National Institute for Health and Care Excellence

Final

# 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 1.4.4 to 1.4.6, 1.4.9, 1.4.11, 1.4.15 to 1.4.17, 1.4.19 to 1.4.24, 1.6.6 to 1.6.7 and the research recommendation on long-term effectiveness of selective laser trabeculoplasty in the NICE guideline*

*January 2022*

*Final*

*This evidence review was developed by the Guideline Updates Team*

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# Contents

# 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 with 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 with 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 with intraocular pressure-lowering eyedrops in OHT or COAG adult patients**

| | |
|---|---|
| **Population** | **Inclusion**<br>• Adults (18 and over) with OHT<br>• Adults (18 and over) with COAG |

| | |
|---|---|
| | **Exclusion**<br>• People who have received first line treatment for OHT or COAG,<br>• People with secondary glaucoma, for example, neovascular or uveitic glaucoma<br>• People with, or at risk of, primary or secondary angle closure glaucoma<br>• People with primary congenital, infantile or childhood glaucoma<br>• People with angle closure |
| **Intervention** | • Selective laser trabeculoplasty |
| **Comparator** | • Intraocular pressure-lowering eyedrops alone |
| **Outcome (s)** | **Critical outcomes**<br>• IOP (intraocular pressure) level/outcomes<br>• Glaucomatous visual field loss [(a)]<br>• Normal visual field to visual field defect [(a)]<br>• Progression of glaucomatous visual field defect [(a)]<br>• Vision loss<br>• Health-related quality of life<br>• Adverse events<br>**Important outcomes**<br>• Optic nerve head damage<br>• Progression of optic nerve head damage<br>• Normal or suspicious-to- abnormal optic nerve head<br>• Treatment adherence<br>• Treatment discontinuation |

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

### 1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods section in Appendix L.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

### 1.1.4 Effectiveness evidence

#### 1.1.4.1 Included studies

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

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

See section 1.1.13 References – included studies for a list of included references.

#### 1.1.4.2 Excluded studies

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

### 1.1.5 Summary of studies included in the effectiveness evidence

**Table 2: Summary of studies for SLT compared with intraocular pressure-lowering eyedrops in OHT or COAG adult patients**

| Study | Intervention | Comparator | Follow-up | Outcomes |
|---|---|---|---|---|
| Gazzard, 2019<br>Study location: UK | • 360° SLT (n=356 participants; n=613 eyes)<br><br>Next treatment escalation was medical therapy.<br>One re-treatment with 360° SLT was allowed. | • Eye drops (n=362 participants; n=622 eyes)<br><br>Treatment escalation included:<br>• First line: prostaglandin analogues<br>• Second line: β blockers<br>• Third or fourth line: topical carbonic anhydrase inhibitors or α agonists | • 36 months | • Intraocular pressure<br>○ IOP target for OHT<br>- <25 mmHg and >20% reduction<br>○ IOP target for primary open-angle glaucoma (POAG)<br>- Mild disease: <21 mmHg and >20% reduction<br>- Moderate disease: <18 mmHg and >30% reduction<br>- Severe disease: <15 mmHg and >30% reduction<br>• Health-related quality of life<br>• Adverse events<br>• Treatment adherence<br>• Visual field progression<br>• Optic disc progression |
| Katz, 2012<br>Study location: US | • 360° SLT (n=38 participants)<br><br>Sequence of steps:<br>• Step 1: 360° SLT<br>• Step 2: If target IOP not maintained in 1 or both eyes within 4 to 6 weeks, SLT over nasal 180° with 50 applications<br>• 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 | • Eye drops (n=31 participants)<br><br>Sequence of steps:<br>• Step 1: Start with ocular prostaglandin analogue<br>• Step 2: If target IOP not met but initial medication deemed effective, add β blocker<br>• Step 3: Brimonidine<br>• Step 4: Dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol | • 12 months | • Intraocular pressure<br>○ Mean differences of IOP from baseline to follow-up<br>○ 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-(reference IOP + visual field score/100)] x reference IOP. Therefore, if the reference IOP=28mm Hg and the reference visual field score=5, then target IOP= [1-(28+5)/100] x 28= (1-0.33) x 28=0.67 x 28=19mm Hg. |

| Study | Intervention | Comparator | Follow-up | Outcomes |
|---|---|---|---|---|
| | • Step 4: Treating clinician choice of next therapy for intervention failure | | | |
| Lai, 2004<br>Study location: China | • 360° SLT (n=29 eyes) | • Eye drops (n=29 eyes)<br><br>Eye drops included: β blocker, pilocarpine, dorzolamide and latanoprost | • 5 years | • Intraocular pressure<br>○ Mean IOP reduction at follow-up |
| Nagar, 2005<br>Study location: UK | • 360° SLT (n=44 participants; n=44 eyes)<br>• 180° SLT (n=49 participants; n=49 eyes)<br>• 360° SLT (n=35 participants; n=35 eyes) | • Latanoprost (n=39 participants; n=39 eyes) | • 12 months | • Intraocular pressure<br>○ 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<br>• Adverse events |
| Nagar, 2009<br>Study location: UK | • SLT (n=20 participants) | • Latanoprost (n=20 participants) | • 6 months | • Intraocular pressure<br>○ Treatment success for IOP control was defined as at least a 20% reduction from baseline measurement |

See Appendix D for full evidence tables.

### 1.1.6 Summary of the effectiveness evidence

**Comparison: 360° SLT vs eye drops**

**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 |

*a) No meaningful difference: 95% CI completely between MIDs and crossing line of no effect; Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds*
*RR: relative risk; MD: mean difference*

**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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds*

**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)** | | | | |

| No. of studies | Sample size | Effect estimate (95% CI) | Quality | Interpretation of effect[a] |
|---|---|---|---|---|
| Gazzard 2019 | 635 | MD 0.01 (-0.01, 0.03) | High | No meaningful difference |
| **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 |

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

**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 |

*a) No meaningful difference: 95% CI completely between MIDs and crossing line of no effect; Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds; Favours: statistically significant*

**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 |

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

**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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds*

### Comparison: 360° SLT vs latanoprost

**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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID threshold; Favours: statistically significant*

### Comparison: 180° SLT vs latanoprost

**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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID threshold; Favours: statistically significant*

### Comparison: 90° SLT vs latanoprost

**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)** | | | | |

| No. of studies | Sample size | Effect estimate (95% CI) | Quality | Interpretation of effect[a] |
|---|---|---|---|---|
| Nagar 2005 | 48 | RR 1.94 (0.10, 38.01) | Very low | Could not differentiate |
| **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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds; Favours: statistically significant*

**Comparison: SLT (degrees not specified) vs latanoprost**

**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 |

*a) Could not differentiate: 95% CI is crossing line of no effect and also crossing one or two of the MID thresholds; Favours: statistically significant*

See Appendix F for full GRADE tables.

## 1.1.7 Economic evidence

### 1.1.7.1 Included studies

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

### 1.1.7.2 Excluded studies

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<br><br>SLT[4] - £4,119 | Eye drops – 2.62<br><br>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<br><br>SLT - £18,239 | Eye drops – 12.3<br><br>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 uprated 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*

### 1.1.9 Economic model

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

1.1.10 Evidence statement

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

### 1.1.11 The committee's discussion and interpretation of the evidence

#### 1.1.11.1. The outcomes that matter most

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

#### 1.1.11.2 The quality of the evidence

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

The review protocol states that studies including people who have previously received first line treatment for OHT or COAG would be excluded. Two studies (Katz 2012 and Nagar 2005) were identified but it was unclear if the studies included people who were not treatment naïve. The committee highlighted that these studies provide context but that they should be downgraded for indirectness.

Three studies included in this review were conducted in the UK (Gazzard 2019, Nagar 2005 and Nagar 2009), 1 study was conducted in the US (Katz 2012) and 1 study was conducted

in China (Lai 2004). Authors of Lai 2004 highlighted that Asian eyes have more pigmented trabecular meshwork. This means that the laser energy required and the clinical response might be different from eyes with lightly pigmented trabecular meshwork. The committee highlighted that this study is relevant to a subset of the UK population, but it's not directly applicable to the UK general population.

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

The committee highlighted that there was a lack of long-term evidence 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). They also noted that patients care more about vision outcomes compared with other outcomes such as IOP. The committee discussed the importance of investigating these outcomes at longer follow-up times (≥3, 5 and 10 years) to know how effective SLT is at long-term. This evidence could help to target interventions which could prevent progression. Therefore, a research recommendation was developed to cover this gap in the evidence.

#### 1.1.11.3 Benefits and harms

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

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

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

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

The committee agreed that SLT is an appropriate treatment option for people with OHT and COAG but in practice people can be newly diagnosed but have pigment dispersion syndrome. In this population, SLT would not be appropriate. There was no evidence on the use of SLT in people with pigment dispersion syndrome and the committee agreed that eye drop treatment is more suitable for people with pigment dispersion syndrome. Based on the evidence and clinical understanding, the committee noted that SLT as first line treatment was not appropriate for people with pigment dispersion syndrome. Additionally, the LiGHT trial included a small number of people with pseudoexfoliation. Based on their clinical understanding, the committee did not think it was appropriate to exclude pseudoexfoliation from the recommendations but as the evidence based was relatively small, they opted to not explicitly highlight the condition in the recommendation.

Based on the new evidence, the committee agreed that 360° SLT should be offered as first-line treatment to people with newly diagnosed OHT with IOP of 24 mmHg or more (and if they are at risk of visual impairment within their lifetime) or COAG, however this should exclude cases associated with pigment dispersion syndrome. For people with newly diagnosed OHT, a threshold of 24 mmHg or more was identified based on existing NICE guidance. Additionally, in the LiGHT trial, baseline characteristics showed that mean IOP in the SLT arm was 24.5 (SD 5.2) and 24.4 (SD 5.0) in the eye drops arm.

To aid decision making, the committee further stated that information should be provided on the possibility of needing eye drops treatment after SLT, the time that SLT takes to improve IOP, the SLT specific side effects and complications including the type and duration, and that they might need further SLT treatment at a later date. The committee highlighted that when a generic prostaglandin analogue (PGA) is given as interim treatment to people waiting for an SLT procedure, it is important to follow recommendations on reassessment to use clinical judgement regarding IOP control and risk of progression.

The committee further highlighted that in general, treatment to reduce IOP has to work for at least 6 months to be considered successful, however this can also be based on clinician discretion. In the case of SLT procedures, there may be an initial reduction in the IOP level, but over time this level may begin to increase. This can occur at any time, meaning that re-treatment with SLT may be required. The committee highlighted that, recommendations on repeating SLT were required as re-treatment with SLT is usually done in practice.

In the LiGHT trial, patients who were not at target IOP after a single SLT received another treatment of 360° SLT at the same energy setting, with re-evaluation after 2 weeks. SLT was also repeated in Katz 2012, where participants in the laser arm were offered repeat 180° SLT. However, it should be noted that this study (Katz 2012) was downgraded for indirectness as it was unclear if the study included people who were not treatment naive (see section 1.1.11.2 for more details).

Based on their clinical expertise and applicability of evidence to current practice, the committee opted to follow the treatment protocol highlighted in the LiGHT trial. Based on these factors the committee further recommended that a second 360° SLT could be considered for people with OHT and COAG if the effect of an initial successful SLT has subsequently reduced over time. This means that the IOP level has gone up and clinicians need to decide if there is risk of progression of COAG or conversion of OHT to COAG. The second SLT should be given at the discretion of the treating consultant ophthalmologist. Based on their clinical experience, the committee further noted that any effect from SLT might be reduced after repeating the procedure more than 2 or 3 times.

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

treatment. Therefore, eye drops were recommended as first line treatment for this population. It was also recommended that healthcare professionals should demonstrate correct eye drop instillation technique and observe the person using the correct technique when eye drops are first prescribed.

The committee noted that the first line use of SLT to treat OHT or COAG might lead to a significant change in practice that requires better organisation of care and the establishment of a multidisciplinary team. The committee also noted that larger centres may see more referrals, resulting in an increase in the number of clinics per week. The committee highlighted that, although the increase should not be significant, any increase means there will be a change to the organisation of care. They also discussed the safety of the SLT procedure and agreed that healthcare professionals should discuss with the responsible consultant ophthalmologist the decision to offer SLT and how it will be performed. This means that healthcare professionals such as specialty doctors, associate specialists, specialist nurses, optometrists and allied health professionals can perform SLT with support from a consultant ophthalmologist. The committee also wanted to make clear that if SLT is suitable for a person, that person should be referred to a consultant ophthalmologist. Based on this, the committee updated an existing recommendation to state that people should be referred to a consultant ophthalmologist for consideration of a definitive diagnosis and formulation of a management plan if they are suitable for SLT.

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

#### 1.1.11.4 Cost effectiveness and resource use

The committee discussed the published cost-utility evidence relating to selective laser trabeculoplasty (SLT) compared with pharmacological treatment (eyedrops) in ocular hypertension and open-angle glaucoma. This included a published study and a health technology appraisal (HTA) that were both based on the same clinical trial (LiGHT) and both these studies were assessed to be directly relevant to the review question. The difference between the study and the HTA was the time horizon; the study had a three-year time horizon (to match that of the LiGHT trial) whereas the HTA had a lifetime time horizon and extrapolated the data beyond the time horizon of the trial.

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

The committee noted that there was only a small difference in the quality of life between the two comparators and therefore the main reason that SLT was the dominant option was because the SLT arm was less costly. These lower costs were primarily driven by the finding

that using SLT means people are likely to need to use significantly fewer eye drops, which reduces costs both of the medicines themselves, and also appointments to monitor and modify treatment. The committee noted that SLT may need to be repeated and that was included in the analyses (with approximately 15% of people in the SLT arm having a second procedure within the first year) and therefore that gave the committee more confidence in the result, as it reflected their expectations of how the treatment would be used in practice.

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

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

#### 1.1.11.5 Other factors the committee took into account

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

The committee also highlighted that some people with suspected COAG may still be at risk of visual impairment within their lifetime, for example, in some people clinicians may be concerned with the appearance of the optic disc but may not find signs of visual defect but the person may have a strong family history of glaucoma. As there is a risk of visual impairment, such patients may require treatment at clinician's discretion. Based on this understanding, the committee amended the 2017 recommendation to state that treatment should not be offered to people with suspected COAG and IOP less than 24 mmHg, unless they are at risk of visual impairment within their lifetime.

Additionally, the 2017 update included a recommendation on treatment adherence and checking the eye drop instillation technique. If adherence and eye drop instillation were satisfactory, a medicine from another therapeutic class, topical medicine from a different class, laser trabeculoplasty or surgery with pharmacological augmentation (MMC) could be offered. The 2017 update also included a recommendation on offering surgery with pharmacological augmentation (MMC) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment.

The committee noted that these recommendations required further clarity as there were three important messages being conveyed across the two recommendations. Based on this

understanding, the committee amended the 2017 recommendations and split them into 3 separate recommendations. The first recommendation highlights that clinician should check treatment adherence and eye drop instillation technique in people with COAG whose IOP has not been reduced sufficiently to prevent the risk of progression to sight loss, despite pharmacological treatment with a generic PGA.

The second recommendation highlights the treatment options that can be offered to people in whom eye drop instillation technique is satisfactory and IOP has not been reduced. As the evidence identified in the current review focused specifically on SLT, the committee noted it was important that all recommendations in the guideline are in line with the evidence and new recommendations. As SLT is the type of laser trabeculoplasty currently used in clinical practice this recommendation was also updated to specifically highlight SLT as a treatment option for people in whom adherence and eye drop instillation technique are satisfactory.

The third recommendation considers SLT or glaucoma surgery with pharmacological augmentation (MMC) as indicated to people with COAG who are at risk of progressing to sight loss despite treatment with medicines from 2 therapeutic classes. The committee highlighted that the purpose of this recommendation is to discourage polypharmacy with patients being given additional drug therapies and for healthcare professionals to consider SLT and glaucoma surgery as more favourable outcomes before considering further medical treatment.

It should also be noted that the committee suggested to change the term ‘surgery’ to ‘glaucoma surgery’ because the term ‘surgery’ is more general, and it can include other types of eye surgery which are not glaucoma surgery. This change was also made across the guideline.

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

The 2017 update also included recommendations for people with COAG who have undergone surgery, but IOP has not reduced sufficiently to prevent the risk of progression to sight loss. Laser trabeculoplasty or cyclodiode treatment were a suggested treatment option for the group. The committee amended this recommendation to state that SLT can be a treatment option instead of laser trabeculoplasty.

No evidence was identified in people with advanced COAG as the LiGHT trial excluded people with advanced COAG. Therefore, no specific recommendations were developed. However, the 2017 update, included a recommendation that stated in people with advanced COAG surgery could be offered with pharmacological augmentation. The committee noted that there are instances where surgery might not be suitable (for example due to systemic comorbidities). The 2017 update also included a recommendation stating that for people with COAG who prefer not to have surgery or for whom surgery is not suitable pharmacological treatment, laser trabeculoplasty or cyclodiode laser treatment could be offered. The committee amended this recommendation to explicitly state that SLT can be a treatment option instead of laser trabeculoplasty.

Recommendations for people with OHT have been amended to be in line with the new recommendation which offers SLT as first-line treatment. In particular, SLT was added to the

recommendation to refer people whose IOP cannot be reduced sufficiently with pharmacological treatment to a consultant ophthalmologist.

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

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

The committee acknowledged that there might be waiting times for SLT procedures, and this is why they recommended to offer a generic PGA as interim treatment for people who are waiting for an SLT procedure. The committee also highlighted that SLT procedures should be prioritise to women who are pregnant/breastfeeding because of the side effects that IOP-lowering eye drops could have on women and their children if those were used.

The committee acknowledged that late presentation of glaucoma (usually in the form of advanced glaucoma) might be associated with people who are of black African or black Caribbean family background and with greater individual and area level deprivation. Late presentation of glaucoma might be driven by clinical variation and by variations in healthcare seeking behaviours and healthcare inequalities in referrals or diagnosis. Evidence included in the review, excluded people with advanced glaucoma, therefore specific recommendations could not be drafted for this population. However, the committee agreed that new recommendations were unlikely to have an impact on late presentation of glaucoma because surgery is the main treatment option for advanced glaucoma and this is stated in existing recommendations. As ethnicity is an important risk factor for glaucoma, the committee identified it as an important subgroup in the new research recommendation.

### 1.1.12 Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.4 to 1.4.6, 1.4.9, 1.4.11, 1.4.15 to 1.4.17, 1.4.19 to 1.4.24, 1.6.6 to 1.6.7 and the research recommendation on long-term effectiveness of SLT.

### 1.1.13 References – included studies

#### 1.1.13.1 Effectiveness evidence

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

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

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

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

Nagar M, Ogunyomade A, O'Brart DP et al. (2005) 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 89(11): 1413-1417

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

#### 1.1.13.2 Economic

Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial Lancet. 2019;393(10180):1505-1516. doi:10.1016/S0140-6736(18)32213-X

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).

# Appendices

## Appendix A – Review protocols

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

| ID | Field | Content |
|---|---|---|
| 0. | PROSPERO registration number | Not applicable |
| 1. | Review title | Effectiveness and cost-effectiveness of selective laser trabeculoplasty (SLT) as a first line treatment compared with 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 with 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. |

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| 4. | Searches | The following databases will be searched:<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase<br>• MEDLINE<br><br>Searches will be restricted by:<br>• August 2008 onwards<br>• English language<br>• Human studies<br><br>Other searches:<br>• Reference searching<br>• Citation searching<br>• Inclusion lists of systematic reviews<br>• Websites<br><br>The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion.<br><br>The full search strategies for MEDLINE database will be published in the final review. |

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| 5. | Condition or domain being studied | Ocular hypertension (OHT) or chronic open-angle glaucoma (COAG) in adult patients. |
| 6. | Population | Inclusion:<br>• Adults (18 and over) with OHT<br>• Adults (18 and over) with COAG<br><br>Exclusion:<br>• People who have received first line treatment for OHT or COAG,<br>• People with secondary glaucoma, for example, neovascular or uveitic glaucoma<br>• People with, or at risk of, primary or secondary angle closure glaucoma<br>• People with primary congenital, infantile or childhood glaucoma<br>• People with angle closure |
| 7. | Intervention/Exposure/ Test | • Selective laser trabeculoplasty |
| 8. | Comparator/Reference standard/Confounding factors | • Intraocular pressure-lowering eyedrops alone |

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| 9. | Types of study to be included | • Systematic Review of RCTs<br>• RCTs |
| 10. | Other exclusion criteria | • Other study types<br>• 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) | Critical outcomes:<br>• IOP (intraocular pressure) level/outcomes<br>• Glaucomatous visual field loss*<br>• Normal visual field to visual field defect*<br>• Progression of glaucomatous visual field defect*<br>• Vision loss<br>• Health-related quality of life<br>• Adverse events<br><br>*Follow up for outcomes related to visual field should be restricted to those 6 months or greater. |

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| 13. | Secondary outcomes (important outcomes) | Important outcomes:<br>• Optic nerve head damage<br>• Progression of optic nerve head damage<br>• Normal or suspicious-to- abnormal optic nerve head<br>• Treatment adherence<br>• Treatment discontinuation |
| 14. | Data extraction (selection and coding) | 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.<br><br>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 section 6.2 in Developing NICE guidelines: the manual). |
| 15. | Risk of bias (quality) assessment | Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. |
| 16. | Strategy for data synthesis | 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 outcomes stated above. A fixed effect meta-analysis, with weighted mean differences for |

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| | | continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome.<br>Heterogeneity between the studies in effect measures will be assessed using the $I^2$ statistic and visually inspected.<br>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.<br>GRADE pro will be used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results.<br>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.<br>Network meta-analysis is not planned for this review. |
| 17. | Analysis of sub-groups | Possible sub-groups include;<br>• Older people (over 70 years)<br>• Younger adults with chronic open angle glaucoma or ocular hypertension (under 50 years)<br>• Different ranges of trabecular meshwork treated (90, 180 or 360 degrees)<br>• Different laser application end points (sub-threshold / threshold / supra-threshold)<br>• Patients undergoing early repeat SLT treatment (i.e. within 6 or 12 months of the initial SLT treatment) |
| 18. | Type and method of review | ☒ Intervention<br>☐ Diagnostic |

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|---|---|---|---|---|
| | | ☐ Prognostic<br>☐ Qualitative<br>☐ Epidemiologic<br>☐ Service Delivery<br>☐ 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 | ☑ | ☐ |

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|---|---|---|---|---|
| | | Piloting of the study selection process | ☑ | ☐ |
| | | Formal screening of search results against eligibility criteria | ☑ | ☐ |
| | | Data extraction | ☑ | ☐ |
| | | Risk of bias (quality) assessment | ☑ | ☐ |
| | | Data analysis | ☑ | ☐ |
| 24. | Named contact | **5a. Named contact**<br>NICE Guideline Updates Team<br><br>**5b Named contact e-mail**<br>GUTprospero@nice.org.uk<br><br>**5e Organisational affiliation of the review**<br>National Institute for Health and Care Excellence (NICE) and NICE Guideline Updates Team | | |

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| 25. | Review team members | From the NICE Guideline Updates Team:<br>• Shreya Shukla<br>• Yolanda Martinez<br>• Joshua Pink<br>• Steph Armstrong<br>• Lynda Ayiku |
| 26. | Funding sources/sponsor | This systematic review is being completed by the Guideline Updates Team which receives funding from NICE. |
| 27. | Conflicts of interest | 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. |
| 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 Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage]. |

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| 29. | Other registration details | None |
| 30. | Reference/URL for published protocol | None |
| 31. | Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• 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 | ☐ Ongoing<br>☒ Completed but not published |

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| | | ☐ | Completed and published |
| | | ☐ | Completed, published and being updated |
| | | ☐ | Discontinued |
| 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 | |

# 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 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 Iopidine* or brimonidine* or simbrinza* or brymont* or alphagan* 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 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. (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 eydelto* or trusopt* or vizidor*).tw. (54)
15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
16 (sympathomimetic* or apraclonidine* or Iopidine* 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 ocusert* 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 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. (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* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (46)
15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
16 (sympathomimetic* or apraclonidine* or Iopidine* 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 ocusert* 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 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. (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 eydelto* or trusopt* or vizidor*).tw. (4276)
15 (sympathomimetic* or apraclonidine* or Iopidine* 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 ocusert* 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 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*):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 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*):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 eydelto* 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 Iopidine* 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 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*))) | 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 eyzeeta* 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 Iopidine* 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 Iopidine* or brimonidine* or simbrinza* or brymont* or alphagan* 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 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 disutili$.tw. (436)
74 rosser.tw. (97)
75 quality of wellbeing.tw. (22)
76 quality of well-being.tw. (402)
77 qwb.tw. (194)
78 willingness to pay.tw. (5309)
79 standard gamble$.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 xelor* 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 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 eydelto* or trusopt* or vizidor*).tw. (53)
15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
16 (sympathomimetic* or apraclonidine* or Iopidine* 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 ocusert* 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 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. (553)
13 exp Carbonic Anhydrase Inhibitors/ (0)
14 (carbon* anhydras* inhibitor* or brinzolamide* or azopt* or dorzolamide* or eydelto* or trusopt* or vizidor*).tw. (46)
15 exp Sympathomimetics/ or Brimonidine Tartrate/ (0)
16 (sympathomimetic* or apraclonidine* or Iopidine* 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 ocusert* 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 trabeculotome/ or trabeculotomy/ or trabeculotomy probe/ (11256)
7 (trabecul* or slt or surgical* or surger*).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 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. (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 Iopidine* 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 ocusert* 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 ocusert* 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 |

| | | | |
|---|---|---|---|
| | 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 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*))) | 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 eyzeeta* 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* 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 |

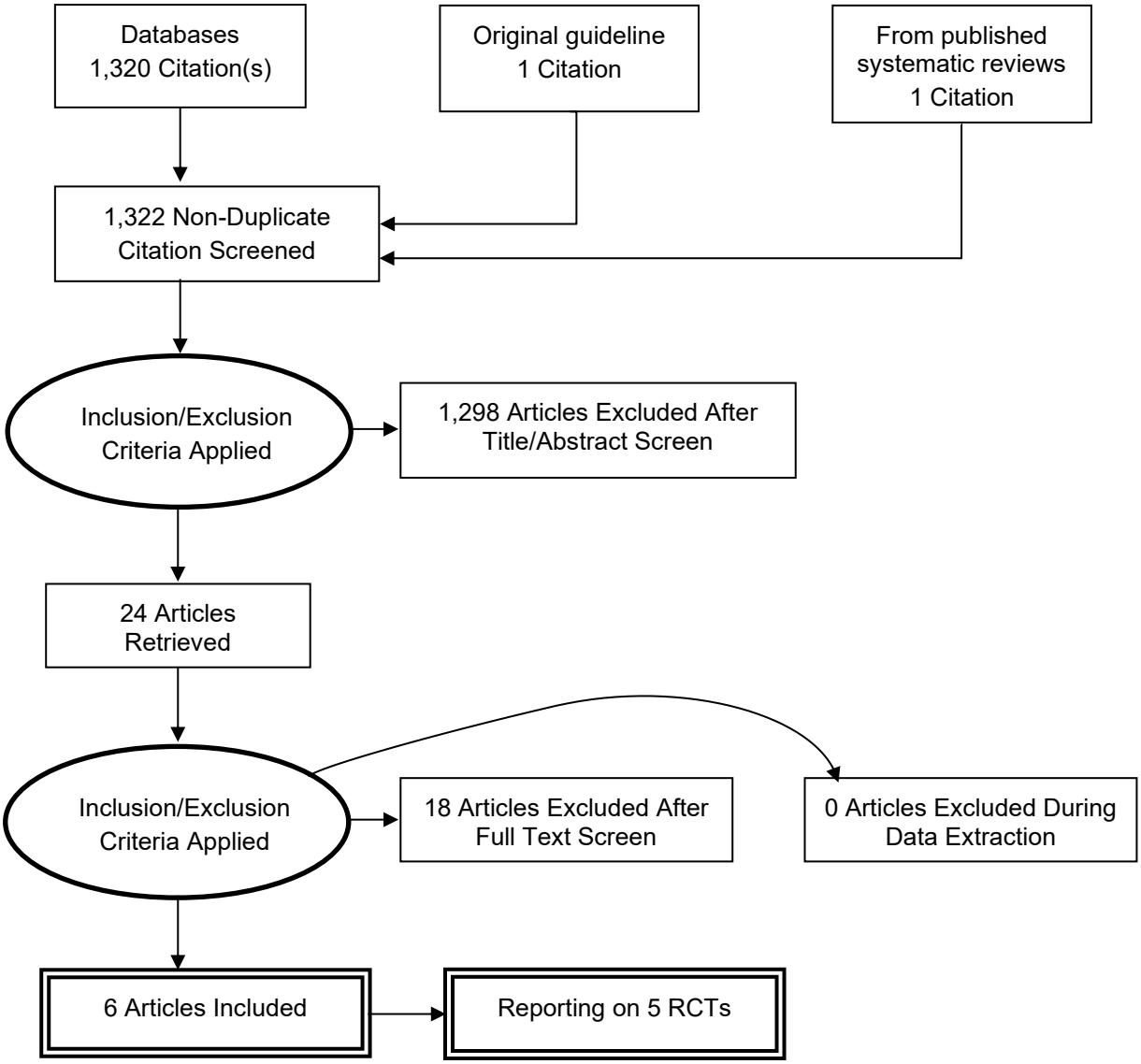
| | | | |
|---|---|---|---|
| | 19 | (((miotic* or pilocarpine* or isopilocarpine* or isoptocarpine* or ocusert* or salagen))) | 12 |
| | 20 | (MeSH DESCRIPTOR Ophthalmic Solutions EXPLODE ALL TREES) | 35 |
| | 21 | (((eyedrop* or drop* or medicat* or medici* or pharm*))) | 22490 |
| | 22 | (#9 OR #10 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 |

**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 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* 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 Iopidine* 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** | 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<br><br>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<br><br>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 |
| **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** | Newly diagnosed, untreated OAG or ocular hypertension in one or both eyes<br><br>Qualified for treatment according to NICE guidelines<br><br>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<br><br>Able to read and understand English<br><br>Visual acuity of 6/36 or better in the eyes to be treated<br><br>No previous intraocular surgery, except uncomplicated phacoemulsification at least 1 year before randomisation<br><br>A decision to treat had been made by a glaucoma specialist consultant ophthalmologist<br><br>Aged >18 years and able to provide informed consent<br><br>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)<br><br>It was possible to perform a VF test in the study eye(s) with <15% false positives |
| **Exclusion criteria** | 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)<br><br>A visually significant cataract in symptomatic patients who want to undergo cataract surgery |

| | |
|---|---|
| | Any current, active treatment for another ophthalmic condition in the hospital eye service (this applied to both eyes, even if one was not in the trial, as the fellow eye might affect the patient's visit frequency)<br><br>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)<br><br>Secondary glaucoma (e.g. pigment dispersion syndrome, rubeosis, trauma, etc.) or any angle closure<br><br>Inability to use topical medical therapy because of, for example, physical infirmity and a lack of carers able to administer daily eyedrops<br><br>A previous treatment for OAG or OHT<br><br>Congenital or early childhood glaucoma<br><br>Any history of retinal ischaemia, macular oedema or diabetic retinopathy<br><br>Age-related macular degeneration with neovascularisation in either eye or geographic atrophy<br><br>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)<br><br>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)<br><br>Pregnancy at the time of recruitment or intention to become pregnant within the duration of the trial<br><br>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)** | **SLT**<br><br>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. |
| **Comparator** | **Eye drops**<br><br>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. |
| **Outcome measures** | Intraocular pressure<br><br>Proportion of visits at target intraocular pressure.<br><br>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.<br><br>**IOP target for OHT**<br><br>• <25 mmHg and >20% reduction<br><br>**IOP target for POAG**<br><br>• Mild disease: <21 mmHg and >20% reduction<br>• Moderate disease: <18 mmHg and >30% reduction<br>• Severe disease: <15 mmHg and >30% reduction |

| | |
|---|---|
| | Health-related quality of life<br><br>EuroQol EQ-5D 5 Levels (EQ-5D-5L) utility scores at 36 months.<br><br>Glaucoma-specific treatment related quality of life assessed with the Glaucoma Utility Index (GUI).<br><br>Patient-reported visual function assessed using the Glaucoma Quality of Life-15 questionnaire (GQL-15).<br><br>Adverse events<br><br>Treatment adherence<br><br>Compliance/concordance was assessed by two questions shown to predict the probability of non-concordance.<br><br>Visual field progression<br><br>"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)<br><br>Optic disc progression<br><br>"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)<br><br>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)<br><br>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**<br>Sample size | n = 165 ; % = 45.6 | n = 156 ; % = 43.8 |
| **Age** (years)<br>Mean (SD) | 62.7 (11.6) | 63.4 (12) |
| **Ethnicity** | | |
| **Asian**<br>Sample size | n = 28 ; % = 7.7 | n = 23 ; % = 6.5 |
| **Black**<br>Sample size | n = 69 ; % = 19.1 | n = 77 ; % = 21.6 |
| **White**<br>Sample size | n = 258 ; % = 71.3 | n = 243 ; % = 68.3 |
| **Other**<br>Sample size | n = 7 ; % = 1.9 | n = 13 ; % = 3.7 |
| **Diagnosis by participant** | | |
| **Primary open angle glaucoma**<br>Sample size | n = 282 ; % = 77.9 | n = 273 ; % = 76.7 |

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

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

| Characteristic | Eye drops (N = 362) | SLT (N = 356) |
|---|---|---|
| **Visual acuity**<br>Eye drops (n=622 eyes); SLT (n=613 eyes)<br><br>Mean (SD) | 0.1 (0.1) | 0.1 (0.2) |
| **Visual field mean deviation (Decibels (dB))**<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant<br><br>Mean (SD) | -3 (3.6) | -3 (3.4) |
| **HRT rim area** ($mm^2$)<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for 62 participants<br><br>Mean (SD) | 1.1 (0.4) | 1.2 (0.4) |
| **Intraocular pressure** (mmHg)<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant<br><br>Mean (SD) | 24.4 (5) | 24.5 (5.2) |
| **Central corneal thickness** (µm)<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for 3 participants<br><br>Mean (SD) | 551.6 (36.2) | 550.7 (38.1) |
| **Pseudo-exfoliation**<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant<br><br>Sample size | n = 12 ; % = 1.9 | n = 5 ; % = 0.8 |
| **Pseudophakia**<br>Eye drops (n=622 eyes); SLT (n=613 eyes); no data for one participant<br><br>Sample size | n = 33 ; % = 5.3 | n = 39 ; % = 6.4 |

| Characteristic | Eye drops (N = 362) | SLT (N = 356) |
|---|---|---|
| **EQ-5D**<br>n=716 participants<br><br>Mean (SD) | 0.92 (0.13) | 0.91 (0.13) |
| **Glaucoma Utility Index** (Higher scores indicate better health-related quality of life)<br>n=716 participants<br><br>Mean (SD) | 0.89 (0.11) | 0.89 (0.12) |
| **Glaucoma Quality of Life-15** (Higher scores indicate worse health-related quality of life)<br><br>Mean (SD) | 18.7 (5.6) | 18.9 (6.6) |
| **Central subscale**<br><br>Mean (SD) | 2.5 (1) | 2.5 (1) |
| **Peripheral subscale**<br><br>Mean (SD) | 8.4 (2.9) | 8.5 (3.4) |
| **Dark subscale**<br><br>Mean (SD) | 7.9 (2.8) | 7.9 (3) |
| **Outdoor subscale**<br><br>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<br>*(There were protocol deviations but unlikely to have an effect on outcomes.)* |
| 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) | *Not applicable* |
| 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<br>*(There were protocol deviations but unlikely to have an effect on outcomes.)* |
| 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 |

## 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 |

| | |
|---|---|
| **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** | 25 to 82 years of age<br><br>IOP ≥24 and ≤31 (higher eye) and IOP ≥20 (lower eye)<br><br>Diagnosis of primary OAG, pseudoexfoliation glaucoma, or mixed mechanism OAG with a narrow angle (if laser peripheral iridotomy was performed >3mo ago)<br><br>Diagnosis of ocular hypertension if central corneal thickness was <600 microns<br><br>Adequate visualisation of angle structures (that is clear media and cooperative patient)<br><br>No previous intraocular surgery<br><br>No glaucoma medications in both eyes for ≥4 weeks<br><br>No systemic medications known to increase IOP (corticosteroids)<br><br>Visual acuity of 20/70 or better in both eyes |
| **Exclusion criteria** | >2 glaucoma medications (fixed combination products are considered 2 drugs)<br><br>Any eye drops for glaucoma 4 weeks before baseline visit |

| | |
|---|---|
| | Collaborative Initial Glaucoma Treatment Study (CIGTS) visual field score that exceeded 16 in either eye<br><br>Evidence of ocular disease other than glaucoma or ocular hypertension, which might affect IOP measurements, assessment of visual function or visual field testing<br><br>Diagnosis of pigmentary OAG or proliferative diabetic retinopathy<br><br>Undergone ophthalmic laser (other than laser peripheral iridotomy >3mo ago) or had refractive, conjunctival, or intraocular surgery in either eye<br><br>Likely to require cataract surgery within 6 months of randomisation<br><br>Current or expected use of corticosteroids<br><br>Pregnant or planning to become pregnant within the next year |
| **Intervention(s)** | **SLT**<br><br>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.<br><br>• **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.<br>• **Step 2**: If target IOP not maintained in 1 or both eyes within 4 to 6 weeks, SLT over nasal 180° with 50 applications.<br>• **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.<br>• **Step 4**: Treating clinician choice of next therapy for intervention failure. |
| **Comparator** | **Eye drops** |

| | |
|---|---|
| | The treatment regimen was not rigidly standardised but the following treatment regimen was recommended:<br><br>• **Step 1**: Start with ocular prostaglandin analogue: latanoprost, bimatoprost, or travoprost<br>• **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<br>• **Step 3**: Brimonidine<br>• **Step 4**: Dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol |
| **Outcome measures** | Intraocular pressure<br><br>Mean differences of IOP from baseline to follow-up 4 to 6 months, and to follow-up 9 to 12 months.<br><br>Percentage of participants who met ≤target IOP.<br><br>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-(reference IOP + visual field score/100)] x reference IOP. Therefore, if the reference IOP=28mm Hg and the reference visual field score=5, then target IOP= [1-(28+5)/100] x 28= (1-0.33) x 28=0.67 x 28=19mm Hg. |
| **Duration of follow-up** | 12 months |
| **Additional comments** | Although Katz (2012) had an eligibility criterion as 'on no glaucoma medications in both eyes for ≥4 weeks', there was no information in the baseline characteristics to confirm that there were participants with previous used of glaucoma medications. |

## 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**<br><br>Sample size | n = 19 ; % = 61.3 | n = 22 ; % = 57.9 |

| Characteristic | Eye drops (N = 31) | SLT (N = 38) |
|---|---|---|
| **Age** | | |
| **Less than 60 years**<br>Sample size | n = 14 ; % = 45.2 | n = 14 ; % = 36.8 |
| **60 years or more**<br>Sample size | n = 17 ; % = 54.8 | n = 24 ; % = 63.2 |
| **Race** | | |
| **White**<br>Sample size | n = 23 ; % = 74.2 | n = 27 ; % = 71.1 |
| **Non-white**<br>Sample size | n = 8 ; % = 25.8 | n = 11 ; % = 28.9 |
| **Glaucoma in immediate family** | | |
| **No or uncertain**<br>Sample size | n = 18 ; % = 58.1 | n = 20 ; % = 52.6 |
| **Yes**<br>Sample size | n = 13 ; % = 41.9 | n = 18 ; % = 47.4 |
| **Hypertension** | | |
| **No**<br>Sample size | n = 20 ; % = 64.5 | n = 26 ; % = 68.4 |

| Characteristic | Eye drops (N = 31) | SLT (N = 38) |
|---|---|---|
| **Yes**<br><br>Sample size | n = 11 ; % = 35.5 | n = 12 ; % = 31.6 |
| **Diabetes** | | |
| **No**<br><br>Sample size | n = 25 ; % = 80.7 | n = 30 ; % = 78.9 |
| **Yes**<br><br>Sample size | n = 6 ; % = 19.4 | n = 8 ; % = 21.1 |

**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<br>*(Two participants crossed over to the alternative treatment (one from each arm) but both were analysed under the intention to treat approach.)* |
| 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<br>*(Two participants crossed over to the alternative treatment (one from each arm) but both were analysed under the intention to treat approach.)* |

| Section | Question | Answer |
|---|---|---|
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Some concerns<br>*(No reasons were given for participants lost to 9 to 12 months follow-up)* |
| 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<br>*(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<br>*(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<br><br>IOP >21 mmHg in both eyes without antiglaucomatous medications<br><br>Those with POAG demonstrated optic disc changes and/or visual field changes typical of glaucomatous damage |
| **Exclusion criteria** | Pregnancy<br><br>Previous laser trabeculoplasty<br><br>Previous intraocular surgery disturbing the aqueous outflow<br><br>Active ocular inflammation<br><br>Poor visualization of the trabecular meshwork<br><br>Single eye<br><br>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**<br><br>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 goniolens 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**<br><br>Topical antiglaucoma medications were used including beta blocker, pilocarpine, dorzolamide and latanoprost were started either as monotherapy or in combination. |
| **Outcome measures** | Intraocular pressure<br><br>Mean IOP reduction at follow-up.<br><br>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.<br><br>To minimize the extent of cross-over effect with medical treatment, participants were instructed to apply digital lacrimal punctual pressure for 5 min after instilling the eye drops.<br><br>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]) |

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**<br><br>Sample size | n = 16 ; % = 55.2 |
| **Age** (years)<br><br>Mean (SD) | 51.9 (14.7) |
| **Diagnosis** | |

| Characteristic | Study (N = 29) |
|---|---|
| **POAG**<br>Sample size | n = 17 ; % = 58.6 |
| **OHT**<br>Sample size | n = 12 ; % = 41.4 |

**Arm-level characteristics**

| Characteristic | Eye drops (N = 29) | SLT (N = 29) |
|---|---|---|
| **Baseline IOP** (mmHg)<br>Mean (SD) | 26.2 (4.2) | 26.8 (5.6) |
| **Best-corrected visual acuity**<br>Custom value | ranged from 0.2 to 1.0 | ranged from 0.1 to 1.0 |
| **Cup/disc ratio**<br>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<br>*(There was no information on whether allocation sequence was concealed.)* |
| 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<br>*(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.)* |
| 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) | *Not applicable* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | High<br>*(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.)* |
| 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<br>*(There was no information about a pre-specified analysis plan.)* |
| 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<br><br>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<br><br>Either newly diagnosed or controlled on medical therapy |
| **Exclusion criteria** | Congenital glaucoma<br><br>Any type of angle closure glaucoma |

| | |
|---|---|
| | Eyes with previous laser or surgical glaucoma interventions<br><br>Eyes with previous anterior segment surgery |
| **Intervention(s)** | **Laser techniques**<br><br>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 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.<br><br>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.<br><br>**90° SLT**<br><br>Treatments 25–30 non-overlapping laser spots were applied to 3 clock hours of the inferonasal or inferotemporal trabecular meshwork.<br><br>**180° SLT**<br><br>Treatments 48–53 spots were applied over the inferior 6 clock hours.<br><br>**360° SLT**<br><br>The entire meshwork was treated with 93–102 non-overlapping spots. |
| **Comparator** | **Latanoprost** 0.005% at night |
| **Outcome measures** | Intraocular pressure<br><br>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 |
| **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** | 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.<br><br>Data was not reported on how many participants were controlled on medical therapy.<br><br>At the discretion of the treating surgeons, further laser treatments or antiglaucomatous medications were administered to ensure adequate IOP control.<br><br>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. |

## Study arms

### Latanoprost (N = 39)

| | |
|---|---|
| **Number of participants** | Latanoprost (n=39 participants; n=39 eyes) |

**90° SLT (N = 35)**

| | |
|---|---|
| **Number of participants** | 90° SLT (n=35 participants; n=35 eyes) |

**180° SLT (N = 49)**

| | |
|---|---|
| **Number of participants** | 180° SLT (n=49 participants; n=49 eyes) |

**360° SLT (N = 44)**

| | |
|---|---|
| **Number of participants** | 360° SLT (n=44 participants; n=44 eyes) |

## Characteristics

### Study-level characteristics

| **Characteristic** | **Study (N = 167)** |
|---|---|
| **Female**<br><br>Sample size | n = 90 ; % = 53.9 |
| **Age** (years)<br><br>Custom value | Mean 63 years (range 22 to 90) |

| Characteristic | Study (N = 167) |
|---|---|
| **Ethnicity** | |
| **African or Afro-Caribbean origin**<br><br>Sample size | n = 36 ; % = 22 |
| **White**<br><br>Sample size | n = 131 ; % = 78 |
| **Diagnosis** | |
| **OAG**<br>Primary OAG (n=76); secondary to pigment dispersion syndrome (n=4); secondary to pseudoexfoliation syndrome (n=2)<br><br>Sample size | n = 82 ; % = 49 |
| **OHT**<br><br>Sample size | n = 85 ; % = 51 |

**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 |

| Section | Question | Answer |
|---|---|---|
| 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<br>*(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.)* |
| 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) | *Not applicable* |
| 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<br>*(There was no information about a pre-specified analysis plan.)* |
| Overall bias and Directness | Risk of bias judgement | High |
| Overall bias and Directness | Overall Directness | Partially applicable<br>*(It was not reported how many participants were controlled on medical therapy before participating in the trial.)* |

## 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** | Newly diagnosed OHT or primary OAG<br><br>Aged 40 to 80 years<br><br>Diurnal intraocular pressure fluctuation more than 3 mm Hg<br><br>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<br><br>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<br><br>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) |

| | |
|---|---|
| | In those with OHT, normal optic disc<br><br>In those with OHT, normal visual field using Humphrey visual field on two separate screening visits<br><br>In those with OHT, no evidence of glaucomatous damage<br><br>Willing to undergo selective laser trabeculoplasty versus latanoprost treatment trial |
| **Exclusion criteria** | Diurnal intraocular pressure fluctuation of less than 3 mm Hg<br><br>Diagnoses other than open-angle glaucoma and ocular hypertension (eg, patients with narrow angles, congenital glaucoma)<br><br>Advanced glaucoma<br><br>Normal tension glaucoma<br><br>Previous laser or surgical glaucoma invention or any previous anterior segment surgery<br><br>Pregnancy<br><br>Ocular condition precluding visualisation of trabecular meshwork<br><br>Impairment preventing adequate understanding to sign an informed consent or cooperate during study procedures<br><br>Potential need for other ocular surgery within the 4–6-month follow-up period<br><br>Unable to comply with intended follow-up visits |
| **Intervention(s)** | **SLT**<br><br>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 goniolens was used, and the laser was focused on the trabecular meshwork. Using a 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**<br><br>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<br><br>Treatment success for IOP control was defined as at least a 20% reduction from baseline measurement. |
| **Number of participants** | SLT (n=20)<br><br>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.<br><br>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**<br><br>Sample size | n = 19 ; % = 48 |
| **Age** (years)<br><br>Custom value | Mean 66.4 (range 43 to 88) |
| **Diagnosis** | |

| Characteristic | Study (N = 40) |
|---|---|
| **OAG**<br><br>Sample size | n = 17 ; % = 43 |
| **OHT**<br><br>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<br>*(Unclear if intention-to-treat analysis was used.)* |
| 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) | *Not applicable* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Some concerns<br>*(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 between* |

| Section | Question | Answer |
|---|---|---|
| | | *the standard clinic appointment and the study appointment to monitor diurnal fluctuation".)* |
| 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<br>*(No information on whether there was a pre-specified analysis plan.)* |
| Overall bias and Directness | Risk of bias judgement | Moderate<br>*(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.)* |
| 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)**

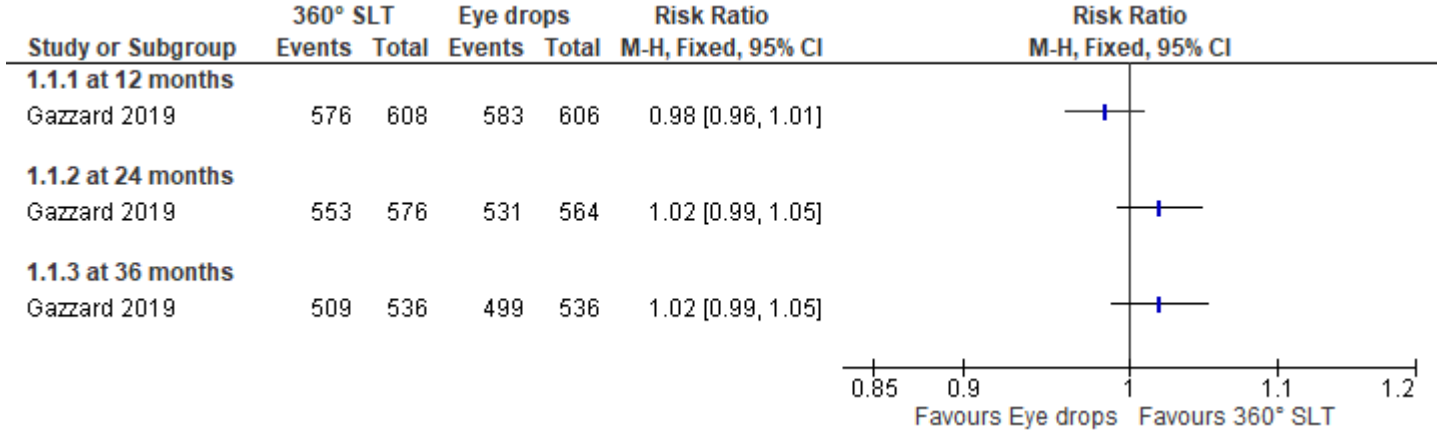
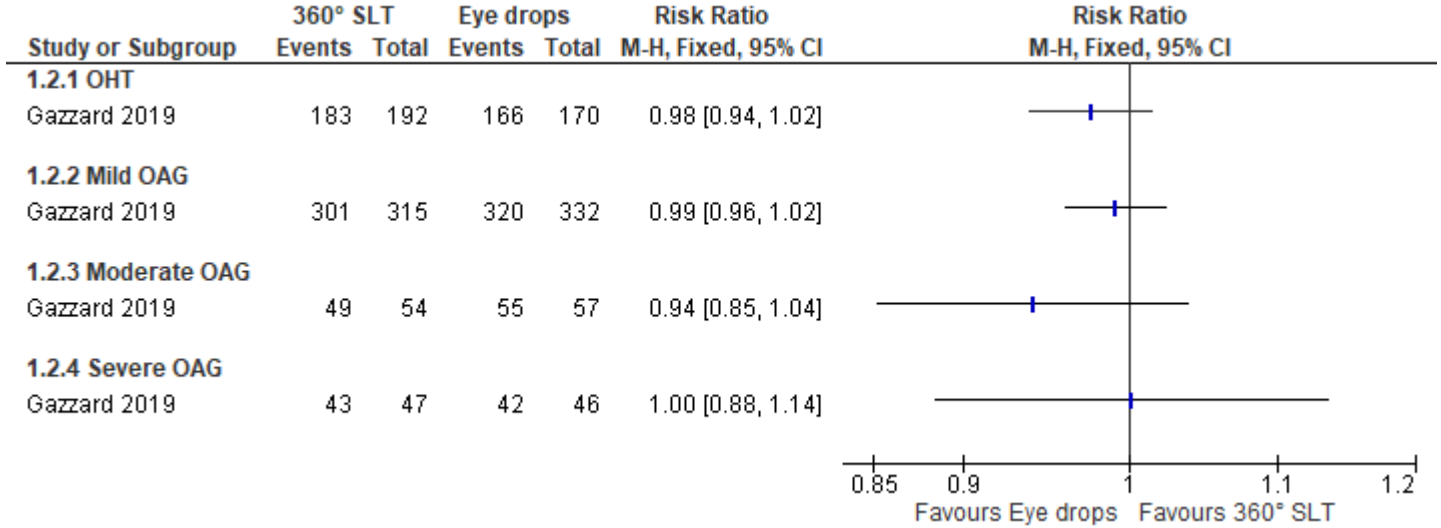
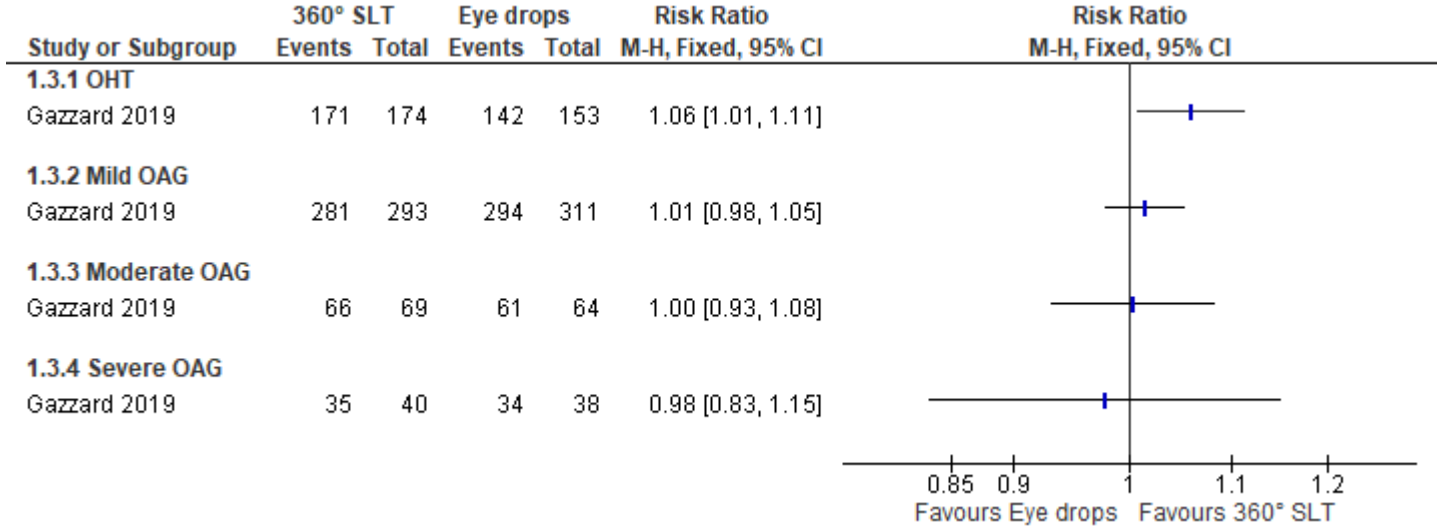


**Figure 2: 360° SLT vs eye drops; Outcome: Eyes at target IOP by type of glaucoma at 12 months (reported by Gazzard 2019 HTA)**



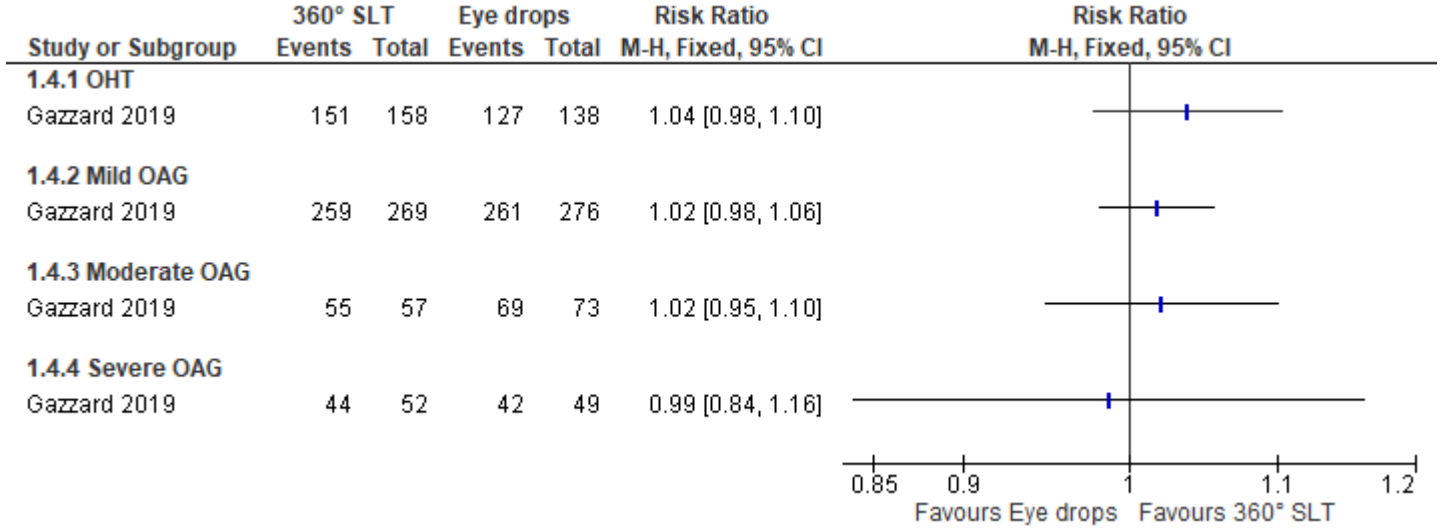

*Totals for each subgroup were calculated by reviewer as Gazzard 2019 HTA only reported percentages*

**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**

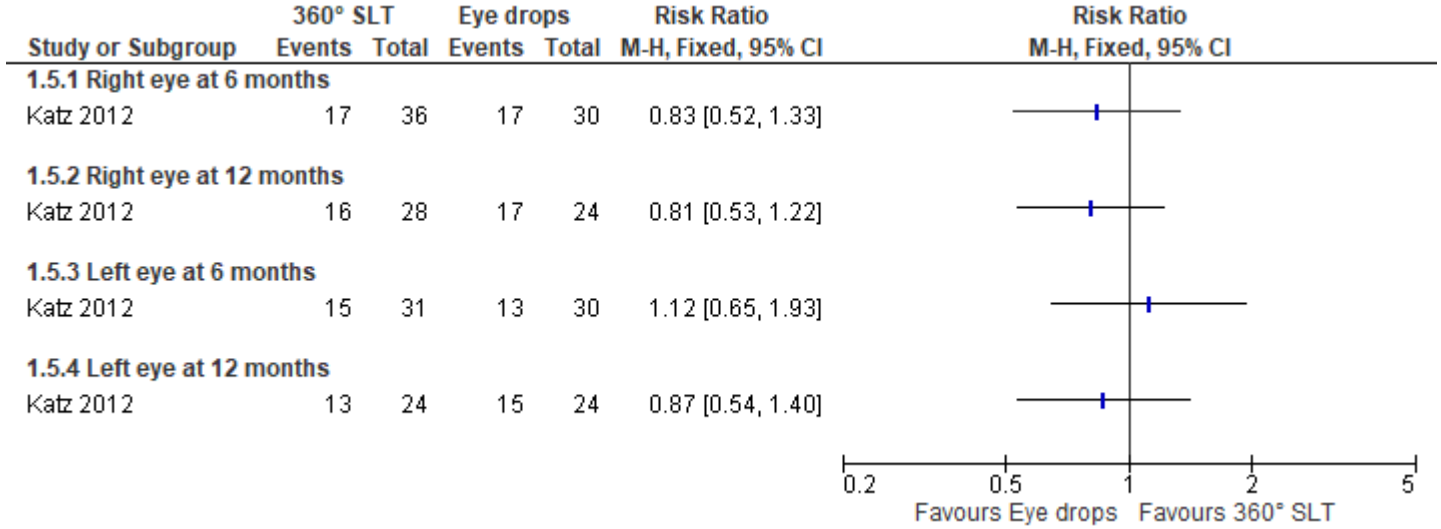
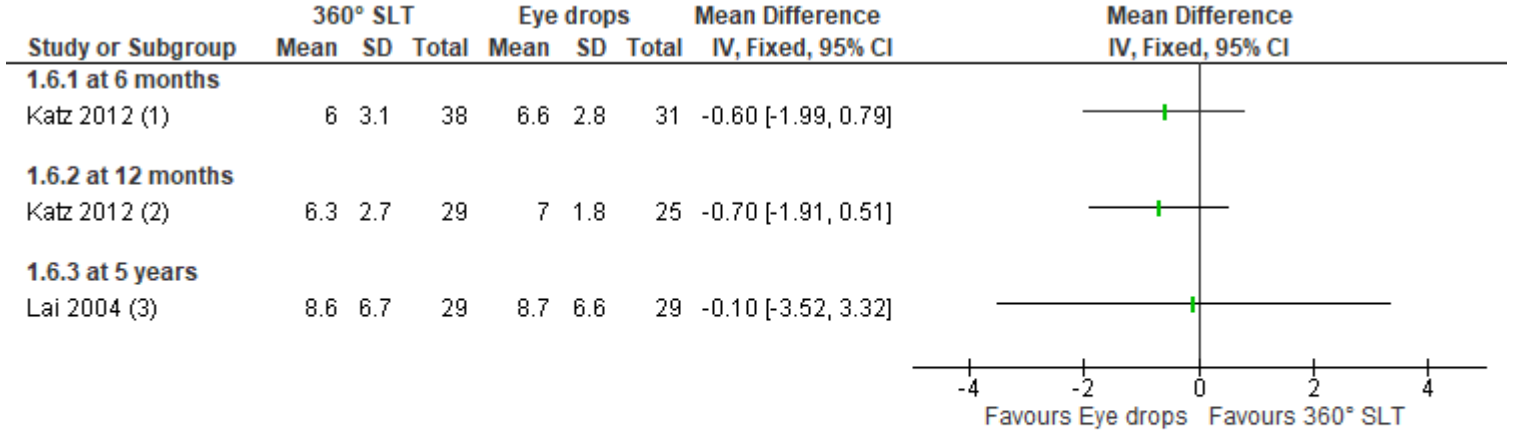


**Figure 6: 360° SLT vs eye drops; Outcome: Mean IOP reduction**




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)**

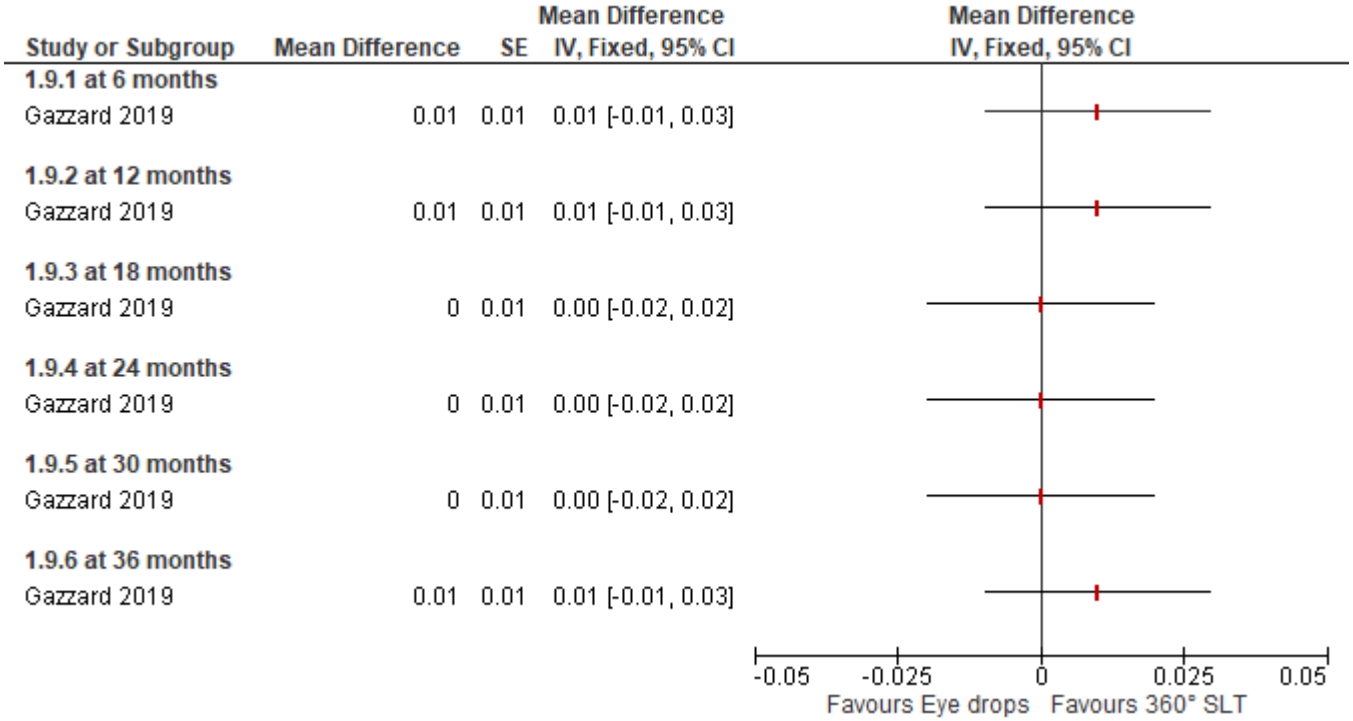


**Figure 8: 360° SLT vs eye drops; Outcome: GUI (reported by Gazzard 2019 Lancet)**

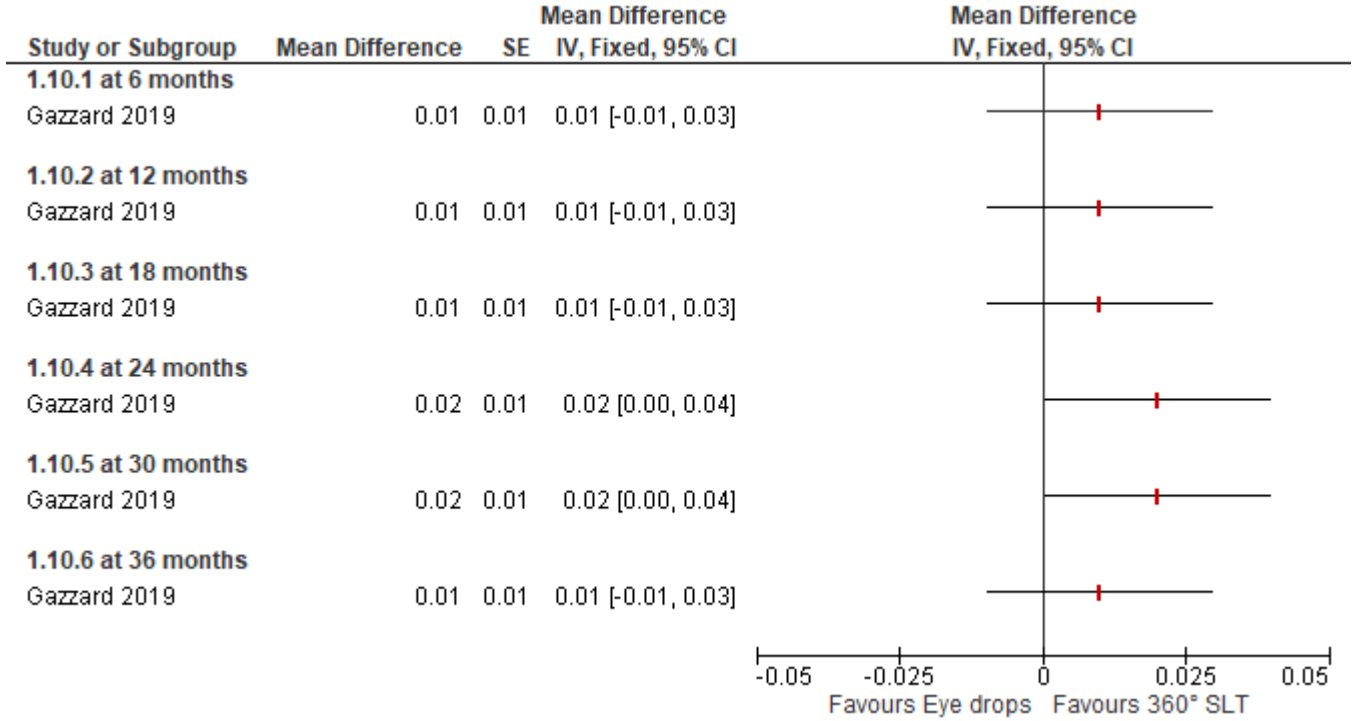


**Figure 9: 360° SLT vs eye drops; Outcome: GQL-15 (reported by Gazzard 2019 Lancet)**

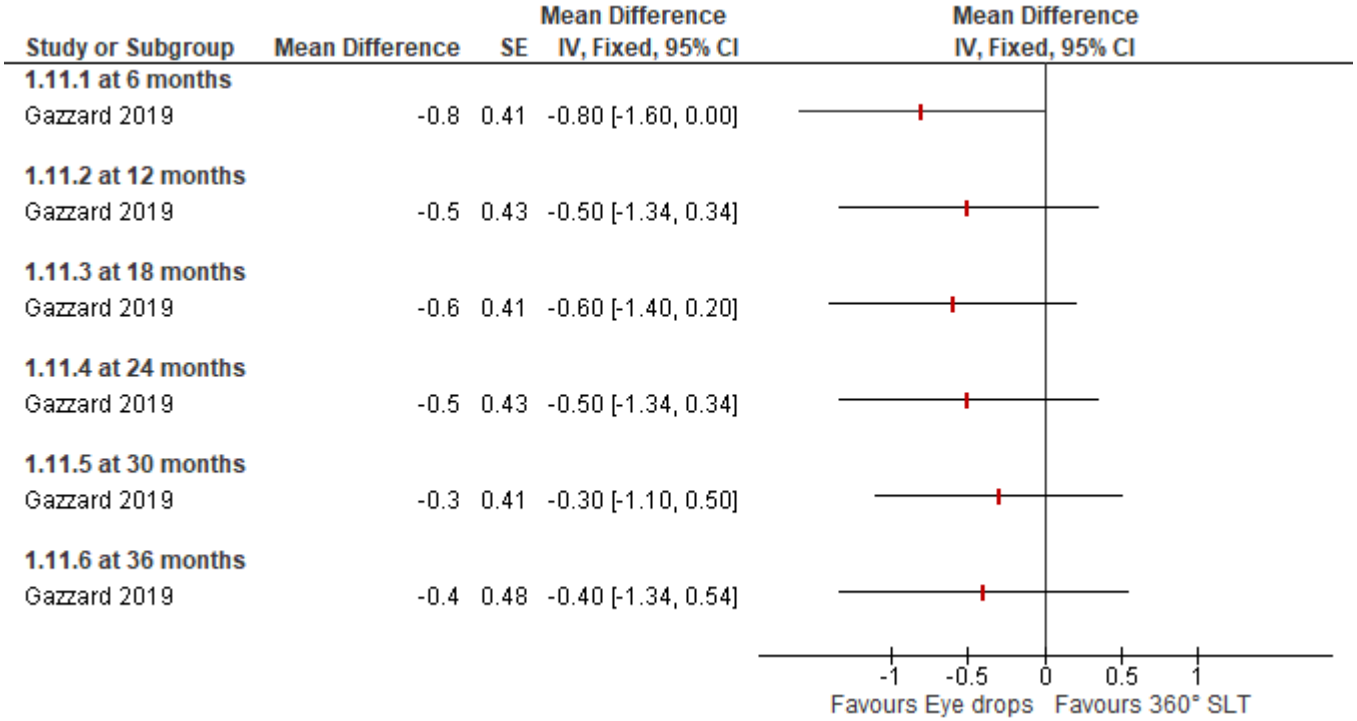


**Figure 10: 360° SLT vs eye drops; Outcome: Ocular adverse events (reported by Gazzard 2019 Lancet)**

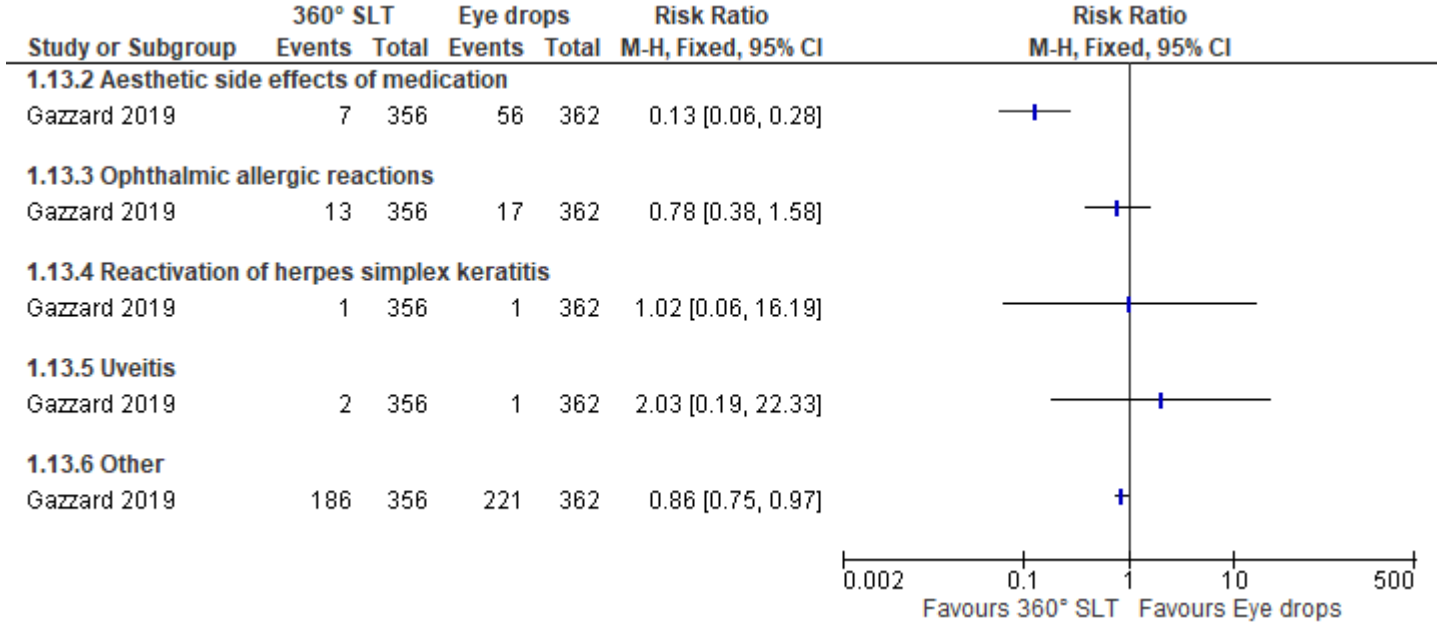


**Figure 11: 360° SLT vs eye drops; Outcome: SLT-related ocular adverse events (reported by Gazzard 2019 Lancet)**

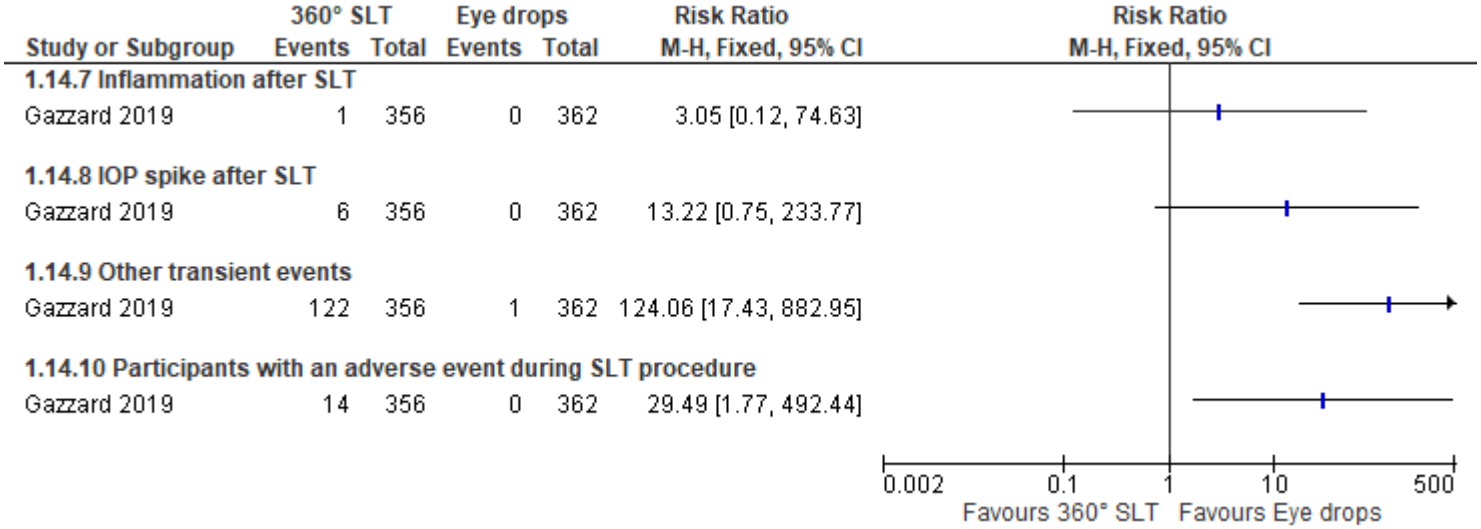


**Figure 12: 360° SLT vs eye drops; Outcome: Systemic adverse events (reported by Gazzard 2019 Lancet)**

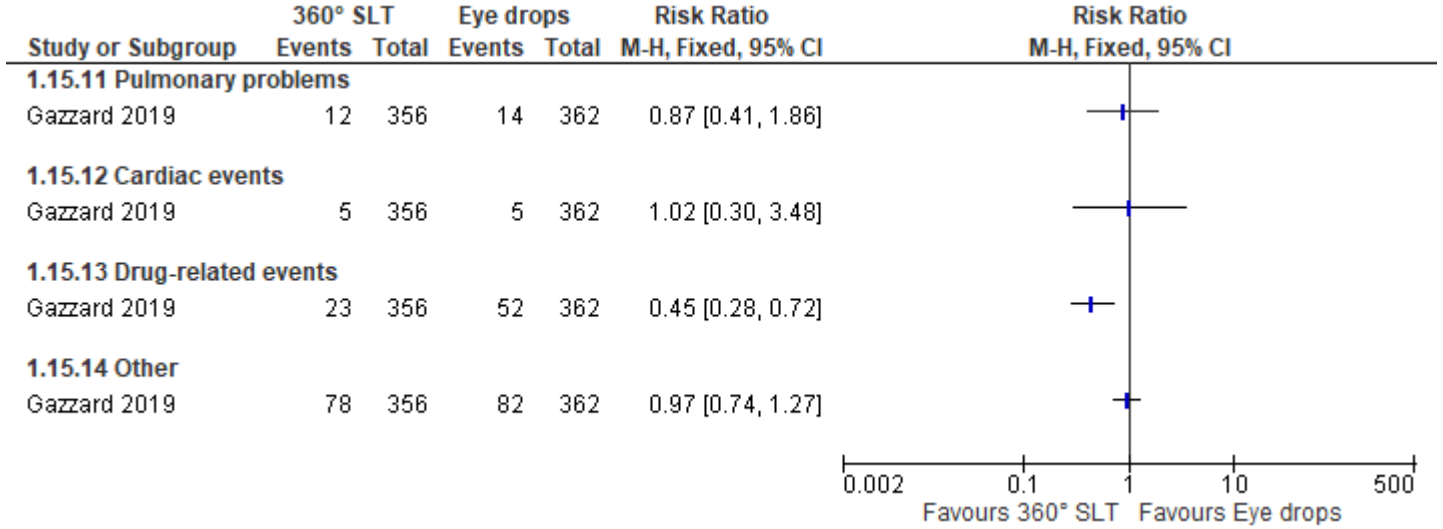
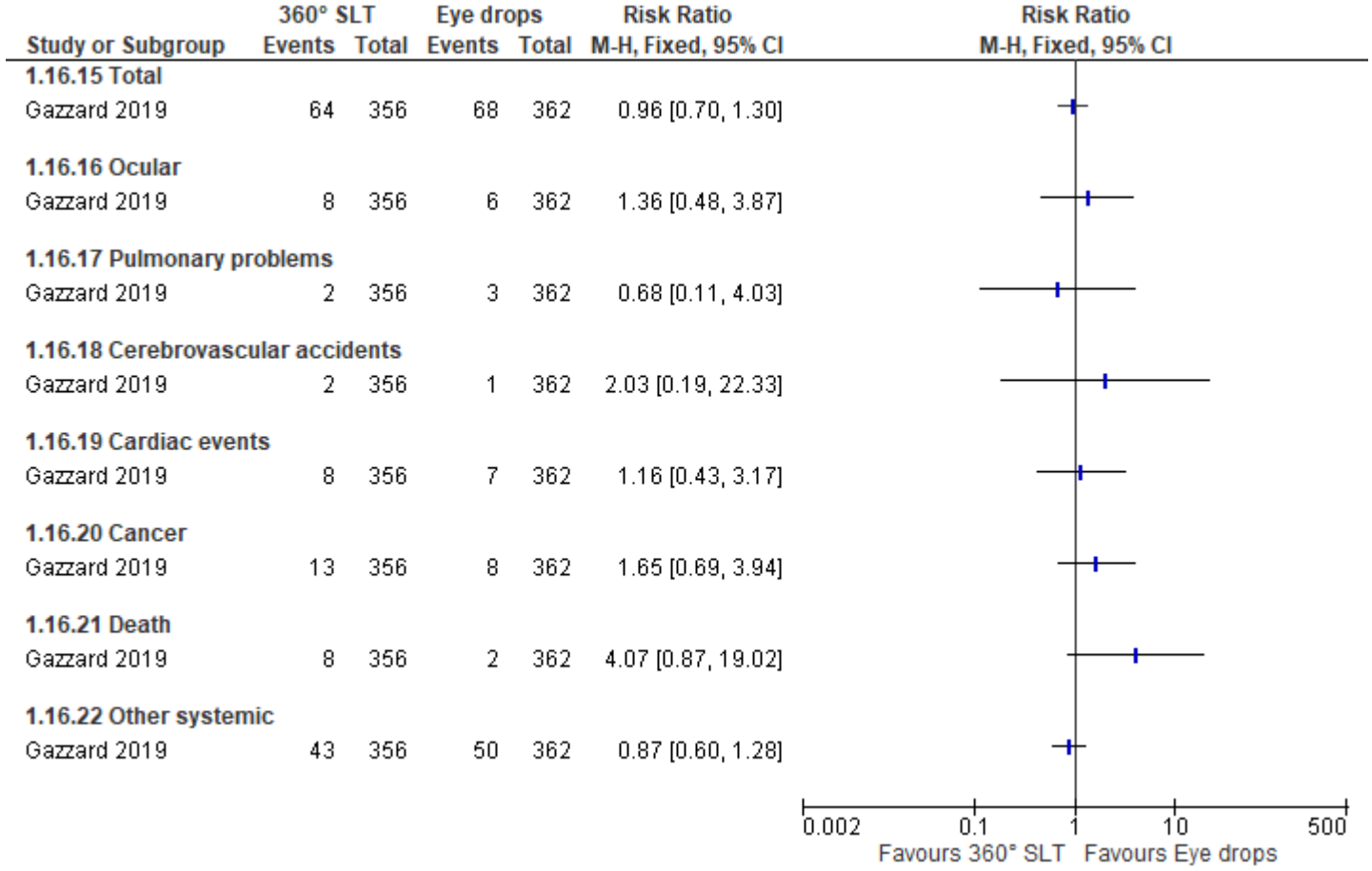


**Figure 13: 360° SLT vs eye drops; Outcome: Serious adverse events (reported by Gazzard 2019 Lancet)**



## Comparison: 360° SLT vs latanoprost

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

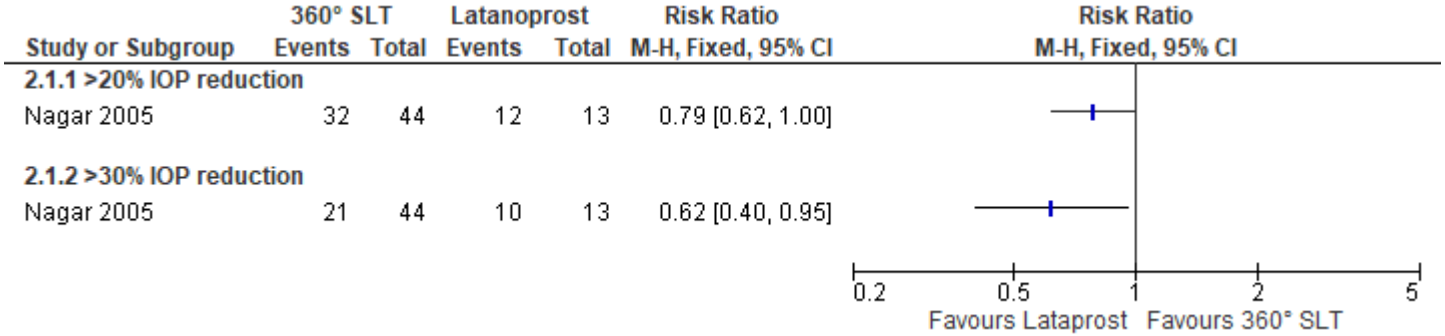
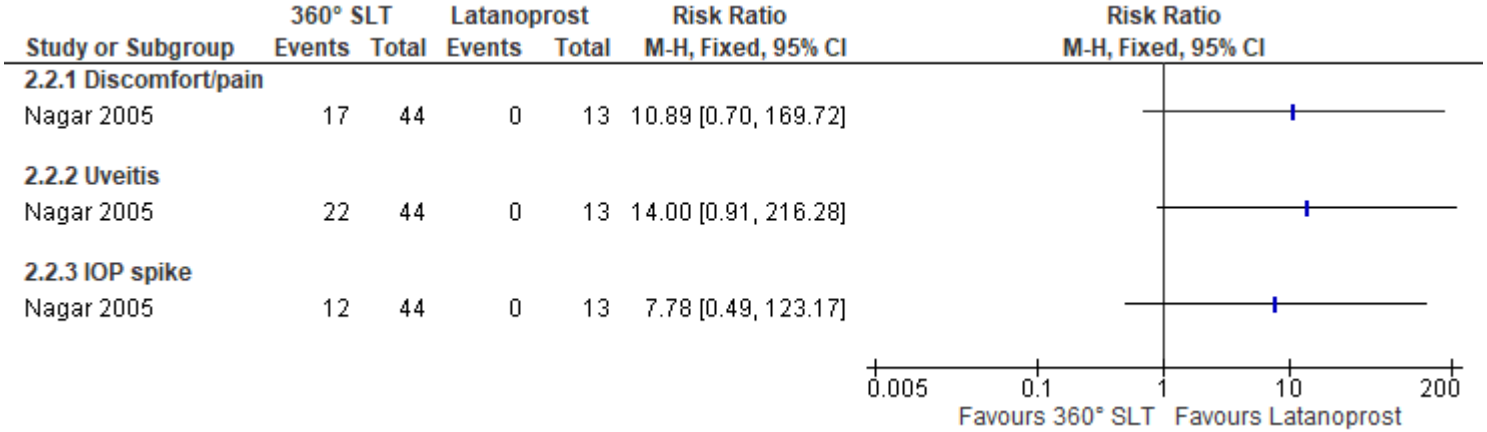



**Figure 15: 360° SLT vs latanoprost; Outcome: Adverse events during first week after treatment**




*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**

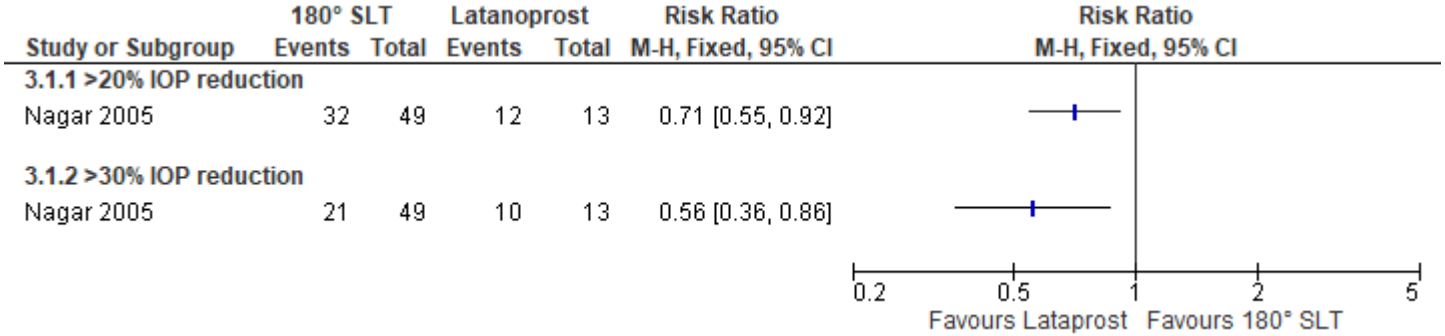
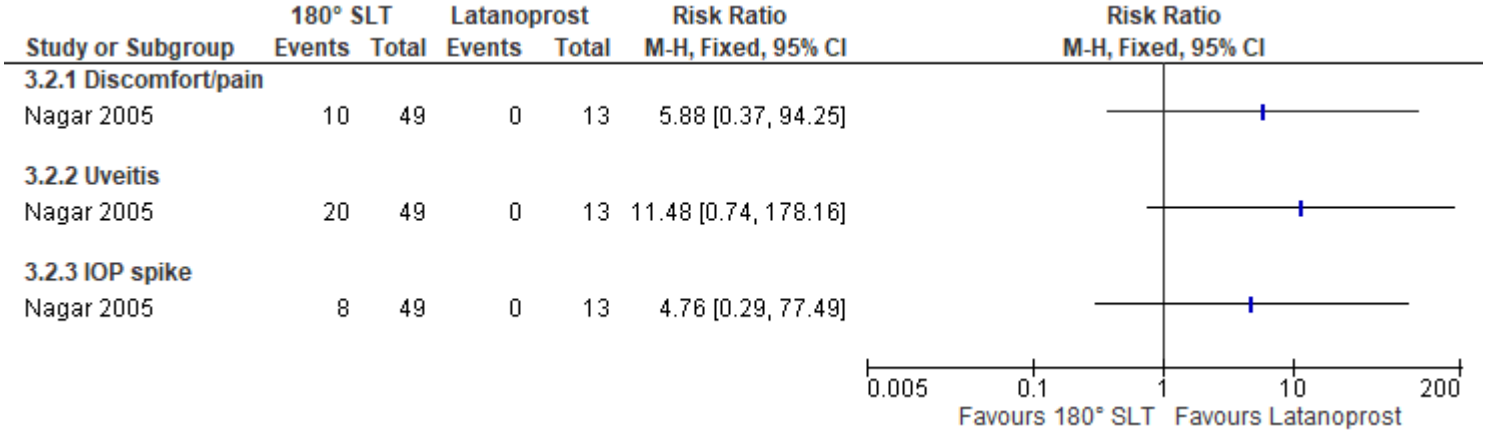



**Figure 17: 180° SLT vs latanoprost; Outcome: Adverse events during first week after treatment**




*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**

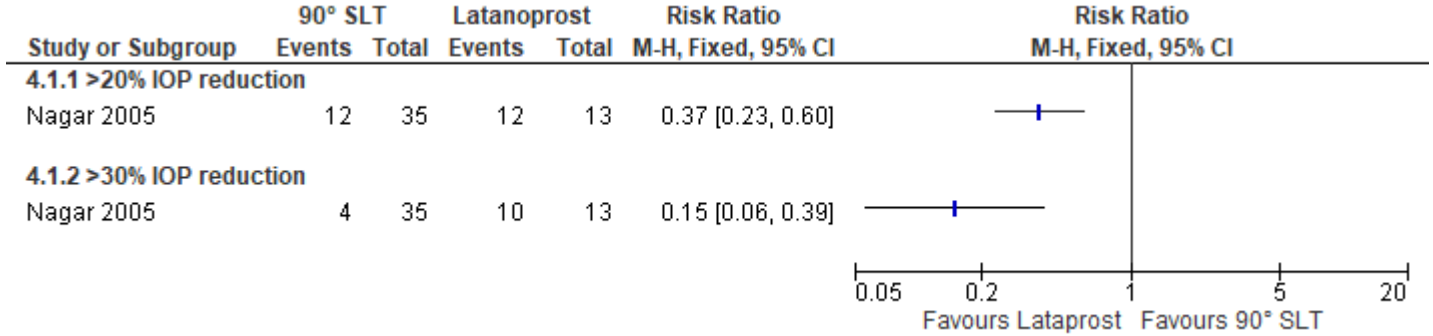
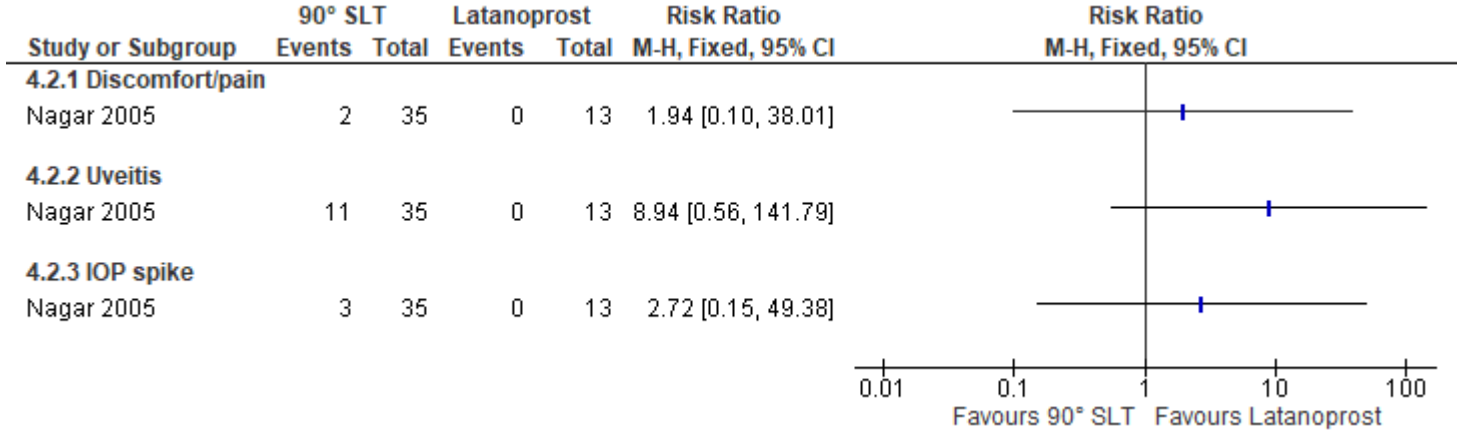


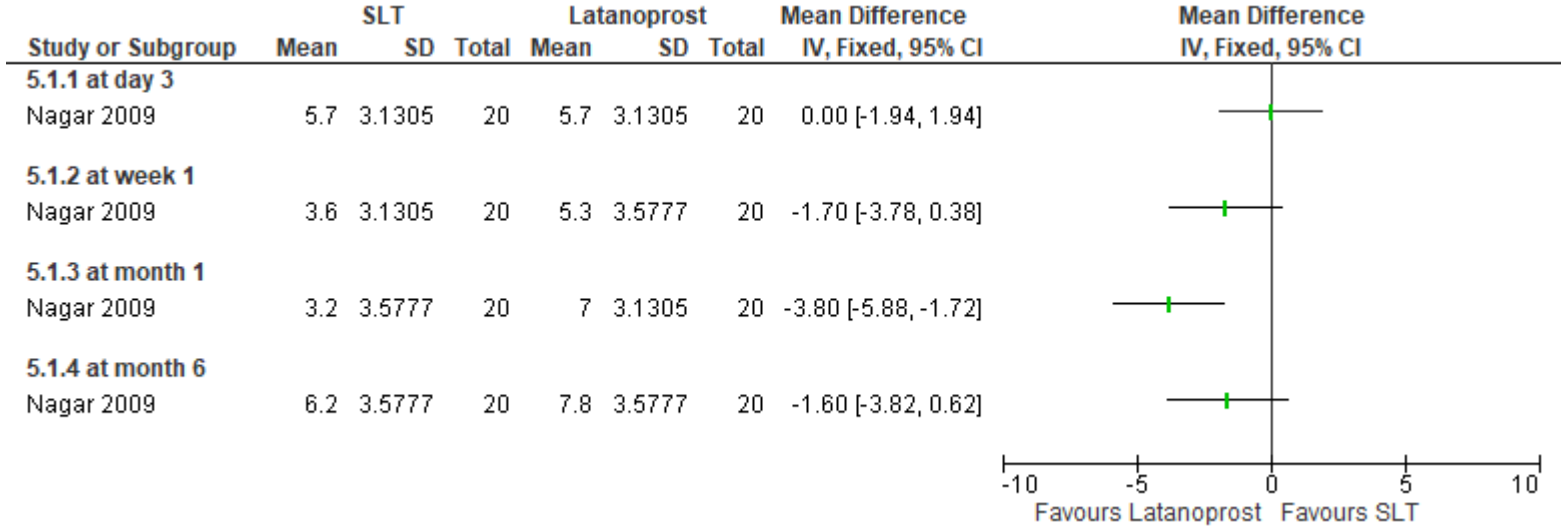

**Figure 19: 90° SLT vs latanoprost; Outcome: Adverse events during first week after treatment**




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

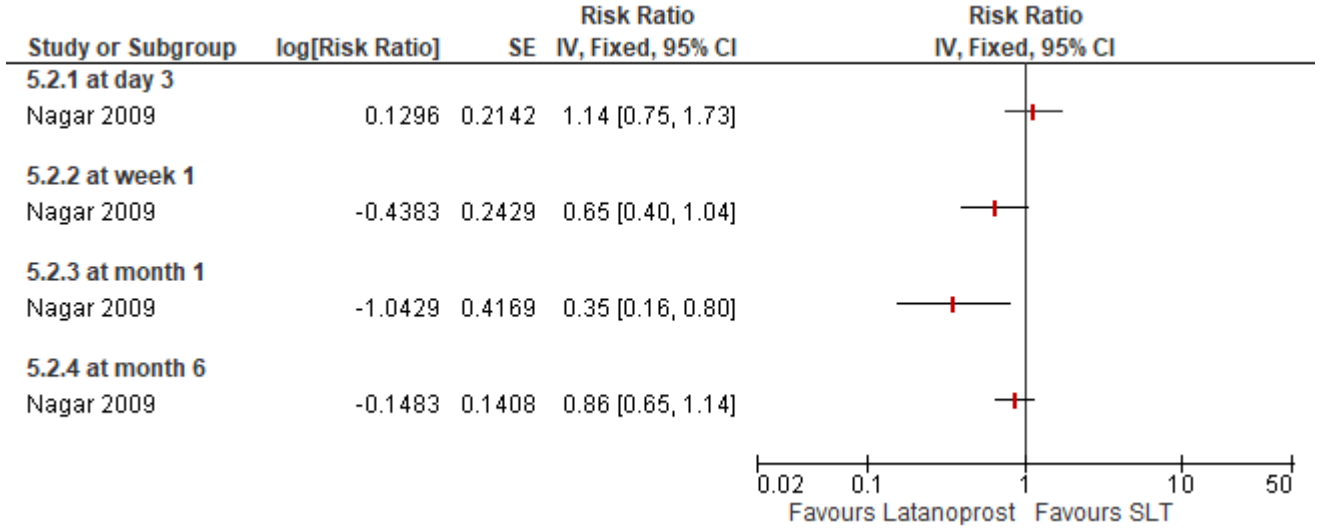
## Comparison: SLT (degree not specified) vs latanoprost

**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)** | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|
| 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**<br>**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 |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | (0.11, 3.97) | | (0 more to 2 more) | | | | | |

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 |

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|---|---|---|---|---|---|---|---|---|---|---|
| **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 |

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*

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**

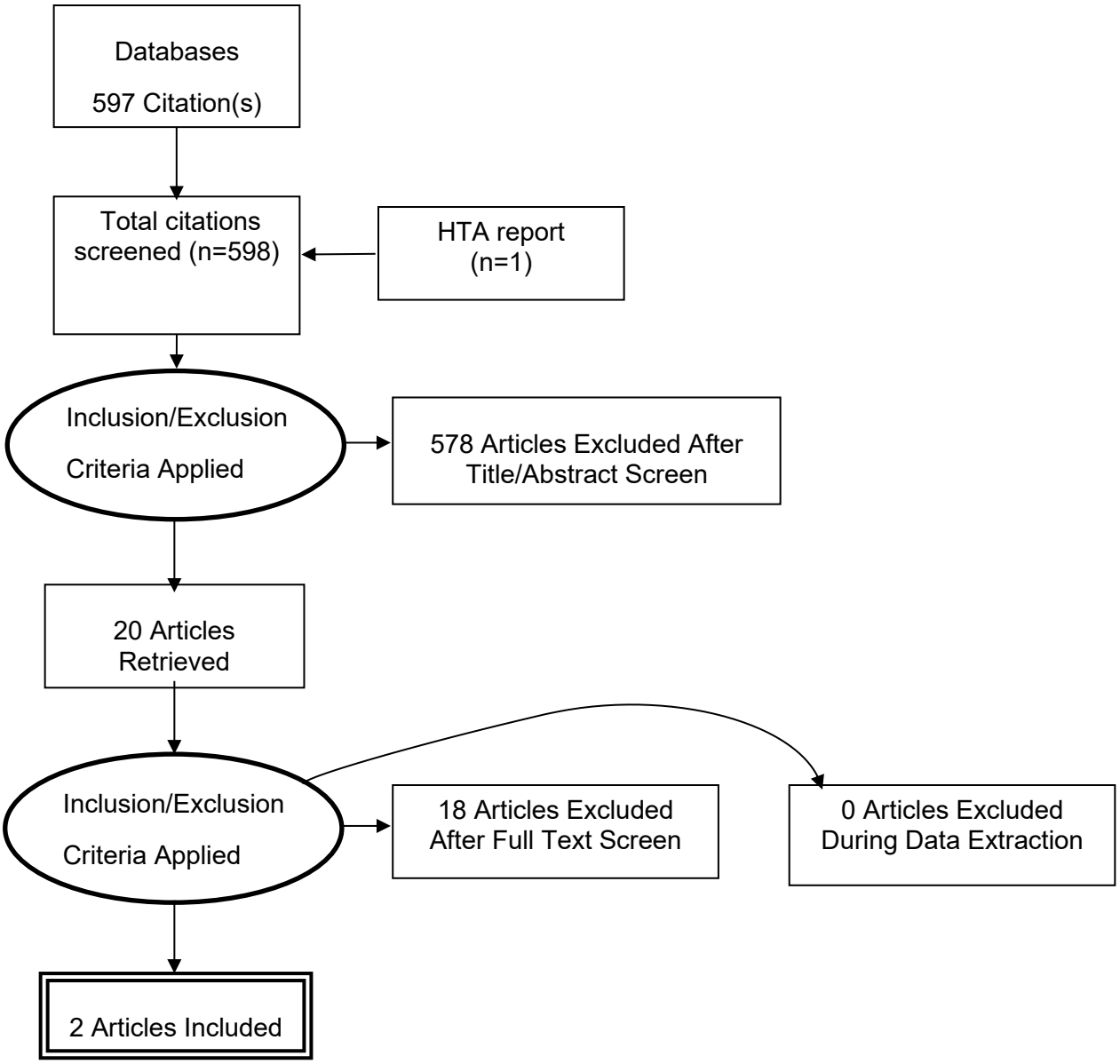
| No. of studies | Study design | Sample size | Effect size (95% CI) | Absolute risk: control | Absolute risk: intervention (95% CI) | Risk of bias | Indirectness | Inconsistency | Imprecision | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| **Mean IOP reduction at day 3 (MD greater than 0 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 |

** 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.*

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<br><br>Minor limitations | UK<br>Hospital setting<br>National health care perspective | **Eye drops**: topical medication to lower intraocular pressure<br><br>**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%<br><br>**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.<br>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<br><br>**Time horizon**: 3 years<br><br>**Discount rate**: 3.5% | **Eye drops:**<br>QALYs: 2.62<br>Costs: £3,993<br><br>**SLT**:<br>QALYs: 2.65<br>Costs: £3,890<br><br>**ICER**: SLT dominates<br><br>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<br>**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<br><br>Minor limitations | UK<br>Hospital setting<br>National health care perspective | **Eye drops**: topical medication to lower intraocular pressure<br><br>**SLT**: primary selective laser trabeculoplasty followed by topical medication | "Assumed to be the same as Gazzard et al. 2019"<br>**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%<br><br>**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.<br>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:**<br>QALYs: 12.3<br>Costs: £20,435<br><br>**SLT**:<br>QALYs: 12.5<br>Costs: £17,541<br><br>**ICER**: SLT dominates<br><br>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<br>**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% | 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.<br>Transition probabilities were obtained from the trial for the first 3 years. Further transition probabilities were extrapolated from the 3-year data.<br>QALYs for each health state were calculated based on glaucoma severity at 35 months and the mean glaucoma utility index.<br>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<br><br>**Time horizon**: lifetime<br><br>**Discount rate**: 3.5% | | | | |

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

**Table 15: Economic evaluation checklist**

| **Study identification**<br>**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<br>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<br>Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.<br>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**<br>**Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.**<br>**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**<br>**Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.**<br>**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 [baseline characteristics show the number of glaucoma medications that participants had before their participation in the study].<br>- The aim of the study was to evaluate the effect of 360° SLT and 0.004% travoprost on the 24-hour circadian IOP of patients with primary open-angle glaucoma and normal-tension glaucoma in habitual positions. |
| Konstantakopoulou, Evgenia, Gazzard, Gus, Vickerstaff, Victoria et al. (2018) The Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre randomised controlled trial: | - Secondary publication of an included study that does not provide any additional relevant information |

| Study | Reason for exclusion |
|---|---|
| baseline patient characteristics. The British journal of ophthalmology 102(5): 599-603 | |
| Lamoureux, Ecosse L, Mcintosh, Rachel, Constantinou, Marios et al. (2015) Comparing the effectiveness of selective laser trabeculoplasty with topical medication as initial treatment (the Glaucoma Initial Treatment Study): study protocol for a randomised controlled trial. Trials 16: 406 | - Participants with primary open angle glaucoma and exfoliation glaucoma (no separate analysis by subtype of glaucoma) |
| Li, Xingyi; Wang, Wei; Zhang, Xiulan (2015) Meta-analysis of selective laser trabeculoplasty versus topical medication in the treatment of open-angle glaucoma. BMC ophthalmology 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. Eye (London, England) 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]. Chinese Journal of Ophthalmology 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. Medwave 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. American Journal of Ophthalmology | - 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. Trials 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. Survey of ophthalmology 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). Ophthalmology 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 | - Only baseline characteristics reported |

| Study | Reason for exclusion |
|---|---|
| Randomized Controlled Trial: Design and Baseline Characteristics. American Journal of Ophthalmology 230: 143-150 | |

**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. Journal of medical economics 20(7): 760-766 | - Study does not contain a relevant intervention<br>*Comparing iStent procedure to medications or SLT*<br><br>- Cost analysis only<br>*No quality of life information* |
| 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. Current medical research and opinion 24(10): 2905-18 | - Cost analysis only<br>*No quality of life data* |
| 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. Clinical drug investigation 29(2): 111-20 | - Cost analysis only<br>*No quality of life data* |
| 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 | - Non economic evaluation<br>*No results* |
| 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 | - Secondary publication of an included study that does not provide any additional relevant information<br>*Light study, already included* |
| 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. Medicine 95(52): e5745 | - Perspective not transferable<br>*Brazilian health care system* |
| 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. JAMA ophthalmology 133(5): 560-7 | - Study does not contain a relevant intervention<br>*Does not include SLT, only Trabeculectomy* |

| Study | Code [Reason] |
|---|---|
| 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 | - Non-economic evaluation<br>*No ICER reported, Light trial included* |
| 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<br>*Does not include SLT* |
| 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<br>*No quality of life data* |
| Sawchyn, Andrea K and Slabaugh, Mark A (2016) Innovations and adaptations in trabeculectomy. Current opinion in ophthalmology 27(2): 158-63 | - Non economic evaluation<br>*Does not include an ICER* |
| 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<br>*Does not include an ICER* |
| 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<br>*Compares Argon laser trabeculoplasty not SLT* |
| Stewart, William C, Stewart, Jeanette A, Nasser, Qasiem J et al. (2008) Cost-effectiveness of treating ocular hypertension. Ophthalmology 115(1): 94-8 | - Study does not contain a relevant intervention<br>*Uses Argon laser trabeculoplasty not SLT* |
| 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<br>*Watchful waiting is the comparator* |

| Study | Code [Reason] |
|---|---|
| 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<br>*Plan of the Light trial, no results* |
| 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<br>*Not an incremental cost effectiveness study, not possible to calculate an ICER* |

# 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 with 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 of 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 | Inclusion:<br>• Adults (18 and over) with OHT<br>• Adults (18 and over) with COAG<br><br>Exclusion:<br>• People who have received first line treatment for OHT or COAG,<br>• People with secondary glaucoma, for example, neovascular or uveitic glaucoma<br>• People with, or at risk of, primary or secondary angle closure glaucoma |

| | |
|---|---|
| | • People with primary congenital, infantile or childhood glaucoma<br>• People with angle closure |
| Intervention | Selective laser trabeculoplasty |
| Comparator | Intraocular pressure-lowering eye drops alone |
| Outcome | • Progression of glaucomatous visual field defect<br>• Vision loss<br>• Progression of optic nerve head damage<br>• Conversion of OHT to COAG |
| Study design | Randomised controlled trial |
| Timeframe | 3 years or more, 5 years and 10 years follow-up |
| Additional information | Subgroups:<br>• Degree of pigmentation<br>• Initial IOP<br>• Ethnicity<br>• 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 | 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.<br>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.<br>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.<br>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 |
| Indirectness | 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.<br>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.<br>Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels. |
| Inconsistency | 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.<br>N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study.<br>Not serious: If the $I^2$ was less than 33.3%, the outcome was not downgraded.<br>Serious: If the $I^2$ was between 33.3% and 66.7%, the outcome was downgraded one level.<br>Very serious: If the $I^2$ was greater than 66.7%, the outcome was downgraded two levels. |
| Imprecision | 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.<br>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.<br>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. |
| Publication bias | 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. |

# 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 18: 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<br>• Three medications<br>• Four medications | 21 (3.9)<br>4 (0.8)<br>1 (0.2) | 99 (18.5)<br>35 (6.5)<br>3 (0.6) |

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

*(b) Includes eyes that had undergone trabeculectomy.*