Corneal Surface Ablation Laser Refractive Surgery for the Correction of Myopia: A Network Meta-analysis

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ABSTRACT

PURPOSE: To systematically compare the efficacy, predictability, safety, postoperative haze, pain scores, and epithelial healing time of four corneal surface ablation procedures.

METHODS: PubMed, Embase, Cochrane Library, and the U.S. trial registry were searched up to June 2018. Randomized controlled trials were selected. Efficacy (uncorrected distance visual acuity of 20/20 or better), predictability (refractive spherical equivalent within ±0.50 diopters [D] of the target), and safety (loss of two or more lines of spectacle corrected distance visual acuity) were set as primary outcome measures. Haze, pain scores, and epithelial healing time were set as secondary outcome measures.

RESULTS: Eighteen studies involving 1,423 eyes were included. According to the Grading of Recommendations Assessment, Development, and Evaluation, the quality of outcomes were moderate to high (70.6%). There were no differences in efficacy, predictability, safety, haze, day 1 pain, and epithelial healing time between treatments. Epithelial laser in situ keratomileusis (epi-LASIK) had statistically significantly higher pain scores on day 3 compared to photorefractive keratectomy (PRK) (weighted mean differences [WMD] = 2.2, 95% credible intervals [CrI] = 0.19 to 4.01) and transepithelial PRK (T-PRK) (WMD = 2.7, 95% CrI = 0.51 to 4.84). The surface under the cumulative ranking curve ranking results (best to worst) showed laser epithelial keratomileusis (LASEK) ranked highest for efficacy, predictability, safety, and day 1 pain scores. Epi-LASIK ranked best for grade 1 haze scores. T-PRK ranked best for haze of 0.5 or higher, haze scores day 3 pain scores, and epithelial healing time.

CONCLUSIONS: Surface laser refractive surgeries are comparable in terms of efficacy, predictability, safety, and postoperative haze except for day 3 pain scores, with epi-LASIK being more painful compared to PRK and T-PRK.

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Uncorrected refractive error is the leading cause of visual impairment throughout the world.[1-3] Laser corneal refractive surgery is an effective alternative to the correction of refractive errors with spectacles or contact lenses, especially for myopia. During the past 25 years, several surgical techniques have been developed that change refraction by reshaping the cornea through excimer laser photoablative removal of corneal tissue. Photorefractive keratectomy (PRK), which involves mechanically debriding the central corneal epithelium and then photoablating the under-

lying stromal surface, was the first of these techniques described.[4-6] However, because it is a surface ablation procedure, PRK has limitations such as postoperative pain, delayed epithelial healing, and anterior stromal haze development.[7,8] As such, PRK declined in popularity with the introduction and development of intrastromal ablative techniques such as laser in situ keratomileusis (LASIK).[9-11] However, surface ablation procedures such as PRK retain certain advantages over LASIK, such as inflicting less corneal biomechanical insult and avoiding both intraoperative and late flap-related complications.[12-14] Therefore, during the past two decades, other surface ablation procedures have been developed to try to overcome some of the limitations of PRK while retaining its advantages. These procedures include transepithelial photorefractive keratectomy (T-PRK), laser epithelial keratomileusis (LASEK),[15] and epithelial LASIK (epi-LASIK).[16,17]

A fundamental difference between the various surface ablative techniques is the method of epithelial removal. Alcohol or mechanical debridement has been advocated for the preservation of the epithelium as a flap, as in LASEK and epi-LASIK, respectively.[18] This flap can then be placed over the ablated stromal surface to reduce postoperative pain and speed epithelial healing time. Alternatively, epithelial removal can be undertaken by the laser itself as in T-PRK. This technique has several perceived advantages, including no instrument contact with the cornea, reduced intervention time, and the potential to minimize the size of the epithelial defect required for stromal ablation, as well as the avoidance of alcohol and potential toxicity as in LASEK.[19] Although these new approaches to surface laser ablation offer apparent theoretical improvements over traditional PRK, they each have different advantages and disadvantages. What is currently lacking is a comprehensive evidence-based approach to determine the relative merits of each of these procedures over each other and PRK.

Although several conventional pairwise meta-analyses of the four surface refractive ablation procedures (PRK, LASEK, epi-LASIK, and T-PRK) have been published,[20-23] these publications share several limitations. First, they are unable to provide clear hierarchies for these four available treatments due to a lack of head-to-head comparisons. Second, some previous analyses included non-randomized controlled trials that might influence the quality of the evidence. However, a network meta-analysis can combine direct evidence from individual trials and indirect evidence gleaned using statistical techniques across trials, enabling simultaneous "all-way" comparisons of multiple interventions.[24] This technique is therefore particularly suitable to address questions relating to the relative safety and benefits of different treatment modalities for a single condition. We therefore performed this network meta-analysis of available randomized controlled trials (RCTs) to systematically compare the efficacy, predictability, safety, postoperative haze, pain scores, and epithelial healing time of the four major surface ablative procedures described above and to provide evidence-based rankings of these treatments.

METHODS

This systematic review complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) network meta-analysis extension statement.[25]

OUTCOME MEASUREMENTS

Efficacy (uncorrected distance visual acuity [UDVA] of 20/20 or better), predictability (refractive spherical equivalent [SE] within ±0.50 diopters [D] of the target), and safety (loss of two or more lines of spectacle corrected distance visual acuity [CDVA]) were set as primary outcome measures. Haze, pain scores, and epithelial healing time were set as secondary outcome measures. Pain data were assessed using a 10-point scale at days 1 and 3 postoperatively. When data at day 3 were not available, the outcome at the follow-up time point closest to day 3, such as day 2 or day 4, was used. The results of efficacy, predictability, safety, and haze were analyzed at 6 months postoperatively. When data at 6 months were not available, the outcome at the follow-up time point closest to 6 months was used.

ELIGIBILITY CRITERIA

Trials were included if they met the following criteria: (1) treated population: patients with myopia; (2) interventions: PRK, T-PRK, LASEK, or epi-LASIK; (3) comparisons: two or more laser corneal surface ablation techniques (as listed above); (4) at least one of the following outcomes: efficacy, safety, predictability, postoperative haze, pain, and epithelial healing time; and (5) study design: RCTs. We excluded trials if they contained only one of the surface ablation techniques, did not use randomization for treatment allocation, used mitomycin C (MMC) during surgery, or if participants were followed up for less than 3 months after surgery. MMC was not included due to the controversial nature of the use of this drug.

SEARCH METHODS

A systematic literature review was conducted using PubMed, Embase, The Cochrane Library, and the U.S. trial registry (www.ClinicalTrial.gov) for RCTs

published up to June 2018 without language restrictions. The full search strategies are shown in **Table A** (available in the online version of this article). We also manually examined the reference lists of clinical trials, related meta-analyses, and systematic reviews to identify relevant studies.

STUDY SELECTION

Screening was performed by two independent investigators (YH, BS). They retrieved the full-text articles that appeared relevant after reviewing the titles and abstracts and independently assessed them for final eligibility. Any discrepancies were resolved by focused discussion or consultation with an additional investigator (RT).

DATA EXTRACTION AND RISK OF BIAS ASSESSMENT

Two investigators independently extracted information into an electronic database, including the participant and intervention characteristics, outcomes, and quantitative results for treatment effects. For data that were missing or could not be directly obtained, we contacted the authors of trial reports or used GetData GraphDigitizer 2.24 (http://getdata-graph-digitizer.com) to read data from figures.

To appraise the study quality, the Cochrane Collaboration risk-of-bias method was used.[26] In this method, we graded all reports at low, high, or unclear risk of bias for each of the following items: random sequence generation and allocation concealment (both items relate to selection bias), masking of participants and personnel (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases. Two investigators also independently assessed the quality of the body of evidence for outcomes within the network meta-analysis according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method as very low, low, moderate, or high.[27] The GRADE considered the following domains: study limitations, indirectness, inconsistency, imprecision of effect estimates, and risk of reporting bias.

DATA ANALYSIS

We first conducted traditional pairwise meta-analyses for direct comparisons using random-effects models. For binary outcomes, relative effect sizes were calculated as odds ratios (ORs) with 95% confidence intervals (CIs). For continuous outcomes, relative effect sizes were calculated as weighted mean differences (WMDs) with 95% CI. For positive outcomes (ie, efficacy and predictability, where a greater value indicates a better result), an OR of greater than 1 or WMD of greater than 0 corresponded

to beneficial treatment effects of the first treatment compared with the second treatment. When the outcomes were negative (ie, safety, haze, pain, or epithelial healing time, where a greater value indicates a worse result), an OR of less than 1 or WMD of less than 0 corresponded to beneficial treatment effects of the first treatment compared with the second treatment. We used visual inspection of the forest plots and the I^2 statistic[28] (values of 50% or more indicated substantial heterogeneity) to investigate the possibility of statistical heterogeneity. We used STATA software (version 12.0; StataCorp LP, College Station, TX) for statistical analyses.

To incorporate indirect comparisons, we performed Bayesian random-effects network meta-analyses using Markov chain Monte Carlo methods in GeMTC GUI 0.14.3[29] to estimate pooled ORs and WMD with 95% credible intervals (CrI). We used four parallel chains and obtained 50,000 samples after a 20,000-sample burn-in in each chain. To check convergence, we used the Gelman and Rubin diagnostic[30] and trace plots. We ranked treatments based on the analysis of ranking probabilities and the surface under the cumulative ranking curve (SUCRA).[31] The SUCRA values, expressed as a percentage, showed the relative probability of an intervention being the best option. Inconsistency between direct and indirect evidence was assessed by a "node-splitting" approach.[32] When high heterogeneity or inconsistency was found, a "leave-one-out procedure" in which each trial is left out, one at a time, was done for further sensitivity analyses. Funnel plots were used to evaluate publication bias in the results between small and large studies.[33]

RESULTS

STUDY SELECTION

Figure A (available in the online version of this article) shows the detailed steps of the study selection process. The literature search yielded 608 potentially relevant studies (the detailed search strategy is shown in **Table A**). Of these, 36 potentially eligible studies were retrieved from the electronic databases and 5 additional studies were located from the references of selected studies, making a total of 41. After excluding 23 studies on the basis of the predefined inclusion criteria, 18 studies were included in the network meta-analysis.

STUDY CHARACTERISTICS AND NETWORK GEOMETRY

A summary of all eligible studies is shown in **Table B** (available in the online version of this article). Included trials were published between 2001 and 2014. A total of 1,399 eyes that underwent one of the four different interventions were evaluated: 606 eyes in the

PRK group, 616 eyes in the LASEK group, 105 eyes in the epi-LASIK group, and 72 eyes in the T-PRK group (**Figure B**, available in the online version of this article). All trials had two treatment arms, with the exception of O'Doherty et al.,[34] which had three treatment arms. Of the included 18 trials, 5 (27.8%) recruited participants from Europe, 7 (38.9%) recruited participants from Asia, 4 (22.2%) recruited participants from North America, and 2 (11.1%) recruited participants from Brazil.

QUALITY OF THE EVIDENCE

The quality of the studies included in the network meta-analysis is shown in **Table C-1** (Quality of the Included Trials) and **Table C-2** (Analysis by Synthesis) (available in the online version of this article). In relation to the complete outcome data, almost 25% of trials were rated as "high risk of bias" (4 trials, 22.2%), but most were rated as "low risk of bias" (11 trials, 61.1%). Those rated as "unclear risk of bias" reported allocation concealment and masking of outcome assessment (14 and 12 trials, respectively). The results of the GRADE are shown in **Table C-3** (available in the online version of this article). Across the outcomes of the network meta-analysis, we found 8 comparisons (15.7% of all comparisons) of high quality, 28 (54.9%) of moderate quality, and 15 (29.4%) of low quality. The comparisons were all assessed as moderate-high quality for efficacy, predictability, safety, and pain scores on day 3, and low-moderate for haze, pain scores on day 1, and epithelial healing time. For most of the outcomes, the main issues that reduced confidence in estimates were risk of bias and imprecision.

RESULTS OF META-ANALYSIS

Direct Comparisons. **Table 1** shows the results of efficacy, predictability, and safety based on direct comparisons. Ten articles reported the percentage of eyes with UDVA of 20/20 or better postoperatively (defined as efficacy). The results show that there was no statistically significant difference between the four major types of corneal surface ablation laser refractive surgery and high heterogeneity for all comparisons. Predictability was measured by the proportion of eyes where the postoperative refractive error was within ±0.50 D of the target refraction. We found that 8 studies had sufficient data for this analysis. Statistical analyses of these data showed no statistically significant effect of the type of corneal surface ablation laser refractive surgery. The proportion of eyes with a loss of two or more lines of CDVA was used as a measure of safety. This parameter was reported in 6 studies. The results show that there was no statistically significant

difference between the types of corneal surface ablation laser refractive surgery and high heterogeneity for all comparisons ($I^2 < 50\%$).

Tables 2-3 show the results of postoperative haze, pain scores, and epithelial healing time based on direct comparisons. Six trials reported haze scores. We found one statistically significant difference between LASEK and PRK (WMD = -0.19, 95% CI = -0.37 to -0.01), whereas high heterogeneity was observed between LASEK and PRK ($I^2 = 88.9\%$) (forest plots in **Table D**, available in the online version of this article). We also analyzed the data at two different grades (grade 0.5 or higher and grade 1.0 or higher) in 7 trials; no statistically significant difference between the types of corneal surface ablation laser refractive surgery was found and high heterogeneity was found for both grades ($I^2 < 50\%$).

Six studies reported postoperative pain scores. We analyzed the postoperative pain scores at days 1 and 3. Statistically significant differences were found between PRK and T-PRK at day 1 (WMD = 1.24, 95% CI = 1.00 to 1.48), LASEK and T-PRK at day 1 (WMD = -1.23, 95% CI = -2.10 to -0.36), PRK and epi-LASIK at day 3 (WMD = -2.16, 95% CI = -3.55 to -0.77), and PRK and T-PRK at day 3 (WMD = 0.48, 95% CI = 0.23 to 0.73). There was no high heterogeneity for all comparisons ($I^2 < 50\%$).

Twelve studies reported epithelial healing time. A statistically significant difference was found between PRK and T-PRK (WMD = 1.57, 95% CI = 1.33 to 1.75). We also found high heterogeneity between PRK and epi-LASIK ($I^2 = 91.4\%$), PRK and LASEK ($I^2 = 97.1\%$), and LASEK and epi-LASIK ($I^2 = 76.6\%$) (forest plots are shown in **Table D**).

Combination of Direct and Indirect Comparisons. **Figure C** (available in the online version of this article) shows the results of efficacy, predictability, and safety based on Bayesian network meta-analyses that combine direct and indirect comparisons. The ranking probabilities for all procedures are presented in **Table E** (available in the online version of this article), along with the ranking probabilities of other results. For the primary outcomes, there were no statistically significant differences in any comparison in terms of efficacy, safety, and predictability ($P > .05$). For the ranking results, LASEK came first in efficacy, predictability, and safety on the SUCRA values (**Figure 1**). The results for postoperative haze based on Bayesian network meta-analyses are shown in **Figure D** (available in the online version of this article). There was no statistically significant difference between any of the studied techniques ($P > .05$). For haze scores, epi-LASIK had the least haze as per the SUCRA values. T-PRK ranked first in haze scores at grade 0.5 or higher, whereas epi-LASIK ranked first with haze scores at grade 1 or higher (**Figure 2**).

TABLE 1
Postoperative Efficacy, Predictability, and Safety From Direct Comparisons Between Each Pair of Treatments

Treatment	UDVA of 20/20 or Better			Refractive SE Within ±0.50 D of the Target			Losing ≥ 2 Lines of CDVA		
	No. of Studies	Odds Ratio (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²
PRK vs									
Epi-LASIK	2	1.23 (0.45, 3.34)	0.0%	2	0.87 (0.30, 2.47)	0.0%	1	1.00 (0.05, 17.90)	—
LASEK	7	0.86 (0.58, 1.26)	0.0%	6	0.84 (0.58, 1.21)	0.0%	4	1.24 (0.32, 4.78)	0.0%
T-PRK	—	—	—	—	—	—	1	1.00 (0.06, 16.51)	—
LASEK vs									
Epi-LASIK	2	1.49 (0.62, 3.60)	0.0%	2	1.30 (0.47, 3.60)	0.0%	—	—	—
T-PRK	1	1.56 (0.24, 10.05)	—	—	—	—	—	—	—

UDVA = uncorrected distance visual acuity; SE = spherical equivalent; D = diopters; CDVA = corrected distance visual acuity; CI = confidence interval; PRK = photorefractive keratectomy; Epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratomileusis; T-PRK = transepithelial photorefractive keratectomy

TABLE 2
Postoperative Haze From Direct Comparisons Between Each Pair of Treatments

Treatment	Haze Scores			Haze Grade ≥ 0.5			Haze Grade ≥ 1.0		
	No. of Studies	Mean Difference (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²
PRK vs									
Epi-LASIK	—	—	—	1	2.80 (0.53, 14.74)	—	1	7.5 (0.73, 76.77)	—
T-PRK	—	—	—	1	2.03 (0.83, 4.95)	—	1	2.70 (0.49, 14.79)	—
LASEK vs									
Epi-LASIK	1	0.08 (-0.02, 0.18)	—	1	1.00 (0.25, 4.00)	—	1	1.00 (0.06, 16.89)	—
PRK	4	-0.19 (-0.37, -0.01)[a]	88.9%	4	1.16 (0.71, 1.90)	0.0%	4	1.36 (0.57, 3.26)	0.0%
T-PRK	1	-0.01 (-0.13, 0.11)	—	—	—	—	—	—	—

CI = confidence interval; LASEK = laser epithelial keratomileusis; Epi-LASIK = epithelial laser in situ keratomileusis; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy
[a]Statistically significant (P < .05).

TABLE 3
Postoperative Pain Scores and Epithelial Healing Time From Direct Comparisons Between Each Pair of Treatments

Treatment	Pain Scores on Day 1			Pain Scores on Day 3			Epithelial Healing Time		
	No. of Studies	Odds Ratio (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²	No. of Studies	Odds Ratio (95% CI)	I²
PRK vs									
Epi-LASIK	1	-0.01 (-1.76, 1.66)	—	1	-2.16 (-3.55, -0.77)[a]	—	2	0.13 (-1.63, 1.90)	91.4%
LASEK	3	0.23 (-0.37, 0.83)	0.0%	3	-0.07 (-0.52, 0.38)	0.0%	8	0.04 (-0.54, 0.61)	97.1%
T-PRK	1	1.24 (1.00, 1.48)[a]	—	1	0.48 (0.23, 0.73)[a]	—	1	1.57 (1.39, 1.75)[a]	—
LASEK vs									
Epi-LASIK	—	—	—	—	—	—	3	-0.18 (-0.81, 0.46)	76.6%
T-PRK	1	-1.23 (-2.10, -0.36)[a]	—	1	0.87 (-0.39, 2.13)	—	—	—	—

CI = confidence interval; PRK = photorefractive keratectomy; Epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratomileusis; T-PRK = transepithelial photorefractive keratectomy
[a]Statistically significant (P < .05).
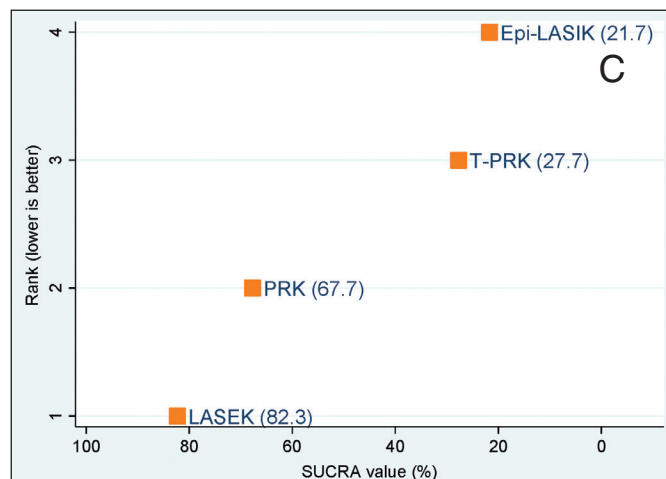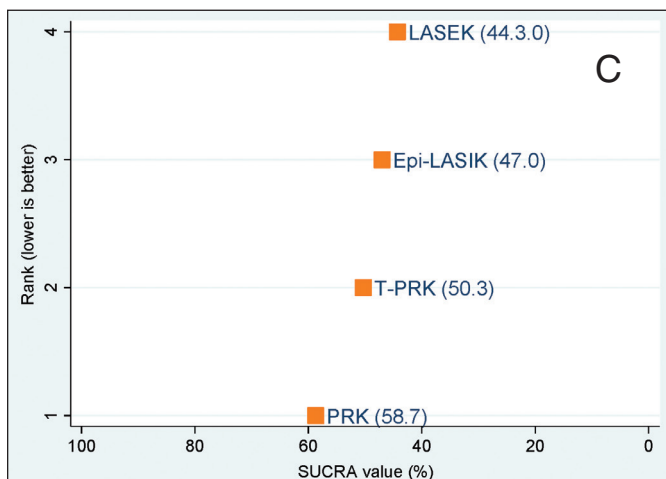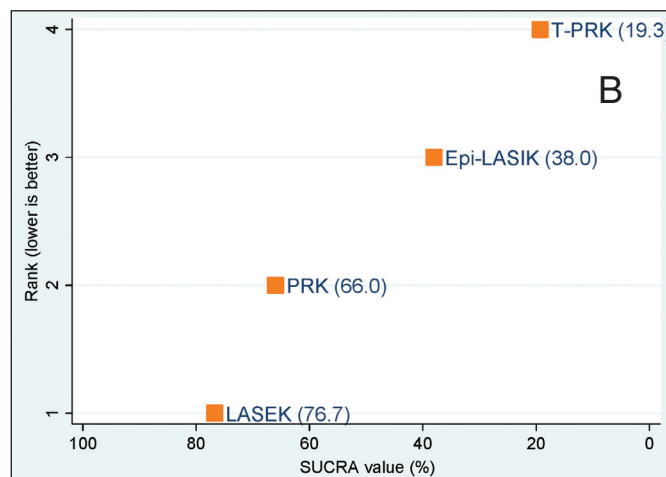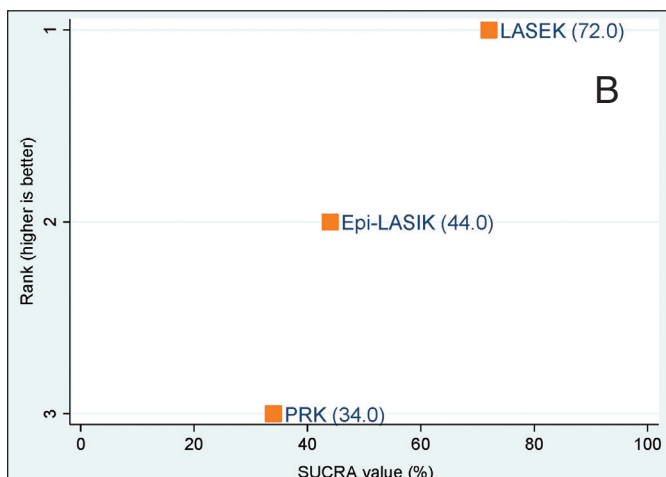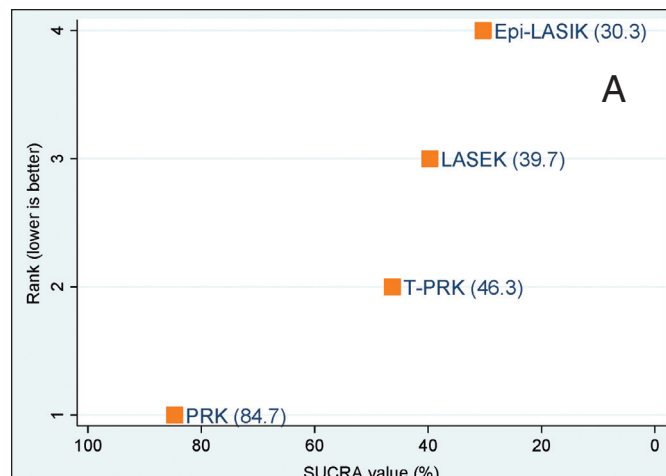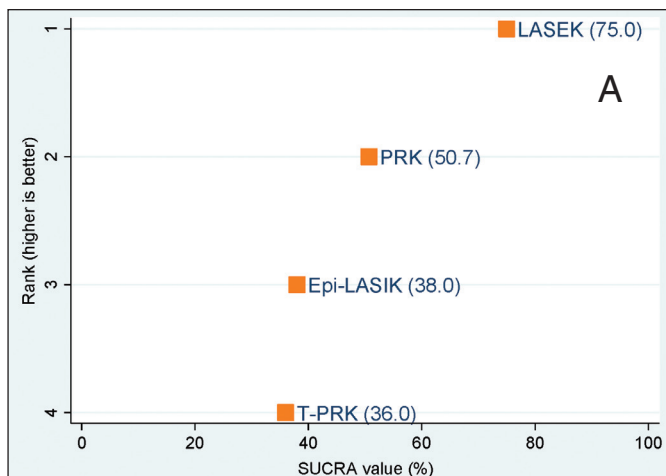
Figure 1. Ranking plot of the surface ablation surgery network based on surface under the cumulative ranking curve (SUCRA) values for (A) postoperative efficacy (uncorrected distance visual acuity [UDVA] of 20/20 or better), (B) predictability (refractive spherical equivalent [SE] within ±0.50 diopters [D] of the target refraction), and (C) safety (losing two or more lines of corrected distance visual acuity [CDVA]). epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

Figure 2. Ranking plot of procedures based on surface under the cumulative ranking curve (SUCRA) values for (A) postoperative haze scores, (B) haze grade of 0.5 or higher, and (C) haze grade of 1.0. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratomileusis; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy
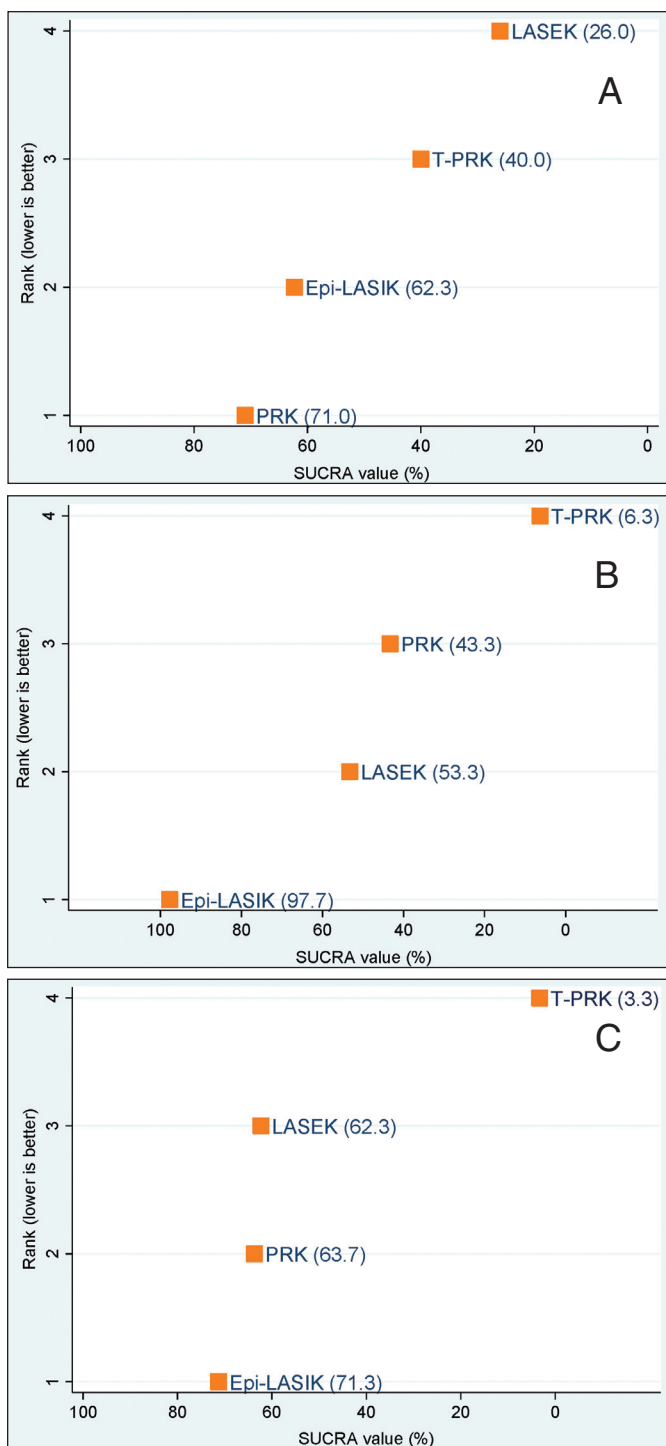
Figure 3. Ranking plot of procedures based on surface under the cumulative ranking curve (SUCRA) values for postoperative pain scores on (A) day 1 and (B) day 3 and (C) epithelial healing time. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratomileusis; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

The results for pain scores and epithelial healing time can be seen in **Figure E** (available in the online version of this article). As shown, statistically signifi-

cant differences only exist when epi-LASIK was compared with PRK (WMD = 2.17, 95% CrI = 0.19 to 4.01) and T-PRK (WMD = 2.69, 95% CrI = 0.51 to 4.84) in terms of pain scores on day 3. LASEK ranked highest for pain on day 1 and T-PRK had the least pain on day 3. T-PRK ranked first in terms of epithelial healing time (**Figure 3**).

Inconsistency. Node-splitting analysis between LASEK, PRK, and T-PRK for closed-loop comparisons in terms of pain score on day 1 shows significant inconsistency ($P = .05$). However, for other results comparisons between direct and indirect estimates did not suggest significant inconsistency between direct and indirect evidence (**Table F**, available in the online version of this article, P value varying from .22 to .99).

Sensitivity Analysis. For further sensitivity analyses, we undertook a "leave-one-out procedure" in which each trial is left out, one at a time (full process and data shown in **Table G**, available in the online version of this article). This process produced no significant change in the results.

For the postoperative haze scores in direct comparison of LASEK and PRK (WMD = -0.19, 95% CrI = -0.37 to -0.01, $I^2 = 88.9\%$), there was a statistically significant difference. When removing any single article, I^2 values were all still greater than 65% and the result turned to no statistically significant difference except when removing Ghanem et al.[35] (WMD = -0.25, 95% CrI = -0.44 to -0.07, $I^2 = 84.8\%$). For pain score on day 1, no statistically significant difference between any of the studied techniques was found when removing any study.

For epithelial healing time, high heterogeneity was found. This heterogeneity remained even after removing the two largest contributors, which prevented any meaningful sensitivity analysis for this outcome. This variability indicates the need for cautious interpretation of our data on epithelial healing time.

Publication Bias. Comparison-adjusted funnel plots for each outcome including all primary outcomes and secondary outcomes are provided in **Table H** (available in the online version of this article). Most of these plots show that the included studies lie symmetrically around the 0 line (vertical line); we did not find evidence of a small-study effect or significant publication bias in the network.

DISCUSSION

This study provides an in-depth statistical comparison of the four major excimer laser corneal surface ablation refractive procedures: PRK, T-PRK, LASEK, and epi-LASIK, for correcting myopia, combining data from 18 trials and 1,399 eyes. In addition to efficacy,

predictability, and safety, it also considers a wide range of clinically relevant outcomes including postoperative pain, haze, and epithelial healing time. The variety of available surface ablation techniques and the lack of large definitive trials with multiple treatment arms make a network meta-analysis particularly useful in this field. According to GRADE, the quality of outcomes within this network meta-analysis was mostly evaluated as moderate or high (70.6%), which indicated an acceptable level of evidence.

The main conclusion of our network meta-analysis is the confirmation[36] that all surface laser refractive technologies included in this analysis have excellent efficacy, predictability, and safety, at least in the short term (6 months after surgery). For many of the outcomes analyzed, no statistically significant differences were found (ie, in relation to efficacy, predictability, safety, postoperative haze, day 1 pain score, and epithelial healing time) (**Tables 1-3**). However, in terms of pain score on day 3, epi-LASIK was significantly more painful compared to PRK and T-PRK (**Table 3**).

In addition to determining the statistical differences of specific outcomes between procedures, our analysis (using SUCRA) provides a numerical ranking of all procedures for each outcome. SUCRA values show the relative probability of an intervention being the best option, providing an estimate of the relative dominance of the treatment in the absence of significant differences in statistical analysis. LASEK demonstrates relative advantages in three visual outcomes (efficacy, predictability, and safety) compared with the other techniques assessed, but results in greater postoperative corneal haze. Epi-LASIK demonstrates better haze scores while performing less well in relation to postoperative comfort (pain score and epithelial healing time). T-PRK tops the rankings in relation to postoperative haze grade 0.5 or higher, pain scores, and epithelial healing time, whereas PRK fails to achieve top ranking in any of the studied outcomes.

Efficacy, predictability, and safety are the most important outcomes in evaluations of corneal refractive surgery.[37,38] There are several trials and meta-analyses that compare the direct evidence for these three outcomes between different surface laser procedures. In 2010, Zhao et al.[20] performed a meta-analysis to examine possible differences in efficacy and predictability between LASEK and PRK. They indicated that LASEK had no significant benefits over PRK in terms of efficacy (OR = 0.86, 95% CI = 0.61 to 1.20) or predictability (OR = 0.90, 95% CI = 0.63 to 1.29). Wu et al.[21] compared epi-LASIK and PRK in relation to efficacy and predictability, reporting no statistically significant differences in either efficacy (relative risk = 1.43, 95%

CI = 0.85 to 2.40) or predictability (relative risk = 1.03, 95% CI = 0.92 to 1.16). These findings are similar to our results, although we also found no statistically significant difference in safety when PRK was compared with either epi-LASIK or LASEK. However, we found that LASEK demonstrated relative advantages in these three outcomes in terms of ranking and that PRK ranks lowest for both predictability and safety.

Postoperative haze formation is an important factor that may directly influence the efficacy, safety, and visual quality of corneal refractive surgery. Zhao et al.[20] contrasted LASEK and PRK in terms of corneal haze, reporting that no statistically significant difference was observed between the LASEK-treated groups and PRK-treated groups at 6 months after surgery (WMD = 0.14, 95% CI = -0.02 to 0.30), which was similar to our results (**Table 2**). We found that epi-LASIK and T-PRK performed best on SUCRA ranking in terms of haze. These findings may be associated with the release of transforming growth factor (TGF)-1. The researchers found TGF-1 is released into the tear film by the lacrimal gland after corneal epithelial injury and TGF-1 levels correlated positively with the degree of haze, whereas tear fluid TGF-1 levels were less following epi-LASIK than after LASEK.[39,40] As previously mentioned, high heterogeneity was found in direct comparison of LASEK and PRK, and we could not identify a particular study as the source of high heterogeneity through sensitivity analysis. We propose that the variability between studies may be attributed to the relatively small sample size and the subjective nature of assessing haze.[41,42]

Postoperative pain and epithelial healing time are two important factors that influence patient preference for a specific procedure. In 2002, Litwak et al.[43] reported that LASEK induced more pain than standard PRK. However, in our study, the results showed that there was no statistically significant difference between PRK and LASEK, and the SUCRA ranking showed that PRK was more likely to cause pain than LASEK at 1 day postoperatively. These differences may be attributable to the devitalized flap in LASEK, or it may be the result of the release of chemical factors such as prostaglandin, histamine, and substance P by corneal tissue.[44] Interestingly, our study found that epi-LASIK resulted in more pronounced pain compared to PRK and T-PRK at day 3 postoperatively. This might be due to delayed epithelial wound healing; Hondur et al.[45] reported slightly longer epithelial healing time with epi-LASIK compared to LASEK.

However, in relation to epithelial healing time, our statistical results indicate that heterogeneity is too high to draw reliable conclusions. Differing postoperative topical drug regimens and the variable use of bandage

contact lenses may influence postoperative epithelial healing time and could have contributed to this high heterogeneity.

In terms of our study limitations, the difference between the internal characteristics of research and studies based on the small sample sizes can be the key factors that influence both heterogeneity in direct comparisons and transitivity in indirect comparison.[46,47] For our study, although there are some differences in characteristics among the included studies (eg, the race of the study population, the choice of laser device, and the type or frequency of postoperative medication), factors that may have a potential impact on results were reasonably consistent (eg, mean dioptric correction [range: -6.32 to -2.04 D] and mean age [range: 23 to 35.7 years]). There were only two trials involving T-PRK, and with such paucity of data we should be cautious with the interpretation of the results involving T-PRK. We chose the follow-up time point closest to 6 months postoperatively to analyze outcomes for some studies because of the lack of data after 6 months postoperatively.

It is important to note that our findings are only applicable to the treatment of myopia without the use of MMC. Additional evaluation of the comparative safety and effectiveness of corneal surface laser refractive surgery with and without MMC is warranted.

Although a range of outcomes was assessed in this study, higher order aberrations, contrast sensitivity, and patient-reported outcomes such as subjective quality of vision[48,49] were not included due to a lack of data in the form of RCTs. This meta-analysis was also specifically designed to compare different corneal surface ablation techniques rather than excimer laser ablation profiles.

This network meta-analysis demonstrates that the four major corneal surface laser refractive surgeries for the correction of myopia are comparable in efficacy, predictability, safety, postoperative haze, and comfort, with the exception of pain score on day 3. Epi-LASIK was significantly more painful compared to PRK and T-PRK on postoperative day 3.

AUTHOR CONTRIBUTIONS

Study concept and design (DW, IF, DO, CM, JH); data collection (DW, RT, YH, BS); analysis and interpretation of data (DW, IF, QW, AY, LH, YZ, FB, YY, HL, LH, RLK, ES, DO, IP, JM, CM, JH); writing the manuscript (DW, RT, IF, BS, DO, CM, JH); critical revision of the manuscript (DW, IF, QW, YH, AY, LH, YZ, FB, YY, HL, LH, RLK, ES, DO, IP, JM, CM, JH); statistical expertise (DW, AY, YY, HL, CM, JH); administrative, technical, or material support (QW, FB, JH); supervision (JH)

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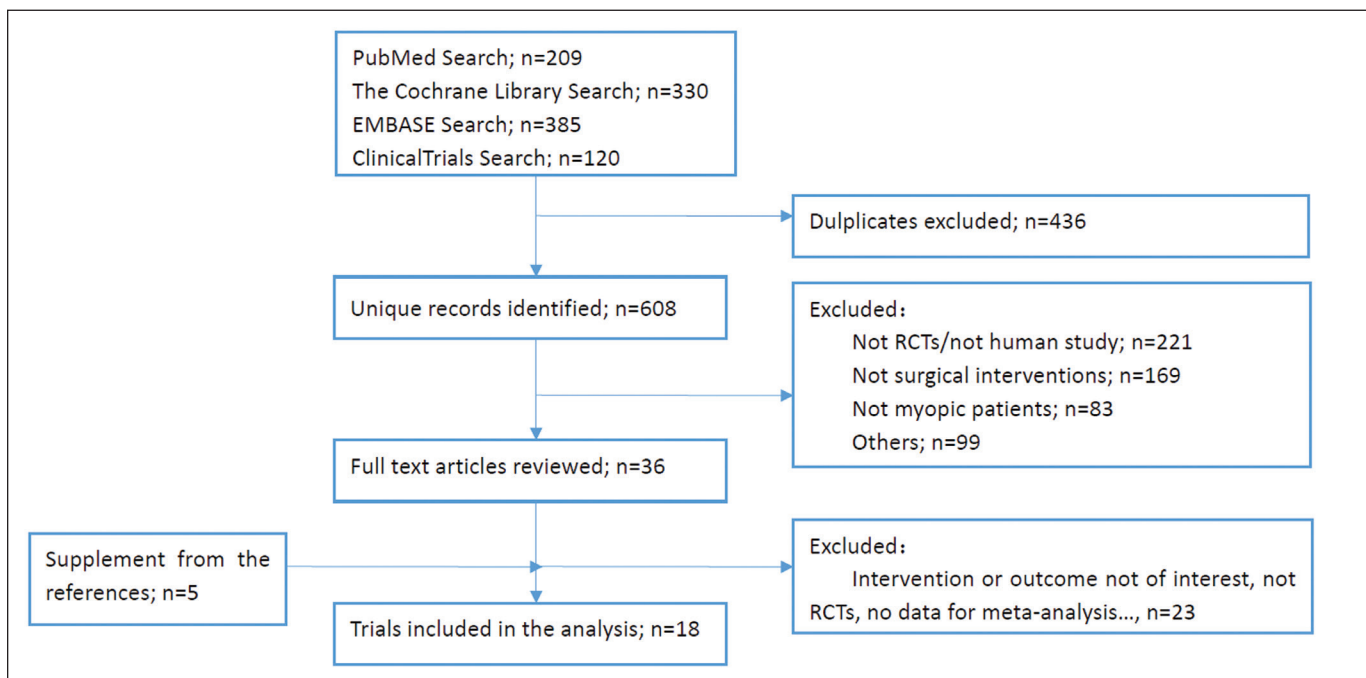
Figure A. Study selection process. RCT = randomized controlled trial
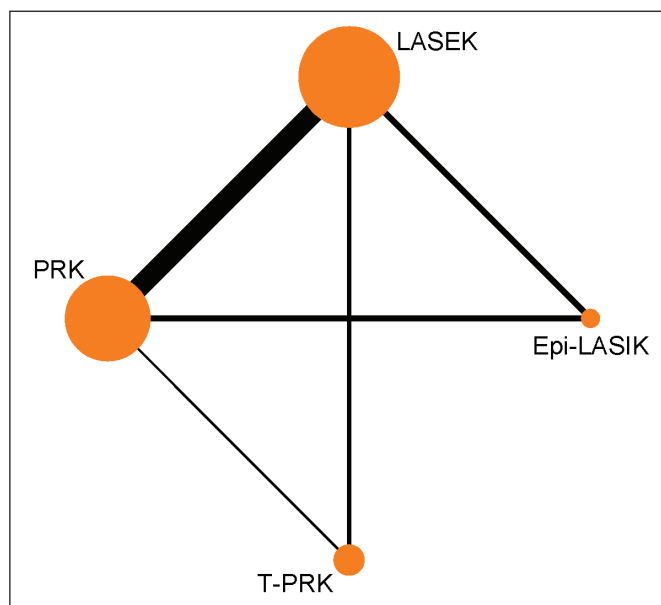
Figure B. Network of direct comparison for the corneal refractive surgery of myopia. Each node represents one treatment. The size of the node is proportional to the number of participants randomized to that treatment. The edges represent direct comparisons, and the width of the edge is proportional to the number of trials. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratomileusis; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

Epi-LASIK			
E: 0.75 (0.31, 1.75) P: 0.85 (0.37, 2.11) S: 0.90 (0.03, 49.55)	LASEK		
E: 0.86 (0.36, 2.00) P: 1.03 (0.43, 2.51) S: 0.75 (0.01, 25.85)	E: 1.16 (0.75, 1.79) P: 1.20 (0.77, 1.84) S: 0.77 (0.19, 2.95)	PRK	
E: 1.27 (0.13, 12.86) P: NA S: 0.91 (0.01, 101.18)	E: 1.62 (0.25, 13.72) P: NA S: 0.86 (0.03, 35.08)	E: 1.43 (0.21, 12.46) P: NA S: 1.23 (0.04, 31.24)	T-PRK

Odds Ratio (95% CrI) are calculated by column; E = Efficacy (UCVA of 20/20 or better); P = Predictability (Refractive SE within ± 0.50 D of the target); S = Safety (Losing two or more lines of BSCVA); NA = Not available.

Figure C. Summary comparison for postoperative efficacy, predictability, and safety of all treatments derived from the network meta-analysis. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratectomy; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

Epi-LASIK			
HS: -0.08 (-0.62, 0.46) H0.5: 0.60 (0.16, 2.13) H1: 0.20 (0.02, 2.04)	LASEK		
HS: -0.27 (-0.87, 0.33) H0.5: 0.67 (0.18, 2.25) H1: 0.27 (0.02, 2.57)	HS: -0.19 (-0.46, 0.08) H0.5: 1.10 (0.58, 2.12) H1: 1.33 (0.40, 4.78)	PRK	
HS: -0.09 (-0.86, 0.67) H0.5: 1.39 (0.22, 8.40) H1: 0.85 (0.03, 26.38)	HS: -0.01 (-0.55, 0.52) H0.5: 2.26 (0.55, 9.89) H1: 4.31 (0.28, 75.55)	HS: 0.17 (-0.42, 0.77) H0.5: 2.05 (0.59, 7.65) H1: 3.28 (0.26, 43.00)	T-PRK

Odds Ratio (95% CrI) and Mean difference (95% CrI) are calculated by column; HS = Haze scores; H0.5 = Haze grade 0.5 or higher; H1 = Haze grade 1.0 or higher.

Figure D. Summary comparisons for postoperative haze of all treatments derived from the network meta-analysis. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratectomy; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

Figure E. Summary comparison for postoperative pain scores and epithelial healing time of all treatments derived from the network meta-analysis. epi-LASIK = epithelial laser in situ keratomileusis; LASEK = laser epithelial keratectomy; PRK = photorefractive keratectomy; T-PRK = transepithelial photorefractive keratectomy

Table A

Search Strategy

MEDLINE (Pubmed)

("Keratectomy, Subepithelial, Laser-Assisted"[Mesh] OR Laser-Assisted Subepithelial Keratectomy OR Laser Subepithelial Keratomileusis OR Laser-Assisted Subepithelial Keratomileusis OR LASEK OR epipolis laser in situ keratomileusis OR Epipolis laser in situ keratomileusis OR Epi-LASIK OR "Photorefractive Keratectomy"[Mesh] OR Photorefractive Keratectomy OR PRK OR TransPRK OR transepithelial PRK OR transepithelial photorefractive keratectomy OR refractive surgery OR laser surgery) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh]) AND ((short OR near*) AND sight* OR myop* OR myopia[MeSH]) AND (pain [MeSH] OR pain* OR haze OR heal OR healing)

Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (Wiley)

#1 MeSH descriptor: [Myopia] explode all trees

#2 (short OR near*) next sight*

#3 myop*

#4 (#1 OR #2 OR #3)

#5 MeSH descriptor: [Keratectomy, Subepithelial, Laser-Assisted] explode all trees

#6 Laser-Assisted Subepithelial Keratectomy OR Laser Subepithelial Keratomileusis OR Laser-Assisted Subepithelial Keratomileusis OR LASEK

#7 epipolis laser in situ keratomileusis OR Epipolis laser in situ keratomileusis OR Epi-LASIK

#8 MeSH descriptor: [Photorefractive Keratectomy] explode all trees

#9 Photorefractive Keratectomy OR PRK OR TransPRK OR transepithelial PRK OR transepithelial photorefractive keratectomy OR refractive surgery OR laser surgery

#10 (#5 OR #6 OR #7 OR #8 OR #9)

#11 (#4 AND #10)

#12 MeSH descriptor: [pain] explode all trees

#13 pain*

#14 haze

#15 heal*

#16 (#12 OR #13 OR #14 OR #15)

#17 (#16 AND #11)   --(Restrict to trials)

EMBASE

1. myopia/exp

2. myop*

3. (short or near*) near/3 sight*

4. OR/1-3

5. 'laser epithelial keratomileusis'/exp

6. 'keratomileusis'/exp

7. 'photorefractive keratectomy'/exp

8. 'refractive surgery'/exp

9. 'laser assisted' AND subepithelial AND keratectomy

10. laser AND subepithelial AND keratomileusis

11. 'laser assisted' AND subepithelial AND keratomileusis

12. lasek

13. epipolis AND laser AND in AND situ AND keratomileusis or AND lasik

14. epipolis AND laser AND in AND situ AND keratomileusis

15. 'epi lasik'

16. photorefractive AND keratectomy

17. prk

18. 'trans prk'

19. refractive AND surgery

20. laser AND surgery

21. OR/5-20

22. random*

23. blind*

24. placebo

25. 'meta analysis'

26. OR/22-25

27. 'human'/de

28. 4 AND 21 AND 26 AND 27

29. pain/exp

30. pain*

31. haze

32. heal*

33. OR/29-32

34. 28 AND 33

ClinicalTrials.gov search strategy

(PRK OR LASIK OR LASEK OR EPI-LASIK OR SBK OR FLEX OR SMILE) AND Myopia

Table B

Summary of Randomized Controlled Trials Included in the Meta-analysis

Study (Author, Year)	Country	Follow-up, mo	Treatment	Laser Machine	Number Of Eyes	Mean Age (SD), y	Mean pre-op refraction (SD), D	Postoperative proportion of eyes at 6 months, events/total					Postoperative Haze scores at 6 months (SD)	Postoperative pain scores (SD)	
								UCVA of 20/20 or better	Refractive SE within ±0.50 D of the target	Losing two or more lines of BSCVA	Haze grade 0.5 or higher	Haze grade 1.0 or higher		Day 1	Day 3
Autrata 2003[1]	Czech	24m	PRK	Nidek EC-5000	92	18 to 39	-4.78(2.93)	62/92	52/92	0/92			1.06(0.52)		
			LASEK	Nidek EC-5000	92		-4.9(3.01)	67/92	57/92	0/92			0.61(0.4)		
Celik 2014[2]	Turkey	12m	T-PRK	Amaris	42	28.5(6.3)	-2.88(1.24)			0/42	13/42	2/42		4.28(0.55)	3.08(0.41)
			PRK	Amaris	42		-2.44(1)			0/42	20/42	5/42		5.52(0.58)	3.56(0.7)
Gamaly 2007[3]	Oman	6m	Epi-LASIK	Nidek EC-5000 CX II	12	24.8	-2.67	9/12	8/12	0/12	7/12	0/12			
			PRK	Nidek EC-5000 CX II	12			8/12	7/12	0/12	15/12	4/12			
Ghanem2008[4]	Brazil	12m	PRK	MEL 70 G-scan	51	28.06(4.13)		49/50	45/48	0/51	4/51	1/51	0.08(0.32)		
			LASEK	MEL 70 G-scan	51			47/49	40/44	0/51	7/51	1/51	0.09(0.24)		
Ghanem2008+[5]	Brazil	12m	PRK	MEL 70 G-scan	51	28.06(4.13)									
			LASEK	MEL 70 G-scan	51										
Ghirlando 2007[6]	Italy	12m	LASEK	InPro	50	34.5(2.3)	-3.59(1.29)		44/50		9/50	4/50			
			PRK	InPro	50		-4.37(1.35)		46/50		12/50	2/50			
Hashemi 2004[7]	Iran	3m	PRK	Nidek EC-5000/	42	29.1(7.8)	-3.44(1.13)	26/32	23/32		8/32	1/32			
			LASEK	Technolas 217C	42		-3.57(1.25)	25/32	26/32		10/32	4/32			
				Nidek EC-5000/											

				Technolas 217C												
He 2004[8]	China	6m	PRK	Nidek EC-5000	46	23.2(4)	-4.5(1.28)		36/46					0.32(0.25)		
			LASEK	Nidek EC-5000	46		-4.38(1.23)		40/46					0.16(0.23)		
Hondur 2008[9]	Turkey	12m	LASEK	ESIRIS	25	26.8(8.4)	-3.91(1.39)	23/25	23/25			5/25	0/25			
			Epi-LASIK	ESIRIS	25		-3.95(1.49)	23/25	23/25			5/25	0/25			
Lee 2001[10]	Germany	3m	PRK	Keratome II	27	25(3.2)	-4.82(1.07)	7/27						0.45(0.27)		
			LASEK	Keratome II	27		-4.69(0.96)	8/27						0.29(0.26)		
Litwak 2002[11]	Mexico	1m	PRK	Nidek EC-5000	25	28.7(5.9)	-3(1.9)			0/25						
			LASEK	Nidek EC-5000	25		-3.1(2)			0/25						
Long 2006[12]	China	3m	LASEK	MEL80	10	28.3	-4.5(1.44)							0.31(0.14)		
			Epi-LASIK	MEL80	10		-4.9(1.26)							0.23(0.08)		
O'Doherty 2007[13]	Ireland	3m	Epi-LASIK	Bausch & Lomb 217	38	30	-3.51(1.65)	24/38	30/38							
			LASEK	Bausch & Lomb 217	38	30	-3.18(1.15)	28/38	32/38							
			PRK	Bausch & Lomb 217	19	32	-3.72(1.59)	14/19	15/19							
Pirouzian 2004[14]	USA	1m	PRK	VISX Star 3	32	21 to 46								4.27(3.5)	2.27(2)	
			LASEK	VISX Star 3	32									4.17(3.5)	2.17(1.5)	
Saleh 2003[15]	U.K.	2d	PRK	Nidek EC-5000	14	22 to 43	-2.035							4.09(2.48)	2.21(2.55)	
			LASEK	Nidek EC-5000	14		-2.267							3.71(2.84)	2.86(3.43)	
Sia 2014[16]	USA	12m	LASEK	LADARVision 4000	83	35.7(8)	-5.85(1.38)	64/75	51/75	1/75	18/75	5/75		1(2.19)	0.64（1.81）	
			PRK	LADARVision 4000	83		-5.89(1.42)	64/75	47/75	2/75	15/75	6/75		1.23(2.28)	0.54（1.76）	
Torres 2007[17]	USA	6d	PRK	NIDEK EC-5000	20									4.21(2.37)	2.53(2.22)	
			Epi-LASIK	NIDEK EC-5000	20									4.26(3.1)	4.69(2.28)	
Wang 2014[18]	China	3m	LASEK	SCHWIND	30	23(4.59)	-6.27(2.30)	28/30						0.26(0.21)	3.2(1.833)	5.27(2.638)
			T-PRK	SCHWIND	30		-6.32(2.21)	27/30						0.27(0.25)	4.43(1.612)	4.4(2.343)

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Table C

The Quality of the Included Trials

3-1 Quality of the included trials

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Autrata 2003	?	?	+	?	+	+	+
Celik 2014	?	?	+	+	+	−	+
Gamaly 2007	+	?	+	?	?	+	−
Ghanem2008	+	−	+	?	+	+	?
Ghanem 2008	+	−	+	?	+	+	?
Ghirlando 2007	?	?	+	?	+	?	−
Hashemi 2004	+	?	?	?	?	+	−
He 2004	?	?	?	?	+	−	?
Hondur 2008	−	−	?	?	+	?	?
Lee 2001	?	?	?	?	+	+	?
Litwak 2002	?	?	+	+	+	−	−
Long 2006	+	?	?	?	+	?	−
O'Doherty 2007	?	+	+	?	+	+	−
Pirouzian 2004	+	?	+	?	+	+	+
Saleh 2003	?	+	?	?	+	+	−
Sia 2014	?	?	?	?	?	+	+
Torres 2007	?	+	+	+	+	+	?
Wang 2014	−	−	?	?	+	−	+

3-2 Analysis by synthesis
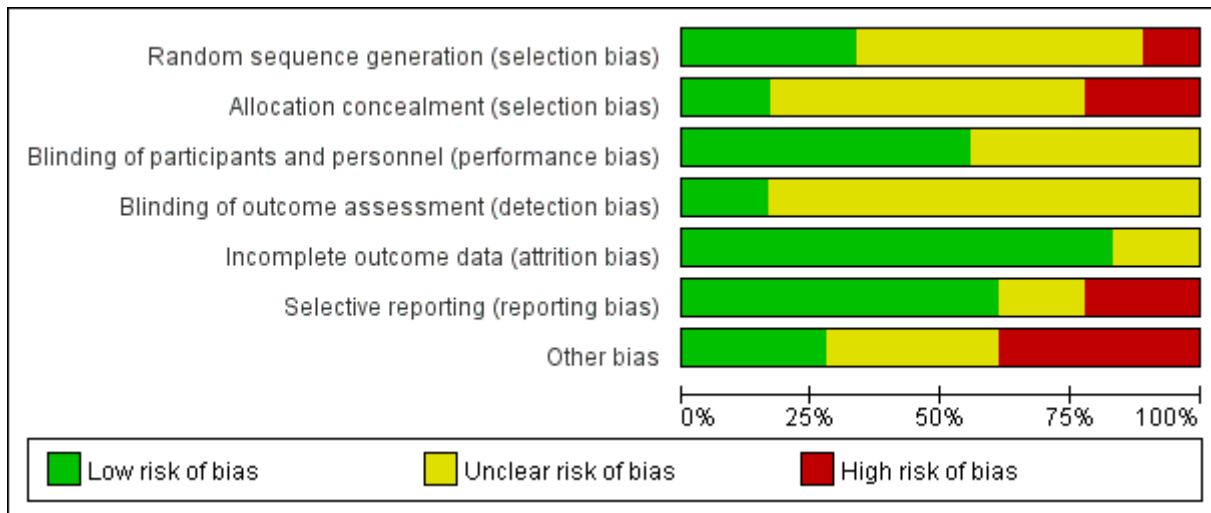
3-3 GRADE result for quality ratings

Efficacy						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odds radio (95% confidence interval)	Quality of evidence	Odds radio (95% conference interval)	Quality of evidence	Odds radio (95% confidence interval)	Quality of evidence
PRK vs T-PRK	/	/	1.43 (0.21,12.46)	Moderate	1.43 (0.21,12.46)	Moderate
PRK vs LASEK	1.16 (0.76,1.82)	Moderate	0.72 (0.05, 8.76)	Moderate	1.16 (0.75, 1.79)	Moderate
PRK vs Epi-LASIK	0.86 (0.30,1.97)	High	1.67 (0.13,12.06)	Moderate	0.86 (0.36,1.99)	High
T-PRK vs LASEK	1.56 (0.24, 10.05)	Moderate	/	/	1.62 (0.25,13.72)	Moderate
T-PRK vs Epi-LASIK	/	/	1.27 (0.13,12.86)	Moderate	1.27 (0.13,12.86)	Moderate
LASEK vs Epi-LASIK	1.45 (0.55, 3.67)	Moderate	1.46 (0.47,4.95)	Moderate	1.34 (0.57, 3.19)	Moderate
Predictability						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odds radio (95% conference interval)	Quality of evidence	Odds radio (95% confidence interval)	Quality of evidence	Odds radio (95% conference interval)	Quality of evidence

Comparison	Direct evidence					
PRK vs T-PRK	/	/	/	/	/	/
PRK vs LASEK	1.21 (0.75, 1.84)	Moderate	1.13 (0.08, 13.20)	Moderate	1.21 (0.77, 1.84)	Moderate
PRK vs Epi-LASIK	1.05 (0.40, 2.80)	High	1.27 (0.06, 10.18)	Moderate	1.03 (0.43, 2.51)	High
T-PRK vs LASEK	/	/	/	/	/	/
T-PRK vs Epi-LASIK	/	/	/	/	/	/
LASEK vs Epi-LASIK	1.23 (0.41, 3.56)	Moderate	0.99 (0.30, 3.32)	Moderate	1.17 (0.47, 2.66)	Moderate

Safety						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odds radio (95% confidence interval)	Quality of evidence	Odds radio (95% conference interval)	Quality of evidence	Odds radio (95% confidence interval)	Quality of evidence
PRK vs T-PRK	1.00 (0.06, 16.51)	High	/	/	1.23 (0.04,31.24)	High
PRK vs LASEK	1.24 (0.32, 4.78)	High	/	/	0.77 (0.19,2.95)	High
PRK vs Epi-LASIK	1.00 (0.05, 17.90)	Moderate	/	/	0.75 (0.01,25.85)	Moderate
T-PRK vs LASEK	/	/	0.86 (0.03,35.08)	High	0.86 (0.03,35.08)	High
T-PRK vs Epi-LASIK	/	/	0.91 (0.01,101.18)	Moderate	0.91 (0.01,101.18)	Moderate
LASEK vs Epi-LASIK	/	/	0.90 (0.03,49.55)	Moderate	0.90 (0.03,49.55)	Moderate

Haze score						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Weighted mean differences (95% conference interval)	Quality of evidence	Weighted mean differences (95% confidence interval)	Quality of evidence	Weighted mean differences (95% conference interval)	Quality of evidence
PRK vs T-PRK	/	/	0.17 (-0.42,0.77)	Low	0.17 (-0.42,0.77)	Low
PRK vs LASEK	-0.19 (-0.37, -0.01)	Low	/	/	-0.19 (-0.46,0.08)	Low
PRK vs Epi-LASIK	/	/	-0.27 (-0.87,0.33)	Low	-0.27 (-0.87,0.33)	Low

T-PRK vs LASEK	-0.01 (-0.13, 0.11)	Moderate	/	/	-0.01 (-0.55,0.52)	Moderate
T-PRK vs Epi-LASIK	/	/	-0.09 (-0.86,0.67)	Moderate	-0.09 (-0.86,0.67)	Moderate
LASEK vs Epi-LASIK	0.08 (-0.02, 0.18)	High	/	/	-0.08 (-0.62,0.46)	High

Haze grade 0.5 or higher						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odds radio (95% confidence interval)	Quality of evidence	Odds radio (95% conference interval)	Quality of evidence	Odds radio (95% confidence interval)	Quality of evidence
PRK vs T-PRK	2.03 (0.83, 4.95)	Low	/	/	2.05 (0.59,7.65)	Low
PRK vs LASEK	1.17 (0.61,2.34)	Moderate	0.3 2(0.03,3.90)	Moderate	1.11 (0.58,2.12)	Moderate
PRK vs Epi-LASIK	0.35 (0.05,2.29)	Moderate	1.19 (0.19,7.24)	Moderate	0.67 (0.18,2.25)	Moderate
T-PRK vs LASEK	/	/	2.26 (0.55,9.89)	Low	2.26 (0.55,9.89)	Low
T-PRK vs Epi-LASIK	/	/	1.39 (0.22,8.40)	Low	1.39 (0.22,8.40)	Low
LASEK vs Epi-LASIK	0.98 (0.19,5.75)	Moderate	3.39 (0.51,28.22)	Moderate	1.67 (0.47,6.23)	Moderate

Haze grade 1.0 or higher						
Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Odds radio (95% conference interval)	Quality of evidence	Odds radio (95% confidence interval)	Quality of evidence	Odds radio (95% conference interval)	Quality of evidence
PRK vs T-PRK	2.70 (0.49, 14.79)	Low	/	/	3.28 (0.26,43.00)	Low
PRK vs LASEK	1.63 (0.46,6.17)	Moderate	0.09 (0.00,13.74)	Moderate	1.34 (0.40,4.81)	Moderate
PRK vs Epi-LASIK	0.10 (0.00,1.65)	Moderate	1.65 (0.03,89.12)	Moderate	0.28 (0.02,2.56)	Moderate
T-PRK vs LASEK	/	/	4.31 (0.28,75.55)	Low	4.31 (0.28,75.55)	Low
T-PRK vs Epi-LASIK	/	/	0.85 (0.03,26.38)	Low	0.85 (0.03,26.38)	Low
LASEK vs Epi-LASIK	0.94 (0.02,42.10)	Moderate	17.64 (0.84,1096.63)	Moderate	4.95 (0.49,62.18)	Moderate
Pain day1						

Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Weighted mean differences (95% confidence interval)	Quality of evidence	Weighted mean differences (95% conference interval)	Quality of evidence	Weighted mean differences (95% confidence interval)	Quality of evidence
PRK vs T-PRK	1.25 (-0.06, 2.56)	Low	-0.97 (-2.82, 0.81)	Low	0.49 (-0.99, 1.82)	Low
PRK vs LASEK	-0.22 (-1.27, 0.78)	Moderate	-2.44 (-4.51, -0.46)	Low	-0.69 (-1.79, 0.50)	Moderate
PRK vs Epi-LASIK	-0.01 (-1.76, 1.66)	Moderate	/	/	0.06 (-2.43,2.49)	Moderate
T-PRK vs LASEK	-1.20 (-2.72, 0.29)	Low	1.04 (-0.62, 2.65)	Low	-0.20 (-1.69, 1.22)	Low
T-PRK vs Epi-LASIK	/	/	0.54 (-2.34,3.27)	Low	0.54 (-2.34,3.27)	Low
LASEK vs Epi-LASIK	/	/	0.75 (-2.00,3.41)	Moderate	0.75 (-2.00,3.41)	Moderate

<table>
<tr><td colspan="7" style="background-color:yellow;text-align:center">Pain day3</td></tr>
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Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Weighted mean differences (95% conference interval)	Quality of evidence	Weighted mean differences (95% confidence interval)	Quality of evidence	Weighted mean differences (95% conference interval)	Quality of evidence
PRK vs T-PRK	0.49 (-1.27, 2.27)	Moderate	0.82 (-1.71, 3.20)	Low	0.51 (-0.51, 1.67)	Moderate
PRK vs LASEK	0.07 (-1.08, 1.39)	Moderate	0.37 (-2.44, 3.14)	Low	0.12 (-0.69, 1.04)	Moderate
PRK vs Epi-LASIK	-2.16 (-3.55, -0.77)	High	/	/	2.17 (0.19,4.01)	High
T-PRK vs LASEK	0.81 (-1.22, 3.00)	Low	0.59 (-1.54, 2.84)	Moderate	0.64 (-0.39, 1.88)	High
T-PRK vs Epi-LASIK	/	/	2.69 (0.51,4.84)	Moderate	2.69 (0.51,4.84)	Moderate
LASEK vs Epi-LASIK	/	/	2.03 (-0.16,4.03)	Moderate	2.03 (-0.16,4.03)	Moderate

<table>
<tr><td colspan="7" style="background-color:yellow;text-align:center">Epithelial healing time</td></tr>
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Comparison	Direct evidence		Indirect evidence		Network meta-analysis	
	Weighted mean differences (95% confidence interval)	Quality of evidence	Weighted mean differences (95% conference interval)	Quality of evidence	Weighted mean differences (95% confidence interval)	Quality of evidence

PRK vs T-PRK	1.57 (1.39, 1.75)	Moderate	/	/	1.57 (-0.04,3.15)	Moderate
PRK vs LASEK	-0.03 (-0.67, 0.58)	Moderate	-0.33 (-2.18, 1.56)	Low	-0.01 (-0.56, 0.56)	Moderate
PRK vs Epi-LASIK	-0.12 (-1.47, 1.24)	Low	0.17 (-1.37, 1.58)	Low	0.08 (-0.81, 0.99)	Low
T-PRK vs LASEK	/	/	1.56 (-0.14,3.23)	Moderate	1.56 (-0.14,3.23)	Moderate
T-PRK vs Epi-LASIK	/	/	1.6 5(-0.21,3.46)	Low	1.65 (-0.21,3.46)	Low
LASEK vs Epi-LASIK	-0.15 (-1.13, 0.90)	Low	0.29 (-1.18, 1.64)	Low	-0.09 (-0.96, 0.76)	Low

Table D

High Heterogeneity Among Some Comparisons (Forest Plots)

4-1 LASEK vs PRK for postoperative Haze scores

Study		Relative Effect (95% CI)
Autrata 2003		-0.45 (-0.58, -0.32)
Ghanem2008		0.01 (-0.10, 0.12)
He 2004		-0.16 (-0.26, -0.06)
Lee 2001		-0.16 (-0.30, -0.02)
Combined		-0.19 (-0.37, -0.01)

-0.6   0   0.2

Mean Difference

Favours LASEK   Favours PRK

Heterogeneity = 26.94 (I^2 = 88.9%)
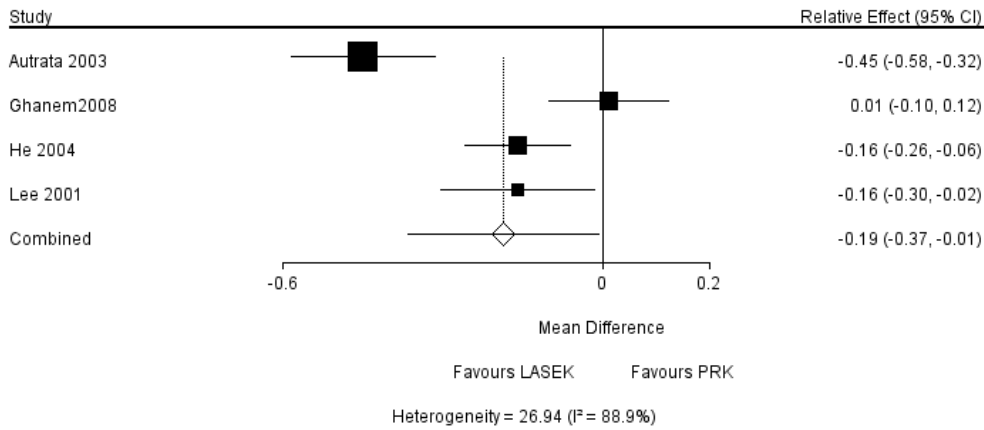
4-2 LASEK vs Epi-LASIK for postoperative epithelial healing time

Study		Relative Effect (95% CI)
Hondur2008		-0.68 (-1.03, -0.33)
Long2006		0.50 (-0.61, 1.61)
O'Doherty 2007		0.00 (-0.46, 0.46)
Combined		-0.18 (-0.81, 0.46)

-2   0   2

Mean Difference

Favours LASEK   Favours Epi-LASIK

Heterogeneity = 8.55 (I^2 = 76.6%)

4-3 PRK vs Epi-LASIK for postoperative epithelial healing time

Study		Relative Effect (95% CI)
O'Doherty 2007		1.00 (0.44, 1.56)
Torres 2007		-0.80 (-1.71, 0.11)
Combined		0.13 (-1.63, 1.90)

-2   0   2

Mean Difference

Favours PRK   Favours Epi-LASIK

Heterogeneity = 11.60 (I^2 = 91.4%)
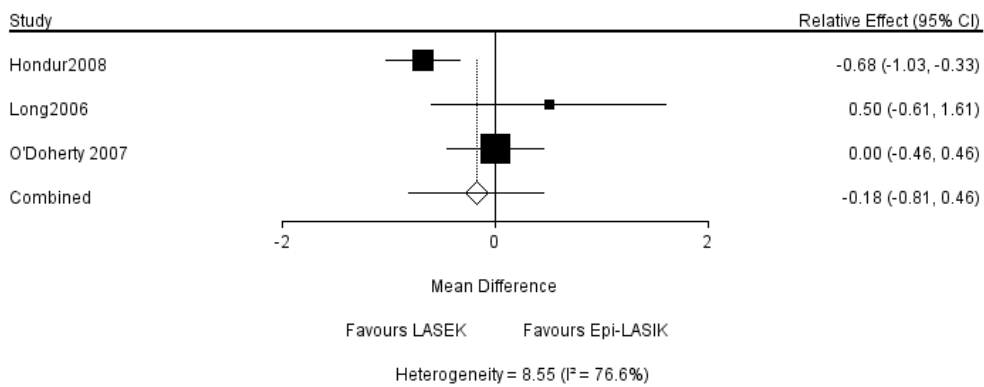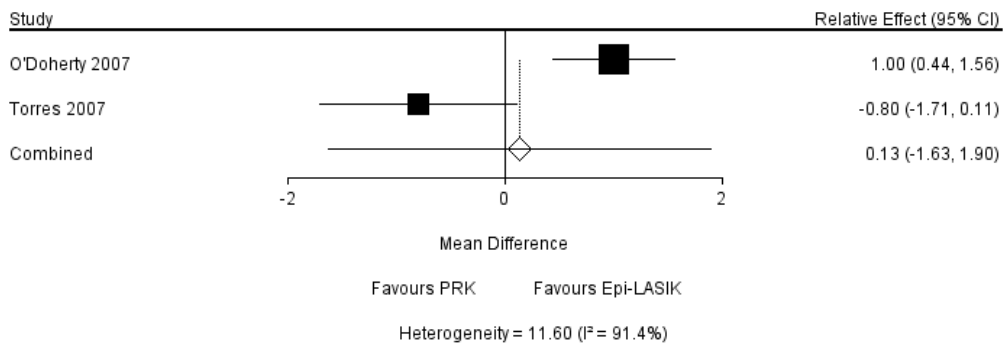
4-4 PRK vs LASEK for postoperative epithelial healing time

Study		Relative Effect (95% CI)
Autrata 2003		1.19 (1.01, 1.37)
Ghanem2008+		-0.40 (-0.64, -0.16)
Ghirlando 2007		0.23 (-0.08, 0.54)
Hashemi 2004		-0.28 (-0.78, 0.22)
He 2004		-0.62 (-0.85, -0.39)
Lee 2001		-0.46 (-0.77, -0.15)
Litwak2002		-0.30 (-0.58, -0.02)
O'Doherty 2007		1.00 (0.44, 1.56)
Combined		0.04 (-0.54, 0.61)

-1   0   2

Mean Difference

Favours PRK   Favours LASEK

Heterogeneity = 239.47 (I² = 97.1%)
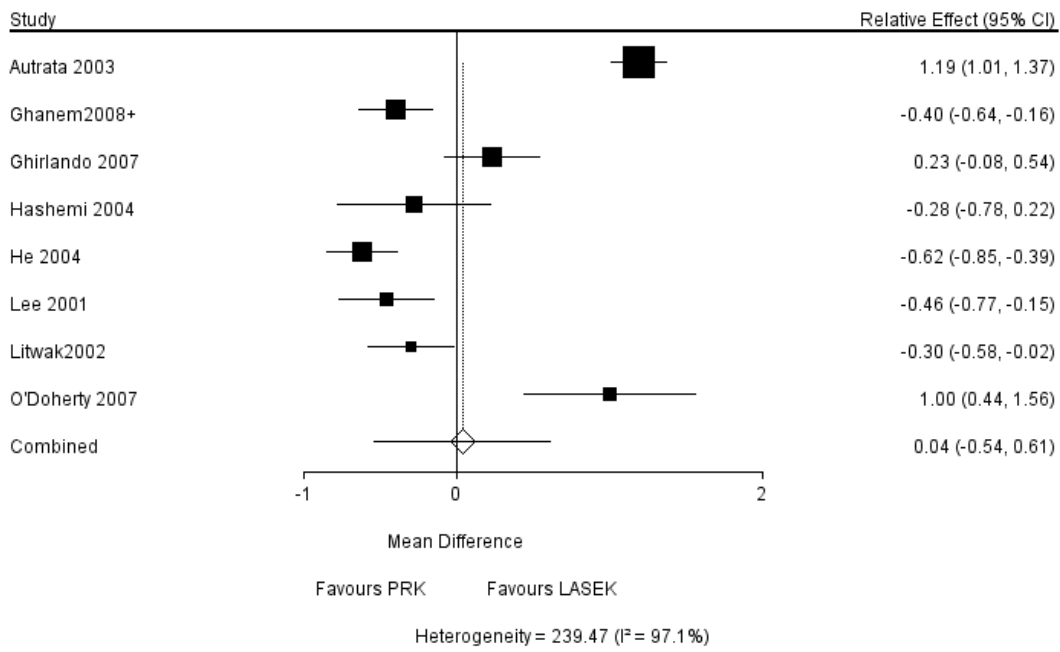
Table E

Ranking Probabilities

5-1 Efficacy (UCVA of 20/20 or better)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.16	0.15	0.36	0.32
LASEK	0.43	0.41	0.14	0.02
PRK	0.14	0.36	0.38	0.12
T-PRK	0.27	0.08	0.11	0.54

5-2 Predictability (Refractive SE within ±0.50 D of the target)

Drug	Rank 1	Rank 2	Rank 3
Epi-LASIK	0.34	0.2	0.46
LASEK	0.54	0.36	0.1
PRK	0.12	0.44	0.44

5-3 Safety (Losing two or more lines of BSCVA)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.32	0.14	0.17	0.38
LASEK	0.16	0.24	0.37	0.22
PRK	0.19	0.45	0.29	0.08
T-PRK	0.33	0.17	0.18	0.32

5-4 Postoperative haze scores

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.12	0.17	0.21	0.51
LASEK	0.02	0.32	0.49	0.17
PRK	0.65	0.26	0.07	0.02
T-PRK	0.22	0.25	0.23	0.3

5-5 Postoperative haze grade 0.5 or higher

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.17	0.13	0.37	0.33
LASEK	0.49	0.35	0.13	0.02
PRK	0.27	0.46	0.25	0.02
T-PRK	0.07	0.06	0.25	0.62

5-6 Postoperative Haze grade 1.0 or higher

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.05	0.07	0.36	0.52
LASEK	0.61	0.27	0.10	0.01
PRK	0.24	0.57	0.17	0.02
T-PRK	0.10	0.08	0.37	0.45

5-7 Postoperative pain scores on day 1

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.48	0.15	0.13	0.24
LASEK	0.05	0.14	0.35	0.45
PRK	0.34	0.48	0.15	0.03
T-PRK	0.13	0.22	0.37	0.28

5-8 Postoperative pain scores on day 3

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.96	0.02	0.01	0.01
LASEK	0.02	0.62	0.3	0.05
PRK	0.01	0.33	0.61	0.06
T-PRK	0.01	0.04	0.08	0.88

5-9 Postoperative epithelial healing time

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.48	0.2	0.3	0.03
LASEK	0.23	0.42	0.34	0.02
PRK	0.27	0.38	0.34	0.01
T-PRK	0.02	0.01	0.02	0.95

Table F

Node-splitting Analysis of Inconsistency

Name	Outcome	Direct estimate (95% Cl)	Indirect estimate (95% Cl)	Overall (95% Cl)	P-value for inconsistency
LASEK vs Epi-LASIK	Efficacy	0.37 (-0.59, 1.30)	0.38 (-0.76, 1.60)	0.29 (-0.56, 1.16)	0.99
Epi-LASIK vs PRK	Efficacy	-0.15 (-1.19, 0.68)	0.51 (-2.07, 2.49)	-0.15 (-1.01, 0.69)	0.62
LASEK vs PRK	Efficacy	0.15 (-0.27, 0.60)	-0.33 (-2.97, 2.17)	0.15 (-0.28, 0.58)	0.71
LASEK vs Epi-LASIK	Predictability	0.21 (-0.88, 1.27)	-0.01 (-1.22, 1.20)	0.16 (-0.75, 0.98)	0.75
Epi-LASIK vs PRK	Predictability	0.05 (-0.92, 1.03)	0.24 (-2.74, 2.32)	0.03 (-0.84, 0.92)	0.86
LASEK vs PRK	Predictability	0.19 (-0.29, 0.61)	0.12 (-2.50, 2.58)	0.19 (-0.26, 0.61)	0.96
LASEK vs Epi-LASIK	Haze grade 0.5 or higher	-0.02 (-1.68, 1.75)	1.22 (-0.67, 3.34)	0.51 (-0.76, 1.83)	0.32
Epi-LASIK vs PRK	Haze grade 0.5 or higher	-1.04 (-3.07, 0.83)	0.17 (-1.66, 1.98)	-0.40 (-1.73, 0.81)	0.34
LASEK vs PRK	Haze grade 0.5 or higher	0.16 (-0.49, 0.85)	-1.15 (-3.67, 1.36)	0.10 (-0.54, 0.75)	0.33
LASEK vs Epi-LASIK	Haze grade 1.0 or higher	-0.06 (-3.91, 3.74)	2.87 (-0.18, 7.00)	1.60 (-0.71, 4.13)	0.22
Epi-LASIK vs PRK	Haze grade 1.0 or higher	-2.31 (-6.26, 0.50)	0.50 (-3.48, 4.49)	-1.29 (-3.76, 0.94)	0.23
LASEK vs PRK	Haze grade 1.0 or higher	0.49 (-0.77, 1.82)	-2.38 (-7.26, 2.62)	0.29 (-0.92, 1.57)	0.23
LASEK vs PRK	Pain scores on day 1	-0.22 (-1.27, 0.78)	-2.44 (-4.51, -0.46)	-0.69 (-1.79, 0.50)	0.05
LASEK vs T-PRK	Pain scores on day 1r	-1.20 (-2.72, 0.29)	1.04 (-0.62, 2.65)	-0.20 (-1.69, 1.22)	0.05

PRK vs T-PRK	Pain scores on day 1	1.25 (-0.06, 2.56)	-0.97 (-2.82, 0.81)	0.49 (-0.99, 1.82)	0.05
LASEK vs PRK	Pain scores on day 3	0.07 (-1.08, 1.39)	0.37 (-2.44, 3.14)	0.12 (-0.69, 1.04)	0.79
LASEK vs T-PRK	Pain scores on day 3	0.81 (-1.22, 3.00)	0.59 (-1.54, 2.84)	0.64 (-0.39, 1.88)	0.85
PRK vs T-PRK	Pain scores on day 3	0.49 (-1.27, 2.27)	0.82 (-1.71, 3.20)	0.51 (-0.51, 1.67)	0.74
LASEK vs Epi-LASIK	epithelial healing time	-0.15 (-1.13, 0.90)	0.29 (-1.18, 1.64)	-0.09 (-0.96, 0.76)	0.60
Epi-LASIK vs PRK	epithelial healing time	-0.12 (-1.47, 1.24)	0.17 (-1.37, 1.58)	0.08 (-0.81, 0.99)	0.76
LASEK vs PRK	epithelial healing time	-0.03 (-0.67, 0.58)	-0.33 (-2.18, 1.56)	-0.01 (-0.56, 0.56)	0.74

Sensitivity Analyses Using a Leave-One-Out Procedure in Which Each Trial Is Left Out, One at a Time

7-1 Direct comparison between PRK and LASEK for postoperative Haze scores (removed Autrata 2003)

Study		Relative Effect (95% CI)
Ghanem2008		0.01 (-0.10, 0.12)
He 2004		-0.16 (-0.26, -0.06)
Lee 2001		-0.16 (-0.30, -0.02)
Combined		-0.10 (-0.22, 0.01)

-0.4   0   0.2

Mean Difference

Favours LASEK   Favours PRK

Heterogeneity = 5.91 (I^2 = 66.1%)
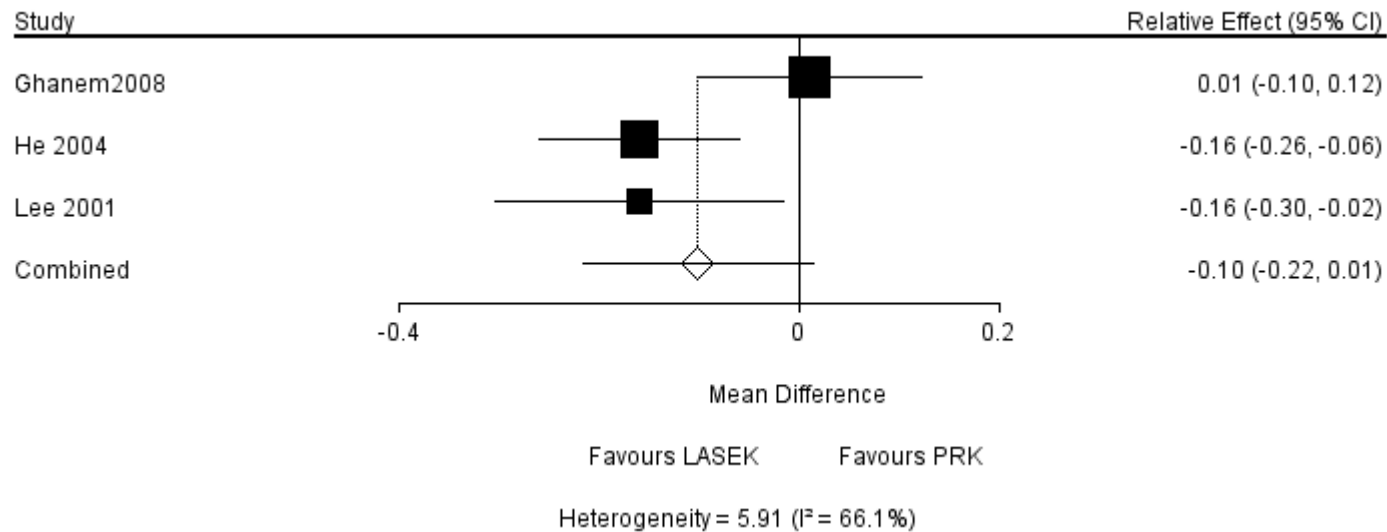
7-2 Comparison for postoperative haze scores of all treatments derived from network meta-analysis (removed Autrata 2003)

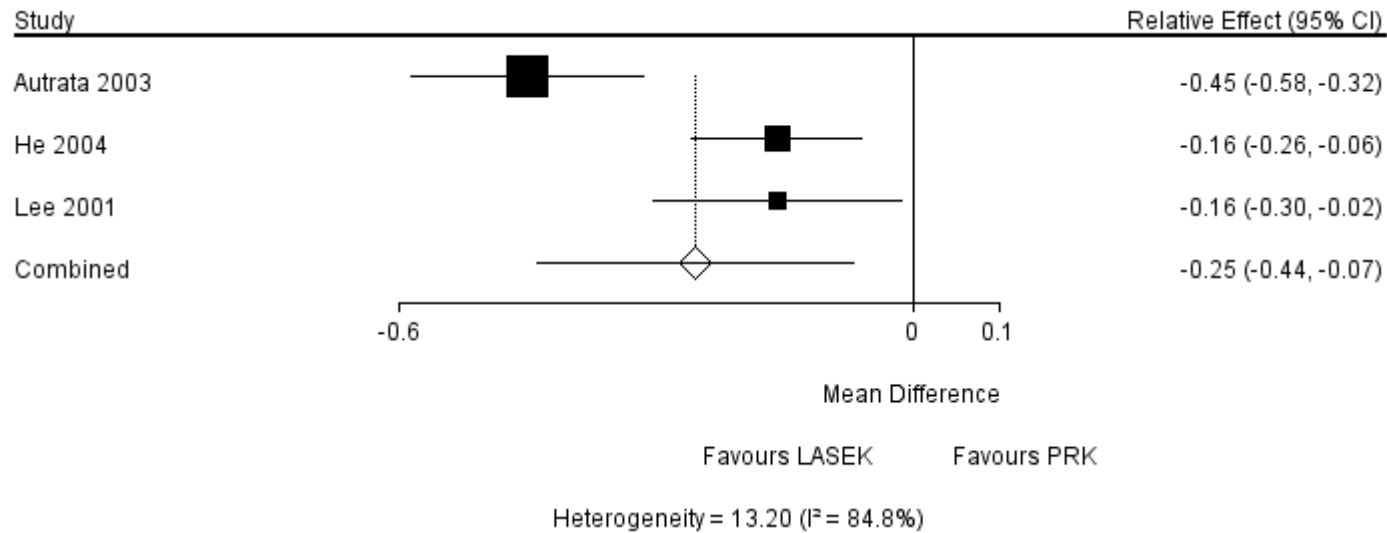|			
Epi-LASIK	0.08 (-0.14, 0.30)	0.18 (-0.08, 0.44)	0.09 (-0.22, 0.41)
-0.08 (-0.30, 0.14)	LASEK	0.10 (-0.03, 0.23)	0.01 (-0.22, 0.23)
-0.18 (-0.44, 0.08)	-0.10 (-0.23, 0.03)	PRK	-0.09 (-0.35, 0.17)
-0.09 (-0.41, 0.22)	-0.01 (-0.23, 0.22)	0.09 (-0.17, 0.35)	T-PRK

Mean difference (95% CrI)

7-3 Ranking probabilities of postoperative haze scores (removed
Autrata 2003)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.05	0.10	0.18	0.67
LASEK	0.02	0.37	0.51	0.10
PRK	0.73	0.21	0.04	0.01
T-PRK	0.21	0.31	0.27	0.21

7-4 SUCRA value of postoperative haze scores
(removed Autrata 2003)

Treatment	SUCRA value (%)
Epi-LASIK	17.7
LASEK	43.7
PRK	88.3
T-PRK	50.7

7-5 Direct comparison between PRK and LASEK for postoperative Haze scores (removed Ghanem 2008)

Study		Relative Effect (95% CI)
Autrata 2003		-0.45 (-0.58, -0.32)
He 2004		-0.16 (-0.26, -0.06)
Lee 2001		-0.16 (-0.30, -0.02)
Combined		-0.25 (-0.44, -0.07)

Mean Difference

Favours LASEK   Favours PRK

Heterogeneity = 13.20 (I^2 = 84.8%)

7-6 Comparison for postoperative haze scores of all treatments derived from network
meta-analysis (removed Ghanem 2008)

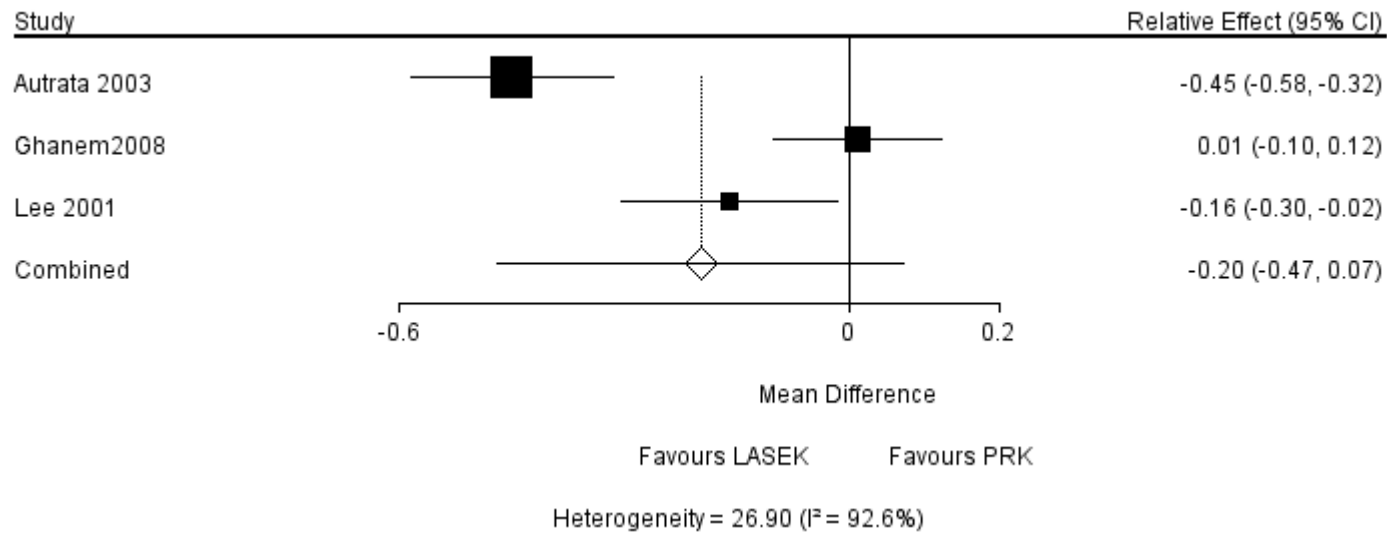|			
Epi-LASIK	0.08 (-0.44, 0.62)	0.33 (-0.28, 0.95)	0.09 (-0.66, 0.83)
-0.08 (-0.62, 0.44)	LASEK	0.25 (-0.06, 0.57)	0.01 (-0.52, 0.54)
-0.33 (-0.95, 0.28)	-0.25 (-0.57, 0.06)	PRK	-0.25 (-0.84, 0.38)
-0.09 (-0.83, 0.66)	-0.01 (-0.54, 0.52)	0.25 (-0.38, 0.84)	T-PRK

Mean difference (95% CrI)

7-7 Ranking probabilities of postoperative haze scores (removed
  Ghanem 2008)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.08	0.18	0.22	0.52
LASEK	0.01	0.33	0.49	0.17
PRK	0.76	0.18	0.05	0.01
T-PRK	0.14	0.31	0.25	0.29

7-8 SUCRA value of postoperative haze scores
  (removed Ghanem 2008)

Treatment	SUCRA value (%)
Epi-LASIK	27.3
LASEK	39.3
PRK	89.7
T-PRK	43.0

7-9 Direct comparison between PRK and LASEK for postoperative Haze scores (removed He 2004)

Study		Relative Effect (95% CI)
Autrata 2003		-0.45 (-0.58, -0.32)
Ghanem2008		0.01 (-0.10, 0.12)
Lee 2001		-0.16 (-0.30, -0.02)
Combined		-0.20 (-0.47, 0.07)

-0.6   0   0.2

Mean Difference

Favours LASEK   Favours PRK

Heterogeneity = 26.90 (I² = 92.6%)

7-10 Comparison for postoperative haze scores of all treatments derived from network meta-analysis (removed He 2004)

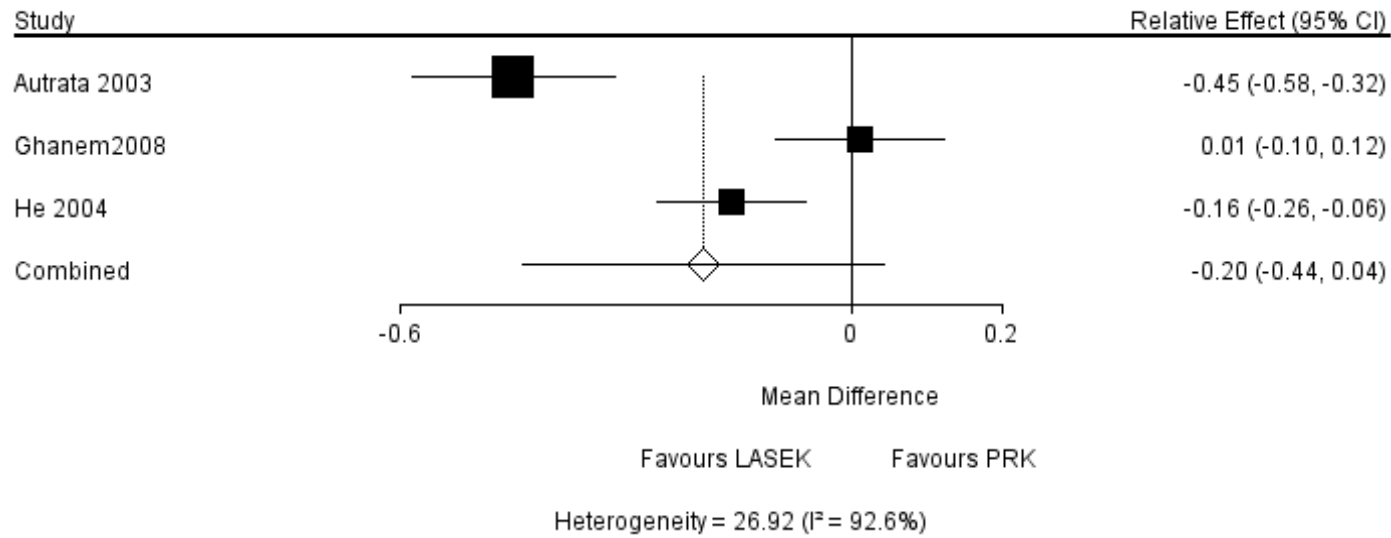| Epi-LASIK	0.08 (-0.53, 0.69)	0.28 (-0.41, 0.97)	0.09 (-0.76, 0.94)
-0.08 (-0.69, 0.53)	LASEK	0.20 (-0.14, 0.54)	0.01 (-0.60, 0.60)
-0.28 (-0.97, 0.41)	-0.20 (-0.54, 0.14)	PRK	-0.19 (-0.89, 0.50)
-0.09 (-0.94, 0.76)	-0.01 (-0.60, 0.60)	0.19 (-0.50, 0.89)	T-PRK

Mean difference (95% CrI)

7-11 Ranking probabilities of postoperative haze scores (removed
He 2004)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.13	0.17	0.21	0.49
LASEK	0.03	0.33	0.47	0.17
PRK	0.62	0.26	0.09	0.03
T-PRK	0.22	0.24	0.23	0.31

7-12 SUCRA value of postoperative haze
scores (removed He 2004)

Treatment	SUCRA value (%)
Epi-LASIK	31.3
LASEK	40.7
PRK	82.3
T-PRK	45.7

7-13 Direct comparison between PRK and LASEK for postoperative Haze scores (removed Le 2001)

Study		Relative Effect (95% CI)
Autrata 2003		-0.45 (-0.58, -0.32)
Ghanem2008		0.01 (-0.10, 0.12)
He 2004		-0.16 (-0.26, -0.06)
Combined		-0.20 (-0.44, 0.04)

-0.6   0   0.2

Mean Difference

Favours LASEK   Favours PRK

Heterogeneity = 26.92 (I² = 92.6%)

7-14 Comparison for postoperative haze scores of all treatments derived from network meta-analysis (removed Le 2001)

Epi-LASIK	0.08 (-0.50, 0.67)	0.28 (-0.40, 0.96)	0.09 (-0.74, 0.94)
-0.08 (-0.67, 0.50)	LASEK	0.20 (-0.15, 0.54)	0.01 (-0.59, 0.61)
-0.28 (-0.96, 0.40)	-0.20 (-0.54, 0.15)	PRK	-0.19 (-0.88, 0.51)
-0.09 (-0.94, 0.74)	-0.01 (-0.61, 0.59)	0.19 (-0.51, 0.88)	T-PRK

Mean difference (95% CrI)

7-15 Ranking probabilities of postoperative haze scores (removed
  Le 2001)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.13	0.17	0.21	0.49
LASEK	0.03	0.33	0.47	0.17
PRK	0.62	0.26	0.09	0.04
T-PRK	0.22	0.24	0.23	0.31

7-16 SUCRA value of postoperative haze
  scores (removed Le 2001)

Treatment	SUCRA value (%)
Epi-LASIK	31.3
LASEK	40.7
PRK	82.3
T-PRK	45.7

7-17 Comparison for postoperative pain scores on day 1 of all treatments derived
  from network meta-analysis (removed Wang 2014)

Epi-LASIK	-0.25 (-2.57, 2.01)	-0.03 (-2.12, 2.03)	-1.25 (-3.68, 1.12)
0.25 (-2.01, 2.57)	LASEK	0.23 (-0.78, 1.25)	-0.99 (-2.62, 0.67)
0.03 (-2.03, 2.12)	-0.23 (-1.25, 0.78)	PRK	-1.23 (-2.54, 0.10)
1.25 (-1.12, 3.68)	0.99 (-0.67, 2.62)	1.23 (-0.10, 2.54)	T-PRK

Mean difference (95% CrI)

7-18 Ranking probabilities of postoperative pain scores on day 1
  (removed Wang 2014)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.48	0.14	0.27	0.12
LASEK	0.18	0.33	0.43	0.06
PRK	0.33	0.50	0.16	0.01
T-PRK	0.01	0.03	0.14	0.82

7-19 SUCRA value of postoperative pain scores
  on day 1 (removed Wang 2014)

Treatment	SUCRA value (%)
Epi-LASIK	66.3
LASEK	54.3
PRK	71.7
T-PRK	7.7

7-20 Comparison for postoperative pain scores on day 1 of all treatments derived
  from network meta-analysis (removed Celik 2014)

Epi-LASIK	-0.27 (-2.58, 2.02)	-0.03 (-2.14, 1.99)	0.98 (-1.81, 3.63)
0.27 (-2.02, 2.58)	LASEK	0.23 (-0.77, 1.24)	1.24 (-0.23, 2.73)
0.03 (-1.99, 2.14)	-0.23 (-1.24, 0.77)	PRK	1.03 (-0.77, 2.80)
-0.98 (-3.63, 1.81)	-1.24 (-2.73, 0.23)	-1.03 (-2.80, 0.77)	T-PRK

Mean difference (95% CrI)

7-21 Ranking probabilities of postoperative pain scores on day 1
  (removed Celik 2014)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.20	0.29	0.14	0.37
LASEK	0.01	0.19	0.34	0.46
PRK	0.05	0.35	0.46	0.15
T-PRK	0.74	0.18	0.06	0.02

7-22 SUCRA value of postoperative pain scores
  on day 1 (removed Celik 2014)

Treatment	SUCRA value (%)
Epi-LASIK	44.0
LASEK	25.0
PRK	43.7
T-PRK	88,0

7-23 Comparison for postoperative pain scores on day 1 of all treatments derived
  from network meta-analysis (removed Pirouzian 2004)

Epi-LASIK	-0.92 (-3.64, 1.91)	-0.06 (-2.52, 2.39)	-0.62 (-3.45, 2.29)
0.92 (-1.91, 3.64)	LASEK	0.86 (-0.52, 2.13)	0.29 (-1.22, 1.83)
0.06 (-2.39, 2.52)	-0.86 (-2.13, 0.52)	PRK	-0.57 (-1.99, 0.98)
0.62 (-2.29, 3.45)	-0.29 (-1.83, 1.22)	0.57 (-0.98, 1.99)	T-PRK

Mean difference (95% CrI)

7-24 Ranking probabilities of postoperative pain scores on day 1
  (removed Pirouzian 2004)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.48	0.17	0.13	0.21
LASEK	0.04	0.12	0.34	0.50
PRK	0.35	0.48	0.14	0.03
T-PRK	0.12	0.22	0.40	0.26

7-25 SUCRA value of postoperative pain scores
  on day 1 (removed Pirouzian 2004)

Treatment	SUCRA value (%)
Epi-LASIK	63.7
LASEK	23.3
PRK	71.7
T-PRK	40.0

7-26 Comparison for postoperative pain scores on day 1 of all treatments derived
  from network meta-analysis (removed Saleh 2003)

Epi-LASIK	-0.79 (-3.57, 1.99)	-0.04 (-2.48, 2.39)	-0.53 (-3.33, 2.35)
0.79 (-1.99, 3.57)	LASEK	0.75 (-0.65, 2.00)	0.25 (-1.29, 1.81)
0.04 (-2.39, 2.48)	-0.75 (-2.00, 0.65)	PRK	-0.51 (-1.91, 1.10)
0.53 (-2.35, 3.33)	-0.25 (-1.81, 1.29)	0.51 (-1.10, 1.91)	T-PRK

Mean difference (95% CrI)

7-27 Ranking probabilities of postoperative pain scores on day 1
  (removed Saleh 2003)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.47	0.17	0.13	0.23
LASEK	0.05	0.14	0.33	0.47
PRK	0.34	0.47	0.16	0.03
T-PRK	0.14	0.22	0.37	0.26

7-28 SUCRA value of postoperative pain scores
  on day 1 (removed Saleh 2003)

Treatment	SUCRA value (%)
Epi-LASIK	62.7
LASEK	25.3
PRK	70.7
T-PRK	41.0

7-29 Comparison for postoperative pain scores on day 1 of all treatments derived
  from network meta-analysis (removed Sia 2004)

Epi-LASIK	-1.24 (-3.72, 1.76)	-0.10 (-2.40, 2.30)	-0.85 (-3.33, 2.17)
1.24 (-1.76, 3.72)	LASEK	1.13 (-0.50, 2.41)	0.47 (-1.09, 1.87)
0.10 (-2.30, 2.40)	-1.13 (-2.41, 0.50)	PRK	-0.75 (-1.96, 0.90)
0.85 (-2.17, 3.33)	-0.47 (-1.87, 1.09)	0.75 (-0.90, 1.96)	T-PRK

Mean difference (95% CrI)

7-30 Ranking probabilities of postoperative pain scores on day 1
(removed Sia 2004)

Drug	Rank 1	Rank 2	Rank 3	Rank 4
Epi-LASIK	0.53	0.19	0.12	0.17
LASEK	0.03	0.09	0.27	0.61
PRK	0.34	0.53	0.10	0.02
T-PRK	0.10	0.20	0.51	0.20

7-31 SUCRA value of postoperative pain scores
on day 1 (removed Sia 2004)

Treatment	SUCRA value (%)
Epi-LASIK	69.7
LASEK	18.0
PRK	72.7
T-PRK	40.3

Table H

Comparison-Adjusted Funnel Plots

8-1 Funnel plot to confirm the risk of publications bias for the ten included studies which reported postoperative efficacy
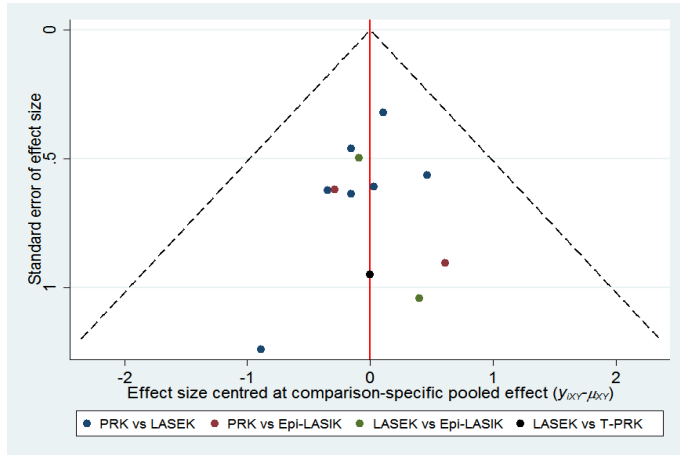
8-2 Funnel plot to confirm the risk of publications bias for the eight included studies which reported postoperative predictability
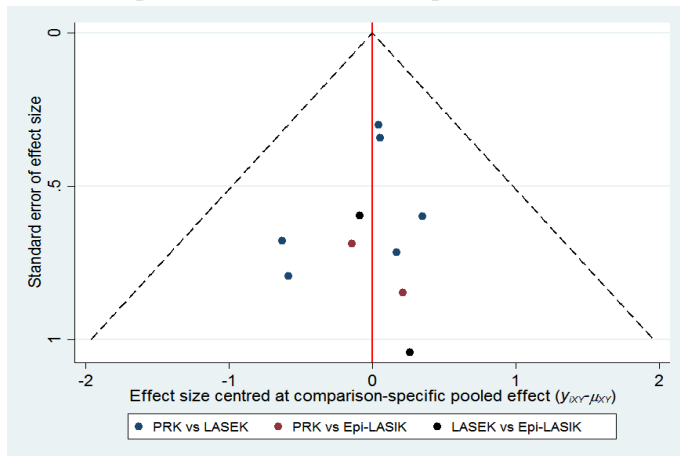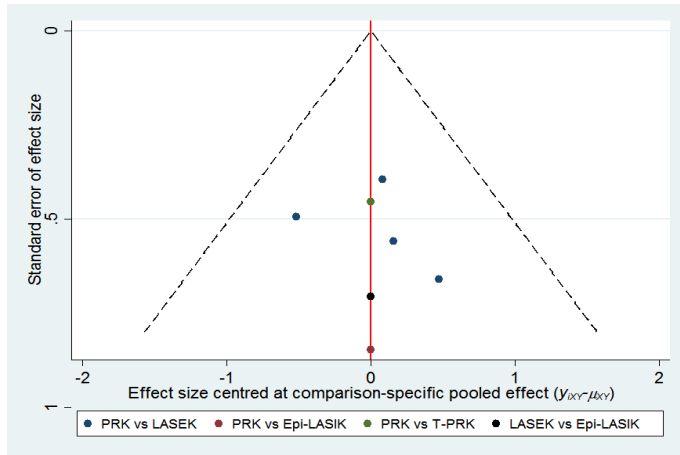
8-3 Funnel plot to confirm the risk of publications bias for the six included studies which reported postoperative safety
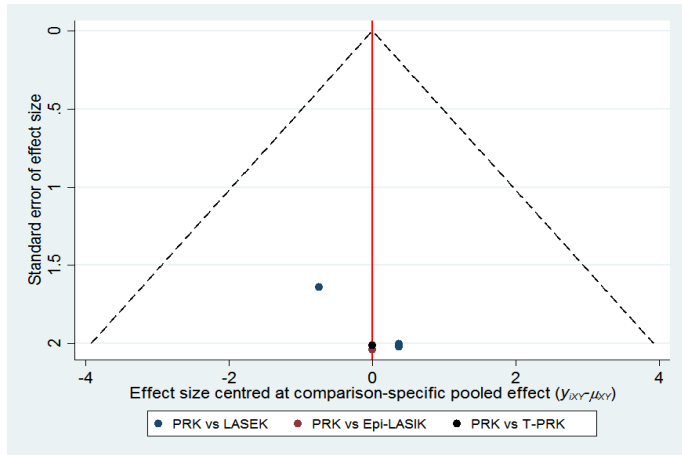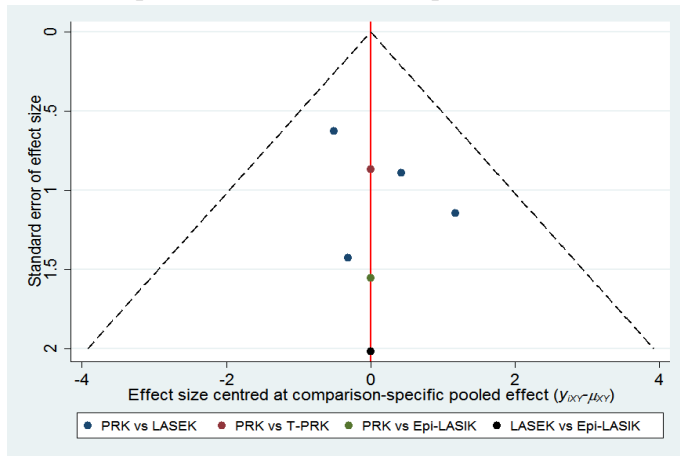

8-4 Funnel plot to confirm the risk of publications bias for the six included studies which reported postoperative haze scores
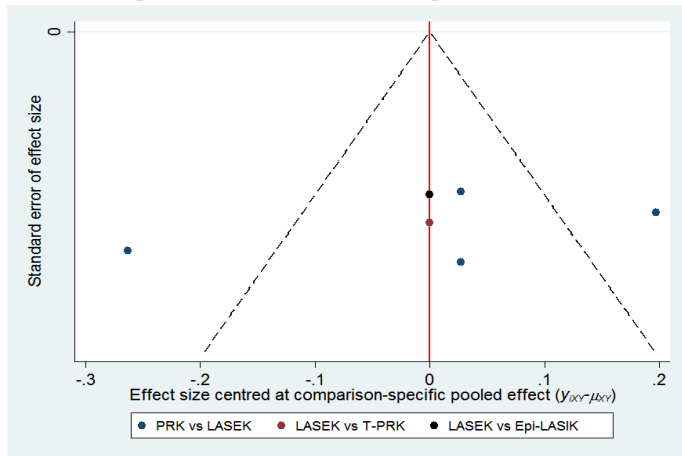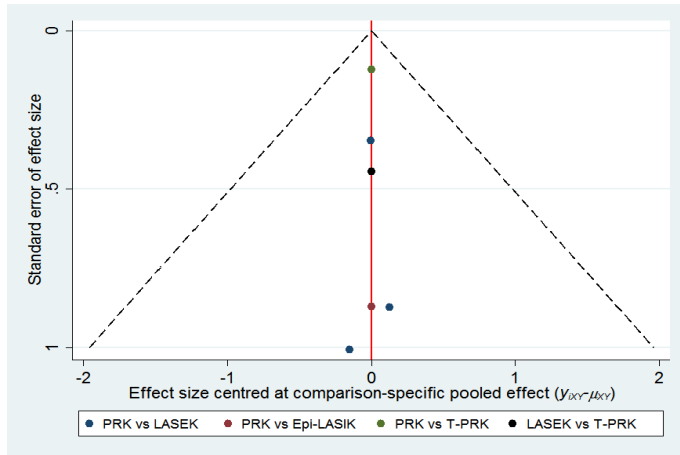
8-5 Funnel plot to confirm the risk of publications bias for the seven included studies which reported postoperative haze grade 0.5 or higher
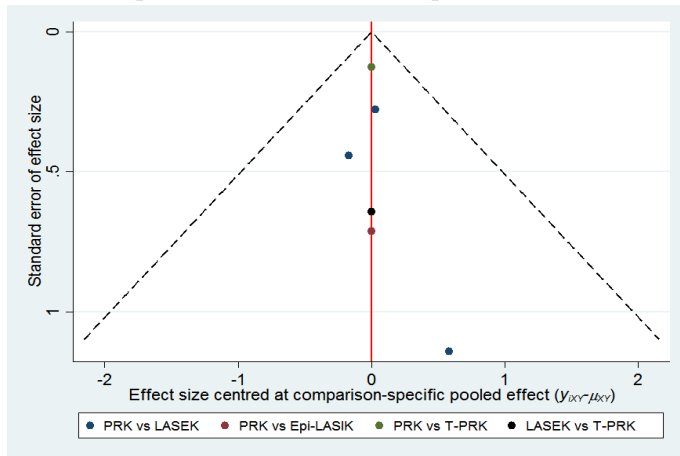

8-6 Funnel plot to confirm the risk of publications bias for the seven included studies which reported postoperative haze grade 1.0 or higher

8-7 Funnel plot to confirm the risk of publications bias for the six included studies which reported postoperative pain scores at day 1

8-8 Funnel plot to confirm the risk of publications bias for the six included studies which reported postoperative pain scores at day 3

8-9 Funnel plot to confirm the risk of publications bias for the twelve included studies which reported postoperative epithelial healing time