Efficacy, predictability, safety, haze and comfort of corneal surface ablation laser refractive surgery: A systematic review and network meta-analysis

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ABSTRACT

OBJECTIVE: To systematically compare the efficacy, predictability, safety, post-operative haze, pain scores and epithelial healing time of four corneal surface ablation procedures (PRK, T-PRK, LASEK and Epi-LASIK) and to provide evidence-based rankings of these treatments.

DESIGN: Systematic review and network meta-analysis.

DATA SOURCES: PubMed, Embase, The Cochrane Library and the US trial registry (until September 2016).

ELIGIBILITY CRITERIA: Databases were searched without language restrictions for randomized controlled trials of comparisons between two or more of the included procedures. Studies using mitomycin C (MMC) during surgery or with less than 3 months of follow-up after randomization were excluded.

OUTCOME MEASURES: The primary outcomes in this study were efficacy, predictability and safety. Haze, pain scores and epithelial healing time were analyzed as secondary outcomes.

RESULTS: A total of 18 studies involving 1423 eyes were included. There were no statistically significant differences in efficacy, predictability, safety, haze, pain scores on day 1 and epithelial healing time between any pair of treatments analyzed. Epi-LASIK had statistically significantly higher pain scores on day 3 when compared

with PRK (weighted mean differences [WMD] 2.17, 95% credible intervals [CrI] 0.19-4.01) and T-PRK (WMD 2.69, 95% CrI 0.51-4.84). The SUCRA (Surface under the Cumulative RAnking curve) ranking results (from best to worst) showed that LASEK ranked highest in terms of efficacy, predictability, safety and pain scores on day 1 (SUCRA values were 75.0%, 72.0%, 44.3% and 26.0% respectively). Epi-LASIK ranked best for haze scores at grade 1 (SUCRA values 30.3% and 21.7% respectively). T-PRK ranked best for haze scores at grade 0.5 or higher, pain scores on day 3 and epithelial healing time (SUCRA values are 19.3%, 6.3%, 3.3% respectively).

CONCLUSIONS: This network meta-analysis demonstrates that all the surface laser refractive surgeries are comparable in terms of efficacy, predictability, safety, post-operative haze and comfort with the exception of pain scores on day 3. Epi-LASIK was significantly more painful when compared with PRK and T-PRK on post-operative day 3.

INTRODUCTION

Uncorrected refractive error, particularly myopia, is the leading cause of visual impairment throughout the world.[1-3] Laser corneal refractive surgery is an effective alternative to optical correction of refractive errors with glasses or contact lenses, particularly for myopia. A range of surgical techniques have been developed that change refraction by reshaping the cornea through the photoablative removal of corneal tissue. Photorefractive keratectomy (PRK) was the first corneal refractive surgical technique using the excimer laser and was introduced more than 25 years ago.[4, 5]

During the intervening years, traditional PRK declined in popularity with the introduction of intra-stromal ablative techniques such as LASIK,[6, 7] which addressed the principle limitations of PRK: post-operative pain, delayed epithelial healing, and post-operative stromal haze. PRK does, however, retain certain advantages over LASIK such as inflicting less corneal biomechanical insult and avoiding both intraoperative and late flap-related complications.[8] Several other surface ablation procedures have been developed, all of which can be considered derivations of PRK, most notably transepithelial photo-refractive keratectomy (T-PRK), laser epithelial keratomileusis (LASEK)[9] and epipolis laser in situ keratomileusis (Epi-LASIK).[10, 11] These alternative surface ablation approaches have evolved to avoid the shortcomings of PRK while retaining its biomechanical advantages.[12, 13]

A key component of the surface ablative techniques is the method of epithelial

removal. Alcohol or mechanical debridement may be used or the preservation of the epithelium as a flap. Another alternative is T-PRK, where epithelial removal is performed using laser phototherapeutic (PTK) ablation followed by a stromal laser refractive ablation. This has several advantages, including no instrument contact with the cornea, reduced intervention time, and the potential to minimize the size of an epithelial defect required for stromal ablation, as well as the avoidance of alcohol and, thus, potential toxicity.[14] Although these new technologies have offered apparent improvements over traditional PRK with alcohol, they each have different advantages and disadvantages. What is currently lacking is a comprehensive evidence based approached to determine the relative merits of each procedure.

The speed with which refractive surgery techniques have evolved has created several challenges, in particular, the evidence comparing specific procedures is often lacking. Several conventional pair wise meta-analyses of four refractive surgery techniques above have been published,[15-18] but these publications share several limitations. Firstly, they are unable to provide clear hierarchies for all available treatments due to a lack of head to head comparisons. Secondly, some previous analyses included some non-randomized controlled trials that might influence the quality of evidence. 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.[19] This technique is therefore particularly suitable to address questions relating to the relative safety and benefits of different corneal surface ablation techniques. We performed this network

meta-analysis of available randomized controlled trials (RCTs) to systematically compare the efficacy, predictability, safety and post-operative haze, pain scores and epithelial healing time of the four major forms of surface ablative procedures and to provide evidence-based rankings of these treatments.

METHODS

This systematic review complies with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) network meta-analysis extension statement.[20]

Outcome Measurements

Efficacy (uncorrected visual acuity (UCVA) of 20/20 or better), predictability (refractive spherical equivalent [SE] within ±0.50 D of the target) and safety (losing two or more lines of best spectacle corrected visual acuity [BSCVA]) were set as primary outcome measures. Haze, pain scores and epithelial healing time were set as secondary outcome measures. Pain data was assessed using a 10-point scale at day 1 and day 3 post-operatively. 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 post-operatively. 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, Epi-LASIK (see ***Table* 1** for the full name of these surgical abbreviations); (3) comparisons: two or more laser corneal surface ablation techniques (as listed above); (4) at least one of the following outcomes: efficacy, safety, predictability, post-operative haze, pain and epithelial healing time; and (5) study design: randomized controlled trial. We excluded trials if they contained only one or none 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..

Search Methods

A systematic literature review was conducted using PubMed, Embase, The Cochrane Library and the US trial registry (www.ClinicalTrial.gov) for RCTs published up to September 2016 without language restrictions. The full search strategies are shown in appendix 1. 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 (YYH, BHS). They retrieved the full-text articles that appeared relevant after reviewing the titles and abstracts. They independently assessed full-text articles for final eligibility. Any

discrepancies were resolved by focused discussion or consultation with an additional investigator (RXT).

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.[21] 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), blinding of participants and personnel (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other biases.

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 (OR) with 95% confidence intervals (CI). For continuous outcomes, relative effect sizes were calculated as weighted mean differences (WMD) with 95% CI. For positive outcomes (i.e. efficacy and predictability where a greater value

indicates a better result), OR >1 or WMD >0 correspond to beneficial treatment effects of the first treatment compared with the second treatment. When the outcomes are negative (i.e. safety, haze, pain, epithelial healing time, where a greater value indicates a worse result), OR <1 or WMD <0 correspond 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[22] (values of 50% or more indicate substantial heterogeneity) to investigate the possibility of statistical heterogeneity. We used STATA 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[23] to estimate pooled ORs and WMD with 95% credible intervals (CrI). We used four parallel chains and obtained 50000 samples after a 20000-sample burn-in in each chain. To check convergence, we used the Gelman and Rubin diagnostic[24] and trace plots. We ranked treatments based on the analysis of ranking probabilities and the Surface Under the Cumulative RAnking curve (SUCRA)[25]. The SUCRA values, expressed as a percentage, show the relative probability of an intervention being the best option. Inconsistency between direct and indirect evidence was assessed by a "node-splitting" approach.[26] Further sensitivity analyses were undertaken by removal of trials that caused high heterogeneity in direct comparisons or appeared to introduce statistical inconsistency in the network meta-analyses.

RESULTS

Study Selection

***Figure* 1** shows the detailed steps of the study selection process. The literature search yielded 514 potentially relevant studies (detailed search strategy is shown in ***Appendix* I**). Of these, 33 potentially eligible studies were retrieved from the electronic databases and 4 additional studies were located from the references of selected studies, making a total of 37. After excluding 19 studies on the basis of the pre-defined 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 Appendix 2. Included trials were published between 2001 and 2015. A total of 1423 eyes which underwent one of the four different interventions were evaluated; 618 eyes were in the PRK group, 616 eyes in the LASEK group, 117 eyes in the Epi-LASIK group, and 72 eyes in the T-PRK group (***Figure* 2**). Almost all trials had two treatment arms with the exception of O'Doherty 2007[27] 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 Latin America (all from Brazil).

Quality of Trials

The quality of the studies included in the Network Meta-Analysis (NMA) is shown in Appendix **3**. In relation to the complete outcome data, almost one quarter of trials were rated as "high risk of bias" (4 trials, 22.2%), but the majority of trials were rated at "low risk of bias", because they reported the masking of participants and personnel (10 trials, 55.6%), used appropriate randomization techniques (10, 55.6%) and did not selectively report outcomes (11 trials, 61.1%). Those rated as "unclear risk of bias" were trials that reported allocation concealment and masking of outcome assessment (14 and 12, respectively).

Results of meta-analysis

Direct comparisons

***Table* 2** shows the results of efficacy, predictability and safety based on direct comparisons. Twelve articles reported the percentage of eyes with UCVA of 20/20 or better post-operatively (defined as efficacy). The results show that there was no statistically significant difference as well as high heterogeneity for all comparisons. Predictability was measured by the proportion of eyes where the post-operative refractive error was within ±0.5 D of the target refraction. We found that 10 studies had sufficient data for this analysis. Statistical analyses of these data found no statistically significant effect. The proportion of eyes losing 2 or more lines of BSCVA was used as a measure of safety. This parameter was reported in 7 studies. The results show that there was no statistically significant difference as well as high heterogeneity for all comparisons.

Similarly, ***Tables* 3** and **4** show the results of post-operative haze, pain scores and epithelial healing time based on direct comparisons. Six trials reported haze scores. We found one statistically significant difference between LASEK vs PRK (WMD -0.19, 95% CI -0.37 to -0.01), while high heterogeneity was observed between LASEK vs PRK with I^2 = 88.9% (forest plots in Appendix IV). We also analyzed the data at two different grades (grade 0.5 or higher and grade 1.0 or higher) in 7 trials, for both grades, no statistically significant difference was found and high heterogeneity was found.

Six studies reported post-operative pain scores. We analyzed the post-operative pain scores at day 1 and day 3. Statistically significant differences were found between PRK vs T-PRK at day 1 (WMD 1.24, 95% CI 1.00 to 1.48), LASEK vs T-PRK at day 1 (WMD -1.23, 95% CI -2.10 to -0.36), PRK vs Epi-LASIK at day 3 (WMD -2.16, 95% CI -3.55 to -0.77), and PRK vs T-PRK at day 3 (WMD -0.48, 95% CI -0.23 to -0.73). There was no high heterogeneity for all comparisons.

Fourteen 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 vs Epi-LASIK (I^2 = 91.4%), PRK vs LASEK (I^2 = 97.1%), LASEK vs Epi-LASIK (I^2 = 76.6%) (forest plots in Appendix 4).

Combination of direct and indirect comparisons

***Figure* 3** shows the results of efficacy, predictability and safety based on Bayesian

network meta-analyses that combines direct and indirect comparisons. The ranking probabilities for all procedures are presented in Appendix 5, along with the ranking probabilities of other results. For the primary outcomes, there were no statistically significant difference in efficacy, safety and predictability. As for the ranking results, the efficacy ordered from the best to worst on the SUCRA values (***Figure* 6**) were as follows: LASEK (75.0%), PRK (50.7%), Epi-LASIK (38.0%), T-PRK (36.0%). The predictability ordered from the best to worst on the SUCRA values (***Figure* 7**) were as follows: LASEK (72.0%), Epi-LASIK (44.0%), PRK (34.0%). The safety ordered from the best to worst (safe to unsafe) on the SUCRA values (***Figure* 8**) were as follows: LASEK (44.3%), Epi-LASIK (47.0%), T-PRK (50.3%), PRK (58.7%).

The results for post-operative haze based on Bayesian network meta-analyses is shown in ***Figure 4***. There was no statistically significant difference between any of the studied techniques. The haze scores were ranked from the best (least haze) to worst (most haze) depending on the SUCRA values (***Figure* 9**) as follows: Epi-LASIK (30.3%), LASEK (39.7%), T-PRK (46.3%), PRK (84.7%). The haze scores at grade 0.5 or higher, were ranked from best to worst (***Figure* 10**) as follows: T-PRK (19.3%), Epi-LASIK (38.0%), PRK (66.0%), LASEK (76.7%). The haze scores at grade 1.0 or higher, were ranked from best to worst (***Figure* 11**) as follows: Epi-LASIK (21.7%), T-PRK (27.7%), PRK (67.7%), LASEK (82.3%).

The results for pain scores and epithelial healing time can be seen in ***Figure 5.*** As shown, there are statistically significant differences when Epi-LASIK is compared

with PRK (WMD 2.17, 95% CrI 0.19-4.01) and T-PRK (WMD 2.69, 95% CrI 0.51-4.84) in terms of pain scores on day 3. For pain on the first day, the rank from best result to worst (***Figure* 12**) is as follows: LASEK (26.0%), T-PRK (40.0%), Epi-LASIK (62.3%), PRK (71.0%). For pain on the third day, the rank from best result to worst (***Figure* 13**) is: T-PRK (6.3%), PRK (43.3%), LASEK (53.3%), Epi-LASIK (97.7%). The rank of the epithelial healing time from best to worst (***Figure* 14**) is: T-PRK (3.3%), LASEK (62.3%), PRK (63.7%), Epi-LASIK (71.3%), more closely matching the rank for pain on day 3, than pain on day 1.

Inconsistency

Node-splitting analysis between LASEK, PRK and T-PRK for close-loop comparisons in terms of pain score on day 1 shows significant inconsistency (p=0.05). However, for other results comparisons between direct and indirect estimates did not suggest significant inconsistency between direct and indirect evidence (Appendix 6, p-value varying from 0.22 to 0.99).

Sensitivity Analysis

As mentioned above, we found some high heterogeneity and inconsistency for certain comparisons, so we performed a sensitivity analysis by removing trials that contributed the highest heterogeneity in direct comparisons or introduced statistical inconsistency in network meta-analyses. For the post-operative haze scores in direct comparison of PRK vs LASEK, Autrata (2003)[28] was removed as it was identified as

the main source of heterogeneity. This changed the rank and SUCRA values as follows: Epi-LASIK (17.7%), LASEK (43.7%), T-PRK (50.7%), PRK (88.3%). When Wang 2014[29] (LASEK vs T-PRK for post-operative pain scores on day 1) was removed from the analysis of pain scores at day 1 (on account of contributing significant inconsistency in close-loop comparisons), the rank and SUCRA value changed to T-PRK (7.7%), LASEK (54.3%), Epi-LASIK (66.3%), PRK (71.7%).

For direct comparisons, high heterogeneity is apparent for epithelial healing time. This heterogeneity remains even after removing the two largest contributors, which prevents any meaningful sensitivity analysis for this outcome. This variability also points to the need for cautious interpretation of the data on epithelial healing time.

DISCUSSION

This study provides an in-depth statistical comparison of the major laser corneal surface ablation refractive procedures for correcting myopia, combining data from 18 trials and 1423 eyes. It also considers a wide range of clinically relevant outcomes including post-operative 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.

The main conclusion of this analysis is the confirmation[30] that all the surface laser refractive technologies included in this analysis have excellent efficacy, predictability

and safety, at least in the short term. For many of the outcomes analyzed no statistically significant differences were found, i.e. in relation to efficacy, predictability, safety, post-operative haze, pain score on day 1 and epithelial healing time. However, in terms of pain score on day 3, Epi-LASIK was significantly more painful when compared with PRK and T-PRK.

As well as determining the statistical differences of specific outcomes between procedures, our analysis (using SUCRA) provides a numerical ranking of all the procedures for each outcome (as shown in Figures 6-14). LASEK demonstrates relative advantages in three visual outcomes (efficacy, predictability and safety) compared with the other techniques assessed, but results in greater post-operative corneal haze. Epi-LASIK demonstrates better haze scores while performing less well in relation to post-operative comfort (pain score and epithelial healing time). T-PRK tops the rankings in relation to post-operative haze grade 0.5 or higher, pain scores and epithelial healing time. Notably, traditional PRK fails to achieve top ranking in any of the studied outcomes. The SUCRA values showed the relative probability of an intervention being the best option. This provides an estimate of the relative dominance of the treatment in the absence of significant differences in statistical analysis.

Efficacy, predictability and safety are perhaps the most important outcomes in evaluations of corneal refractive surgery.[31, 32] 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.[15] 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 0.61-1.20) or predictability (OR 0.90, 95% CI 0.63-1.29). Wu et al.[16] compared Epi-LASIK and PRK in relation to efficacy and predictability, reporting no statistically significant differences in either efficacy (RR 1.43, 95% CI 0.85-2.40) or predictability (RR 1.03, 95% CI 0.92-1.16). These findings are similar to our research results, but we also found no statistical significant difference in safety when PRK is compared with either Epi-LASIK or LASEK. Furthermore, we found that LASEK demonstrates relative advantages in these three outcomes in terms of ranking and that PRK ranks lowest for both predictability and safety. Lee et al.[33] proposed that the remaining epithelial flap in LASEK acts as a smooth refractive surface and enables better initial visual acuity when LASEK is compared with PRK. When comparing visual outcomes between LASEK and Epi-LASIK, subclinical scarring or induced irregularity in Bowman's layer from superficial stromal cuts in Epi-LASIK may directly affect the visual quality.[34] Comparisons of Epi-LASIK and T-PRK in relation to predictability are limited by a lack of data, and future trials may provide more solid evidence in this regard.

Post-operative haze formation is an important factor that may directly influence the efficacy, safety and visual quality of corneal refractive surgery. Zhao et al.[15] contrasted LASEK and PRK in terms of corneal haze, reporting that LASEK-treated eyes showed less corneal haze at one month after surgery (WMD 0.25, 95% CI

0.10-0.39) and three months after surgery (WMD 0.14, 95% CI 0.01-0.26) compared with PRK but no statistically significant difference was observed between the two groups at six months after surgery (WMD 0.14, 95% CI -0.02-0.30). In our results, there is also no statistical difference between LASEK and PRK at six months. We found that Epi-LASIK and T-PRK performed best on SUCRA ranking in terms of haze. Epi-LASIK ranked best for any haze and also for haze scores greater than 1 whereas T-PRK ranked best for haze scores greater than 0.5. This may be associated with the release of TGF-1. Baldwin et al.[35] found cytokines and growth factors such as TGF-1 are released into the tear film by the lacrimal gland after corneal epithelial injury. Further, Long et al.[36] found tear fluid TGF-1 levels were less following Epi-LASIK than after LASEK. TGF-1 levels correlated positively with the degree of haze, which was lower after Epi-LASIK compared to LASEK.

Post-operative pain and epithelial healing time are two important factors that influence patient preference for a specific procedure. In 2002, Litwork et al.[37] 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 SUCRA ranking showed that PRK was more likely to cause pain than LASEK 1 day post-operatively, which may be due to the exposure of sensitive nerve endings in the cornea following PRK, which is avoided in LASEK. It may also be the result of the release in chemical factors such as prostaglandin, histamine, and substance P by corneal tissue.[38] Our study also found that Epi-LASIK showed more pronounced pain compared to PRK and T-PRK at day 3 post-operatively.

In relation to epithelial healing time, our statistical results indicate that there is too high heterogeneity to draw reliable conclusions. Furthermore, post-operative topical drug regimes and the use of corneal contact lenses may influence post-operative epithelial healing time. In the present study, T-PRK achieves the highest ranking in terms of post-operative pain. This may be due to the precise, smooth, and regular epithelial ablation and lack of epithelial islands on the stromal bed.

In terms of study limitations, like any traditional meta-analysis, the results are restricted by the differences between the included trials. These differences include: the race of study population, patient age, dioptric correction, choice of laser device including the year of manufacture and different post-operative medications. These factors may certainly have potential impacts on our results, but we found that the heterogeneity and inconsistency of studies to be low except in relation to epithelial healing time. Furthermore, the sensitivity analyses, whereby we removed studies with high heterogeneity or inconsistencies, this did not significantly alter the results. Also, these findings are only applicable to myopia as hyperopic treatments were not included and also studies using MMC were excluded.

We chose six months post-surgery as the time point to analyze outcomes. This choice was driven by the availability of data from the various trials but does mean that we cannot evaluate the long-term stability of the outcomes. However, most long-term follow-up studies have shown that the operative results tend to stabilize by six months.[39-41] Although a range of outcomes were assessed in this study, outcomes such

as higher-order aberrations (HOAs), contrast sensitivity (CS) and patient reported outcomes such as subjective quality of vision (QoV) were not included due to a lack of data in the form of RCTs. This meta-analysis was also designed to compare techniques that differed in surgical design, rather than in relation to excimer laser ablation profile.

In conclusion, this network meta-analysis demonstrates that all the surface laser refractive surgeries are comparable in efficacy, predictability safety, post-operative haze and comfort with the exception of pain score on day 3. Epi-LASIK was significantly more painful when compared with PRK and T-PRK on post-operative day 3.

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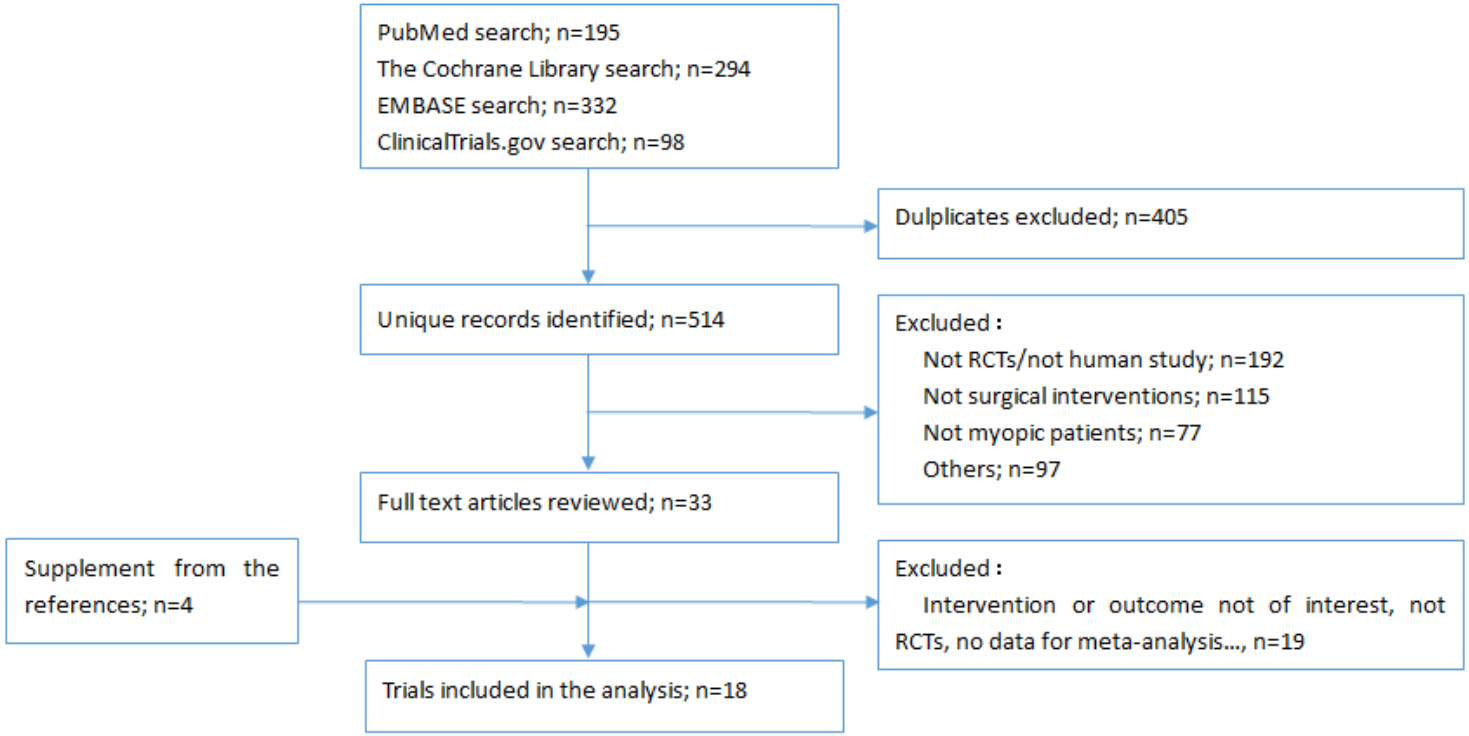


Figure 1: Study selection process

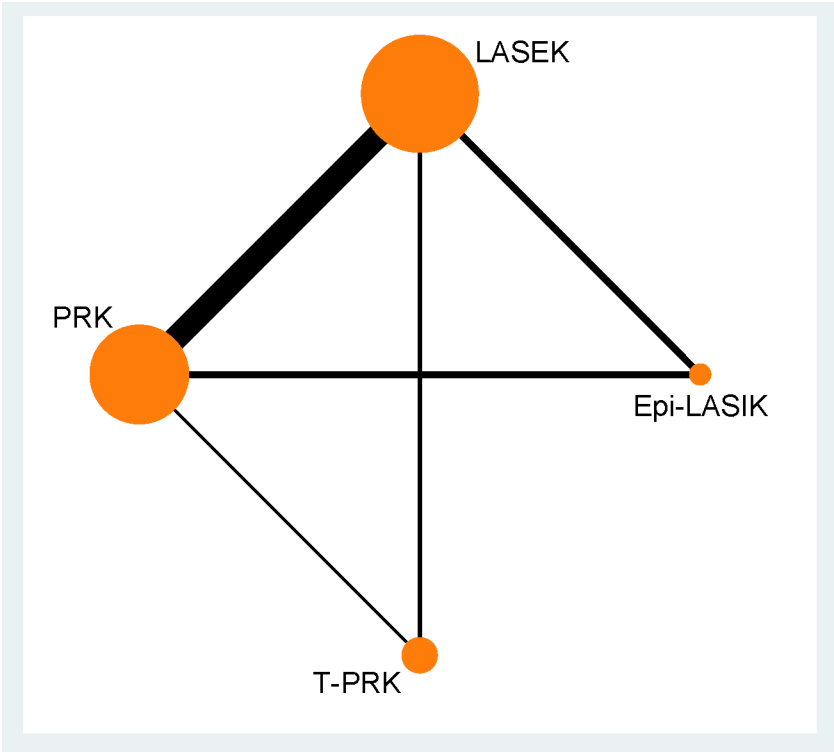


Figure 2: Network of direct comparisons for corneal surface ablation surgeries for myopia. Each node represents 1 treatment. The size of the node is proportional to the number of participants randomized to that treatment. The edges represent direct comparisons, and the width of the edge is proportional to the number of trials.

Epi-LASIK			
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 ratios (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 refraction); S = Safety (Losing two or more lines of BSCVA); NA = Not available.

Figure 3: Summary comparison for postoperative efficacy, predictability and safety of all treatments derived from the network meta-analysis.

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**

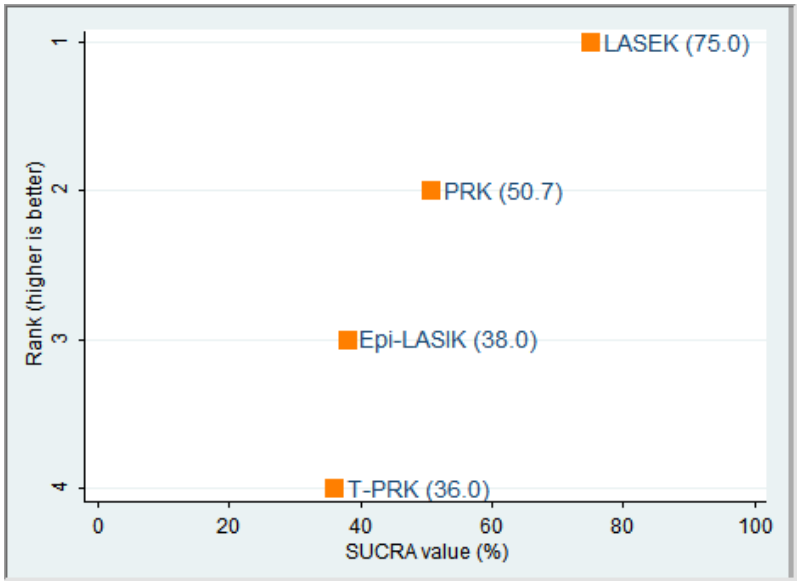
Odds ratio (95% CrI) and mean difference (95% CrI) are calculated by column; HS = Haze scores; H0.5 = Haze grade 0.5 or higher; H1 = Haze grade 1.0 or higher.

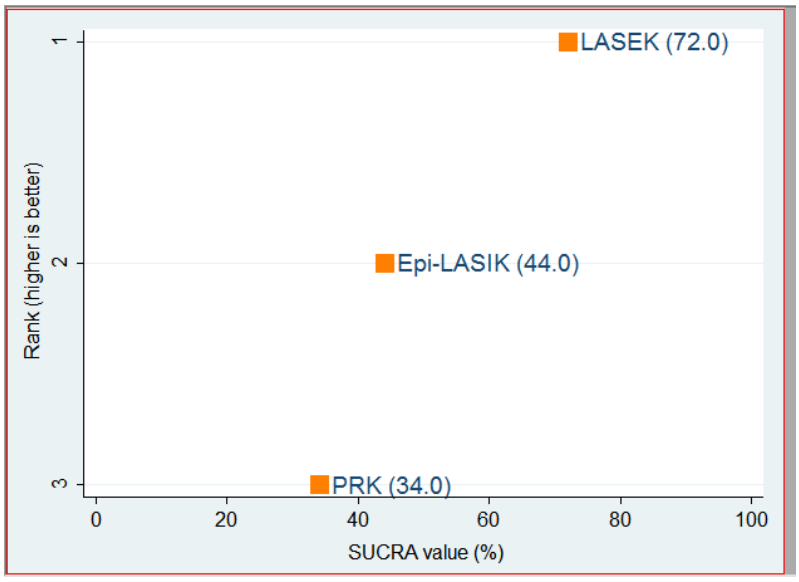
Figure 4: Summary comparisons for postoperative haze of all treatments derived from the network meta-analysis.

Epi-LASIK			
PS1: 0.75 (-2.00, 3.41) PS3: 2.03 (-0.16, 4.03) EH: 0.09 (-0.76, 0.96)	**LASEK**		
PS1: 0.06 (-2.43, 2.49) PS3: <u>2.17 (0.19, 4.01)</u> EH: 0.08 (-0.81, 0.99)	PS1: -0.69 (-1.79, 0.50) PS3: 0.12 (-0.69, 1.04) EH: -0.01 (-0.56, 0.56)	**PRK**	
PS1: 0.54 (-2.34, 3.27) PS3: <u>2.69 (0.51, 4.84)</u> EH: 1.65 (-0.21, 3.46)	PS1: -0.20 (-1.69, 1.22) PS3: 0.64 (-0.39, 1.88) EH: 1.56 (-0.14, 3.23)	PS1: 0.49 (-0.99, 1.82) PS3: 0.51 (-0.51, 1.67) EH: 1.57 (-0.04, 3.15)	**T-PRK**

Mean differences (95% CrI) are calculated by column; PS1 = pain scores on day 1; PS3 = pain scores on day 3; EH = epithelial healing time. The underlined data indicate a statistically significant effect ($p < 0.05$).

Figure 5: Summary comparison for post-operative pain scores and epithelial healing time of all treatments derived from the network meta-analysis.





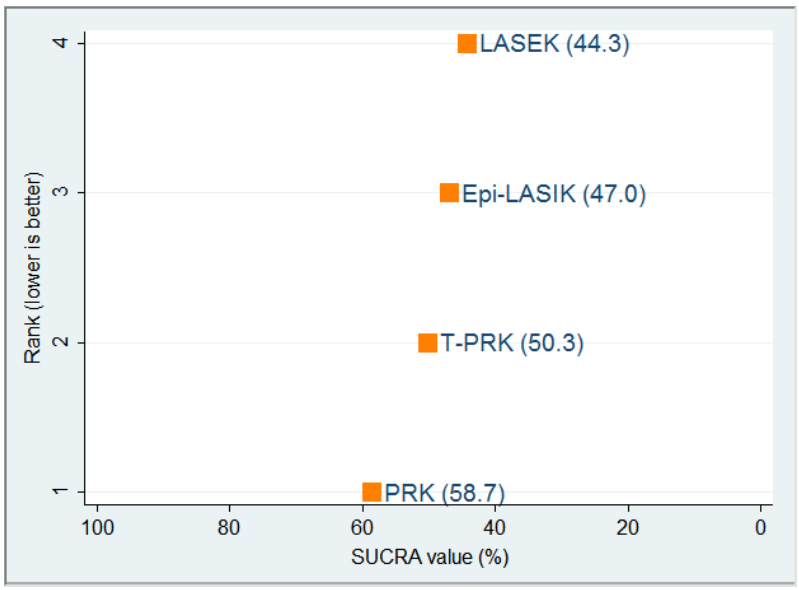
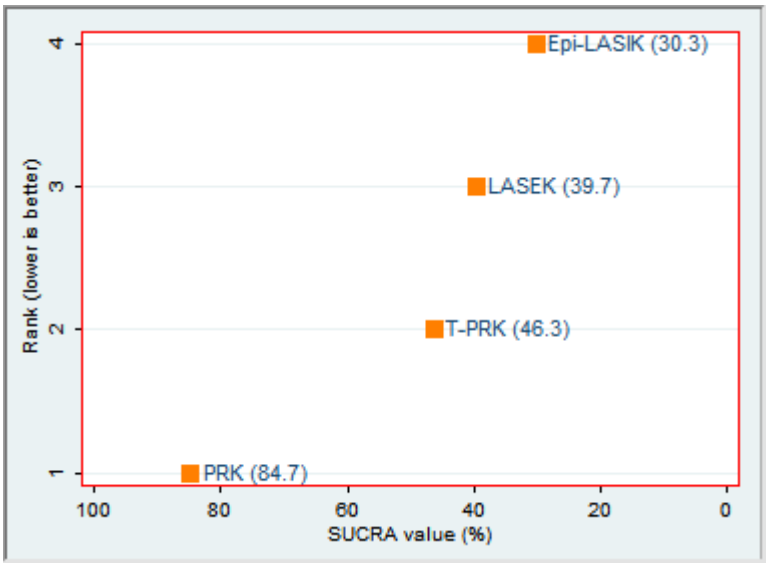
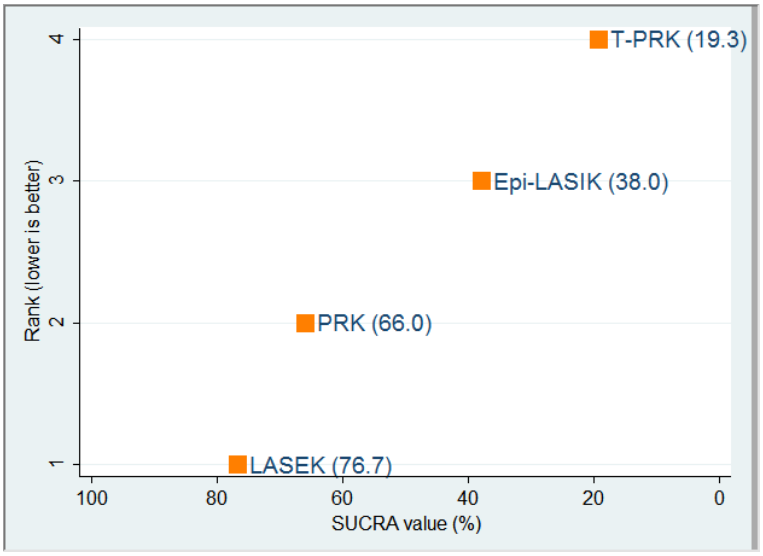


Figure 6-8: Ranking plot of the surface ablation surgery network based on SUCRA values for post-operative efficacy (UCVA of 20/20 or better), predictability (refractive SE within ±0.50 D of the target refraction) and safety (losing two or more lines of BSCVA).





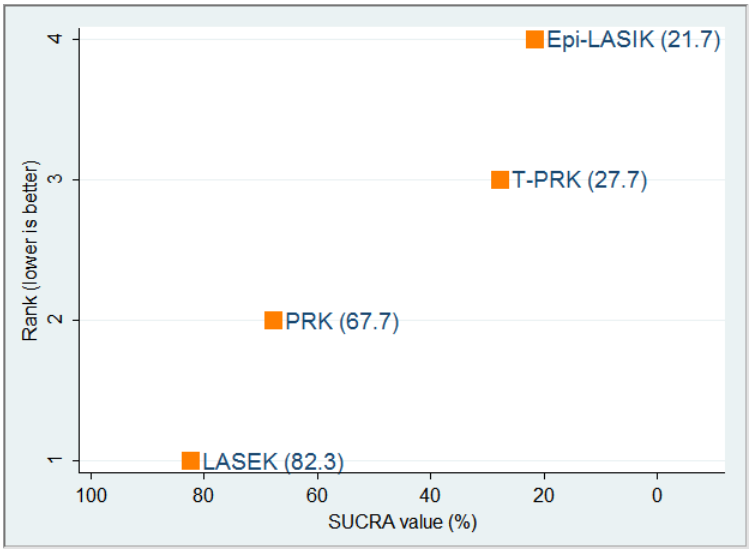
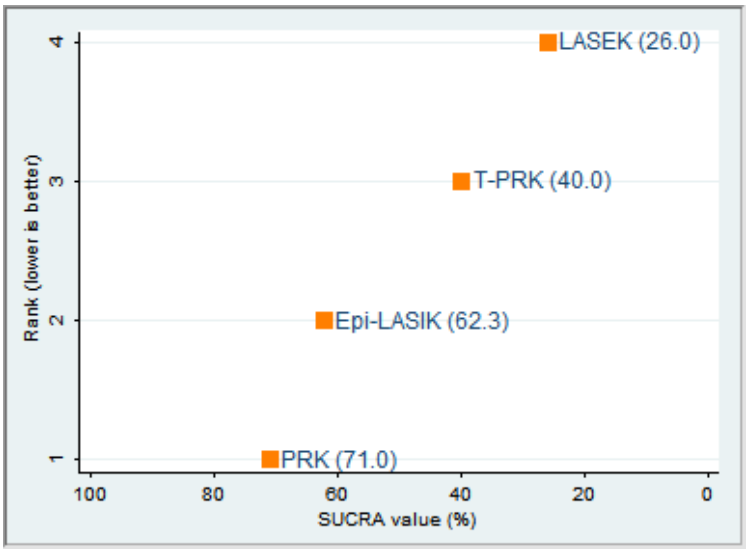
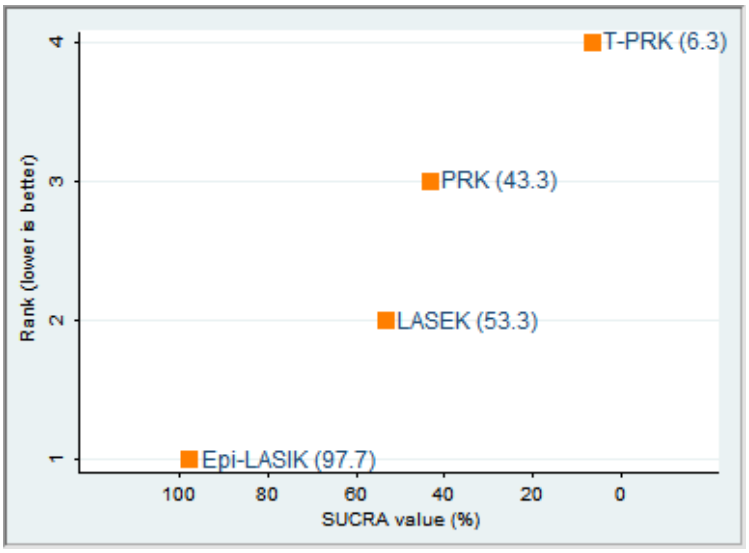


Figure 9-11: Ranking plot of procedures based on SUCRA value for post-operative haze scores, haze grade 0.5 or higher and haze grade 1.0 or higher.





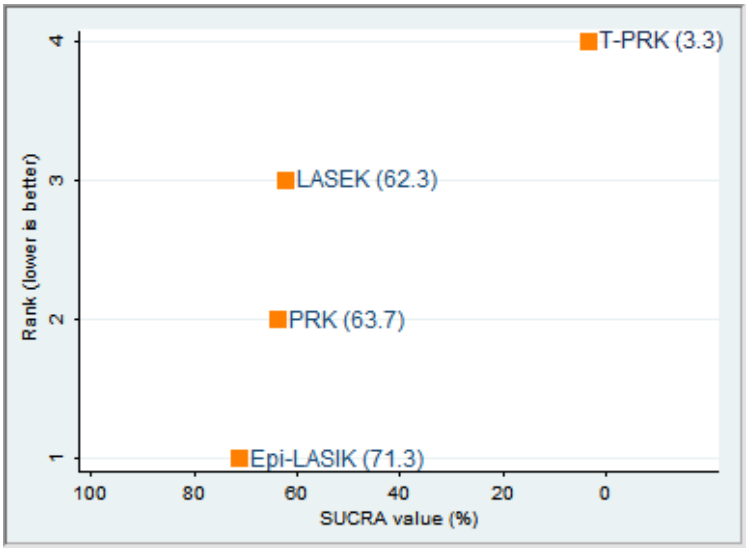


Figure 12-14: Ranking plot of procedures based on SUCRA value for post-operative pain scores on day 1, day 3 and epithelial healing time.

Table 1 Names of treatment included in network meta-analyses

Epi-LASIK = Epithelial laser in situ keratomileusis
LASEK = Laser-assisted subepithelial keratectomy
PRK = Photorefractive keratectomy
T-PRK = Transepithelial photorefractive keratectomy

Table 2 Post-operative efficacy, predictability and safety from direct comparisons between each pair of treatments

	UCVA of 20/20 or better			Refractive SE within ±0.50 D of the target			Losing two or more lines of BSCVA		
	Number of Studies	**Odds Ratio (95% CI)**	**I^2**	**Number of Studies**	**Odds Ratio (95% CI)**	**I^2**	**Number of Studies**	**Odds Ratio (95% CI)**	**I^2**
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)					1	1.00 (0.06, 16.62)	

UCVA = uncorrected visual acuity; SE = spherical equivalent; BSCVA = best spectacle corrected visual acuity

Table 3 Post-operative haze from direct comparisons between each pair of treatments

	Haze Scores			Haze grade 0.5 or higher			Haze grade 1.0 or higher		
	Number of Studies	**Mean difference (95% CI)**	**I^2**	**Number of Studies**	**Odds Ratio (95% CI)**	**I^2**	**Number of Studies**	**Odds Ratio (95% CI)**	**I^2**
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)	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)							
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)	

The underlined data indicate that there is statistically significant effect ($p < 0.05$).

Table 4 Post-operative pain scores and epithelial healing time from direct comparisons between each pair of treatments

	Pain scores on day 1			Pain scores on day 3			Epithelial healing time		
	Number of Studies	**Mean difference (95% CI)**	**I^2**	**Number of Studies**	**Mean difference (95% CI)**	**I^2**	**Number of Studies**	**Mean difference (95% CI)**	**I^2**
PRK vs									
Epi-LASIK	1	-0.01 (-1.76, 1.66)		1	<u>-2.16 (-3.55, -0.77)</u>		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	<u>1.24 (1.00, 1.48)</u>		1	<u>-0.48 (0.23, 0.73)</u>		1	<u>1.57 (1.39, 1.75)</u>	
LASEK vs									
Epi-LASIK							3	-0.18 (-0.81, 0.46)	76.6%
T-PRK	1	<u>-1.23 (-2.10, -0.36)</u>		1	0.87 (-0.39, 2.13)				

The underlined data indicate that there is statistically significant effect ($p < 0.05$)

Appendix

Appendix 1

Search strategy

MEDLINE (Pubmed)

("Keratectomy, Subepithelial, Laser-Assisted"[Mesh] OR Laser-Assisted Subepithelial Keratectomy OR Laser Subepithelial Keratomileusis OR Laser-Assisted Sub epithelial Keratomileusis
OR LASEK OR epipolis laser in situ keratomileusis OR Epipolis laser in situ keratomileusis OR Epi-LASIK OR "Photorefractive Keratectomy"[Mesh] OR Photore fractive 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 keratomileusisor 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/30-33
27.'human'/de
28.4 AND 34 AND 35
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

Appendix 2

Summary of randomized controlled trials included in the meta-analysis

Study (Author, Year)	Country	Follow-up, mo	Treatment	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)		Epithelial healing time (SD), d
							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	92	18 to 39	-4.78(2.93)	62/92	52/92	0/92			1.06(0.52)	1.82（1.34）	0.81（0.54）	3.95(0.71)
			LASEK	92		-4.9(3.01)	67/92	57/92	0/92			0.61(0.4)	1.06（0.90）	0.30（0.43）	2.76(0.47)
Celik 2014[2]	Turkey	12m	T-PRK	42	28.5(6.3)	-2.88(1.24)			0/42	13/42	20/42	0.17	4.28(0.55)	3.08(0.41)	2.19(0.39)
			PRK	42		-2.44(1)			0/42	20/42	5/42	0.33	5.52(0.58)	3.56(0.7)	3.76(0.43)
Gamaly 2007[3]	Oman	6m	Epi-LASIK	24	24.8	-2.67	9/24	8/24	0/24	7/24，	0/24	0.145			
			PRK	24			8/24	7/24	0/24	15/24	8/24	0.705			
Ghanem2008[4]	Brazil	12m	PRK	51	28.06(4.13)		49/50	45/48	0/51	4/51	2/51	0.054			
			LASEK	51			47/49	40/44	0/51	8/51	2/51	0.077			
Ghanem2008+[5]	Brazil	12m	PRK	51	28.06(4.13)								0.73（1.08）	0.63（1.02）	4.35(0.48)
			LASEK	51									1.14(1.23)	0.53（0.86）	4.75(0.72)
Ghirlando 2007[6]	Italy	12m	LASEK	50	34.5(2.3)	-3.59(1.29)		44/50		9/50	4/50	0.13		2.62（0.6）	2.29(0.52)
			PRK	50		-4.37(1.35)		46/50		12/50	2/50	0.14		2.17（0.87）	2.52(0.99)
Hashemi 2004[7]	Iran	3m	PRK	42	29.1(7.8)	-3.44(1.13)	26/32	23/32		8/32	1/32	0.1405	1.0（0.7）		3.69(1.03)
			LASEK	42		-3.57(1.25)	25/32	26/32		10/32	4/32	0.219	0.8（0.7）		3.97(1.27)
He 2004[8]	China	6m	PRK	46	23.2(4)	-4.5(1.28)	36/46					0.32(0.25)			2.87(0.49)
			LASEK	46		-4.38(1.23)	40/46					0.16(0.23)			3.49(0.62)

Hondur 2008[9]	Turkey	12m	LASEK	25	26.8(8.4)	-3.91(1.39)	23/25	23/25		5/25	0/25	0.1			4.18(0.58)
			Epi-LASIK	25		-3.95(1.49)	23/25	23/25		5/25	0/25	0.1			4.86(0.64)
Lee 2001[10]	Germany	3m	PRK	27	25(3.2)	-4.82(1.07)	7/27					0.45(0.27)		2.36（0.67）	3.18(0.5)
			LASEK	27		-4.69(0.96)	8/27					0.29(0.26)		2.04（0.76）	3.64(0.63)
Litwak 2002[11]	Mexico	1m	PRK	25	28.7(5.9)	-3(1.9)			0/25						3.3(0.5)
			LASEK	25		-3.1(2)			0/25						3.6(0.5)
Long 2006[12]	China	3m	LASEK	10	28.3	-4.5(1.44)						0.31(0.14)			5.3(0.9)
			Epi-LASIK	10		-4.9(1.26)						0.23(0.08)			4.8(1.4)
O'Doherty 2007[13]	Ireland	3m	Epi-LASIK	38	30	-3.51(1.65)	24/38	30/38					0.156		3(1)
			LASEK	38	30	-3.18(1.15)	28/38	32/38					0.452		3(1)
			PRK	19	32	-3.72(1.59)	14/19	15/19					0.326		4(1)
Pirouzian 2004[14]	USA	1m	PRK	32	21 to 46								4.27(3.5)	2.27(2)	
			LASEK	32									4.17(3.5)	2.17(1.5)	
Saleh 2003[15]	U.K.	2d	PRK	14	22 to 43	-2.035							4.09(2.48)	2.21(2.55)	
			LASEK	14		-2.267							3.71(2.84)	2.86(3.43)	
Sia 2014[16]	USA	12m	LASEK	83	35.7(8)	-5.85(1.38)	64/75	51/75	1/75		4/75	0.029	1(2.19)	0.64（1.81）	
			PRK	83		-5.89(1.42)	64/75	47/75	2/75		5/75	0.124	1.23(2.28)	0.54（1.76）	
Torres 2007[17]	USA	6d	PRK	20									4.21(2.37)	2.53(2.22)	3.95(1.39)
			Epi-LASIK	20									4.26(3.1)	4.69(2.28)	4.75(1.44)
Wang 2014[18]	China	3m	LASEK	30	23(4.59)	-6.27(2.30)	28/30					0.26(0.21)	3.2(1.833)	5.27(2.638)	
			T-PRK	30		-6.32(2.21)	27/30					0.27(0.25)	4.43(1.612)	4.4(2.343)	

[a] Data of total; [b] Data from graph

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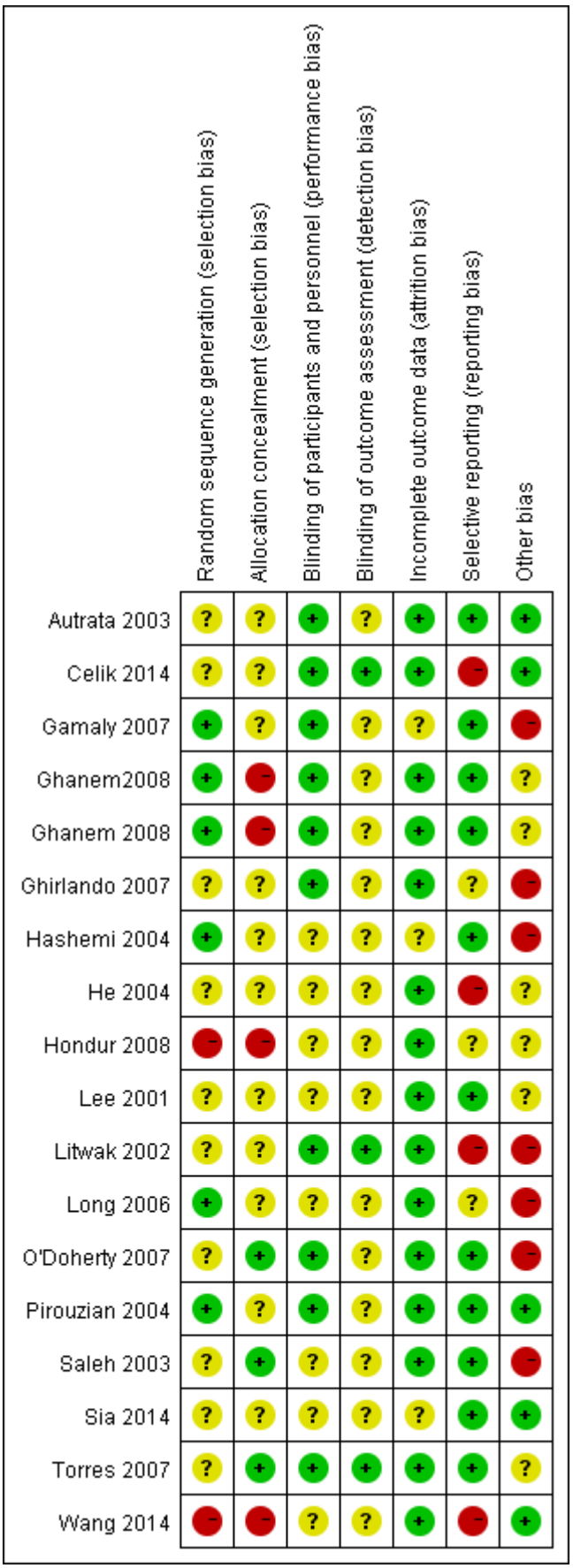
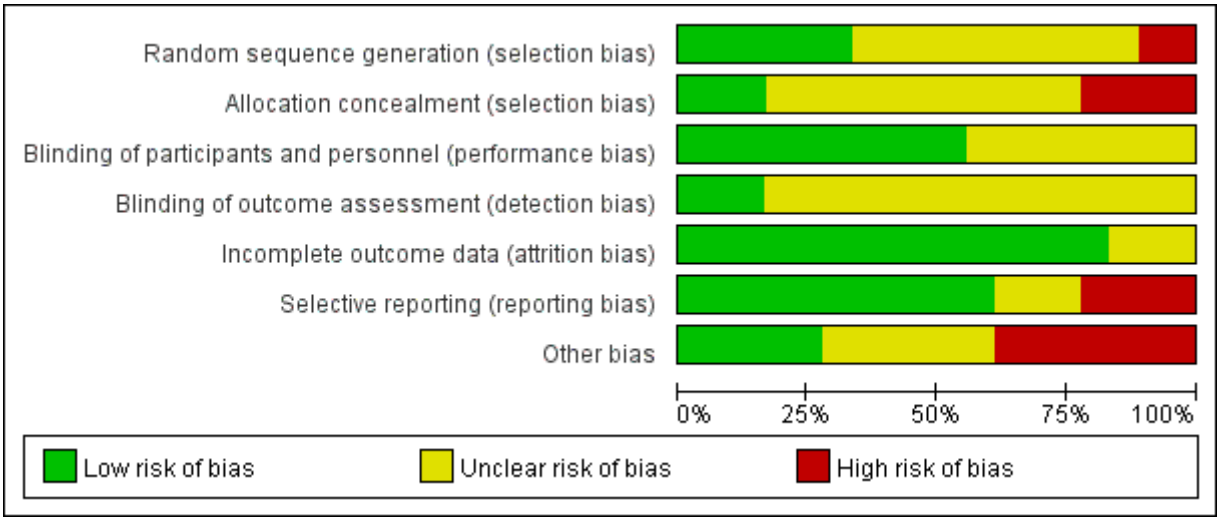
Appendix 3: The quality of the included trials

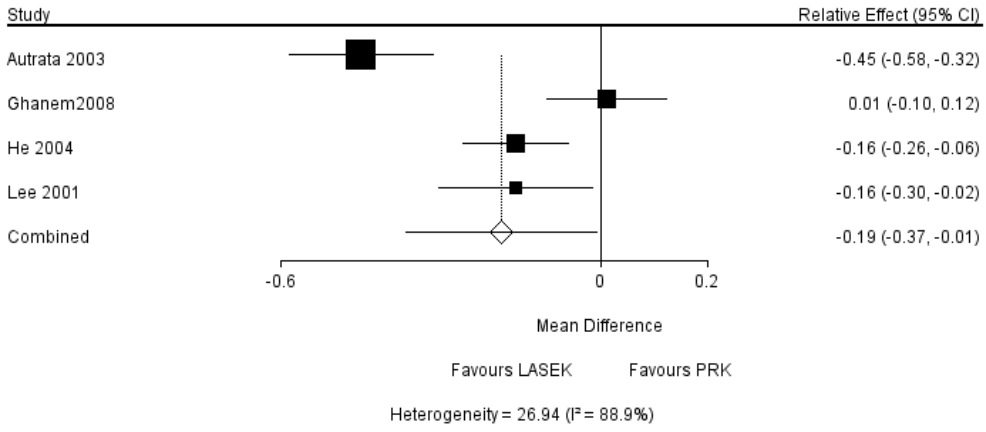



Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias

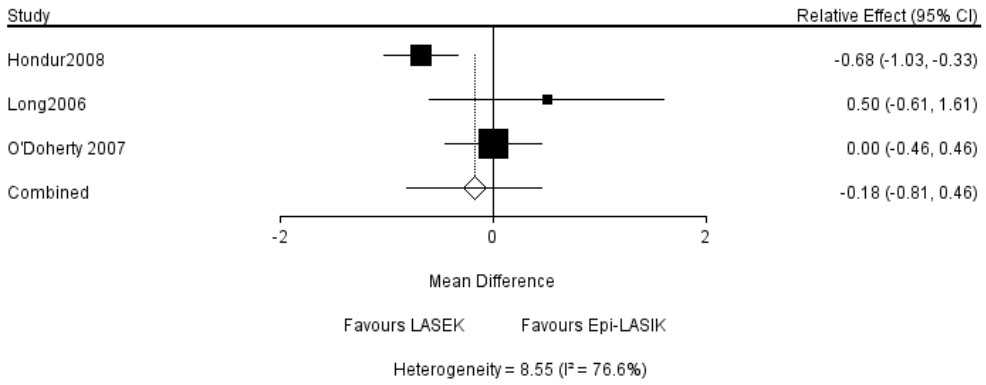
Appendix 4

High heterogeneity among some comparisons (Forest plots)

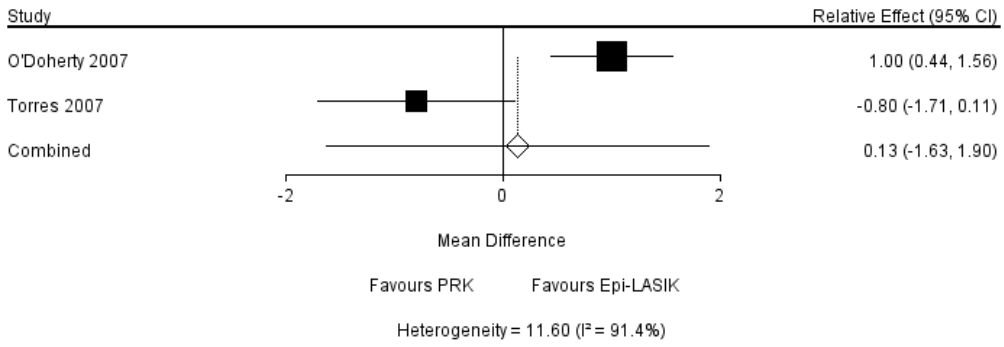
LASEK vs PRK for postoperative Haze scores



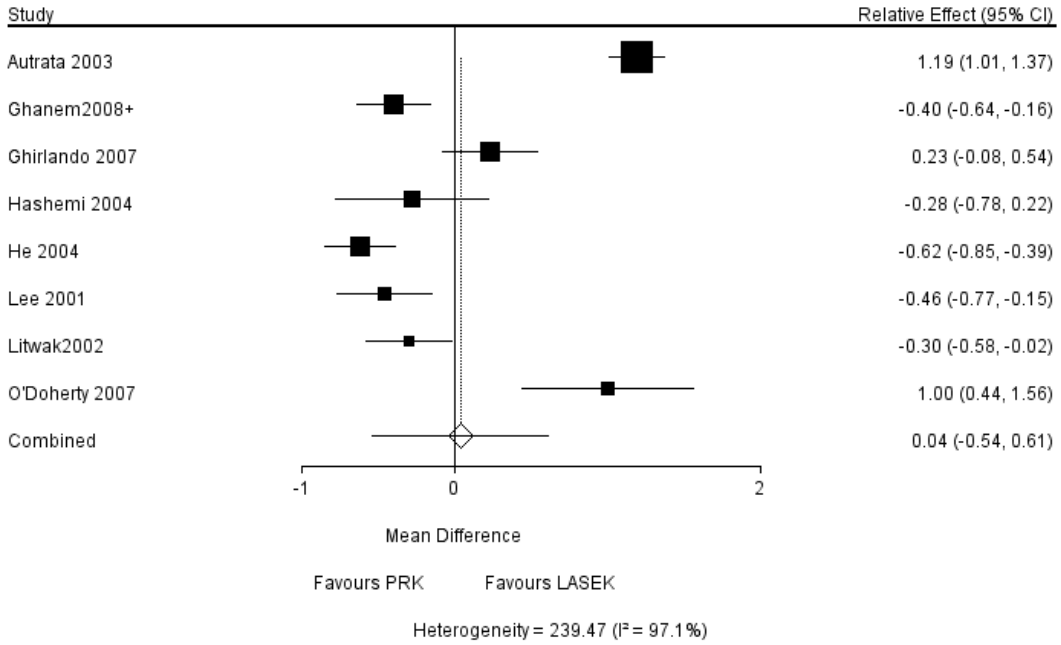
LASEK vs Epi-LASIK for postoperative epithelial healing time



PRK vs Epi-LASIK for postoperative epithelial healing time



PRK vs LASEK for postoperative epithelial healing time



Appendix 5

Ranking probabilities

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

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

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

Post-operative 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

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

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

Post-operative 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

Post-operative 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

Post-operative pain scores on day 3

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

Appendix 6

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

Appendix 7

Sensitivity analyses

Removed trials that introduced high heterogeneity or statistical inconsistency across studies (outcome of post-operative haze scores in Autrata 2003 and outcome of pain scores on day 1 in Wang 2014)

Comparison for postoperative haze scores of all treatments derived from network meta-analysis

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)

Ranking probabilities of postoperative haze scores

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

SUCRA value of postoperative haze scores

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

T-PRK	50.7

Comparison for postoperative pain scores on day 1 of all treatments derived from network meta-analysis

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)

Ranking probabilities of post-operative pain scores on day 1

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

SUCRA value of post-operative pain scores on day 1

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