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Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery (Review)

Day AC, Gore DM, Bunce C, Evans JR

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[Intervention Review]

Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery

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ABSTRACT

Background

Cataract is the leading cause of blindness in the world, and cataract surgery is one of the most commonly performed operations in the Western world. Preferred surgical techniques have changed dramatically over the past half century with associated improvements in outcomes and safety. Femtosecond laser platforms that can accurately and reproducibly perform key steps in cataract surgery, including corneal incisions, capsulotomy and lens fragmentation, are now available. The potential advantages of laser-assisted surgery are broad, and include greater safety and better visual outcomes through greater precision and reproducibility.

Objectives

To compare the effectiveness of laser-assisted cataract surgery with standard ultrasound phacoemulsification cataract surgery by gathering evidence on safety from randomised controlled trials (RCTs).

Search methods

We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 4), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to May 2016), EMBASE (January 1980 to May 2016), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to May 2016), the ISRCTN registry (www.isrctn.com/ editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov), the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en) and the U.S. Food and Drugs Administration (FDA) website (www.fda.gov). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 10 May 2016.

Selection criteria

We included randomised controlled trials where laser-assisted cataract surgery was compared to standard ultrasound phacoemulsification cataract surgery. We graded the certainty of the evidence using GRADE.

Data collection and analysis

Two review authors independently screened the search results, assessed risk of bias and extracted data using the standard methodological procedures expected by Cochrane. The primary outcome for this review was intraoperative complications in the operated eye, namely anterior capsule and posterior capsule tears. The secondary outcomes were visual acuity (corrected distance visual acuity (CDVA) and uncorrected distance visual acuity (UDVA)), refractive outcomes, quality of vision (as measured by any validated visual function score), postoperative complications and cost-effectiveness.

Main results

We included 16 RCTs conducted in Germary, Hungary, Italy, India, China and Brazil that enrolled a total of 1638 eyes of 1245 adult participants. Overall, the studies were at unclear or high risk of bias. In 11 of the studies the authors reported financial links with the manufacturer of the laser platform evaluated in their studies. Five of the studies were within-person (paired-eye) studies with one eye allocated to one procedure and the other eye allocated to the other procedure. These studies were reported ignoring the paired nature of the data.

The number of anterior capsule and posterior capsule tears reported in the included studies for both laser cataract surgery and manual phacoemulsification cataract surgery were low. There were four anterior capsule tears and one posterior capsule tear in 1076 eyes reported in 10 studies (2 anterior capsule tears in laser arms, 2 anterior capsule tears and 1 posterior capsule tear in standard phacoemulsification arms). We are very uncertain as to the effect of laser-assisted surgery compared to standard phacoemulsification surgery with respect to these two outcomes. For postoperative cystoid macular oedema and elevated postoperative intraocular pressures, again the evidence was inconclusive (odds ratio (OR) 0.58, 95% confidence interval (CI) 0.20 to 1.68; 957 eyes, 9 studies, low certainty evidence; and OR 0.57, 95% CI 0.11 to 2.86; 903 eyes, 8 studies, low certainty evidence).

We found little evidence of any important difference in postoperative visual acuity between laser-assisted and standard phacoemulsification arms. There was a small advantage for laser-assisted cataract surgery at six months in CDVA. However, the mean difference (MD) was -0.03 logMAR (95% CI -0.05 to -0.00; 224 eyes, 3 studies, low certainty evidence) which is equivalent to 1.5 logMAR letters and is therefore, clinically insignificant. No studies reported patient-reported outcome measures such as visual function.

There were no data reported on costs or resource use but three studies reported the time taken to do the surgery. There was little evidence of any major difference between the two procedures in this respect (MD 0.1 minutes, 95% CI -0.02 to 0.21; 274 eyes, low certainty evidence).

Authors' conclusions

The evidence from the 16 randomised controlled trials RCTs included in this review could not determine the equivalence or superiority of laser-assisted cataract surgery compared to standard manual phacoemulsification for our chosen outcomes due to the low to very low certainty of the evidence available from these studies. As complications occur rarely, large, adequately powered, well designed, independent RCTs comparing the safety and efficacy of laser-assisted cataract surgery with standard phacoemulsification cataract surgery are needed. Standardised reporting of complications and visual and refractive outcomes for cataract surgery would facilitate future synthesis. Data on patient-reported outcomes and cost-effectiveness are needed. Paired-eye studies should be analysed and reported appropriately.

PLAIN LANGUAGE SUMMARY

Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery

What is the aim of this review?

The aim of this Cochrane Review was to find out what the benefits and harms of laser-assisted cataract surgery are compared with standard ultrasound phacoemulsification cataract surgery. Cochrane researchers collected and analysed all relevant studies to answer this question and found 16 studies.

Key messages

There is currently not enough evidence to determine the benefits and harms of laser-assisted cataract surgery compared with standard ultrasound cataract surgery. The evidence is uncertain because current studies have not been large enough to provide a reliable answer to this question.

What was studied in the review?

As people become older, the lens inside the eye can become cloudy. This is known as a cataract, and it is the leading cause of blindness in the world. Cataract surgery is one of the most commonly performed operations. During standard cataract surgery, the doctor removes the cloudy lens material and places an artificial lens in the remaining bag or capsule. The aim of laser-assisted cataract surgery is to provide more precise control over the steps involved in cataract surgery. This could make it easier to do the operation more reliably, and faster, than if it is done in the standard way. This may result in fewer complications, such as tears to the person's lens capsule, which in turn could lead to better vision and quality of life for people who have had cataract surgery.

What are the main results of the review?

The review authors found 16 relevant studies. Most studies (13) were from Europe and three studies were from Brazil, India and China. All these studies compared laser-assisted cataract surgery with standard ultrasound phacoemulsification cataract surgery for people with cataracts. Eleven of the studies were either funded by the manufacturer of the laser machine or the investigators reported financial links with the manufacturer.

The review authors were uncertain as to whether laser-assisted cataract surgery reduces the number of tears to the capsule because there were very few cases of capsule tears in these studies. They judged this as very low certainty evidence.

Other complications were also infrequent for both laser-assisted and standard cataract surgery. The authors judged this as low certainty evidence.

There may be little difference in vision after laser-assisted cataract surgery compared with standard cataract surgery (low certainty evidence).

Laser-assisted cataract surgery and standard cataract surgery may require the same amount of theatre time (low certainty evidence).

None of the studies reported the effect of the operations on people's quality of life.

How up-to-date is this review?

The review authors searched for studies that had been published up to 16 May 2016.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery

Patient or population: people with age-related cataract
Setting: eye hospital
Intervention: laser-assisted cataract surgery
Comparison: standard ultrasound phacoemulsification cataract surgery

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of eyes (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard ultrasound phacoemulsification	Risk with laser-assisted cataract surgery				
Intraoperative complications: anterior capsule tear	Only 4 events, 2 in each group		-	1076 (10 RCTs)	⊕◯◯◯ Very low [1]	
Intraoperative complications: posterior capsule tear	Only 1 event, in standard group		-	1076 (10 RCTs)	⊕◯◯◯ Very low [2]	
Corrected distance visual acuity assessed with: logMAR acuity chart (lower scores = better vision, scale from: -0.3 to 1.3) at least six months after surgery	The mean corrected distance visual acuity ranged from 0.038 to -0.03 logMAR units	The mean corrected distance visual acuity in the intervention group was 0.03 logMAR units lower (better vision) (0.05 lower to 0.00)	-	224 (3 RCTs)	⊕⊕◯◯ Low [3]	
Patient reported outcome measures (PROMs) at least one month after surgery	See comments					Not reported

Postoperative complications: cystoid macular oedema	20 per 1000	11 per 1000 (4 to 33)	OR 0.58 (0.20 to 1.68)	957 (9 RCTs)	⊕⊕◯◯ Low [3]	
Postoperative complications: elevated intraocular pressure (1 day to 1 week after surgery)	13 per 1000	8 per 1000 (2 to 33)	OR 0.57 (0.11 to 2.86)	903 (8 RCTs)	⊕⊕◯◯ Low [3]	
Costs and resource use: total duration of procedure	The mean total duration of procedure in the control group ranged from 6.04 to 10.5 minutes	The mean total duration of procedure in the intervention group was 0.10 minutes more (0.02 fewer to 0.21 more)	-	274 (3 RCTs)	⊕⊕◯◯ Low [3]	No information on costs or other resources reported.

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

CI: confidence interval; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded for: risk of bias (-1) because studies were poorly reported and largely judged to be at unclear or high risk of bias; imprecision (-1) because very few events; inconsistency as effect estimates in the 3 trials reporting events were 0.33, 1.13 and 3.03.
[2] Downgraded for: risk of bias (-1) and imprecision (-2) as only 1 event.
[3] Downgraded for risk of bias (-1) and imprecision (-1) as effect estimate imprecise with 95% CIs including or close to null (no effect).

BACKGROUND

Description of the condition

Age-related cataract is the leading cause of visual impairment worldwide (Quigley 2006); and cataract surgery is the most commonly performed eye operation worldwide, with an estimated 19.5 million procedures carried out in 2011 (Lawless 2012). Preferred surgical techniques have changed dramatically over the past half century, with associated improvements in outcomes and safety (Riaz 2006). With this increase in safety and improvements in visual outcomes, lens extraction with intraocular lens implantation is now increasingly performed for the treatment of other conditions, including refractive error and angle closure glaucoma (Friedman 2006; Packard 2005).

Description of the intervention

Lasers have been used in corneal surgery for over a decade. More recently, femtosecond laser platforms that may accurately and reproducibly perform key steps in cataract surgery, including corneal incisions, capsulotomy and lens fragmentation, are now available. The potential advantages of laser-assisted surgery are broad and include greater safety and better visual outcomes through greater precision and reproducibility. These systems are expensive at outset; however, the costs may be mitigated by a reduction in complication rates, less repeat surgery and better patient outcomes.

How the intervention might work

Phacoemulsification (ultrasound) is a highly successful technique first introduced over 40 years ago. It is the standard method of cataract surgery today in higher income countries, with reported rates of major complications (posterior capsule rupture or vitreous loss) of 1.95% (95% confidence interval (CI) 1.89% to 2.02%); and overall intraoperative complication rates of 4.2% (95% CI 4.1 to 4.3%) (Day 2015). It consists of a series of manual steps, including corneal incision creation, capsulorhexis (circular opening of the front of the cataract lens capsule), removal of the cataract with ultrasound and placement of an intraocular lens into the capsular bag. Each step is dependent on successful completion of the preceding steps and, therefore, surgical ability is critical to visual outcome.

Femtosecond lasers have revolutionised corneal surgery such as for LASIK flap creation, and femtosecond laser cataract surgery platforms are now available. These can automate over half of these steps including creation of the corneal incisions (with or without additional incision to reduce astigmatism), capsulotomy and lens fragmentation, facilitating lens removal. The remaining steps are removal of the fragmented crystalline lens and insertion of the intraocular lens, which still have to be completed by hand. The femtosecond laser platforms use photo-dissection to create tissue planes accurate to 5μm in the anterior segment through the formation of cavitation bubbles, and as the focused pulses are ultrashort (10^{-15} seconds), this is thought to almost eliminate any collateral damage to surrounding tissues (Donaldson 2013). The laser energy imparted to the eye, however should not be considered to be insignificant.

While the overall range of possible operative complications in either laser-assisted or manual phacoemulsification surgery are similar, rates would be expected to be lower in laser-assisted procedures as laser completed steps should be more precise and more reproducible than those completed by hand. Ultimately, this should also translate to fewer complications and better patient outcomes.

There is increasing evidence to support an advantage for laser-assisted procedures with more accurate capsulotomy positioning, shape and size reported when compared to manual capsulorhexis (Friedman 2011; Kránitz 2011; Nagy 2011). This is associated with better intraocular lens centration (ensuring correct centring of the lens) (Kránitz 2011; Kranitz 2012; Nagy 2011), and less intraocular lens tilt with fewer internal higher order aberrations (Kranitz 2012; Mihältz 2011). By using a laser to fragment the crystalline lens, less phacoemulsification (ultrasound) energy is subsequently required to complete its removal. Reductions in effective phacoemulsification time have been reported, with zero phacoemulsification time being possible in 30% of operations in a series by Abell 2013. This study also reported a 36% lower endothelial cell loss in the laser-assisted procedures compared to the manual phacoemulsification (Abell 2013).

Data on the surgical learning curve (Bali 2012; Roberts 2013a), and complication rates in laser-assisted cataract surgery procedures have been reported in large case-series (Roberts 2013a, Abell 2015; Chee 2015), with the complication rates appearing favourable when compared to those from large series of manual phacoemulsification (Roberts 2013a).

A recent large comparative case-series of more than 4000 eyes undergoing cataract surgery (1852 eyes in a laser-assisted group versus 2228 eyes in a standard phacoemulsification group) reported that both techniques appeared "equally safe" and that rates of significant intraoperative complications were low (Abell 2015). A recent case-series of 1105 eyes undergoing laser-assisted cataract surgery reported a 0.81% anterior capsule tear rate and a 0.27% posterior capsule tear rate (Chee 2015). Studies comparing postoperative visual acuities and intraocular lens power calculation predictability for laser-assisted surgery with manual phacoemulsification procedures have shown inconsistent results with some reporting better CDVA (Kranitz 2012), higher proportions of those achieving 20/20 or better UDVA (Chee 2015), and better intraocular lens power predictability for laser-assisted surgery (Filkorn 2012), whilst others have reported no difference in CDVA (Filkorn 2012; Lawless 2012; Mihältz 2011), UDVA (Lawless 2012; Mihältz 2011) or intraocular lens power predictability (Lawless 2012; Roberts 2013b).

Why it is important to do this review

Laser-assisted lens surgery platforms are now increasingly being used for lens extraction and intraocular lens implantation. There are currently five commercially available systems in Europe: Catalys™ (Abbott Medical Optics), LENSAR™ (LENSAR Inc), LenSx® (Alcon), VICTUS™ (Bausch & Lomb Inc) and the Femto LDV Z8 (Ziemer). The aims of this review are to compare effectiveness of laser-assisted cataract surgery with standard phacoemulsification cataract surgery and gather evidence from RCTs on safety.

OBJECTIVES

To compare the effectiveness of laser-assisted cataract surgery with standard phacoemulsification cataract surgery by gathering evidence on safety from randomised controlled trials (RCTs).

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) that met the inclusion criteria.

Types of participants

We included all participants who were enrolled in the respective RCT whereby either the participant or one of their eyes was randomised to either laser-assisted cataract surgery or standard phacoemulsification and intraocular lens implantation. Participants were adults (18 years old or more).

Types of interventions

We included all RCTs comparing laser-assisted cataract surgery to standard ultrasound phacoemulsification, with implantation of a posterior chamber intraocular lens in both techniques.

Types of outcome measures

Primary outcomes

The primary outcome was intraoperative complications in the operated eye.

Secondary outcomes

The secondary outcomes for this review were the following.

- Distance visual acuity in the operated eye after initial cataract surgery. We considered corrected distance visual acuity (CDVA) and uncorrected distance visual acuity (UDVA) separately. CDVA demonstrates intervention safety, whilst UDVA demonstrates intervention efficacy (see How the intervention might work above). We considered long-term data, where reported.
- Patient reported outcome measures (PROMs) at least one month after surgery. These include patient satisfaction and/or vision-related quality of life as measured by any validated questionnaire, such as the Catquest-9SF.
- Any postoperative or long-term complications reported within one year of initial surgery. We anticipated these may be reported as overall risk of any complication, or more specifically such as cystoid macular oedema, elevated intraocular pressure, corneal decompensation, retinal detachment and posterior capsule opacification.
- Costs and resource use (e.g. total duration of procedure, number of operating rooms/practitioners).
- Refractive outcomes, including deviation from the predicted refractive outcome.

Search methods for identification of studies

Electronic searches

We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 4), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to May 2016), EMBASE (January 1980 to May 2016), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to May 2016), the ISRCTN registry (www.isrctn.com/editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov), the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en) and the U.S. Food and Drugs Administration (FDA) website (www.fda.gov). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 10 May 2016. See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), LILACS (Appendix 4), ISRCTN (Appendix 5), ClinicalTrials.gov (Appendix 6), the ICTRP (Appendix 7) and the FDA website (Appendix 8).

Searching other resources

We searched the reference lists of included studies to identify any additional trials. We did not handsearch conference proceedings or journals for this review.

Data collection and analysis

Selection of studies

Two review authors (ACD, DMG) working independently reviewed the titles and abstracts from the electronic literature searches. They removed duplicate records and obviously irrelevant reports. They classified abstracts as 'exclude', 'unsure' or 'include'. The full-text for abstracts classified as 'unsure' by both review authors were retrieved and reassessed for inclusion. They sought to link together multiple reports of the same study. They planned to deal with potential discrepancies on unclear studies by contacting the trial authors for clarification and additional information, however this was not required. Studies labelled as 'exclude' by both review authors were excluded, and those labelled 'include' were assessed for methodological quality. We organised translation of non-English language reports, as needed.

Data extraction and management

Two review authors (ACD, DMG) extracted data using a standard form developed by Cochrane Eyes and Vision. We compared these and resolved discrepancies by discussion. One author (ACD) entered the data into Review Manager 5 (RevMan 2014), following the guidelines set out in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* and this was verified by a second review author (DMG) (Higgins 2011a).

Assessment of risk of bias in included studies

Each review author independently assessed risk of bias in the included studies using the recommended tool in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We assessed studies for the following criteria: sequence generation and allocation concealment (selection bias), masking (blinding) of participants and personnel (performance bias) and outcome assessors (detection bias), incomplete outcome data (attrition bias) and selective outcome reporting (reporting bias).

Selection bias

We considered adequacy of random sequence generation and allocation concealment. Methods of sequence generation considered to be at low risk of bias include referring to random number tables or a list of random assignments generated by a computer. Methods at high risk of bias include sequence generation, for example, by odd or even dates of birth. We assessed any method of allocation concealment (such as central randomisation, use of sequential numbered, opaque, sealed envelopes) which meets or exceeds the minimal criteria for judging concealment of allocation sequence (as detailed in section 8.10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b)) at low risk of bias. Methods such as using an open random allocation schedule may allow participants or investigators to possibly foresee assignment, thus introducing selection bias, and we judged such studies at high risk of bias.

Performance and detection bias

We considered the masking of outcome assessors by study outcomes or group of outcomes in the included studies. Masking of surgeons and participants was not possible with the interventions being examined. High risk of bias was defined as no masking, or incomplete masking, where the outcome was considered likely to be influenced by lack of masking; or if masking of the outcome assessor was attempted, but likely that the masking could have been broken, and the outcome measurement likely to be influenced by a lack of masking.

Attrition bias

We examined for missing outcome data, rates of follow-up, reasons for losses to follow-up and analysis by the principle of intention-to-treat. This included whether follow-up rates for the laser-assisted lens surgery and manual phacoemulsification arms were similar, and whether there were missing data for the outcomes of interest. We considered studies to be at low risk of bias if, for example, there were no missing data or reasons for missing outcome data were unlikely to be related to the outcomes.

Reporting bias

We investigated for selective reporting by comparing published reports to the study protocol, when available. We considered a study to be at low risk of bias if the outcomes of interest were reported in the prespecified way in both the protocol and in the published report. We considered the risk of bias to be high if, for example, not all of the study's prespecified primary outcomes were reported.

The judgement for each criterion was reported as 'satisfactory' (low risk of bias), 'unsatisfactory' (high risk of bias) or 'unclear' (insufficient information to assess). Review authors were not masked to the report authors and trial results during the assessment, and any disagreements between the review authors were resolved by discussion. We planned to contact the report authors for additional information on issues that were unclear after reviewing the original study report, however this was not required.

Measures of treatment effect

Our primary outcome was a dichotomous outcome (whether or not the eye suffers a complication during surgery). We used the

odds ratio (OR) with 95% confidence intervals (CIs). For continuous outcomes we used the mean difference (MD) between comparison groups with 95% CIs.

Unit of analysis issues

The main unit of analysis issue is how the studies dealt with both eyes. There are three options: (i) people are randomised to intervention/comparator and one eye per person enrolled in the trial; (ii) people are randomised but both eyes are included and the same intervention/comparator applied to both eyes (iii) one eye is randomly allocated to intervention and the other eye to comparator (within-person study). We documented which design was used. We planned to record whether the study authors stated explicitly why they opted for a particular design, how the study eye was selected and, for within-person studies, how each eye was randomised but in the event none of the included studies provided this level of information. None of the studies including more than one eye per person took this into account in the analysis; we have analysed the data as reported.

Dealing with missing data

We originally planned to contact the original investigators where any data in regard to prespecified trial outcomes were not reported in the final publication, however this was not required (with the exception of the trial by Schargus 2015 where we were provided with the postoperative CDVA standard deviation values following request). We have done an available case analysis - none of the studies had performed any imputation.

Assessment of heterogeneity

We assessed for methodological and statistical heterogeneity by careful review of the studies, examination of the forest plots of results of the studies and by examining the I^2 statistic (%) to assess inconsistency between studies.

Assessment of reporting biases

We planned to investigate publication bias by examination of funnel plots for signs of asymmetry. However, there were not sufficient trials contributing data to the meta-analyses (fewer than 10) to make this worthwhile.

Data synthesis

We performed data analysis according to Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). We pooled data using a random-effects model, unless there were three or fewer trials contributing to the analysis, in which case we used a fixed-effect model.

Subgroup analysis and investigation of heterogeneity

To date there are five commercially available femtosecond laser cataract surgery systems: Catalys™ (Abbott Medical Optics Inc), LENSAR™ (LENSAR Inc), LenSx® (Alcon), VICTUS™ (Bausch & Lomb Inc) and the Femto LDV Z8 (Ziemer Ophthalmic Systems AG) and it is possible that outcomes may differ between manufacturers. We therefore report the results detailing the platform manufacturer for each relevant study. Currently there are not enough trials for a subgroup analysis.

Sensitivity analysis

We planned to conduct a sensitivity analysis excluding trials at high risk of bias, but there were too few RCTs contributing data for each analysis to enable us to do this.

'Summary of findings' table

In a modification to our published protocol, we prepared a 'Summary of findings' table presenting relative and absolute risks for the outcomes listed below. One review author (JE) independently assessed the overall certainty of the evidence for each outcome using the GRADE classification system (GRADEpro 2015); this was checked by the other review authors.

1. Intraoperative complications: anterior capsule tear.
2. Intraoperative complications: posterior capsule tear.
3. Corrected distance visual acuity (CDVA) at least one month after surgery.
4. Patient reported outcome measures (PROMs) at least one month after surgery
5. Postoperative complications: cystoid macular oedema.
6. Postoperative complications: elevated intraocular pressure.
7. Costs and resource use: total duration of procedure

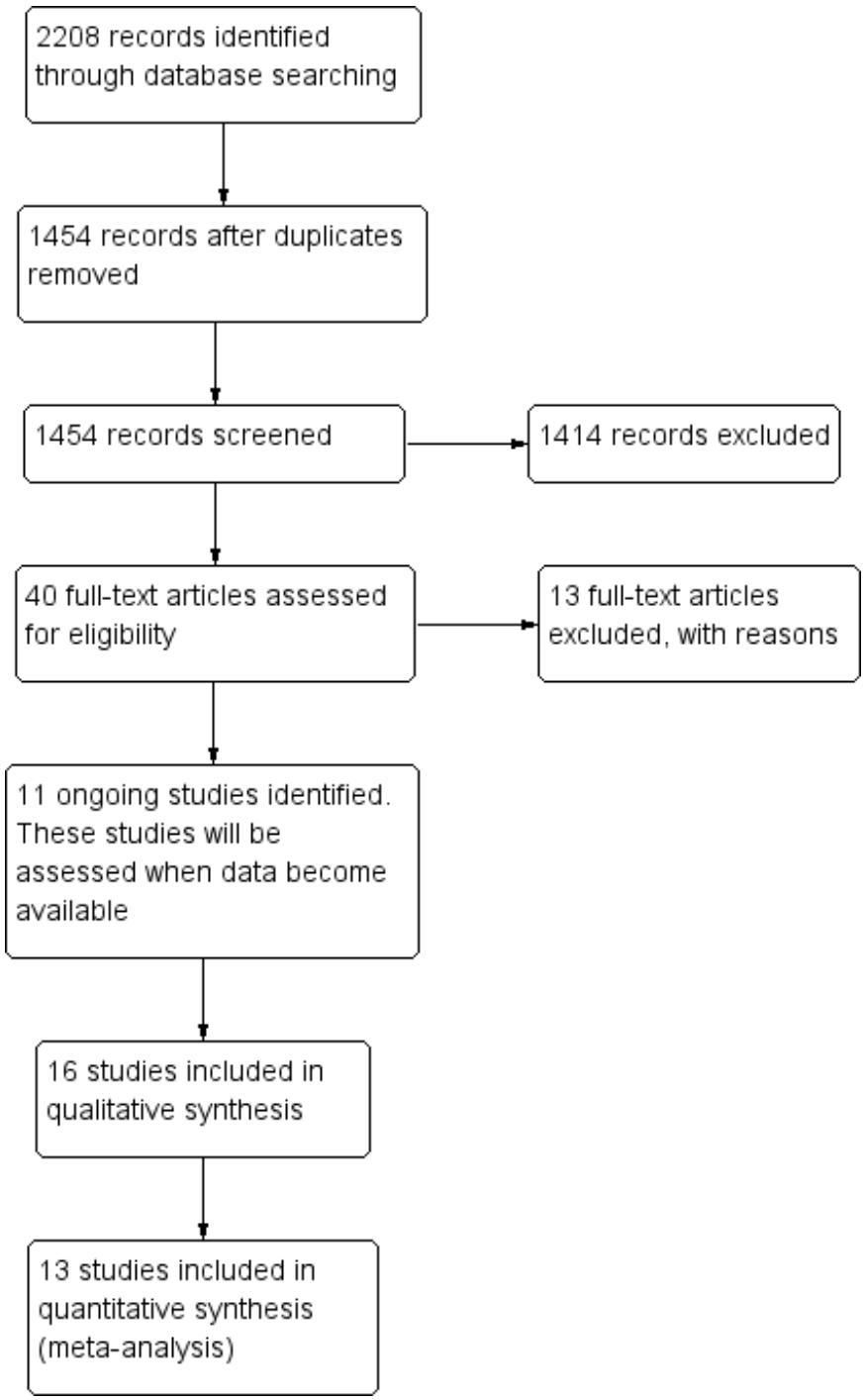
RESULTS

Description of studies

Results of the search

The electronic searches yielded a total of 2208 references (Figure 1). The Cochrane Information Specialist removed 754 duplicate records and we screened the remaining 1454 reports. We rejected 1414 records after reading the abstracts and obtained the full-text reports of 40 references for further assessment. We identified 16 studies which met the inclusion criteria and excluded 13 studies, see Characteristics of excluded studies for details. In addition, we identified another 11 studies as ongoing or completed but with no data currently available. When the review is next updated we will check to see if these studies have published data and if so assess them for inclusion in the review.

Figure 1. Study flow diagram.



Included studies

Below is a summary of the 16 studies included in this review. Further details of these can be found in the Characteristics of included studies tables.

Design

The studies by Conrad-Hengerer 2013, Conrad-Hengerer 2014, Conrad-Hengerer 2015, Dick 2014 and Schargus 2015 were within-person studies, where one eye of each participant had manual phacoemulsification and the other eye laser-assisted cataract surgery. None of these studies did a paired analysis. We have used the data as reported.

Filkorn 2012, Hida 2014, Kovacs 2014, Kranitz 2012, Mastropasqua 2014a, Mastropasqua 2014b, Nagy 2011, Nagy 2014, Reddy 2013, Takacs 2012 and Yu 2015 were parallel group RCTs. The majority of these trials included one eye per person. In Nagy 2011 6% of enrolled participants had bilateral surgery (111 eyes, 105 people) and in Yu 2015 50% of cases were bilateral (54 eyes, 36 people). No adjustment was made for within-person correlation in these studies. We have used the data as reported.

Participants

The within-person studies in Germany by Conrad-Hengerer 2013, Conrad-Hengerer 2014, Dick 2014, Schargus 2015 and Conrad-Hengerer 2015 enrolled 75 participants (150 eyes), 104 participants (208 eyes), 53 participants (106 eyes), 37 participants (74 eyes) and 100 participants (200 eyes), respectively.

For the parallel group RCTs, Reddy 2013 recruited a total of 131 participants (131 eyes) in India. In Hungary, Kranitz 2012 enrolled 45 participants (45 eyes), Filkorn 2012 134 participants (134 eyes), Takacs 2012 76 participants (76 eyes), Nagy 2014 40 participants (40 eyes) and Kovacs 2014 79 participants (79 eyes). Mastropasqua 2014a and Mastropasqua 2014b recruited 60 participants (60 eyes), and 90 participants (90 eyes) in Italy, respectively. Hida 2014 recruited 80 participants (80 eyes) in Brazil.

In two studies both eyes of some participants were reported: Yu 2015 recruited 36 participants (54 eyes) in China and Nagy 2011 enrolled 105 participants (111 eyes).

Interventions

All included studies compared laser-assisted cataract surgery to standard ultrasound phacoemulsification cataract surgery. Conrad-Hengerer 2013, Conrad-Hengerer 2014, Conrad-Hengerer 2015, Dick 2014 and Schargus 2015 used the Catalys laser platform (OptiMedica, AMO). Reddy 2013 used the VICTUS™ laser platform (Bausch & Lomb Technolas). Filkorn 2012, Hida 2014, Kovacs 2014, Kranitz 2012, Nagy 2011, Nagy 2014, Mastropasqua 2014a, Mastropasqua 2014b and Takacs 2012 used the LenSx platform (Alcon Laboratories, Inc., Fort Worth, TX). Yu 2015 used the LensAR platform.

Outcomes

Outcomes for each study are reported separately below.

- Nagy 2011: Circularity and area of capsulotomy, intraocular lens decentration.
- Kranitz 2012: Intraocular lens decentration and tilt, refraction, uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA).
- Takacs 2012: Postoperative central corneal oedema, endothelial cell count and endothelial cell function expressed by volume stress index.
- Filkorn 2012: Manifest refraction spherical equivalent, CDVA, mean absolute error, mean error, postoperative keratometry.
- Conrad-Hengerer 2013: Primary outcome measures: Corneal endothelial cell loss and corneal thickness at three months. Additional data reported: effective phacoemulsification time, mean irrigation fluid volume, mean surgical time, intraoperative and postoperative complications.
- Reddy 2013: Primary outcome measure: effective phacoemulsification time. Secondary outcome measures: mean phacoemulsification energy, mean phacoemulsification time, volume of balanced salt solution, subjective surgeon assessment of ease of phacoemulsification. Additional data reported: capsulotomy comparisons, intraocular lens decentration, safety data including posterior capsule tear and iris damage. Follow-up was limited to one day postoperatively.
- Conrad-Hengerer 2014: Primary outcome measures: laser flare counts and changes in macular thickness and volume. Secondary outcome measures: absolute and effective phacoemulsification time, and intraoperative and postoperative complications. Follow-up was six months postoperatively.
- Dick 2014: Primary outcome measures: capsular bag diameters and intraindividual difference in millimetres. Additional data reported: phacoemulsification energy used. Follow-up was three months.
- Nagy 2014: Surgically induced astigmatism and corneal higher order aberrations. Additional data reported: intraoperative and postoperative complications. Follow-up was three months.
- Kovacs 2014: Subgroup analysis of previous RCT (no further data on this given). Primary outcome measure: quantification of posterior capsule opacification at 18-26 months postoperatively. Additional data: intraocular lens tilt and decentration.
- Mastropasqua 2014a: UDVA, CDVA, keratometric astigmatism, corneal endothelial cell count, corneal thickness at the incision site and higher order corneal aberrations. Follow-up was six months.
- Mastropasqua 2014b: Stated aim to report capsulotomy

features including circularity and size. Study also reports UDVA and CDVA, subjective refraction data.

- Hida 2014: Capsulotomy size and shape parameters. Additional data: intraoperative complications in the laser arm (there is no description of the occurrence or non-occurrence of complications in the manual phacoemulsification arm) and refractive outcomes. The follow-up period is not described.
- Schargus 2015: Primary outcome: corneal endothelial cell count measurements. Secondary outcomes: corneal thickness, intraocular pressure, CDVA, overall surgery time and quantity of fluid passing through the eye. Follow-up was six months.
- Conrad-Hengerer 2015: Primary outcome measures were early and late CDVA and the deviation from the target refraction using the spherical equivalent refraction. Secondary outcome measures were anterior chamber depth and keratometry values.
- Yu 2015: Various outcome measures including average and effective phacoemulsification time, total cataract surgery time, capsulotomy size, corneal endothelial cell density, postoperative refraction and CDVA.

Excluded studies

We excluded 13 studies and details of these are in the Characteristics of excluded studies table.

Risk of bias in included studies

We assessed the included studies for possible biases, with findings as below.

Allocation

See Figure 2; Figure 3.

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

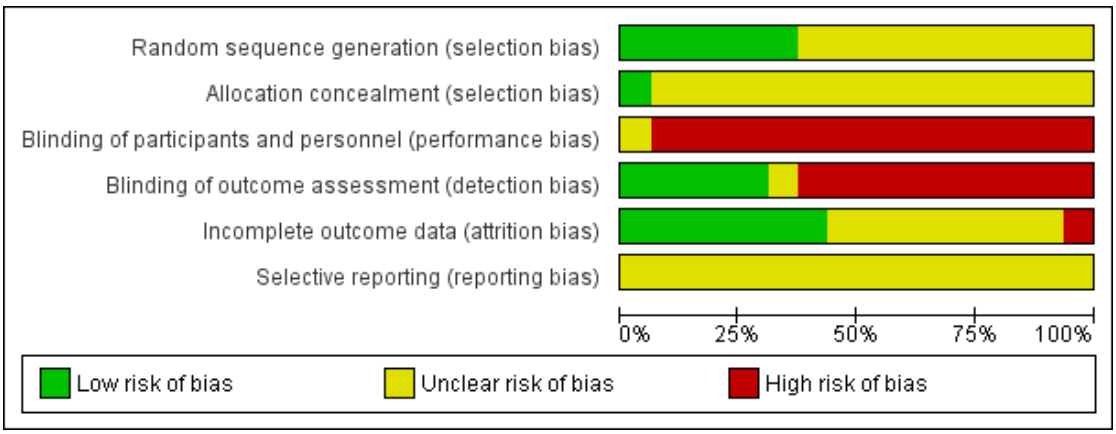
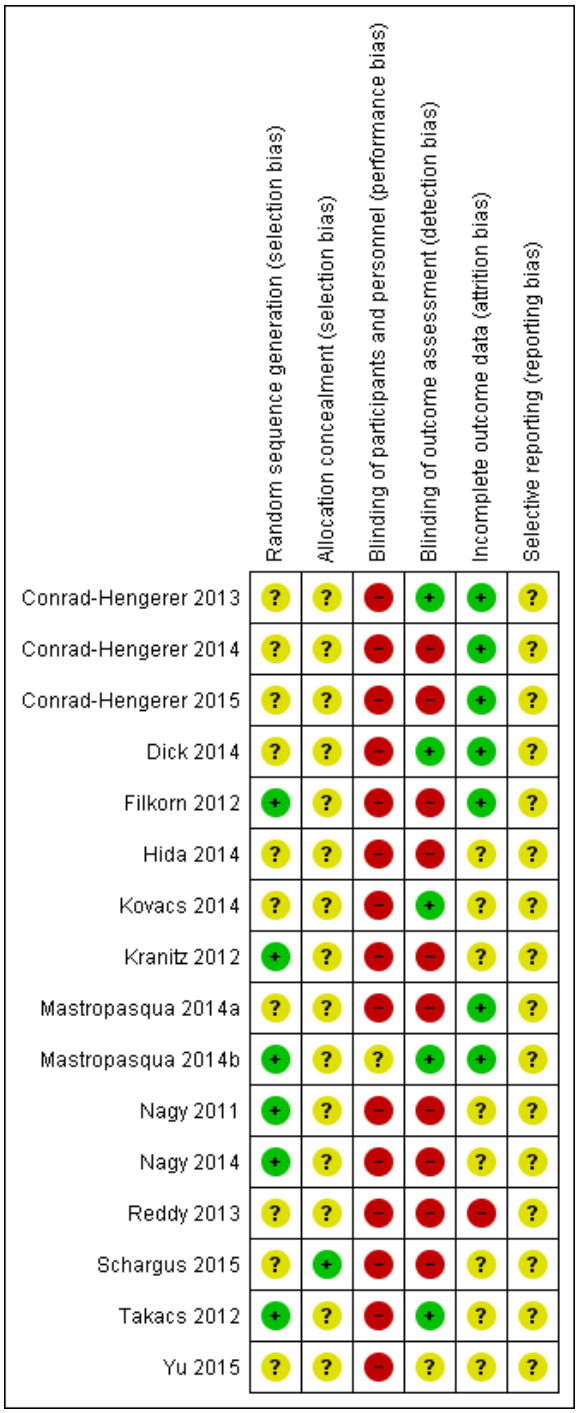


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias in each included study.



Although all studies were described as randomised, there was variable reporting as to the method of randomised sequence generation used. Kranitz 2012, Nagy 2014 and Filkorn 2012 report randomisation was done using "computer-generated tables" or a "computer randomization chart." Nagy 2011 and Takacs 2012 used "computer randomization." At best, Mastropasqua 2014b state a "computer-generated, 6-block, 15-patient randomization list was generated using an in-house closed-source software developed in MATLAB (MATLAB 2009). Patients were assigned to 1 of the 3 treatments with an equal probability for each group." Other studies did not describe the method of sequence generation and were judged at unclear risk of bias.

The methods of allocation concealment were insufficiently or not described in all but one study (Schargus 2015), in which: "The enclosed assignments were inserted into sequentially numbered, opaque, well sealed envelopes for allocation concealment, which were continuously monitored. Investigators ensured that the envelopes were opened sequentially and only after the participant's name and other details were written on the appropriate envelope." We judged this study to be at low risk of allocation concealment bias. The studies by Conrad-Hengerer 2013, Conrad-Hengerer 2014, Conrad-Hengerer 2015 and Dick 2014 used envelopes for allocation concealment and "the surgeon opened the corresponding envelope" at the time of surgery. As no further details about the allocation concealment methodology were given (e.g. use of sequentially numbered envelopes), we judged these studies to be at unclear risk of bias. None of the other trials gave details on the methods of allocation concealment used and we judged them to be at unclear risk of bias.

Blinding

Surgeon masking was not possible and in general participant masking was not described so most studies were judged to be high risk for performance bias. In Mastropasqua 2014b "*The patients were masked to group assignment until the study was completed"* however it was unclear how the patients could remain masked unless sham laser was performed, and there was no description of this, so we judged this to be unclear risk of bias. Reddy 2013 was described as open label and was considered to be definitely not masked and judged to be at high risk of both performance and detection bias. Masking of any outcome assessment was described in 6 studies. For the studies by Conrad-Hengerer 2013 and Dick 2014, a masked technician performed the "full clinical examination" and "all slit-lamp measurements" respectively, following surgery. In Mastropasqua 2014b the "examiners performing preoperative and postoperative assessments were masked to group assignment until the study was completed." In Takacs 2012, "examiners were not aware of which surgical procedure had been used when performing the postoperative examinations." In the study by Kovacs 2014, masking of posterior capsule opacification measurement only is described (study primary outcome).

For Yu 2015, capsulorhexis size only was measured by a masked examiner but masking of other outcomes was not described.

No outcome assessment masking was described in the other included studies.

Incomplete outcome data

There was variable reporting of data attrition with only eight of the 16 included studies providing any detail.

In the study by Conrad-Hengerer 2013, 2/75 participants (4/150 eyes) were excluded at the three-month follow-up (one due to poor health - cancer; and one had moved abroad). Conrad-Hengerer 2014 and Conrad-Hengerer 2015 state that 102/104, and 196/200 eyes respectively, were included and analysed at six months postoperatively. In the study by Dick 2014, "all patients were included in the 3-month follow-up." For Mastropasqua 2014a, based on the number of eyes reported in figure 1, there was no loss to follow-up. For Mastropasqua 2014b, based on the results ("Each group comprised 30 eyes (30 patients)"), there was no loss to follow-up. For Filkorn 2012, the number of patients at baseline was the same as those with postoperative data. We assessed these seven studies to be at low risk of bias.

A total of 14/131 participants were excluded in Reddy 2013. One eye in the laser-assisted group was excluded from analysis because of a protocol violation (no details of this are given). Seven eyes in the laser-assisted group and four in the manual group were also excluded from further analysis with the reason for this being described as "to guarantee correct data analysis and rule out preoperative bias" by ensuring "equal cataract grade distributions in the 2 study groups" were present. We judged this study to be at high risk of bias.

Selective reporting

All studies reported prespecified outcome measures in their methodology, however, it was unclear whether these were truly prespecified, as no study protocol was available and the trials were not registered on a clinical trials' database. It was unclear if the statistical analysis methods were prespecified, and therefore, although none of the included studies appeared to demonstrate selective reporting, we judged all to be at unclear risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery

Intraoperative complications in the study eye (primary outcome)

There was variable reporting of types and detail regarding intraoperative complications between studies.
See Analysis 1.1

Anterior capsule tears

The number of anterior capsule tears reported in the included studies was low. In Conrad-Hengerer 2013 there was one tear in 75 eyes in the control group and none in the laser group. In Reddy 2013 there was one anterior capsule tear in the laser group (out of 56 eyes) and one in the control group (63 eyes). In Conrad-Hengerer 2015 there was one in the laser group and none in the standard phacoemulsification group.
We assume that in Nagy 2011, Kranitz 2012, Conrad-Hengerer 2014, Nagy 2014, Kovacs 2014 and Schargus 2015 there were no anterior capsule tears in either arms, as they reported there were either no intraoperative complications or described other intraoperative complications, but did not specifically describe the occurrence of any anterior capsular tear. Hida 2014 reported no intraoperative complications in the laser-assisted arm, but did not report any data on complications for the phacoemulsification arm. In Filkorn 2012, Mastropasqua 2014a and Mastropasqua 2014b complications were excluded and therefore not reported. Takacs 2012 and Dick 2014 did not provide data on complications. In Yu 2015 there were no anterior capsule tears in either arm.
The estimates of the effect in the three studies contributing events were different (0.33, 1.13, 3.03) and with very wide confidence intervals (Analysis 1.1). We did not pool the data because an average of these three different estimates would be unlikely to be informative.
We graded this evidence as very low certainty. We downgraded for risk of bias, imprecision and inconsistency (Summary of findings for the main comparison).

Posterior capsule tears

Schargus 2015 reported one posterior capsular tear (1/37 eyes) in the standard phacoemulsification arm and none (0/37) in the laser-assisted arm. In the trial by Yu 2015 there were no posterior capsule tears in either arm. We assume that in Nagy 2011, Kranitz 2012, Conrad-Hengerer 2014, Nagy 2014 and Kovacs 2014, there were no posterior capsule tears as they report there were no intraoperative complications. For Conrad-Hengerer 2013 and Conrad-Hengerer 2015 occurrence of anterior capsule tears are described and the other cases are described as "uneventful" or "without further complications." Reddy 2013 describes a range of intraoperative complications and states in the discussion that there were no posterior capsular tears in either group. In Filkorn 2012, Mastropasqua 2014a and Mastropasqua 2014b complications were excluded and therefore not reported. Hida 2014 reported no intraoperative complications in the laser-assisted arm, but did not report any data on complications for the phacoemulsification arm. Takacs 2012 and Dick 2014 did not provide data on complications.
We graded the certainty of evidence as very low. We downgraded one level for risk of bias and two levels for imprecision (Summary of findings for the main comparison).

Distance visual acuity in the operated eye at least one month after cataract surgery

Seven studies reported data on postoperative visual acuity. In summary, Mastropasqua 2014a and Mastropasqua 2014b found no statistically significant difference in uncorrected distance visual acuity (UDVA) or corrected distance visual acuity (CDVA) between laser-assisted and standard phacoemulsification groups. Filkorn 2012, Schargus 2015 and Yu 2015 found no statistically significant difference in CDVA between laser-assisted and manual phacoemulsification groups. Kranitz 2012 found no difference in UDVA at one month or one year; however, CDVA was statistically significantly better in the laser arm at both these time points.
Conrad-Hengerer 2015 reported that "the mean UDVA improved faster in the femtosecond laser-assisted group than in the conventional group. There was a statistically significant between-group difference 2 hours, 3 days, and 1 week postoperatively ($P < 0.05$). Beginning from 1 month on, no statistically significant differences were detected." No further comparisons on postoperative visual acuities were made.

Corrected distance visual acuity

In Kranitz 2012, CDVA was 0.89 decimal Snellen (standard deviation (SD) 0.17) and 0.77 decimal Snellen (SD 0.25) in laser-assisted and standard phacoemulsification arms, respectively, at one week postoperatively ($P > 0.05$). One month postoperatively, CDVA was 0.94 decimal Snellen (SD 0.11) and 0.84 decimal Snellen (SD 0.16) in laser-assisted and standard phacoemulsification arms, respectively ($P = 0.031$). At one year postoperatively, CDVA values were 0.97 decimal Snellen (SD 0.06) and 0.92 decimal Snellen (SD 0.09) laser-assisted and manual phacoemulsification arms, respectively ($P = 0.038$).
In Filkorn 2012, CDVA was 0.03 (SD 0.06) logMAR and 0.02 (SD 0.04) logMAR laser-assisted and standard phacoemulsification arms, respectively, at mean 10 weeks postoperatively.
In Mastropasqua 2014a, CDVA was 0.18 (SD 0.18) logMAR and 0.16 (0.12) logMAR laser-assisted and standard phacoemulsification arms, respectively, at one month postoperatively. At six months postoperatively, CDVA values were -0.08 (0.09) and -0.03 (0.12) logMAR laser-assisted and manual phacoemulsification arms, respectively. They found no statistically significant difference between study arms for CDVA at either time point.
In Mastropasqua 2014b, mean CDVA at one week was -0.03 (SD 0.05) and -0.03 (0.14) in laser groups 1 and 2, respectively, compared to 0.01 (0.07) in the standard phacoemulsification group.

Mean CDVA at one month was -0.08 (0.05) and -0.09 (0.12) in laser groups 1 and 2, respectively, compared to -0.06 (0.10) in the standard phacoemulsification arm. Mean CDVA at six months was -0.09 (0.12) and -0.08 (0.05) in laser groups 1 and 2, respectively, compared to -0.06 (0.10) in the standard phacoemulsification arm. They found no statistically significant difference between arms at any time point.

In Schargus 2015, CDVA was reported as 0.049 logMAR at three months and 0.024 logMAR at six months in the laser-assisted arm. In the manual phacoemulsification arm, CDVA was 0.057 logMAR at three months and 0.038 logMAR at six months. They found no statistically significant difference between the two groups (P = 0.46).

In Yu 2015, CDVA at one day postoperatively was 0.16 (0.20) logMAR and 0.35 (0.45) logMAR in the laser and manual phacoemulsification arms, respectively. At one week postoperatively, the CDVA was 0.06 (0.15) logMAR and 0.18 (0.21) logMAR in the laser and manual phacoemulsification arms, respectively. At one month, CDVA was 0.09 (0.10) logMAR and 0.19 (0.44) logMAR in the laser and manual phacoemulsification arms, respectively. At three months, CDVA was 0.12 (0.09) logMAR and 0.33 (0.56) logMAR in laser and manual phacoemulsification arms, respectively.

CDVA data from Kranitz 2012 was not included in the meta-analysis due to visual acuity data being reported in Snellen rather than logMAR. Whilst conversion of mean Snellen values to logMAR is possible, conversion of SDs is not.

As seen in Analysis 1.2, there were no differences in either CDVA or UDVA between arms with the exception of CDVA at six months. Here we found some evidence to support a very small advantage for the laser-assisted arm (MD -0.03 logMAR, 95% CI -0.05 to -0.00; eyes = 224). This difference is equivalent to 1.5 logMAR letters between groups and is not thought to be of any clinical significance.

Overall, we graded the certainty of visual acuity evidence as low. We downgraded for risk of bias and imprecision (Summary of findings for the main comparison).

Uncorrected distance visual acuity

Kranitz 2012, Mastropasqua 2014a, Mastropasqua 2014b and Conrad-Hengerer 2015 report data on UDVA outcomes.

In Kranitz 2012, UDVA at one week was 0.59 decimal Snellen (SD 0.23) and 0.51 decimal Snellen (SD 0.29) laser-assisted and standard phacoemulsification arms, respectively. At one month, UDVA values were 0.69 decimal Snellen (SD 0.19) laser-assisted versus 0.61 decimal Snellen (SD 0.28) standard phacoemulsification. At one year, UDVA values were 0.63 decimal Snellen (SD 0.23) laser-assisted versus 0.60 decimal Snellen (SD 0.25) in the standard phacoemulsification arm. They found no statistically significant difference between arms at any time point.

In Mastropasqua 2014a, UDVA at one month postoperatively was 0.35 (0.23) logMAR in the laser arm and 0.28 (0.13) in the standard phacoemulsification arm. At six months postoperatively, mean UDVA was 0.13 (0.21) and 0.08 (0.15) logMAR in the laser-assisted and standard phacoemulsification arms, respectively. No statistically significant difference in UDVA values between arms were found.

In Mastropasqua 2014b, mean UDVA at one week was 0.08 (0.08) logMAR in laser arm 1, 0.07 (0.09) in laser arm 2 and 0.18 (0.05) in the standard phacoemulsification group. At one month, mean UDVAs were 0.10 (0.10), 0.09 (0.13) and 0.21 (0.09), laser arms 1 & 2, and standard phacoemulsification arm, respectively. At six months postoperatively, mean UDVAs were 0.09 (0.08), 0.10 (0.05) and 0.25 (0.05), laser arms 1 & 2, and standard phacoemulsification arm, respectively. They found no statistically significant difference between arms at any time point.

Conrad-Hengerer 2015 found early differences in UDVA between arms, however no differences were found after one month with up to six months follow-up. No details on postoperative visual acuity values were given.

Patient reported outcome measures (PROMs) at least one month after cataract surgery

No data on patient-reported outcome measures were reported by any of the 16 included studies.

Postoperative or long-term complications reported within one year of cataract surgery

Cystoid macular oedema

Four studies reported cystoid macular oedema (Conrad-Hengerer 2013; Conrad-Hengerer 2014; Conrad-Hengerer 2015; Schargus 2015). Two out of 73 eyes (Conrad-Hengerer 2013), 2/104 (Conrad-Hengerer 2014), 0/37 (Schargus 2015) and 1/100 (Conrad-Hengerer 2015) in the laser groups developed postoperative cystoid macular oedema compared to 3/73, 3/104, 1/37 and 2/100 eyes in the manual phacoemulsification arms, respectively. In the studies by Nagy 2011, Kranitz 2012, Nagy 2014 and Kovacs 2014 it is stated that there were no postoperative complications and thus we assume there were no cases of cystoid macular oedema. In Mastropasqua 2014a and Mastropasqua 2014b complications were excluded, and therefore not reported. Filkorn 2012, Takacs 2012, Dick 2014 and Hida 2014 did not provide data on complications. Yu 2015 provides some information on raised postoperative intraocular pressure, but does not specifically mention any cases of cystoid macular oedema following surgery, and so we assume there were no cases.

Overall, this gives: odds ratio (OR) 0.58, 95% CI 0.20 to 1.68; eyes = 957, studies = 9 (Analysis 1.4). We graded this as low certainty evidence. We downgraded for risk of bias and imprecision (Summary of findings for the main comparison).

Raised intraocular pressure

Five studies specifically reported intraocular pressure in the postoperative period and 4 of these gave data at specified time points (Conrad-Hengerer 2013; Conrad-Hengerer 2014; Conrad-Hengerer 2015; Schargus 2015). The study by Yu 2015 does not give the time point at which the raised IOP was identified. In the study by Schargus 2015, it must be noted that no ophthalmic viscosurgical device was used in the laser arm, but was in the standard phacoemulsification arm. Additionally those in the standard phacoemulsification arm were given oral acetazolamide for intraocular pressure prophylaxis, whilst those in the laser arm were not. Follow-up in the study by Reddy 2013 was limited to one day and "no adverse events were observed." In the studies by Nagy 2011, Kranitz 2012, Nagy 2014 and Kovacs 2014, it is stated that there were no postoperative complications, and thus it is assumed there were no cases of elevated intraocular pressure. In Mastropasqua 2014a and Mastropasqua 2014b, complications were excluded and therefore not reported. Filkorn 2012, Takacs 2012, Dick 2014 and Hida 2014 did not provide data on complications.

Considering elevated intraocular pressure immediately after surgery, the number of events was low: 2/75, 1/104, 0/37 and 3/100 eyes in the laser arms of Conrad-Hengerer 2013, Conrad-Hengerer 2014, Schargus 2015 and Conrad-Hengerer 2015 respectively; compared to 2/75, 2/104, 1/37 and 2/100 for the standard phacoemulsification arms: OR 0.88, 95% CI 0.29 to 2.66; eyes = 1022, studies = 9) (Analysis 1.4).

Considering elevated intraocular pressure reported between one day and one week postoperatively, the number of events was low: 1/75, 0/104, 1/37 and 0/100 eyes in the laser arms of Conrad-Hengerer 2013, Conrad-Hengerer 2014, Schargus 2015 and Conrad-Hengerer 2015, respectively; compared to 0/75, 1/104, 3/37 and 0/100 for the standard phacoemulsification arms: OR 0.57, 95% CI 0.11 to 2.86; eyes = 903, studies = 8; I^2 = 0% (Analysis 1.4). Yu 2015 reported one eye (1/29) in the manual phacoemulsification arm had steroid response ocular hypertension, and none (0/25) in the laser arm. They do not describe the time after surgery at which this occurred and so this data has not been included in Analysis 1.4.

We judged the evidence for postoperative complications to be of low certainty and downgraded for risk of bias and imprecision (Summary of findings for the main comparison).

Posterior capsule opacification

Only Kovacs 2014 and Yu 2015 reported posterior capsule opacification rates. In Yu 2015, 2/29 eyes in the control required YAG laser posterior capsulotomy at one and three months, respectively, following surgery. No eyes (0/25) in the laser arm required YAG capsulotomy.

Kovacs 2014 investigated posterior capsule opacification development between arms for between 18-26 months postoperatively. They found higher posterior capsule opacification scores in the standard phacoemulsification arm, however, no patients in either arm required YAG laser posterior capsulotomy (0/39 standard phacoemulsification arm, 0/40 laser-assisted arm).

Other complications

No study specifically mentioned any cases of postoperative corneal decompensation or retinal detachment, and thus we assume none occurred.

Costs and resource use

No data on costs were reported by any of the 16 included studies. Three studies reported data on the duration of the procedure (Analysis 1.3). There was little evidence for a difference between the procedures: mean difference (MD) 0.10 minutes, (95% CI -0.02 to 0.21; eyes = 274, studies = 3). (Summary of findings for the main comparison). One additional study (Conrad-Hengerer 2014) did report procedure durations, but did state there was no significant difference in surgery times between arms.

Refractive outcomes

Five studies reported data on refractive outcomes (Filkorn 2012, Hida 2014, Mastropasqua 2014b, Yu 2015 and Conrad-Hengerer 2015). There were differences in how the refractive results were reported between studies which limited comparisons between trial arm.

Filkorn 2012 reported the achieved postoperative spherical equivalents were -0.50 diopters (D) (SD 1.06) and -0.58 D (1.28) for laser-assisted and standard phacoemulsification arms, respectively. Mean errors were -0.03 D (0.47) and 0.07 D (0.63) laser-assisted and standard phacoemulsification arms, respectively. Mean absolute errors (MAE, mean of the individual prediction errors without regard for its sign) were 0.38 D (0.28) and 0.50 D (0.38) for laser-assisted and standard phacoemulsifications arms, respectively. They found the MAE to be significantly lower in the laser-assisted arm (P = 0.04), otherwise they found no significant differences between arms. 42% eyes were within ±0.25D of target refraction in the laser arm compared to 28% in the standard phacoemulsification arm. 69% eyes were within ±0.50D of target refraction in the laser arm compared to 65% in the standard phacoemulsification arm. 99% eyes were within ±1.0D of target refraction in the laser arm compared to 88% in the standard phacoemulsification arm. These data were "measured 6 to 12 weeks after surgery."

Hida 2014 reported the mean predicted and achieved postoperative spherical equivalents were -0.30 D (SD 0.39) and -0.16 D (0.38) for the laser-assisted arm. For the manual phacoemulsification arm these were +0.33 D (SD 0.33) and -0.03 D (0.28). They found no statistically significant differences between arms. Data

on mean absolute errors were not reported, or proportions within ±0.50 or ±1.0 diopters target refraction were not reported.

Mastropasqua 2014b report data on postoperative refractive outcomes and found the mean postoperative spherical equivalents at one month to be -0.25D (0.38), -0.23 (0.64) and -0.39 (0.33) in laser arms 1 and 2, and the standard phacoemulsification arm, respectively. The mean postoperative spherical equivalents at six months were -0.25D (0.54), -0.26 (0.40) and -0.41 (0.39) in laser arms 1 and 2, and the standard phacoemulsification arm, respectively. Mean absolute errors were 0.42 (0.16), 0.36 (0.36) and 0.54 (0.43) in laser arms 1 and 2, and standard phacoemulsification arm, respectively at one month. Mean absolute errors were 0.44 (0.31), 0.43 (0.10) and 0.56 (0.39) in laser arms 1 and 2, and standard phacoemulsification arm, respectively at six months. They found statistically significant differences between groups for postoperative spherical equivalent and mean absolute error. Proportions within ±0.50 or ±1.0 diopters target refraction were not reported.

Conrad-Hengerer 2015 reported the postoperative spherical equivalents by various time points. At one month, postoperative spherical equivalent was -0.05 D (0.28) in the laser arm versus -0.18 D (0.54) in the manual phacoemulsification arm, and at six months -0.05 D (0.28) versus -0.11 D (0.55), respectively. Ninety eyes (92%) in the femtosecond laser-assisted group and 70 eyes (71%) in the conventional group were within ±0.50 D of the target refractive outcome and 98 eyes (100%) in both groups were within ±1.00 D at 6 months postoperatively. Data on mean absolute errors were not reported.

Yu 2015 reported the absolute deviation between the attempted and achieved spherical equivalents at one day, one week, one month and three months postoperatively. They found no significant difference except at three months postoperatively, where the absolute deviation was statistically significantly lower in the laser arm compared to the manual phacoemulsification arm (0.16 D (0.16), versus 0.74 (0.65) P = 0.00, laser versus manual phacoemulsification, respectively). Proportions within ±0.50 or ±1.0 diopters target refraction were not reported.

The definition in Yu 2015 for "absolute deviation between the attempted and achieved spherical equivalent" was consistent with that for "mean absolute error" in the studies by Filkorn 2012 and Mastropasqua 2014b, and so these studies were used for Analysis 1.5. Only data from the longest follow-up time point were used for the analysis. We found some evidence for a difference in MAE between the procedures: mean difference (MD) -0.18D for the laser arm (95% CI: -0.27 to -0.09), eyes = 278, studies = 3). We judged the evidence for postoperative refractive predictability to be of low certainty. We downgraded for imprecision (the confidence intervals include a clinically insignificant effect) and inconsistency (I^2=83%).

DISCUSSION

Summary of main results

We found 16 small randomised studies meeting the inclusion criteria. Reporting was variable on the types of intraoperative and postoperative complications. Ten of 16 trials reported data on intraoperative complications, in six of these trials, there were either no anterior or posterior capsule tears. In the four trials in which these complications occurred, there were few events and there was only one trial where posterior capsular rupture occurred (one eye, standard phacoemulsification arm).

Only seven studies reported data on overall postoperative visual acuity outcomes, of which data from five were sufficient to combine for analyses. We found little evidence of any important difference in postoperative visual acuity between laser-assisted and standard phacoemulsification arms. There was a small advantage for the laser-assisted arm at six months in corrected distance visual acuity that just met statistical significance. However, the difference was equivalent to 1.5 logMAR letters and we considered this to be clinically insignificant. There was a small difference in postoperative refraction prediction error (mean absolute error) in favour of laser-assisted surgery but the confidence intervals for this estimate included a clinically insignificant effect.

None of the trials were powered to investigate for differences in complication rates or postoperative visual acuity outcomes between arms or reported data on patient-reported outcome measures (visual function questionnaires) or cost-effectiveness. Further appropriately powered randomised controlled trials (RCTs) are recommended to address these issues.

Overall completeness and applicability of evidence

Of the 16 RCTs that met the inclusion criteria, none reported data for every outcome measure. Data on anterior or posterior capsule tears were reported by 10 of the 16 included trials, however only three reported usable data on visual outcomes with at least six months follow-up. No studies reported data on visual function, measured by patient-reported outcome measures, or data on cost-effectiveness.

Certainty of the evidence

Overall, we graded the certainty of the evidence to be low or very low. We downgraded for risk of bias because the trials were poorly reported, and largely it was unclear as to the extent to which bias had been avoided; we judged most trials to be at high risk of performance bias and one trial to be at high risk of performance, detection and attrition bias. The investigators in at least 11 trials had financial links with the manufacturers of the laser platforms.

None of the trials were prospectively registered and most of the trials were published by two research groups; it was not always possible to tell whether patients were double-counted, although the investigators assured us that this was not the case.
We downgraded for imprecision because the trials were small and complications occurred rarely, so the estimates of effect from the pooled results were imprecise. In some cases the results of different studies were inconsistent.

Potential biases in the review process

We had hoped to explore whether or not the differences in trial designs, namely unilateral versus bilateral (paired-eye studies) impacted on results. Whilst we found both paired and unpaired studies in our review, the paired studies had been analysed as unpaired. Analysis ignoring this pairing lowers the chance of detecting a significant difference between groups, but data was not presented in a way that allowed us to explore this.
Femtosecond laser-assisted cataract surgery is a rapidly developing area, and although we re-ran searches during the review to ensure they were up-to-date, it is possible that a recently published study may have been missed.

Agreements and disagreements with other studies or reviews

A number of large case series have been published reporting outcomes of laser assisted cataract surgery. Anterior capsular tear rates range from 0.08% to 1.84%, (Roberts 2013a, Day 2014, Chee 2015, Abell 2015, Roberts 2015) and posterior capsular tear rates from 0.27 to 0.43%.(Chee 2015, Abell 2015, Roberts 2013a) In a prospective consecutive comparative case-series of 1852 laser-assisted and 2228 control cases (Abell 2015); the rates of significant intraoperative complications were low in both groups, and both techniques were thought to be equally safe, although anterior capsule tear rates were statistically significantly higher in laser-assisted cases (1.84% versus 0.22% in the standard phacoemulsification arm, P < 0.001). Chee 2015 compared visual outcomes in a non-randomised case-series of 794 laser cataract operations with 420 matched manual phacoemulsification controls. They found the proportion with a postoperative UDVA of 20/25 or better to be significantly higher in the laser cases (68.6% vs 56.3%; P < 0.0001), and a non-significant trend towards lower MAE in the laser cataract surgery cases was found (0.30D, SD 0.25D laser vs 0.33D, SD 0.25D controls, P = 0.062). A recent comparative case series by Ewe 2016 found no clinically meaningful difference in visual outcomes between 988 laser assisted cataract surgery and 888 manual phacoemulsification cataract surgery cases (laser postoperative CDVA 0.09 logMAR (SD 0.13) vs standard phacoemulsification 0.12 logMAR (SD 0.22), P = 0.001), and also a high MAE in laser assisted cases (0.41D vs 0.35 D; P < 0.0011).

AUTHORS' CONCLUSIONS

Implications for practice

The evidence from the 16 randomised controlled trials (RCTs) included in this review could not determine the equivalence or superiority of laser-assisted cataract surgery compared to standard manual phacoemulsification for our chosen outcomes due to the low to very low certainty of the evidence available from these studies.

Implications for research

As complications occur rarely, large adequately powered, well designed, independent RCTs comparing the safety and efficacy of laser-assisted cataract surgery with standard phacoemulsification cataract surgery are needed. Standardised reporting of intraoperative and postoperative complications, visual and refractive outcomes for cataract surgery would facilitate future synthesis of trials. Data on patient-reported outcomes and cost-effectiveness are needed. Unit of analysis issues must be considered when conducting ophthalmic RCTs.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Conrad-Hengerer 2013

Methods	Within-person (paired-eye) RCT
Participants	Number of participants randomised: 75 Number of eyes included: 150 Country: Germany Average age: 71 years Sex: 63% female Ethnic group: not described Inclusion criteria: *"All patients enrolled had a visually significant cataract, dilated pupil width of 6.0 mm or larger, and were willing to volunteer for the trial after giving informed consent"* Exclusion criteria: *"The exclusion criteria included a history of serious coexisting ocular disease, uncontrolled glaucoma, optic atrophy or ocular tumors, use of topical or systemic steroids or nonsteroidal anti-inflammatory drugs (NSAIDs) during the previous 3 months, relevant corneal opacities, poorly dilating pupils (pupil % 6.0 mm), known zonular weakness, age less than 22 years, or participation in another clinical study"*
Interventions	Laser-assisted cataract surgery using the Catalys platform (Catalys Precision Laser System, AMO) or manual phacoemulsification using a Stellaris phaco machine (Bausch & Lomb)
Outcomes	Primary outcome measures: Corneal endothelial cell loss and corneal thickness at up to 3 months. Additional data reported: effective phacoemulsification time, mean irrigation fluid volume, mean surgical time, intraoperative and postoperative complications
Notes	Funding source: not reported Declaration of interest: *"Dr. Dick is a member of the medical advisory board of OptiMedica Corp"* Date study conducted: February 2012 to July 2012 Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	*"the surgeon opened the corresponding envelope, receiving information about the procedure to use in each eye; that is, femtosecond laser - assisted or standard phacoemulsification"*

Conrad-Hengerer 2013 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible; no efforts to mask participants are described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	*"All patients had a full clinical examination by the same masked trained technician"*
Incomplete outcome data (attrition bias) All outcomes	Low risk	*"Two patients were excluded at the 3-month follow-up because they missed their previous visits. One patient had cancer and was not available for further visits; the other moved to another county"*
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Conrad-Hengerer 2014

Methods	Within-person (paired-eye) RCT
Participants	Number of participants randomised: 104 Number of eyes included: 208 Country: Germany Average age: 71 years Sex: 56% female Ethnic group: not described Inclusion criteria: only the exclusion criteria below are given Exclusion criteria: *"history of coexistent ocular disease (eg, glaucoma, high myopia, retinal diseases affecting the macula, optic atrophy, or ocular tumors), use of topical or systemic steroids or nonsteroidal anti-inflammatory drugs during the prior 3 months, relevant corneal opacities, age younger than 22 years, or participation in another clinical study"*
Interventions	Laser-assisted cataract surgery using the Catalys platform (Catalys Precision Laser System, AMO) or manual phacoemulsification using a Stellaris phaco machine (Bausch & Lomb)
Outcomes	Primary outcome measures: laser flare counts and changes in macular thickness and volume. Secondary outcome measures: absolute and effective phacoemulsification time; and intraoperative and postoperative complications. Follow-up was 6 months postoperatively
Notes	Funding source: not reported. Declaration of interest: *"Dr. Dick was a member of the medical advisory board of OptiMedica. The remaining authors have no financial or proprietary interest in the materials presented herein"* Date study conducted: March 2012 to October 2012 Trial registration number: not reported

Conrad-Hengerer 2014 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	*"After positioning the patient on the operating bed, the surgeon opened the corresponding envelope indicating which procedure to choose (ie, femtosecond laser-assisted or standard phacoemulsification)"*
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible, no efforts to mask participants are described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Low risk	*"Two hundred two eyes (97%) were included and analyzed at 6 months postoperatively."* No further information is given
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Conrad-Hengerer 2015

Methods	Within-person (paired-eye) RCT
Participants	Number of participants randomised: 100 Number of eyes included: 200 Country: Germany Average age: 72 years Sex: 56% female Ethnic group: not described Inclusion criteria: "*a potential corrected visual acuity of 0.8 (20/25) in both eyes*" Exclusion criteria: "*amblyopia, a history of serious coexistent ocular disease (eg, pseudoexfoliation, uncontrolled glaucoma, macular pathologies, high myopia, or hyperopia, defined as an axial length [AL] < 21.5 mm or > 27.5 mm), corneal astigmatism of more than 1.5 diopters (D), optic atrophy, ocular tumors, use of topical or systemic steroids or nonsteroidal anti-inflammatory drugs during the previous 3 months, relevant corneal opacities, Fuchs dystrophy, cornea guttata, an age younger than 22 years, and participation in another clinical study. Furthermore, a dilated pupil of at least 6.0 mm preoperatively was necessary*"

Conrad-Hengerer 2015 (*Continued*)

Interventions	Laser-assisted cataract surgery using the Catalys platform to produce capsulotomy and lens fragmentation; or manual phacoemulsification cataract surgery
Outcomes	*"Primary outcome measures were early and late corrected distance visual acuity (CDVA) and the deviation from the target refraction using the spherical equivalent (SE) refraction. Secondary outcome measures were anterior chamber depth (ACD) and keratometry values"*
Notes	Funding source: not reported Declaration of interest: "*Dr. Dick is a member of the medical advisory board of Abbott Medical Optics, Inc. No other author has a financial or proprietary interest in any material or method mentioned*" Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	*"After placing the patient on the laser system's operating bed, the surgeon opened the corresponding envelope providing the information about which procedure to use; that is, femtosecond laser-assisted cataract surgery or regular phacoemulsification"*
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible; no efforts to mask participants are described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Low risk	*"Six months postoperatively, 196 eyes were included and analyzed."* No further details are given
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Dick 2014

Methods	Within-person (paired-eye) RCT
Participants	Number of participants randomised: 53 Number of eyes included: 106 Country: Germany Average age: 71 years old Sex: 57% female Ethnic group: not described Inclusion criteria: "a visually significant cataract (corrected distance visual acuity < 20/25) in both eyes, dilated pupil width of 6.0 mm or greater, and were willing to volunteer for the trial after giving an informed consent " Exclusion criteria: "included corneal scars, corneal diseases, corneal astigmatism of 1.5 diopters or greater, reduced endothelial cells, glaucoma, pseudoexfoliation syndrome, zonular weakness, single eye, malformations, history of ocular surgery, intraocular tumours, active or past inflammations, age-related macular degeneration, diabetic retinopathy, axial length difference (greater than 0.5 mm and less than 21.5 mm or greater than 26 mm), pregnancy, reduced compliance, age younger than 22 years, or participation in another clinical study "
Interventions	Laser-assisted cataract surgery using the Catalys platform (Catalys Precision Laser System, AMO) or manual phacoemulsification using a Stellaris phaco machine (Bausch & Lomb)
Outcomes	Primary outcome measures: absolute capsular bag diameters and intraindividual difference in milliammeters. Additional data reported: phacoemulsification energy used. Follow-up was 3 months
Notes	Funding source: not reported Declaration of interest: *"The authors have no financial or proprietary interest in the materials presented herein*" Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	*"For randomization, the patient was placed on the operating bed of the laser system and a corresponding envelope with the information about the receiving procedure was opened by the surgeon*"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described

Dick 2014 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	*"All slit-lamp measurements were done by a single trained technician who was blinded to the surgical technique"*
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients were included in the 3 month follow-up
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Filkorn 2012

Methods	Parallel-group RCT
Participants	Number of participants randomised: 134 (77 laser arm, 57 control arm) Number of eyes included: 134 (77 laser arm, 57 control arm) Country: Hungary Average age: 65 years laser arm, 64 years control arm Ethnic group: not described Inclusion criteria: not described Inclusion criteria: previous ocular surgery, corneal diseases such as keratoconus, known zonular weakness, corneal astigmatism 3.00 D, anterior capsule tear, posterior capsule rupture, severe macular disease, and amblyopia
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx (Alcon Laboratories Inc) or manual phacoemulsification (Accurus, Alcon Laboratories Inc)
Outcomes	Intraocular lens power calculation, visual and refractive outcomes
Notes	Funding source: not reported Declaration of interest: *"Drs Knorz and Nagy are consultants to Alcon LenSx Inc. All remaining authors have no financial interest in the materials presented herein"* Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned to each group using a computer randomisation chart
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described

Filkorn 2012 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Based on the number of patients/eyes reported in figure 2, there was no loss to follow-up
Selective reporting (reporting bias)	Unclear risk	"Patients with CDVA 20/40 or worse were excluded (one patient in each group) to avoid errors in manifest refraction" No access to study protocol or trials registry entry (trial was not registered)

Hida 2014

Methods	Parallel-group RCT
Participants	Number of participants randomised: 80 (40 laser arm, 40 control arm) Number of eyes included: 80 (40 laser arm, 40 control arm) Country: Brazil Average age: 67 years laser arm, 65 years control arm Ethnic group: not described Inclusion criteria: not described Exclusion criteria: not described
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx (Alcon Laboratories Inc) or manual phacoemulsification (phacoemulsification system not described)
Outcomes	Capsulotomy/capsulorhexis circularity and postoperative spherical equivalent
Notes	Funding source: not reported. Declaration of interest: *"The authors declare no conflicts of interest"* Date study conducted: October 2013 to January 2014 Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described

Hida 2014 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Kovacs 2014

Methods	Parallel-group RCT
Participants	Number of participants randomised: 79 (40 laser arm, 39 control arm) Number of eyes included: 79 (40 laser arm, 39 control arm) Country: Hungary Average age: 66 years laser arm, 69 years control arm Sex: 70% female laser arm, 74% female control arm Ethnic group: not described Inclusion criteria: only exclusion criteria are given Exclusion criteria: *"previous ocular surgery, trauma, active ocular disease (eg. pseudoexfoliation syndrome and uveitis), poorly dilated pupils, or known zonular weakness"*
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx (Alcon Laboratories, Inc.) or manual phacoemulsification using the Infinity Vision System (Alcon Laboratories, Inc.)
Outcomes	Subgroup analysis of previous RCT (no further data on this given). Primary outcome measure: quantification of posterior capsule opacification at 18-26 months postoperatively. Additional data: intraocular lens tilt and decentration
Notes	"*All patients from a previous prospective, randomised study on femtosecond laser surgery with a minimum follow-up time of 18 months were identified in our database and their data were processed for further statistical analyses.*" No publication reference is given for the original RCT Funding source: not reported Declaration of interest: "*Drs. Nagy, Donnenfeld, and Knorz are consultants of LenSx Lasers, Inc. The remaining authors have no financial or proprietary interest in the materials presented herein*" Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Kovacs 2014 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described. Patients included were those with a minimum follow-up time of 18 months from a previous RCT
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Kranitz 2012

Methods	Parallel-group RCT
Participants	Number of participants randomised: 45 (20 laser arm, 25 control arm) Number of eyes included: 45 (20 laser arm, 25 control arm) Country: Hungary Average age: 64 years laser arm, 68 years control arm Sex: 75% female laser arm, 92% female control arm Ethnic group: not described Inclusion criteria: only exclusion criteria are given Exclusion criteria: *"Patients with previous ocular surgery, trauma, active ocular disease, poorly dilated pupils, or known zonular weakness were excluded from the study*"
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx (Alcon Laboratories, Inc.) or manual phacoemulsification using the Accurus phacoemulsification machine (Alcon Laboratories, Inc.)
Outcomes	Intraocular lens decentration and tilt, Refraction, UDVA and CDVA
Notes	Funding source: not reported. Declaration of interest: "*Drs Knorz and Nagy are consultants to Alcon LenSx Inc. The remaining authors have no financial interest in the materials presented herein.*" Date study conducted; not reported Trial registration number: not reported
Risk of bias	

Kranitz 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done using computer-generated tables
Allocation concealment (selection bias)	Unclear risk	Randomisation was done using computer-generated tables
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Mastropasqua 2014a

Methods	Parallel-group RCT
Participants	Number of participants randomised: 60 Number of eyes included: 60 (right eyes) Country: Italy Average age: 70 years Sex: not described Ethnic group: not described Inclusion criteria: "*age between 65 and 75 years, axial length between 23.0 and 24.0 mm, corneal astigmatism less than 2.00 diopters (D), nuclear cataract of grade 2 to 3 (nuclear opalescence 3/4) (Lens Opacities Classification System III), and corneal en- dothelial cell count greater than 1,200/mm* " Exclusion criteria: *"pathological alterations of the anterior segment (eg, corneal opacities, keratoconus, chronic uveitis, zonular dialysis, pseudoexfoliation syndrome, glaucoma, and diabetes mellitus), other ocular pathologies impairing visual function, previous anterior or posterior segment surgery, and intraoperative or postoperative complications"*
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx platform (Alcon Inc, Fort Worth, TX, USA) or manual phacoemulsification using the Alcon Constellation System (Alcon Laboratories, Inc.)
Outcomes	UDVA and CDVA (logMAR), keratometric astigmatism, corneal endothelial cell count, corneal thickness at the incision site and higher order corneal aberrations. Follow-up was 6 months

Mastropasqua 2014a (*Continued*)

Notes	Funding source: not reported Declaration of interest: *"The authors have no financial or proprietary interest in the materials presented herein"* Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The method of sequence generation is not described
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Based on the number of eyes reported in Figure 1, there was no loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Mastropasqua 2014b

Methods	Parallel-group RCT
Participants	Number of participants randomised: 90 Number of eyes included: 90 Country: Italy Average age: 69 years Sex: not described Ethnic origin: not described Inclusion criteria: The inclusion criteria were age between 65 years and 75 years, nuclear cataract grade 3 to 4 (nuclear opalescence [NO] 3/4 on Lens Opacities Classification System III), and a corneal endothelial cell count greater than 1200 cells/mm^2 Exclusion criteria: poor pupil dilation, pathology that could alter the anterior segment (e.g. corneal opacities, keratoconus, chronic uveitis, zonular dialysis, pseudoexfoliation syndrome, glaucoma, diabetes), other ocular pathology that can impair visual function, previous anterior or posterior segment surgery, and intraoperative or postoperative complications

Interventions	Participants were randomised to one of 3 treatments with equal probability for each group: a) laser-assisted cataract surgery using a Lensx femtosecond laser (Alcon Laboratories Inc); the capsulotomy, lens fragmentation and corneal incisions were performed using the femtosecond laser b) laser-assisted cataract surgery using a Lensar femtosecond laser (Lensar Inc); the capsulotomy and lens fragmentation were performed using the femtosecond laser c) manual phacoemulsification
Outcomes	Difference in the distance between the intraocular lens centroid and the pupil centroid 180 days after surgery, visual parameters, refractive parameters, circularity, capsulorhexis area, intraocular lens centroid-pupil centroid distance, and capsulorhexis centroid-pupil centroid distance)
Notes	Funding source not reported Declaration of interest: "*No author has a financial or proprietary interest in any material or method mentioned"* Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A computer-generated, 6-block, 15-patient randomisation list was generated using an in-house closed-source software developed in Matlab 2009b. Patients were assigned to 1 of the 3 treatments with an equal probability for each group
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The trial methodology states: *"The surgeon and the operating room staff were aware of group assignment. The patients were masked to group assignment until the study was completed."* However it is unclear how the patients could remain masked unless sham laser was performed, and there is no description of this
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"*examiners performing preoperative and postoperative assessments were masked to group assignment until the study was completed*"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Based on the results ("Each group comprised 30 eyes (30 patients)"), it would appear that no patients were lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Nagy 2011

Methods	Parallel-group RCT
Participants	Number of participants randomised: 105 (53 laser arm, 52 control arm) Number of eyes included: 111 (54 laser arm, 57 control arm) Country: Hungary Average age: 65 years old laser group, 68 years old control group Sex: 72% female laser group, 70% female control group Ethnic group: not described Inclusion criteria: only exclusion criteria are given Exclusion criteria: "*Patients with previous ocular surgery, trauma, active ocular disease, poorly dilated pupils, or known zonular weakness were excluded from the study*"
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx (Alcon Laboratories, Inc.) or manual phacoemulsification using the Accurus phacoemulsification machine (Alcon Laboratories, Inc.)
Outcomes	Circularity and area of capsulotomy and intraocular lens decentration
Notes	Funding source: not reported Declaration of interest: *"Drs Nagy and Knorz are consultants to LenSx Lasers Inc. The remaining authors have no proprietary interest in the materials presented herein*" Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Using computer randomisation, patients and their right/left eyes were randomly selected for femtosecond and manual surgery
Allocation concealment (selection bias)	Unclear risk	Using computer randomisation, patients and their right/left eyes were randomly selected for femtosecond and manual surgery
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Nagy 2014

Methods	Parallel-group RCT
Participants	Number of participants randomised: 40 (20 laser arm, 20 control arm) Number of eyes included: 40 (20 laser arm, 20 control arm) Country: Hungary Average age: 70 years laser group versus 62 years control group Sex: not described Ethnic group: not described Inclusion criteria: only exclusion criteria are given Exclusion criteria: "*previous ocular surgery, trauma, active ocular disease, poorly dilated pupils, or known zonular weakness were excluded*"
Interventions	Surgical intervention: Laser-assisted cataract surgery using the LenSx platform (Alcon Laboratories Inc) or manual phacoemulsification (platform not described)
Outcomes	Surgically induced astigmatism and corneal higher order aberrations. Additional data reported: intraoperative and postoperative complications. Follow-up was 3 months
Notes	Funding source: not reported Declaration of interest: *"Dr. Nagy is a consultant for Alcon Laboratories, Inc. The remaining authors have no financial or proprietary interest in the materials presented herein"* Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was done using computer-generated tables (Microsoft Excel; Microsoft Corporation, Redmond, WA)"
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment is not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Reddy 2013

Methods	Parallel-group RCT
Participants	Number of participants randomised: 131 Number of eyes: 131 Country: India Average age: 59 years laser arm, 61 control arm Sex: 46% female laser arm, 41% female control arm Ethnic group: not described Inclusion criteria: Eligible patients were at least 18 years old with clear corneal media and elected to have routine cataract surgery" Exclusion criteria for all patients: • poorly dilating pupil or other pupil defect that prevents iris from adequate retraction peripherally • lens/zonule instability such as, but not restricted to, Marfan syndrome, pseudoexfoliation syndrome • previous intraocular or corneal surgery of any kind, including any kind of surgery for refractive or therapeutic purposes in either eye • known sensitivity to planned concomitant medications • disorders of the ocular muscle, such as nystagmus or strabismus • keratoconus • wound-healing disorders, such as connective tissue disease, autoimmune illnesses, immunodeficiency illnesses, ocular herpes zoster or simplex, endocrine diseases, lupus, rheumatoid arthritis • abnormal examination results from slitlamp, fundus, partial coherence interferometry • autoimmune disease, collagenosis, or clinically significant atopy • pregnancy or nursing Additional exclusion criteria for those having laser-assisted procedures: • minimal and maximal K values in central 3.0mm zone that do not differ by more than 5.0 D on a keratometric map of the cornea • maximal K-value that does not exceed 60.0D and minimum value that is smaller than 37.0 D • corneal disease or pathology that precludes transmission of laser wavelength or distortion of laser light • abnormal examination results from scanning-slit corneal topography • anterior chamber depth < 2.4 mm or > 4.5 mm measured by ultrasonic examination The study enrolled 131 patients (laser group, 64; manual group, 67)
Interventions	Surgical intervention: Laser-assisted cataract surgery using the VICTUS™ platform (Bausch & Lomb Technolas) or manual phacoemulsification using the Stellaris Vision Enhancement System (Bausch & Lomb)
Outcomes	Primary outcome measure: effective phacoemulsification time Secondary outcome measures: mean phacoemulsification energy, mean phacoemulsification time, volume of balanced salt solution, subjective surgeon assessment of ease of phacoemulsification Additional data reported: capsulotomy comparisons, intraocular lens decentration, safety data including posterior capsule tear and iris damage

Reddy 2013 (*Continued*)

	Follow-up was limited to 1 day postoperatively
Notes	Funding source: not reported Declaration of interest: *"Dr. Reddy has received travel and research grants from Technolas Perfect Vision GmbH, Dr. Kandulla is an employee of Technolas Perfect Vision GmbH (a Bausch & Lomb company), and Dr. Auffarth has received travel and research grants as well as lecture fees from Technolas Perfect Vision GmbH/Bausch & Lomb"* Date study conducted: not reported Trial registration number: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not described, other than "open-label"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not described, other than "open-label"
Incomplete outcome data (attrition bias) All outcomes	High risk	One eye in the laser-assisted group was excluded from analysis because of a protocol violation (no details of this are given). Also: *"During the clinical trial, it became evident that the P values of all phacoemulsification parameters (EPT, mean phaco energy, mean phaco time, and balanced salt solution volume) were both surgeon dependent and cataract grade dependent. Evaluation by the Mann-Whitney U test showed that median cataract grade between the 2 treatment groups was equal except for those operated on by 1 surgeon. To ensure equal cataract grade distributions in the 2 study groups to guarantee correct data analysis and rule out preoperative bias, 7 eyes in the laser-assisted group and 4 in the manual group were excluded from further analysis. This resulted in 56 eyes in the laser-assisted group and 63 in the manual group that had subsequent analysis"*
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Schargus 2015

Methods	Within-person (paired-eye) RCT
Participants	Number of participants randomised: 37 Number of eyes included: 74 Country: Germany Average age: 72 years Sex: 59% female Ethnic group: not described Inclusion criteria: had a visually significant cataract (NC2 to NC5 on the Lens Opacities Classification System III [LOCS III]), corrected distance visual acuity (CDVA) decreased 0.1logMAR in both eyes, dilated pupil width of 6.0 mm or greater, and were willing to volunteer for the trial after giving informed consent Exclusion criteria: corneal scars, corneal diseases, corneal astigmatism of 1.5 D or greater, reduced endothelial cell count (ECC) (less than 1500 cells/mm^2), CCT less than 500 μm, glaucoma, pseudoexfoliation syndrome, zonular weakness, single eye, malformations, history of ocular surgery, intraocular tumours, active or past inflammations, age-related macular degeneration, diabetic retinopathy, axial length difference (greater than 0.5 mm) and axial length less than 21.5 mm or greater than 26 mm, pregnancy, reduced compliance, age younger than 22 years, or participation in another clinical study within 30 days of the preoperative visit
Interventions	Laser-assisted cataract surgery using the Catalys platform (Catalys Precision Laser System, AMO) or manual phacoemulsification using a Stellaris phaco machine (Bausch & Lomb)
Outcomes	Primary outcome measure: endothelial cell count before surgery and 3 and 6 months postoperatively Secondary outcome measurements included evaluation of corneal thickness, intraocular pressure, CDVA, overall surgery time, and quantity of fluid passing through the eye during surgery
Notes	Funding source: not reported Declaration of interest: *"Dr Dick is a paid consultant for Abbott Medical Optics. The remaining authors have no financial or proprietary interest in the materials presented"* Date study conducted: October 2012 to May 2013 Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Both treatment group allocations were printed on a separate sheet, which were sealed in sequentially numbered identical envelopes according to the randomised allocation sequence
Allocation concealment (selection bias)	Low risk	The enclosed assignments were inserted into sequentially numbered, opaque, well sealed envelopes for allocation concealment, which were continuously monitored. Investigators ensured that the en-

Schargus 2015 (*Continued*)

		velopes were opened sequentially and only after the participant's name and other details were written on the appropriate envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	High risk	No masking of the outcome assessment is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Takacs 2012

Methods	Parallel-group RCT
Participants	Number of participants randomised: 76 Number of eyes: 76 Country: Hungry Average age: 67 years laser arm, 67 years control arm Sex: 74% female laser arm, 61% female manual phacoemulsification arm Ethnic group: not described Inclusion criteria: only exclusion criteria stated Exclusion criteria: *"Patients showing low cooperation, dense (grade 4) or white cataract, corneal scars or opacities, anterior segment abnormalities, floppy iris syndrome, and poor pupillary dilation were not included in the study*"
Interventions	Laser-assisted cataract surgery using the LenSx femtosecond laser (Alcon Laboratories Inc) or manual phacoemulsification using the Alcon Infinity phacoemulsification system (Alcon Laboratories Inc)
Outcomes	Postoperative central corneal oedema, endothelial cell count, and endothelial cell function expressed by volume stress index
Notes	Funding source: not reported Declaration of interest: "*Drs Nagy and Knorz are consultants to Alcon LenSx Inc. The remaining authors have no financial interest in the materials presented herein*" Date study conducted; February 2010 to February 2011 Trial registration number: not reported
Risk of bias	

Takacs 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned (using computer randomisation) to either group by the surgeon (ZZN)
Allocation concealment (selection bias)	Unclear risk	No further details other than above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Examiners were not aware of which surgical procedure had been used when performing the postoperative examinations
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

Yu 2015

Methods	Parallel-group RCT
Participants	Number of participants randomised: 36 Number of eyes: 54 Country: China Average age: 62 years laser arm, 57 years control arm Sex: not described Ethnic group: not described Inclusion criteria: Normal and transparent cornea; Pupillary diameter of at least 6mm under dilation; Preoperative best corrected visual acuity worse than LogMAR 0.3 Exclusion criteria: No local or systematic contraindications for cataract surgery
Interventions	Laser-assisted cataract surgery using the LENSAR femtosecond laser or manual phacoemulsification using the Bausch & Lomb Stellaris system
Outcomes	Phacoemulsification time, energy, and complications during operation were recorded. Postoperative refraction at 1 day, 1 week, 1 and 3 months, the capsulorhexis size and corneal endothelial density at 1 and 3 months were also measured
Notes	Funding source: funded by the International Cooperation Project of the Science and Technology Bureau of Zhejiang province, China (Grant No. 2013C14010) Declaration of interest: *"All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported"* Date study conducted; October 2013 to November 2013 Trial registration number: not reported

Yu 2015 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon masking is not feasible for the study methodology described. No masking of participants is described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Corneal endothelial cell density and capsulorhexis size were measured by a masked examiner. No masking of other outcomes is described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There is no reporting of reporting of data attrition to permit judgement
Selective reporting (reporting bias)	Unclear risk	No access to study protocol or trials registry entry (trial was not registered)

CDVA: corrected distance visual acuity
D: diopters
RCT: randomised controlled trial
UDVA: uncorrected distance visual acuity

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

Study	Reason for exclusion
Conrad-Hengerer 2012a	Not a RCT
Conrad-Hengerer 2013b	Not a RCT
Conrad-Hengerer 2014b	Not a RCT
Ecsedy 2011	Not a RCT
Espaillat 2016	Not a RCT
Hatch 2015	Not a RCT

(*Continued*)

Kerr 2013	Not a RCT
Kranitz 2011	Not a RCT
Krarup 2014	Although this is a within-person paired-eye study, eyes were not randomised to the intervention ("To evaluate whether FLACS was superior to CPS regarding ECL, the eye with most dense cataract was operated with femtosecond laser assisted cataract surgery and the eye with less cataract with conventional cataract surgery")
Nagy 2012	Insufficient information to confirm eligibility (conference abstract only), no mention of randomisation to the intervention
Szigeti 2012	Both arms involved laser-assisted cataract surgery, no phacoemulsification control arm
Toto 2015	Not a RCT
Wang 2015	Unable to source a copy of the paper from either the journal website or the contact author

RCT: randomised controlled trial

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

ISRCTN77602616

Trial name or title	The FACT trial: a randomised comparison of femtosecond laser-assisted vs. manual phacoemulsification cataract surgery for adults with visually significant cataract
Methods	Allocation: randomised
Participants	808
Interventions	Arm A: manual phacoemulsification cataract surgery in the study eye Arm B: laser-assisted phacoemulsification cataract surgery in the study eye
Outcomes	Primary outcome measures Unaided distance visual acuity (UDVA, logMAR) at 3 months following surgery in the study eye measured using a standard ETDRS chart at a distance of 4 metres Secondary outcome measures 1. Unaided distance visual acuity (UDVA) in the study eye at 12 months after surgery 2. Corrected distance visual acuity (logMAR) at 3 and 12 months after surgery in the study eye (ETDRS logMAR chart at 4 metres) 3. Ocular complications within 3 and 12 months of surgery in the study eye (and second eye). A complication will be defined as any event that causes unintentional injury to an ocular structure, or requires additional treatment, or has a negative effect on a patient's health or eyesight 4. Unaided and corrected visual distance acuity and complications in the second eye (for those with bilateral cataracts), and with both eyes open at 3 and 12 months after surgery

ISRCTN77602616 (*Continued*)

	5. Percentage of patients within 0.5 and within 1 dioptre of intended refractive outcome 6. Patient-reported outcomes measures: vision health status using Rasch validated patient-reported outcome measures at 3 and 12 months: (Catquest-9SF) 7. Cost-utility analysis: within-trial cost-effectiveness analyses at 3 and 12 months and expected cost- effectiveness over patient lifetime. The analysis will conform to accepted economic evaluation methods and will use the EQ-5D-3L+vision bolt-on question (EQ-5DV) 8. Corneal endothelial cell count change (additional safety measure) at 3 and 12 months
Starting date	01/05/2015
Contact information	ctu.fact@ucl.ac.uk
Notes	Overall trial end date: 28/02/2018

NCT01693211

Trial name or title	Prospective evaluation of circularity and diameter of femtosecond laser versus manual anterior capsulotomy in Singapore National Eye Centre
Methods	Allocation: randomised Endpoint classification: efficacy study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment
Participants	48
Interventions	Device: femtosecond laser (VICTUS™ femtosecond laser platform) Device: manual phacoemulsification cataract surgery (continuous curvilinear capsulorrhexis technique with Utrata forceps)
Outcomes	Primary outcome measure: circularity of created rhexis Secondary outcome measure: diameter of the created rhexis Other outcome measure: centration of the created rhexis relative to the pupil
Starting date	September 2012
Contact information	Principal investigator: Soon Phaik Chee, Assoc Prof, Singapore National Eye Center
Notes	Study completion date: June 2014 No study results posted

NCT01769313

Trial name or title	A single centre study to analyze cataract surgery following femtosecond laser-assisted and manual cataract surgery
Methods	Allocation: randomised Endpoint classification: efficacy study Intervention model: parallel assignment Masking: single-blind (caregiver) Primary purpose: treatment
Participants	30
Interventions	Device: laser-assisted cataract surgery Device: manually performed cataract surgery
Outcomes	Capsulotomy overlap, effective lens position, difference in pre- to postoperative flare, refractive outcome prediction error
Starting date	January 2013
Contact information	Principal investigator: Gerd U Auffarth, Prof. Universitäts-Augenklinik Heidelberg
Notes	Study completion date: October 2014 No study results posted

NCT01971177

Trial name or title	A multi-centre, multi-surgeon, randomised, controlled, prospective, post-market clinical follow-up study to investigate the impact of cataract grade on the efficacy and safety of femtosecond laser-assisted lens fragmentation procedure
Methods	Allocation: randomised Endpoint classification: safety/efficacy study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment
Participants	136
Interventions	Device: femtosecond laser cataract surgery Procedure: manual cataract surgery
Outcomes	Primary outcome measures: effective phacoemulsification time Secondary outcome measures: adverse events
Starting date	October 2013
Contact information	Principal investigator: Pavel Stodulka, Dr. med Gemini clinic, Zlin, Czech Republic 76001

NCT01971177 (*Continued*)

Notes	Study completion date: February 2014 No study results posted

NCT01982006

Trial name or title	Impact médico-economique de la chirurgie de la cataracte au laser femtoseconde
Methods	Allocation: randomised Endpoint classification: safety/efficacy study Intervention model: parallel assignment Masking: single blind (subject) Primary purpose: treatment
Participants	1050
Interventions	Procedure: cataract surgery with phacoemulsification Device: femtosecond laser-assisted cataract surgery
Outcomes	Primary outcome measures: • incremental cost/effectiveness ratio defined as cost per incremental therapeutic success Therapeutic success will be defined by the association of the following criterion • No severe intraoperative or postoperative complications • Best Corrected Visual Acuity of 0 LogMAR • A refractive error inferior or equal to 0.75 diopter • Corneal surgically-induced astigmatism inferior or equal to 0.5 diopter and a postoperative change of astigmatism axis inferior or equal to 20° Secondary outcome measures: • quality of life • quality of life evaluation using Visual Function 14 questionnaire • learning curve of the femtosecond laser-assisted cataract surgery • overall costs of cataract surgery in both arms from the hospital perspective • incremental cost-utility ratio defined as incremental cost/QALY (Quality Adjusted Life Year) for healthcare insurance in both arms • no severe intraoperative or postoperative complications • best corrected visual acuity of 0 LogMAR • refractive error inferior or equal to 0.75 diopter • corneal surgically-induced astigmatism inferior or equal to 0.5 diopter and a postoperative change of astigmatism axis inferior or equal to 20°
Starting date	October 2013
Contact information	Principal investigator: Cédric SCHWEITZER, University Hospital Bordeaux, France
Notes	Estimated study completion date: April 2016

NCT01991717

Trial name or title	An open-label investigator-masked study comparing femtosecond laser assisted with conventional phacoemulsification cataract surgery
Methods	Allocation: randomised Intervention model: parallel assignment Masking: single-blind (investigator) Primary purpose: treatment
Participants	50
Interventions	Device: VICTUS™ Device: conventional phacoemulsification
Outcomes	Primary outcome measures: effective phacoemulsification time Secondary outcome measures: intraocular lens overlap, intraocular lens centration Other outcome measures: patient subjective perception, effects on the cornea and retina as assessed by optical coherence tomography (OCT), pentacam or endothelial cell count
Starting date	December 2013
Contact information	Principal investigator: Matthias Bolz, AKh Linz, Ophthalmology
Notes	Estimated study completion date: January 2015

NCT02110212

Trial name or title	A prospective, randomised study of cataract surgery with the assistance of the OptiMedica femtosecond laser system compared to standard surgical procedure of continuous curvilinear capsulorhexis and ultrasonic phacoemulsification
Methods	Allocation: randomised Endpoint classification: safety/efficacy study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment
Participants	17
Interventions	Procedure: ultrasound surgery and continuous curvilinear capsulorrhexis Device: femtosecond laser surgery
Outcomes	Primary outcome measure: capsulotomy dimension Secondary outcome measure: cumulative dissipated energy
Starting date	April 2011
Contact information	Principal investigator: Juan F. Batlle, Laser Center, Santo Domingo, Dominican Republic

NCT02110212 (*Continued*)

Notes	Study completion date: February 2014 No study results posted: this study has been terminated

NCT02351271

Trial name or title	A single centre randomised eye study to compare the performance and safety of femtosecond laser-assisted cataract procedures with conventional ultrasound-assisted cataract surgery
Methods	Allocation: randomised Endpoint classification: safety/efficacy study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment
Participants	130
Interventions	Device: Femto LDV Z8 Device: manual capsulorhexis and lens fragmentation
Outcomes	Primary outcome measure: effective phacoemulsification time Secondary outcome measures: ease of phacoemulsification, completeness of capsulotomy Other outcome measures: safety outcomes
Starting date	February 2015
Contact information	Principal investigator: Bojan Pajic, Augenzentrum ORASIS AG
Notes	Estimated study completion: September 2016

NCT02403206

Trial name or title	Femtosecond laser assisted cataract surgery in intumescent cataracts
Methods	Allocation: randomised Endpoint classification: safety study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment
Participants	425
Interventions	Device: femtosecond laser Procedure: continuous curvilinear capsulorhexis
Outcomes	Primary outcome measure: percentage of capsular tears (anterior or posterior) Secondary outcome measure: operating time

NCT02403206 (*Continued*)

Starting date	March 2015
Contact information	Study director: Kristi Rushin, Alcon Research
Notes	Estimated study completion date: August 2016

NCT02492659

Trial name or title	Clinical research of femtosecond laser-assisted cataract surgery: randomised clinical trial
Methods	Allocation: randomised Intervention model: single group assignment Masking: single-blind (investigator) Primary purpose: treatment
Participants	54
Interventions	Procedure: femtosecond laser-assisted cataract surgery Procedure: conventional phacoemulsification
Outcomes	Primary outcome measure: the proteins in the aqueous humor after femtosecond laser operation Secondary outcome measures: the electrolyte in the aqueous humor after femtosecond laser operation; morphology of the anterior capsule after femtosecond laser operation Other outcome measures: • phacoemulsification energy • phacoemulsification time • postoperative refraction • the capsulorhexis size • corneal endothelial density
Starting date	October 2013
Contact information	Principal investigator: A-Yong Yu, Wenzhou Medical University
Notes	Study completion date: June 2014

NCT02561104

Trial name or title	Outcomes of resident-performed laser-assisted versus manual traditional phacoemulsification
Methods	Allocation: randomised Endpoint classification: safety/efficacy study Intervention model: parallel assignment Masking: open-label Primary purpose: treatment

NCT02561104 (*Continued*)

Participants	180
Interventions	Procedure: laser-assisted cataract surgery Procedure: traditional manual phacoemulsification
Outcomes	Primary outcome measures: • complication rates • bilateral best spectacle corrected visual acuity Secondary outcome measures: • patient benefit perception • corneal endothelial cell count • lens removal time
Starting date	September 2015
Contact information	Bonnie Miller, University of Texas Southwestern Medical Center
Notes	Estimated study completion date: January 2017

DATA AND ANALYSES

Comparison 1. Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intraoperative complications	10		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 Anterior capsule tear	10		Odds Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Posterior capsule tear	10		Odds Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Visual acuity	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Corrected distance visual acuity 1 week	3	204	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.10, 0.01]
2.2 Corrected distance visual acuity 1-3 months	5	412	Mean Difference (IV, Random, 95% CI)	-0.00 [-0.03, 0.02]
2.3 Corrected distance visual acuity 6 months or more	3	224	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.05, -.00]
2.4 Uncorrected distance visual acuity 1 week	2	150	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.19, 0.14]
2.5 Uncorrected distance visual acuity 1-3 months	2	150	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.21, 0.15]
2.6 Uncorrected distance visual acuity 6 months or more	2	150	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.26, 0.14]
3 Total duration of procedure	3	274	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.02, 0.21]
4 Postoperative complications	10		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Cystoid macular oedema	9	957	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.20, 1.68]
4.2 Elevated intraocular pressure (up to 1 day after surgery)	9	1022	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.29, 2.66]
4.3 Elevated intraocular pressure (1 day to 1 week after surgery)	8	903	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.11, 2.86]
5 Refractive outcomes - mean absolute error	3	278	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.27, -0.09]

CONTRIBUTIONS OF AUTHORS

ACD and CB contributed to the concept, design and writing of the protocol. DMG contributed to the design and provided feedback for the protocol. ACD and DMG reviewed the titles and abstracts from the electronic literature searches and extracted data from these for the review. JE assisted with data analysis and write-up. All authors contributed to responding to editorial and peer review comments, and approved the final version of the review for publication.

DECLARATIONS OF INTEREST

Alex Day is the sub-Principal Investigator for the ongoing FACT trial (ISRCTN77602616). Catey Bunce is a Co-Applicant for the ongoing FACT trial (ISRCTN77602616).

Daniel Gore, Jennifer Evans: None to declare.

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External sources

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The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS, or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The differences between the Day 2013 protocol and the review are summarised below.

We changed the title to "Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery". The title previously was "Laser assisted versus manual phacoemulsification for lens extraction."

We modified the outcomes to include outcomes of relevance to the proposed National Institute for Health and Care Excellence (NICE) Cataract Surgery Guidelines. In particular we included refractive outcomes (including deviation from the predicted refractive outcome), we included patient-reported outcomes such as satisfaction, and included resources used, such as total duration of procedure, in addition to costs.

We added the methods for GRADE assessment that were not included in the original protocol.

Some planned methods could not be performed because there were too few trials supplying relevant data. We therefore did not do any subgroup analysis according to type of laser system used and we did not do a sensitivity analysis excluding trials at high risk of bias.

INDEX TERMS

Medical Subject Headings (MeSH)

Anterior Capsular Rupture, Ocular [etiology]; Cataract Extraction [adverse effects; *methods]; Laser Therapy [adverse effects; *methods]; Macular Edema [etiology]; Ocular Hypertension [etiology]; Phacoemulsification [adverse effects; methods]; Posterior Capsular Rupture, Ocular [etiology]; Randomized Controlled Trials as Topic; Visual Acuity

MeSH check words

Adult; Humans