Chinese eyes.; Clinical & experimental ophthalmology; 2004; vol. 32 (no. 4)

Study details

Trial registration number and/or trial name	None reported
Study location	China
Study setting	University hospital
Study dates	Participants were included in the study from March to June 1998.

Sources of funding	Not reported
Inclusion criteria	Newly diagnosed with POAG or OHT IOP >21 mmHg in both eyes without antiglaucomatous medications Those with POAG demonstrated optic disc changes and/or visual field changes typical of glaucomatous damage
Exclusion criteria	Pregnancy Previous laser trabeculoplasty Previous intraocular surgery disturbing the aqueous outflow Active ocular inflammation Poor visualization of the trabecular meshwork Single eye If the baseline IOP of one eye differed from the fellow eye by more than 15% at either of the two screening visits
Intervention(s)	360° SLT Topical anaesthesia with proparacaine was used. One drop of 1% apraclonidine was instilled into the eye to receive SLT 1 h prior to treatment. The Selecta 7000 frequency doubled Q-switched Nd:YAG laser (Coherent, Palo Alto, CA, USA) was used. A 3-mirror Goldmann gonioscope was placed on the cornea and the trabecular meshwork was brought into focus using the modified Coherent LDS-10 slit lamp with LAS-10 spot mirror illumination. The initial laser energy was set at 0.8 mJ. A single laser pulse was delivered starting at the 12 o'clock position. The energy was then increased or decreased by 0.1 mJ until bubble formation became just invisible. Treatment was then continued in single-burst mode at this energy level until about 100 non-overlapping laser spots were placed throughout 360° of the trabecular meshwork. Immediately following laser treatment, one drop of 1% apraclonidine and 1% prednisolone acetate were administered to the laser-treated eye. The prednisolone acetate eye drop was continued at a frequency of 4 times per day for 7 days.

Comparator	Eye drops Topical antiglaucoma medications were used including beta blocker, pilocarpine, dorzolamide and latanoprost were started either as monotherapy or in combination.
Outcome measures	Intraocular pressure Mean IOP reduction at follow-up. Failure was defined as IOP >21 mmHg.
Duration of follow-up	5 years
Loss to follow-up	Three participants were excluded within 6 months because they failed at follow-up. Five more participants were lost within 5 years follow-up. No details were given about which arm were these participants allocated.
Methods of analysis	
Additional comments	One eye of each participant was randomised to receive SLT and the fellow eye received eye drops. To minimize the extent of cross-over effect with medical treatment, participants were instructed to apply digital lacrimal punctal pressure for 5 min after instilling the eye drops. Eye drops were given 2 hours after SLT.

Study arms

Eye drops (N = 29)

Number of participants	Eye drops (n=32 participants; n=32 eyes [one eye randomised to receive eye drops and the fellow eye received SLT])
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Topical antiglaucoma medications

SLT (N = 29)

Number of participants	SLT (n=32 participants; n=32 eyes [one eye randomised to receive SLT and the fellow eye received eye drops])
360° SLT	

Characteristics**Study-level characteristics**

Characteristic	Study (N = 29)
Female	n = 16 ; % = 55.2
Sample size	
Age (years)	51.9 (14.7)
Mean (SD)	
Diagnosis	
POAG	n = 17 ; % = 58.6
Sample size	
OHT	n = 12 ; % = 41.4
Sample size	

Arm-level characteristics

Characteristic	Eye drops (N = 29)	SLT (N = 29)
Baseline IOP (mmHg) Mean (SD)	26.2 (4.2)	26.8 (5.6)
Best-corrected visual acuity Custom value	ranged from 0.2 to 1.0	ranged from 0.1 to 1.0
Cup/disc ratio Mean (SD)	0.5 (0.2)	0.4 (0.2)

Critical appraisal - GUT Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns <i>(There was no information on whether allocation sequence was concealed.)</i>
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High <i>(There was no information on whether there were any deviations that arose from the experimental context or whether either intention-to-treat analyses or modified intention to treat analyses were used.)</i>
Domain 2b: Risk of bias due to deviations from the intended	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	<i>Not applicable</i>

Section	Question	Answer
interventions (effect of adhering to intervention)		
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High <i>(There was no information about how many participants were lost to follow-up from each arm. Reasons for loss to follow-up were not given for the 5 participants that were lost within 5 years follow-up.)</i>
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns <i>(There was no information about a pre-specified analysis plan.)</i>
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Nagar, 2005

Bibliographic Reference

Nagar M; Ogunyomade A; O'Brart DP; Howes F; Marshall J; A randomised, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma.; The British journal of ophthalmology; 2005; vol. 89 (no. 11)

Study details

Trial registration number and/or trial name	None reported
Study type	Randomised controlled trial (RCT)
Study location	UK
Study setting	Department of Ophthalmology Eye Centre
Study dates	Not reported
Sources of funding	The study was supported by provision of A Selectra 7000 laser by Lumenis (Coherent Medical Group, Palo Alto, CA, USA).
Inclusion criteria	OHT or primary or secondary OAG Either newly diagnosed or controlled on medical therapy
Exclusion criteria	Congenital glaucoma Any type of angle closure glaucoma Eyes with previous laser or surgical glaucoma interventions Eyes with previous anterior segment surgery
Intervention(s)	Laser techniques Immediately before the laser procedure a single application of amethocaine 1% was instilled into the operative eye. A Coherent Selectra 7000 laser (Lumenis, Coherent, Inc, Palo Alto, CA, USA) was used in all cases. This was a frequency

	<p>doubled, q-switched Nd:YAG laser emitting at 532 nm, with a pulse duration of 3 ns, a spot size of 400 mm, and pulse energies ranging from 0.2–1.7 mJ, coupled to a slit lamp delivery system with a helium-neon laser (HeNe) aiming system.</p> <p>Postoperatively, participants were prescribed either dexamethasone 0.1% eye drops four times a day for 5 days or ketorolac eye drops four times a day for 5 days.</p> <p>90° SLT</p> <p>Treatments 25–30 non-overlapping laser spots were applied to 3 clock hours of the inferonasal or inferotemporal trabecular meshwork.</p> <p>180° SLT</p> <p>Treatments 48–53 spots were applied over the inferior 6 clock hours.</p> <p>360° SLT</p> <p>The entire meshwork was treated with 93–102 non-overlapping spots.</p>
Comparator	Latanoprost 0.005% at night
Outcome measures	<p>Intraocular pressure</p> <p>Success was defined both as a 20% or more reduction in IOP from baseline measurements and also as a 30% or greater IOP reduction from baseline with no additional antiglaucomatous interventions.</p> <p>Adverse events</p>
Duration of follow-up	Mean follow-up was 10.3 months (ranging from 1 to 12 months).
Loss to follow-up	Not reported

Methods of analysis	
Additional comments	<p>It was noted that participants were not excluded from the study on the basis of their age, race, and number and types of antiglaucomatous medications.</p> <p>Data was not reported on how many participants were controlled on medical therapy.</p> <p>At the discretion of the treating surgeons, further laser treatments or antiglaucomatous medications were administered to ensure adequate IOP control.</p> <p>It was also noted that if indicated, both eyes of each patient received identical treatments on the basis of randomisation. However, only one eye of each patient was entered into the study. This was either the eye with the highest IOP measurement at baseline examination or, if the pressures were identical, the right eye was chosen.</p>

Study arms

Latanoprost (N = 39)

Number of participants	Latanoprost (n=39 participants; n=39 eyes)
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90° SLT (N = 35)

Number of participants	90° SLT (n=35 participants; n=35 eyes)
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180° SLT (N = 49)

Number of participants	180° SLT (n=49 participants; n=49 eyes)
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360° SLT (N = 44)

Number of participants	360° SLT (n=44 participants; n=44 eyes)
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Characteristics**Study-level characteristics**

Characteristic	Study (N = 167)
Female	n = 90 ; % = 53.9
Sample size	
Age (years)	Mean 63 years (range 22 to 90)
Custom value	
Ethnicity	
African or Afro-Caribbean origin	n = 36 ; % = 22
Sample size	
White	n = 131 ; % = 78

Characteristic	Study (N = 167)
Sample size	
Diagnosis	
OAG Primary OAG (n=76); secondary to pigment dispersion syndrome (n=4); secondary to pseudoexfoliation syndrome (n=2)	n = 82 ; % = 49
Sample size	
OHT	n = 85 ; % = 51
Sample size	

Critical appraisal - GUT Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High <i>(There was no information on whether there were any deviations that arose from the experimental context or whether either intention-to-treat analyses or modified intention to treat analyses were used.)</i>

Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	<i>Not applicable</i>
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns (<i>There was no information about a pre-specified analysis plan.</i>)
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable (<i>It was not reported how many participants were controlled on medical therapy before participating in the trial.</i>)

Nagar, 2009

Bibliographic Reference

Nagar, M; Luhishi, E; Shah, N; Intraocular pressure control and fluctuation: the effect of treatment with selective laser trabeculoplasty.; The British journal of ophthalmology; 2009; vol. 93 (no. 4); 497-501

Study details

Trial registration number and/or trial name	None reported
Study type	Randomised controlled trial (RCT)
Study location	UK
Study setting	Eye centre
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	<p>Newly diagnosed OHT or primary OAG</p> <p>Aged 40 to 80 years</p> <p>Diurnal intraocular pressure fluctuation more than 3 mm Hg</p> <p>In those with OAG, a classification of “outside normal limit” involving same visual-field area at two initial pre-screening visits using glaucoma hemifield test</p> <p>In those with OAG, “borderline” classification was acceptable only if obvious glaucomatous optic disc cupping was present in an area corresponding to the visual-field defect</p> <p>In those with OHT, intraocular pressure between 24 and 32 mm Hg in one eye and 21 and 32 mm Hg in the other (determined on two visits)</p> <p>In those with OHT, normal optic disc</p>

	<p>In those with OHT, normal visual field using Humphrey visual field on two separate screening visits</p> <p>In those with OHT, no evidence of glaucomatous damage</p> <p>Willing to undergo selective laser trabeculoplasty versus latanoprost treatment trial</p>
Exclusion criteria	<p>Diurnal intraocular pressure fluctuation of less than 3 mm Hg</p> <p>Diagnoses other than open-angle glaucoma and ocular hypertension (eg, patients with narrow angles, congenital glaucoma)</p> <p>Advanced glaucoma</p> <p>Normal tension glaucoma</p> <p>Previous laser or surgical glaucoma intervention or any previous anterior segment surgery</p> <p>Pregnancy</p> <p>Ocular condition precluding visualisation of trabecular meshwork</p> <p>Impairment preventing adequate understanding to sign an informed consent or cooperate during study procedures</p> <p>Potential need for other ocular surgery within the 4–6-month follow-up period</p> <p>Unable to comply with intended follow-up visits</p>
Intervention(s)	<p>SLT</p> <p>The laser used was the Ellex Tango ophthalmic laser system (Ellex, Adelaide, Australia), a frequency doubled, q-switched Nd:YAG laser emitting at 532 nm, with a pulse duration of 3 ns, a spot size of 400 mm and pulse energies ranging from 0.2 to 1.4 mJ, coupled to a slit-lamp delivery system with a He–Ne aiming system. One surgeon performed the laser procedures. Immediately prior to treatment, an application of amethocaine 1% was instilled into the eye. The patient was seated at the slit lamp, a single mirror gonioscope was used, and the laser was focused on the trabecular meshwork. Using a</p>

	400 mm spot the entire width of the trabecular meshwork was irradiated with each pulse. The laser energy was initially set at 0.8 mJ, and a single pulse was delivered at the 12 o'clock position. If cavitation bubbles appeared, the energy was reduced by 0.1 mJ increments until no bubble formation or fine champagne bubbles were observed and treatment continued at this energy level. If no cavitation bubbles occurred, the energy was increased by increments of 0.1 mJ until bubble formation and then decreased as described above. The entire meshwork was treated with 100 (SD 5) non-overlapping spots. The total number of pulses and the energy delivered were recorded. Postoperatively, non-steroidal anti-inflammatory drops (ketorolac tromethamine), were prescribed four times a day for 5 days.
Comparator	Latanoprost Patients allocated to this group were instructed to instil one drop of latanoprost 0.005% into the eye every night. Compliance was stressed, and any questions that the patients had were addressed during the teaching session.
Outcome measures	Intraocular pressure Treatment success for IOP control was defined as at least a 20% reduction from baseline measurement.
Number of participants	SLT (n=20) Latanoprost (n=20)
Duration of follow-up	6 months
Loss to follow-up	Unclear; it was only reported that 30 participants attended all appointments.
Additional comments	It was noted that if indicated, both eyes of each patient received identical treatments on the basis of randomisation. However, only one eye of each patient was entered into the study. At the end of the study, eyes that had not achieved adequate IOP control were treated with laser or latanoprost at the discretion of the chief investigator.

Study arms

SLT (N = 20)

Number of participants	SLT (n=20 participants; n=20 eyes)
	Selective laser trabeculoplasty

Latanoprost (N = 20)

Number of participants	Latanoprost (n=20 participants; n=20 eyes)
	Eye drops

Characteristics

Study-level characteristics

Characteristic	Study (N = 40)
Female	n = 19 ; % = 48
Sample size	
Age (years)	Mean 66.4 (range 43 to 88)
Custom value	
Diagnosis	

Characteristic	Study (N = 40)
OAG	
Sample size	n = 17 ; % = 43
OHT	
Sample size	n = 23 ; % = 57

Critical appraisal - GUT Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns <i>(Unclear if intention-to-treat analysis was used.)</i>
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	<i>Not applicable</i>
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns <i>(Of the 40 participants, 30 attended all appointments. It was not reported how many of these participants were from each arm. It was reported that "incomplete follow-up occurred mainly because of the short interval</i>

		<i>between the standard clinic appointment and the study appointment to monitor diurnal fluctuation".)</i>
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns <i>(No information on whether there was a pre-specified analysis plan.)</i>
Overall bias and Directness	Risk of bias judgement	Moderate <i>(Unclear if intention-to-treat analysis was used. It was not reported how many of the participants attending all appointments were from each arm. No information on whether there was a pre-specified analysis plan.)</i>
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

Comparison: 360°SLT vs eye drops

Figure 1: 360°SLT vs eye drops; Outcome: Eyes at target IOP (all participants; reported by Gazzard 2019 Lancet)

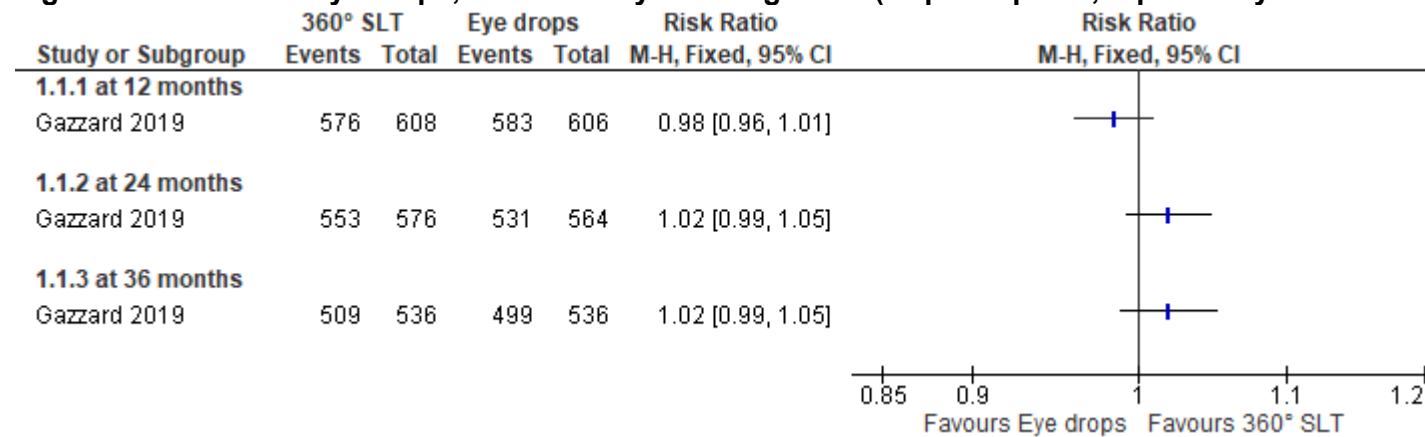
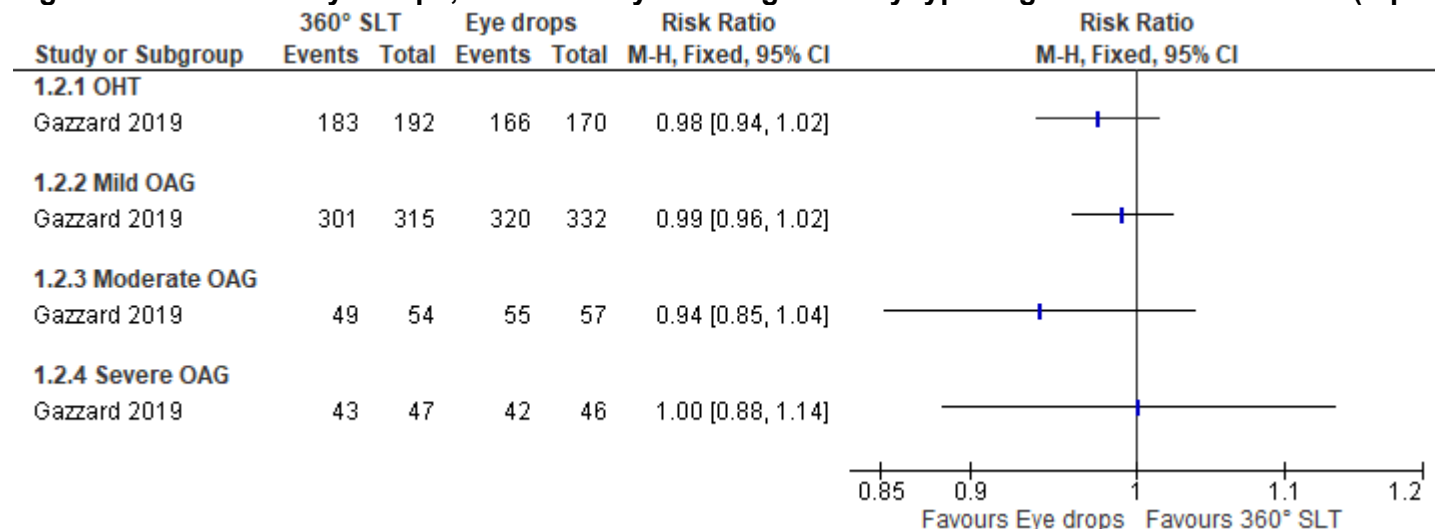
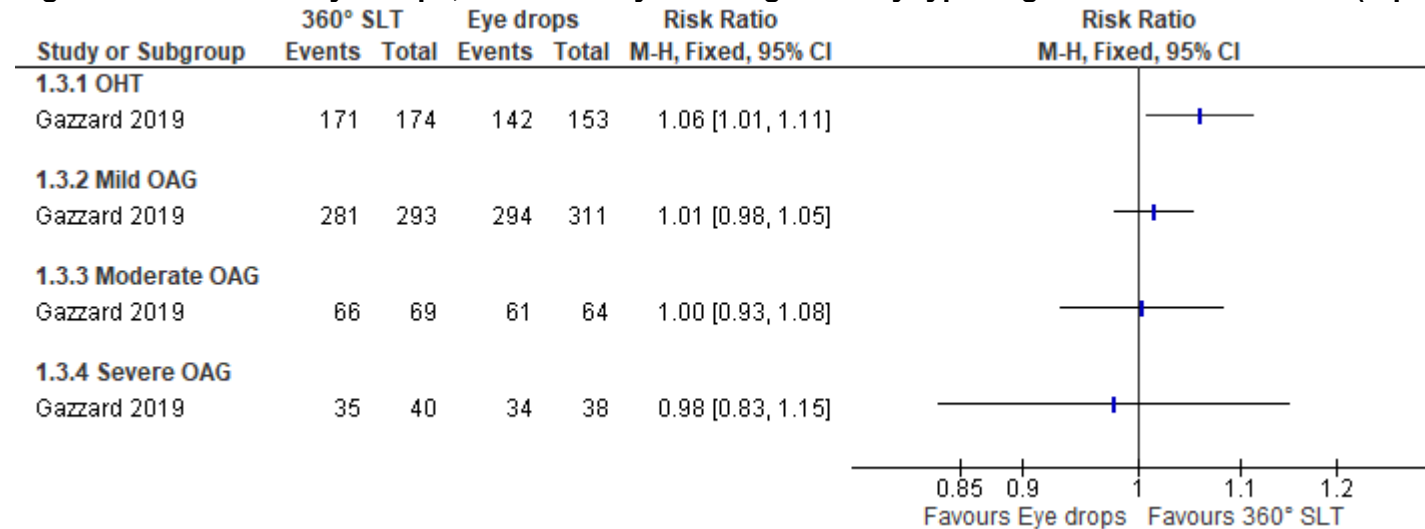


Figure 2: 360°SLT vs eye drops; Outcome: Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA)



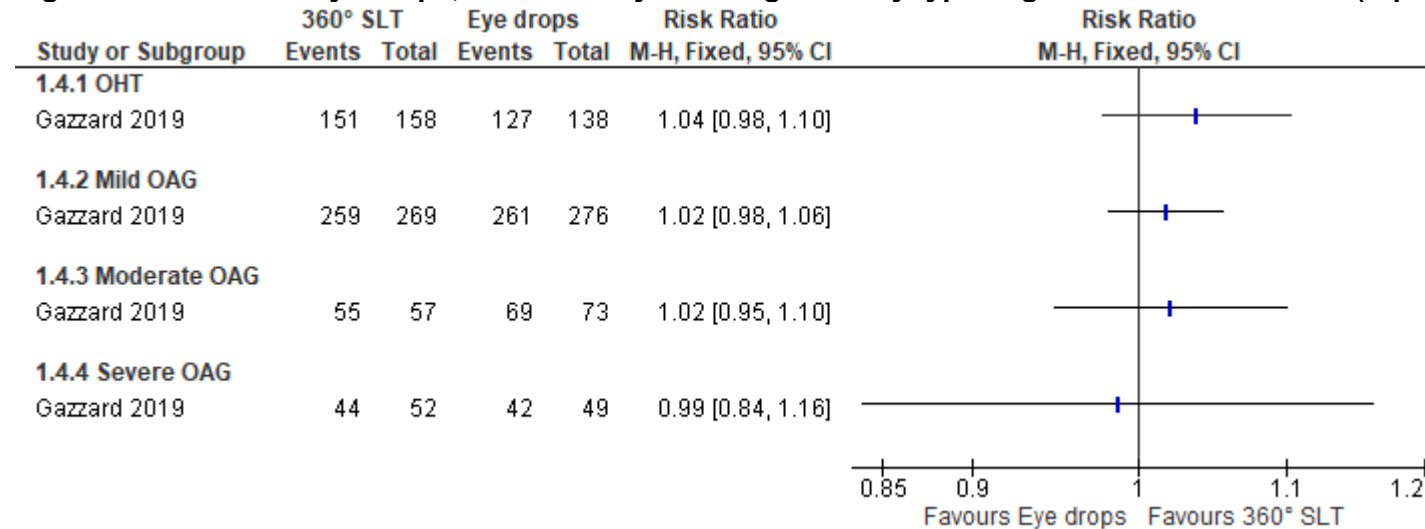
Totals for each subgroup were calculated by reviewer as Gazzard 2019 HTA only reported percentages

Figure 3: 360°SLT vs eye drops; Outcome: Eyes at target IOP by type of glaucoma at 24 months (reported by Gazzard 2019 HTA)



Totals for each subgroup were calculated by reviewer as Gazzard 2019 HTA only reported percentages

Figure 4: 360°SLT vs eye drops; Outcome: Eyes at target IOP by type of glaucoma at 36 months (reported by Gazzard 2019 HTA)



Totals for each subgroup were calculated by reviewer as Gazzard 2019 HTA only reported percentages

Figure 5: 360°SLT vs eye drops; Outcome: Right and left eyes at target IOP

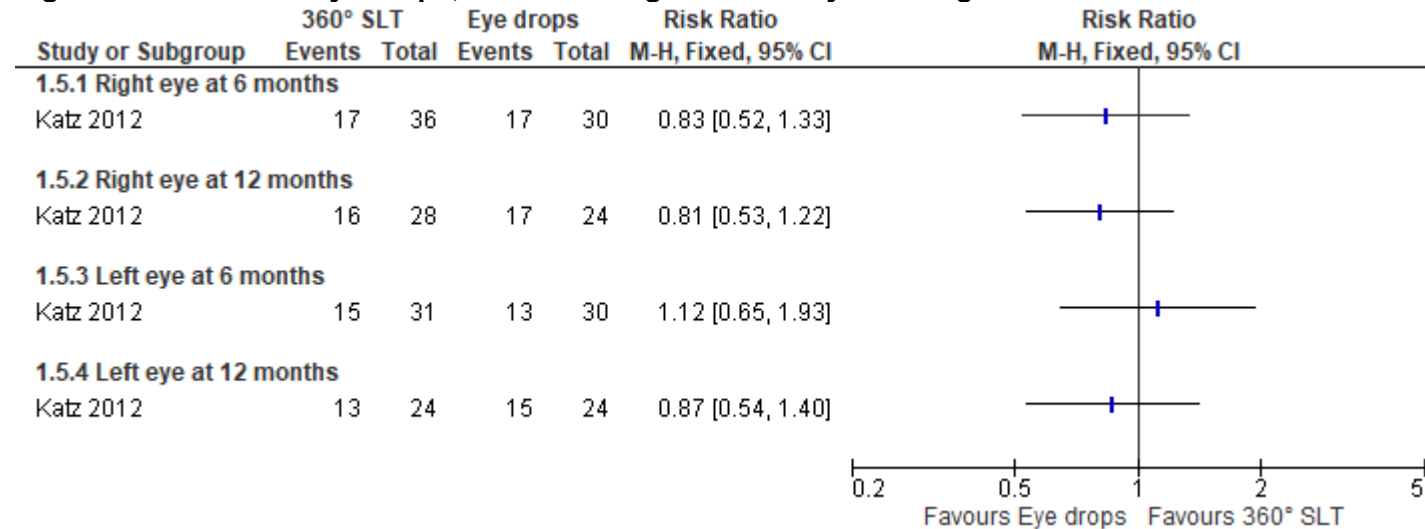
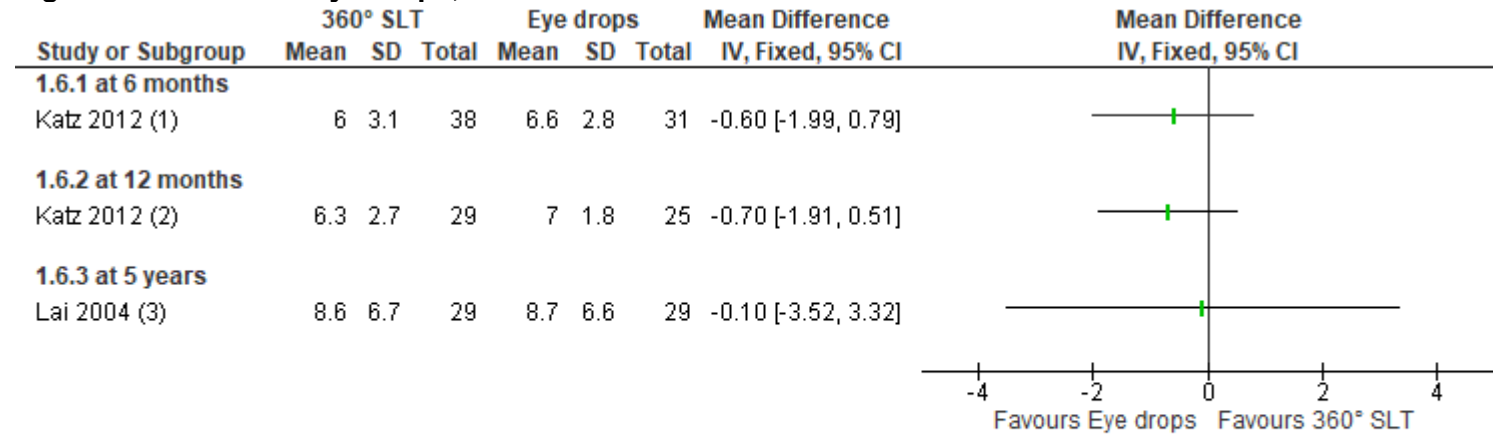


Figure 6: 360°SLT vs eye drops; Outcome: Mean IOP reduction



Footnotes

(1) Mean of both eyes

(2) Mean of both eyes

(3) 29 eyes per arm (n=29 participants in total)

Figure 7: 360°SLT vs eye drops; Outcome: EQ-5D (reported by Gazzard 2019 Lancet)

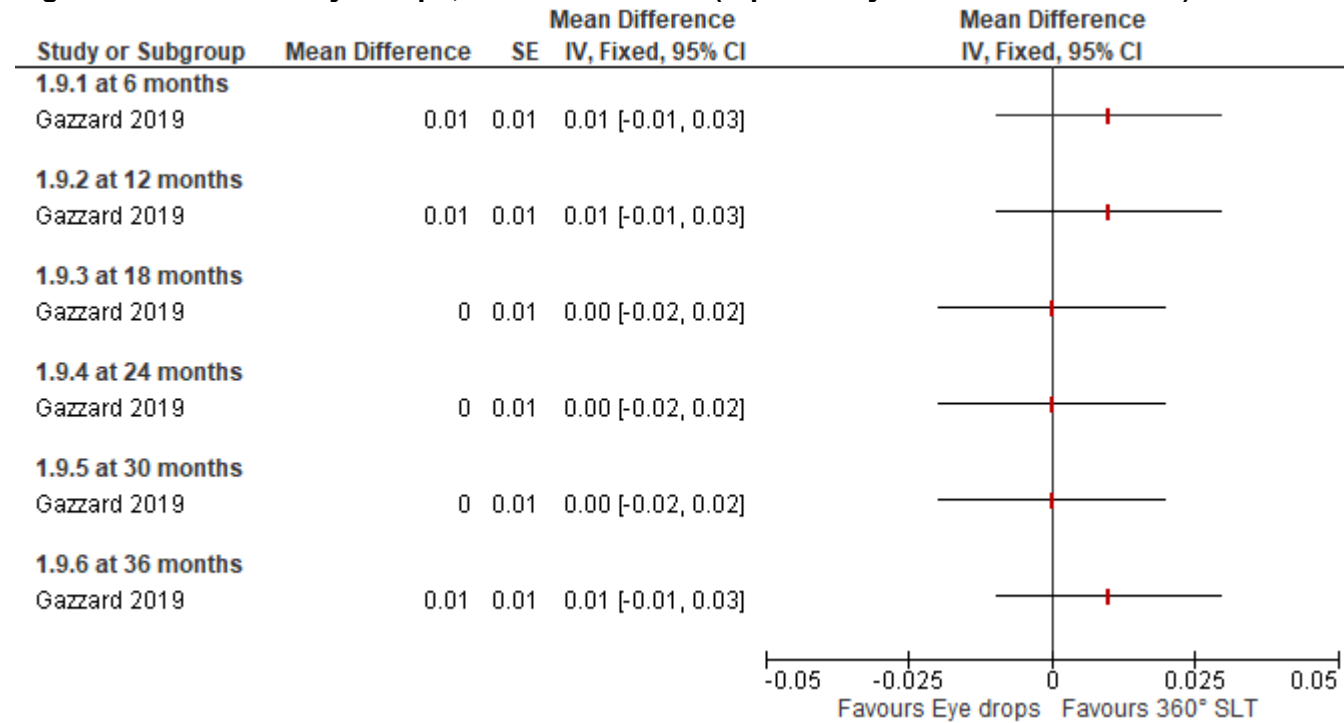


Figure 8: 360°SLT vs eye drops; Outcome: GUI (reported by Gazzard 2019 Lancet)

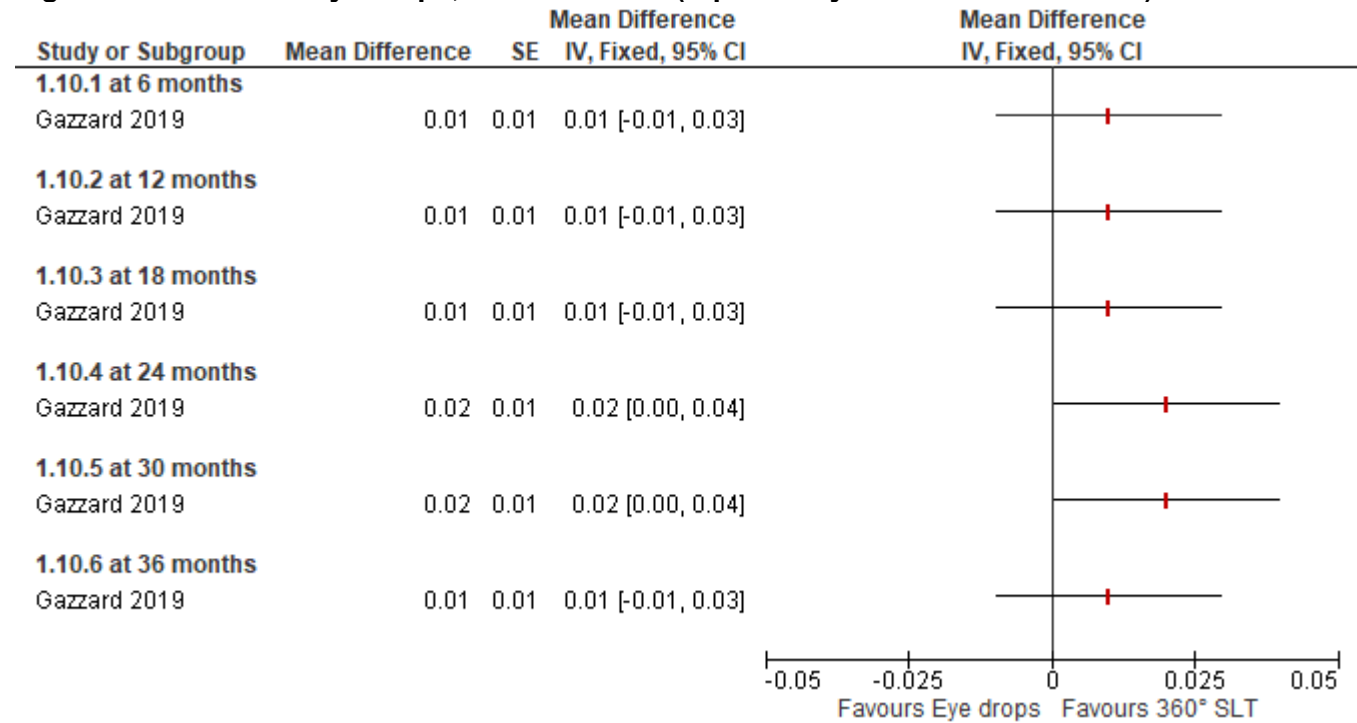


Figure 9: 360°SLT vs eye drops; Outcome: GQL-15 (reported by Gazzard 2019 Lancet)

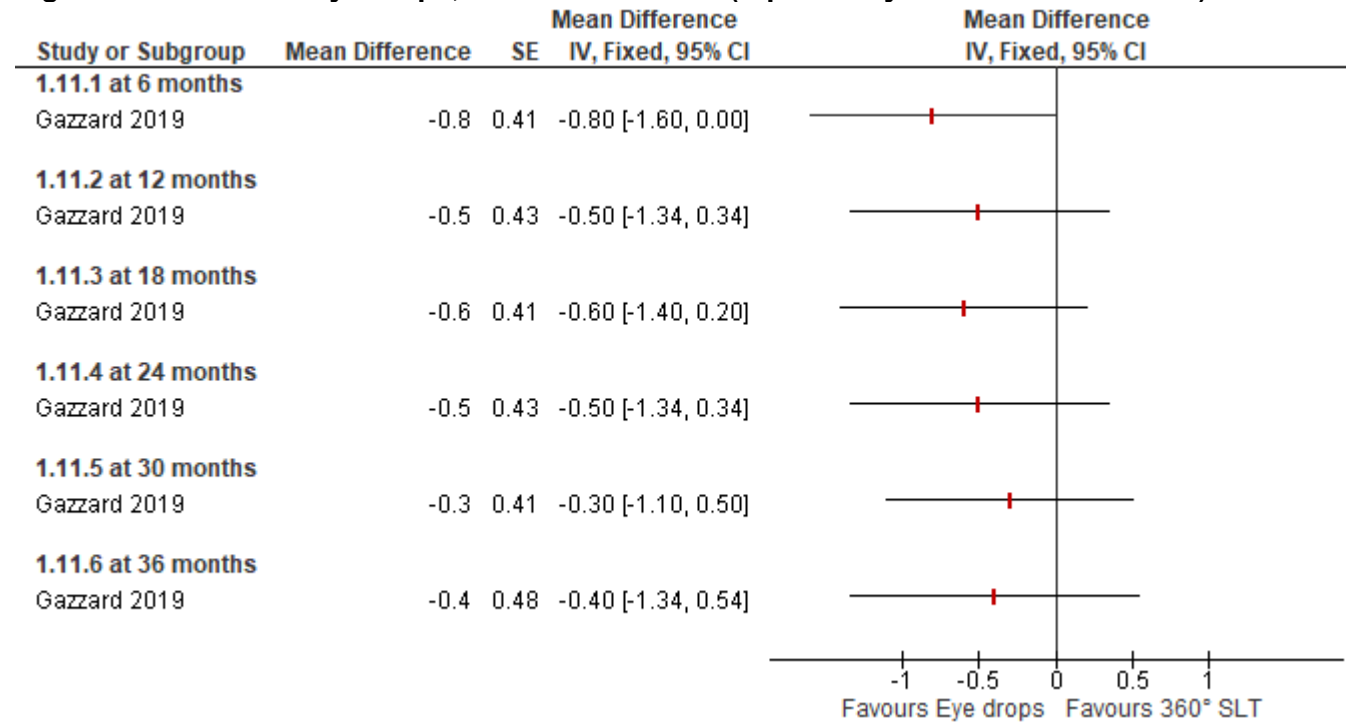


Figure 10: 360°SLT vs eye drops; Outcome: Ocular adverse events (reported by Gazzard 2019 Lancet)

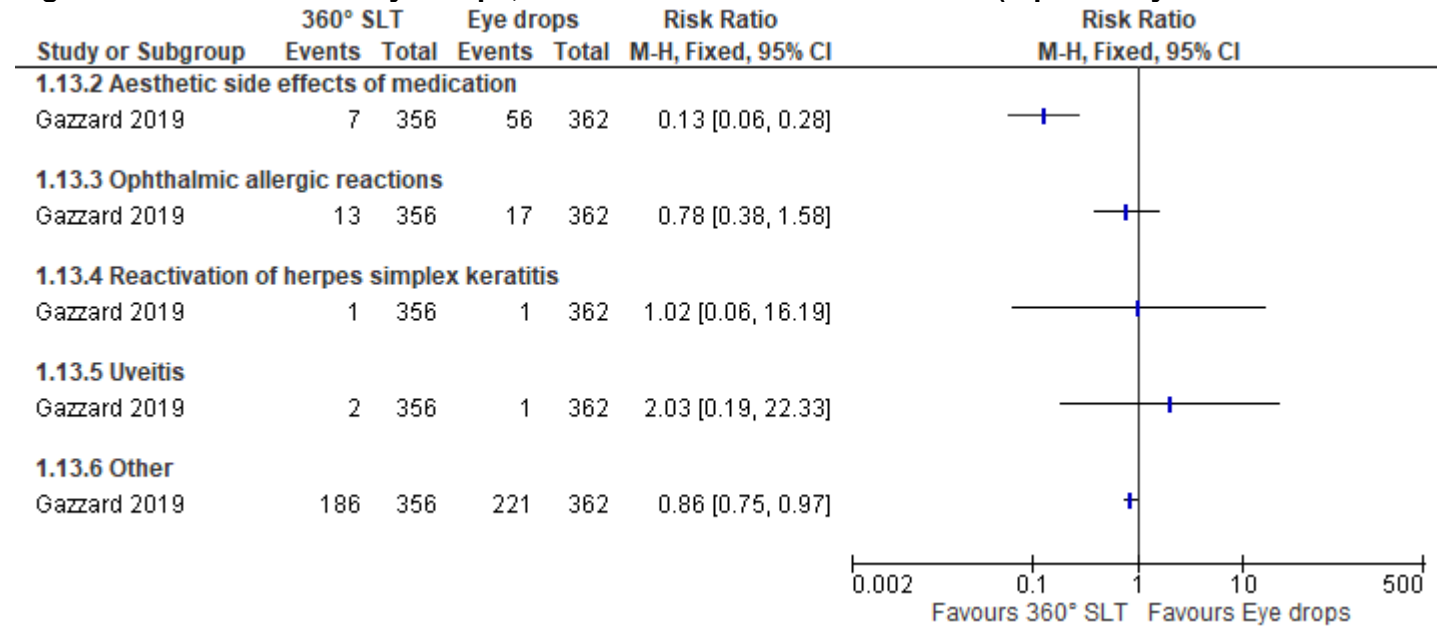


Figure 11: 360°SLT vs eye drops; Outcome: SLT-related ocular adverse events (reported by Gazzard 2019 Lancet)

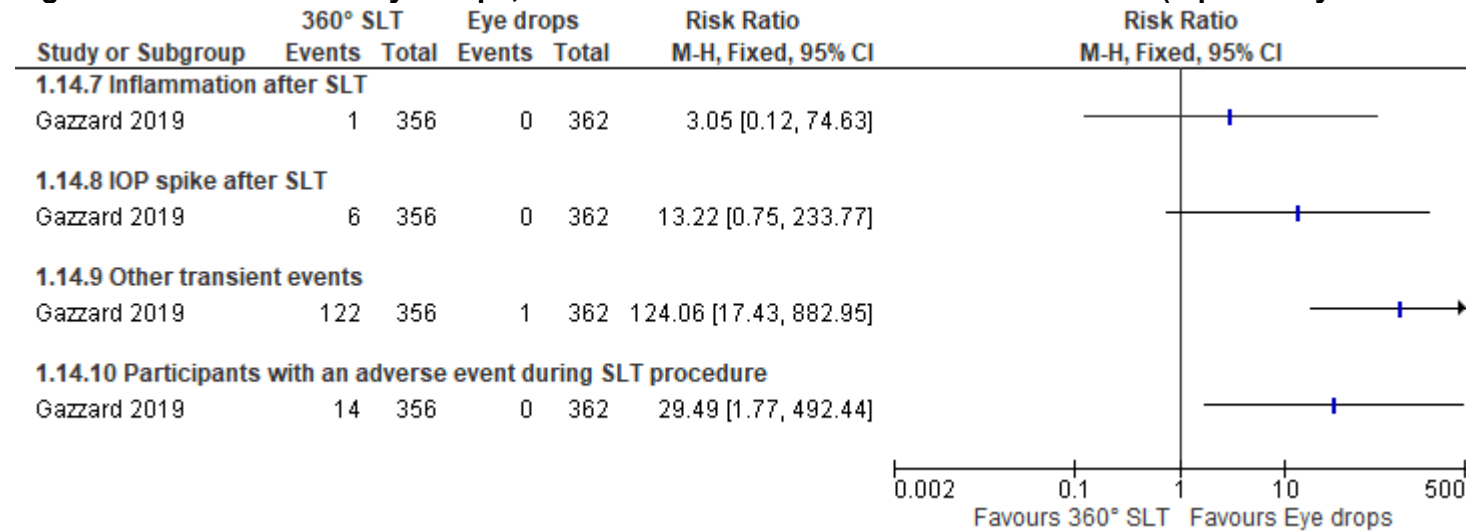


Figure 12: 360°SLT vs eye drops; Outcome: Systemic adverse events (reported by Gazzard 2019 Lancet)

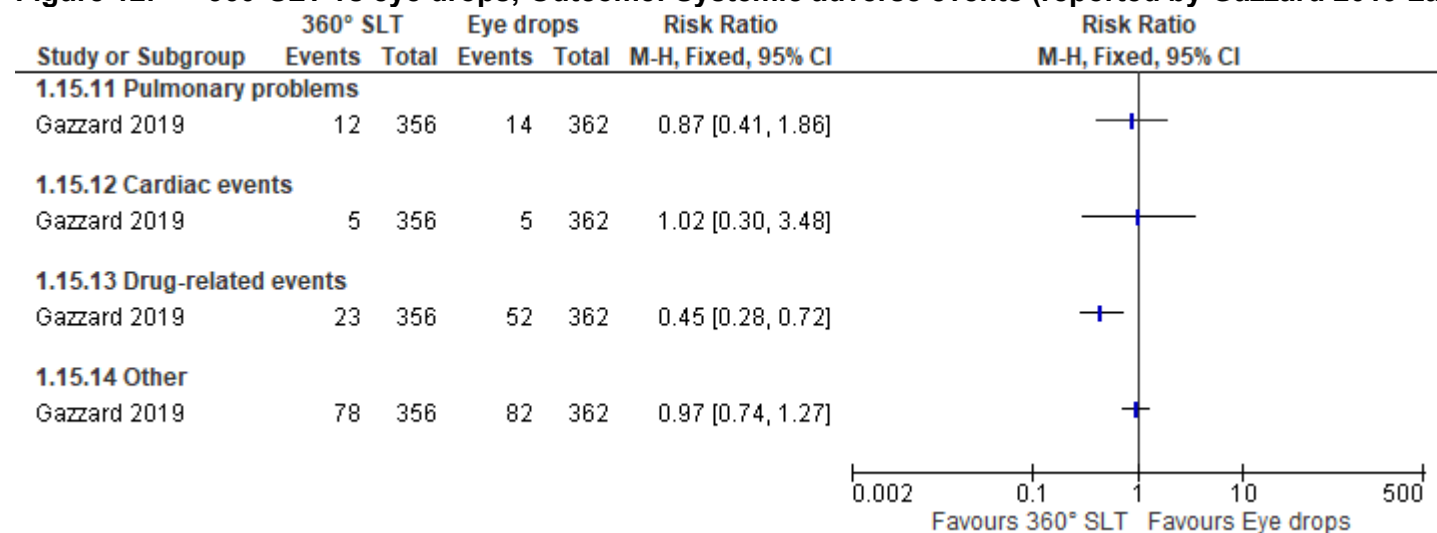
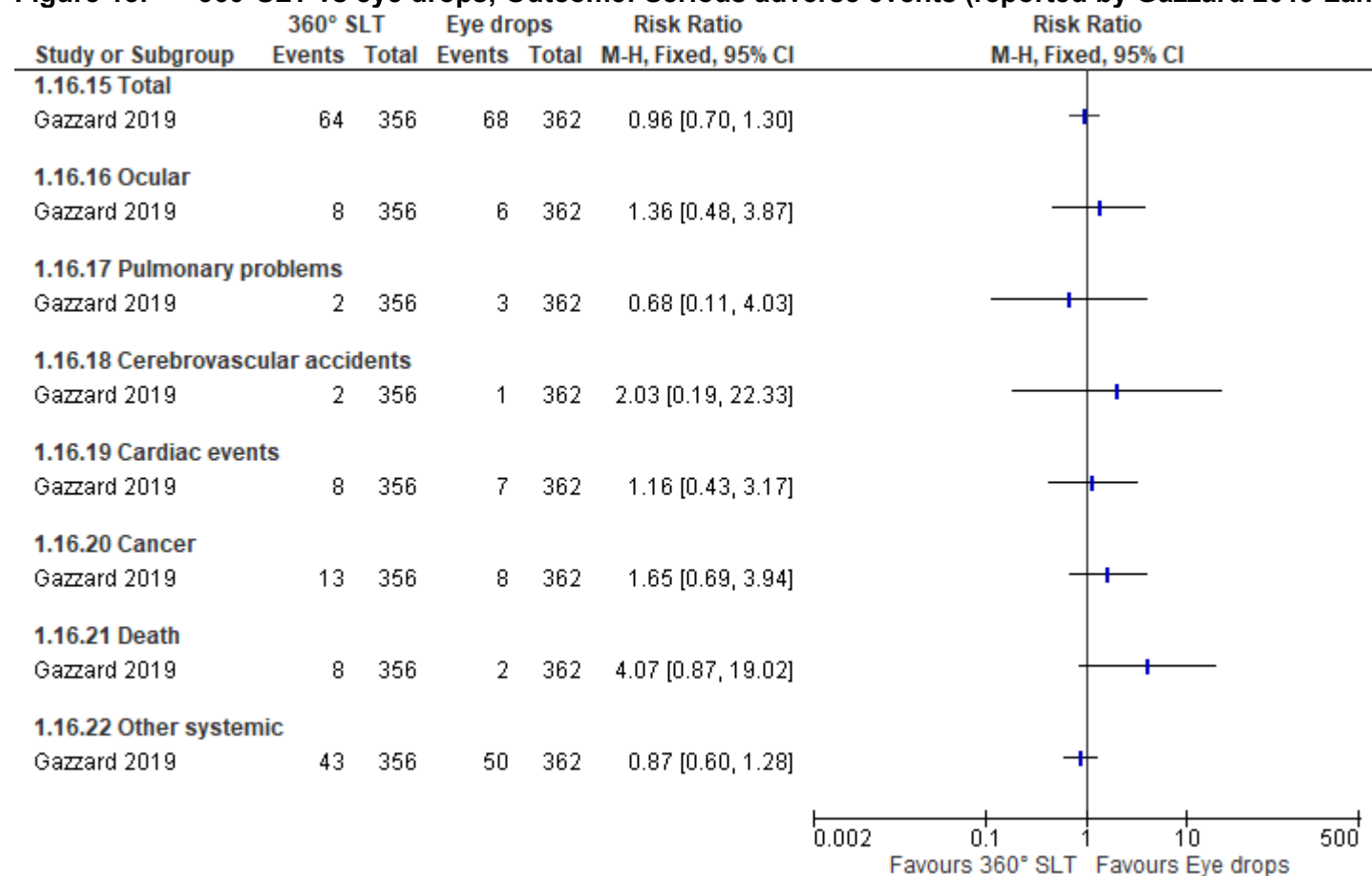


Figure 13: 360°SLT vs eye drops; Outcome: Serious adverse events (reported by Gazzard 2019 Lancet)

Comparison: 360°SLT vs latanoprost

Figure 14: 360°SLT vs latanoprost; Outcome: Eyes at target IOP at 12 months

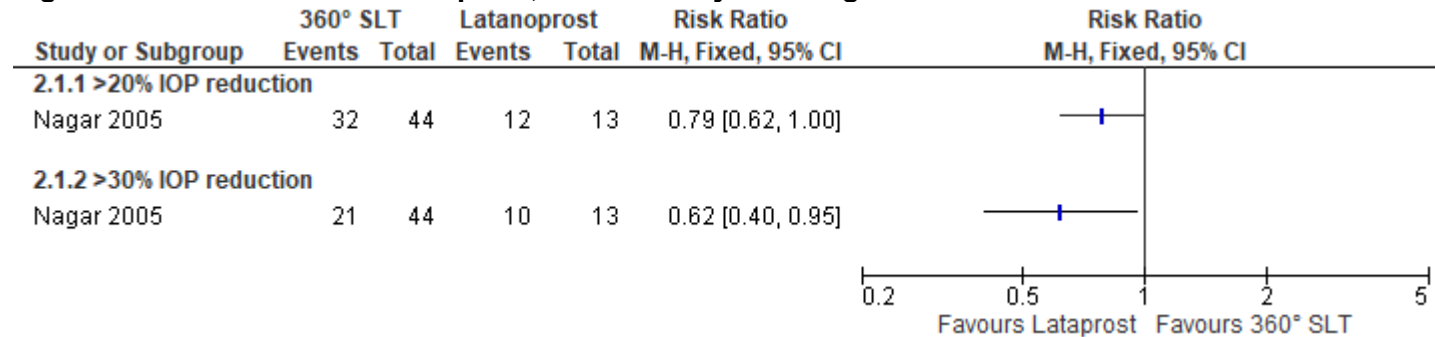
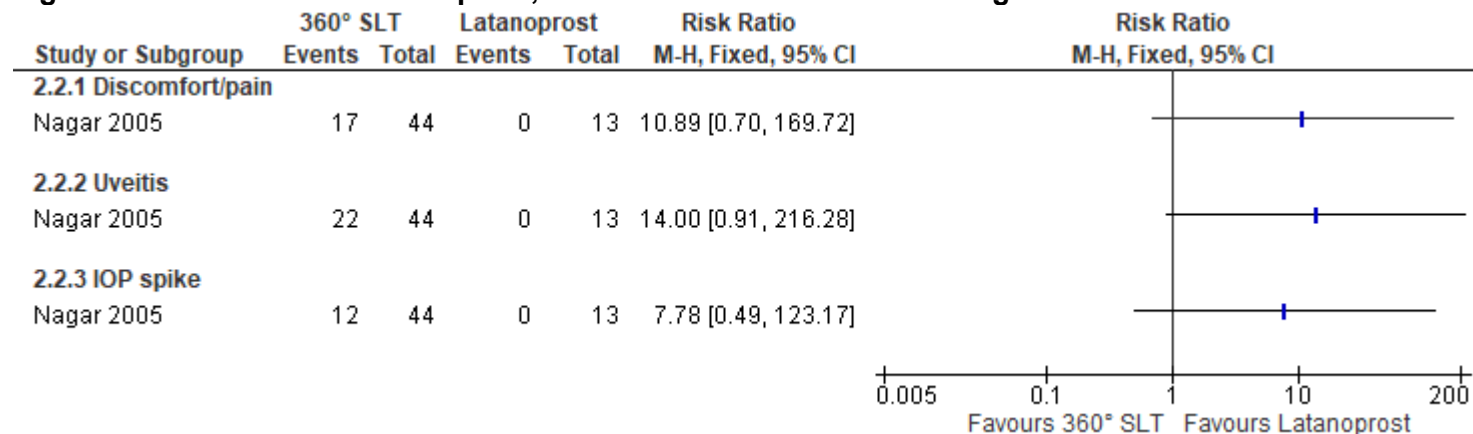


Figure 15: 360°SLT vs latanoprost; Outcome: Adverse events during first week after treatment



Events (discomfort/pain and uveitis) were calculated by reviewer because Nagar 2005 only reported percentages

Comparison: 180°SLT vs latanoprost

Figure 16: 180°SLT vs latanoprost; Outcome: Eyes at target IOP at 12 months

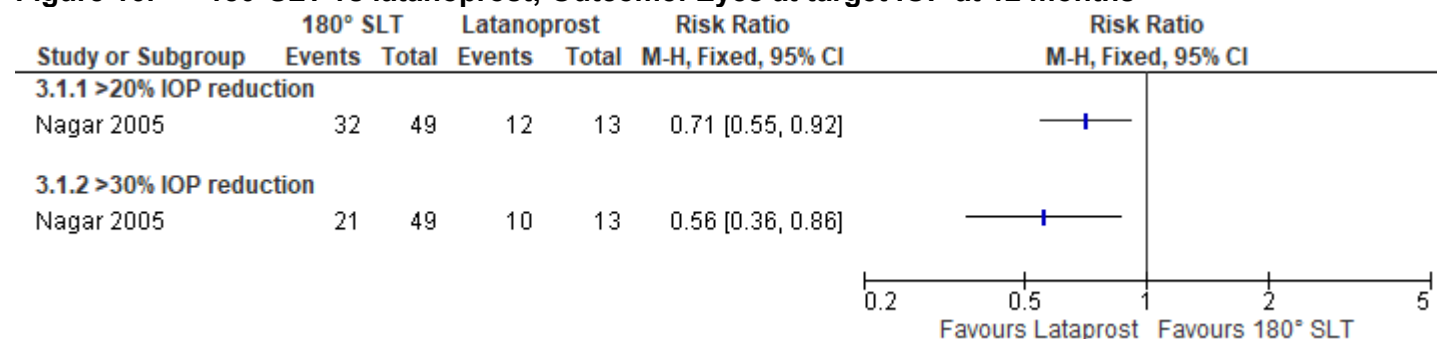
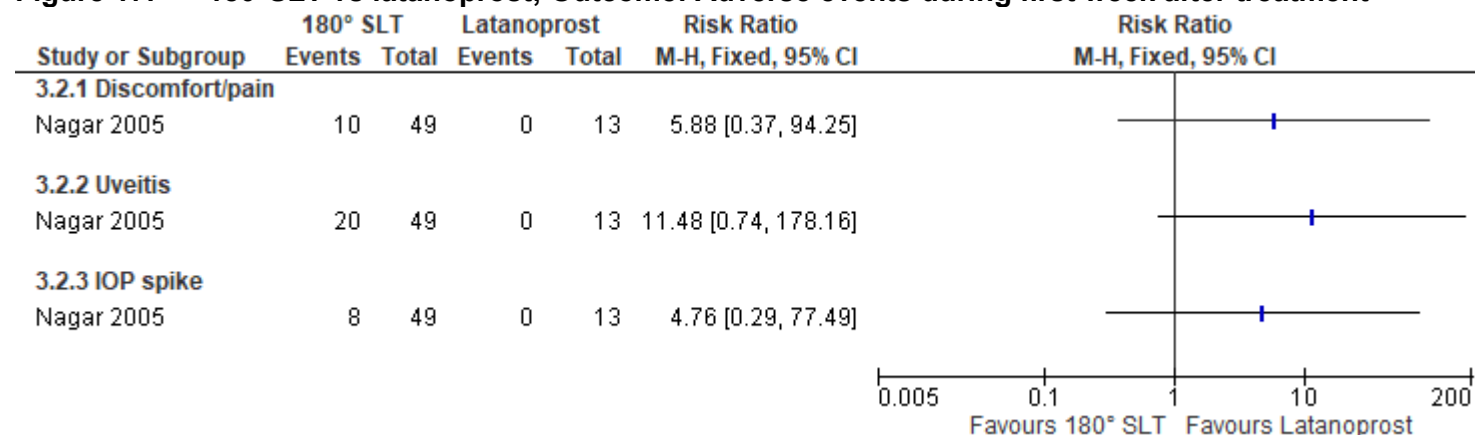


Figure 17: 180°SLT vs latanoprost; Outcome: Adverse events during first week after treatment



Events (discomfort/pain and uveitis) were calculated by reviewer because Nagar 2005 only reported percentages

Comparison: 90°SLT vs latanoprost

Figure 18: 90°SLT vs latanoprost; Outcome: Eyes at target IOP at 12 months

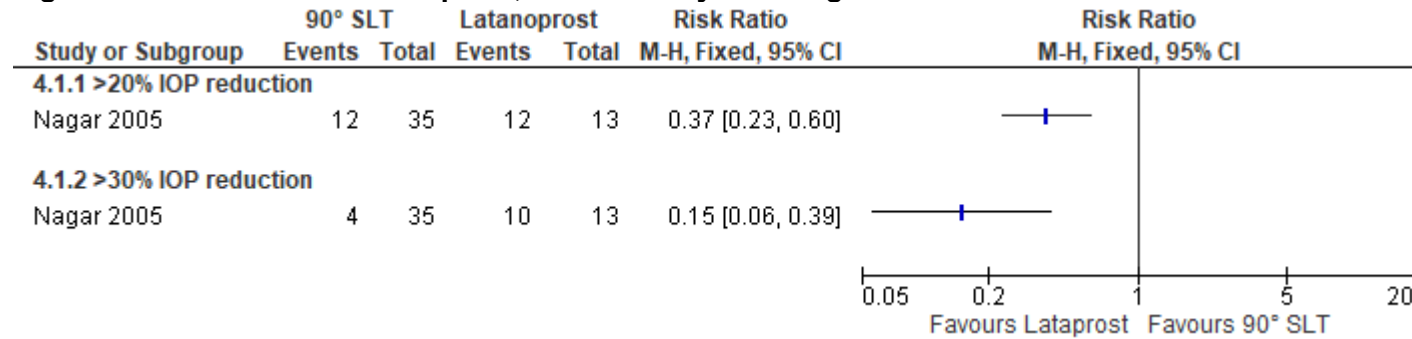
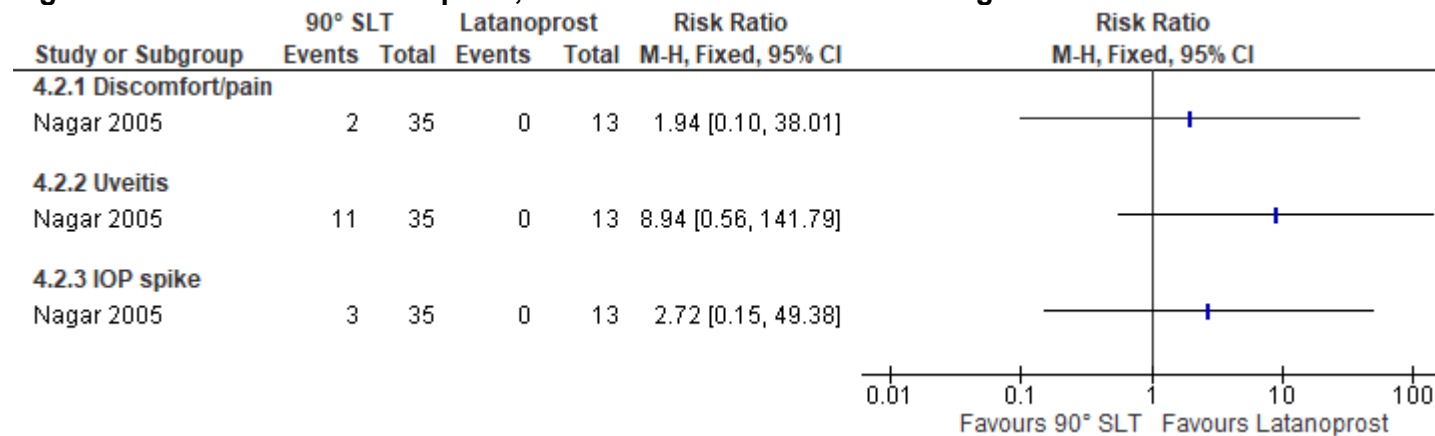
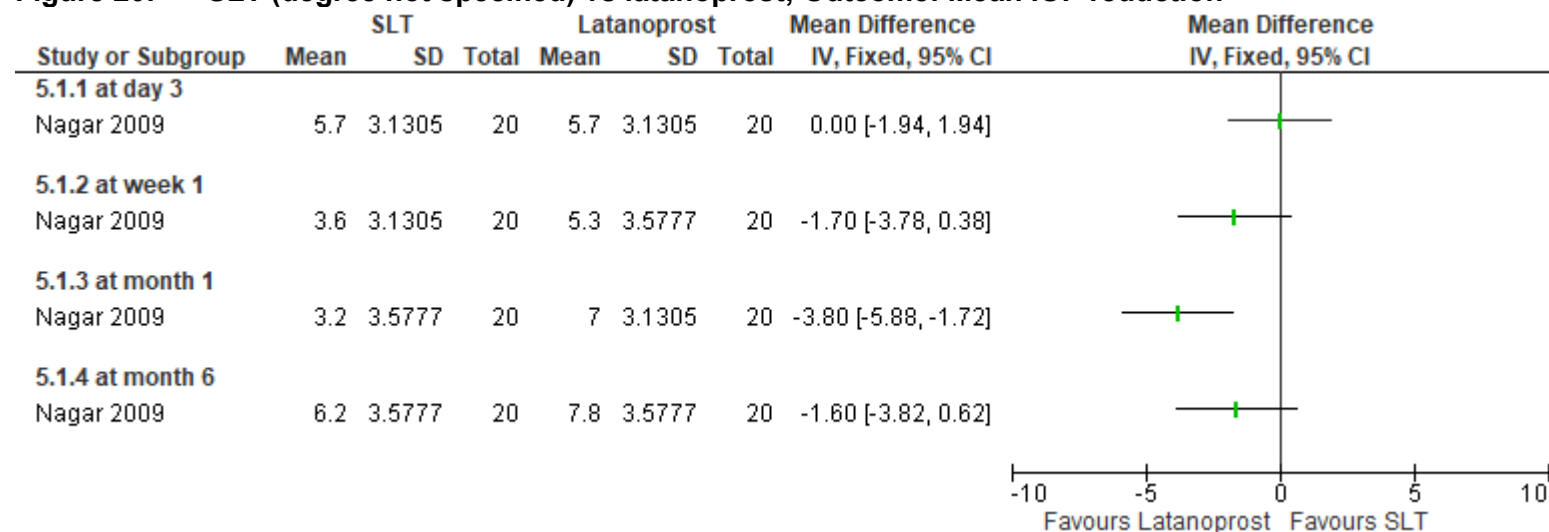


Figure 19: 90°SLT vs latanoprost; Outcome: Adverse events during first week after treatment

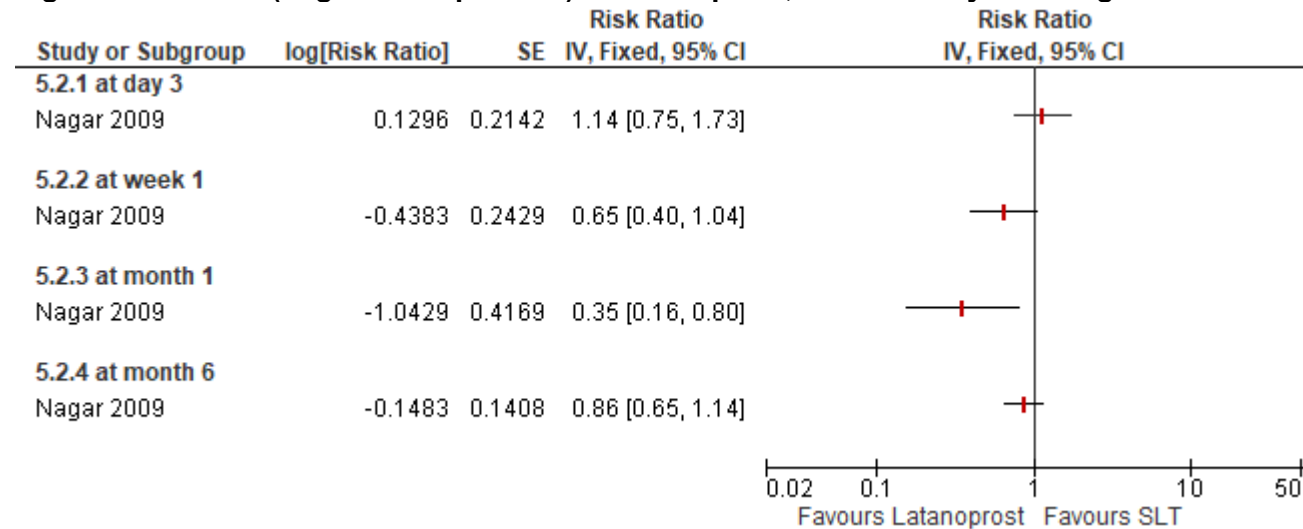


Events (discomfort/pain and uveitis) were calculated by reviewer because Nagar 2005 only reported percentages

Comparison: SLT (degree not specified) vs latanoprost**Figure 20: SLT (degree not specified) vs latanoprost; Outcome: Mean IOP reduction**

Number of participants was not reported at each follow-up; total numbers in the plot represent randomised participants

Figure 21: SLT (degree not specified) vs latanoprost; Outcome: Eyes at target IOP



Appendix F – GRADE tables

Comparison: 360°SLT vs eye drops

Outcome: Intraocular pressure

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Eyes at target IOP at 12 months (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	1214	RR 0.98 (0.96, 1.01)	96 per 100	1 fewer per 100 (4 fewer to 1 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP at 24 months (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	1140	RR 1.02 (0.99, 1.05)	94 per 100	2 more per 100 (1 fewer to 4 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP at 36 months (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	1072	RR 1.02 (0.99, 1.05)	93 per 100	2 more per 100 (1 fewer to 5 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA) OHT (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	362*	RR 0.98 (0.94, 1.02)	98 per 100	2 fewer per 100 (6 fewer to 1 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA) Mild OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	647*	RR 0.99 (0.96, 1.02)	96 per 100	1 fewer per 100 (4 fewer to 2 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA)										

Moderate OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	111*	RR 0.94 (0.85, 1.04)	96 per 100	6 fewer per 100 (14 fewer to 4 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA)										
Severe OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	93*	RR 1.00 (0.88, 1.14)	91 per 100	0 more per 100 (11 fewer to 12 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 24 months (reported by Gazzard 2019 HTA)										
OHT (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	327*	RR 1.06 (1.01, 1.11)	93 per 100	5 more per 100 (1 more to 10 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 24 months (reported by Gazzard 2019 HTA)										
Mild OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	604*	RR 1.01 (0.98, 1.05)	95 per 100	1 more per 100 (2 fewer to 5 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 24 months (reported by Gazzard 2019 HTA)										
Moderate OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	133*	RR 1.00 (0.93, 1.08)	95 per 100	0 more per 100 (6 fewer to 8 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 24 months (reported by Gazzard 2019 HTA)										
Severe OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	78*	RR 0.98 (0.83, 1.15)	89 per 100	2 fewer per 100 (15 fewer to 13 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 36 months (reported by Gazzard 2019 HTA)										
OHT (RR greater than 1 favours 360°SLT)										

Gazzard 2019	RCT	296*	RR 1.04 (0.98, 1.10)	92 per 100	4 more per 100 (2 fewer to 9 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 36 months (reported by Gazzard 2019 HTA)										
Mild OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	545*	RR 1.02 (0.98, 1.06)	95 per 100	2 more per 100 (2 fewer to 5 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 36 months (reported by Gazzard 2019 HTA)										
Moderate OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	130*	RR 1.02 (0.95, 1.10)	95 per 100	2 more per 100 (5 fewer to 9 more)	Not serious	Not serious	NA ⁴	Not serious	High
Eyes at target IOP by type of glaucoma at 36 months (reported by Gazzard 2019 HTA)										
Severe OAG (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	101*	RR 0.99 (0.84, 1.16)	86 per 100	1 fewer per 100 (14 fewer to 14 more)	Not serious	Not serious	NA ⁴	Not serious	High
Right and left eyes at target IOP										
Right eye at 6 months (RR greater than 1 favours 360°SLT)										
Katz 2012	RCT	66	RR 0.83 (0.52, 1.33)	57 per 100	9 fewer per 100 (27 fewer to 19 more)	Serious ¹	Serious ³	NA ⁴	Very serious ⁵	Very low
Right and left eyes at target IOP										
Right eye at 12 months (RR greater than 1 favours 360°SLT)										
Katz 2012	RCT	52	RR 0.81 (0.53, 1.22)	71 per 100	14 fewer per 100 (33 fewer to 15 more)	Serious ¹	Serious ³	NA ⁴	Serious ⁶	Very low
Right and left eyes at target IOP										
Left eye at 6 months (RR greater than 1 favours 360°SLT)										
Katz 2012	RCT	61	RR 1.12 (0.65, 1.93)	43 per 100	5 more per 100	Serious ¹	Serious ³	NA ⁴	Very serious ⁵	Very low

					(15 fewer to 40 more)						
Right and left eyes at target IOP											
Left eye at 12 months (RR greater than 1 favours 360°SLT)											
Katz 2012	RCT	48	RR 0.87 (0.54, 1.40)	62 per 100	8 fewer per 100 (29 fewer to 25 more)	Serious ¹	Serious ³	NA ⁴	Very serious ⁵	Very low	
Mean IOP reduction (mean of both eyes) at 6 months (MD greater than 0 favours 360°SLT) – MID +/-1.4											
Katz 2012	RCT	69	MD -0.60 (-1.99, 0.79)	-	-	Serious ¹	Serious ³	NA ⁴	Serious ⁶	Very low	
Mean IOP reduction (mean of both eyes) at 12 months (MD greater than 0 favours 360°SLT) – MID +/-0.9											
Katz 2012	RCT	54	MD -0.70 (-1.91, 0.51)	-	-	Serious ¹	Serious ³	NA ⁴	Serious ⁶	Very low	
Mean IOP reduction (29 eyes per arm from 29 participants) at 5 years (MD greater than 0 favours 360°SLT) – MID +/-3.3											
Lai 2004	RCT	58	MD -0.10 (-3.52, 3.32)	-	-	Very serious ²	Not serious	NA ⁴	Very serious ⁵	Very low	
* Total for subgroup was calculated by reviewer as Gazzard 2019 only reported percentages											
1. Study at moderate risk of bias											
2. Study at high risk of bias											
3. Partially applicable study											
4. Only one study so no inconsistency											
5. 95% confidence intervals cross both ends of the defined MIDs											
6. 95% confidence intervals cross one end of the defined MIDs											

Outcomes: Visual field progression; optic disc progression

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Eyes with visual field progression at 36 months (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	1072	RR 0.67 (0.37, 1.20)	5 per 100	2 fewer per 100 (3 fewer to 1 more)	Not serious	Not serious	NA ¹	Serious ²	Moderate
Eyes with optic disc progression at 36 months (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	1072	RR 0.67	1 per 100	0 fewer per 100	Not serious	Not serious	NA ¹	Very serious ³	Low

		(0.11, 3.97)		(0 more to 2 more)					
<ol style="list-style-type: none"> 1. Only one study so no inconsistency 2. 95% confidence intervals cross one end of the defined MIDs 3. 95% confidence intervals cross both ends of the defined MIDs 									

Outcome: Quality of life

No. of studies	Study design	Sample size	MIDs	Effect size (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
EQ-5D at 6 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	662	+/- 0.075	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
EQ-5D at 12 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	654	+/- 0.07	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
EQ-5D at 18 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	654	+/- 0.08	MD 0.00 (-0.02, 0.02)*	Not serious	Not serious	NA ¹	Not serious	High
EQ-5D at 24 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	652	+/- 0.07	MD 0.00 (-0.02, 0.02)*	Not serious	Not serious	NA ¹	Not serious	High
EQ-5D at 30 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	637	+/- 0.075	MD 0.00 (-0.02, 0.02)*	Not serious	Not serious	NA ¹	Not serious	High
EQ-5D at 36 months (primary analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	673	+/- 0.09	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 6 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	659	+/- 0.055	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 12 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	635	+/- 0.06	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 18 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	608	+/- 0.06	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 24 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	603	+/- 0.06	MD 0.02 (0.00, 0.04)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 30 months (repeated measures analysis) (MD greater than 0 favours 360°SLT)									
Gazzard 2019	RCT	590	+/- 0.06	MD 0.02 (0.00, 0.04)*	Not serious	Not serious	NA ¹	Not serious	High
GUI at 36 months (primary analysis) (MD greater than 0 favours 360°SLT)									

Gazzard 2019	RCT	602	+/- 0.065	MD 0.01 (-0.01, 0.03)*	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 6 months (repeated measures analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	647	+/- 2.8	MD -0.80 (-1.60, 0.00)*	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 12 months (repeated measures analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	632	+/- 3.6	MD -0.50 (-1.34, 0.34)*	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 18 months (repeated measures analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	600	+/- 3.2	MD -0.60 (-1.40, 0.20)*	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 24 months (repeated measures analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	587	+/- 3.65	MD -0.50 (-1.34, 0.34) ⁸	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 30 months (repeated measures analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	580	+/- 3.9	MD -0.30 (-1.10, 0.50)*	Not serious	Not serious	NA ¹	Not serious	High
GQL-15 at 36 months (primary analysis) (MD less than 0 favours 360°SLT)									
Gazzard 2019	RCT	601	+/- 3.56	MD -0.40 (-1.34, 0.54)*	Not serious	Not serious	NA ¹	Not serious	High
* Mean differences were adjusted for baseline score, severity, centre, baseline intraocular pressure, and number of eyes affected at baseline.									
1. Only one study so no inconsistency									

Outcome: Adverse events

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Total adverse events (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.02 (0.93, 1.12)	72 per 100	1 more per 100 (5 fewer to 8 more)	Not serious	Not serious	NA ¹	Not serious	High
Ocular adverse events: Aesthetic side effects of medication (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.13 (0.06, 0.28)	15 per 100	14 fewer per 100 (15 fewer to 11 fewer)	Not serious	Not serious	NA ¹	Not serious	High
Ocular adverse events: Ophthalmic allergic reactions (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.78 (0.38, 1.58)	5 per 100	1 fewer per 100 (3 fewer to 3 more)	Not serious	Not serious	NA ¹	Very serious ²	Low

Ocular adverse events: Reactivation of herpes simplex keratitis (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.02 (0.06, 16.19)	0 per 100	0 more per 100 (0 more to 4 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Ocular adverse events: Uveitis (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 2.03 (0.19, 22.33)	0 per 100	0 more per 100 (0 more to 6 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Ocular adverse events: Other (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.86 (0.75, 0.97)	61 per 100	9 fewer per 100 (15 fewer to 2 fewer)	Not serious	Not serious	NA ¹	Serious ³	Moderate
SLT-related ocular adverse events: Inflammation after SLT (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 3.05 (0.12, 74.63)	0 per 100	0 fewer per 100 (0 more to 0 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
SLT-related ocular adverse events: IOP spike after SLT (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 13.22 (0.75, 233.77)	0 per 100	0 fewer per 100 (0 more to 0 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
SLT-related ocular adverse events: Other transient events (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 124.06 (17.43, 882.95)	0 per 100	34 more per 100 (5 more to 244 more)	Not serious	Not serious	NA ¹	Not serious	High
SLT-related ocular adverse events: Participants with an adverse event during SLT procedure (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 29.49 (1.77, 492.44)	0 per 100	0 more per 100 (0 more to 4 more)	Not serious	Not serious	NA ¹	Not serious	High
Systemic adverse events: Pulmonary problems (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.87 (0.41, 1.86)	4 per 100	0 fewer per 100 (2 fewer to 3 more)	Not serious	Not serious	NA ¹	Very serious ²	Low

Systemic adverse events: Cardiac events (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.02 (0.30, 3.48)	1 per 100	0 more per 100 (1 fewer to 3 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Systemic adverse events: Drug-related events (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.45 (0.28, 0.72)	14 per 100	8 fewer per 100 (10 fewer to 4 fewer)	Not serious	Not serious	NA ¹	Not serious	High
Systemic adverse events: Other (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.97 (0.74, 1.27)	23 per 100	1 fewer per 100 (6 fewer to 6 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Total (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.96 (0.70, 1.30)	19 per 100	1 fewer per 100 (6 fewer to 6 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Ocular (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.36 (0.48, 3.87)	2 per 100	1 more per 100 (1 fewer to 5 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Pulmonary problems (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.68 (0.11, 4.03)	1 per 100	0 fewer per 100 (1 fewer to 3 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Cerebrovascular accidents (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 2.03 (0.19, 22.33)	0 per 100	0 more per 100 (0 more to 6 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Cardiac events (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.16 (0.43, 3.17)	2 per 100	0 more per 100 (1 fewer to 4 more)	Not serious	Not serious	NA ¹	Very serious ²	Low

Serious adverse events: Cancer (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.65 (0.69, 3.94)	2 per 100	1 more per 100 (1 fewer to 6 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
Serious adverse events: Death (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 4.07 (0.87, 19.02)	1 per 100	2 more per 100 (0 more to 10 more)	Not serious	Not serious	NA ¹	Serious ³	Moderate
Serious adverse events: Other systemic (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 0.87 (0.60, 1.28)	14 per 100	2 fewer per 100 (6 fewer to 4 more)	Not serious	Not serious	NA ¹	Very serious ²	Low
<ol style="list-style-type: none"> 1. Only one study so no inconsistency 2. 95% confidence intervals cross both ends of the defined MIDs 3. 95% confidence intervals cross one end of the defined MIDs 										

Outcome: Treatment adherence

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Treatment adherence (self-reported concordance at 36 months) (RR greater than 1 favours 360°SLT)										
Gazzard 2019	RCT	626	RR 1.00 (0.98, 1.02)*	99 per 100	0 more per 100 (2 fewer to 2 more)	Not serious	Not serious	NA ¹	Not serious	High
* Events calculated by reviewer because Gazzard 2019 only reported percentages										
<ol style="list-style-type: none"> 1. Only one study so no inconsistency 										

Outcome: Treatment discontinuation

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Treatment discontinuation (RR less than 1 favours 360°SLT)										
Gazzard 2019	RCT	718	RR 1.81 (0.81, 4.04)	2 per 100	2 more per 100 (0 more to 6 more)	Not serious	Not serious	NA ¹	Serious ²	Moderate

1. Only one study so no inconsistency
2. 95% confidence intervals cross one end of the defined MIDs

Reasons for treatment discontinuation

360°SLT: 1 was no longer contactable, 1 moved to another hospital, 3 withdrew from trial, 8 died, 3 ill health and unfit to continue.

Eye drops: 1 was no longer contactable, 3 moved to another hospital, 1 withdrew from trial, 2 died, 2 ill health and unfit to continue.

Comparison: 360°SLT vs latanoprost**Outcomes: Intraocular pressure; adverse events**

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Eyes at target IOP at 12 months >20% IOP reduction (RR greater than 1 favours 360°SLT)										
Nagar 2005	RCT	57	RR 0.79 (0.62, 1.00)	92 per 100	20 fewer per 100 (35 fewer to 0 more)	Very serious ¹	Serious ²	NA ³	Serious ⁴	Very low
Eyes at target IOP at 12 months >30% IOP reduction (RR greater than 1 favours 360°SLT)										
Nagar 2005	RCT	57	RR 0.62 (0.40, 0.95)	77 per 100	29 fewer per 100 (46 fewer to 4 fewer)	Very serious ¹	Serious ²	NA ³	Serious ⁴	Very low
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 360°SLT)										
Nagar 2005	RCT	57	RR 10.89 (0.70, 169.72)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁵	Very low
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 360°SLT)										
Nagar 2005	RCT	57	RR 14.00 (0.91, 216.28)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Serious ⁴	Very low
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 360°SLT)										
Nagar 2005	RCT	57	RR 7.78 (0.49, 123.17)	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁵	Very low

* Events were calculated by reviewer because Nagar 2005 only reported percentages

1. Study at high risk of bias
2. Partially applicable study
3. Only one study so no inconsistency
4. 95% confidence intervals cross one end of the defined MIDs

5. 95% confidence intervals cross both ends of the defined MIDs

Comparison: 180°SLT vs latanoprost

Outcomes: Intraocular pressure; adverse events

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Eyes at target IOP at 12 months >20% IOP reduction (RR greater than 1 favours 180°SLT)										
Nagar 2005	RCT	62	RR 0.71 (0.55, 0.92)	92 per 100	27 fewer per 100 (42 fewer to 8 fewer)	Very serious ¹	Serious ²	NA ³	Serious ⁴	Very low
Eyes at target IOP at 12 months >30% IOP reduction (RR greater than 1 favours 180°SLT)										
Nagar 2005	RCT	62	RR 0.56 (0.36, 0.86)	77 per 100	34 fewer per 100 (49 fewer to 10 fewer)	Very serious ¹	Serious ²	NA ³	Serious ⁴	Very low
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 180°SLT)										
Nagar 2005	RCT	62	RR 5.88 (0.37, 94.25)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁵	Very low
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 180°SLT)										
Nagar 2005	RCT	62	RR 11.48 (0.74, 178.16)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁵	Very low
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 180°SLT)										
Nagar 2005	RCT	62	RR 4.76 (0.29, 77.49)	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁵	Very low
* Events were calculated by reviewer because Nagar 2005 only reported percentages										
1. Study at high risk of bias										
2. Partially applicable study										
3. Only one study so no inconsistency										
4. 95% confidence intervals cross one end of the defined MIDs										

5. 95% confidence intervals cross both ends of the defined MIDs

Comparison: 90°SLT vs latanoprost**Outcomes: Intraocular pressure; adverse events**

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Eyes at target IOP at 12 months >20% IOP reduction (RR greater than 1 favours 90°SLT)										
Nagar 2005	RCT	48	RR 0.37 (0.23, 0.60)	92 per 100	58 fewer per 100 (71 fewer to 37 fewer)	Very serious ¹	Serious ²	NA ³	Not serious	Very low
Eyes at target IOP at 12 months >30% IOP reduction (RR greater than 1 favours 90°SLT)										
Nagar 2005	RCT	48	RR 0.15 (0.06, 0.39)	77 per 100	65 fewer per 100 (73 fewer to 47 fewer)	Very serious ¹	Serious ²	NA ³	Not serious	Very low
Adverse events during first week after treatment: Discomfort/pain (RR less than 1 favours 90°SLT)										
Nagar 2005	RCT	48	RR 1.94 (0.10, 38.01)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁴	Very low
Adverse events during first week after treatment: Uveitis (RR less than 1 favours 90°SLT)										
Nagar 2005	RCT	48	RR 8.94 (0.56, 141.79)*	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁴	Very low
Adverse events during first week after treatment: IOP spike (RR less than 1 favours 90°SLT)										
Nagar 2005	RCT	48	RR 2.72 (0.15, 49.38)	0 per 100	0 fewer per 100 (0 more to 0 more)	Very serious ¹	Serious ²	NA ³	Very serious ⁴	Very low
* Events were calculated by reviewer because Nagar 2005 only reported percentages										
1. Study at high risk of bias										
2. Partially applicable study										
3. Only one study so no inconsistency										
4. 95% confidence intervals cross both ends of the defined MIDs										

Comparison: SLT (degrees not specified) vs latanoprost**Outcome: Intraocular pressure**

No. of studies	Study design	Sample size	Effect size (95% CI)	Absolute risk: control	Absolute risk: intervention (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
Mean IOP reduction at day 3 (MD greater than 0 favours SLT) – MID +/-1.57										
Nagar 2009	RCT	40	MD 0.00 (-1.94, 1.94)	-	-	Serious ¹	Not serious	NA ²	Very serious ³	Very low
Mean IOP reduction at week 1 (MD greater than 0 favours SLT) – MID +/-1.79										
Nagar 2009	RCT	40	MD -1.70 (-3.78, 0.38)	-	-	Serious ¹	Not serious	NA ²	Serious ⁴	Low
Mean IOP reduction at month 1 (MD greater than 0 favours SLT) – MID +/-1.57										
Nagar 2009	RCT	40	MD -3.80 (-5.88, -1.72)	-	-	Serious ¹	Not serious	NA ²	Not serious	Moderate
Mean IOP reduction at month 6 (MD greater than 0 favours SLT) – MID +/-1.79										
Nagar 2009	RCT	40	MD -1.60 (-3.82, 0.62)	-	-	Serious ¹	Not serious	NA ²	Serious ⁴	Low
Eyes at target IOP at day 3										
Nagar 2009	RCT	40	RR 1.14 (0.75, 1.73)*	35 per 100	5 more per 100 (13 fewer to 26 more)	Serious ¹	Not serious	NA ²	Very serious ³	Very low
Eyes at target IOP at week 1										
Nagar 2009	RCT	40	RR 0.65 (0.40, 1.04)*	55 per 100	20 fewer per 100 (39 fewer to 2 more)	Serious ¹	Not serious	NA ²	Serious ⁴	Low
Eyes at target IOP at month 1										
Nagar 2009	RCT	40	RR 0.35 (0.16, 0.80)*	65 per 100	42 fewer per 100 (61 fewer to 13 fewer)	Serious ¹	Not serious	NA ²	Serious ⁴	Low
Eyes at target IOP at month 6										

Nagar 2009	RCT	40	RR 0.86 (0.65, 1.14)*	75 per 100	10 fewer per 100 (43 fewer to 10 more)	Serious ¹	Not serious	NA ²	Serious ⁴	Low
<p>* Nagar 2009 reported odds ratios (ORs) comparing latanoprost versus SLT rather than comparing SLT versus latanoprost. Therefore, reviewer back calculated the ORs and 95% CIs diving 1/OR and 1/each of the ends of the 95% CI to show the same direction of effect as the rest of included studies. These were converted to risk ratios to aid interpretation as suggested by the methods of this review in Appendix L.</p> <ol style="list-style-type: none"> 1. Study at moderate risk of bias 2. Only one study so no inconsistency 3. 95% confidence intervals cross both ends of the defined MIDs 4. 95% confidence intervals cross one end of the defined MIDs 										

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Table 14: Economic evidence table

Study	Study type	Study quality	Setting	Interventions	Population	Methods of analysis	Base-case results ¹	Sensitivity analyses	Limitations	Additional comments
Gazzard et al. 2019	Cost-utility analysis alongside an RCT	Directly applicable Minor limitations	UK Hospital setting National health care perspective	Eye drops: topical medication to lower intraocular pressure SLT: primary selective laser trabeculoplasty followed by topical medication	Eye drops: n=362, mean age: 62.7, 45.6% female, 77.9% open angle glaucoma, 22.1% ocular hypertension, Asian 7.7%, Black 19.1%, White 71.3%, Other 1.9% SLT: n=356, mean age: 63.4, 43.8% female, 76.7% open angle glaucoma, 23.3% ocular hypertension, Asian 6.5%, Black 21.6%, White 68.3%, Other 3.7%	QALYs derived from EQ-5D-5L done at baseline, 6, 12, 18, 24, 30 and 36 months of LIGHT trial. Costs sourced from NHS reference costs 2018, Personal Social Services Research Unit (PSSRU). Costs included were cost of SLT, medicine, surgery, adverse events, clinical appointments Time horizon: 3 years Discount rate: 3.5%	Eye drops: QALYs: 2.62 Costs: £3,993 SLT: QALYs: 2.65 Costs: £3,890 ICER: SLT dominates Results include imputed data for missing values	Probabilistic sensitivity analysis: There is a 97% probability that SLT is cost effective at a £20,000 willingness-to-pay threshold and a 93% probability that SLT is cost effective at a £30,000 willingness-to-pay threshold.	The EQ-5D-5L is not good at discriminating between differing severity of glaucoma.	Funded by National Institute of Health Research Authors' conclusions: Primary selective laser trabeculoplasty is a cost-effective alternative to drops that can be offered to patients with OAG or ocular hypertension needing treatment to lower intraocular pressure.
Gazzard et al. 2019 (HTA)	Cost-utility analysis: Markov model based on data from an RCT	Directly applicable Minor limitations	UK Hospital setting National health care perspective	Eye drops: topical medication to lower intraocular pressure SLT: primary selective laser trabeculoplasty followed by topical medication	“Assumed to be the same as Gazzard et al. 2019” Eye drops: n=362, mean age: 62.7, 45.6% female, 77.9% open angle glaucoma, 22.1% ocular hypertension, Asian 7.7%, Black 19.1%, White 71.3%, Other 1.9% SLT: n=356, mean age: 63.4, 43.8% female, 76.7% open	Health states: Ocular hypertension (OHT), Glaucoma ‘mild’, Glaucoma ‘moderate’, Glaucoma ‘severe’, dead. Eye drops treatment pathway, four different types of eyedrops are tried and surgery can be done at any point. After surgery the patient may go to eye drop free before starting the escalation of eyedrops again.	Eye drops: QALYs: 12.3 Costs: £20,435 SLT: QALYs: 12.5 Costs: £17,541 ICER: SLT dominates Results include imputed data	Probabilistic sensitivity analysis: There is a 90% probability that SLT is cost effective at a £20,000 willingness-to-pay threshold	The EQ-5D-5L is not good at discriminating between differing severity of glaucoma.	Funded by National Institute of Health Research Authors' conclusions: Primary selective laser trabeculoplasty is a cost-effective alternative to drops that can be offered to patients with OAG or ocular hypertension needing treatment to lower intraocular pressure.

Study	Study type	Study quality	Setting	Interventions	Population	Methods of analysis	Base-case results ¹	Sensitivity analyses	Limitations	Additional comments
					angle glaucoma, 23.3% ocular hypertension, Asian 6.5%, Black 21.6%, White 68.3%, Other 3.7%	<p>SLT treatment pathway is the same as eyedrops except the patients receive one or two SLT first and can then move into the eye drop free state.</p> <p>Transition probabilities were obtained from the trial for the first 3 years. Further transition probabilities were extrapolated from the 3-year data.</p> <p>QALYs for each health state were calculated based on glaucoma severity at 35 months and the mean glaucoma utility index.</p> <p>Costs sourced from NHS reference costs 2018, Personal Social Services Research Unit (PSSRU). Costs included were cost of SLT (which included the cost of the machine), medicine, surgery, adverse events, clinical appointments</p> <p>Time horizon: lifetime</p> <p>Discount rate: 3.5%</p>				

¹ Costs in GBP in 2019, costs updated to GBP in 2021 in summary in main text

Table 15: Economic evaluation checklist

Study identification		
Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. Lancet (London, England) 393(10180): 1505-1516		
Category	Rating	Comments
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	
1.2 Are the interventions appropriate for the review question?	Yes	
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	
1.4 Is the perspective for costs appropriate for the review question?	Yes	
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Partly	EQ-5D-5L was used rather than EQ-5D-3L
1.8 OVERALL JUDGEMENT	DIRECTLY APPLICABLE	
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	3 years
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	

Study identification		
Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. Lancet (London, England) 393(10180): 1505-1516		
Category	Rating	Comments
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	No	Financial conflicts of interests have been declared; some authors have received grants from SLT producers but no significant concerns as the model appears robust
2.12 OVERALL ASSESSMENT	MINOR LIMITATIONS	

Table 16: Economic evaluation checklist

Study identification		
Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al. Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. Health Technol Assess 2019;23(31).		
Category	Rating	Comments
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	
1.2 Are the interventions appropriate for the review question?	Yes	

Study identification		
Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.		
Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. Health Technol Assess 2019;23(31).		
Category	Rating	Comments
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	
1.4 Is the perspective for costs appropriate for the review question?	Yes	
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Partly	EQ-5D-5L was used rather than EQ-5D-3L
1.8 OVERALL JUDGEMENT	DIRECTLY APPLICABLE	
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Lifetime
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	

Study identification		
Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al. Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. Health Technol Assess 2019;23(31).		
Category	Rating	Comments
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	No	Financial conflicts of interests have been declared; some authors have received grants from SLT producers but no significant concerns as the model appears robust
2.12 OVERALL ASSESSMENT	MINOR LIMITATIONS	

Appendix I – Health economic model

No original health economic modelling was undertaken for this review question.

Appendix J – Excluded studies

Effectiveness evidence

Study	Reason for exclusion
Ang, Ghee Soon, Fenwick, Eva K, Constantinou, Marios et al. (2020) Selective laser trabeculoplasty versus topical medication as initial glaucoma treatment: the glaucoma initial treatment study randomised clinical trial. The British journal of ophthalmology 104(6): 813-821	- Participants with primary open angle glaucoma and exfoliation glaucoma (no separate analysis by subtype of glaucoma)
Anonymous. (2019) Erratum: Department of Error (The Lancet (2019) 393(10180) (1505-1516), (S014067361832213X), (10.1016/S0140-6736(18)32213-X)). The Lancet 394(10192): e1	- Secondary publication of an included study that does not provide any additional relevant information [Erratum of the LiGHT trial (Gazzard 2019)]
Chi, Sheng Chu, Kang, Yi-No, Hwang, De-Kuang et al. (2020) Selective laser trabeculoplasty versus medication for open-angle glaucoma: systematic review and meta-analysis of randomised clinical trials. The British journal of ophthalmology 104(11): 1500-1507	- Systematic review used as source of primary studies
Garg, Anurag, Vickerstaff, Victoria, Nathwani, Neil et al. (2019) Primary Selective Laser Trabeculoplasty for Open-Angle Glaucoma and Ocular Hypertension: Clinical Outcomes, Predictors of Success, and Safety from the Laser in Glaucoma and Ocular Hypertension Trial. Ophthalmology 126(9): 1238-1248	- Secondary publication of an included study that does not provide any additional relevant information
Garg, Anurag, Vickerstaff, Victoria, Nathwani, Neil et al. (2020) Efficacy of Repeat Selective Laser Trabeculoplasty in Medication-Naive Open-Angle Glaucoma and Ocular Hypertension during the LiGHT Trial. Ophthalmology 127(4): 467-476	- Secondary publication of an included study that does not provide any additional relevant information
Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2018) Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre, randomised controlled trial: design and methodology. The British journal of ophthalmology 102(5): 593-598	- Secondary publication of an included study that does not provide any additional relevant information
Kiddee, Weerawat and Atthavuttisilp, Supreeya (2017) The effects of selective laser trabeculoplasty and travoprost on circadian intraocular pressure fluctuations: A randomized clinical trial. Medicine 96(6): e6047	- Participants received previous treatment for glaucoma
Konstantakopoulou, Evgenia, Gazzard, Gus, Vickerstaff, Victoria et al. (2018) The Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre randomised controlled trial: baseline patient characteristics. The British journal of ophthalmology 102(5): 599-603	- Secondary publication of an included study that does not provide any additional relevant information
Lamoureux, Ecosse L, Mcintosh, Rachel, Constantinou, Marios et al. (2015) Comparing the effectiveness of selective laser trabeculoplasty with topical medication as initial	- Participants with primary open angle glaucoma and exfoliation glaucoma (no separate analysis by subtype of glaucoma)

Study	Reason for exclusion
treatment (the Glaucoma Initial Treatment Study): study protocol for a randomised controlled trial. <i>Trials</i> 16: 406	
Li, Xingyi; Wang, Wei; Zhang, Xiulan (2015) Meta-analysis of selective laser trabeculoplasty versus topical medication in the treatment of open-angle glaucoma. <i>BMC ophthalmology</i> 15: 107	- Systematic review used as source of primary studies
McAlinden, C (2014) Selective laser trabeculoplasty (SLT) vs other treatment modalities for glaucoma: systematic review. <i>Eye (London, England)</i> 28(3): 249-58	- Systematic review used as source of primary studies
Peng W, Zhong X, Yu M (2014) [Meta-analysis of randomized controlled trials comparing selective laser trabeculoplasty with prostaglandin analogue in the primary treatment of open-angle glaucoma or ocular hypertention]. <i>Chinese Journal of Ophthalmology</i> 50(5): 343-348	- Study not reported in English
Perez, Efrain; Rada, Gabriel; Maul, Eugenio (2015) Selective laser trabeculoplasty compared with medical treatment for the initial management of open angle glaucoma or ocular hypertension. <i>Medwave</i> 15suppl3: e6337	- Systematic review used as source of primary studies
Sha, Sha, Zhou, Rouxi, Wang, Wei et al. (2020) Laser Trabeculoplasty for Open-Angle Glaucoma: A Systematic Review and Network Meta-Analysis. <i>American Journal of Ophthalmology</i>	- Systematic review used as source of primary studies
Vickerstaff, Victoria, Ambler, Gareth, Bunce, Catey et al. (2015) Statistical analysis plan for the Laser-1st versus Drops-1st for Glaucoma and Ocular Hypertension Trial (LiGHT): a multi-centre randomised controlled trial. <i>Trials</i> 16: 517	- Secondary publication of an included study that does not provide any additional relevant information
Wong, Mandy Oi Man, Lee, Jacky Wai Yip, Choy, Bonnie Nga Kwan et al. (2015) Systematic review and meta-analysis on the efficacy of selective laser trabeculoplasty in open-angle glaucoma. <i>Survey of ophthalmology</i> 60(1): 36-50	- Systematic review used as source of primary studies
Wright, David M., Nathwani, Neil, Garg, Anurag et al. (2020) Visual Field Outcomes from the Multicenter, Randomized Controlled Laser in Glaucoma and Ocular Hypertension Trial (LiGHT). <i>Ophthalmology</i> 127(10): 1313-1321	- Secondary publication of an included study that does not provide any additional relevant information
Yang, Yangfan, Huang, Shitong, Zhang, Xinyi et al. (2021) Laser in Glaucoma and Ocular Hypertension Trial (LiGHT) in China - A Randomized Controlled Trial: Design and Baseline Characteristics. <i>American Journal of Ophthalmology</i> 230: 143-150	- Only baseline characteristics reported

Economic evidence

Study	Code [Reason]
Berdahl, John P, Khatana, Anup K, Katz, L Jay et al. (2017) Cost-comparison of two trabecular micro-bypass stents versus selective laser trabeculoplasty or medications only for intraocular pressure control for patients with open-angle glaucoma. <i>Journal of medical economics</i> 20(7): 760-766	<ul style="list-style-type: none"> - Study does not contain a relevant intervention <i>Comparing iStent procedure to medications or SLT</i> - Cost analysis only <i>No quality of life information</i>
Cantor, Louis B, Katz, L Jay, Cheng, J Wang et al. (2008) Economic evaluation of medication, laser trabeculoplasty and filtering surgeries in treating patients with glaucoma in the US. <i>Current medical research and opinion</i> 24(10): 2905-18	<ul style="list-style-type: none"> - Cost analysis only <i>No quality of life data</i>
De Natale, Renato; Lafuma, Antoine; Berdeaux, Gilles (2009) Cost effectiveness of travoprost versus a fixed combination of latanoprost/timolol in patients with ocular hypertension or glaucoma: analysis based on the UK general practitioner research database. <i>Clinical drug investigation</i> 29(2): 111-20	<ul style="list-style-type: none"> - Cost analysis only <i>No quality of life data</i>
Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2018) Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre, randomised controlled trial: design and methodology. <i>The British journal of ophthalmology</i> 102(5): 593-598	<ul style="list-style-type: none"> - Non economic evaluation <i>No results</i>
Gazzard, Gus, Konstantakopoulou, Evgenia, Garway-Heath, David et al. (2019) Selective laser trabeculoplasty versus drops for newly diagnosed ocular hypertension and glaucoma: the LiGHT RCT. <i>Health technology assessment (Winchester, England)</i> 23(31): 1-102	<ul style="list-style-type: none"> - Secondary publication of an included study that does not provide any additional relevant information <i>Light study, already included</i>
Guedes, Ricardo Augusto Paletta, Guedes, Vanessa Maria Paletta, Gomes, Carlos Eduardo de Mello et al. (2016) Maximizing cost-effectiveness by adjusting treatment strategy according to glaucoma severity. <i>Medicine</i> 95(52): e5745	<ul style="list-style-type: none"> - Perspective not transferable <i>Brazilian health care system</i>
Kaplan, Richard I, De Moraes, C Gustavo, Cioffi, George A et al. (2015) Comparative Cost-effectiveness of the Baerveldt Implant, Trabeculectomy With Mitomycin, and Medical Treatment. <i>JAMA ophthalmology</i> 133(5): 560-7	<ul style="list-style-type: none"> - Study does not contain a relevant intervention <i>Does not include SLT, only Trabeculectomy</i>
Konstantakopoulou, Evgenia, Gazzard, Gus, Vickerstaff, Victoria et al. (2018) The Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre randomised controlled trial:	<ul style="list-style-type: none"> - Non-economic evaluation <i>No ICER reported, Light trial included</i>

Study	Code [Reason]
baseline patient characteristics. The British journal of ophthalmology 102(5): 599-603	
Ontario Health, (Quality) (2019) Minimally Invasive Glaucoma Surgery: A Budget Impact Analysis and Evaluation of Patients' Experiences, Preferences, and Values. Ontario health technology assessment series 19(9): 1-57	- Not a peer-reviewed publication
Orme, Michelle; Collins, Sarah; Loftus, Jane (2012) Long-term medical management of primary open-angle glaucoma and ocular hypertension in the UK: optimizing cost-effectiveness and clinic resources by minimizing therapy switches. Journal of glaucoma 21(7): 433-49	- Study does not contain a relevant intervention <i>Does not include SLT</i>
Real, J P, Lafuente, M C, Palma, S D et al. (2020) Direct costs of glaucoma: Relationship between cost and severity of the disease. Chronic illness 16(4): 266-274	- Cost analysis only <i>No quality of life data</i>
Sawchyn, Andrea K and Slabaugh, Mark A (2016) Innovations and adaptations in trabeculectomy. Current opinion in ophthalmology 27(2): 158-63	- Non economic evaluation <i>Does not include an ICER</i>
Seider, Michael I; Keenan, Jeremy D; Han, Ying (2012) Cost of selective laser trabeculoplasty vs topical medications for glaucoma. Archives of ophthalmology (Chicago, Ill. : 1960) 130(4): 529-30	- Non economic evaluation <i>Does not include an ICER</i>
Stein, Joshua D, Kim, David D, Peck, Will W et al. (2012) Cost-effectiveness of medications compared with laser trabeculoplasty in patients with newly diagnosed open-angle glaucoma. Archives of ophthalmology (Chicago, Ill. : 1960) 130(4): 497-505	- Study does not contain a relevant intervention <i>Compares Argon laser trabeculoplasty not SLT</i>
Stewart, William C, Stewart, Jeanette A, Nasser, Qasim J et al. (2008) Cost-effectiveness of treating ocular hypertension. Ophthalmology 115(1): 94-8	- Study does not contain a relevant intervention <i>Uses Argon laser trabeculoplasty not SLT</i>
Van Gestel, Aukje, Schouten, Jan S. A. G., Beckers, Henny J. M. et al. (2014) The long term effectiveness and cost-effectiveness of initiating treatment for ocular hypertension. Acta Ophthalmologica 92(6): 513-523	- Comparator in study does not match that specified in protocol <i>Watchful waiting is the comparator</i>
Vickerstaff, Victoria, Ambler, Gareth, Bunce, Catey et al. (2015) Statistical analysis plan for the Laser-1st versus Drops-1st for Glaucoma and Ocular Hypertension Trial (LiGHT): a multi-centre randomised controlled trial. Trials 16: 517	- Secondary publication of an included study that does not provide any additional relevant information <i>Plan of the Light trial, no results</i>

Study	Code [Reason]
Yong, M H and Che Hamzah, J (2020) Selective laser trabeculoplasty vs. topical medications for step-up treatment in primary open angle glaucoma: comparing clinical effectiveness, quality of life and cost-effectiveness. The Medical journal of Malaysia 75(4): 342-348	- Cost analysis only <i>Not an incremental cost effectiveness study, not possible to calculate an ICER</i>

Appendix K – Research recommendations – full details

K.1.1 Research recommendation

What is the long-term effectiveness and cost-effectiveness of selective laser trabeculoplasty (SLT) as a first line treatment compared to intraocular pressure-lowering eyedrops in ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) adult patients?

K.1.2 Why this is important

New evidence showed that SLT is cost-effective in the treatment of adults with OHT or COAG but there was not sufficient long-term data on progression of glaucomatous visual field defect and progression of optic nerve head damage (only 1 RCT reported both outcomes at 36 months follow-up). The committee discussed the importance of investigating these outcomes at longer follow-up times (5 and 10 years). This evidence could help to target interventions which could prevent progression.

K.1.3 Rationale for research recommendation

Importance to 'patients' or the population	Little is known about the long-term effects associated with the use of SLT or eye drops for OHT or COAG. There is significant concern about the risk of progression from glaucoma in people delivering and receiving care.
Relevance to NICE guidance	SLT and eye drops have been considered in this guideline and there is a lack of data on long-term risk of progression from glaucoma.
Relevance to the NHS	The outcome would affect the types of treatment for OHT or COAG provided by the NHS and may also predict future healthcare needs for adults who receive this treatment.
National priorities	High
Current evidence base	Minimal long-term data
Equality considerations	None known

K.1.4 Modified PICO table

Population	<p>Inclusion:</p> <ul style="list-style-type: none"> Adults (18 and over) with OHT Adults (18 and over) with COAG <p>Exclusion:</p> <ul style="list-style-type: none"> People who have received first line treatment for OHT or COAG, People with secondary glaucoma, for example, neovascular or uveitic glaucoma People with, or at risk of, primary or secondary angle closure glaucoma
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	<ul style="list-style-type: none"> • People with primary congenital, infantile or childhood glaucoma • People with angle closure
Intervention	Selective laser trabeculoplasty
Comparator	Intraocular pressure-lowering eye drops alone
Outcome	<ul style="list-style-type: none"> • Progression of glaucomatous visual field defect • Vision loss • Progression of optic nerve head damage • Conversion of OHT to COAG
Study design	Randomised controlled trial
Timeframe	5 and 10 years follow-up
Additional information	<p>Subgroups:</p> <ul style="list-style-type: none"> • Degree of pigmentation • Initial IOP • Ethnicity • Different ranges of trabecular meshwork treated (90, 180 or 360 degrees)

Appendix L – Methods

Methods of combining evidence

Data synthesis for intervention studies

Where possible, meta-analyses were conducted to combine the results of quantitative studies for each outcome. When there were 2 treatment alternatives, pairwise meta-analysis was used to compare interventions.

Pairwise meta-analysis

Pairwise meta-analyses were performed in Cochrane Review Manager V5.3. A pooled relative risk was calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event, and a pooled incidence rate ratio was calculated for dichotomous outcomes reporting total numbers of events. Both relative and absolute risks were presented, with absolute risks calculated by applying the relative risk to the risk in the comparator arm of the meta-analysis (calculated as the total number events in the comparator arms of studies in the meta-analysis divided by the total number of participants in the comparator arms of studies in the meta-analysis).

A pooled mean difference was calculated for continuous outcomes (using the inverse variance method) when the same scale was used to measure an outcome across different studies.

For continuous outcomes analysed as mean differences, change from baseline values were used in the meta-analysis if they were accompanied by a measure of spread (for example standard deviation). Where change from baseline (accompanied by a measure of spread) were not reported, the corresponding values at the timepoint of interest were used. If only a subset of trials reported change from baseline data, final timepoint values were combined with change from baseline values to produce summary estimates of effect. If some studies only reported data as a change from baseline, analysis was done on these data, and for studies where only baseline and final time point values were available, change from baseline standard deviations were estimated, assuming a correlation coefficient derived from studies reporting both baseline and endpoint data, or if no such studies were available, assuming a correlation of 0.5 as a conservative estimate (Follman et al., 1992; Fu et al., 2013).

Random effects models were fitted when there was significant between-study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. This decision was made and recorded before any data analysis was undertaken.

For all other syntheses, fixed- and random-effects models were fitted, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met, even after appropriate pre-specified subgroup analyses were conducted, random-effects results are presented. Fixed-effects models were deemed to be inappropriate if there was significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

However, in cases where the results from individual pre-specified subgroup analyses were less heterogeneous (with $I^2 < 50\%$) the results from these subgroups were reported using fixed effects models. This may have led to situations where pooled results were reported from random-effects models and subgroup results were reported from fixed-effects models.

Where sufficient studies were available, meta-regression was considered to explore the effect of study level covariates.

Appraising the quality of evidence

Intervention studies (relative effect estimates)

RCTs were quality assessed using the Cochrane Risk of Bias Tool. Evidence on each outcome for each individual study was classified into one of the following groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.

Each individual study was also classified into one of three groups for directness, based on if there were concerns about the population, intervention, comparator and/or outcomes in the study and how directly these variables could address the specified review question. Studies were rated as follows:

- Direct – No important deviations from the protocol in population, intervention, comparator and/or outcomes.
- Partially indirect – Important deviations from the protocol in one of the following areas: population, intervention, comparator and/or outcomes.
- Indirect – Important deviations from the protocol in at least two of the following areas: population, intervention, comparator and/or outcomes.

Minimally important differences (MIDs) and clinical decision thresholds

The Core Outcome Measures in Effectiveness Trials (COMET) database was searched to identify published minimal clinically important difference thresholds relevant to this guideline that might aid the committee in identifying clinical decision thresholds for the purpose of GRADE. Identified MIDs were assessed to ensure they had been developed and validated in a methodologically rigorous way, and were applicable to the populations, interventions and outcomes specified in this guideline. In addition, the Guideline Committee were asked to prospectively specify any outcomes where they felt a consensus clinical decision threshold could be defined from their experience. In particular, any questions looking to evaluate non-inferiority (that one treatment is not meaningfully worse than another) required a clinical decision threshold to be defined to act as a non-inferiority margin.

Clinical decision thresholds were used to assess imprecision using GRADE and aid interpretation of the size of effects for different outcomes. For continuous outcomes expressed as a mean difference where no other clinical decision threshold was available, a clinical decision threshold of 0.5 of the median standard deviations of the comparison group arms was used (Norman et al. 2003). For relative risks, where no other clinical decision threshold was available, a default clinical decision threshold for dichotomous outcomes of 0.8 to 1.25 was used. Odds ratios were converted to risk ratios before presentation to the committee to aid interpretation.

GRADE for intervention studies analysed using pairwise analysis

GRADE was used to assess the quality of evidence for the outcomes specified in the review protocol. Data from randomised controlled trials were initially rated as high quality. The

quality of the evidence for each outcome was downgraded or not from this initial point, based on the criteria given in [Table 17](#).

Table 17: Rationale for downgrading quality of evidence for intervention studies

GRADE criteria	Reasons for downgrading quality
Risk of bias	<p>Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded.</p> <p>Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level.</p> <p>Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels.</p> <p>Extremely serious: If greater than 33.3% of the weight in a meta-analysis came from studies at critical risk of bias, the outcome was downgraded three levels</p>
Indirectness	<p>Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded.</p> <p>Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level.</p> <p>Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels.</p>
Inconsistency	<p>Concerns about inconsistency of effects across studies, occurring when there is unexplained variability in the treatment effect demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic.</p> <p>N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study.</p> <p>Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded.</p> <p>Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level.</p> <p>Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels.</p>
Imprecision	<p>If an MID other than the line of no effect was defined for the outcome, the outcome was downgraded once if the 95% confidence interval for the effect size crossed one line of the MID, and twice if it crosses both lines of the MID.</p> <p>If the line of no effect was defined as an MID for the outcome, it was downgraded once if the 95% confidence interval for the effect size crossed the line of no effect (i.e. the outcome was not statistically significant), and twice if the sample size of the study was sufficiently small that it is not plausible any realistic effect size could have been detected.</p> <p>Outcomes meeting the criteria for downgrading above were not downgraded if the confidence interval was sufficiently narrow that the upper and lower bounds would correspond to clinically equivalent scenarios.</p>
Publication bias	<p>Where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias. When a funnel plot showed convincing evidence of publication bias, or the review team became aware of other evidence of publication bias (for example, evidence of unpublished trials where there was evidence that the effect estimate differed in published and unpublished data), the outcome was downgraded once. If no evidence of publication bias was found for any outcomes in a review (as was often the case), this domain was excluded from GRADE profiles to improve readability.</p>

Appendix M– Additional evidence

The LiGHT trial (Gazzard 2017 HTA publication) reported data on the number of SLT treatments and the number of eye drops medications during the trial which was considered to be helpful to have as additional evidence in this review.

Table 188: Number of SLT treatments and number of eye drops reported by the LiGHT trial

Number of treatments	SLT given as first line treatment for glaucoma n (%)	Eye-drops given as first line treatment for glaucoma n (%)
Number of SLT treatments per eye at 12 months ^a	701	4
• One SLT treatment	521 (85.3)	4
• Two SLT treatments	90 (14.7)	0
• Three SLT treatments ^b	0	0
Number of medications per eye at target IOP at 12 months ^b		
• No medication	522 (85.9)	6 (0.1)
• One medication	49 (8.1)	498 (88.2)
• Two medications	4 (0.7)	67 (11.1)
• Three medications	1 (0.1)	11 (1.8)
• Four medications	0	1 (0.2)
Number of SLT treatments per eye at 24 months ^a	733	4
• One SLT treatment	489 (80)	4
• Two SLT treatments	122 (20)	0
• Three SLT treatments ^b	0	0
Number of medications per eye at target IOP at 24 months ^b		
• No medication	470 (81.6)	14 (2.5)
• One medication	73 (12.7)	403 (71.5)
• Two medications	8 (1.4)	94 (16.7)
• Three medications	2 (0.3)	18 (3.2)
• Four medications	0	2 (0.4)
Number of SLT treatments per eye at 36 months ^a	770	6
• One SLT treatment	453 (74.0)	6
• Two SLT treatments	157 (26.0)	0
• Three SLT treatments ^b	1 (0.2)	0
Number of medications per eye at target IOP at 36 months ^b		
• No medication	419 (78.2)	16 (0.3)
• One medication	64 (12.0)	346 (64.6)

Number of treatments	SLT given as first line treatment for glaucoma n (%)	Eye-drops given as first line treatment for glaucoma n (%)
• Two medications	21 (3.9)	99 (18.5)
• Three medications	4 (0.8)	35 (6.5)
• Four medications	1 (0.2)	3 (0.6)

(a) Includes eyes that were not at target IOP.

(b) Includes eyes that had undergone trabeculectomy.