NICE National Institute for Health and Care Excellence

2021 exceptional surveillance of cataracts in adults: management (NICE guideline NG77)

Surveillance report

Published: 25 November 2021

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Surveillance decision

We will not update the NICE guideline on cataracts in adults: management at this time.

We will await the publication of the update of the Cochrane review on Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery (Day et al. 2016) to make a decision on whether or not to update the recommendation that femtosecond laser-assisted cataract surgery is only used as part of a randomised controlled trial (RCT).

Reason for the exceptional review

In the NICE guideline on management of cataracts, the section on surgical timing and techniques advises use of standard phacoemulsification cataract surgery and that femtosecond laser-assisted cataract surgery should only be used as part of a RCT that includes collection of resource-use data, comparing femtosecond laser-assisted cataract surgery with ultrasound phacoemulsification (recommendation 1.6.1). Two recently-published RCTs provide further evidence on use of the laser-assisted cataract surgery:

- Femtosecond laser-assisted cataract surgery compared with phacoemulsification: the FACT non-inferiority RCT (Day et al. 2021).
- Femtosecond laser-assisted versus phacoemulsification cataract surgery (FEMCAT): a multicentre participant-masked randomised superiority and cost-effectiveness trial (Schweitzer et al. 2020).

This exceptional review examined the impact of these studies.

Methods

The exceptional surveillance process consisted of:

- Considering the evidence used to develop the guideline in 2017.
- Considering the new evidence that triggered the exceptional review.
- A focused literature search to identify any additional relevant evidence.

- Feedback from topic experts.
- Contact with Cochrane Eyes and Vision group.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Information considered when developing the NICE guideline

During guideline development, RCT evidence published up to May 2016 was searched for the review question 'What is the effectiveness of laser-assisted phacoemulsification cataract surgery [aka femtosecond laser-assisted cataract surgery] compared with standard ultrasound phacoemulsification cataract surgery?' The evidence review was undertaken by the Cochrane Eyes and Vision group, in collaboration with the NICE internal clinical guidelines team and published as a Cochrane review: 'Laser‐assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery' (Day et al. 2016).

Sixteen RCTs were identified for inclusion in the review. The studies enrolled a total of 1,638 eyes (n=1,245 adults). Study quality was assessed using GRADE and studies were assessed as low or very low quality.

The rates of intraoperative complications (anterior capsule and posterior capsule tears) were low across studies and there was no significant difference in rates of complications between those given laser-assisted cataract surgery versus those given standard ultrasound phacoemulsification (10 RCTs with 1,076 participants). There was also no significant difference between surgical interventions in postoperative complications (rates of cystoid macular oedema or elevated intraocular pressure; 9 RCTs with 957 participants).

For visual acuity, measured by corrected distance visual acuity (CDVA) or uncorrected distance visual acuity (UDVA) at 1 week, 1 to 3 months, or ≥6 months after cataract surgery, the only difference between surgical interventions was for CDVA ≥6 months (3 RCTs, 338 participants), which indicated a small statistical advantage for laser-assisted cataract surgery equivalent to a 1 to 1.5 letter improvement. This was judged by the committee not to be a clinically meaningful difference, particularly as it was not replicated at other time points, nor was a difference identified in UDVA.

A literature search for health economic publications identified only 1 cost–utility study, which was assessed as only partly applicable as it was a non-UK study. It also had potentially serious limitations, due to large amounts of the parameter inputs being based solely on assumptions. The study findings suggested that laser-assisted cataract surgery is not cost-effective when compared with standard phacoemulsification techniques.

No studies reported patient-reported outcome measures.

The guideline committee agreed that there was no evidence to suggest a clinical difference between using laser-assisted and standard phacoemulsification surgery and therefore agreed that it would be inappropriate for laser-assisted cataract surgery to be regularly used. The committee agreed that there could be value in additional trials comparing laser-assisted surgery with ultrasound phacoemulsification because of the relative scarcity and low quality of the evidence base, and that there are specific situations when laser-assisted surgery may have benefits (for example, to improve outcomes for inexperienced surgeons).

The committee agreed that while the economic evidence was not directly relevant to the decision problem at hand, nor particularly robust, it still provided useful evidence to inform its decision, as it demonstrated that the benefits necessary for laser-assisted surgery to be cost-effective at a population level were much larger than those shown by currently published trials. The committee noted that results from the (then ongoing) FACT trial and the FEMCAT trial may offer new evidence. The committee also considered that additional research could be undertaken to examine whether femtosecond laser-assisted surgery enables greater surgical throughput and therefore has health-economic benefits through increasing capacity, which may offset the higher costs of laser-assisted surgery. The committee felt an 'only in research' recommendation was appropriate, and that it should specify that resource use data is collected, 'as this will be a key element in deciding on the long-term place of laser assistance in cataract surgery.'

This reflects the conclusions from the Cochrane review that also highlighted the need for large, adequately powered, well designed RCTs comparing the efficacy and safety of laser-assisted versus standard phacoemulsification cataract surgery because of the low complications rate.

Studies considered in this exceptional surveillance review

FACT trial

This was a UK-based pragmatic, randomised controlled non-inferiority trial comparing the impact of FLACS (femtosecond laser-assisted cataract surgery; n=392) versus PCS (phacoemulsification; n=393) in adults (18 years or older) who needed surgery for age-related cataracts. The primary outcome of interest was UDVA in the study eye at 3-months and 12-months follow-up. Secondary outcomes included CDVA, refractive outcomes, adverse events, health-related quality of life, patient-reported vision health status. Resource use and costs were also measured.

Participants were aware of which procedure they received. Surgeons (by necessity) were aware of the cataract procedure they were performing. Outcomes were measured by optometrists who were masked to the trial intervention.

A sample size analysis was undertaken to ensure recruitment of enough patients for identifying a treatment effect size of 1 logMAR (logarithm of the minimum angle of resolution) line UDVA, which was considered as 'clinically important to patients and ophthalmologists as determined by prior patient and public involvement in the trial design'. The sample size analysis also took into consideration the clustering of patients within operating surgeons (which meant that each patient could not be assumed to generate independent information) and an anticipated 15% dropout rate. A total sample size of 808 patients were required to 'provide 90% power to be sure that a 95% two-sided confidence interval (CI) would exclude the non-inferiority limit of 0.1 logMAR, assuming a common standard deviation of 0.32'. While the trial recruited slightly fewer participants than planned (n=785), the authors reported that 'based on the pre-recruitment power calculation, the 95% CI for the difference in visual acuity … did not include our non-inferiority margin of 0.1 logMAR that was considered to be appropriate for cataract drug efficacy trials' (see results below).

The 3 months follow-up was attended by 90% of FLACS participants (n=352) and 81% of PCS participants (n=317). For the primary outcome, the mean ±SD for UDVA logMAR was 0.13±0.23 in the FLACS arm and 0.14±0.27 in the PCS arm. The mean UDVA difference between the treatment arms was non-significant at 0.01 logMAR (95% CI=0.05 to 0.03).

The 12 months follow-up was attended by 79% of FLACS participants (n=311) and 74% of PCS participants (n=292). The UDVA logMAR was 0.14±0.22 in the FLACS arm and 0.17±0.25 in the PCS arm. The mean UDVA difference between treatment arms was non-significant at 0.03 logMAR (95% CI=0.06 to 0.01 logMAR).

The only significant difference in secondary outcome measures between the treatment arms was for mean binocular CDVA difference at 12 months follow-up, which favoured the FLACS arm: 0.02 logMAR (95% CI=0.05 to 0.00 logMAR; p=0.036); however the authors reported that this is not considered a clinically meaningful difference.

There was a low events rate for intraoperative complications, with only 2 posterior capsule tears in the PCS arm and none in the FLACS arm, 3 anterior capsule tears in FLACS arm and 2 in PCS arm. Rates of postoperative complications were similar between arms at 3 months and 12 months, with the most common complication being postoperative anterior uveitis (38 cases in the FLACS arm and 33 in the PCS arm at 12 months). Macular oedema was observed in 9 cases in the FLACS arm and 14 in the PCS arm at 12 months. At 12 months there were 7 study eyes in the FLACS arm and 3 in the PCS arm that had elevated intraocular pressure requiring treatment.

The economic evaluation reported that the mean cost difference of FLACS minus PCS in the UK was £167.62 per patient (95% of iterations for the imputed, bootstrapped, adjusted data were between -£14.12 and £341.67); and the mean QALY difference was 0.001 (95% of iterations between -0.011 and 0.015), which represents an incremental cost-effectiveness ratio (ICER) of £167,620. The authors reported that 'for the threshold analysis from a health and social care cost perspective, assuming that FLACS results in an additional 0.001 QALYs per patient, FLACS needs to cost £138 less than it currently does to potentially be cost-effective at a willingness-to-pay threshold of £30,000 for a QALY gained'.

The conclusions from the findings of the FACT trial were that FLACS is not worse (inferior to) PCS on visual, refractive or safety outcome measures; but given FLACS is more expensive than PCS, FLACS is not currently a cost-effective technique.

The authors of the study speculated that 'It is possible that FLACS may offer advantages over PCS for patients with certain subtypes of cataract, or for lens replacement surgery using multifocal or other 'premium' intraocular lens, but further research may be required'.

FEMCAT trial

This was a French-based randomised parallel superiority clinical trial comparing the impact of FLACS (n=704) and PCS (n=685) in adults (aged 22 years or older) who needed unilateral or bilateral cataract surgery. The primary outcome of interest was 'success rate of surgery' at 3 months follow-up which was measured by: absence of severe intraoperative or postoperative complications, a best-corrected visual acuity of 0.0 LogMAR or better, an absolute refractive error ≤0.75 dioptres, and unchanged postoperative corneal astigmatism power (≤0.5 dioptres) and axis (≤20°). Resource use and costs were also measured. Secondary outcomes included measurement of intraocular pressure and central corneal thickness, measurements of central macular thickness and vision-related quality of life. Each component of the composite primary outcome was also analysed separately.

Surgeons were aware of the cataract procedure they were performing but participants and those assessing outcomes were masked to the surgical treatment.

Sample size analysis was based on the requirements of the cost-effectiveness model considering: the costs of severe perioperative ophthalmological complication to the French healthcare system, an anticipated success rate of 75% with PCS and 82% with FLACS, and assumption that 90% of the patients would present a bilateral cataract. This resulted in a requirement of 2,000 eyes to be included in the trial, which would enable 'the power to distinguish a 6-point difference in the success rate between both groups, with an anticipated 75% rate of success in the PCS group, and 90% power at an alpha risk level of 5% (χ^2 test).' While the overall sample size achieved was only 1,389 eyes, the observed difference in the primary outcome between FLACS and PCS was 'far lower than the hypothesis' on which the sample size calculation was based, 'and the observed differences in all outcomes were in favour of PCS' (see results below), so the authors concluded that the smaller sample size did not affect the interpretation of results.

A modified intention-to-treat analysis with missing data considered as treatment failure was undertaken for the primary clinical outcome analysis. There was no significant difference in the success rate of surgery between FLACS (41.1% success rate, n=289 eyes) and PCS (43.6%, n=299 eyes; adjusted odds ratio=0.85, 95% CI 0.64 to 1.12). The overall success rate was similar in an as-treated analysis, whereby analysis is based on the treatment someone received rather than according to the treatment they were assigned to (FLACS=50.0% success rate, n=268/536 eyes, and PCS=51.0%, n=320/627 eyes; adjusted odds ratio=0.88, 95% CI 0.66 to 1.17).

There were no significant differences between treatment arms for any of the secondary outcomes and no severe adverse events were observed during either procedure. Posterior capsule tears were observed in 10 eyes in the FLACS arm and 11 in the PCS arm. For postoperative complications, there were 21 cases of cystoid macular oedema after FLACS and 27 after PCS.

Cost-effectiveness was analysed at the patient level according to the modified intention-to-treat analysis. FLACS was found to be more expensive and less effective than PCS. The ICER was €10,703 saved per additional patient who had treatment success with PCS compared with FLACS.

As in the FACT trial, the findings in the FEMCAT trial indicate that FLACS is not superior to PCS in cataract surgery outcomes and, because of the higher costs associated with FLACS, it is not considered cost-effective.

Additional evidence

To ensure that other relevant studies were included in this review, we undertook a focused search for RCTs published since May 2016.

Search and selection strategy

We searched for new evidence related to the review question 'What is the effectiveness of laser-assisted phacoemulsification cataract surgery compared with standard ultrasound phacoemulsification cataract surgery?' The original search strategy for this review question was re-run (see appendix D: Review search strategies, Table 19: Cochrane strategy RQ13). We found 119 studies in a search for RCTs published between 1 May 2016 and 14 May 2021.

For RCTs to be included they had to meet the original inclusion criteria (see appendix C: Review protocols); plus, given concerns about the power of studies to detect differences in outcomes between FLACS and PCS, we chose a conservative cut-off of a sample size of at least 200 eyes. This resulted in 7 studies for inclusion, 3 of which reported findings from the FACT trial (Day et al. 2020a and Day et al. 2020b, Day et al. 2021) and 1 reported findings from the FEMCAT trial (Schweitzer et al. 2020), details of which are reported above. There were also 3 publications reporting on the outcomes of a UK single-centre RCT, which assessed the clinical effectiveness and resource implications of FLACS versus PCS (Roberts et al. 2018, Roberts et al. 2019 and Stanojcic et al. 2021; see UK trial from

Guy's and St Thomas' hospital).

UK trial from Guy's and St Thomas' hospital

In this RCT 400 patients undergoing cataract surgery were randomised to receive either PCS or FLACS, with 200 planned in each arm, however in the FLACS group 7 patients were not able to complete the treatment and received PCS instead. The primary outcome of interest was UDVA at 4 weeks post-surgery. Secondary outcomes included intraoperative and postoperative complications, quality of life and patient-reported quality of vision. Participants and surgeons were aware of the cataract procedure they were performing. Outcomes were measured by an optometrist or technician who were masked to the trial intervention.

A sample size analysis was undertaken before the study which indicated that to have an 85% chance of detecting a 0.1 difference in logMAR visual acuity a sample size of 370 was needed. Patients were followed-up at 4 weeks (n=193 in the PCS arm and n=198 in the FLACS arm; Roberts et al. 2019) and at 12 months (n=118 in the PCS arm and n=116 in the FLACS arm; Stanojcic et al. 2021).

At 4 weeks follow-up the rate of posterior capsule rupture was found to be significantly higher in the PCS compared with FLACS arm (n=6 and n=0 respectively). However, as with the FACT and FEMCAT trial, the number of complications was low, and the study authors noted that because of the low rate of complications the study was not sufficiently powered to detect differences in these events between the different surgical techniques. There were no other significant differences reported between the surgical interventions for intraoperative or postoperative complications. At 12-months follow-up there were also no significant differences in postoperative complications between the surgical interventions.

There were no significant differences between FLACS and PCS in measures of visual acuity at 4 weeks or 12 months follow-up. At 4 weeks the mean ±SD for UDVA (logMAR) after PCS was 0.15±0.21 and 0.15±0.19 after FLACS; at 12 months this was 0.13±0.19 after PCS and 0.12±0.18 after FLACS.

For patient-reported outcomes at 4 weeks and 12 months follow-up, the only significant different between groups was found at 4 weeks for the EQ-5D visual analogue score, which was unchanged in the FLACS group, but showed an improvement in the PCS group. For all other patient-reported outcomes improvements were found post-surgery for both

surgical techniques.

A health economics analysis was also undertaken to assess whether a 'hub-and-spoke' service model for FLACS could improve cataract operating room (OR) productivity and whether the number of cases per theatre session could be increased sufficiently to offset the additional costs of femtosecond laser technology (Roberts et al. 2018). The hub-and-spoke model aimed to increase the number of surgical cases undertaken by having a separate room for femtosecond laser and then 'feeding patients into several ORs for completion of surgery' (2 theatres functioning in parallel, with staff working between the 2).

Operation time and total time in the OR were both significantly lower with FLACS compared with PCS, which meant that 1 extra FLACS case per 4-hour theatre list could be undertaken compared with the PCS-only lists. This represented an average 12.5% increase in daily productivity. FLACS cost £144.60 more than PCS per case. Changes in costs if a third or fourth OR was added to the hub-and-spoke model were also assessed. A fourth OR was viewed as the maximal number possible. In these scenarios the differences in costs between FLACS and PCS would be reduced to £131 and £125 respectively. An economic analysis indicated that, depending on patient list size (number of patients operated on per year) and the number of ORs in the hub-and-spoke model, FLACS would only be cost neutral if there was a discount of between 78% and 99% on the cost of the femtosecond laser patient interface. Therefore, even when using a service model that improved productivity, FLACS was not considered cost-effective in comparison to PCS.

Topic expert feedback

In this exceptional review we contacted the 6 topic experts who were members of the guideline development group for the NICE guideline on cataracts in adults. Two topic experts responded: a consultant ophthalmologist and consultant optometrist.

One topic expert agreed that the findings reported in the FACT and FEMCAT trials indicate that recommendation 1.6.1 should be updated. The other topic expert said that while the results of the trials could be interpreted as indicating that FLACS should not be offered, 'there may be a role and a potential cost saving if femtosecond laser surgery was used for a subset of cataract operations. For example, those patients with significant pre-operative astigmatism. It is also possible that femtosecond laser posterior capsulorrhexis at the time of cataract surgery may prove to be both safe and cost-effective by reducing the number of patients requiring subsequent YAG capsulotomies'. The topic expert said that they

therefore thought 'it is important to continue to allow further research, whilst making it clear to purchasers that they should not pay for laser-assisted surgery on routine cataract cases'.

We checked the studies considered in this exceptional surveillance review for evidence on the impact of FLACS versus PCS in people requiring cataract surgery who have significant pre-operative astigmatism. In the FACT trial the statistical model for assessing differences in visual acuity outcomes between FLACS and PCS was adjusted for baseline astigmatism, and no significant differences were found for visual acuity outcomes between the interventions. In the FEMCAT study postoperative astigmatism was an outcome, but it is not reported that analysis adjusted for baseline astigmatism. In the Guy's and St Thomas' hospital trial those patients who had corneal astigmatism greater than 0.9 dioptre received either manual limbal relaxing incisions (LRIs) performed during PCS (n=51 at 4 weeks follow-up and n=33 at 12 months follow-up) or femtosecond laser arcuate keratotomy (iFAK) during FLACS (n=53 at 4 weeks and n=36 at 12 months follow-up). For corneal astigmatic outcomes at 4 week and 12 months follow-up, the iFAK group had a significantly greater correction index and significantly smaller mean difference vector (equivalent to postoperative corneal astigmatism), indicating that those patients with significant pre-operative astigmatism had more astigmatism corrected in the FLACS intervention compared with PCS. However, as noted by the study authors, the sample size is small and further investigation of whether FLACS (using iFAKs) does result in better stability of astigmatic correction than LRIs during PCS is needed.

YAG laser capsulotomy is a procedure that is needed to restore vision after a cataract operation if there is postoperative thickening of the lens capsule, which can be identified by posterior capsular opacification (PCO). A check of the studies considered in this exceptional surveillance review revealed that PCO rates at 12 months postoperatively were reported in the FACT and Guy's and St Thomas' hospital trial and neither study found a significant difference in PCOs between FLACS and PCS. The Guy's and St Thomas' hospital trial also reported that the rate of YAG laser capsulotomies for significant PCO was the same in both groups (2/116 in FLACS and 2/118 in PCS).

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

Since the publication of recommendation 1.6.1 in 2017, 3 large RCTs, including 2 which were UK-based, have been published which compare the clinical- and cost-effectiveness of FLACS with ultrasound PCS for cataract surgery. These RCTs found no clinically meaningful difference in measures of visual acuity, intraoperative or postoperative complications between FLACS and PCS; and concluded that FLACS, at its current cost, is not considered a cost-effective intervention for the treatment of cataracts. However, the evidence was mixed concerning FLACS improving astigmatism outcomes in people requiring cataract surgery who have significant pre-operative astigmatism. There may therefore be a reason to continue research comparing FLACS with PCS within this subgroup of cataract patients.

In addition, while the evidence indicates that there is no difference in complications between FLACS and PCS, all study authors noted that due to complications being rare, studies were not powered to identify differences in complications such as posterior capsule tears. Additional meta-analysis is therefore needed to investigate possible differences in rare events as this will provide a more precise estimate of the effect size and improve the generalisability of the results of individual studies. A meta-analysis may also indicate whether FLACS compared with PCS reduces the number of patients requiring subsequent YAG capsulotomies. We contacted the Cochrane Eyes and Vision group to ask whether the 2016 Cochrane review on Laser-assisted cataract surgery versus standard ultrasound phacoemulsification cataract surgery could be updated with new RCT evidence; and we were told that an update is currently underway.

It is therefore proposed that recommendation 1.6.1 in cataracts in adults: management is not considered for update until the findings of the updated Cochrane review are available, which is expected to include meta-analysis of results including complications (where statistically appropriate).

ISBN: 978-1-4731-4357-9