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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Laser Refractive Surgery for Vision Correction: A Review of Clinical Effectiveness and Cost-effectiveness

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	June 22, 2018
Report Length:	21 Pages

CADTH

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Cite As: Laser refractive surgery for vision correction. Ottawa: CADTH; 2018 June. (CADTH rapid response report: summary with critical appraisal).

Acknowledgments:

ISSN: 1922-8147 (online)

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Context and Policy Issues

Refractive errors are vision defects caused by the change in shape of the cornea, a transparent surface that covers the eye ball, leading to improper focus of light rays on the retina.[1,2] Laser refractive eye surgery refers to the use of laser techniques to correct refractive errors, such as myopia (nearsightedness), hyperopia (farsightedness) or astigmatism (uneven focusing).[2,3] It uses excimer laser to reshape the cornea's curvature to restore the refractive power of the eye, and ultimately to reduce or eliminate the need to wear glasses or contact lenses.[1]

There are two main techniques of laser refractive eye surgery for vision correction:[4]

- Flap or lamellar procedures: A thin flap of the corneal tissue is cut with either a microkeratome or a femtosecond laser and is lifted. A precise amount of tissue of the corneal stroma is removed with the microkeratome, an excimer laser or a specialized instrument, and then the flap is replaced. Three currently available procedures are Automated Lamellar Keratoplasty (ALK), Laser-Assisted in situ Keratomileusis (LASIK), and Refractive Lenticule Extraction (ReLEx), which is further subcategorized as Femtosecond Lenticule Extraction (FLEX) and Small Incision Lenticule Extraction (SMILE).
- Surface procedures: The most anterior tissue of the corneal stroma is ablated with an excimer laser without the need of a partial cut to create a corneal flap. Five different procedures are Photorefractive Keratectomy (PRK), Transepithelial photorefractive Keratectomy (TransPRK), Laser-Assisted Sub-Epithelial Keratomileusis (LASEK), Epithelial Laser Keratomileusis (Epi-LASIK), and customized Transepithelial No-touch (C-TEN).

Recent systematic review and meta-analysis found no significant differences in visual outcomes (efficacy and safety) or visual quality (post-operative higher-order aberrations and contrast sensitivity) among common used refractive surgical techniques, including LASIK, PRK, LASEK and Epi-LASIK.[5] The visual outcomes were often accomplished in short-term studies, while long-term outcomes are still unclear.[2] The aim of this report is to review the long-term clinical effectiveness of laser refractive surgery for vision correction in adults, with particular emphasis on the length of time to avoid corrective eye wear, patient satisfaction and quality of life. Cost-effectiveness of laser refractive surgery is also taken into consideration in this review.

Research Questions

1. What is the long term clinical effectiveness of laser refractive surgery for vision correction?
2. What is the comparative clinical effectiveness of laser refractive surgery procedures for vision correction?
3. What is the cost-effectiveness of laser refractive surgery versus other vision correction or versus other laser techniques for vision correction?

Key Findings

Evidence on long-term clinical effectiveness of laser refractive surgery for vision correction defined as the number of years that a patient remains independent of corrective eyewear

was not identified. Patients who underwent Laser-Assisted in situ Keratomileusis reported having higher overall patient satisfaction compared to those wearing contact lenses. No difference in patient satisfaction or vision-related quality of life was detected among refractive eye surgery techniques. No relevant literature on the cost-effectiveness of laser refractive eye surgery was identified.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD), Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to systematic reviews, meta-analyses, health technology assessments, randomized controlled trials, non-randomized studies, and economic studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and May 27, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults undergoing laser refractive surgery

Intervention	Q1, Q2, Q3: Laser refractive surgery including:
	- Flap procedures
	  ○ Including ALK, LASIK, ReLEx
	- Excimer Laser:
	  ○ Including PRK, TransPRK, LASEK, EPI-LASEK, C-TEN

Comparator	Q1: Other vision correction (prescription glasses, contact lenses); historical control group or other control Q2: Other type of laser refractive surgery (flap procedures, eximer laser) Q3: Other vision correction, other type of laser refractive surgery, historical control group or other control
Outcomes	Q1, Q2: - Length of time to maintain clinical effectiveness defined by the number of years patients avoid the need for eye glasses - Quality of life - Patient satisfaction - Need for corrective eye wear Q3 Cost effectiveness, cost-benefit, cost savings (particularly with respect to corrective eye wear)
Study Designs	Health technology assessments (HTAs), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), non-randomized studies, and economic evaluations

ALK = Automated Lamellar Keratoplasty; C-TEN = Customized Transepithelial No-touch; EPI-LASEK = Epithelial Laser Keratomileusis; LASEK = Laser Assisted Sub-Epithelium Keratomileusis; LASIK = Laser Assisted in situ Keratomileusis; PRK = Photorefractive Keratectomy; ReLEx = Refractive Lenticule Extraction; TransPRK = Transepithelial photorefractive Keratectomy

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria in Table 1 and if they were published prior to 2013.

Critical Appraisal of Individual Studies

The SIGN checklists were used to assess the quality of the included RCTs[6] and non-randomized studies.[7] Summary scores were not calculated for the included study; rather, a review of the strengths and limitations were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 567 citations were identified in the literature search. Following screening of titles and abstracts, 557 citations were excluded and 10 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, one publication was excluded due to irrelevant outcomes, while nine publications met the inclusion criteria and was included in this report. Appendix 1 presents the PRISMA flowchart of the study selection.

Summary of Study Characteristics

The characteristics of the identified studies including three RCTs[8-10] and six non-randomized studies[11-16] are summarized below and are presented in **Appendix 2**.

Study Design

All three RCTs recruited patients from a single centre. Two RCTs[9,10] were open-label, two arms, parallel, and had a 1:1 ratio. One RCT[8] was prospective, paired-eye, single-masked study, in which each patient was randomized to undergo one procedure in one eye and other procedure in the other eye (performed by the same surgeon) on the same day.

Of the six non-randomized studies, three were retrospective cohort studies,[11,12,15] two were prospective cohort studies,[13,14] and one was comparative case series.[16]

Country of Origin

The studies were conducted in the USA,[10,13] the UK,[12] Denmark,[15] Singapore,[8,14] Pakistan,[11] Iran,[9] and Spain,[16] and were published in 2018,[8] 2017,[11,12] 2016,[13] and 2015.[9,10,14-16]

Population

Patients were adults with mean age ranging from 25 to 54 years with stable refraction. They underwent different types of laser refractive surgery to improve visual acuity and to seek independence from glasses or contact lenses. The refractive variables (e.g., sphere diopters [D], cylinder D, and spherical equivalent D) were comparable between groups, but varied across studies.

Interventions and Comparators

Eight of nine studies compared different techniques of refractive laser surgery. Two studies compared two different methods of flap procedures (i.e., LASIK versus SMILE).[8,14] One study compared two different methods of surface procedures (i.e., LASEK versus PRK).[15] One study compared a flap procedure with a surface procedure (i.e., LASIK versus PRK).[11] One study compared a flap procedure (LASIK) with refractive lens exchange surgery using a femtosecond laser.[12] Three studies compared a flap or a surface procedure of different platforms (i.e., symmetrical PresbyLASIK versus asymmetrical PresbyLASIK,[16] tissue-saving PRK versus wavefront-optimized PRK,[9] Wavefront-guided PRK versus Wavefront-optimized PRK[10]). One study compared LASIK with contact lenses, where patients switching from contact lenses to LASIK were compared with those who continued wearing contact lenses.[13]

Outcomes

The identified outcomes from the included studies were patient satisfaction[8-13,15,16] and visual-related quality of life[14] using validated questionnaires. Other outcomes such as length of time to maintain clinical effectiveness (defined by number of years patients avoid the need for eye glasses or contact lenses) and the need for corrective eye wear were not identified.

Follow-up Period

Follow-up period ranged from three months[8,9,12,14] to seven years.[15]

Analysis

Data analysis in two RCTs was performed using per protocol approach.[8,10] Sample size calculation was applied in two RCTs[8,9] and one cohort study.[14] The remaining studies did not report on methods of analysis or sample size calculation. Instead, only *P* value set at 0.05 or 0.01 was used for the comparison between interventions.

Summary of Critical Appraisal

The summary of the quality assessment for the RCTs and observational studies was described below and is presented in **Appendix 3**.

The RCTs had an explicit research question, method of randomization, balance in patient characteristics between groups, and validated methods for outcome assessment. The nature of the study prohibited the blinding of staff and patients to condition assignment during treatment and follow-up periods that may have a risk of assessment bias. High follow-up rates were reported in two RCTs.[8,10] Intention-to-treat analysis was not conducted in the RCTs. Overall, the RCTs were of moderate quality.

All non-randomized studies addressed an appropriate and clearly focused question, had balance patients characteristics between groups, and used reliable and validated methods of assessment. All studies had high risk of selection bias as the participant rate was not defined in the prospective cohort studies,[13,14] or it was not applicable in the retrospective cohort studies.[11,12,15] The rate of follow-up between groups was not reported in the prospective cohort studies[13,14] or in the longitudinal comparative case series[16] that may result in the risk of attrition bias. Blinding was not possible in retrospective cohort studies and many prospective cohort studies that may have a risk of detection bias. All studies did

not identify and control for potential confounding variables in their analyses. Overall, the included observational studies were at high risk for bias.

Summary of Findings

The main findings and conclusions of the included studies are presented in **Appendix 4**.

What is the long term clinical effectiveness of laser refractive surgery for vision correction?

One prospective, longitudinal, parallel group, multicenter survey[13] was identified that compared patient satisfaction among patients who continued wearing contact lenses with those elected to switch from contact lenses to refractive surgery using LASIK.

Overall satisfaction (i.e., strongly agree that they would recommend their current method to a friend or a family member) was higher in LASIK after contact lens group (88%, 84%, 88%) than contact lens control groups (60%, 61%, 54%) at 1-, 2-, and 3-year surveys, respectively. The proportion of patients who reported no difficulty with night-driving and night visual disturbances were also higher in LASIK group compared to contact lens group. The frequencies of other outcomes such as dry eye, difficulty reading small print, depression, eye infection, eye ulcer and eye abrasion did not change from baseline to follow-up surveys and were comparable between groups.

1. *What is the comparative clinical effectiveness of laser refractive surgery procedures for vision correction?*

Two studies compared two different methods of flap procedures (i.e., LASIK versus SMILE).[8,14]

The RCT by Damgaard et al., 2018[8] found no significant differences between LASIK and SMILE for all visual symptoms (light sensitivity, eye discomfort, eye dryness, excessive tearing, gritty sensation, glare, halos, blurring, fluctuations in vision) at the 3-month follow-up.

The prospective cohort study by Ang et al., 2015[14] found no significant difference in visual-related quality life (assessed using Quality of Life Impact of Refractive Correction questionnaire) between LASIK and SMILE at the 1- and 3-month follow-ups.

One study compared two different methods of surface procedures (i.e., LASEK versus PRK).[15]

The retrospective cohort study by Hansen et al., 2015[15] found high patient satisfaction rates in both LASEK and PRK groups with no significant difference (92% versus 100%; $P = 0.87$) at an average follow-up time of 6.0 years and 4.6 years, respectively.

One study compared a flap procedure with a surface procedure (i.e., LASIK versus PRK).[11]

The retrospective cohort study by Hashmani et al., 2017[11] found high and comparable in overall patient satisfaction rates between LASIK and PRK (93.3% versus 95.6%). Follow-up time was not specified.

One study compared a flap procedure (LASIK) with refractive lens exchange surgery using a femtosecond laser.[12]

The retrospective cohort study by Schallhorn et al., 2017[12] found overall vision satisfaction (94.3% versus 79.1%; $P < 0.01$) and intention to recommend the procedure to a friend or a

relative (98.9% versus 90.7%; $P < 0.01$) was significantly higher in LASIK compared to refractive lens exchange surgery in patients with moderate to higher myopia at the 3-month follow-up. However, no significant difference in patient satisfaction between groups for other refractive categories (i.e., low myopia, plano presbyopia, hyperopia).

Three studies compared a flap or a surface procedure of different platforms.[9,10,16]

The longitudinal, comparative case series by Soler Tomas et al., 2015[16] reported comparative results of patient satisfaction between symmetrical and asymmetrical presbyLASIK after 18 months. The study found no significant difference in patient satisfaction between the two procedures.

The RCT by Nassiri et al., 2015[9] found no significant difference in patient satisfaction between tissue-saving PRK and wavefront-optimized PRK procedures.

The RCT by Sia et al., 2015[10] found no significant difference in patient satisfaction between wavefront-guided PRK versus wavefront-optimized PRK procedures.

2. *What is the cost-effectiveness of laser refractive surgery versus other vision correction or versus other laser techniques for vision correction?*

No relevant literature was identified.

Limitations

This review did not find any evidence on the long term clinical effectiveness of laser refractive eye surgery defined by the number of years that post-operative patients could stay independent from prescription glasses or contact lenses. Patient satisfaction and visual-related quality of life were identified as relevant outcomes in the included studies. One study compared LASIK with contact lenses, while the remaining eight studies compared different techniques of refractive laser surgery. Across studies, significant heterogeneity was noted for study designs, sample sizes, patient characteristics, surgery techniques, comparisons, patient satisfaction questionnaires, and follow-up periods. Seven out of nine studies were short-term with follow-up period ranging from 3 to 18 months, while one study had follow-up time of 3 years and the other had average follow-up time up to 6 years. Patient's subjective experience, self-reported outcomes, and physician-related bias may have significant impacts in the study findings. All associated limitations (e.g., risk of selection and recalling bias, and confounders) of the non-randomized studies, particularly retrospective studies, would apply. No relevant literature could be identified for comparative cost-effectiveness of laser refractive surgery with other laser techniques or with other methods of vision correction.

Conclusions and Implications for Decision or Policy Making

A laser refractive surgery for vision correction such as LASIK technology was found to yield higher levels of patient satisfaction compared to contact lens wear. There was no significant difference in subjective visual symptoms, patient satisfaction, or visual-related quality of life between different laser refractive surgery techniques, or between different platforms of a laser refractive surgery technique. Due to short-term follow-up and limited number of studies identified for each type of comparison (often single study), it is still uncertain about the reproducibility of the findings, thus the interpretation should be taken with caution. The current literature regarding laser refractive eye surgery primarily emphasizes visual and refractive outcomes, and showed no significant differences among

most surgical techniques. Studies that aim to determine the number of years for which laser refractive eye surgery for vision correction could keep patients from returning to prescription glasses or contact lens wear would reduce uncertainty. Additionally, as no cost-effectiveness studies were identified, high quality studies examining the comparative cost-effectiveness of the various surgery techniques are needed in order to determine cost-effectiveness.

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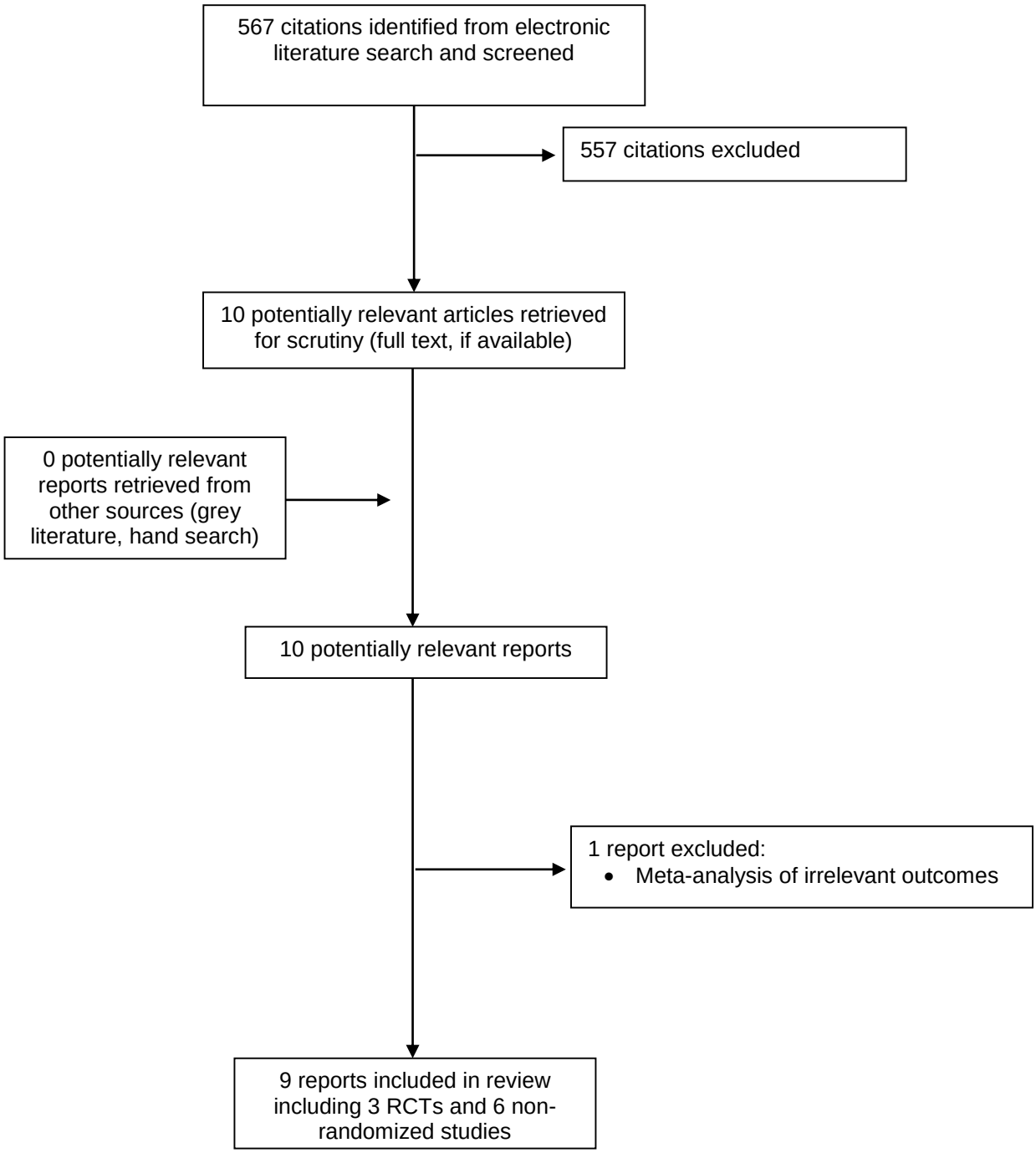
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Studies

Table 2: Characteristics of Included Primary Studies

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
Damgaard et al., 2018[8] Singapore Funding: NR	Prospective, paired-eye, single-masked, single center RCT Analysis: PP Sample size calculation: Yes, minimum of 63 patients (126 eyes) to have a non-inferiority limit of 0.6 in mean postoperative symptom scores, SD of 1.2, power of 80%, and significant level of 2.5%.	70 adult patients Mean age (SD): 28.3 (5.21) years Sex: 36% male Race: 96% Asian Sphere: -9.25 D to -2.00 D Cylinder: -2.50 D to 0.00 D Spherical equivalent: -9.50 D to -2.0 D	Femtosecond LASIK	SMILE	Patient experience using post-operative questionnaire at 1- and 3-month follow-up Items in the questionnaire: light sensitivity, eye discomfort, eye dryness, excessive tearing, gritty sensation, glare, halos, blurring, and fluctuation in vision. Score: 1 to 6 (1 = not at all, 6 = very severe/extremely)
			Each patient was randomized to undergo LASIK in one eye and SMILE in the other eye in the same day performed by the same surgeon.		
Hashmani et al., 2017[11] Pakistan Funding: The Hashmanis Foundation	Retrospective cohort study Analysis: *P* value set at 0.05 Sample size calculation: No	207 adult patients (409 eyes) Mean age (SD), years – LASIK: 27.0 (7.3) – PRK: 25.0 (5.8) Sex – LASIK: 31% male – PRK: 27% male Sphere	Femtosecond LASIK (n = 117 patients; 229 eyes)	PRK (n = 90 patients; 180 eyes)	Patient satisfaction (overall) Satisfaction level: “extremely satisfied”, “very satisfied”, “satisfied”, and “not satisfied” Follow-up: post-operative (NR on time)

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
		– LASIK: -9.8 D to 6.8 D – PRK: -14.5 D to 2.0 D Cylinder – LASIK: -12.8 D to 3.3 D – PRK: -5.0 D to 0.25 D Spherical equivalent – LASIK: -13.4 D to 8.0 D – PRK: -15.5 D to 0.0 D	PRK was performed by three surgeons; LASIK was performed by one surgeon.		
Schallhorn et al., 2017[12] UK Funding: NR	Retrospective cohort study Analysis: *P* value set at 0.05 Sample size calculation: No	1,198 adults patients Mean age (SD), years – LASIK: 51.9 (3.8) – RLE: 54.0 (3.7) Sex – LASIK: 38.5% male – RLE: 50.7% male Patient classification: – Moderate to high myopia – Low myopia – Plano presbyopia – Hyperopia (There were some differences in baseline visual variables between patients underwent LASIK and RLE)	Monovision LASIK (n = 608) Surgeries were performed at 37 centers by 27 ophthalmologists	RLE (n = 590)	Patient satisfaction using post-operative questionnaire at 1 day, 1 week, 1 month and 3 months Six questions, score from 1 to 5 (1 = very satisfied, 5 = very dissatisfied)
Price et al., 2016[13] USA Funding: NR	Prospective, longitudinal, parallel-group, multicenter survey Analysis: *P* value set at 0.01 Sample size calculation: No	1,800 adult patients Mean age (SD), years – Contact lenses continuing: 34 (12) – Contact lenses to LASIK: 34 (9) – Glasses to LASIK: 37	Contact lenses continuing (n = 694) Contact lenses to LASIK (n = 819) Glasses to LASIK (n = 287)		Patient satisfaction was assessed using survey instrument at 1, 2, and 3 years of follow-up Components included: – Overall satisfaction – Night-driving difficulties and night visual disturbances

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
		(11) 2/3 contact lens wearers were female >1/2 glasses wearers were male Age, gender and duration of contact lenses: significant differences between groups Type of lenses were balanced between contacts groups Mean spherical equivalent in myopic eyes and in hyperopic eyes: significant differences between groups			– Dry eyes – Artificial tear use – Difficulty reading small print – Depression – Infection, ulceration, and abrasion
Ang et al., 2015[14] Singapore Funding: National Research Foundation-Funded Translational & Clinical Research Program Grant	Prospective cohort study Analysis: *P* value set at 0.05 Sample size calculation: Yes 413 eyes of LASIK and 126 eyes of SMILE to achieve power of 82% to detect a difference of 0.1 in mean of efficacy index For QIRC analysis, 17 patients in each group would achieve 80.7% power to detect a difference of 10.0	Adult patients Mean age (SD), years – LASIK: 32 (7) – SMILE: 32 (8) Sex: NR Race (Chinese) – LASIK: 82% – SMILE: 80% Most patients in both groups had myopia and spherical equivalents were similar in both groups	Femtosecond LASIK (n = 688 eyes)	SMILE (n = 172 eyes)	Visual-related QoL using validated QIRC at 3-month follow-up 20 items covering visual function, symptoms, convenience, concerns, and emotional well-being. Each item was score on 5-point response scale spaced evenly, ranging from “not at all” to “extremely”
Hansen et al., 2015[15] Denmark	Retrospective cohort study	81 adult patients Mean age (SD), years – LASEK: 37 (8)	LASEK (n = 35 patients)	Cooling PRK (n = 46 patients)	Patient satisfaction assessed using two questions:

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
Funding: Odense University Hospital Research Foundation	Analysis: *P* value set at 0.05 Sample size calculation: No	– PRK: 38 (6) Sex: NR Myopia – LASEK: 92% – PRK: 97% Sphere – LASEK: -12.75 D to -1.75 D – PRK: -11.75 D to -3.00 D Astigmatism – LASEK: -3.00 D to 0.00 D – PRK: -3.00 D to 0.00 Spherical equivalent – LASEK: -13.00 D to -1.75 D – PRK: -11.75 D to -4.50 D			1. "How satisfied are you right now with your laser surgery for near-sightedness, on a scale from 0 to 10, where 10 is the most satisfied and 0 is the most dissatisfied?" 2. "Would you recommend the surgery to a friend or relative?" Follow-up – LASEK: 5.4 to 6.7 years (average 6.0 years) – PRK: 4.1 to 5.0 years (average 4.6 years)
Nassiri et al., 2015[9] Iran Funding: NR	Open-label, parallel, 1:1 ratio, single center RCT Analysis: unclear about ITT or PP Sample size calculation: Yes, based on difference of 0.2, SD of 0.26, and 95% confidence interval in contrast sensitivity (primary outcome)	80 adult patients (152 eyes) Mean age (SD): 27 (5.5) years Sex: 23.8% male Sphere: -6.25 D to -3.00 D Cylinder: -1.25 D to 1.25 D Spherical equivalent: -6.63 D to -2.88 D	Tissue-saving PRK (n = 76 eyes)	Wavefront-optimized PRK (n = 76 eyes)	Patient satisfaction using post-operative questionnaire at 3-month follow-up – Ten questions on patient perception of glare, light sensitivity, hazy or foggy vision, dry eye, foreign body sensation, vision fluctuation, double vision. – Total satisfaction with vision (scale 1 to 10)
Sia et al., 2015[10] USA	Open-label, parallel, 1:1 ratio, single center RCT Analysis: PP	108 adult patients Mean age (SD): 30.3 (6.3) years	Wavefront-guided PRK (n = 55 patients)	Wavefront-optimized PRK (n = 53 patients)	Patient satisfaction using post-operative questionnaire at 12-month follow-up

First Author, Publication Year, Country, Study Name (if reported), Funding	Study Design and Analysis	Patient Characteristics	Interventions	Comparators	Clinical Outcomes, Length of Follow-up
Funding: US Army Medical Research Acquisition Activity Award	Sample size calculation: NR	Sex: 77.8% male Spherical equivalent (SD): -3.51 (1.63) D Sphere and cylinder were similar in both groups			Items in the questionnaire: difficulty performing daily activities, dry eye, vision fluctuation, double vision, nighttime glare, halo, overall vision expectation, patient satisfaction
Soler Tomas et al., 2015[16] Spain Funding: No funding	Longitudinal, comparative case series Analysis: *P* value set at 0.01 No sample size calculation	30 adult patients (40 eyes), hyperopic presbyopes seeking independence from reading glasses Mean age (SD): 53.5 (2.3) years for symmetrical and 51.9 (2.5) years for asymmetrical PresbyLASIK Sex: NR Spherical equivalent: +1 D to +2.5 D Astigmatism: up to 1 D Maximum difference between subjective and cycloplegic refraction: ≤ +0.5	Symmetrical PresbyLASIK (16 patients; 19 eyes)	Asymmetrical PresbyLASIK (14 patients; 21 eyes)	Patient satisfaction using modified cataract TyPE Spec questionnaire at 18-month follow-up – General satisfaction (0 to 10 points – Reading satisfaction (0 to 10 points) – Distance, near, and intermediate vision difficulties (0 to 4 points) – Halos difficulties (0 to 4 points) – Willing to repeat the procedure (0 to 4 points)

D = diopters; ITT = intention-to-treat; LASEK = laser-assisted subepithelial keratectomy; LASIK = laser in-situ keratomileusis; NR = not reported; PP = per protocol; PRK = photorefractive keratectomy; QIRC = Quality of Life Impact of Refractive Correction; QoL = quality of life; RCT = randomized controlled trial; RLE = refractive lens exchange; SD = standard deviation; SMILE = small incision lenticule extraction

Appendix 3: Quality Assessment of Included Studies

Table 3: Quality Assessment of Primary Studies

SIGN Checklist for Randomized Controlled Trials: Internal Validity[6]	Damgaard et al., 2018[8]	Nassiri et al., 2015[9]	Sia et al., 2015[10]
1. The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes
2. The assignment of subjects to treatment groups is randomized.	Yes	Yes	Yes
3. An adequate concealment method is used.	Can't say	Yes	Can't say
4. Subjects and investigators are kept 'blind' about treatment allocation.	No	Yes	No
5. The treatment and control groups are similar at the start of trial.	Yes	Yes	Yes
6. The only difference between groups is the treatment under investigation.	Yes	Yes	Yes
7. All relevant outcomes are measured in a standard, valid and reliable way.	Yes	Yes	Yes
8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	At 1 month, follow-up rates were 90% in both groups. At 3 months, follow-up rates were 83% and 90% for LASIK and SMILE, respectively	Can't say	Follow-up rates in both groups at 1, 3, 6 and 12 months were over 87%
9. All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	No	Can't say	No
10. Where the study is carried out more than one site, results are comparable for all sites.	NA	NA	NA

SIGN Checklist for Comparative non-Randomized Studies: Internal Validity[7]	Hashmani et al., 2017[11]	Schallhorn et al., 2017[12]	Price et al., 2016[13]	Ang et al., 2015[14]	Hansen et al., 2015[15]	Soler Tomas et al., 2015[16]
1. The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes	Yes	Yes
SELECTION OF SUBJECTS						
2. The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Yes	Yes	Yes	Yes	Yes	Yes
3. The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Does not apply	Does not apply	No	No	Does not apply	No
4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Does not apply	Does not apply	Does not apply	Does not apply	Does not apply	Does not apply
5. What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed.	Does not apply	Does not apply	Can't say	Can't say	Does not apply	Can't say
6. Comparison is made between full participants and those lost to follow up, by exposure status.	Does not apply	Does not apply	Does not apply	Can't say	Does not apply	Can't say
ASSESSMENT						
7. The outcomes are clearly defined.	Yes	Yes	Yes	Yes	Yes	Yes
8. The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable	Does not apply	Does not apply	Does not apply	No	Does not apply	No
9. Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	Does not apply	Does not apply	Does not apply	Can't say	Does not apply	Can't say
10. The method of assessment of exposure is reliable.	Yes	Yes	Yes	Yes	Yes	Yes
11. Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	Yes	Yes	Yes	Yes	Yes	Yes
12. Exposure level or prognostic factor is assessed more than once.	No	No	Yes	Yes	No	Yes
CONFOUNDING						
13. The main potential confounders are identified and taken into account in the design and analysis.	No	No	No	No	No	No
STATISTICAL ANALYSIS						
14. Have confidence intervals been provided?	No	Yes	Yes	Yes	Yes	Yes

Appendix 4: Main Study Findings and Author's Conclusions

Table 4: Summary of Findings of Included Primary Studies

Main Study Findings	Author's Conclusions
Damgaard et al., 2018[8]	
Comparisons between LASIK (n = 70 eyes) and SMILE (n = 70 eyes) for patient experience (visual symptoms) At 1-month follow-up – Visual blurring: 1.8 ± 0.7 in LASIK versus 2.1 ± 0.8 in SMILE; *P* = 0.025 – Other visual symptoms: no significant differences between groups At 3-month follow-up: – All visual symptoms: no significant differences between groups	*"Subjective visual symptoms were comparable after 3 months"*[8] p.92
Hashmani et al., 2017[11]	
Comparisons between LASIK (n = 75 patients) and PRK (n = 46 patients) for patient satisfaction (follow-up time not specified) • Extremely satisfied: 13.3% in LASIK versus 15.2% in PRK • Very satisfied: 40.0% in LASIK versus 30.4% in PRK • Satisfied: 40.0% in LASIK versus 50.0% in PRK • Not satisfied: 6.7% in LASIK versus 4.3% in PRK • Overall satisfaction: 93.3% in LASIK versus 95.6% in PRK	*"Our study shows superior visual outcomes in patients undergoing* LASIK*. However, we found a higher satisfaction rate in those that underwent PRK, perhaps due to higher cost of* LASIK"[11] p.1
Schallhorn et al., 2017[12]	
Comparisons between LASIK (n = 608 patients) and RLE (n = 590 patients) for patient satisfaction at 3-month follow-up • Overall vision satisfaction: – Moderate to higher myopia: 94.3% for LASIK versus 79.1% for RLE; *P* < 0.01 – Other refractive categories: No significant difference • Percentage of patients who would recommend the procedure to their friends or relatives: – Moderate to higher myopia: 98.9% with LASIK versus 90.7% with RLE; *P* < 0.01 – Other refractive categories: No significant difference • In plano presbyopia group, all visual outcomes were similar in both procedures • In moderate to high myopia, low myopia and hyperopia groups, some visual outcomes were in favor of LASIK procedure	*"Monovision LASIK and refractive lens exchange are both reasonable options for presbyopic patients"*[12] p.749
Price et al., 2016[13]	
Comparisons between LASIK after contacts (n = 819) and contact lenses (n = 649) at baseline, 1-, 2- and 3-year follow-up • Overall satisfaction (Strongly agree that they would recommend their current method to close friends or family members) – LASIK after contacts: 40%, 88%, 84%, 88% for baseline, 1 year, 2 years and 3 years, respectively – Contacts: 63%, 60%, 61%, 54% for baseline, 1 year, 2 years and 3 years, respectively • Difficulty in driving at night (None) – LASIK after contacts: 42%, 63%, 61%, 60% for baseline, 1 year, 2 years and 3 years, respectively – Contacts: 36%, 8%, 40%, 37% for baseline, 1 year, 2 years and 3 years, respectively • Difficulty with vision at night because of starbursts or halos around bright lights (None) – LASIK after contacts: 49%, 62%, 60%, 60% for baseline, 1 year, 2 years and 3 years, respectively	*"Compared with contact lens wear, current LASIK technology improved ease of night driving, did not significantly increase dry eye symptoms, and resulted in higher levels of satisfaction at 1, 2, and 3 years follow-up."*[13] p.1659

Main Study Findings	Author's Conclusions
– Contacts: 45%, 56%, 51%, 46% for baseline, 1 year, 2 years and 3 years, respectively • Feeling of dry eyes during the past week (None) – LASIK after contacts: 44%, 42%, 45%, 50% for baseline, 1 year, 2 years and 3 years, respectively – Contacts: 29%, 34%, 31%, 29% for baseline, 1 year, 2 years and 3 years, respectively • Difficulty reading small print (Not at all) – LASIK after contacts: 67%, 79%, 74%, 72% for baseline, 1 year, 2 years and 3 years, respectively – Contacts: 55%, 63%, 59%, 57% for baseline, 1 year, 2 years and 3 years, respectively • Feeling down, depression or hopeless (Not at all) – LASIK after contacts: 94%, 93%, 93%, 93% for baseline, 1 year, 2 years and 3 years, respectively – Contacts: 87%, 89%, 88%, 87% for baseline, 1 year, 2 years and 3 years, respectively • Eye infection (Yes) – LASIK after contacts: 3%, 4%, 3% for 1 year, 2 years and 3 years, respectively – Contacts: 8%, 11%, 8% for 1 year, 2 years and 3 years, respectively • Any type of eye ulcer (Yes) – LASIK after contacts: 0.2%, 0%, 1% for 1 year, 2 years and 3 years, respectively – Contacts: 1%, 2%, 2% for 1 year, 2 years and 3 years, respectively • Eye abrasion (Yes) – LASIK after contacts: 2%, 2%, 3% for 1 year, 2 years and 3 years, respectively – Contacts: 4%, 6%, 5% for 1 year, 2 years and 3 years, respectively	
Ang et al., 2015[14]	
At 1-month follow-up • QIRC functional scores – LASIK: 60.1 ± 18.5 – SMILE: 50.5 ± 20.7; *P* = 0.10 • Emotional scores – LASIK: 43.8 ± 23 – SMILE: 29.3 ± 16.6; *P* = 0.054 At 3-month follow-up • QIRC functional scores – LASIK: 66.7 ± 15.7 – SMILE: 55.3 ± 22.2; *P* = 0.064 • Emotional scores – LASIK: 42.7 ± 23.2 – SMILE: 37.9 ± 23.8; *P* = 0.394	*"The study, 3-month predictability, safety, and VRQoL scores were not statistically different between small-incision lenticule extraction and LASIK."*[14] p.2136
Hansen et al., 2015[15]	
Four to seven years after surgery • Patient satisfaction (satisfied or very satisfied) – LASEK: 92% – Colling PRK: 100%; *P* = 0.87 • Would recommend the surgery to a friend or a relative: All patients	*"cPRK and LASEK seemed safe and with high patient satisfaction 4 to 7 years after surgery for high myopia."*[15] p.1027
Nassiri et al., 2015[9]	

Main Study Findings	Author's Conclusions
Patient satisfaction at 3 months after tissue-saving PRK and Wavefront-optimized PRK • Glare at night (*P* = 0.473) • Glare at day (*P* = 0.921) • Haze (*P* = 0.662) • Halos (*P* = 0.672) • Clarity at night (*P* = 0.478) • Clarity at day (*P* = 0.284) • Vision quality (*P* = 0.770) • Dry eye (*P* = 0.094) • Dry eye severity (*P* = 0.074) • Gritty, scratchy, or sandy feeling (*P* = 0.377) • Vision fluctuation (*P* = 0.915) • Double vision ghost images (*P* = 0.742) • Total satisfaction (*P* = 0.817)	*"Both platforms were effective in correcting moderate myopia with or without astigmatism. No difference in refractive outcome, contrast sensitivity changes, and patient satisfaction between the groups was observed."*[9] p.683
Sia et al., 2015[10]	
Subjective visual complaints and patient satisfaction between wavefront-guided PRK and wavefront-optimized PRK at 12 months of follow-up • Difficulty performing daily activities (P = 0.894) • Dry eye (*P* = 0.075) • Visual fluctuation (*P* = 0.233) • Double vision (*P* = 0.799) • Nighttime glare (*P* = 0.589) • Halo (*P* = 0.303) • Overall vision expectation (*P* = 0.336) • Patient satisfaction (*P* = 0.981)	*"There was no significant difference between treatment groups in visual symptoms, overall visual expectation, and satisfaction (P > .075)."*[10] p.2152
Soler Tomas et al., 2015[16]	
Patient satisfaction between symmetrical and asymmetrical PresbyLASIK at 18 months of follow-up • General satisfaction (*P* > 0.01) • Reading satisfaction (*P* > 0.01) • Far vision difficulty (*P* > 0.01) • Near vision difficulty (*P* > 0.01) • Intermediate vision difficulty (*P* > 0.01) • Halos (*P* > 0.01) • Would repeat the procedure: 60% versus 71% said yes	*"Symmetrical and asymmetrical presbyLASIK significantly improved distance UCVA, near UCVA, after 18 months."*[16] p.651

D = diopters; ITT = intention-to-treat; LASEK = laser-assisted subepithelial keratectomy; LASIK = laser in-situ keratomileusis; NR = not reported; PP = per protocol; PRK = photorefractive keratectomy; QIRC = Quality of Life Impact of Refractive Correction; QoL = quality of life; RCT = randomized controlled trial; RLE = refractive lens exchange; SD = standard deviation; SMILE = small incision lenticule extraction; UCVA = uncorrected visual acuity; VRQoL = vision-related quality of life