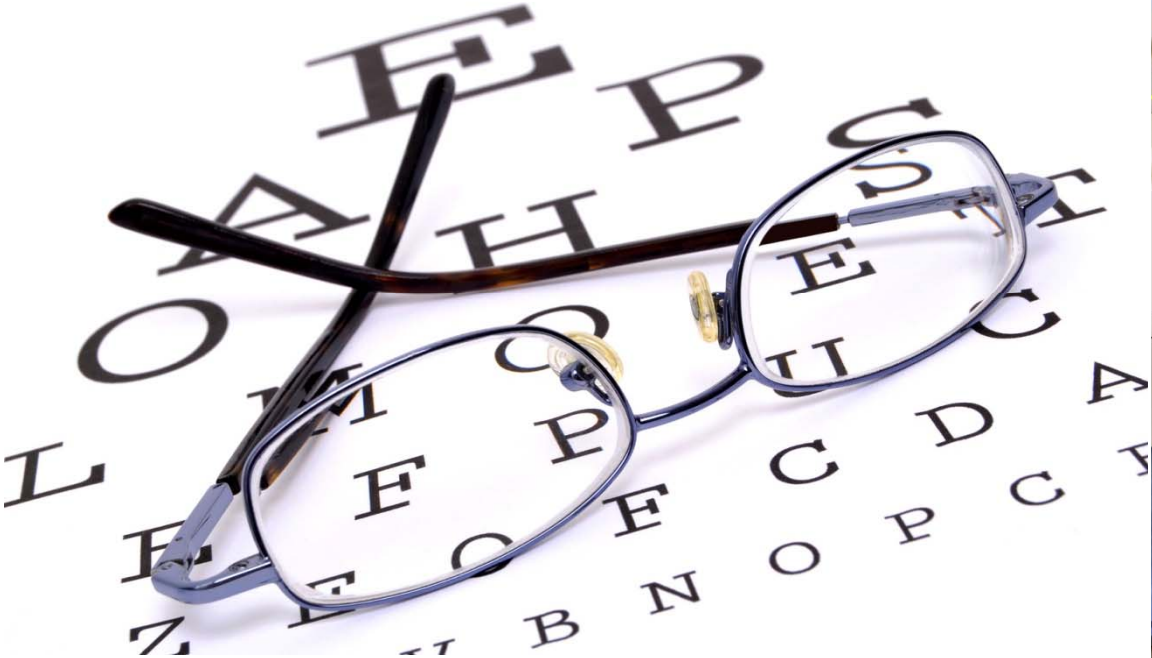
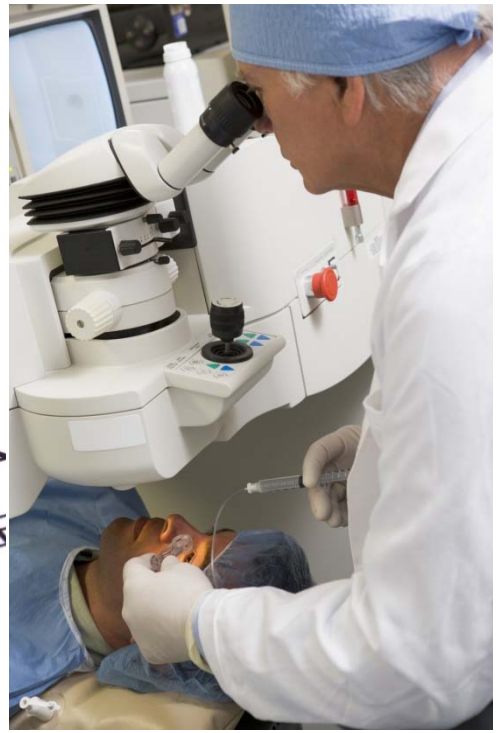
KCE REPORT 215S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

CORRECTION OF REFRACTIVE ERRORS OF THE EYE IN ADULTS – PART 2: LASER SURGERY AND INTRAOCULAR LENSES

APPENDIX





KCE REPORT 215S
HEALTH TECHNOLOGY ASSESSMENT

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CORRECTION OF REFRACTIVE ERRORS OF THE EYE IN ADULTS – PART 2: LASER SURGERY AND INTRAOCULAR LENSES

APPENDIX

CAROLINE OBYN, YOLBA SMIT, PIET POST, LAURENCE KOHN, NOÉMIE DEFOURNY, WENDY CHRISTIAENS, DOMINIQUE PAULUS

COLOPHON

Title :	Correction of refractive errors of the eye in adults – Part 2: laser surgery and intraocular lenses - Appendix
Authors :	Caroline Obyn (KCE), Yolba Smit, Piet Post, Laurence Kohn (KCE), Noémie Defourny (KCE), Wendy Christiaens (KCE), Dominique Paulus (KCE)
Reviewers :	Irina Cleemput (KCE), Lorena San Miguel (KCE)
External Experts and stakeholders :	Gilles Berdeaux (IMS Health), Jacques Boly (Alliance Nationale des Mutualités Chrétiennes), Ann Ceuppens (Onafhankelijke Ziekenfondsen), Ilse Claerhout (AZ Maria Middelares – Campus Sint-Jozef - Gentbrugge), Ignace Fransman (Algemene Professionele Opticiens en Optometristen Bond van België), René Trau (UZ Antwerpen), Rob Van Horenbeeck (Belgian Society of Cataract and Refractive Surgeons), Dominique Vandijck (Universiteit Hasselt), Bert Winnen (RIZIV – INAMI), Antonine Wyffels (RIZIV – INAMI)
External Validators :	Damien Gatinel (Fondation Ophtalmologique A. de Rothschild, Paris), Diana De Graeve (Universiteit Antwerpen)
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Layout :	Ine Verhulst

Disclaimer :	• **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.** • **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.** • **Finally, this report has been approved by common assent by the Executive Board.** • **Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE**

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APPENDIX REPORT

LIST OF FIGURES

Figure 1 – Meta-analysis of ⩾1 lines of BCVA lost at 1-24 months post-treatment, PRK vs. LASEK 6
Figure 2 – Meta-analysis of ⩾1 lines of BCVA lost at ⩾6 months post-treatment, PRK vs. LASIK 16
Figure 3 – Meta-analysis of % of eyes with an UCVA of 20/20 or better at 12 months post-treatment, IOL vs. laser surgery 28
Figure 4 – Meta-analysis of % of eyes within ± 0.5 D of target refraction at 12 months, IOL vs. laser surgery 29

LIST OF TABLES

Table 1 – PRK vs. LASEK for myopia with or without astigmatism, randomised data 3
Table 2 – Summary of findings for PRK vs. LASEK for patients with myopia with/without astigmatism, randomised data [1, 2] 7
Table 3 – PRK vs. LASEK for hyperopia with or without astigmatism, randomised data 9
Table 4 – Summary of findings for PRK vs. LASEK for patients with hyperopia with/without astigmatism, randomised data [2] 11
Table 5 – PRK vs. LASIK for myopia with or without astigmatism, randomised data 12
Table 6 – Summary of findings for PRK vs. LASIK for patients with myopia with/without astigmatism, randomised data [3] 17
Table 7 – PRK vs. LASIK for hyperopia with or without astigmatism, randomised data 19
Table 8 – LASEK vs. LASIK for myopia with or without astigmatism, randomised data 20
Table 9 – Summary of findings for LASEK vs. LASIK for patients with myopia with/without astigmatism, randomised data [2] 21
Table 10 – LASEK vs. LASIK for hyperopia with or without astigmatism, randomised data 23
Table 11 – Intra-ocular lenses vs. laser refractive eye surgery for myopia with or without astigmatism, randomised data 24
Table 12 – Summary of findings for intra-ocular lenses vs. laser refractive surgery for patients with myopia with/without astigmatism, randomised data [6, 7] 29
Table 13 – Intra-ocular lenses vs. laser refractive eye surgery for hyperopia with or without astigmatism, randomised data 32
Table 14 – PRK for myopia, observational data 32
Table 15 – Summary of findings for visual acuity and safety of PRK for patients with myopia, observational data [2, 10-15] 39

Table 16 – PRK for myopic astigmatism, observational data 40
Table 17 – Summary of findings for visual acuity and safety of PRK for patients with myopic astigmatism, observational data 42
Table 18 – PRK for hyperopia with or without astigmatism, observational data 43
Table 19 – Summary of findings for visual acuity and safety of PRK for patients with hyperopia with/without astigmatism, observational data 45
Table 20 – LASEK for myopia with or without astigmatism, observational data 46
Table 21 – Summary of findings for visual acuity and safety of LASEK for patients with myopia with/without astigmatism, observational data [2, 16] 48
Table 22 – LASIK, observational data 49
Table 23 – Summary of findings for visual acuity and safety of LASIK for patients with myopia with/without astigmatism, observational data [2, 13, 17-24, 26, 27] 60
Table 24 Summary of findings for visual acuity and safety of LASIK for patients with hyperopia with/without astigmatism, observational data [2] 61
Table 25 – LASIK vs. intra-ocular lenses, observational data 62
Table 26 – Intra-ocular lenses, observational data 67
Table 27 – Summary of findings for visual acuity and safety of intra-ocular lenses for patients with myopia with/without astigmatism, observational data [9 29 28, 30-32] 79
Table 28 – Summary of findings for visual acuity and safety of intra-ocular lenses for patients with hyperopia with/without astigmatism, observational data [9] 80

Table 1 – PRK vs. LASEK for myopia with or without astigmatism, randomised data

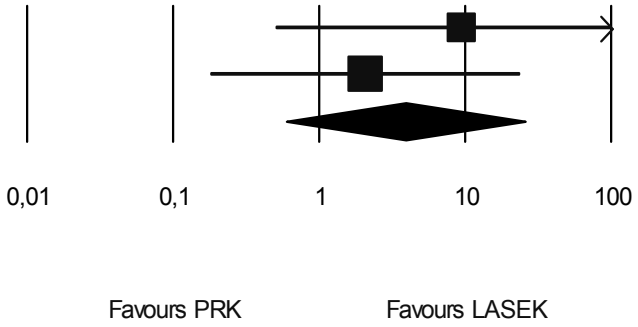
Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Zhao 2010 [1]	• SR + MA • Funding: none; CoI: none • Databases searched: Medline, EMBASE, CENTRAL, references, related articles (Medline) • Search date: July 2008 • Languages included: all • Number of studies included: 11 RCTs, 1 CCT	• Eligibility criteria: comparative studies; patients aged 18-60y, any degree of myopia, up to 3 D of astigmatism • Exclusion criteria: significant co-pathology, history of previous ocular surgeries, systemic diseases associated with impaired or abnormal wound healing • Patient characteristics: mean age range 23.2-34.5y • Median follow-up 11 RCTs: 3 months (range: 48 hours-1 year)	LASEK vs. PRK	<u>Visual acuity</u>: • Preoperative Mean Refractive Spherical Equivalent: 10 studies, 885 eyes (PRK vs. LASEK) WMD = -0.08, 95%CI -0.28 to 0.12, p=0.43 • Final Mean Refractive Spherical Equivalent: 8 studies, 785 eyes (PRK vs. LASEK) WMD = 0.00, 95%CI -0.08 to 0.07, p=0.95; sensitivity analysis with RCTs only (7 studies, 731 eyes): WMD = -0.02, 95%CI -0.10 to 0.06, p=0.57 • % refractions within 0.5 D of intended spherical equivalent correction: 4 RCTs, 545 eyes (PRK vs. LASEK) OR=0.81, 95%CI 0.52 to 1.26, p=0.34 • % eyes with final UCVA of 20/20 or better: 6 studies, 634 eyes (PRK vs. LASEK) OR = 0.86, 95%CI 0.61 to 1.20, p=0.37; sensitivity analysis with RCTs only (5 studies, 580 eyes): OR = 0.78, 95%CI 0.52 to 1.16, p=0.22 • % eyes with final UCVA of 20/40 or less: 5 studies, 584 eyes (PRK vs. LASEK) OR = 1.26, 95%CI 0.63 to 2.51, p=0.52; sensitivity analysis with RCTs only (4 studies, 530 eyes): OR = 1.63, 95%CI 0.73 to 3.66, p=0.23 <u>Return to work</u>: Not reported <u>Rehabilitation time</u>:	Included studies: Ghirlando 2007, O'Doherty 2007, Pirouzian 2006, Saleh and Almasri 2003, He 2004, Hashemi 2004, Autrata and Rehurek 2003, Lee 2002, Lee 2001, Lee 2005, Litwak 2002, Ghanem 2008 Author´s quality assessment with Jadad score (5-point scale): RCTs scored 3 (n=3), 4 (n=5) or 5 (n=3). The non-RCT scored 0. Not reported for which items RCTs did not score

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				Not reported Quality of life: Not reported Safety: • Postoperative pain: 9 studies, 878 eyes (PRK vs. LASEK); SMD = 0.24, 95%CI -0.15 to 0.63, p=0.23; sensitivity analysis with RCTs (8 studies, 824 eyes) only: SMD = 0.26, 95%CI -0.20 to 0.72, p=0.27 • Postoperative pain on day 1: 5 studies, 604 eyes (PRK vs. LASEK); SMD = 0.08, 95%CI -0.29 to 0.45, p=0.67 • Healing time of corneal epithelium: 9 studies, 893 eyes (PRK vs. LASEK); WMD = 0.08, 95%CI -0.44 to 0.59, p=0.77; sensitivity analysis with RCTs only (8 studies, 839 eyes): WMD = 0.04, 95%CI -0.54 to 0.61, p=0.89 • Mean corneal haze scores at 1 month post-treatment: 6 studies, 510 eyes (PRK vs. LASEK); WMD = 0.25, 95%CI 0.10 to 0.39, p=0.0007 • Mean corneal haze scores at 3 months post-treatment: 6 studies, 544 eyes (PRK vs. LASEK); WMD = 0.14, 95%CI 0.01 to 0.26, p=0.03 • Mean corneal haze scores at 6 months post-treatment: 5 studies, 576 eyes (PRK vs. LASEK); WMD = 0.14, 95%CI -0.02 to 0.30, p=0.08; sensitivity analysis with RCTs only: OR = 0.17, 95%CI -0.02 to 0.36, p=0.07 • Mean corneal haze scores at 12 months post-treatment: 3 studies, 348 eyes (PRK vs. LASEK); WMD = 0.09, 95%CI -0.09 to 0.28, p=0.34	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 10 RCT	• Comparative studies on patients with myopia	LASEK vs. PRK	<u>Safety data not reported on by Zhao 2010</u>: • Post-operative complications such as infections or recurrent erosion syndrome: 0% (2 RCTs, 238 eyes) • Eyes that lost ≥ 1 line of BCVA 1-24 months post-treatment: in 4 RCTs (362 eyes) the rate of loss of one line BCVA was 6/181 (median 2.2%, range 0% to 6.0%)) for PRK vs. 1/181 (median 0%, range 0% to 3.0%) for LASEK • Eyes that lost ≥ 2 line of BCVA 3-24 months post-treatment: no events in 2 RCTs (248 eyes) • Mean halo score: mean halo score at 3 months was 1.71 (SD: 1.27) vs.1.62 (1.31) (1 RCT, 64 eyes) • <u>Self-reported mean glare score at 3 months: 1.83 (1.13) vs. 1.79 (SD: 1.18) (1 RCT, 64 eyes)</u>	Only safety data not reported on by Zhao 2010 reported here Included studies Autrata 2003, Hashemi 2004, Lee 2001, Litwak 2002, Pirouzian 2004, Saleh 2003, Al Fayez 2002, Al Fayez 2004, Ghirlando 2002, Rooij 2003 Negative scores in author´s quality assessment of the 6 full-text RCTs (the quality of 4 abstracts was not assessed): 2/6 unconcealed allocation; 1/6 eligibility criteria unspecified; 1/6 participants unblinded; 3/6 follow-up not long enough to detect important effects; 2/6 no ITT analysis

Figure 1 – Meta-analysis of ≥1 lines of BCVA lost at 1-24 months post-treatment, PRK vs. LASEK

Study name	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	PRK	LASEK
Autrata 2003	Loss of 1 or more lines of BCVA (1-24 months)	9,407	0,499	177,270	1,496	0,135	4 / 92	0 / 92
Hashemi 2004	Loss of 1 or more lines of BCVA (1-24 months)	2,067	0,178	24,006	0,580	0,562	2 / 32	1 / 32
		3,852	0,587	25,303	1,404	0,160		



Q-value= 0.60; I^2=0%

Meta-analysis using the primary studies identified in NICE 2005 (table 66). Two studies with a total of 114 eyes had no events in either arm and are not depicted in the figure

Table 2 – Summary of findings for PRK vs. LASEK for patients with myopia with/without astigmatism, randomised data [1, 2]

Outcome (follow-up)	Absolute effect: WMD (95%CI)	Relative effect: OR (95%CI)	N of primary studies (N of eyes)	Quality of the evidence (GRADE)	Comments
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR			
UCVA 20/20 or better (at final follow-up)	NR	0.78 (0.52 to 1.16) [1]	5 (580)	⊕⊕ ⊙⊙ low §	
UCVA 20/40 or less (at final follow-up)	NR	1.63 (0.73 to 3.66) [1]	4 (530)	⊕⊕ ⊙⊙ low #	
Within 0.5 D target refraction (≥6 months)	NR	0.81 (0.52 to 1.26) [1]	4 (545)	⊕⊕ ⊙⊙ low £	
Within 1 D target refraction (≥6 months)	NR	NR			
Postoperative spherical equivalent	-0.02 (-0.10 to 0.06) [1]	NR	7 (731)	⊕⊕ ⊕⊙ moderate ¥	
Return to work	NR	NR			
Rehabilitation time	NR	NR			
Quality of life	NR	NR			
Loss of ≥1 line of BCVA (1-24 months)	NR	3.85 (0.59 to 25.30)	4 (362)	⊕⊕ ⊙⊙ low ¤	In 4 RCTs the rate of loss of one line BCVA was 6/181 (median 2.2%, range 0% to 6.0%)) for PRK vs. 1/181 (median 0%, range 0% to 3.0%) for LASEK [2]
Loss of ≥2 lines of BCVA (3-24 months)	NR	NR	2 (248)	⊕⊕ ⊕⊙ moderate ¶	In 2 RCTs no events occurred [2]
Corneal ectasia	NR	NR			
Keratitis/infection (post-operative)	NR	NR	2 (238)	⊕⊕ ⊕⊙ moderate $	2 RCTs did not report any post-operative infections [2]
Healing time (days) of corneal epithelium	0.04 (-0.54 to 0.61) [1]	NR	8 (839)	⊕⊕ ⊙⊙ low ₴	

Retinal detachment	NR	NR			
Choroidal neovascularisation	NR	NR			
Epithelial in growth	NR	NR			
Raised intraocular pressure	NR	NR			
Re-treatment	NR	NR			
Mean corneal haze scores (12 months)	0.09 (-0.09 to 0.28)[1]	NR	3 (348)	⊕⊕ ⊕⊙ moderate ¥	
Haloes and/or glare (3 months)	NR	NR	1 (64)	⊕⊕ ⊕⊙ moderate ₮	In 1 RCT the mean halo score was 1.71 (SD: 1.27) vs.1.62 (1.31) and the mean glare score was 1.83 (SD: 1.13) vs. 1.79 (1.18) [2]
Night driving problems	NR	NR			
Dryness	NR	NR			
Mean post-operative pain score	0.26 (-0.20 to 0.72) [1]	NR	8 (824)	⊕⊕ ⊙⊙ low ₮	

Abbreviations: BCVA: best corrected visual acuity; CI: confidence interval; D: diopter; N: number; NR: not reported; OR: odds ratio; SD: standard deviation; UCVA: uncorrected visual acuity; WMD: weighted mean difference
§: Serious risk of bias (1/5 included studies scored 5 on the Jadad scale, 3/5 studies scored 4 and 1/5 studies scored 3); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 1); no other considerations
#: Serious risk of bias (3/4 studies scored 4 on the Jadad scale and 1/4 studies scored 3); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 1); no other considerations
£: Serious risk of bias (2/4 included studies scored 5 on the Jadad scale, 1/4 studies scored 4 and 1/4 studies scored 3); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 1); no other considerations
¥: Serious risk of bias (3/7 included studies scored 5 on the Jadad scale, 3/7 studies scored 4 and 1/7 studies scored 3); no serious inconsistency; no serious indirectness; no serious imprecision; no other considerations
¤: Serious risk of bias (2 trials did not perform an intention to treat analysis, 2 trials had a follow-up that was too short, no allocation concealment in 1 trial); no serious inconsistency; no serious indirectness; serious imprecision (very few (7) events and 95%CI includes 1); no other considerations
¶: No serious risk of bias; no serious inconsistency; no serious indirectness; serious imprecision (238 eyes with no events); no other considerations
$: Serious risk of bias (treatment allocation unconcealed and participants non-blinded in 1 trial); no serious inconsistency; no serious indirectness; no serious imprecision; no other considerations
₴: Serious risk of bias (2/8 included studies scored 5 on the Jadad scale, 4/8 studies scored 4 and 3/8 studies scored 3); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 0); no other consideration
¥: No serious risk of bias; no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 0); no other considerations
₮: No serious risk of bias; no serious inconsistency; no serious indirectness; serious imprecision; no other considerations
₮: Serious risk of bias (2/8 included studies scored 5 on the Jadad scale, 4/8 studies scored 4 and 3/8 studies scored 3); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 0); no other consideration

Table 3 – PRK vs. LASEK for hyperopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 1 RCT	• Eligibility criteria: adults undergoing photorefractive surgery for correction of hyperopia • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: range hyperopia 2.0-5.0 D, mean age 38.7y • Follow-up: 24 months	PRK vs. LASEK	<u>Visual acuity</u>: • Efficacy index at 24 months: 0.953 vs. 1.056, p=0.047 • % refractions within 0.5 D of intended spherical equivalent correction: 1 study, 216 eyes (LASEK vs. PRK) • 78% (85/108) vs. 57% (62/108), p=0.04 • % refractions within 1 D of intended spherical equivalent correction: 1 study, 216 eyes (LASEK vs. PRK) 92% (99/108) vs. 86% (93/108), p=0.13 • % eyes with final UCVA of 20/20 or better: 1 study, 216 eyes (LASEK vs. PRK) 67% (72/108) vs. 73% (79/108), p-value not reported • % eyes with final UCVA of 20/40 or better: 1 study, 216 eyes (LASEK vs. PRK) 91% (98/108) vs. 81% (87/108), p-value not reported <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>: Not reported <u>Safety</u>:	One trial included: Autrata 2003 Author´s quality appraisal with 18-question checklist for case series and 15-question checklist for RCTs: the 1 included trial scored well on 10 out of 15 items and unclear on 5 items

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				• % eyes that lost ≥ 1 line of BCVA post-treatment: 1 study, 216 eyes (LASEK vs. PRK) 14% vs. 12%, p-value not reported • % eyes that lost ≥ 2 line of BCVA post-treatment: 1 study, 216 eyes (LASEK vs. PRK) 0% in both arms • No postoperative complications such as infection, corneal melt, recurrent erosion syndrome, or dry-eye problems • Mean haze at 24 months: 1 study, 216 eyes (LASEK vs. PRK); 0.20 (SD 0.27) vs. 0.45 (SD 0.31), p<0.05 • Mean postoperative pain for days 1-3: 1 study, 216 eyes (LASEK vs. PRK); 0.59 (SD 0.52) vs. 1.13 (SD 0.95), p<0.05 • Re-treatment: 8 vs. 0 eyes due to regression	

Table 4 – Summary of findings for PRK vs. LASEK for patients with hyperopia with/without astigmatism, randomised data [2]

Outcome (follow-up)	Absolute effect: WMD (95%CI)	Relative effect: OR (95%CI)	N of primary studies (N of eyes)	Quality of the evidence (GRADE)	Comments
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively) (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	0.953 vs. 1.056, p=0.047 [2]
UCVA 20/20 or better (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	73% (79/108) vs. 67% (72/108), p=0.29 [2]
UCVA 20/40 or better (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	81% (87/108) vs. 91% (98/108), p=0.03 [2]
Within 0.5 D target refraction (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	57% (62/108) vs. 78% (85/108) p=0.04 [2]
Within 1 D target refraction (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	86% (93/108) vs. 92% (99/108) p=0.13 [2]
Postoperative spherical equivalent	NR	NR			
Return to work	NR	NR			
Rehabilitation time	NR	NR			
Quality of life	NR	NR			
Loss of 1 line of BCVA (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	12 (13/108) vs.14% (15/108), p=0.69 [2]
Loss of ≥2 lines of BCVA (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	0% in both arms [2]
Corneal ectasia	NR	NR			
Keratitis/infection	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	No postoperative complications such as infection, corneal melt, recurrent erosion syndrome, or dry-eye problems reported [2]
Healing time of corneal epithelium	NR	NR			
Retinal detachment	NR	NR			
Choroidal neovascularisation	NR	NR			

Epithelial in growth	NR	NR			
Raised intraocular pressure	NR	NR			
Re-treatment	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	8 vs. 0 eyes, p=0.004 [2]
Mean corneal haze (24 months)	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	0.45 (SD 0.31) vs. 0.20 (SD 0.27), p<0.05 [2]
Haloes and/or glare	NR	NR			
Night driving problems	NR	NR			
Dryness	NR	NR			
Pain day 1-3	NR	NR	1 (216)	⊕⊕ ⊕⊙ moderate $	1.13 (SD 0.95) vs. 0.59 (SD 0.52), p<0.05 [2]

Abbreviations: BCVA: best spectacle corrected visual acuity; CI: confidence interval; D: diopter; N: number; NR: not reported; OR: odds ratio; SD: standard deviation; UCVA: uncorrected visual acuity; WMD: weighted mean difference
$: No serious risk of bias; no serious inconsistency; no serious indirectness; serious imprecision (1 trial with 216 eyes and small differences between groups leading to fragility of results); no other considerations

Table 5 – PRK vs. LASIK for myopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Shortt 2013 [3]	• SR + MA • Funding: Moorfields Eye Hospital NHS Trust, UK; CoI: one author uses LASIK as first choice for myopia • Databases searched: CENTRAL, Medline, EMBASE, LILACS, mRCT, ClinicalTrials.gov, WHO ICTRP, reference lists, Science Citation Index • Search date: November	• Eligibility criteria: RCTs; age 18-60y, any degree of myopia, up to 3 D of myopic astigmatism • Exclusion criteria: age <18y or > 60y, treatment for correction of refractory errors other than primary myopia; co-existing ocular	LASIK (including SBK) vs. PRK	Visual acuity: • % eyes with UCVA of 20/15 or better at 2-4 weeks post-treatment: 4 trials, 566 eyes (LASIK vs. PRK) OR = 5.89, 95%CI 3.34 to 10.39, p<0.00001 • % eyes with UCVA of 20/15 or better at 6 months post-treatment: 5 trials, 682 eyes (LASIK vs. PRK) OR = 1.13, 95%CI 0.75 to 1.69, p=0.55 • % eyes with UCVA of 20/15 or better at 12 months post-treatment: 2 trials, 372 eyes (LASIK vs. PRK) OR = 1.08, 95%CI 0.58 to 2.00, p=0.81 • % eyes with UCVA of 20/20 or better at 2-4 weeks post-treatment: 8 trials, 1079 eyes (LASIK vs. PRK) OR = 3.69, 95%CI 2.55 to 5.36, p<0.00001	Included studies: Barreto 2010, Durrie 2008, el Danasoury 1999, el Maghraby 1999, Forseto 2000, Hatch 2011, Hjortdal 2005, Manche 2011, Moshirfar 2010, Schallhorn 2009, SUMMIT 1998, Wallau 2008, Wang 1997 Author´s quality appraisal with

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	2012 • Languages included: all • Number of studies included: 13 RCTs	disease or systemic disease associated with abnormal or impaired wound healing • Patient characteristics: 100% stable refraction for at least 1y, range myopia -0.25 to -14.48		• % eyes with UCVA of 20/20 or better at 6 months post-treatment: 10 studies, 1113 eyes (LASIK vs. PRK) OR = 1.41, 95%CI 1.00 to 2.00, p=0.049 • % eyes with UCVA of 20/20 or better at 12 months post-treatment: 7 studies, 1007 eyes (LASIK vs. PRK) OR = 1.64, 95%CI 1.10 to 2.45, p=0.016 • Mean spherical equivalent at 2-4 weeks post-treatment: 9 studies, 1041 eyes (LASIK vs. PRK) Not pooled because of heterogeneity (I^2 83%); range -0.60 to 0.14 D • Mean spherical equivalent at 6 months post-treatment: 9 studies, 1024 eyes (LASIK vs. PRK) Not pooled because of heterogeneity (I^2 59%); range -0.26 to 0.60 D • Mean spherical equivalent at 12 months post-treatment: 6 studies, 599 eyes (LASIK vs. PRK) MD = -0.01, 95%CI -0.06 to 0.04, p=0.73 • % eyes with final BCVA 20/40 or worse at 6 months post-treatment: 6 studies, 442 eyes (LASIK vs. PRK) Only 2 events, in LASIK arm OR = 0.12, 95% CI 0.01 to 1.93; p=0.13 <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>:	Cochrane Risk of Bias Tool: one trail did not use an adequate sequence generation; two trials did not use adequate allocation concealment; 12 trials did not blind participants or personnel; eight trials did not blind outcome assessors for the outcome visual acuity or other outcomes; none of the trials reported outcome data incomplete; and none of the trials reported outcomes selectively. The quality of the evidence was considered low for most outcomes

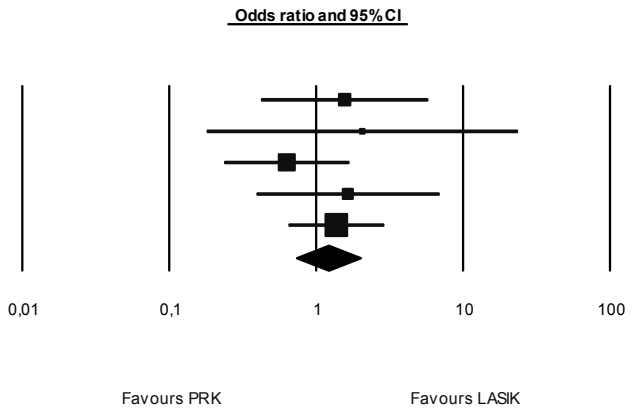
Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				Not reported <u>Safety</u>: • % eyes that lost ≥ 1 line of BCVA at 6 months post-treatment: 6 studies, 746 eyes (LASIK vs. PRK) OR = 0.88, 95%CI 0.51 to 1.50, p=0.63 • % eyes that lost ≥ 2 lines of BCVA at 6 months post-treatment: 11 studies, 1446 eyes (LASIK vs. PRK) OR = 0.47, 95%CI 0.23 to 0.98, p=0.043 • Pain scores: intraoperative pain was less with PRK (1 study) and postoperative pain was less after LASIK (2 studies) • Sub epithelial haze at 6-12 months post-PRK: o At 6 months: grade 0 range 41.7-96.1%, grade +1/2 to +2 range 3.9-58.4%, grade 3-4 range 0-4.4% o At 12 months: grade 0 range 54.2-100%, grade +1/2 to +2 range 0-41.7%, grade 3-4 range 0-3% • Flap-related complications in LASIK eyes: overall rate 3.8%, range 0.7-15% (6 studies) • Optical side effect: reported by 6 studies, but only 1 study reported a difference between treatments with more symptoms 2 years after PRK (35% vs. 21% reported glare, halos or flare) • Higher order aberrations (HOAs): reported by 7 studies; all but one of these studies show that both LASIK and PRK resulted in a statistically significant increase in HOAs post-treatment. One study found that HOAs were reduced in both PRK and LASIK post-treatment. When postoperative HOAs were compared between LASIK and PRK, only one study found a statistically significant difference, with fewer HOAs in the LASIK group	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Gamaly 2007 [4]	• RCT • Funding: not reported; CoI: none • Setting: single centre, Oman • Sample size: N=16, 32 eyes • Duration: not clearly reported, 6-month results presented	• Eligibility criteria: patients with myopia with or without astigmatism, age > 18 years, documented stable refraction for the past 12 months, poor candidates for LASIK because of thin corneas (< 500 µm) • Exclusion criteria: unstable refraction, keratoconus, suspected keratoconus, pellucid marginal degeneration, previous ocular surgery, active ocular or systemic disease that could affect corneal wound healing • Patient characteristics: mean age 24.8y; males 69.7%; mean preoperative manifest refractive spherical	Epithelial LASIK vs. PRK	<u>Visual acuity</u>: • % eyes with UCVA of 20/25 or better at 6 months post-treatment: 93.8% vs. 87.5%, NS • % eyes with UCVA of 20/20 or better at 6 months post-treatment: 75% vs. 68.8%, p-value not provided • % eyes with UCVA of 20/30 or better at 6 months post-treatment: 93.8% in both groups • % eyes with UCVA of 20/40 or better at 6 months post-treatment: 100% in both groups • % eyes within -0.5 D of intended manifest refractive spherical equivalent at 6 months post-treatment: 81.2% vs. 81.3%, p-value not provided <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>: Not reported <u>Safety</u>: • No complications during surgery in either group • % eyes that lost ≥ 2 lines of BCVA at 6 months post-treatment:	Randomization schedule generated by a biostatistician Treatment with LASIK in one eye and PRK in other eye Patients were blinded to allocation Unclear allocation concealment, blinding of assessors After 6 months only 75% available for follow-up

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		equivalent -2.76 D		0% in both treatment groups • Subepithelial haze at 6 months: grade 0: 71% vs. 36%; trace: 29% vs. 29%; grade 1: 0% vs. 21%; grade 2: 0% vs. 7%; grade 3: 0% vs. 7%; grade 4: 0% vs. 0% • Postoperative pain: no actual numbers or p-values provided	

Figure 2 – Meta-analysis of ≥1 lines of BCVA lost at ≥6 months post-treatment, PRK vs. LASIK

Study name	Outcome	Statistics for each study					Events / Total	
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	PRK	LASIK
Gamaly 2007	Lostone or more lines of BCVA at six months or more post-treatment	1,565	0,418	5,864	0,664	0,507	7 / 24	5 / 24
Manche 2011	Lostone or more lines of BCVA at six months or more post-treatment	2,065	0,178	23,942	0,580	0,562	2 / 33	1 / 33
Morshirfar 2010	Lostone or more lines of BCVA at six months or more post-treatment	0,631	0,234	1,703	-0,908	0,364	8 / 61	11 / 57
Schallhorn 2009	Lostone or more lines of BCVA at six months or more post-treatment	1,647	0,388	7,001	0,676	0,499	5 / 176	3 / 172
SUMMIT 1998	Lostone or more lines of BCVA at six months or more post-treatment	1,375	0,641	2,948	0,818	0,413	22 / 68	16 / 62
		1,193	0,721	1,972	0,686	0,492		



Q-value= 2.26; I^2=0%
Meta-analysis using the primary studies identified in Shortt 2013 (analysis 1.13) plus another identified RCT (Gamaly 2007). Two studies with a total of 42 eyes in each arm had no events in either arm and are not depicted in the figure

Table 6 – Summary of findings for PRK vs. LASIK for patients with myopia with/without astigmatism, randomised data [3]

Outcome (follow-up)	Absolute effect: WMD (95%CI)	Relative effect: OR (95%CI)	N of primary studies (N of eyes)	Quality of the evidence (GRADE)	Comments
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR			
UCVA 20/20 or better (12 months)	NR	0.61 (0.41 to 0.91) [3]	7 (1007)	⊕⊕ ⊕⊙ moderate $	Excluding 2 studies at high risk of selection bias gave an OR of 0.72 (0.33 to 1.54) [3]
UCVA 20/40 or better	NR	NR			
Within 0.5 D target refraction (12 months)	NR	0.69 (0.48 to 1.01) [3]	7 (1007)	⊕⊕ ⊕⊙ moderate $	Excluding 2 studies at high risk of selection bias gave an OR of 0.75 (0.51 to 1.11) [3]
Within 1 D target refraction	NR	NR			
Postoperative spherical equivalent (12 months)	The mean postoperative spherical equivalent in the LASIK groups was 0 higher (0.06 lower to 0.04 higher) [3]	NR	6 (598)	⊕⊕ ⊕⊙ moderate $	
Return to work	NR	NR			
Rehabilitation time	NR	NR			
Quality of life	NR	NR			
Loss of ≥1 line of BCVA (≥6 months)	NR	1.19 (0.72 to 1.97) [3, 4] §	7 (794) [3, 4]	⊕⊕ ⊙⊙ low £	
Loss of ≥2 lines of BCVA (6 months)	NR	2.13 (1.02 to 4.35) [3] #	11 (1494) [3, 4]	⊕⊕ ⊕⊙ moderate $	
Corneal ectasia	NR	NR			

Keratitis/infection	NR	NR		
Healing time of corneal epithelium	NR	NR		
Retinal detachment	NR	NR		
Choroidal neovascularisation	NR	NR		
Epithelial in growth	NR	NR		
Raised intraocular pressure	NR	NR		
Re-treatment	NR	NR		
Sub-epithelial haze (6-12 months)	NR	NR	9 (NR)	Grade 2: median 2.1% (range: 0-13%). Grade 3: median 0% (range: 0-7%); grade 4: 0% (range: 0-3%) in PRK treated eyes [3, 4]
Haloes and/or glare	NR	NR	7 (NR)	Optical side-effects were reported by 6 RCTs; only one RCT reported a difference in treatments with more side-effects 2 years after PRK (35% vs. 21% reported glare, halos or flare) [3] 7 RCTs reported on higher order aberrations: 6 out of 7 studies show that both LASIK and PRK resulted in a statistically significant increase in aberrations post-treatment. One study found that aberrations were reduced in both PRK and LASIK post-treatment. When postoperative aberrations were compared between LASIK and PRK, only one study found a statistically significant difference, with fewer HOAs in the LASIK group [3]
Night driving problems	NR	NR		
Dryness	NR	NR		
Flap-related complications	NR	NR	6 (NR)	Median 5.0% in LASIK-eyes (range:

				0 to 15%) [3, 4]
Pain	See comment	Not estimable	3 (NR)	3 studies reported pain scores; significantly more pain experienced in the PRK group[3]

Abbreviations: BCVA: best spectacle corrected visual acuity; CI: confidence interval; D: diopter; N: number; NR: not reported; OR: odds ratio; SD: standard deviation; UCVA: uncorrected visual acuity; WMD: weighted mean difference
$ Serious risk of bias (none of the trials were masked and so were considered to be at risk of performance and detection bias; in two trials allocation was not properly concealed and therefore they were at risk of selection bias); no serious inconsistency; no serious indirectness; no serious imprecision; no other considerations
§ Meta-analysis using data from six primary studies selected by Shortt 2013 (analysis 1.13), plus the RCT we identified that was not included by Shortt 2013, Gamaly 2007 [4] (Figure 2)
£: Serious risk of bias (none of the trials were masked and so were considered to be at risk of performance and detection bias; in two trials allocation was not properly concealed and therefore they were at risk of selection bias); no serious inconsistency; no serious indirectness; serious imprecision (the 95%CI includes 1 with a substantial effect size in either direction); no other considerations
 # No events in the Gamaly 2007 trial so the meta-analysis result from Shortt 2013 applies

Table 7 – PRK vs. LASIK for hyperopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Settas 2012 [5]	• SR • Funding: not reported; CoI: none • Databases searched: CENTRAL, Medline, EMBASE, LILACS, mRCT, ClinicalTrials.gov, WHO ICTRP, reference lists, Science Citation Index, reference lists, Science Citation Index • Search date: February 2012 • Languages included: all • Number of studies included: 0	• Eligibility criteria: RCTs; age > 18y, any degree of primary hyperopia (including hyperopic astigmatism) • Exclusion criteria: history of previous refractive or other eye surgery, co-existing ocular pathology, systemic disease that affects wound healing • Patient characteristics: no trials included	LASIK vs. PRK	<u>Visual acuity</u>: Not reported <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>: Not reported <u>Safety</u>: Not reported	• In the absence of RCTs, the authors discuss 5 non-randomized trials. However, their search was not focused on this type of studies

Table 8 – LASEK vs. LASIK for myopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 3 RCTs (of which 1 in abstract form)	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: range myopia -1.0 to -13.0 D, range mean age 20.5-26.8y • Follow-up: 3-12 months	LASEK vs. LASIK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction: 1 study, 40 eyes (LASEK vs. LASIK) 65% (13/20) vs. 95% (19/20), p-value not reported • % refractions within 1 D of intended spherical equivalent correction: 1 study, 394 eyes (LASEK vs. LASIK) 85% (156/184) vs. 84% (176/210), p>0.05 • % eyes with final UCVA of 20/20 or better: 1 study, 394 eyes (LASEK vs. LASIK) 85% (156/184) vs. 84% (176/210), p=0.64 • % eyes with final UCVA of 20/40 or better: 1 study, 40 eyes (LASEK vs. LASIK) 70% (14/20) vs. 95% (19/20), p-value not reported Return to work: Not reported Rehabilitation time: Not reported Quality of life: Not reported Safety: • % eyes that lost 1 or 2 lines of BCVA post-treatment: 3 studies, 498 eyes (LASEK vs. LASIK)	Included studies: Kaya 2004, Sheng 2004, Bansal 2003 Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the main risks for bias in the two full text studies were as follows (the RCT in abstract form was not appraised): participants were not blinded in one study (unclear in the other assessed study); and the analysis did not include an intention to treat analysis in one RCT. The paired nature of eyes was taken into account in the analyses. The source of funding was unclear for all three studies

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				4/236, median 0% (range 0-20%) vs. 2/262, median 0% (range 0-1%) • No data reported on potentially serious complications • Undesired postoperative consequences (LASEK vs. LASIK): punctate corneal defect (Sheng 2004): 16% vs. ?%; flap complications: 9% (Kaya 2004) vs. 1% (Sheng 2004); epithelial ingrowth: ? vs. 0.5% (Sheng 2004); increased intra-ocular pressure: 1.6% (Sheng 2004) vs. ? • Haze at 3 months: LASEK vs. LASIK o Bansal 2003: grade 2 or more: 35% vs. 0%, no p-value reported o Sheng 2004: grade 1: 9% vs. 0%, no p-value reported	

Table 9 – Summary of findings for LASEK vs. LASIK for patients with myopia with/without astigmatism, randomised data [2]

Outcome (follow-up)	Absolute effect: WMD (95%CI)	Relative effect: OR (95%CI)	N of primary studies (N of eyes)	Quality of the evidence (GRADE)	Comments
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR			
UCVA 20/20 or better (6 months)	NR	NR	1 (394)	⊕⊕⊕ moderate § ⊙	85% (156/184) vs. 84% (176/210), p=0.64 [2]
UCVA 20/40 or better (3 months)	NR	NR	1 (40)	⊕⊕⊕ moderate $ ⊙	70% (14/20) vs. 95% (19/20), p=0.04 [2]
Within 0.5 D target refraction (3 months)	NR	NR	1 (40)	⊕⊕⊕ moderate $ ⊙	65% (13/20) vs. 95% (19/20), p=0.02 [2]
Within 1 D target refraction (6 months)	NR	NR	1 (394)	⊕⊕⊕ moderate § ⊙	85% (156/184) vs. 84% (176/210), p>0.05 [2]
Postoperative spherical equivalent	NR	NR			

Return to work	NR	NR			
Rehabilitation time	NR	NR			
Quality of life	NR	NR			
Loss of ≥1 line of BCVA (3-12 months)	NR	NR	3 (498)	⊕⊕ ⊙⊙ low #	4/236, median 0% (range 0-20%) vs. 2/262, median 0% (range 0-1%) [2]
Loss of ≥2 lines of BCVA (6 months)	NR	NR	1 (64)	⊕⊕ ⊙⊙ low #	0/32 vs. 0/32 [2]
Corneal ectasia	NR	NR			
Keratitis/infection	NR	NR			
Healing time of corneal epithelium	NR	NR			
Retinal detachment	NR	NR			
Choroidal neovascularisation	NR	NR			
Epithelial in growth	NR	NR	1 (210)	Not applicable £	Reported in 1/210 LASIK patients [2]
Raised intraocular pressure	NR	NR	1 (184)	Not applicable £	3/184 LASEK patients [2]
Re-treatment	NR	NR			
Haze grade ≥2 (3 months)	NR	NR	1 (40)	⊕⊕⊕ ⊙ moderate $	35% (7/20) vs. 0% (0/20), p=0.004 [2]
Haloes and/or glare	NR	NR			
Night driving problems	NR	NR			
Dryness	NR	NR			
Flap-related complications	NR	NR	2 (242)	Not applicable £	3/32 LASEK patients in 1 RCT and in 2/210 LASIK patients in another trial
Pain	NR	NR			

Abbreviations: BCVA: best spectacle corrected visual acuity; CI: confidence interval; D: diopter; N: number; NR: not reported; OR: odds ratio; SD: standard deviation; UCVA: uncorrected visual acuity; WMD: weighted mean difference

§: Serious risk of bias (non-blinded participants); no serious inconsistency; no serious indirectness; no serious imprecision; no other considerations

#: Serious risk of bias (non-blinded participants in 1 study; no ITT analysis in 1 study); no serious inconsistency; no serious indirectness; serious imprecision (very few events leading to fragility of results); no other considerations

$: No serious risk of bias; no serious inconsistency; no serious indirectness; serious imprecision (1 trial with 40 eyes leading to fragility of results); no other considerations

£: non-comparative outcome. Rate of one trial arm reported

Table 10 – LASEK vs. LASIK for hyperopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 0 RCTs	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: no trials	LASEK vs. LASIK	<u>Visual acuity</u>: Not reported <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>: Not reported <u>Safety</u>: Not reported	

Table 11 – Intra-ocular lenses vs. laser refractive eye surgery for myopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Albarran-Diego 2012 [6]	• RCT • Funding: supported in part by Ministerio de Ciencia e Innovación Research Grant (#SAF2009-13342#); CoI: none • Setting: single centre, Spain • Sample size: N=46, 92 eyes • Duration: not clearly reported, 12-month results presented	• Eligibility criteria: patients with moderate myopia (-6.0 to -9.0 D), astigmatism ≤1.0 D, age> 18 years, corrected distance visual acuity of 0.3 logMAR (20/40 Snellen) or better, stable refraction, clear central cornea • Exclusion criteria: previous corneal refractive surgery, anterior chamber depth measured from the endothelium < 2.8 mm, corneal endothelial cell density < 2000 cells/mm2, mesopic pupil size > 7.0 mm, and history of uveitis, amblyopia, glaucoma, retinal detachment, diabetic retinopathy, macular degeneration, neuro-ophthalmic disease	Bilateral femtosecond laser-assisted LASIK vs. Phakic intra-ocular lens implantation (Artiflex)	<u>Visual acuity</u>: • % eyes with UDVA of 20/25 or better at 12 months post-treatment: 93.5% vs. 100%, NS • % eyes with UDVA of 20/20 or better at 12 months post-treatment: 37% (n=17) vs. 41.3% (n=19), NS • % eyes with spherical equivalent refraction within +/- 0.5 D at 12 months post-treatment: 91.3% (n=42) vs. 89.1% (n=41), NS • Mean spherical equivalent refraction at 12 months post-treatment (before retreatment): -0.07 D ±0.36 vs. -0.17 D ±0.33, p=0.19 • Efficacy index at 12 months post-treatment: 0.95 vs. 1.00 <u>Return to work</u>: Not reported <u>Rehabilitation time</u>: Not reported <u>Quality of life</u>: Not reported	Randomization by computer Unclear allocation concealment, blinding and intention-to-treat analysis

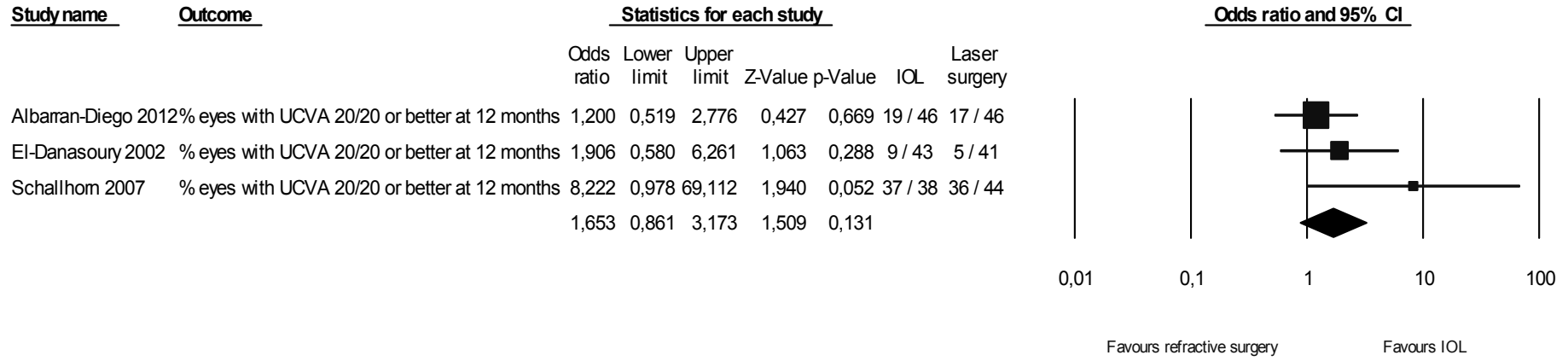
Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		• Patient characteristics: no significant group differences; mean age 31.4 vs. 30.5y; corneal thickness 562 vs. 557 µm, anterior chamber depth 3.08 vs. 3.11 mm, spherical equivalent -7.15 vs. -7.37 D, uncorrected distance visual acuity 1.31 vs. 1.42 logMAR, intraocular pressure 15.6 vs. 16.2 mmHg		Safety: • % eyes that lost ≥ 1 line of CDVA at 12 months post-treatment: 0% in both treatment groups • Pigment deposits: 6.5% after lens implantation • Superficial punctate keratopathy: 91.3% vs. 34.8% at 1 week postoperatively, p<0.001 • Artificial tears use at 12 months: 56.6% vs. 21.7%, p=0.06 • Night halos at 12 months: 17.4% vs. 13.0%, p=0.69 • Retreatment rate: 10.9% vs. 17.4%, p=0.37	
Barsam 2012a [7] **Barsam 2012b** [8]	• SR + MA • Funding: not reported; CoI: none • Databases searched: CENTRAL, Medline, EMBASE, LILACS, mRCT, ClinicalTrials.gov, WHO ICTRP, reference lists, experts, Science Citation Index, FDA trials database • Search date: November 2011 • Languages included: all • Number of studies	• Eligibility criteria: RCTs; age 21-60y, myopia > 6.0 D • Exclusion criteria: age > 60y, myopia < 6.0 D; other refractive errors, e.g. post corneal graft; participants with any other simultaneous ocular disease • Patient characteristics (N=132): 228 treated eyes, age	Phakic intraocular lens (IOL) insertion (Artisan phakic IOL in 2 RCTs and Visian Implantable Collamer Lens in 1 RCT) vs. excimer laser refractive surgery (PRK in 1 study, LASIK in 2 studies)	Visual acuity: • % eyes with UCVA of 20/20 or better at 12 months post-treatment: 2 trials, 166 eyes OR = 1.33, 95%CI 0.08 to 22.55, p=0.84 • % eyes with UCVA of 20/20 or better at 6 months post-treatment: 2 trials, 157 eyes OR = 0.99, 95%CI 0.25 to 3.91, p=0.99 • % eyes with UCVA of 20/40 or better at 6 months post-treatment: 2 trials, 125 eyes OR = 0.71, 95%CI 0.36 to 1.39,	Included studies: el Danasoury 2012, Malecaze 2002, Schallhorn 2007 Author´s quality appraisal with Cochrane Risk of Bias Tool: the main risk of bias was that participants were not blinded in all three studies. One out of three RCTs blinded the outcome assessors; for the other two trials this was unclear

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	included: 3 RCTs	range 21-52y, myopia range 6.0-20.0 D (with up to 4.0 D of myopic astigmatism)		p=0.32 • % eyes with UCVA of 20/40 or better at 12 months post-treatment: 2 trials, 134 eyes OR = 0.66, 95%CI 0.36 to 1.22, p=0.18 • % refractions within 0.5 D of intended spherical equivalent correction at 12 months: 3 studies, 216 eyes OR = 0.72, 95%CI 0.40 to 1.29 • % refractions within 1 D of intended spherical equivalent correction at 12 months: 3 studies, 216 eyes OR = 1.01, 95%CI 0.42 to 2.45 Return to work: Not reported Rehabilitation time: Not reported Quality of life: Not reported Safety: • % eyes that lost ≥ 2 lines of BCVA at 6 months post-treatment: 1 study 0% in both treatment groups % eyes that lost ≥ 2 lines of BCVA at	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				12 months post-treatment: 3 studies, 216 eyes OR = 0.35, 95%CI 0.19 to 0.66, p=0.001 • % eyes that lost ≥ 1 line of BCVA at 6 months post-treatment: 1 study No differences, p=0.12 • % eyes that lost ≥ 1 line of BCVA at 12 months post-treatment: 3 studies, 216 eyes OR = 0.41, 95%CI 0.33 to 0.51, p=0.00001 • Incidence of flap/interface/decentred ablation/haze related complications in laser treated eyes: 1 in 45 LASIK treatments (1 study) • Endothelial cell loss: no significant differences in 2 studies • Incidence of cataract in the phakic IOL group: 2.3% in 1 study (1 patient, 2 year follow-up), no reported cases in 2 studies =1 out of 106 IOL patients (1%) • Incidence of glaucoma uveitis in the phakic IOL group: no cases of glaucoma or uveitis; 4.4% transient ocular hypertension in 1 study • Need for IOL exchange in the phakic IOL group: 2.2-2.3% in 2 studies =2 out of 106 patients (1.9%) • Changes in contrast sensitivity:	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				benefit in favour of phakic IOL, not significant in 1 study, significant in 1 study, significance not reported in 1 study • Quality of vision: all 3 studies showed that glare and halos were more of a problem with excimer laser than with phakic IOL	

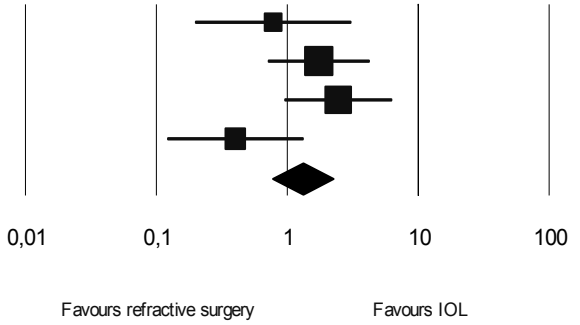
Figure 3 – Meta-analysis of % of eyes with an UCVA of 20/20 or better at 12 months post-treatment, IOL vs. laser surgery



Update of the meta-analysis from Barsam 2012 with the newer RCT by Albarran-Diego 2012, using data of the primary studies selected in Barsam 2012
Q-value: 2.79; I^2=28.46

Figure 4 – Meta-analysis of % of eyes within ± 0.5 D of target refraction at 12 months, IOL vs. laser surgery

Study name	Outcome	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	IOL	Laser surgery
Albarran-Diego 2012	% eyes within ±0.5 D of target refraction at 12 months	0,781	0,196	3,115	-0,350	0,726	41 / 46	42 / 46
El-Danasoury 2002	% eyes within ±0.5 D of target refraction at 12 months	1,740	0,704	4,303	1,199	0,230	18 / 43	12 / 41
Schallhorn 2007	% eyes within ±0.5 D of target refraction at 12 months	2,449	0,941	6,374	1,835	0,067	29 / 38	25 / 44
Malecaze 2002	% eyes within ±0.5 D of target refraction at 12 months	0,402	0,120	1,349	-1,476	0,140	6 / 25	11 / 25
		1,293	0,759	2,204	0,944	0,345		



Update of the meta-analysis from Barsam 2012 with the newer RCT by Albarran-Diego 2012, using data of the primary studies selected in Barsam 2012
Q-value: 6.21; I^2=51.72%

Table 12 – Summary of findings for intra-ocular lenses vs. laser refractive surgery for patients with myopia with/without astigmatism, randomised data [6, 7]

Outcome (follow-up)	Absolute effect: WMD (95%CI)	Relative effect: OR (95%CI)	N of primary studies (N of eyes)	Quality of the evidence (GRADE)	Comments
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR			
UCVA 20/20 or better (12 months)	NR	1.65 (0.86 to 3.17) [6, 7]	3 (258) #	⊕⊕ ⊙⊙ low $	
UCVA 20/40 or better (12 months)	NR	0.66 (0.36 to 1.22) [7]	2 (134)	⊕⊕ ⊙⊙ low $	
Within 0.5 D target refraction	NR	1.29 (0.76 to 2.20) [6, 7]	4 (308) #	⊕⊕ ⊙⊙ low $	
Within 1 D target refraction	NR	NR			
Postoperative spherical equivalent	NR	NR			
Return to work	NR	NR			

Rehabilitation time	NR	NR			
Quality of life	NR	NR			
Loss of ≥1 line of BCVA (12 months)	NR	0.41 (0.33 to 0.51) [6, 7]	4 (308) §	⊕⊕ moderate £	⊕⊙
Loss of ≥2 lines of BCVA (12 months)	NR	0.35 (0.19 to 0.66) [6, 7]	4 (308) §	⊕⊕ moderate £	⊕⊙
Corneal ectasia	NR	NR			
Keratitis/infection	NR	NR			
Healing time of corneal epithelium	NR	NR			
Retinal detachment	NR	NR			
Choroidal neovascularisation	NR	NR			
Epithelial in growth	NR	NR			
Raised intraocular pressure	NR	NR			
Re-treatment	NR	NR	3 (152)		Median need for IOL exchange in the IOL groups: 2.3% (range: 2.2 to 17.4%) (10 out of 152 eyes) [6, 7]
Haze grade ≥2	NR	NR			
Haloes and/or glare	NR	NR	4 (308)		Three studies showed that glare and halos were more of a problem with laser surgery than with IOL [7] One study showed no difference in night halos (13% vs. 17.4%, p=0.69) [6]
Night driving problems	NR	NR			
Dryness	NR	NR	1 (92)	⊕⊕ moderate £	⊕⊙ Artificial tears use at 12 months: 21.7% vs. 56.6%, p=0.06 [6]
Flap-related complications	NR	NR	1 (45)		Incidence of flap/interface/de-centered ablation/haze related

				complications in laser treated eyes: 1 in 45 LASIK treatments [7]
Cataract, glaucoma or uveitis	NR	NR	3 (106)	Incidence of cataract in the IOL group: 1 patient in 1 study, no reported cases in 2 studies (1 out of 106 eyes; 1%)[7] Incidence of glaucoma uveitis in the IOL group: no cases of glaucoma or uveitis; 4.4% transient ocular hypertension in 1 study [7]
Pain	NR	NR		

Abbreviations: BCVA: best spectacle corrected visual acuity; CI: confidence interval; D: diopter; IOL: intra-ocular lens; N: number; NR: not reported; OR: odds ratio; UCVA: uncorrected visual acuity; WMD: weighted mean difference

 # Update of the meta-analysis of Barsam 2012 with the newly identified RCT of Albarran-Diego 2012 (Figure 3 and Figure 4)

$: Serious risk of bias (due to likely non-blinded participants and outcome assessors); no serious inconsistency; no serious indirectness; serious imprecision (95%CI includes 1 with a substantial effect on either side); no other considerations

§ The newly identified RCT of Albarran-Diego did not contribute to the existing meta-analysis of Barsam 2012 as it had zero events in both trial arms for this outcome. Number of eyes were added to the number of eyes in Barsam 2012

£: Serious risk of bias (due to likely non-blinded participants and outcome assessors); no serious inconsistency; no serious indirectness; no serious imprecision; no other considerations

Table 13 – Intra-ocular lenses vs. laser refractive eye surgery for hyperopia with or without astigmatism, randomised data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
OHTAS 2009 [9]	• SR • Funding: Ontario Ministry of Health and Long-Term Care; CoI: none • Databases searched: Medline, EMBASE, Cochrane Library, INAHTA, CRD • Search date: 2003 – January 2009 • Languages included: English • Number of studies included: 0 RCTs	• Eligibility criteria: adult patients (at least 18y) with myopia, hyperopia or astigmatism • Exclusion criteria: studies with <20 eyes for each refractive error type • Patient characteristics: no studies	LASIK vs. Phakic intraocular lens (IOL) insertion	Visual acuity: Not reported Return to work: Not reported Rehabilitation time: Not reported Quality of life: Not reported Safety: Not reported	

Table 14 – PRK for myopia, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Goreishi 2009 [10]	• Retrospective study • Funding: not reported; CoI: not reported • Setting: single centre, Iran • Years: 2006-2007 • Number of patients: 1250 eyes • Follow-up: 1 year	• Eligibility criteria: 18 years of age; good ocular and general health; refractive error had been stable for at least one year • Exclusion criteria: corneal or anterior segment pathology, eyelid	PRK	Visual acuity: • % eyes with UCVA of 20/20 or better at 1 year: 92.1% • % refractions within 0.5 D of intended spherical equivalent correction at 1 year: 69.4% • % refractions within 1 D of intended spherical equivalent correction at 1 year: 91% Safety:	• Consecutive eyes

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		disease, uncontrolled glaucoma, untreated retinal pathology, progressive or unstable myopia, and previous intraocular or corneal surgery • Patient characteristics: mean preoperative spherical equivalent refractive error: -4.85±2.27 D (range: -2.50 to -13.5); mean astigmatism 2.35± 1.25 D (range, 0 to -3.5); mean age 31.5 ±12 years		• % eyes that lost 1 or 2 lines of BCVA 1 year post-treatment: 4.9% • % eyes with haze grade 3 at 1 year: 0.3% • % eyes with haze grade 4 at 1 year: 0.2% • Infectious keratitis: 0% • Corneal ectasia: 0%	
Leccisotti 2007 [11]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, Italy • Years: 2001-2005 • Number of patients: 6543 eyes	• Eligibility criteria: myopia or myopic astigmatism • Exclusion criteria: incomplete data or follow-up; any kind of preoperative corneal scar, including severe post-PRK haze; previous corneal	PRK	Visual acuity: • Not reported Safety: • % eyes with corneal ectasia: 0.03%	• Consecutive eyes • Patients with incomplete follow-up were excluded • A myopic and/or myopic astigmatic refractive change >1 D in the postoperative period was

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	• Follow-up: ≥ 18 months	surgery other than PRK • Patient characteristics: not reported			considered essential to confirm the diagnosis of corneal ectasia, as well as a reduction in BCVA
Lee 2005 [12]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, South Korea • Years: not reported • Number of patients: 1011 eyes • Follow-up: mean 13 months (range 6-27 months)	• Eligibility criteria: healthy myopic patients 18 years of age or older; refractive error had to be stable for at least 1 year • Exclusion criteria: no history of ocular surgery or trauma and no ocular pathology other than refractive error • Patient characteristics: mean preoperative spherical equivalent: -7.82 D ±2.64; mean age 29 years ±6.2	PRK	Visual acuity: • % eyes with UCVA of 20/20 or better at 6 months: 86% • % refractions within 1 D of intended spherical equivalent correction at 6 months: 93% • % refractions within 0.5 D of intended spherical equivalent correction at 6 months: 86% Safety: • % eyes that lost 1 line of BCVA 6 months post-treatment: 8% • % eyes that lost ≥ 2 line of BCVA 6 months post-treatment: 0% • % eyes with haze ≥ grade 1 at 6 months: 3.2% • % eyes with haze ≥ grade 2 at 6 months: 0.5% • % eyes with haze ≥ grade 3 at 6 months: 0.2%	• Consecutive eyes • No loss to follow-up at 6 months; 408 eyes (40.4%) had a follow-up >6 months
Lee 2006 [13]	• Retrospective study • Funding: not reported; CoI: not reported	• Eligibility criteria: myopic Singapore residents with ≥1 year follow-up	PRK	Visual acuity: • Not reported	• Eyes with a follow-up <1 year were excluded

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	• Setting: single centre, Singapore • Years: 1998-2001 • Number of patients: 1982 eyes • Follow-up: ≥ 1 year	after PRK • Exclusion criteria: not reported • Patient characteristics: mean age 33 ±8 years; mean preoperative spherical equivalent -4.43 ±1.83 D (range: -16.88 to -0.25)		Safety: • % eyes with retinal detachment: 0.2% (4/1982)	• Article is letter • Different denominators mentioned in article: 1982 seems right one as is mentioned most frequently and in all tables
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism; full-text prospective studies with > 50 eyes or retrospective studies with > 100 eyes • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error	PRK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 3-6 months: 7 studies, 1 726 eyes median 75.9%, range 53.9-92.3% • % refractions within 1 D of intended spherical equivalent correction at 3-6 months: 8 studies, 2 135 eyes median 93%, range 48.0-97.8% • % refractions within 0.5 D of intended spherical equivalent correction after at least 12 months: 10 studies, 1 909 eyes median 68%, range 56.5-87.4% • % refractions within 1 D of intended spherical equivalent correction after at least 12 months: 13 studies, 2 587 eyes median 86%, range 39.1-95.8% • % eyes with UCVA of 20/20 or better at 3-6 months: 5 studies, 1 046 eyes	Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the main quality appraisal findings across 40 studies (including those on hyperopia and astigmatism) were: • 13/40 studies did not describe the inclusion/exclusion criteria of the patients clearly • One out of 40 studies did not select participants

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	included: 30 case series (+/- 15 785 eyes)	following cataract or corneal graft surgery • Patient characteristics: mean age 22-46y, mean spherical equivalent -2.10 to -11.43 D		median 66.7%, range 54.9-69.9% • % eyes with UCVA of 20/40 or better at 3-6 months: 6 studies, 1 309 eyes median 93%, range 48.9-98.6% • % eyes with UCVA of 20/20 or better after at least 12 months: 10 studies, 1 991 eyes median 70.4%, range 39.1-87.0% • % eyes with UCVA of 20/40 or better after at least 12 months: 9 studies, 1 900 eyes median 92.3%, range 37.6-98.8% Safety: 30 studies, +/- 15 785 eyes (range 51 – 5 936), follow-up range 1 month to 12 years • % eyes that lost 1 line of BCVA post-treatment: 9 studies, 1 173 eyes 4.5%, range 0.7-15.3% • % eyes that lost ≥ 2 line of BCVA post-treatment: 12 studies, 2 165 eyes 0.5%, range 0-20.5% • No studies reported incidence of ectasia • Rate of potentially serious complications (1 study each): keratitis/infection (54 eyes) 0%, persistent epithelial defect (54 eyes) 0%, retinal detachment (5 936 eyes) 0.15%, choroidal neovascularization (5 936 eyes) 0.02%, epithelial ingrowth (161 eyes) 0.62% • Undesired complications: infiltrates 0.62-2.5% (2 studies, 21 eyes), delayed re-epithelisation 1.3-4.1%, regression 3.9-20.8%, over correction 3.2-8.0%, under correction 4.0-	consecutively (unclear for 24 studies) • 14 out of 40 studies collected data retrospectively (unclear for four studies) • 29 out of 40 studies did not report data on non-respondents and dropouts • In six out of 40 studies participants lost to follow-up were considered likely to introduce bias (unclear for 33 studies) • In 11 out of 40 studies the paired nature of eyes was taken into account in the analyses (unclear for 27 studies)

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				9.9%, raised intraocular pressure 0-7.6% (5 studies, 1108 patients), re-treatment median 1.5% (range: 1.2-3.6%, 3 studies, 948 eyes); haze: median % eyes with haze grade 2 or more 0% (range 0-31.4%) (10 studies, 1 443 eyes) at 1 month to 12 years • Participant reported outcomes: haloes and/or glare median 17% (range: 2.-23.8%, 5 studies 2 126 eyes; 6-18 months), problems with night driving 5.2-57.7% (divers definitions), night vision problems 12%, epiphora 44.2%, photophobia 36.5%, foreign body sensation 5.9-38.5%, itching 38.5%, dryness 41.1%, soreness 27%, eyelid sticking 15.4%, sharp pains 20.3%; pain: % with Present Pain Intensity score 4-5 days post-surgery ≥3 (distressing to excruciating pain): median 28% (range: 25-31%) (2 studies, 132 eyes)	
Sia 2012 [14]	• Retrospective chart review • Funding: none; CoI: none • Setting: United States • Years: 2008-2010 • Number of patients: 1431 eyes • Follow-up: ≥6 months	• Eligibility criteria: patients who underwent either brush or alcohol-assisted PRK for spherical myopia or myopic astigmatism, with ≥ 6 months follow-up • Exclusion criteria: LASIK patients; hyperopic or mixed astigmatic treatments; retreatment cases	PRK	Visual acuity: • % eyes with UCVA of 20/20 or better at 6 months: 94.5% • % eyes with UCVA of 20/20 or better at 1 year: 94.8% • % refractions within 0.5 D of intended spherical equivalent correction at 6 months: 92.5% • BCVA same or better than preoperatively: 95.9% Safety: • % eyes that lost 1 line of BCVA 6 months post-treatment: 4%	• Only cases with a follow-up of ≥6 months included (90% of all cases) • Follow-up at 1 year: 55% • Study compared brush vs. alcohol technique; data combined here

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		• Patient characteristics: active military personnel; mean age ~33 years; mean spherical equivalent ~ -3.5 D		• % eyes that lost ≥ 2 line of BCVA 6 months post-treatment: 0% • % eyes with haze ≥ grade 1 at 1 year: 0% • ´Infection, delayed epithelial healing, steroid induced glaucoma and recurrent corneal erosions were comparably infrequent between the two treatment groups at each postoperative visit´ (actual data not reported)	
Wrobleski 2006 [15]	• Retrospective chart review • Funding: none; CoI: none • Setting: multicentre, United States • Years: 1995-2004 • Number of patients: 25337 eyes • Follow-up: 1 year	• Eligibility criteria: not reported • Exclusion criteria: not reported • Patient characteristics: not reported	PRK	Visual acuity: • % Not reported Safety: • Culture proven or clinically suspicious infectious keratitis: 0.02% (5/25337; 4 Staphylococcus (2 MRSA) and 1 culture negative)	• Consecutive eyes • Loss to follow-up unclear, 3-month follow-up of 1 centre currently 61%

Table 15 – Summary of findings for visual acuity and safety of PRK for patients with myopia, observational data [2, 10-15]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR	
UCVA 20/20 or better (≥12 months)	76.0% [2, 10]	39.1-94.8%	12 (3 872)
UCVA 20/40 or better (≥12 months)	92.3%	37.6-98.8%	9 (1 900)
Within 0.5 D target refraction (≥12 months)	69.4% [2, 10]	56.5-87.4%	9 (2 949)
Within 1 D target refraction (≥12 months)	91.0% [2, 10]	39.1-95.8%	11 (3 361)
Postoperative spherical equivalent	NR	NR	
Loss of 1 line of BCVA (≥6 months)	4.5% [2, 12, 14]	0.7-15.3%	11 (3 705)
Loss of ≥2 lines of BCVA (≥6 months)	0.3% [2, 12, 14]	0-20.5%	14 (4 607)
Corneal ectasia	0.015% [10, 11]	0 to 0.03%	2 (7 793)
Keratitis/infection (≥6 months)	0% [2, 10, 15]	0-0.02%	3 (26 641)
Persistent epithelial defect (6 months)	0%	NA	1 (54)
Retinal detachment (≥ 1 year)	0.18% [2, 13]	0.15 to 0.2%	2 (7 918)
Choroidal neovascularisation (26 months)	0.02%	NR	1 (5 936)
Epithelial in growth (NR)	0.62%	NA	1 (161)
Cataract	NR	NR	
Raised intraocular pressure (1 months-12 years)	1.9%	0-7.6%	5 (1 108)
Re-treatment (6-18 months)	1.5%	1.2-3.6%	3 (948)
Haze grade ≥2 (1 month-12 years)	0% [2, 12, 14]	0-31.4%	12 (3 885)
Haloes and/or glare (6-18 months)	17%	2.4-23.8%	5 (2 126)
Night vision/driving problems (1 week-6 months)	31.1%	5.2-57.7%	3 (1 249)
Dryness (6 months)	41.1%	NA	1 (241)
Pain (PPI≥3, 4 to 5 days post-treatment)	28%	25-31%	2 (132)

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; PPI: present pain intensity score; UCVA: uncorrected visual acuity

Table 16 – PRK for myopic astigmatism, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 6 case series (+/- 7 009 eyes)	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism; full-text prospective studies with > 50 eyes or retrospective studies with > 100 eyes • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: mean age 32-43y, mean spherical equivalent -4.63 to -7.18 D	PRK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 3-6 months: 2 studies, 718 eyes median 58.7%, range 55.0-62.3% • % refractions within 1 D of intended spherical equivalent correction at 3-6 months: 3 studies, 774 eyes median 75%, range 62.5-86.1% • % refractions within 0.5 D of intended spherical equivalent correction after at least 12 months: 2 studies, 6 156 eyes median 55.3%, range 40.7-69.8% • % refractions within 1 D of intended spherical equivalent correction after at least 12 months: 3 studies, 6 630 eyes median 83.8%, range 81.3-87.9% • % eyes with UCVA of 20/20 or better at 3-6 months: 2 studies, 717 eyes median 60.2%, range 56.0-64.3% • % eyes with UCVA of 20/40 or better at 3-6 months: 3 studies, 773 eyes median 83.9%, range 82.0-93.5% • % eyes with UCVA of 20/20 or better after at least 12 months: 2 studies, 536 eyes median 62.6%, range 58.0-67.1% • % eyes with UCVA of 20/40 or better after at least 12 months: 3 studies, 6 633 eyes median 93.5%, range 91.2-95.0%	Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the main quality appraisal findings across 40 studies (including those on myopia and hyperopia) are presented above

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				Safety: 6 studies, +/- 7 009 eyes (range 70 – 6 097), follow-up range 3-24 months • % eyes that lost 1 line of BCVA post-treatment: 1 study, 56 eyes 7.1% • % eyes that lost ≥ 2 line of BCVA post-treatment: 3 studies, 592 eyes 0.6%, range 0-1.6% • No studies reported incidence of ectasia • Potentially serious complications: keratitis/infection 0.13% (1 study, 749 eyes, 18 months follow-up), infiltrates 0.1%, optic neuropathy 0.13%, corneal oedema 0.4%, vitreous haemorrhage 0.13% • Undesired complications: over correction 5.1%, under correction 13.6%, raised intraocular pressure 0.6%, re-treatment 25.8%; haze: in 1 study at 2y 0% moderate-severe haze, in 1 study at 6m 0.3% moderate haze, in 1 study no haze > grade 2 at any time during follow-up • Participant reported outcomes: increase from pre-PRK in halo score 37.3%, significant increase (unspecified) at 2 years; increase in glare score 27.1% at 1 year and non-significant increase (unspecified) at 2 years	

Table 17 – Summary of findings for visual acuity and safety of PRK for patients with myopic astigmatism, observational data

Outcome (follow-up)	Median [2]	Range [2]	N of primary studies (N of eyes) [2]
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR	
UCVA 20/20 or better (≥12 months)	62.6%	58.0-67.1%	2 (536)
UCVA 20/40 or better (≥12 months)	93.5%	91.2-95.0%	3 (633)
Within 0.5 D target refraction (≥12 months)	55.3%	40.7-69.8%	2 (6 156)
Within 1 D target refraction (≥12 months)	83.8%	81.3-87.9%	3 (6 630)
Postoperative spherical equivalent	NR	NR	
Loss of 1 line of BCVA	7.1%	NA	1 (56)
Loss of ≥2 lines of BCVA	0.6%	0-1.6%	3 (592)
Corneal ectasia	NR	NR	
Keratitis/infection (18 months)	0.13%	NA	1 (749)
Persistent epithelial defect (18 months)	0.13%	NA	1 (749)
Retinal detachment (18 months)	0.13%	NA	1 (749)
Choroidal neovascularisation	NR	NR	
Cataract	NR	NR	
Epithelial in growth	NR	NR	
Raised intraocular pressure (18 months)	0.6%	NA	1 (749)
Re-treatment (24 months)	25.8%	NA	1 (93)
Haze grade ≥2	3 different scales used in 3 different studies		
Haloes (12 months)	37.3%	NA	1 (NR)
Night driving problems	NR	NR	
Dryness	NR	NR	
Pain	NR	NR	

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; UCVA: uncorrected visual acuity

Table 18 – PRK for hyperopia with or without astigmatism, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 6 case series (+/- 1 599 eyes)	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism; full-text prospective studies with > 50 eyes or retrospective studies with > 100 eyes • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: mean age 35.4-51.8y, mean spherical equivalent 2.48-5.64 D	PRK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 3-6 months: 3 studies, 371 eyes median 67.4%, range 63.3-76.3% • % refractions within 1 D of intended spherical equivalent correction at 3-6 months: 3 studies, 371 eyes median 88.4%, range 86.7-91.3% • % refractions within 0.5 D of intended spherical equivalent correction after at least 12 months: 5 studies, 1 345 eyes median 60.8%, range 53.8-79.0% • % refractions within 1 D of intended spherical equivalent correction after at least 12 months: 5 studies, 1 345 eyes median 78.9%, range 69.6-86.0% • % eyes with UCVA of 20/20 or better at 3-6 months: 3 studies, 351 eyes median 39%, range 37.8-72.5% • % eyes with UCVA of 20/40 or better at 3-6 months: 3 studies, 351 eyes median 85.4%, range 85.0-89.1% • % eyes with UCVA of 20/20 or better after at least 12 months: 5 studies, 1 332 eyes median 59%, range 48.8-84.0% • % eyes with UCVA of 20/40 or better after at least 12 months: 5 studies, 1 332 eyes median 85.5%, range 72.1-95.1%	Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the main quality appraisal findings across 40 studies (including those on myopia and astigmatism) are presented above

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments

				Safety: 6 studies, +/- 1 599 eyes (range 52-800), follow-up range 6-36 months
				• % eyes that lost 1 line of BCVA 6-24 months post-treatment: 5 studies, 1 425 eyes
				16.3%, range 5.5-27.0%
				• % eyes that lost ≥ 2 line of BCVA 6-24 months post-treatment: 5 studies, 1 425 eyes
				7.0%, range 0-13.5%
				  • In eyes with +3.5 or lower: 2.1% (range: 0-11.3%)
				  • In eyes with hyperopia higher than +3.5: 20.2% (range: 9.6-30.8%)
				• No studies reported incidence of ectasia
				• Potentially serious complications: keratitis/infection 0% (1 study, 200 patients, at 12 months), corneal oedema 0.4%, recurrent corneal erosion 0-0.4%
				• Undesired complications: superficial punctuate keratitis 2.5%, infiltrates 0-1.1%, delayed re-epithelisation 1.9-4.3%, regression of UCVA 57%, over correction 1.0-1.8%, under correction 21.7%, raised intraocular pressure median: 8.6% (range: 8.5-8.6%, 2 studies, 1 000 eyes), re-treatment 0.7%; average haze at 12 months: < 3.5 D 0.16-0.22, > 3.5 D 0.24-0.34
				• Participant reported outcomes: haloes and/or glare at 1 week-12 months median 12.0% (range: 7.7-15.0%, 4 studies, 1 132 eyes); problems with night driving at 6-12 months: median 18% (range: 3.4-26.8%, 4 studies, 1 260 eyes); photophobia 7.7%, foreign body sensation 0.4%	

Table 19 – Summary of findings for visual acuity and safety of PRK for patients with hyperopia with/without astigmatism, observational data

Outcome (follow-up)	Median [2]	Range [2]	N of primary studies (N of eyes) [2]
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR	
UCVA 20/20 or better (≥12 months)	59%	48.8-84.0%	5 (1 332)
UCVA 20/40 or better (≥12 months)	85.5%	72.1-95.1%	5 (1 332)
Within 0.5 D target refraction (≥12 months)	60.8%	53.8-79.0%	5 (1 345)
Within 1 D target refraction (≥12 months)	78.9%	69.6-86.0%	5 (1 345)
Postoperative spherical equivalent	NR	NR	
Loss of 1 line of BCVA (6-24 months)	16.3%	5.5-27.0%	5 (1 425)
Loss of ≥2 lines of BCVA (6-24 months)	7.0%	0-13.5%	5 (1 425)
Corneal ectasia	NR	NR	
Keratitis/infection (12 months)	0%	NA	1 (200)
Persistent epithelial defect	NR	NR	
Retinal detachment	NR	NR	
Choroidal neovascularisation	NR	NR	
Epithelial in growth	NR	NR	
Cataract	NR	NR	
Raised intraocular pressure (NR)	8.6%	8.5-8.6%	2 (1 000)
Re-treatment (12 months)	0.7%	NA	1 (276)
Haze grade ≥2	NR	NR	
Haloes and/or glare (1 week-12 months)	12.0%	7.7-15%	4 (1 132)
Night driving problems (6-12 months)	18%	3.4-26.8%	4 (1 260)
Dryness	NR	NR	
Pain	NR	NR	

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; UCVA: uncorrected visual acuity

Table 20 – LASEK for myopia with or without astigmatism, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Kulkarni 2013 [16]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, Canada • Years: not reported • Number of patients: 560 eyes • Follow-up: minimum 3 months; 1 year follow-up data were available for 70-85% of patients	• Eligibility criteria: refraction -1.0 to -8.0 D, cylinder of 0 to +2D • Exclusion criteria: previous ocular or refractive surgery; other ocular pathology; unsuccessful wavefront capture; retreatment • Patient characteristics: mean age around 39 years (range: 20-62); 361 eyes had LASEK and 199 eyes had LASEK flap-off	LASEK	Visual acuity: • % eyes with UCVA of 20/20 or better at 1 year: ~90.5% (exact number of eyes with follow-up at 1 year unclear) • % refractions within 1 D of intended spherical equivalent correction at 1 year: 100% • Efficacy index at 1 year: 1.13 LASEK; 1.03 LASEK flap-off Safety: • % eyes that lost 1 line of BCVA 1 year post-treatment: ~5% (data in a figure, not in text) • % eyes that lost ≥ 2 line of BCVA 1 year post-treatment: 0% • % eyes with haze ≥ grade 1 at 1 year: 0% • Retreatment for under correction: 1.4% • Infection: 0%	• Consecutive eyes • Exact number of eyes lost to follow-up unclear
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism; full-text prospective studies with > 25 eyes or abstracts or retrospective	LASEK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 3-6 months: 14 studies median 75%, range 19-98% • % refractions within 1 D of intended spherical equivalent correction at 3-6 months: 14 studies median 92%, range 67-96% • % refractions within 0.5 D of intended spherical equivalent correction beyond 6 months: 8 studies , >1 080 eyes median 82%, range 42-96%	Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the most important negative findings in the quality assessment of the 17 full text studies were:

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	Controlled Trials, FDA database, conference proceedings, abstracts, reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 26 case series (5 091 eyes) of which 9 were only available as abstract	studies with > 50 eyes • Exclusion criteria: photorefractive surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: range mean age 26-42y, % women 52-73%, range mean preoperative spherical equivalent -2.48 to -12.0 D • Three studies included some patients with hyperopia; the inclusion criteria in two studies were unclear		• % refractions within 1 D of intended spherical equivalent correction beyond 6 months: 9 studies, >548 eyes median 90%, range 67-97% • % eyes with UCVA of 20/20 or better at 3-6 months: median 66%, range 39-100% • % eyes with UCVA of 20/40 or better at 3-6 months: median 96%, range 95-100% • % eyes with final UCVA of 20/20 or better at 12-24 months: 8 studies, >974 eyes median 62%, range 38-89% • % eyes with final UCVA of 20/40 or better at 12-24 months: 7 studies, >890 eyes median 92%, range 77-100% <u>Safety</u>: • % eyes that lost 1 line of BCVA 3-12 months post-treatment: 13 studies (1 722 eyes) median 2.2%, range 0-16% • % eyes that lost ≥ 2 line of BCVA 3-24 months post-treatment: 20 studies (2 545 eyes) median 0%, range 0-8.2% • Potentially serious complications, median: ectasia: 0% (1 study, 171 eyes, mean follow-up 8 months), perforation 0%, decentration of ablation 0-0.7%, acute epithelial complications 0%, recurrent erosion 0-1%, keratitis/infection 1.6% (0-3.4%, 4 studies, 952 eyes; 3-12 months follow-up), stromal melting 0%, scarring 0%, irregular astigmatism 1.4%, macular cyst 0.3%	• 3 out of 17 studies did not select participants consecutively • 4 out of 17 studies collected data retrospectively • 4 out of 17 studies did not report data on non-respondents and dropouts • in 7 out of 17 studies participants lost to follow-up were considered likely to introduce bias • in 2 out of 17 studies the paired nature of eyes was taken into account in the analyses

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				• Undesired complications: flap complications median: 2.0% (range: 0-14%, 9 studies, 959 eyes, 3-26 months follow-up); alcohol leakage 4%, central island 1.9%, raised intraocular pressure 1.2% (1 study, 84 eyes, 6 months follow-up); over or under correction 4%, regression 0-12.3%, retreatment median 1.0 (0-5.5%, >923 eyes) corneal haze of at least grade 2: 0% (0-25%, 16 studies, 2093 eyes; 3-12 months follow-up) • Participant reported outcomes: strong-severe post-operative pain median: 4.0% (range: 0-19%; 5 studies, 849 eyes; 6-26 months follow-up); dry eye syndrome median 3.0% (range. 0-33%; 4 studies, 489 eyes; 6-12 months follow-up)	

Table 21 – Summary of findings for visual acuity and safety of LASEK for patients with myopia with/without astigmatism, observational data [2, 16]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/mean BCVA preoperatively, 1 year)	NR	1.03-1.13 [16]	1 (560)
UCVA 20/20 or better (12-24 months)	64% [2, 16]	38-90.5%	9 (>1 534)
UCVA 20/40 or better (12-24 months)	92%	77-100%	7 (>890)
Within 0.5 D target refraction (≥6 months)	82%	42-96%	8 (>1 080)
Within 1 D target refraction (>6 months)	91.5% [2, 16]	67-100%	8 (1 210)
Postoperative spherical equivalent	NR	NR	
Loss of 1 line of BCVA (3-12 months)	2.2%	0-16%	13 (1 722)
Loss of ≥2 lines of BCVA (3-24 months)	0% [2, 16]	0-8.2%	21 (3 105)
Corneal ectasia (mean 8 months)	0%	NA	1 (171)
Keratitis/infection (3-12 months)	0.6% [2, 16]	0-3.4%	5 (1 512)
Persistent epithelial defect	NR	NR	
Retinal detachment	NR	NR	

Choroidal neovascularisation	NR	NR	
Epithelial in growth	NR	NR	
Cataract	NR	NR	
Raised intraocular pressure (6 months)	1.2%	NA	1 (84)
Flap complications (3-26 months)	2.0%	0-14%	9 (959)
Re-treatment (unclear)	1.15% [2, 16]	0-5.5%	8 (1 483)
Haze grade ≥2 (3-12 months)	0%	0-25%	16 (2 093)
Haloes and/or glare	NR	NR	
Night driving problems	NR	NR	
Dry eyes syndrome (6-12 months)	3.0%	0-33%	4 (489)
Strong-severe post-operative pain (6-26 months)	4.0%	0-19%	5 (849)

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; UCVA: uncorrected visual acuity

Table 22 – LASIK, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
Abdallat 2011[17]	• Retrospective study • Funding: not reported; CoI: not reported • Setting: single centre, Jordan • Years: 2006-2007 • Number of patients: 1000 eyes • Follow-up: mean 30 months (range: 24-36 months)	• Eligibility criteria: myopia patients that underwent LASIK at the centre • Exclusion criteria: not reported • Patient characteristics: mean preoperative spherical equivalent -4.15 D; mean age 33 years	LASIK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 1 year: 85% -mild myopia (0 to -3.0 D): 94% -moderate (-3.0 to -6.0 D): 76% -severe (>6.0 D): 52% • % refractions within 1 D of intended spherical equivalent correction at 1 year: 96% -mild myopia (0 to -3.0 D): 98% -moderate (-3.0 to -6.0 D): 93% -severe (>6.0 D): 66% • % refractions within 0.5 D of intended spherical equivalent correction at 3 years: 80%	• No loss to follow-up at 1 year • Glare and night vision problems (32%), debris (3%), halos (3%) and striae (1%) were reported harms but it was unclear at what time point these were assessed

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				-mild myopia (0 to -3.0 D): 96% -moderate (-3.0 to -6.0 D): 70% -severe (>6.0 D): 48% • % refractions within 1 D of intended spherical equivalent correction at 3 years: 89% -mild myopia (0 to -3.0 D): 98% -moderate (-3.0 to -6.0 D): 91% -severe (>6.0 D): 62% Safety: • % eyes that lost ≥1 line of BCVA 1 year post-treatment: 10% • % eyes that lost ≥ 2 line of BCVA 1 year post-treatment: 0% • Retreatment for regression at 3 years: 1.1%	
Al-Mezaine 2009 [18]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, Saudi-Arabia • Years: 1999-2008 • Number of patients: 4250 eyes • Follow-up: mean 31.7 ±30.4 weeks (range: 3.0-101.4)	• Eligibility criteria: ≥18 years of age; stable refraction for at least 1 year • Exclusion criteria: pregnant, with a history of ocular pathology or corneal disease, previous ocular surgery including refractive corneal surgery, or contact lens wear for the 2 weeks before	LASIK	Visual acuity: • Not reported Safety: • % with buttonhole flaps: 0.4%:	• Consecutive eyes • Cohort includes hyperopia patients

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		surgery • Patient characteristics: mean preoperative spherical equivalent -4.16 ±2.75 D (range +4.25 to -9.00 D)			
Arevalo 2012 [19]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, Venezuela • Years: 1995-1999 • Number of patients: 22296 eyes • Follow-up: 10 years	• Eligibility criteria: myopia ≤ -10 D without astigmatism • Exclusion criteria: history of prior refractive surgery, keratoconus, prior cataract surgery, proliferative diabetic retinopathy, collagen vascular disease • Patient characteristics: mean spherical equivalent -4.5 D ±3.7 (range: -1.5 to -10)	LASIK	Visual acuity: • Not reported Safety: • % Rhegmatogenous retinal detachment: 0.05% (11/22296) at 1 year, 0.15% (18/11371) at 5 years, and 0.19% (22/11594) at 10 years	• Consecutive eyes • Loss to follow-up at 10 years: 48%
Bamashmus 2010 [20]	• Retrospective chart review • Funding: not reported; CoI: not reported • Setting: single centre,	• Eligibility criteria: myopia or hyperopia • Exclusion criteria: other refractive	LASIK	Visual acuity: • Not reported Safety:	• Consecutive eyes • 351/2480 (14%) patients (LASIK (2227) + PRK 253)) were lost to

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	Yemen • Years: 2005-2008 • Number of patients: 4217 eyes • Follow-up: ≥1 year (range: 12-36 months)	procedures • Patient characteristics: age 18-53 years		• % Rhegmatogenous retinal detachment: 0.04%	follow-up <1 months • 32/248 patients had hyperopia
Clare 2011 [21]	• Retrospective chart review • Funding: not reported; CoI: 1/7 authors reported CoI • Setting: single centre, United Kingdom • Years: not reported • Number of patients: 23997 eyes • Follow-up: ≥12 months	• Eligibility criteria: myopia or hyperopia patients that underwent LASIK at the centre • Exclusion criteria: not reported • Patient characteristics: not reported separately for microkeratome patients	LASIK	Visual acuity: • Not reported Safety: • % Flap displacements: 0.033% (all occurred <48 hours post-surgery) - Myopia: 0.005% - Hyperopia: 0.179%	• Consecutive eyes • 3914 hyperopic eyes and 19766 myopic eyes included
Lee 2006 [13]	• Retrospective study • Funding: not reported; CoI: not reported • Setting: single centre, Singapore • Years: 1998-2001 • Number of patients: 7065 eyes • Follow-up: ≥ 1 year	• Eligibility criteria: myopic Singapore residents with ≥1 year follow-up after LASIK • Exclusion criteria: not reported • Patient characteristics: mean age 34 ±8 years; mean preoperative	LASIK	Visual acuity: • Not reported Safety: • % eyes with retinal detachment: 0.84% (6/7065)	• Eyes with a follow-up <1 year were excluded • Article is letter

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		spherical equivalent -6.37 ±2.81 D (range: -24.25 to -0.13)			
Lee 2011 [22]	• Retrospective chart review linked to health insurance claims database • Funding: not reported; CoI: not reported • Setting: multicentre, South-Korea • Years: 2002-2005 • Number of patients: 1637 patients • Follow-up: 3-8 years	• Eligibility criteria: patients who had LASIK surgery • Exclusion criteria: history of eye disease, diabetes, hyperopia, different surgery techniques for both eyes • Patient characteristics: not reported	LASIK	Visual acuity: • Not reported Safety: • Cataract 3-8 years post surgery: 0.3% • Glaucoma 3-8 years post-surgery: 0.2% • Retinal detachment 3-8 years post-surgery: 0.7%	• Consecutive eyes • Reported as an abstract only
NICE 2005 [2]	• SR + MA • Funding: core grant from the Scottish Executive Health Department; CoI: none • Databases searched: Medline, EMBASE, BIOSIS, Science Citation Index, CENTRAL, National Research Register, Clinical Trials, Current Controlled Trials, FDA database, conference proceedings, abstracts,	• Eligibility criteria: adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism; full-text prospective studies with > 300 eyes or retrospective studies with > 500 eyes • Exclusion criteria: photorefractive	LASIK	Visual acuity: • % refractions within 0.5 D of intended spherical equivalent correction at 3-12 months: 23 studies, >9 542 eyes, myopia median 75.2%, range 53.4-90.4% - low/moderate myopia <7.15 D (7 studies, 2 230 eyes): 84.6%, range 74.8-90.4% - high myopia (6 studies, >1 443 eyes): 62.3%, range 53.4-74.0% - myopic astigmatism (4 studies, 919 eyes): 73.3%, range 56.2-87.2% • % refractions within 1 D of intended spherical equivalent correction at 3-6 months: 23 studies, >8 885 eyes, myopia	Author´s quality appraisal with 18-question checklist for case series and 14-question checklist for RCTs: the most important negative findings in the quality assessment of the 64 studies were: • 34 out of 64 studies did not describe the inclusion/exclusion criteria of the

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	reference lists • Search date: 2000 – December 2004 • Languages included: English • Number of studies included: 64 case series	surgery for therapeutic reasons, such as to correct refractive error following cataract or corneal graft surgery • Patient characteristics: range mean age 16-75y, % women 41-67%, range mean preoperative spherical equivalent -11.69 to 2.7 D		median 92.4%, range 74.7-100% • % refractions within 0.5 D of intended spherical equivalent correction at 6-12 months: hyperopia median 62%, range 59.0-74.1% (5 studies, 530 eyes) • % refractions within 1 D of intended spherical equivalent correction at 6-12 months: hyperopia median 88%, range 86.0-91.4% (5 studies, 530 eyes) • % eyes with UCVA of 20/20 or better at 1-24 months: myopia (26 studies, >14 527 eyes) median 64% (range: 14.7-90.1) -low/moderate myopia ≤7 D (8 studies, 3231 eyes): 80.6%, range 44.1-90.1% -high myopia ≥ 6 D (8 studies, 2194 eyes): 45.2%, range: 14.7-74.3% -myopic astigmatism (3 studies, 579 eyes): 87.8%, range 52.0-90.1% • % eyes with UCVA of 20/40 or better at 1-24 months: myopia (25 studies, >14 388 eyes) median 94%, range: 76.2-100% • % eyes with UCVA of 20/20 or better at 6-24 months: hyperopia median 51.5%, range 51.0-64.8%; 5 studies, >369 eyes • % eyes with UCVA of 20/40 or better at 6-24 months: hyperopia median 95.9%, range 93.9-100%; 5 studies, >369 eyes <u>Safety</u>:	participants clearly (unclear for two studies) • None out of 64 studies did not select participants consecutively, but this was unclear for 33 studies • 39 out of 64 studies collected data retrospectively (unclear for two studies) • 51 out of 64 studies did not define the intervention clearly (unclear for three studies) • 46 out of 64 studies did not consider all important outcomes • 43 out of 64 studies did not report data on non-respondents and dropouts (unclear for one study)

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				• % eyes that lost ≥ 2 lines of BCVA 2-13 months post-treatment: 21 studies, 16 816 eyes, myopia, overall median 0.6%, range 0-3% • % eyes that lost ≥ 2 lines of BCVA post-treatment: 6 studies, 2 828 eyes, low-moderate myopia median 0.7%, range 0-1.6% • % eyes that lost ≥ 2 lines of BCVA post-treatment: 5 studies, 1 669 eyes, high myopia median 0.9%, range 0-1.8% • % eyes that lost ≥ 2 lines of BCVA ≥12 months post-treatment: 2 studies, 396 eyes, hyperopia median 3.4%, range 2.2-4.7% (2 studies, 396 eyes) • % eyes with induced astigmatism >2 D, myopia, 6 studies, 3 167 eyes median 0.15%, range 0-0.97% • Flap complications (myopia & hyperopia): buttonhole flap (9 studies, 140 316 eyes) 0-0.53% (median 0.13%), free cap (15 studies, 148 438 eyes) 0-2% (median 0.13%), torn flap (2 studies, 8 179 eyes) 0.03-0.09% (median 0.06%), incomplete flap (20 studies, 152 694 eyes) 0-2.86% (median 0.28%), thin flap (9 studies, 143 185 eyes) 0-0.86% (median 0.23%), flap folds/striae (14 studies, 10 679 eyes) 0.03-5.52% (median 0.77%), dislodged flap (9 studies, 5 308 eyes) 0.29-2.41% (median 1.2%) • Epithelial complications: epithelial in growth (19 studies, 17 715 eyes) 0-4.44% (median 1.4%), epithelial defects (20 studies, 23 679 eyes) 0-10.2% (median 1.7%) • Keratitis: microbial keratitis (6 studies, 4 499 eyes) 0-0.16%, diffuse lamellar keratitis (26 studies, 40 097	• In 23 out of 64 studies participants lost to follow-up were considered likely to introduce bias (unclear for 36 studies) • In 44 out of 64 studies the paired nature of eyes was not taken into account in the analyses

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				eyes) 0-7.72% (median 1.4%) • Potentially serious complications: ectasia (5 studies, 10 806 eyes) 0-0.9% (median 0.2%), raised intraocular pressure (4 studies, 2 071 eyes) 0-0.86% (median 0.14%), vitreo-retinal complications (7 studies, 44 209 eyes) 0-0.84%: retinal detachment: median 0.23% (2 studies, 41 832 eyes); choroidal neovascularisation: 0.33% (1 study, 3 009 eyes) • Undesired complications: corneal haze (7 studies, 4 760 eyes) 0%, range 0-2.08%, corneal oedema (4 studies, 1 530 eyes) 0.26-1.88% • Retreatment: median 10.7% (range: 1.6-37.0%, 18 studies, 14 621 eyes) for myopia and 6.1% for hyperopia (range 0-23.6%, 5 studies >931 eyes). In eyes with low to moderate myopia, a median of 3.4% (range 1.6% to 5.1%) were retreated. Highly myopic eyes were retreated in a median of 22.6% (range 2.6% to 37.0%) of cases. • Participant reported outcomes: blurring vision: worse 10.3-37.9%, better 14.4-41.2%; burning: worse 4.3-13.6%, better 1.3-7.2%; dry eye: worse 17-44%, better 9.8-28.6%; fluctuation of vision: worse 14.7-42.3%, better 7.5-12.1%; glare (7 studies): worse 10.3-29.9%, better 10.9-24.6%; halos: worse 14.4-42.9%, better 6.0-15.6%; light sensitivity: worse 4.4-36.8%, better 23.0-42.4%; night driving difficulty: worse 10.3-36.6%, better 22.7-40.3%; pain: worse 0.7-5.7%, better 4.6-9.1% (6 studies)	
Qin 2007 [23]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre,	• Eligibility criteria: LASIK for myopia; age 20-60 years; pre-operative BCVA ≥20/200	LASIK	<u>Visual acuity</u>: • Not reported <u>Safety</u>:	• Consecutive eyes • 215/9598 (2%) of patients lost to follow-up • All detachment

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	China • Years: 1998-2005 • Number of patients: 18342 eyes • Follow-up: mean 20 months (range: 4-27)	• Exclusion criteria: corneal disease; previous refractive surgery; cataract surgery; glaucoma • Patient characteristics: mean age 36.7 years; mean spherical equivalent -7.21 D (range: -0.75 to -15)		• % retinal detachment: 0.033%	cases were spontaneous
Sanders 2006[24]	• Retrospective chart review • Funding: not reported; CoI: none • Setting: single centre, United States • Years: 1998-2001 • Number of patients: 1678 eyes • Follow-up: 6 months	• Eligibility criteria: not reported • Exclusion criteria: not reported • Patient characteristics: mean pre-operative spherical equivalent -5.6 ±1.1D (range -4 to -7.88); mean age 34.9 ±6.44 years (range 21–45 years)	LASIK	Visual acuity: • % eyes with UCVA of 20/20 or better at 6 months: 57% • % refractions within 1 D of intended spherical equivalent correction at 6 months: 88% • % refractions within 0.5 D of intended spherical equivalent correction at 6 months: 70% Safety: • % eyes that lost ≥1 line of BCVA at 6 months: 11% • % eyes that lost ≥ 2 line of BCVA at 6 months: 1% • Retreatment for enhancement: 25% • Diffuse lamellar keratitis: 4.8% • Striae corneal flap: 1.8% (30 eyes, in 24 eyes the flap was lifted to smooth out the striae) • Free cap: 0.06%	• Consecutive eyes • Loss to follow-up 70% at 6 months
Schallh	• SR	• Eligibility criteria:	Wavefro	Visual acuity:	Poor-quality review

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
orn 2008 [25]	• Funding: American Academy of Ophthalmology; CoI: 6/8 authors declared potential conflicts of interest • Databases searched: Medline, Cochrane Library databases • Search date: last date May 2007 • Languages included: English for PubMed, no restriction for Cochrane Library • Number of studies included: 11 RCTs, 2 non-randomized comparative studies, 1 prospective cohort study, 33 low-quality observational studies	patients with primary myopia with or without astigmatism • Exclusion criteria: not reported • Patient characteristics: not reported in aggregated way	nt-guided LASIK	• % refractions within 0.5 D of intended spherical equivalent correction: Published studies: range 72-100% FDA studies: at 6 months (1 015 eyes), range 75.9-94.6% • % eyes with UCVA of 20/20 or better: Published studies: range 56-100% FDA studies (premarket approval): at 6 months (1 015 eyes), range 84.1-93.9% • % eyes with UCVA of 20/40 or better: Published studies: nearly every study participant FDA studies: at 6 months (1 015 eyes), range 97.4-100% <u>Safety</u>: • % eyes that lost ≥ 2 lines of BCVA post-treatment at finale follow-up: Published studies: 0% FDA studies (1 015 eyes): range 0-0.6% • Complications reported in FDA studies (1 015 eyes): free cap 0.3%, poorly created flap 0.3%, flap striae 0.3%, epithelial defect 0.6%, epithelium in the interface 0.3%, diffuse lamellar keratitis 0.9%; glare, halos, night driving difficulty and double vision at 6 months: range 0-7.1%	Two studies included after search date: unclear on what base Levels of evidence provided, but no individual quality appraisal results
Schraepen 2005 [26]	• Retrospective chart review • Funding: not reported; CoI: not reported	• Eligibility criteria: correction for myopia • Exclusion criteria: not reported	LASIK	<u>Visual acuity</u>: • % eyes with UCVA of 20/20 or better at 1-3 years: 42.7% -Low myopia: 65%	• Consecutive eyes -Low myopia <3 D: 183 (18% -Moderate -3.25 to

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	• Setting: two centres, Belgium and Russia • Years: not reported • Number of patients: 1035 eyes • Follow-up: 1-3 years	• Patient characteristics: mean associated astigmatism -0.5 ±0.9 D		-Moderate: 51% -High: 23% -Very high: 0% • % refractions within 1 D of emmetropia at 1 to 3 years: 87.9% -Low myopia: 99.1% -Moderate: 98.9% -High: 83% -Very high: 21% • % refractions within 0.5 D of emmetropia at 1 to 3 years: 72.9% -Low myopia: 95.6% -Moderate: 85.4% -High: 54.3% -Very high: 5% Safety: • % eyes that lost ≥ 2 line of BCVA 1 to 3 years post-treatment: 0% • % eyes with haze grade ≥ 2 1 to 3 years: 4.0% -Low myopia: 0% -Moderate: 4.5% -High: 2.4% -Very high: 12.7%	-6 D: 540 (52%) -High -6.25 to -10 D: 210 (20%) -Very high -10.25 to -20 D: 102 (10%) • Loss to follow-up not reported
Spadea 2012 [27]	• Retrospective chart review • Funding: University of L´Aquila; CoI: none	• Eligibility criteria: myopia patients operated by one surgeon	LASIK	Visual acuity: • Not reported Safety:	• Consecutive eyes • No loss to follow-up

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	• Setting: single centre, Italy • Years: 1999-2003 • Number of patients: 4027 eyes • Follow-up: ≥7 years	• Exclusion criteria: not reported • Patient characteristics: mean age 31.6 ± 8.45 years; mean manifest spherical equivalent −8.11 ± 4.48 D, range: -1.62 to -21.12		• Corneal ectasia: 0.57%	

Table 23 – Summary of findings for visual acuity and safety of LASIK for patients with myopia with/without astigmatism, observational data [2, 13, 17-24, 26, 27]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR	
UCVA 20/20 or better (1-36 months)	64% [2, 26]	14.7 to 90.1%	27 (>15 562)
UCVA 20/40 or better (1-24 months)	94% [2]	76.2 to 100%	25 (>14 388)
Within 0.5 D target refraction (3-12 months)	76.0% [2, 17, 24]	53.4 to 90.4%	25 (>12 220)
Within 1 D target refraction (3-6 months)	92.6% [2, 24]	74.7 to 100%	24 (>10 563)
Postoperative spherical equivalent	NR	NR	
Loss of ≥1 line of BCVA (≥6 months)	10.5% [17, 24]	10 to 11%	2 (2 678)
Loss of ≥2 lines of BCVA (2 months – 3 years)	0.62% [2, 17, 24, 26]	0-3%	23 (20 529)
Button hole flap § (unclear)	0.17% [2, 18]	0 to 0.53%	10 (144 566)
Dislodged flap § (unclear)	1.2% [2, 21]	0.033 to 2.41%	10 (29 305)
Corneal ectasia § (unclear)	0.25% [2, 27]	0 to 0.9%	6 (14 833)
Microbial keratitis § (>1-12)	0% [2]	0 to 0.16%	6 (4 499)
Epithelial defect §	1.7% [2]	0 to 10.2%	20 (23 679)

Retinal detachment (mean 20-64 months)	0.19% [2, 13, 19, 20, 22, 23]	0.033-0.84%	7 (95 389)
Choroidal neovascularisation	0.33% [2]	NA	1 (3 009)
Glaucoma (3 to 8 years)	0.2% [22]	NA	1 (1 637)
Cataract (3 to 8 years)	0.3% [22]	NA	1 (1 637)
Epithelial in growth §	1.4% [2]	0 to 4.4%	19 (17 715)
Raised intraocular pressure §	0.14% [2]	0 to 0.86%	4 (2 071)
Re-treatment (2-24 months)	10.7% [2, 17, 24]	1.1 to 37.0%	20 (17 299)
Corneal haze # § (1 week-12 months)	0% [2]	0-2.08%	7 (4 760)
Haloes and/or glare §	Glare: reported worse 10.3-29.9%, better 10.9-24.6% Halos: reported worse 14.4-42.9%, better 6.0-15.6% (7 studies) [2]		
Night driving difficulty §	Worse 10.3-36.6%, better 22.7-40.3% (7 studies) [2]		
Dryness §	Worse 17-44%, better 9.8-28.6% (7 studies) [2]		
Pain §	Worse 0.7-5.7%, better 4.6-9.1% (6 studies) [2]		

§ Including patients with hyperopia

Varying definitions of haze: detectable haze, late onset of haze with loss of ≥2 lines BCVA, haze greater than grade 3, moderate or marked haze at 1 week, significant corneal haze

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; UCVA: uncorrected visual acuity

Table 24 Summary of findings for visual acuity and safety of LASIK for patients with hyperopia with/without astigmatism, observational data [2]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/ mean BCVA preoperatively)	NR	NR	
UCVA 20/20 or better (6-24 months)	51.5% [2]	51.0-64.8%	5 (>396)
UCVA 20/40 or better (6-24 months)	95.9% [2]	93.9-100%	5 (>396)
Within 0.5 D target refraction (6-12 months)	62% [2]	59.0 to 74.1%	5 (530)
Within 1 D target refraction (6-12 months)	88% [2]	86.0 to 91.4%	5 (530)
Postoperative spherical equivalent	NR	NR	
Loss of 1 line of BCVA	NR	NR	

Loss of ≥2 lines of BCVA (≥ 12 months)	3.4% [2]	2.2-4.7%	2 (396)
Corneal ectasia	See myopia table		
Microbial keratitis	See myopia table		
Persistent epithelial defect	See myopia table		
Retinal detachment	See myopia table		
Choroidal neovascularisation	See myopia table		
Epithelial in growth	See myopia table		
Raised intraocular pressure	See myopia table		
Re-treatment (5-24 months)	6.1% [2]	0 to 23.6%	5 (>931)
Haze grade ≥2	See myopia table		
Haloes and/or glare	See myopia table		
Night driving problems	See myopia table		
Dryness	See myopia table		
Pain	See myopia table		

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NR: not reported; UCVA: uncorrected visual acuity

Table 25 – LASIK vs. intra-ocular lenses, observational data

OHTAS 2009 [9]	• SR • Funding: Ontario Ministry of Health and Long-Term Care; CoI: none • Databases searched: Medline, EMBASE, Cochrane Library, INAHTA, CRD • Search date: 2003 – January 2009 • Languages included: English	• Eligibility criteria: adult patients (at least 18y) with myopia, hyperopia or astigmatism • Exclusion criteria: studies with <20 eyes for each refractive error type; anterior chamber lenses (not iris fixated) • Patient characteristics: not	LASIK vs. Phakic intraocular lens (IOL) insertion	Visual acuity: **Moderate myopia**: 1 study, 1 822 eyes • % eyes with UCVA of 20/20 or better: (LASIK vs. IOL) At day 1: 38% vs. 28%, p=0.019 At 1 week: 55% vs. 48%, p=0.15 At 1 month: 58% vs. 55%, p=0.53 At 6 months: 57% vs. 67%, p=0.027 • % eyes with UCVA of 20/40 or better: (LASIK vs. IOL) At day 1: 92% vs. 69%, p<0.001 At 1 week: 96% vs. 93%, p=0.076	Included studies: Kamiya 2008, Sanders 2008, Sanders 2007, Sanders 2006, Sanders 2003 GRADE system used, but no individual results of quality appraisal (although GRADE tables provided in appendix)

• Number of studies included: 5 comparative case series, 0 RCTs	provided	At 1 month: 95% vs. 96%, p=0.84 At 6 months: 92% vs. 96%, p=0.11 • Mean spherical equivalent: (LASIK vs. IOL) Preoperative: -5.6 D vs. -6.4 D, p<0.001 At 1 week: -0.01 D vs. -0.24 D, p<0.001 At 1 month: -0.24 D vs. -0.15 D, p=0.89 At 6 months: -0.35 D vs. -0.08 D, p<0.001 • % eyes that gained ≥ 2 lines of BCVA: (LASIK vs. IOL) At 1 week: 0.7% vs. 3%, p=0.029 At 1 month: 0.9% vs. 5%, p=0.001 At 6 months: 0.8% vs. 4%, p=0.013 **Moderate-high myopia**: 1 study, 328 eyes • % eyes with UCVA of 20/20 or better: (LASIK vs. IOL) At 1 week: 45% vs. 49%, p=0.48 At 1 month: 43% vs. 59%, p=0.011 At 6 months: 49% vs. 63%, p=0.01 • % eyes with UCVA of 20/40 or better: (LASIK vs. IOL) At 1 week: 92% vs. 94%, p=0.65 At 1 month: 90% vs. 96%, p=0.055 At 6 months: 95% vs. 99%, p=0.104 • Mean spherical equivalent: (LASIK vs. IOL) At 1 week: -0.18 D vs. -0.25 D, p=093 At 1 month: -0.25 D vs. -0.14 D, p=0.58 At 6 months: -0.33 D vs. -0.09 D, p=0.001 • % eyes that gained ≥ 2 lines of BCVA: (LASIK vs. IOL) At 1 week: 2% vs. 3%, p=0.69

At 1 month: 4% vs. 4%, p=1.0

At 6 months: 3% vs. 3%, p=0.747

High myopia: 1 study, 769 eyes

- % eyes with UCVA of 20/20 or better: (LASIK vs. IOL)

  At 1 week: 26% vs. 38%, p=0.002

  At 1 month: 31% vs. 43%, p=0.005

  At 6 months: 50% vs. 35%, p<0.001

  At 12 months: 36% vs. 52%, p=0.01

- % eyes with UCVA of 20/40 or better: (LASIK vs. IOL)

  At 1 week: 85% vs. 85%, p=1.0

  At 1 month: 82% vs. 89%, p=0.02

  At 6 months: 87% vs. 81%, p=0.1

  At 12 months: 89% vs. 87%, p=0.57

- Mean spherical equivalent: (LASIK vs. IOL)

  At 1 week: -0.06 D vs. -0.39 D, p-value not reported

  At 1 month: -0.18 D vs. -0.27 D, p-value not reported

  At 6 months: -0.33 D vs. -0.27 D, p-value not reported

  At 12 months: -0.30 D vs. -0.30 D, p-value not reported

- % eyes that gained ≥ 2 lines of BCVA: (LASIK vs. IOL)

  At 1 week: 1% vs. 5%, p=0.005

  At 1 month: 3% vs. 6%, p=0.07

  At 6 months: 3% vs. 7%, p=0.04

  At 12 months: 2% vs. 5%, p=0.34

Myopic astigmatism:

- % eyes with UCVA of 20/20 or better: 2 studies (LASIK vs. IOL)

  At 1 week (Kamiya 2008): 79% vs. 97%, p-value not reported

  At 1 month (Kamiya 2008): 88% vs. 97%, p-value not reported

  At 6 months:

  - Kamiya 2008: 83% vs. 100%, p-value not reported
  - Sanders 2008: 3-7 D, VISX 80%, Alcon 91%, IOL 94%; 7-11 D: VISX 71%, Alcon 82%, IOL 84%; p>0.05
- % eyes with UCVA of 20/40 or better: 1 study (LASIK vs. IOL)

  At 6 months: 92% vs. 96%, p=0.11

  - Sanders 2008: 3-7 D, VISX 94%, Alcon 97%, IOL 97%; 7-11 D: VISX 97%, Alcon 100%, IOL 97%; p>0.05
- Mean spherical equivalent: 1 study (LASIK vs. IOL)

  At 1 week: 0.57 D vs. -0.10 D, p-value not reported

  At 1 month: 0.32 D vs. -0.12 D, p-value not reported

  At 6 months: -0.60 D vs. -0.13 D, p-value not reported
- Mean postoperative efficacy index: 1 study (LASIK vs. IOL)

  At 6 months: 1.01 vs. 1.28, p-value not reported
- % eyes that gained ≥ 2 lines of BCVA: 1 study (LASIK vs. IOL)

  At 6 months: VISX 11%, Alcon 2%, IOL 20%, p<0.001 vs. both lasers combined

Return to work:
Not reported

Rehabilitation time:
Not reported

Quality of life:
Not reported

Safety:
Moderate myopia: 1 study, 1 822 eyes

- IOL (144 eyes): 2 lenses replaced, 1 lens repositioned, 1 asymptomatic lens opacity
- LASIK (1 678 eyes): diffuse lamellar keratitis 4.8%, striae in corneal flap 1.8%, free cap 0.06%
- % eyes that lost ≥ 2 lines of BCVA: (LASIK vs. IOL)
  At 1 week: 6% vs. 0.7%, p=0.008
  At 1 month: 2% vs. 0%, p=0.101
  At 6 months: 1% vs. 0%, p=0.245

Moderate-high myopia: 1 study, 328 eyes

- IOL (164 eyes): 1 lens replaced, 1 lens repositioned, 7 eyes additional YAG iridotomies
- LASIK (164 eyes): diffuse lamellar keratitis 6.7%, striae in corneal flap 1.8%, very thin flaps in 2 eyes, corneal ectasia in 1 eye
- % eyes that lost ≥ 2 lines of BCVA: (LASIK vs. IOL)
  At 1 week: 10% vs. 0.6%, p<0.001
  At 1 month: 7% vs. 0%, p=0.001
  At 6 months: 1% vs. 0%, p=0.499

				High myopia: 1 study, 769 eyes • IOL (210 eyes): 1 lens repositioned • LASIK (559 eyes): diffuse lamellar keratitis 3%, striae in corneal flap 3%, free cap 0.2% • % eyes that lost ≥ 2 lines of BCVA: (LASIK vs. IOL) At 1 week: 11% vs. 2%, p<0.001 At 1 month: 6% vs. 0.5%, p<0.001 At 6 months: 2% vs. 0%, p=0.05 At 12 months: 0% vs. 0% **Myopic astigmatism**: • % eyes that lost ≥ 2 lines of BCVA: not observed in either group • No adverse events in either group	

Table 26 – Intra-ocular lenses, observational data

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
OHTAS 2009 [9]	• SR • Funding: Ontario Ministry of Health and Long-Term Care; CoI: none • Databases searched: Medline, EMBASE, Cochrane Library, INAHTA, CRD • Search date: 2003 – January 2009 • Languages included: English • Number of studies	• Eligibility criteria: adult patients (at least 18y) with myopia, hyperopia or astigmatism • Exclusion criteria: studies with <20 eyes for each refractive error type; anterior chamber lenses (non-iris fixated) • Patient characteristics: not summarized	Intra-ocular lenses	Visual acuity: **Efficacy index (weighted mean)** • Iris-fixated lenses for myopia: At 3 months (1 study, 31 eyes): 0.95 At 12 months (3 studies, 704 eyes): 0.85 At 24 months (2 studies, 153 eyes): 0.89 At 36 months (1 study, 20 eyes): 0.43 At 60 months (1 study 19 eyes): 0.63 At 72 months (1 study 89 eyes): 0.83 At 120 months (1 study 89 eyes): 0.80 • Iris-fixated lenses for hyperopia: At 6 months (1 study, 22 eyes): 0.76 At 12 months (1 study, 17 eyes): 0.73	GRADE system used, but no individual results of quality appraisal (although GRADE tables provided in appendix) Observational outcomes were graded low or very low

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	included: 1 SR, 19 pre-post case series			At 24 months (1 study, 15 eyes): 0.69 At 36 months (1 study, 10 eyes): 0.67 • Posterior chamber lenses for myopia: At 6 months (1 study, 65 eyes): 0.86 At 12 months (2 studies, 101 eyes): 0.99 At 24 months (3 studies, 102 eyes): 0.87 At 36 months (1 study, 65 eyes): 0.69 At 48 months (1 study, 65 eyes): 0.84 • Posterior chamber lenses for myopic astigmatism: At 6 months (1 study, 52 eyes): 0.94 **% eyes with UCVA of 20/20 or better** • Iris-fixated lenses for myopia: At 3 months (1 study, 60 eyes): 5% At 4 months (1 study, 93 eyes): 20.4% At 6 months (1 study, 69 eyes): 17.4% At 12 months (2 studies, 554 eyes): 33.9% At 24 months (2 studies, 394 eyes): 32.2% At 36 months (1 study, 231 eyes): 31.2% At 60 months (1 study 19 eyes): 73.7% • Iris-fixated lenses for hyperopia: At 6 months (1 study, 22 eyes): 22.7% • Posterior chamber lenses for myopia: At 6 months (1 study, 317 eyes): 55.8% At 12 months (2 studies, 318 eyes): 58.8% At 24 months (1 study, 258 eyes): 57.4% At 36 months (1 study, 369 eyes): 40.8% • Posterior chamber lenses for myopic astigmatism:	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				At 6 months (1 study, 52 eyes): 78.8% At 12 months (1 study, 186 eyes): 82.7% **% eyes with UCVA of 20/40 or better** • Iris-fixated lenses for myopia: At 3 months (2 studies, 85 eyes): 81% At 4 months (1 study, 93 eyes): 79.6% At 6 months (1 study, 69 eyes): 82.6% At 12 months (3 studies, 643 eyes): 87.2% At 24 months (2 studies, 394 eyes): 86.8% At 36 months (1 study, 231 eyes): 84% At 60 months (1 study 19 eyes): 94.7% At 72 months (1 study, 89 eyes): 78.7% At 120 months (1 study, 89 eyes): 82% • Iris-fixated lenses for hyperopia: At 6 months (1 study, 22 eyes): 90.9% • Posterior chamber lenses for myopia: At 6 months (1 study, 317 eyes): 92.1% At 12 months (2 studies, 318 eyes): 92.1% At 24 months (1 study, 258 eyes): 80.2% At 36 months (1 study, 369 eyes): 81.3% • Posterior chamber lenses for myopic astigmatism: At 6 months (1 study, 52 eyes): 94.2% At 12 months (1 study, 186 eyes): 96.2% **Mean pre- and postoperative manifest refraction spherical equivalent (range)** • Iris-fixated lenses for myopia: Preoperative (8 studies): -18.92 to -10.37	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				At 3 months (2 studies): -0.77 to -0.50 At 6 months (2 studies): -0.68 to -0.26 At 12 months (5 studies): -1.14 to -0.03 At 24 months (4 studies): -1.20 to -0.15 At 36 months (1 study): -0.38 At 60 months (2 studies): -0.71 to -0.37 At 120 months (1 study): -0.70 • Iris-fixated lenses for hyperopia: Preoperative (1 study): 6.80 At 6 months (1 study): -0.08 At 12 months (1 study): -0.03 At 24 months (1 study): -0.15 At 36 months (1 study): 0.10 • Posterior chamber lenses for myopia: Preoperative (2 studies): -16.79 to -8.54 At 3 months (2 studies): -16.23 to -13.42 At 6 months (2 studies): -1.79 to -0.32 At 36 months (2 studies): -1.77 to -0.10 • Posterior chamber lenses for hyperopia: Preoperative (1 study): 5.78 At 120 months (1 study): 0.07 • Posterior chamber lenses for myopic astigmatism: Preoperative (2 studies): -9.36 At 6 months (1 study): 0.02 At 12 months (1 study): 0.05 **% eyes that lost ≥ 2 lines of BCVA** • Iris-fixated lenses for myopia:	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				At 3 months (91 eyes): 0% At 4 months (93 eyes): 0% At 6 months (69 eyes): 0% At 12 months (1 study, 493 eyes): 0.6% At 24 months (355 eyes): 0.3% At 36 months (228 eyes): 0.9% At 60 months (19 eyes): 0% • Iris-fixated lenses for hyperopia: At 6 months (22 eyes): 0% At 36 months (10 eyes): 0.9% • Posterior chamber lenses for myopia: At 6 months (464 eyes): 0.4% At 12 months (2 studies, 452 eyes): 0.7% At 24 months (257 eyes): 1.6% • Posterior chamber lenses for hyperopia: At 120 months (57 eyes): 0% • Posterior chamber lenses for myopic astigmatism: At 6 months (52 eyes): 0% At 12 months (186 eyes): 0.5% **% eyes that gained ≥ 2 lines of BCVA** • Iris-fixated lenses for myopia: At 3 months (91 eyes): 23.1% At 4 months (93 eyes): 43.0% At 6 months (69 eyes): 18.9% At 12 months (493 eyes): 12.4% At 24 months (355 eyes): 13.5% At 36 months (228 eyes): 13.6%	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
				At 60 months (19 eyes): 15.8% • Iris-fixated lenses for hyperopia: At 6 months (22 eyes): 9.1% At 36 months (10 eyes): 20% • Posterior chamber lenses for myopia: At 6 months (464 eyes): 11.9% At 12 months (452 eyes): 10% At 24 months (257 eyes): 10.9% • Posterior chamber lenses for hyperopia: At 120 months (57 eyes): 17.5% • Posterior chamber lenses for myopic astigmatism: At 6 months (52 eyes): 17.3% At 12 months (186 eyes): 18.8% Safety: **Iris-fixated lenses** • SR of Chen et al. (adverse events in >1% of eyes): halo / glare 8.77%, uveitis 4.49%, increased intra-ocular pressure 4.24%, pigment deposits on lens 1.73%, corneal oedema 1.69%, decentration 1.65%, cystic wound / wound leakage 1.44%, pupil ovalization 1.44%, pigment dispersion 1.29%, cataract 1.11% **Posterior chamber lenses** • SR of Chen et al. (adverse events in >1% of eyes): pigment deposits on lens 10.85%, cataract 9.60%, halo / glare 5.93%, increased intra-ocular pressure 4.80%, decentration 3.26%, secondary refractive surgery 2.80%, pigment dispersion 2.63%	
Jiang	• Retrospective chart	• Eligibility criteria:	Intra-	Visual acuity:	• Not stated that

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
2012 [28]	review • Funding: not reported; CoI: not reported • Setting: single centre, China • Years: 2003-2009 • Number of patients: 530 eyes • Follow-up: ≥2 years; mean: 44 months	21-45 years old; stable myopia –3D ~–20D; <5D corneal astigmatism; endothelial cell count greater than 2,500 cells/mm2; normal anterior segment with an anterior chamber depth greater than 3mm; no general health problems • Exclusion criteria: not reported • Patient characteristics: not reported	ocular lenses	• Not reported on Safety: • % retinal detachment: 1.5% (mean time between implantation and detachment: 23.63±18.12 months; mean spherical equivalent before implantation was −17.53±3.86 D)	patients were consecutive, but seems likely • The authors concluded that the risk of retinal detachment after intra-ocular lens implantation seemed similar to the natural history of retinal detachment in highly myopic eyes
Huang 2009 [29]	• SR • Funding: American Academy of Ophthalmology; CoI: 5/5 authors disclosed potential conflicts of interest • Databases searched: Medline, Cochrane Library • Search date: July 2008 • Languages included: English for Medline, all	• Eligibility criteria: patients undergoing intra-ocular lens implantation for correction of myopia and myopic astigmatism; any study design • Exclusion criteria: not reported • Patient characteristics: not	Intra-ocular lenses	Visual acuity: Presented in narrative way in article Safety: **FDA submissions** • Glare / halos: Artisan 18.2%; Visian ICL glare worse at 3y 9.7%, better 12%, halos worse 11.4%, better 9.1% • Mean endothelial cell loss: Artisan 4.75% at 3y; Visian ICL 12.8% cumulative loss • Cataract: Artisan 5.2%; Visian ICL 0.4% visually significant anterior subcapsular cataract, 1% nuclear sclerosis	Level of evidence provided in article, but no individual results presented

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	languages for Cochrane Library • Number of studies included: unclear how many exactly for safety	reported		**Clinical trials** • Anterior chamber angle-supported lenses: endothelial cell density loss 4.18% (at 2y) – 30.31% (at 12y), increased intra-ocular pressure 0.5-2.2%, uveitis 0.59-8.7%, pupil ovalization 11-40%, decentration 4.3-6.51%, night halos/glare 1.18-26.1%, cataract 10.7%, reoperations 1-7.1% • Anterior chamber iris-supported lenses: loss > 2 lines of BCVA 6-120 months: median 0%, range 0-2.99%, 11 studies, 1 792 eyes; endothelial cell density loss 0.7-17.9%, increased intra-ocular pressure 0-15.6% including early post-operative, uveitis 0-9.3%, pupil ovalization 0-1.7%, iris synechiae / atrophy 0-90.63%, decentration 1.49-15.63%, night halos/glare median 12.8%, range 1.4-56.25%, 9 studies 1 067 eyes, cataract median 2.33%, range 0-3.85%, 8 studies, 921 eyes; re-operations median 3.43, range 0-8.8%, 10 studies 1 751 eyes • Posterior chamber lenses: endothelial cell density loss 6.4-26.1%, increased intra-ocular pressure 0-2%, pupil ovalization 5%, iris synechiae / atrophy 5%, subluxation 0-3.77%, night halos/glare 1.6-46%, cataract 0-14.47%, reoperations median 3.28%, range 0-5%, 5 studies 457 eyes at 8 to 24 months	
Ruiz-Moreno 2006 [30]	• Retrospective observational study • Funding: not reported; CoI: none • Setting: single centre, Spain • Years: 1990-2002 • Number of patients: 522	• Eligibility criteria: age 18 to 55 years; spherical equivalent refraction >6.0 D and/or axial length >26mm, which remained stable for at least 2	Intra-ocular lenses	Visual acuity: Not reported Safety: • % retinal detachment: 2.87% (mean time between implantation and detachment: 24.4 ±24.4 months) • No retinal detachments occurred in eyes between -6 and -12 D • Risk of retinal detachment: 0.57% at 3 months, 1.64%	• Consecutive patients • Loss to follow-up: 23.8% (5.4% changed address, rest lived too far and felt well so refused to come for follow-up)

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	eyes • Follow-up: >1 year; mean: 60.4 months (±39.1 months)	years; incapability to wear contact lenses; motivation for not wearing glasses; best corrected visual acuity >20/400; anterior segment without noticeable defects, with anterior chamber depth >3.4 mm and endothelial cell density >2250 cells/mm2; normal retinal periphery or lattice degeneration, trophic holes, or tears that had been treated by argon laser photocoagulation before refractive surgery; no systemic diseases • Exclusion criteria: anisometropic patients with amblyopia and those with previous corneal diseases, glaucoma, or		at 12 months, 2.73% at 36 months, and 4.06% at 92 to 145 months (Kaplan-Meier analysis)	

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		history of ocular trauma • Patient characteristics: mean age: 32.1 years; mean preoperative refraction -18.1 D (± 5.0D); range: -7 to -38 D			
Ruiz-Moreno 2006 [31]	• Retrospective observational study • Funding: not reported; CoI: none • Setting: single centre, Spain • Years: 1990-2002 • Number of patients: 522 eyes • Follow-up: >1 year; mean: 60.4 months (±39.1 months)	• Eligibility criteria: age 18 to 55 years; spherical equivalent refraction >6.0 D and/or axial length >26mm, which remained stable for at least 2 years; incapability to wear contact lenses; motivation for not wearing glasses; best corrected visual acuity >20/400; anterior segment without noticeable defects, with anterior chamber depth >3.4 mm and endothelial cell density >2250 cells/mm2; normal	Intra-ocular lenses	Visual acuity: • Not reported Safety: • Macular choroidal neovascularisation: 2.3% (mean interval between implantation and neovascularisation: 33.7 ±29.6 months) • Cumulative risk of developing neovascularisation was 0.38% at 3 months, 0.57% at 5 months, 0.81% at 18 months, 1.31% at 24 months, 2.19% at 45 months, 2.63% at 63 months, and 3.72% from 87 to 145 months	• Consecutive patients • Loss to follow-up: 23.8% (5.4% changed address, rest lived too far and felt well so refused to come for follow-up) • The authors concluded that the risk of neovascularisation after intra-ocular lens implantation seemed similar to the natural history of neovascularisation in highly myopic eyes

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
		retinal periphery or lattice degeneration, trophic holes, or tears that had been treated by argon laser photocoagulation before refractive surgery; no systemic diseases • Exclusion criteria: anisometropic patients with amblyopia and those with previous corneal diseases, glaucoma, or history of ocular trauma • Patient characteristics: mean age: 32.1 years; mean preoperative refraction -18.1 D (± 5.0D); range: -7 to -38 D			
Sanders 2008[32]	• Observational study • Funding: not reported; CoI: author is a consultant to IOL	• Eligibility criteria: not reported • Exclusion criteria: not reported	Intra-ocular lenses	Visual acuity: • Not reported Safety:	• Unclear whether data were collected prospectively or retrospectively

Reference	Methodology	Patient characteristics	Intervention(s)	Results	Comments
	manufacturer • Setting: multicentre, United States • Years: 1998-2001 • Number of patients: 526 eyes • Follow-up: mean 4.7 ±1.2 years	• Patient characteristics: mean age 36.5 ±5.9 years; mean spherical equivalent: -10.10 D (range: -3.00 D to -20.00 D)		• Cumulative probability anterior subcapsular opacification at 7 years: 7% (Kaplan-Meier analysis) • Cumulative probability cataract at 7 years: 2% (Kaplan Meier analysis)	• Long term follow-up of study included in OTHAS 2009 • 89% (468 eyes), 73% (384 eyes), and 59% (311 eyes) were seen at 3, 4, and 5 years or later • Clinically significant cataract defined as loss of 2 or more lines of BCVA associated with anterior subcapsular opacification, a significant increase in glare symptoms, or cataract extraction

Abbreviations: CCT: controlled clinical trial; CENTRAL: Cochrane Central Register of Controlled Trials; CoI: conflict of interest; D: dioptre; HOA: higher order aberration; ICTRP: International Clinical Trials Registry Platform; LASEK: laser epithelial keratomileusis; LASIK: laser-assisted in situ keratomileusis; LILACS: Latin American and Caribbean Literature on Health Sciences; PRK: photorefractive keratectomy; SBK: sub-Bowmans keratomileusis; SD: standard deviation; SMD: standardized mean difference; WHO: World Health Organization; WMD: weighted mean difference

Table 27 – Summary of findings for visual acuity and safety of intra-ocular lenses for patients with myopia with/without astigmatism, observational data [9] [29] [28, 30-32]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/mean BCVA preoperatively) iris-fixated lenses (12 months)	0.85 # [9]	NR	3 (704)
Efficacy index (mean postoperative UCVA/mean BCVA preoperatively) posterior chamber lenses (12 months)	0.99 # [9]	NR	2 (101)
UCVA 20/20 or better, iris-fixated lenses (12 months)	33.9% # [9]	NR	2 (554)
UCVA 20/20 or better, posterior chamber lenses (12 months)	58.5% # [9]	NR	2 (318)
UCVA 20/40 or better, iris-fixated lenses (12 months)	87.2% # [9]	NR	3 (643)
UCVA 20/40 or better, posterior chamber lenses (12 months)	92.1% # [9]	NR	2 (318)
Within 0.5 D target refraction	NR	NR	
Within 1 D target refraction	NR	NR	
Loss of ≥2 lines of BCVA, iris-fixated lenses (12 months)	0.6% # [9]	NR	1 (493)
Loss of ≥2 lines of BCVA, posterior chamber lenses (12 months)	0.7% # [9]	NR	2 (452)
Corneal ectasia	NR	NR	
Microbial keratitis	NR	NR	
Persistent epithelial defect	NR	NR	
Retinal detachment (≥1 year)	2.2% [28, 30]	1.5 to 2.9%	2 (1 052)
Choroidal neovascularisation (≥1 year)	2.3% [31]	NA	1 (522)
Epithelial in growth	NR	NR	
Raised intraocular pressure	4.24%, 4.80% $ [9]	NR	NR
Cataract	1.11%, 9.60% $ [9], 2% [32]	NR	NR
Re-operation iris-fixated lenses (6-120 months), posterior chamber lenses (8-24 months)	3.43%, 3.28% [29]	0 to 8.8%, 0 to 5%	10 (1 751), 5 (457)
Haze grade ≥2	NR	NR	
Haloes and/or glare	8.77%, 5.93% $ [9]	NR	NR

Night driving problems	NR	NR
Dryness	NR	NR
Pain	NR	NR

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NR: not reported; UCVA: uncorrected visual acuity
 # weighted mean, 95%CI not reported
$ From a systematic review by Chen et al. that reported adverse events in >1% of eyes, either myopic or hyperopic [9]. Iris-fixated lenses, posterior chamber lenses

Table 28 – Summary of findings for visual acuity and safety of intra-ocular lenses for patients with hyperopia with/without astigmatism, observational data [9]

Outcome (follow-up)	Median	Range	N of primary studies (N of eyes)
Efficacy index (mean postoperative UCVA/mean BCVA preoperatively) iris-fixated lenses (12 months)	0.73 [9]	NA	1 (17)
UCVA 20/20 or better, iris-fixated lenses (6 months)	22.7% [9]	NA	1 (22)
UCVA 20/40 or better, iris-fixated lenses (6 months)	90.9% [9]	NA	1 (22)
Within 0.5 D target refraction	NR	NR	
Within 1 D target refraction	NR	NR	
Loss of ≥2 lines of BCVA, iris-fixated lenses (6 months)	0% [9]	NA	1 (22)
Corneal ectasia	NR	NR	
Microbial keratitis	NR	NR	
Persistent epithelial defect	NR	NR	
Retinal detachment	NR	NR	
Choroidal neovascularisation	NR	NR	
Epithelial in growth	NR	NR	
Raised intraocular pressure	See myopia table	NR	
Cataract	See myopia table	NR	
Re-treatment	See myopia table	NR	
Haze grade ≥2	NR	NR	
Haloes and/or glare	See myopia table	NR	
Night driving problems	NR	NR	

Dryness	NR	NR
Pain	NR	NR

Abbreviations: BCVA: best spectacle corrected visual acuity; D: diopter; N: number; NA: not applicable; NR: not reported; UCVA: uncorrected visual acuity

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