



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

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## COLOPHON

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## LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
APOOB	Belgian Association of opticians and optometrists
BCVA	Best corrected visual acuity
D	Diopter
INAMI-RIZIV	Institut national d'assurance maladie-invalidité - Rijksinstituut voor ziekte- en invaliditeitsverzekering (National institute for health and disability insurance)
LASEK	Laser-assisted sub-epithelial keratomileusis
LASIK	Laser in-situ keratomileusis
NEI-RQL	National Eye Institute Refractive Quality of Life
NICE	National Institute for Health and Clinical Excellence
pIOL	Phakic intraocular lense
PRK	Photorefractive keratectomy
QALY	Quality-adjusted life years
QIRC	Quality of life impact of refractive correction
RCT	Randomised controlled trial
RES	Refractive eye surgery
RSVP	Refractive status and vision profile
SR	Systematic review
UCVA	Uncorrected visual acuity



## ■ SCIENTIFIC REPORT

### 1 BACKGROUND AND SCOPE OF THE REPORT

#### 1.1 Background

This report is the second part of a large KCE project on the correction of refractive error.

This topic was proposed to the KCE by four stakeholders: the Minister of Social Affairs and Public Health, the Federal Public Service (Health, Food Chain Safety and Environment), the National Institute for Health and Disability Insurance (INAMI – RIZIV) and a sickness fund. The most important questions related to the cost-effectiveness of refractive surgery: techniques, side effects and patients' satisfaction in comparison with other solutions (glasses or contact lenses). A connected question was the reimbursement of these techniques. A last group of questions related to organization of refractive surgery in extramural centres (quality of care - including safety - and regulations) given the rising number of patients operated in these settings.

Given the number and diverging nature of the questions, the topic has been split into distinct study projects:

- The first report (KCE report 202)<sup>1</sup> described a wide-scale survey on visual acuity disorders (including refractive errors) reported by the population and the perception of refractive error by these persons.
- The initial aim of this report was to provide a health technology assessment of refractive eye surgery techniques: clinical effectiveness and safety, cost-effectiveness, reimbursement schemes in other countries, patients' experiences with refractive surgery. Given the lack of robust outcome data, the part on cost-effectiveness analysis has been reduced to a long term cost comparison.
- A forthcoming report will analyse the regulation of extramuros centres where refractive surgery is often performed.



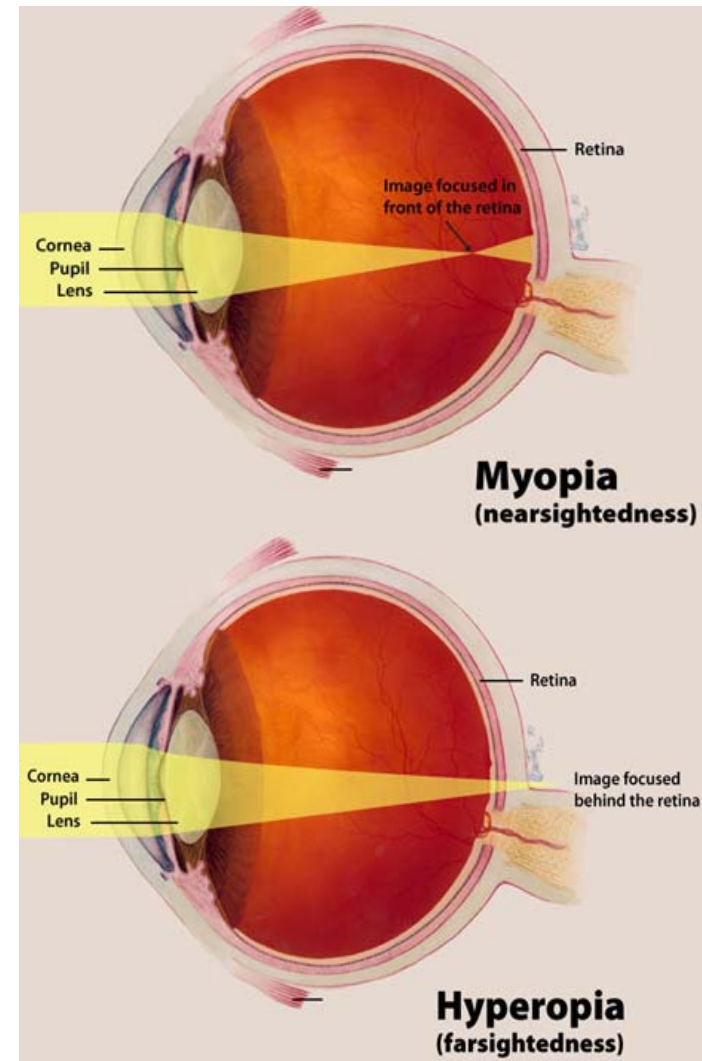
## 1.2 Refractive error and correction methods

The first report<sup>1</sup> provided an overview of the most common refractive errors in adults. They occur when the shape of the eye prevents light from focusing directly on the retina. The eyeball can be too long or too short but also changes in the shape of the cornea or aging of the lens can cause refractive errors. The most common symptoms are reduced visual acuity, blurred vision, eyestrain and headaches.

There are four types of refractive error:

- Myopia (nearsightedness or shortsightedness) is a condition where the light that comes in does not directly focus on the retina but in front of it (see Figure 1). As a result objects close-by appear clearly, while objects far away appear out of focus.
- Hyperopia (farsightedness, hypermetropia or hypermetropy) is a condition where the image of a distant object becomes focused behind the retina (see Figure 1). As a result objects close-by appear out of focus.
- Presbyopia is a specific, age-related type of farsightedness, due to the hardening of the eye lens, impairing accommodation to close objects.
- Astigmatism is an abnormal curvature of the cornea, where the eye does not focus light evenly onto the retina.

Figure 1 – Refractive error in myopia and hyperopia<sup>2</sup>





It should be noted that cataract is not a refractive error: its cause is a clouding of the lens, frequently related to aging. Still the replacement of the intraocular lens in cataract surgery is a technique that has similarities with one technique used for correcting refractive errors (see 1.4.3, insertion of intraocular lenses).

### 1.3 Refractive error: a frequent problem in Belgium and abroad

The previous report showed that refractive error is a frequent disorder that would affect up to two thirds of the adults in Belgium: refractive error and the related correction methods may have an emotional impact and an influence on the social life. This report also summarized epidemiological data on refractive error in other populations.

### 1.4 Possible solutions: glasses, contact lenses or surgery

#### 1.4.1 Glasses and contact lenses

Glasses, contact lenses and surgery are three solutions to correct refractive error<sup>2-5</sup>. The previous report described the different types of glasses, lenses and the possible side effects of these last ones. Their most common inconveniences are irritation of the eyes, redness and blurred vision. These minor symptoms may signal the onset of more severe complications i.e. corneal abrasion and infection, with a possible resulting corneal ulcer.

#### 1.4.2 Laser refractive surgery

The aim of laser surgery is to reshape the cornea in order to modify its refractive properties and thereby correct myopia, hyperopia and/or astigmatism. The most common laser techniques were photorefractive keratectomy (PRK) and laser epithelial keratomileusis (LASEK), progressively replaced now by laser in-situ keratomileusis (LASIK)<sup>4,5</sup>. The most recent technique called ReLEx smile is just mentioned as very few data on effectiveness and safety are available. Those laser procedures are performed under local anaesthesia using anaesthetic drops.

##### 1.4.2.1 Photorefractive keratectomy (PRK)

The surgeon first removes a small area of the cornea epithelium by abrasion (scraping) and then reshapes the cornea using Excimer laser: this computer-controlled beam of light removes microscopic amounts of the surface of the cornea (surface ablation). After the procedure the epithelial layer spontaneously regenerates.

##### 1.4.2.2 Laser-assisted sub-epithelial keratomileusis (LASEK)

This surface ablation technique is similar to PRK but in this procedure, the epithelium is not removed but an epithelial flap is first prepared with the help of ethanol, before the application of the Excimer laser. This epithelial flap is replaced afterwards and will heal during the following days.

##### 1.4.2.3 Laser in-situ keratomileusis (LASIK and Femto LASIK)

The difference with the previously mentioned surface ablation techniques is a thicker flap, involving not only the epithelium but also the outer part of the corneal stroma (thickness of 100-180µ as opposed to ~70µ). In this more recent procedure a flap is made using either a microkeratome (LASIK) or using another type of laser (Femtosecond laser for Femto LASIK). The Excimer laser energy is applied at this deeper level of the corneal stroma.

In many countries this technique has replaced the previous ones because it provides less discomfort and gives a quicker visual recovery.

##### 1.4.2.4 ReLEx smile

This most recent technique creates in a single step a thin lenticule together with a small access in the cornea. The lenticule will be removed through this incision, thereby changing the form of the cornea<sup>6</sup>.





### 1.4.3 Intraocular refractive surgery

The insertion of an intraocular lens of appropriate power is a second type of refractive surgery technique<sup>4, 7</sup>. This procedure can be performed in topical, bulbar or general anaesthesia.

A first possibility is the insertion of an additional lens (phakic intraocular lens, pIOL) in front of the original lens, leaving this original lens in place and keeping the mechanism of accommodation. One advantage is that this procedure is reversible.

A second possibility is the refractive lens exchange: the original lens is removed (as in a cataract operation) and replaced by a synthetic lens.

Intraocular surgery is used for refraction errors (i.e. myopia and hyperopia with or without astigmatism) that are too severe to be corrected with laser (see discussion). The inserted lenses can be either monofocal or multifocal, allowing for pseudo-accommodation. Toric intraocular lenses specifically address astigmatism.

## 1.5 Chapters of this report

This HTA report is subdivided into three parts:

- A systematic literature review on the clinical effectiveness and safety of surgery techniques for hyperopia and myopia (with or without astigmatism);
- An economic part: systematic review on economic evaluations of refractive surgery techniques, a long term cost comparison and overview of the reimbursement rules in other countries;
- A qualitative study on the patients' experiences with refractive surgery.

## 2 REFRACTIVE SURGERY TECHNIQUES: SYSTEMATIC REVIEW OF THE CLINICAL EFFECTIVENESS

### 2.1 Introduction

This chapter deals with the efficacy, effectiveness and safety of refractive surgery techniques. The initial research questions were:

- What is the evidence for the clinical effectiveness of PRK, LASEK, LASIK or phakic intraocular lenses for refractive eye surgery, compared to spectacles or contact lenses, or compared to each other?
- What is the evidence for the safety of the different techniques in terms of risk of vision loss and other side effects (short and long-term)?
- Which refractive errors cannot be sufficiently corrected with glasses/lenses and can only be treated with surgery ?

### 2.2 Methods

The methodology of this systematic review follows the KCE process book (<http://processbook.kce.fgov.be/?q=node/1>) and the Cochrane Handbook<sup>8</sup>, with an iterative approach. First, a search for systematic reviews, meta-analyses and HTA-reports that answer the clinical research question was conducted. If no systematic reviews, meta-analyses or HTA-reports were identified, the search would be extended to RCTs. When a relevant systematic review, meta-analysis or HTA-report was identified, the search for RCTs was limited to studies published after the last search date of the identified study. We searched for observational studies if there were insufficient (recent) data on the need for glasses and/or safety. The methodology is described in detail hereafter.



### Types of studies

The following types of studies were included:

- Systematic reviews, meta-analyses or HTA-reports that included RCTs or observational studies. To be selected, reports needed to have searched in at least Pubmed and to have assessed the study quality of randomized controlled trials in a systematic way, using the risk of bias tool or other appropriate instruments.
- RCTs;
- Observational studies with a follow-up of at least 6 months and:
  - $\geq 500$  eyes for LASEK or intraocular lens techniques;
  - $\geq 1000$  eyes for PRK or LASIK techniques.

This difference in cut off values was set by the researchers given the too large number of studies available for LASIK and PRK to be analysed within the available time and resources constraints.

### Types of patients

Adult patients with myopia, hyperopia and/or astigmatism. Medical conditions related to age such as cataract, presbyopia and other eye conditions (glaucoma, corneal disease and eye injuries) were excluded.

### Types of interventions

The most common surgical methods in refractive eye surgery currently used in Belgium:

- Most commonly used laser treatments:
  - photorefractive keratectomy (PRK)
  - laser-assisted sub-epithelial keratomileusis (LASEK)
  - laser in situ keratomileusis (LASIK) excluding Femto LASIK
- Phakic intraocular lenses: iris supported or sulcus supported intraocular lenses (excluding angle supported intraocular lenses, not used in Belgium).

### Types of control

Either the most common surgical methods in refractive eye surgery mentioned above, or spectacles or contact lenses. Studies that compared different LASIK techniques with each other, or different LASEK or different PRK techniques, were not selected (e.g. wave-front guided vs. wave-front optimized LASIK). For observational studies no control treatment was required.

### Types of outcome measures

The following outcome measures were searched for:

- Visual acuity:
  - primary outcome: the need for glasses or contact lenses,
  - primary outcome: the efficacy index: ratio of the mean postoperative uncorrected visual acuity (UCVA) to the mean preoperative best spectacle corrected visual acuity (BCVA)),
  - primary outcome: UCVA  $\geq 20/20$ ; secondary outcome:  $\geq 20/40$ ,
  - primary outcome: refraction within 0.5 D of target refraction; secondary outcome: within 1 D of target refraction,
- Quality of life,
- Safety.

Return to work, rehabilitation time and stereopsis were considered as well but the results did not give any information on these outcomes.

Visual acuity and safety data were extracted from (reviews that selected) randomized and observational studies. Quality of life data were only extracted from (reviews that selected) randomized studies. This outcome will be further studied in the economic chapter.



### 2.2.1 Search strategies

Medline, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) were searched in Dutch, English, French and German. Detailed search strings can be found in Appendix 1. HTA-reports were identified through a separate search detailed in the economic chapter. References of selected studies were checked to identify additional relevant studies.

Ongoing RCTs were searched for in the metaRegister ([www.controlled-trials.com/mrct](http://www.controlled-trials.com/mrct)), Clinicaltrials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) and the WHO International Clinical Trials Registry Platform ([www.apps.who.int/trialsearch](http://www.apps.who.int/trialsearch)).

Additional safety information was searched in:

- Toxnet ([www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?index.html](http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?index.html));
- The Food and Drug Administration (FDA) database that contains observational studies submitted to the FDA by the manufacturer to obtain approval.

The cell "material vigilance" of the Federal Agency for medications and health products (AFMPS–FAGG) was contacted as well but could not provide any specific information for Belgium.

## 2.2.2 Data collection and analysis

### 2.2.2.1 Selection of studies

Two reviewers (YS,PP) selected studies independently. Differences of opinion were resolved through discussion. If more than one systematic review, meta-analysis or HTA-report was identified for one type of (comparison of a) surgical method (PRK, LASEK or LASIK) and one patient group (myopia, hyperopia and/or astigmatism) we only used the most recent systematic review, meta-analysis or HTA-report. The older studies were checked for RCTs omitted by the newer studies.

### 2.2.2.2 Assessment of methodological quality

The following instruments were used to assess study quality:

- Systematic reviews, meta-analyses and HTA-reports: AMSTAR checklist<sup>9</sup> (for the clinical part of the HTA-report only);
- Randomized controlled trials (effectiveness): the Cochrane Risk of Bias tool<sup>8</sup>;
- Observational studies: McMaster Quality Assessment Scale of Harms (McHarm)<sup>10</sup> instrument, including 15 predefined criteria for assessing the quality of harms reporting.

Two reviewers (YS, PP) assessed study quality independently. Differences of opinion were resolved through discussion.

### 2.2.2.3 Data extraction and management

One reviewer (YS) extracted the data; a second reviewer (PP) checked the extracted data. Data for specific patient populations were extracted when available (age categories, high myopia, severe refractive error).

**The following data were extracted from systematic reviews, meta-analyses or HTA-reports:**

Reference, search date, funding, conflicts of interest, searched databases, language restrictions, inclusion criteria (study types, restrictions), number and type of included studies, quality appraisal included studies (type and outcome), population characteristics, intervention(s) and comparator(s), length of follow-up, outcomes at different time points of follow-up, sponsoring, conflicts of interest, quality appraisal of included studies.

**The following data were extracted from RCTs or observational studies:**

Reference, funding, conflicts of interest, years of inclusion, country and setting, number of patients included, patients characteristics, intervention(s) and comparator(s), length of follow-up, outcomes at different time points, sponsoring, conflicts of interest.



If needed, relative effect sizes were recalculated to reflect the following comparisons:

- PRK vs. LASEK,
- PRK vs. LASIK,
- LASEK vs. LASIK,
- Intraocular lenses vs. refractive surgery.

#### 2.2.2.4 Data analysis

The included studies were described in text and tables. Missing p-values were calculated in Stata 10.1, if needed. Meta-analyses were performed if no existing meta-analysis was identified and included, but RCTs were; or if more recent RCTs were identified after the publication of an included, existing meta-analysis. If the evidence permitted, differences in effectiveness and safety between treatment groups were meta-analysed (odds ratio and rate difference) using Comprehensive Meta-analysis version 2.2. Incidence/prevalence of outcomes from observational studies were not meta-analysed but only extracted from existing systematic reviews, meta-analyses or HTA-reports.

#### 2.2.2.5 Assessment of the strength of the body of evidence

GRADE was used to assess the quality of the evidence from randomized trials as high, moderate, low or very low ([www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)). GRADing was done by two reviewers (YS, PP) independently. Differences of opinion were resolved through discussion. The reasons for up- or downgrading the evidence were stated. Final conclusions were drawn according to the evidence on effectiveness and harms, and the quality of this evidence.

## 2.3 Search results and quality appraisal

### 2.3.1 Overview of the search and selection process

A flow diagram of the search and selection process is given in Appendix 3. The references of studies excluded after full-text review, with the reasons for exclusion, are given in Appendix 2.

#### Systematic reviews

The selection per type of comparison or intervention is summarized in Appendix 4.

This selection left 16 systematic reviews for inclusion: 13 systematic reviews and meta-analyses and 3 HTA-reports. We further excluded eight of these 16 reviews because:

- their search was done before the search of the most recent review, with fewer randomized trials included (3 reviews<sup>11-13</sup>: none of these reviews included randomized trials not included by the more recent reviews);
- their search was done before the search of the most recent review and it included fewer observational studies (2 reviews<sup>14, 15</sup>);
- one rapid review was much less extensive than the finally selected one<sup>16</sup>;
- another one had a poor methodology, with no quality appraisal of the included studies and a narrative presentation of results and conclusions<sup>17</sup>;
- one review was included in a more recent, selected review<sup>18</sup>.

#### Randomized controlled trials

We then searched for RCTs published from 2004 onwards, as the oldest search date of a systematic review was December 2004 (see Appendix 5). Two RCTs (Albarran-Diego 2012<sup>19</sup> and Gamaly 2007<sup>20</sup>) were further included.



### Observational studies

We then searched for observational studies on PRK, LASEK and LASIK published from December 2004 onwards (search date of the NICE 2005<sup>21</sup> systematic review) and for observational studies on intraocular lenses from January 2009 onwards (search data of the OTHAS 2009<sup>22</sup> systematic review). This additional work was performed upon request of the experts, in particular to get more precise information on safety aspects.

### Final selection

Finally, we selected:

- eight systematic reviews (Barsam 2012<sup>7, 23</sup>; Huang 2009<sup>24</sup>; NICE 2005<sup>21</sup>; OTHAS 2009<sup>22</sup>; Settas 2012<sup>25</sup>; Schallhorn 2008<sup>26</sup>; Shortt 2013<sup>27</sup> and Zhao 2010<sup>28</sup>);
- two newer RCTs (Albarran-Diego 2012<sup>19</sup> and Gamaly 2007<sup>20</sup>);
- 21 newer observational studies (Abdallat 2011<sup>29</sup>, Al-Mezaine 2009<sup>30</sup>, Arevalo 2012<sup>31</sup>, Bamashmus 2010<sup>32</sup>, Clare 2011<sup>33</sup>, Ghoreishi 2009<sup>34</sup>, Jiang 2012<sup>35</sup>, Kulkarni 2013<sup>36</sup>, Leccisotti 2007<sup>37</sup>, Lee 2005<sup>38</sup>, Lee 2006<sup>39</sup>, Lee 2011<sup>40</sup>, Qin 2007<sup>41</sup>, Ruiz-Moreno 2006<sup>42</sup>, Ruiz-Moreno 2006<sup>43</sup>, Sanders 2006<sup>44</sup>, Sanders 2008<sup>45</sup>, Schraepen 2005<sup>46</sup>, Sia 2012<sup>47</sup>, Spadea 2012<sup>48</sup> and Wroblewski 2006<sup>49</sup>).

### Additional safety search

The Toxnet database yielded 3 narrative reviews. However, they were not selected for inclusion because they were not based on systematic searches. The Food and Drug Administration database only yielded observational studies, no RCTs or systematic reviews, and therefore they were not retained. Some of these studies however were already included in the selected systematic reviews.

### 2.3.2 Quality appraisal of selected studies

#### Quality of systematic reviews

An overview of the quality of the eight selected systematic reviews is given in Table 22, Appendix 6:

- Three out of the eight reviews provided an 'à priori' design;
- Four reviews had duplicate study selection and data extraction;
- All eight reviews searched the literature comprehensively;
- In three reviews the status of a publication was not used as an inclusion criterion;
- Three reviews provided the list of excluded studies;
- Five reviews provided the characteristics of the included studies;
- Six reviews assessed and documented the scientific quality of included studies (this item was not applicable to one review);
- Three reviews used the scientific quality of the included studies appropriately in formulating their conclusions (this item was not applicable to one review);
- Four reviews used appropriate methods to combine studies' findings (this item was not applicable to the other four reviews);
- None of the reviews assessed the likelihood of publication bias (this item was not applicable to one review);
- Conflicts of interests and funding:
  - Two reviews stated the conflicts of interest or the funding of both the review and included primary studies;
  - The other five reviews stated the conflicts of interest of the review authors only;
  - The review that did not identify any study reported the conflicts of interest of its authors;



- Five reviews were publicly funded and all authors reported no conflicts of interest. The source of funding for the three other reviews was not reported: one out of three authors of Shortt 2013<sup>27</sup> reported potential conflicts of interest as six out of eight authors of Schallhorn 2008<sup>26</sup> did and five out of five authors of Huang 2009<sup>24</sup>.

### Quality of the randomized controlled trials

An overview of the risk of bias of the two selected randomized trials is given in Table 23, Appendix 6. Both trials were at a low risk of selection bias because the randomization sequence generation was adequate. Allocation concealment was unclear. The blinding of patients and personnel was rated as unclear, as was the blinding of outcome assessors. The risk of attrition bias, through the incomplete reporting of outcome data, was unclear for one trial (Albarran-Diego 2012<sup>19</sup>) and high for the other trial (Gamaly 2007<sup>20</sup>), because it was unclear how many patients were actually randomized (no schedule provided) and only 75% of eyes were available for follow-up after 6 months. The risk of reporting bias was unclear for both trials as no study protocols were identified. No other sources of bias were identified.

### Quality of the observational studies

An overview of the quality of the observational studies is given in Table 24 and Table 25 – Quality appraisal of the 21 selected observational studies with the McHarm (part 2) Table 25 in Appendix 6. The main findings of the quality appraisal are that:

- Only three out of 21 studies predefined harms using a standardised or precise definition;
- The mode of harms collecting was assessed as 'active' for nine studies; and as 'passive' for six studies;
- One study specified who collected the harms, and what the training and background of those persons were;
- Twelve studies specified the timing and frequency of harms collection; nine studies did not;
- Four studies used standard scales or checklists for all harms collected; 17 did not though standard scales or checklists may have been used for some harms in those studies;
- For five studies harms seemed to encompass all events collected; for 16 studies harms seemed to be a selective sample (e.g. studies only evaluated retinal detachment);
- Eleven studies did not specify how many patients were lost to follow-up.

## 2.4 Refractive eye surgery: results of randomized controlled trials

### 2.4.1 Refractive eye surgery vs. spectacles or contact lenses

#### 2.4.1.1 Lack of data in the RCTs

We did not identify any systematic review of RCTs that evaluated refractive eye surgery vs. spectacles or contact lenses.

This systematic literature review could not either answer to the third research question i.e. "Which refractive errors cannot be sufficiently corrected with glasses/lenses and can only be treated with surgery?". None of the identified reviews or RCTs gave an indication that some types of refraction errors cannot be corrected sufficiently with spectacles or contact lenses but can only be treated with surgery.

#### 2.4.1.2 Indications from expert consensus

Given this lack of evidence the researchers looked in international guidelines on that topic. Experts pointed out situations that cannot be corrected sufficiently by glasses: either the image obtained is still too small (e.g. in case of severe myopia) or differs too much between eyes (in case of anisometropia).

Experts from the Netherlands published a guideline on refractive surgery, based on consensus, with specific medical indications for the different techniques. As illustrations:

- LASIK is recommended for severe anisometropia (> 4 D) when lenses are not tolerated (also in very complex cases of astigmatism);



- Intraocular lenses are recommended e.g. for severe myopia (over -10 D), or severe hyperopia (over +5 D).

The Dutch insurers based their agreement for reimbursement on this expert consensus: many reports for individual patients have been published on their website.

In a similar way the French “Assurance-Maladie” reimburses contact lenses for very specific indications to allow a better vision than with glasses (see section 3.3.1).

**This systematic review did not identify any systematic reviews or RCTs that evaluated refractive eye surgery versus spectacles or contact lenses (i.e. “usual care”).**

## 2.4.2 PRK vs. LASEK (randomized data)

### 2.4.2.1 For patients with myopia with/without astigmatism

Two selected systematic reviews evaluated PRK vs. LASEK for myopia patients<sup>21, 28</sup>.

The first review by Zhao et al. searched up to July 2008 and included studies on patients with any degree of myopia and up to 3 D of astigmatism<sup>28</sup>. Eleven RCTs and one non-randomized comparative study were included. The results of the 11 RCTs are reported here. The mean age range of patients was 23 to 34.5 years. Median follow-up in the 11 RCTs was three months (range: 48 hours to one year).

The second review by NICE searched up to December 2004 and included ten RCTs<sup>21</sup>. Six of these RCTs were also included by Zhao et al. The remaining four RCTs were abstracts. NICE did not perform a meta-analysis. Therefore, NICE data are only reported here if no data from Zhao 2010 were available for a particular outcome.

There was low quality evidence that PRK-treated eyes had an UCVA of 20/20 or better less often than LASEK-treated eyes (OR: 0.78; 95%CI: 0.52 to 1.16; 5 studies, 580 eyes; at final follow-up) and had a refraction within 0.5 D of target refraction less often (OR: 0.81; 95%CI: 0.52 to 1.26; 4 studies, 545 eyes; at  $\geq 6$  months of follow-up)<sup>28</sup>.

There was low quality evidence that PRK-treated eyes lost  $\geq 1$  line of BCVA more often than LASEK-treated eyes (OR: 3.85; 95%CI: 0.59 to 25.30; 4 studies, 362 eyes at 1-24 months of follow-up) and moderate quality evidence that both treatments had an equal rate of eyes that lost  $\geq 2$  lines of BCVA, with no such events in two trials with 248 treated eyes<sup>28</sup>. Two trials (238 eyes) did not report any postoperative infections (moderate quality evidence)<sup>21</sup>. Healing time of the corneal epithelium was 0.4 days (95%CI: -0.54 to 0.61; 8 studies, 839 eyes; low quality evidence) longer in PRK-treated eyes<sup>28</sup>. The mean corneal haze score was 0.09 (95%CI: -0.09 to 0.28; 3 studies, 348 eyes, moderate quality evidence) higher in PRK treated eyes<sup>28</sup>. One trial (64 eyes) reported on the mean halo score, which was 1.71 (SD 1.27) vs. 1.62 (1.31) and on the mean glare score, which was 1.83 (SD 1.13) vs. 1.79 (1.18) (moderate quality evidence)<sup>21</sup>. There was low quality evidence that the mean postoperative pain score was higher in PRK-treated eyes (weighted mean difference 0.26; 95%CI: -0.20 to 0.72; 8 studies, 824 eyes)<sup>28</sup>.

Detailed evidence tables and a summary of findings table can be found in the supplement.

### 2.4.2.2 For patients with hyperopia with/without astigmatism

One systematic review (NICE 2005) that evaluated PRK vs. LASEK for patients with hyperopia was identified<sup>21</sup>. This review searched up to December 2004 and identified one RCT. This RCT included patients at a mean age of 38.7 years with hyperopia ranging between +2 and +5 D. All outcomes were of moderate quality.

At 24 months the efficacy index in PRK-treated eyes was worse than in LASEK-treated eyes (0.953 vs. 1.056,  $p=0.047$ )<sup>21</sup>. 73% vs. 67% of eyes reached an UCVA of 20/20 or better ( $p=0.29$ ) and 81% vs. 91% reached an UCVA of 20/40 or better ( $p=0.03$ )<sup>21</sup>. 57% vs. 78% of eyes was within 0.5 D of their target refraction ( $p=0.04$ )<sup>21</sup>. 12% vs. 14% ( $p=0.69$ ) lost  $\geq 1$  line of BCVA and no eye in either group lost  $\geq 2$  lines<sup>21</sup>. Postoperative complications such as infection, corneal melt, recurrent erosion syndrome, or dry-eye problems were not reported. Eight vs. zero eyes ( $p=0.004$ ) needed retreatment, all for regression. The mean corneal haze score was higher in PRK-treated eyes (0.45 (SD 0.31) vs. 0.20 (SD 0.27),  $p<0.05$ ), as



was the post-operative pain score on days 1-3 (1.13 (SD 0.95) vs. 0.59 (SD 0.52),  $p < 0.05$ )<sup>21</sup>.

A detailed evidence table and a summary of findings table can be found in the supplement.

#### Keypoints PRK versus LASEK:

- **For myopia**
  - **There was low quality evidence that PRK-treated eyes had a worse visual acuity than LASEK-treated eyes;**
  - **There was moderate quality evidence that no eye in either treatment lost  $\geq 2$  lines of BCVA, or had a postoperative infection; that PRK-treated eyes had a higher corneal haze score; and low quality evidence that the mean postoperative pain score was higher in PRK-than in LASEK treated eyes.**
- **For hyperopia**
  - **There was moderate quality evidence that LASEK-treated eyes had the best visual acuity;**
  - **There was moderate quality evidence that with both treatments no eye lost  $\geq 2$  lines of BCVA; more eyes in the PRK group needed retreatment; the mean corneal haze score was higher in PRK-treated eyes, as was the post-operative pain score.**

### 2.4.3 PRK vs. LASIK (randomized data)

#### 2.4.3.1 For patients with myopia with/without astigmatism

One selected systematic review evaluated PRK vs. LASIK for patients with myopia (Shortt 2013)<sup>27</sup>. RCTs on patients with any degree of myopia and up to 3 D of myopic astigmatism were eligible. The search was executed in November 2012 and 13 RCTs were finally included. Seven trials (1007 eyes) contributed to the main meta-analyses of visual acuity. Patients in the 13 trials had a stable refraction for at least one year; refractions ranged from -0.25 to -14.48. Eleven trials treated both eyes of each patient, either randomizing eyes (nine trials) or patients (two trials).

One additional RCT (Gamaly 2007)<sup>20</sup> was identified that was not included in the systematic review by Shortt et al. It included 16 patients (32 eyes) with myopia (mean manifest spherical equivalent -2.76 D; range: -1.00 to -4.88 D) with or without astigmatism and stable refraction for the past 12 months. Outcomes were reported after a follow-up of six months.

There was moderate quality evidence that PRK-treated eyes had worse visual acuity, compared to LASIK-treated eyes at 12 months post-treatment (OR UCVA 20/20 or better: 0.61 (95%CI: 0.41 to 0.91); OR % eyes within 0.5 D of target refraction: 0.69 (95%CI: 0.48 to 1.01); 7 studies with 1007 eyes included)<sup>27</sup>. There was low quality evidence that more PRK-treated eyes lost  $\geq 1$  line, and moderate quality evidence that more PRK-treated eyes lost  $\geq 2$  lines of BCVA at 6 months or longer post-treatment (OR loss  $\geq 1$  line BCVA: 1.19 (95%CI: 0.72-1.97); 7 studies with 794 eyes; OR loss  $\geq 2$  lines BCVA: 2.13 (95%CI: 1.02-4.35); 11 studies with 1494 eyes included)<sup>20, 27</sup>.

A median of 2.1% (range: 0-13%) of PRK-treated eyes reported a grade 2 sub-epithelial haze six to 12 months post-treatment; with grade 3 in a median of 0% (range: 0-7%) of eyes; and grade 4 in a median of 0% (range: 0-3%) of eyes<sup>20, 27</sup>. Optical side-effects such as glare or halos were reported by 6 RCTs in the Shortt 2013 review; only one RCT reported more side-effects after PRK<sup>27</sup>. Flap-related complications were reported in a median of 5% (range: 0-15%) of LASIK-treated eyes<sup>20, 27</sup>. Three studies reported pain scores, with significantly more pain experienced in the PRK-treated eyes in all studies (a summary effect size was not calculable)<sup>27</sup>.

Detailed evidence tables and a summary of the outcomes with GRADING of the evidence can be found in the supplement.

#### 2.4.3.2 For patients with hyperopia with/without astigmatism

One selected systematic review evaluated PRK vs. LASIK in patients with hyperopia (Settas 2012)<sup>25</sup>. This review searched up to February 2012 and RCTs on patients with any degree of hyperopia were eligible. No RCTs were identified.



**Keypoints PRK versus LASIK**

- **For myopia**
  - **There was moderate quality evidence that PRK-treated eyes had worse visual acuity;**
  - **There was low quality evidence that more PRK-treated eyes lost  $\geq 2$  lines of their BCVA; a median of 2.1% of PRK-treated eyes reported a grade 2 sub-epithelial haze; flap-related complications were reported in a median of 5% of LASIK-treated eyes; more pain was reported in PRK-treated eyes.**
- **For hyperopia no RCTs were identified.**

**2.4.4 LASEK vs. LASIK (randomized data)****2.4.4.1 For patients with myopia with/without astigmatism**

One systematic review by NICE evaluated LASEK vs. LASIK for patients with myopia<sup>21</sup>. The NICE review searched from 2000 up to December 2004; all RCTs comparing LASEK with LASIK in myopia patients with or without astigmatism were eligible. Three RCTs were included, one of which was only described in an abstract. The patients in these trials had a mean age of 21 to 27 years and a mean D of -1 to -13. The source of funding was unclear in all three studies. Follow-up ranged from three to 12 months.

There was evidence of moderate quality that there was no difference in the proportion of eyes with an UCVA of 20/20 or better at 6 months (85% vs. 84%,  $p=0.64$ ; 1 study, 394 eyes) or in the proportion of eyes with a refraction within 1 D of their target refraction (85% vs. 84%,  $p=0.64$ ; 1 study, 394 eyes)<sup>21</sup>. There was evidence of moderate quality that less LASEK-treated eyes had an UCVA of 20/40 or better at 3 months post-treatment (70% vs. 95%,  $p=0.04$ ; 1 study, 40 eyes) and that they had a refraction within 0.5 D of their target refraction less often (65% vs. 95%,  $p=0.02$ ; 1 study, 40 eyes)<sup>21</sup>. There was low quality evidence that the median of eyes that lost  $\geq 1$  line of their BCVA was equal in both treatment arms (median 0%, range 0-20% vs. median 0%, range 0-1%; 3 studies, 498 eyes; 3-12 months post-treatment) and low quality evidence that an equal number of eyes lost  $\geq 2$  lines of their BCVA at six months (0/32 vs.

0/32, 1 study)<sup>21</sup>. At 3 months post-treatment more LASEK-treated patients reported a haze grade  $\geq 2$  (35% vs. 0%,  $p=0.004$ ; 1 study, 40 eyes)<sup>21</sup>. Epithelial in growth was reported in 1/210 (0.5%) LASIK-treated eyes in one study; a raised intraocular pressure was reported in 3/184 (1.6%) LASEK-treated eyes in one study; and flap-related complications were reported in 3/32 (9.4%) LASEK-treated eyes in 1 trial and in 2/210 (9.5%) LASIK-treated eyes in another trial<sup>21</sup>.

Detailed evidence tables and a summary of the outcomes with GRADing of the evidence can be found in the supplement.

**2.4.4.2 For patients with hyperopia with/without astigmatism**

The systematic review by NICE 2005 searched for RCTs that evaluated LASEK vs. LASIK in patients with hyperopia<sup>21</sup>. However, no RCTs were identified.

**Keypoints LASEK versus LASIK**

- **For myopia**
  - **There was moderate quality evidence that there was no difference in visual acuity;**
  - **There was no evidence on the loss of  $\geq 2$  lines of BCVA; more LASEK-treated patients reported a haze grade  $\geq 2$ ; epithelial in growth was reported in 1/210 LASIK-treated eyes; raised intraocular pressure was reported in 3/184 LASEK-treated eyes; and flap-related complications were reported in 3/32 LASEK-treated eyes in 1 trial and in 2/210 LASIK-treated eyes in another trial.**
- **For hyperopia no RCTs were identified.**



### 2.4.5 Intraocular lenses vs. laser refractive surgery (randomized data)

#### 2.4.5.1 For patients with myopia with/without astigmatism

One systematic review that selected RCTs was identified and selected<sup>7</sup>. It evaluated intraocular lenses vs. laser refractive surgery in patients with moderate to high myopia (i.e. at least -6 D or worse). Three RCTs were included, with patients aged 21-52 and a myopic range of -6 to -20 D and up to -4 D with astigmatism. Two RCTs implanted the Artisan phakic intraocular lens and one RCT implanted the Vision Toric Implantable Collamer lens. In one study PRK was used in the refractive surgery group; two studies used LASIK.

One newer RCT was identified that compared intraocular lenses vs. LASIK<sup>19</sup>. It studied 92 eyes of 46 patients with moderate myopia (-6.0 to -9.0 D) and astigmatism  $\leq 1.0$  D. We conducted two new meta-analyses (for the outcomes % eyes with UCVA  $\geq 20/20$  and % eyes  $\leq 0.5$  D of target refraction) to combine the data from the systematic review with the data of this newer RCT (see also the supplement document).

There was low quality evidence that eyes with an intraocular lens had an UCVA  $\geq 20/20$  more often at 12 months post-treatment (OR: 1.65; 95%CI: 0.86 to 3.17; 3 studies, 258 eyes)<sup>7, 19</sup>. There was low quality evidence that eyes with an intraocular lens had an UCVA  $\geq 20/40$  less often at 12 months post-treatment (OR: 0.66; 95%CI: 0.36 to 1.22; 2 studies, 134 eyes)<sup>7</sup>. At 12 months post-treatment, eyes with intraocular lenses were within 0.5 D of their target refraction more often (OR: 1.29; 95%CI: 0.76 to 2.20; 4 studies, 308 eyes; low quality evidence)<sup>7, 19</sup>. There was moderate quality evidence that eyes with intraocular lenses lost  $\geq 1$  line (OR: 0.41; 95%CI: 0.33 to 0.51; 4 studies, 308 eyes) or  $\geq 2$  lines (OR: 0.35; 95%CI: 0.19 to 0.66; 4 studies, 308 eyes) of their BCVA less often, compared to laser surgery-treated eyes<sup>7, 19</sup>. In three studies (152 eyes) the median need for replacement of an intraocular lens was 2.3% (range: 2.2 to 17.4%)<sup>7, 19</sup>. Three studies found that glare and halos were more of a problem with laser surgery than with pIOL<sup>7</sup>; one study found no difference in night halos (13% vs. 17.4%,  $p=0.69$ )<sup>19</sup>. There was evidence of moderate quality that artificial tears were used more often by LASIK-treated patients at 12 months post-treatment (21.7% vs. 56.6%,  $p=0.06$ ; 1 study, 92 patients)<sup>19</sup>.

The incidence of flap/interface/de-centred ablation/haze related complications in laser treated eyes was 1 in 45 (2.2%) LASIK-treated eyes in one study<sup>7</sup>. There was a low risk of developing cataract with intraocular lenses: in one out of three trials (106 eyes) one eye developed cataract (two year follow-up). There was no significant difference in the loss of endothelial cells between treatment arms in two studies<sup>7</sup>.

Detailed evidence tables and a summary of the outcomes with GRADing of the evidence can be found in the supplement.

#### 2.4.5.2 For patients with hyperopia with/without astigmatism

The OTHAS 2009 review searched for RCTs that evaluated intraocular lenses vs. refractive surgery in patients with hyperopia, but did not identify any RCTs<sup>22</sup>. It searched from 2003 up to January 2009.

#### Keypoints intraocular lenses vs. laser refractive surgery

- **For myopia**
  - **There was low quality evidence that eyes with myopia worse than -6 D had better UCVA with an intraocular lens than with laser surgery;**
  - **There was moderate quality evidence that eyes with myopia worse than -6 D lost  $\geq 2$  lines of their BCVA less often with intraocular lenses compared to laser surgery; the median need for replacement of an intraocular lens was 2.3%; glare and halos were more of a problem with laser surgery; the incidence of flap/interface/de-centered ablation/haze related complications in laser treated eyes was 1 in 45 LASIK-treated eyes; one eye (intraocular lens) developed cataract in one out of three trials (106 eyes).**
- **For hyperopia no RCTs were identified.**



## 2.5 Refractive eye surgery: results of observational data

### 2.5.1 PRK (observational data)

The NICE 2005<sup>21</sup> review evaluated visual acuity and safety in patients with myopia, myopic astigmatism and hyperopia with/without astigmatism treated by PRK. In as far as this review described these patient groups separately, the results are described below. In addition, six newer observational studies described visual acuity and adverse effects after PRK (Ghoreishi 2009<sup>34</sup>, Leccisotti 2007<sup>37</sup>, Lee 2005<sup>38</sup>, Lee 2006<sup>39</sup>, Sia 2012<sup>47</sup> and Wroblewski 2006<sup>49</sup>).

#### 2.5.1.1 Patients with myopia

The NICE 2005<sup>21</sup> review evaluated visual acuity and safety in patients with myopia treated by PRK. It searched from 2000 up to December 2004 and included 30 case series or single arms of RCTs that either included >50 eyes (prospective series), or >100 eyes (retrospective series). The patients mean age ranged from 22 to 46 years, and their mean spherical equivalent from -2.10 to -11.43 D. The source of funding was unclear in 19 out of 30 studies. Nine studies received government funding, one study was funded by a manufacturer and one study by a charitable foundation.

The six observational studies included 37 554 patients and were retrospective studies on either visual acuity and safety (Ghoreishi 2009<sup>34</sup>, Lee 2005<sup>38</sup>, Sia 2012<sup>47</sup>) or studied one safety aspect only (Leccisotti 2007<sup>37</sup>, Lee 2006<sup>39</sup>, Wroblewski 2006<sup>49</sup>). All included patients were myopic patients with/without astigmatism except for Wroblewski 2006<sup>49</sup> who did not describe patients' characteristics. Patients with a short follow-up were sometimes excluded<sup>37, 39</sup>; reported loss to follow-up was 0% at six months<sup>38</sup>, at 1 year 45%<sup>47</sup>.

After ≥12 months a median of 76.0% of eyes (range: 39.1 to 94.8%; 12 studies, 3 872 eyes) had an UCVA of ≥20/20<sup>21, 34</sup>, and a median of 92.3% (range: 37.6-98.8%; 9 studies, 1 900 eyes) had an UCVA of ≥20/40<sup>21</sup>. A median of 69.4% (range: 56.5-87.4%; 9 studies, 2 949 eyes) of eyes was ≤0.5 D of their target refraction and a median of 91.0% (range: 39.1-95.8%; 11 studies, 3 361 eyes) was ≤1 D at 12 months or longer post-treatment<sup>21, 34</sup>. After ≥6 months of follow up, a median of 4.5% of eyes (range: 0.7-15.3%; 11 studies, 3 705 eyes) had lost 1 line of BCVA and a median of

0.3% of eyes (range: 0-20.5%; 14 studies, 4 607 eyes) had lost ≥2 lines of their BCVA<sup>21, 38, 47</sup>. A median of 0.015% (range: 0 to 0.03%; 2 studies, 7 793 eyes) of eyes had a corneal ectasia<sup>34, 37</sup>. A median of 0% (range: 0 to 0.02%; 3 studies, 26 641 eyes) of eyes had a keratitis/bacterial infection<sup>21, 34, 49</sup>. No patient had a persistent epithelial defect at six months post-treatment in one study (54 eyes)<sup>21</sup>. A median of 0.18% of eyes (range: 0.15 to 0.2%; 2 studies, 7 918 eyes) had a retinal detachment<sup>21, 39</sup> and at a median follow-up of 26 months 0.02% had choroidal neovascularisation in one study (5 936 eyes), a rate considered similar to that in non-treated myopia<sup>21</sup>. Epithelial in growth was reported in one eye (0.62%) in one study (161 eyes)<sup>21</sup>. A median of 1.9% of eyes (range: 0-7.6%; 5 studies, 108 eyes) had a raised intraocular pressure, one month to 12 years post-treatment. Re-treatment was done in a median of 1.5% of eyes (range: 1.2-3.6%; 3 studies, 948 eyes) after six to 18 months<sup>21</sup>. A haze grade ≥2 was reported by a median of 0% of patients (range: 0-31.4%; 12 studies, 3 3885 patients) one month to 12 years post-treatment<sup>21, 38, 47</sup>. 17% (median, range: 2.4-23.8%; 5 studies, 2 216 eyes) reported haloes and/or glare at six to 18 months of follow-up and night vision/driving problems were reported by a median of 31.1% of patients (range: 5.2-57.7%; 3 studies, 1 249 eyes) at one week to six months of follow-up<sup>21</sup>. Dry eyes were reported by 41.1% of patients in one study (241 eyes) and a median of 28% of patients (range: 25-31%; 2 studies, 132 eyes) scored their pain as distressing to excruciating, at four to five days post-operation<sup>21</sup>.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

#### 2.5.1.2 Patients with myopic astigmatism

The NICE 2005<sup>21</sup> review evaluated visual acuity and safety in patients with myopic astigmatism treated by PRK, described in 6 case series or single arms of RCTs that either included >50 eyes (prospective series), or >100 eyes (retrospective series). The mean age of patients was 32 to 43 years, and their mean spherical equivalent was between -4.63 to -7.18 D. The source of funding was unclear for five studies; the remaining study was partly funded though a number of sources including a charitable foundation and Research to Prevent Blindness Inc.



At  $\geq 12$  months of follow-up a median of 62.6% of eyes (range: 58.0-67.1%; 2 studies, 536 eyes) had an UCVA  $\geq 20/20$  and a median of 93.5% (range: 91.2-95.0%; 3 studies, 633 eyes) had an UCVA  $\geq 20/40$  <sup>21</sup>. A median of 55.3% of eyes (range: 40.7-69.8%; 2 studies, 6 156 eyes) were  $\leq 0.5$  D of their target refraction and a median of 83.3% (range: 81.3-87.9%; 3 studies, 6 630 eyes) were  $\leq 1$  D of their target refraction <sup>21</sup>. 7.1% (1 study, 56 eyes) lost 1 line of their BCVA and a median of 0.6% of eyes (range: 0-1.6%; 3 studies, 592 eyes) lost  $\geq 2$  lines BCVA <sup>21</sup>. One study (749 eyes) with a follow-up of 18 months reported one eye (0.13%) with keratitis, one eye with a persistent epithelial defect and one eye with retinal detachment <sup>21</sup>. The rate of raised intraocular pressure was 0.6% in this study. At 24 months, 25.8% of eyes were re-treated in one Turkish study (93 eyes) published in 2000 <sup>21</sup>. At 12 months 37.7% of patients reported haloes and 27.1% of eyes reported an increase in glare score (compared to pre-PRK) in another study (number of eyes not reported) <sup>21</sup>.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

### 2.5.1.3 Patients with hyperopia with/without astigmatism

The NICE 2005 <sup>21</sup> review evaluated visual acuity and safety in patients with hyperopia treated by PRK, described in six case series or single arms of RCTs that either included  $>50$  eyes (prospective series), or  $>100$  eyes (retrospective series). Patients' mean age ranged from 35.4 to 51.8 years, and their mean spherical equivalent from +2.48 to +5.64 D. The source of funding was unclear for two studies; three studies reported government funding, one study was supported by the manufacturer.

At  $\geq 12$  months the median UCVA was  $\geq 20/20$  in a median of 59% of eyes (range: 48.8-84.0%; 5 studies, 1 332 eyes) and  $\geq 20/40$  in a median of 85.5% of eyes (range: 72.1-95.1%; 5 studies, 1 332 eyes) <sup>21</sup>. A median of 60.8% of eyes (range: 53.8-79.0%; 5 studies 1 345) was  $\leq 0.5$  D of target refraction and a median of 78.9% (range: 69.6-86.0%; 5 studies, 1 345 eyes) was  $\leq 1$  D after a follow-up of  $\geq 12$  months <sup>21</sup>. A median of 16.3% of eyes (range: 5.5-27.0%; 5 studies, 1 425 eyes) lost 1 line of their BCVA and a median of 7.0% (range: 0-13.5%; 5 studies, 1 425 eyes) lost  $\geq 2$  lines. A high median of 21.1% (range: 11.3-30.8%) of eyes with high hyperopia ( $+3.5$  D or higher) lost  $\geq 2$  lines of their BCVA; vs. a median of

2.1% (range: 0-11.3%) of eyes with less severe hyperopia <sup>21</sup>. No keratitis/infection was reported in one study (200 eyes) <sup>21</sup>. The intraocular pressure was raised in a median of 8.6% of eyes (range: 8.5-8.6%; 2 studies, 1 000 eyes) <sup>21</sup>. Re-treatment was needed in 0.6% of eyes in one study on 276 eyes <sup>21</sup>. Haloes and/or glare were reported by a median of 12.0% of patients (range: 7.7-15%; 4 studies, 1 132 eyes) after one week to 12 months of follow-up and night driving problems were reported by a median of 18% of patients (range: 3.4-26.8%; 4 studies, 1 260 eyes) after a follow-up of six to 12 months <sup>21</sup>.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

### Key points PRK (observational data)

- For myopia

- At 12 months post-treatment a median of 76.0% of eyes had an UCVA of  $\geq 20/20$ , and a median of 91.0% was  $\leq 1$  D of their target correction;
- After  $\geq 6$  months a median of 0.3% of eyes had lost  $\geq 2$  lines of their BCVA; no patient had a keratitis or infection; a median of 0.18% of eyes had a retinal detachment; 0.62% had epithelial in growth; a median of 1.9% of eyes had a raised intraocular pressure; re-treatment was done in a median of 1.5% of eyes; a median of 17% reported haloes and/or glare; and a median of 28% of patients scored their pain as distressing to excruciating at four to five days post-operation.

- For myopic astigmatism

- At  $\geq 12$  months post-treatment a median of 62.6% of eyes had an UCVA  $\geq 20/20$  and a median of 83.3% eyes were  $\leq 1$  D of their target refraction



- **A median of 0.6% of eyes lost  $\geq 2$  lines of their BCVA; one study reported one eye (0.13%) with keratitis, one eye with a persistent epithelial defect and one eye with retinal detachment and a rate of 0.6% of raised intraocular pressure; 37.7% of eyes reported haloes and 27.1% of eyes experienced an increase in glare scores compared to pre-PRK in one study.**
- **For hyperopia**
  - **At  $\geq 12$  months the median UCVA was  $\geq 20/20$  in a median of 59% of eyes; a median of 78.9% of eyes was  $\leq 1$  D of their target refraction**
  - **A median of 2.1% of eyes with low hyperopia (maximum +3.5 D) lost  $\geq 2$  lines of their BCVA; no keratitis/infection was reported in one study; the intraocular pressure was raised in a median of 8.6% of eyes; re-treatment was needed in 0.6% of eyes; haloes and/or glare were reported by a median of 12% of patients.**

### 2.5.2 LASEK (observational data)

The NICE 2005<sup>21</sup> review evaluated visual acuity and safety in patients with myopia, myopic astigmatism and hyperopia with/without astigmatism treated by LASEK. In addition, one more recent observational study (Kulkarni 2013<sup>36</sup>) described visual acuity and safety in myopia patients with/without astigmatism.

#### 2.5.2.1 For patients with myopia with/without astigmatism

The NICE 2005<sup>21</sup> review evaluated visual acuity and safety in patients with myopia treated by LASEK, described in 26 case series or single arms of RCTs that either included  $>25$  eyes (prospective series), or  $>50$  eyes (retrospective series and abstracts). The mean age range of included patients was 26 to 42 years, and the range of their mean preoperative spherical equivalent was -2.48 to -12.0 D. Three of these 26 studies included some patients with hyperopia; the inclusion criteria were unclear in two studies. Data were presented for low/moderate myopia participants in seven studies and for high myopia (worse than -6.0 D) in five studies. The source of funding was unclear in 22 out of 26 studies. The Kulkarni

2013<sup>36</sup> study evaluated 560 eyes with myopia -1.0 to -8.0 D and a cylinder of 0 to +2 D.

- At a follow-up of 12-24 months, a median of 64% of eyes (range: 38-90.5%; 9 studies,  $>1534$  eyes) had an UCVA of  $\geq 20/20$ <sup>21, 36</sup> and a median of 92% of eyes (range: 77-100%; 7 studies,  $>890$  eyes) had an UCVA of  $\geq 20/40$ <sup>21</sup>. A median of 82% of eyes (range: 42-96%; 8 studies,  $>1\,080$  eyes)<sup>21</sup> was within 0.5 D of target refraction and a median of 91.5% (range: 67-100%; 8 studies, 1 210 eyes) was within 1.0 D of target refraction after 6 months<sup>21, 36</sup>. At 12 months the efficacy indexed ranged from 1.03 to 1.13 in a study with 560 eyes<sup>36</sup>.

At three to 12 months of follow-up a median of 2.2% of eyes (range: 0-16%; 13 studies, 1 722 eyes) lost 1 line of their BCVA<sup>21</sup> and a median of 0% (range: 0-8.2%; 21 studies, 3 105 eyes) lost  $\geq 2$  lines<sup>21, 36</sup>. Corneal ectasia was not reported in one series of 171 eyes after a mean of eight months of follow-up<sup>21</sup>. A median of 0.6% of eyes had a keratitis or infection (range: 0-3.4%; 5 studies, 1 512 eyes)<sup>21, 36</sup> and one eye (1.2%) with a raised intraocular pressure was found in one study with a follow-up of six months<sup>21</sup>. Epithelial flap-related complications were reported in a median of 2.0% of patients (range: 0-14%; 9 studies, 959 eyes)<sup>21</sup>. Retreatment was done in a median of 1.15% of eyes (range: 0-5.5%; 8 studies, 1 483 eyes)<sup>21, 36</sup>. Haze grade  $\geq 2$  was reported by a median of 0% of patients (range: 0-25%; 16 studies, 2 093 patients) at three to 12 months post-treatment<sup>21</sup>. A median of 3% of patients (range: 0-33%; 4 studies, 489 patients) reported dry eyes syndrome in studies with a follow-up of six to 12 months<sup>21</sup>. Strong to severe post-operative pain was reported by a median of 4.0% of patients (range: 0-19%; 5 studies, 849 patients)<sup>21</sup>.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

#### 2.5.2.2 For patients with hyperopia with/without astigmatism

None of the identified SRs evaluated LASEK for patients with hyperopia. Three out of 26 case series on LASEK, included in the NICE 2005<sup>21</sup> review, included some patients with hyperopia. However, these patients were not reported on separately in the review.

**Keypoints LASEK (observational data)**

- **For myopia**
  - **At 12-24 months post-treatment a median of 64% of eyes had an UCVA of  $\geq 20/20$  and a median of 91.5% of eyes was within 1.0 D of their target refraction;**
  - **Loss of  $\geq 2$  lines of BCVA and haze grade  $\geq 2$  were rarely reported in the studies (median 0%); a median of 0.6% of eyes had a keratitis or infection; one eye (1.2%) had raised intraocular pressure in one study; epithelial flap-related complications were reported in a median of 2.0% of patients; a median of 1.15% of eyes needed retreatment; strong to severe post-operative pain was reported by a median of 4.0% of patients.**
- **For hyperopia: none of the identified SRs evaluated LASEK for patients with hyperopia.**

**2.5.3 LASIK (observational data)**

Two systematic reviews<sup>21, 26</sup> and 11 newer observational studies that included 1000 eyes or more and had a follow-up of 6 months or more (Abdallat 2011<sup>29</sup>, Al-Mezaine 2009<sup>30</sup>, Arevalo 2012<sup>31</sup>, Bamashmus 2010<sup>32</sup>, Clare 2011<sup>33</sup>, Lee 2006<sup>39</sup>, Lee 2011<sup>40</sup>, Qin 2007<sup>41</sup>, Sanders 2006<sup>44</sup>, Schraepen 2005<sup>46</sup>, Spadea 2012<sup>48</sup>) evaluated the visual acuity and safety in patients treated by LASIK.

The NICE 2005<sup>21</sup> review described in 64 case series or single arms of RCTs that either included >300 eyes (prospective series), or >500 eyes (retrospective series). The range of mean ages was 16 to 75 years and the range of mean preoperative spherical equivalents was -11.69 to +2.7 D. Thirty-three studies included participants with myopia or myopic astigmatism, two studies included participants with hyperopia or hyperopic astigmatism, nine studies included participants with both myopia and hyperopia, and 20 studies did not report whether participants had myopia or hyperopia. Four studies were funded by government grants, 10 by manufacturers and 38 studies did not declare their source of funding. The remaining 11 studies were funded by a range of private sources including

seven funded or part-funded by the charity Research to Prevent Blindness (New York).

The Schallhorn 2008<sup>26</sup> review searched up to May 2007 and included 11 RCTs, 2 non-randomized comparative studies, 1 prospective cohort study and 33 low-quality observational studies on patients with primary myopia, with or without astigmatism, treated by wavefront-guided LASIK. The level of evidence was provided, but individual quality appraisal results were not. Six out of eight authors declared potential conflicts of interest because of various ties to the industry.

The 11 observational studies included 89 544 LASIK-treated, mainly myopic, eyes. Eight out of the eleven studies searched for one to three adverse events (retinal detachment, buttonhole flaps, flap displacement etc.) while the other three studies evaluated both visual acuity and safety (Abdallat 2011<sup>29</sup>, Sanders 2006<sup>44</sup>, Schraepen 2005<sup>46</sup>).

**2.5.3.1 For patients with myopia with/without astigmatism**

In the NICE 2005 review plus the observational study of Schraepen 2005 a median of 64% (range: 14.7 to 90.1%; 27 studies, >15 562 eyes) of myopia eyes had an UCVA of 20/20 or better one to 36 months after LASIK<sup>21, 46</sup>, and a median of 94% (range: 76.2 to 100%; 25 studies, >14 388 eyes) of eyes had an UCVA of 20/40 or better<sup>21</sup>. The reported ranges by Schallhorn 2008 were slightly better, with 56-100% of eyes in published studies and 84.1-93.9% of eyes in Food and Drug Administration (FDA) reports (premarket approval) having an UCVA of 20/20 or better<sup>26</sup>. An UCVA  $\geq 20/20$  was attained in a median 80.6% of low/moderate myopia eyes ( $\leq 7$  D; range: 44.1-90.1%; 8 studies, 3231 eyes); in a median of 45.2% of high myopia eyes ( $\geq 6$  D; range: 14.7-74.3; 8 studies, 2194 eyes); and in a median of 87.8% of eyes with myopic astigmatism (range 52.0-90.1%; 3 studies, 579 eyes)<sup>21</sup>.

Three to 12 months after LASIK a median of 76.0% (range: 53.4-90.4%; 25 studies, >12 220 eyes)<sup>21, 29, 44</sup> of eyes was within 0.5 D of their target refraction, and 92.6% (range: 74.7-100%; 24 studies, >10 563 eyes)<sup>21, 44</sup> was within 1D after three to six months. The reported ranges by Schallhorn 2008 were slightly better, with 72-100% of eyes in published studies and 75.9-94.6% of eyes in FDA-reports (premarket approval) having their refraction  $\leq 0.5$  D of their target refraction<sup>26</sup>. Eyes with low/moderate



myopia ( $\leq 7$  D; 8 studies, 3231 eyes) attained a refraction  $\leq 0.5$  D of their target refraction in a median of 80.6% (range 44.1-90.1%); eyes with high myopia ( $\geq 6$  D; 8 studies, 2194 eyes) in a median of 45.2% (range: 14.7-74.3%); and eyes with myopic astigmatism (3 studies, 579 eyes) in a median of 87.8% (range 52.0-90.1%)<sup>21</sup>.

The median percentage of eyes that lost  $\geq 2$  lines of BVCA was 0.62% (range: 0-3%; 23 studies, 20 529 eyes)<sup>21, 29, 44, 46</sup>. The reported ranges by Schallhorn 2008 were slightly better, with 0% of eyes that lost  $\geq 2$  lines of BCVA in published studies and 0 to 0.6% of eyes in FDA-reports<sup>26</sup>. Percentages were similar in patients with low to moderate myopia (median 0.7%; range: 0-1.6%) and patients with high myopia (median 0.9%; range: 0 to 1.8%)<sup>21</sup>.

The complications and patient-reported outcomes hereafter include studies in patients with hyperopia, or patients with a mixed or unreported refraction. Flap-related complications were described in seven subgroups: buttonhole flap in a median of 0.17% of eyes (range: 0-0.53%; 10 studies, 14 566 eyes)<sup>21, 30</sup>; free cap 0.13% (range: 0-2%; 15 studies, 148 438 eyes); torn flap 0.06% (range: 0.03-0.09%; 2 studies, 8 179 eyes); incomplete flap 0.28% (range: 0-2.86%; 20 studies, 152 694 eyes); thin flap 0.23% (range: 0-0.86%; 9 studies, 143 185 eyes); flap folds/striae 0.77% (range: 0.03-5.52%; 14 studies, 10 679 eyes); dislodged flap 1.2% (range: 0.033-2.41%; 10 studies, 29 305 eyes)<sup>21, 33</sup>. Corneal ectasia was reported in a median of 0.25% of eyes (range: 0 to 0.9%; 6 studies, 14 833 eyes)<sup>21, 48</sup> and microbial keratitis in a median of 0% of eyes (range: 0 to 0.16%; 6 studies, 4 499 eyes)<sup>21</sup>. A median of 1.7% of eyes had an epithelial defect (range: 0 to 10.2%; 20 studies, 23 679 eyes) and a median of 0.19% a retinal detachment (range: 0.033-0.84%; 7 studies, 95 389 eyes)<sup>21, 31, 32, 39-41</sup>. Glaucoma and cataract were seen in 0.2% and 0.3% of eyes respectively (1 study, 1 637 eyes)<sup>40</sup>. Choroidal neovascularisation was seen in 0.33% of eyes in one study (3 009 eyes), an incidence similar to non-treated myopic eyes, and epithelial in growth in a median of 1.4% of eyes (range: 0 to 4.4%; 19 studies, 17 715 eyes)<sup>21</sup>. Raised intraocular pressure was seen in a median of 0.14% of eyes (range: 0 to 0.86%; 4 studies, 2 071 eyes) and a median of 10.7% of eyes was re-treated (range: 1.1 to 37.0%; 20 studies, 17 229 eyes)<sup>21, 29, 44</sup>.

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. Corneal haze was reported in a median of 0% of eyes (range: 0-2.08%; 7 studies, 4 760 eyes) with varying definitions of haze used<sup>21</sup>. Glare was reported worse - compared to post operatively - in 10.3-29.9% of patients and better in 10.9-24.6%; halos were reported worse in 14.4-42.9%, and better in 6.0-15.6% (7 studies)<sup>21</sup>. Night driving difficulties were reported worse by 10.3-36.6%, and better by 22.7-40.3% of patients (7 studies)<sup>21</sup>. Dryness of the eyes was reported to be worse by 17-44% of patients, and better by 9.8-28.6% (7 studies)<sup>21</sup>. Pain was reported worse by 0.7-5.7% of patients and better by 4.6-9.1% compared to pre-operatively (6 studies)<sup>21</sup>. It is unclear however how pre-operative pain should be interpreted.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

### 2.5.3.2 For patients with hyperopia with/without astigmatism

A median of 51.5% of eyes (range: 51.0 to 64.8%; 5 studies, >396 eyes) with hyperopia had an UCVA of 20/20 or better, six to 24 months after LASIK, and 95.9% (range: 93.9-100%; 5 studies, >396 eyes) had an UCVA of  $\geq 20/40$ <sup>21</sup>. 62% (range: 59.0 to 74.1%; 5 studies, 530 eyes) of hyperopic eyes were within 0.5 D of their target refraction after six to 12 months; and 88% (range: 86.0 to 91.4%; 5 studies, 530 eyes) was within 1 D<sup>21</sup>. A median of 3.4% (range: 2.2 to 4.7%; 2 studies 396 eyes) of hyperopic eyes lost two or more lines of BCVA after a follow-up of 12 months or longer<sup>21</sup>. Other complications and patients reported outcomes were reported on in the paragraph on patients with myopia/myopic astigmatism (section 2.5.3.1).

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

**Key points LASIK (observational data)**

- **For myopia**
  - **A median of 64% of eyes had an UCVA of 20/20 or better, one to 36 months after LASIK; a median of 92.6% of eyes was within 1D of their target refraction after three to six months;**
  - **A median of 0.62% eyes lost  $\geq 2$  lines of their BVCA.**
- **Side effects for myopia or hyperopia :**
  - **Median flap-related complications: buttonhole flap 0.17% of eyes; free cap 0.13%; torn flap 0.06%; incomplete flap 0.28%; thin flap 0.23%; flap folds/striae 0.77%; dislodged flap 1.2%;**
  - **Corneal ectasia was reported in a median of 0.25% of eyes; microbial keratitis in a median of 0%; a median of 0.19% had a retinal detachment; glaucoma in 0.2% and cataract in 0.3% in another study; epithelial in growth in a median of 1.4% of eyes; raised intraocular pressure was seen in a median of 0.14% of eyes; and a median of 10.7% of eyes was re-treated (range: 1.6 to 37.0%; 18 studies, 14 621 eyes); corneal haze was reported in a median of 0% of eyes.**
- **For hyperopia**
  - **A median of 51.5% of eyes had an UCVA of 20/20 or better, six to 24 months after LASIK; 88% of eyes was within 1 D of their target refraction after six to 12 months;**
  - **A median of 3.4% eyes lost  $\geq 2$  lines of their BCVA.**

**2.5.4 Intraocular lenses (observational data)**

The use of intraocular lenses was evaluated by the OTHAS 2009<sup>22</sup> and Huang 2009<sup>24</sup> reviews and by four newer observational studies that included at least 500 eyes and had a follow-up of at least six months<sup>35, 42, 43, 45</sup>. OTHAS 2009 included iris-fixated (anterior chamber lenses that are anchored to the iris with a claw) and posterior chamber lenses, as these are licensed in Canada. It searched from 2003 up to January 2009 and selected one systematic review and 19 observational studies with  $\geq 20$  eyes included. Patients' characteristics were not summarized. All observational outcomes were GRADEd low or very low. The review by Huang et al. searched up to July 2008 and included an unclear number of studies on safety (visual accuracy data were presented in a narrative way and are not reported here)<sup>24</sup>. As the review by Huang et al. was less transparent compared by the review by OTHAS, outcomes from the OTHAS 2009 review will be described here and outcomes from the Huang 2009 review will only be described if that particular outcome was not described by OTHAS.

The four observational studies included between 500 and 600 eyes and were all concerned with searching for single adverse events (retinal detachment<sup>35, 43</sup>, choroidal neovascularisation<sup>42</sup>, cataract<sup>45</sup>) at a mean of three to four years after intraocular lens implantation.

**2.5.4.1 For patients with myopia with/without astigmatism**

The weighted mean efficacy index (mean postoperative UCVA/mean BCVA preoperatively) of iris-fixated lenses, 12 months post-treatment, was 0.85 (95%CI not reported; 3 studies, 704 eyes) and 0.99 (95%CI not reported; 2 studies, 101 eyes) for posterior chamber lenses<sup>22</sup>. At 12 months, a weighted mean of 33% of eyes (95%CI not reported; 2 studies, 554 eyes) with an iris-fixated lens and 58.5% of eyes with a posterior chamber lens (95%CI not reported; 2 studies, 318 eyes) had an UCVA of  $\geq 20/20$ <sup>22</sup>.





0.6% (iris-fixated lenses; 1 study, 493 eyes) and 0.7% (posterior chamber lenses; 95%CI not reported; 2 studies, 452 eyes) of eyes lost  $\geq 2$  lines of their BCVA<sup>22</sup>. A median of 2.2% of eyes had a retinal detachment (range: 1.5 to 2.9; 2 studies, 1 052 eyes)<sup>35, 43</sup>, which, according to the authors, seemed similar to the rate of retinal detachment occurring naturally in myopic eyes. Macular choroidal neovascularisation was observed in 2.3% of 522 eyes in one study<sup>42</sup>, also considered by the authors to be similar to the natural rate of neovascularisation in myopic eyes. Raised intraocular pressure was observed in 4.24% (iris-fixated lenses) and 4.80% (posterior chamber lenses) of eyes (number of studies or eyes not reported)<sup>22</sup>. Cataract was observed in 1.11% (iris-fixated lenses) and 9.60% (posterior chamber lenses) of eyes (number of studies or eyes not reported)<sup>22</sup> and in 2% of 526 eyes in one other study<sup>45</sup>. Haloes and/or glare were observed in 8.77% (iris-fixated lenses) and 5.93% (posterior chamber lenses) of eyes (number of studies or eyes not reported)<sup>22</sup>. Re-treatment was needed in a median of 3.43% (iris-fixated lenses; range: 0 to 8.8%; 10 studies, 1 751 eyes) and 3.28% (posterior chamber lenses; range: 0 to 5%; 5 studies, 475 eyes) of eyes<sup>24</sup>.

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

#### 2.5.4.2 For patients with hyperopia with/without astigmatism

The weighted mean efficacy index (mean postoperative UCVA/mean BCVA preoperatively) of iris-fixated lenses, 12 months post-treatment, was 0.73 (1 study, 17 eyes)<sup>22</sup>. At 6 months, 22.7% of eyes (1 study, 22 eyes) with an iris-fixated lens had an UCVA of  $\geq 20/20$  and 90.9% had an UCVA of  $\geq 20/40$  (1 study, 22 eyes)<sup>22</sup>.

0% (iris-fixated lenses; 1 study, 22 eyes) of eyes lost  $\geq 2$  lines of their BCVA<sup>22</sup>. Other safety issues are described in the paragraph on patients with myopia (paragraph 2.5.4.1).

Detailed evidence tables and a summary of the outcomes can be found in the supplement.

#### Key points intraocular lenses

- **For myopia**
  - The weighted mean efficacy index (mean postoperative UCVA/mean BCVA preoperatively) of iris-fixated lenses, 12 months post-treatment, was 0.85 and 0.99 for posterior chamber lenses. At 12 months, a weighted mean of 33% of eyes with an iris-fixated lens and 58.5% of eyes with a posterior chamber lens had an UCVA of  $\geq 20/20$ ;
  - 0.6% of eyes with an iris-fixated lens and 0.7% of eyes with a posterior chamber lens lost  $\geq 2$  lines of their BCVA.
- **For myopia or hyperopia**
  - A median of 2.2% of eyes had a retinal detachment and 2.3% of eyes had a macular choroidal neovascularisation. Raised intraocular pressure was observed in 4.24% (iris-fixated lenses) and 4.80% (posterior chamber lenses) of eyes; cataract was observed in 1.11% (iris-fixated lenses) and 9.60% (posterior chamber lenses) of eyes and in 2% of eyes in one other study; haloes and/or glare were observed in 8.77% (iris-fixated lenses) and 5.93% (posterior chamber lenses) of eyes; re-treatment was needed in a median of 3.43% (iris-fixated lenses) and 3.28% (posterior chamber lenses) of eyes.
- **For hyperopia**
  - The weighted mean efficacy index (mean postoperative UCVA/mean BCVA preoperatively) of iris-fixated lenses was 0.73 at 12 months post-treatment. At 6 months, 22.7% of eyes with an iris-fixated lens had an UCVA of  $\geq 20/20$ ;
  - No eye lost  $\geq 2$  lines of BCVA.



## 2.6 Summary of findings

Eight systematic reviews, two additional randomized trials and 21 additional observational studies provided evidence on refractive eye surgery. A summary of the main findings is presented here below.

### 2.6.1 *Direct comparisons (randomized controlled trials)*

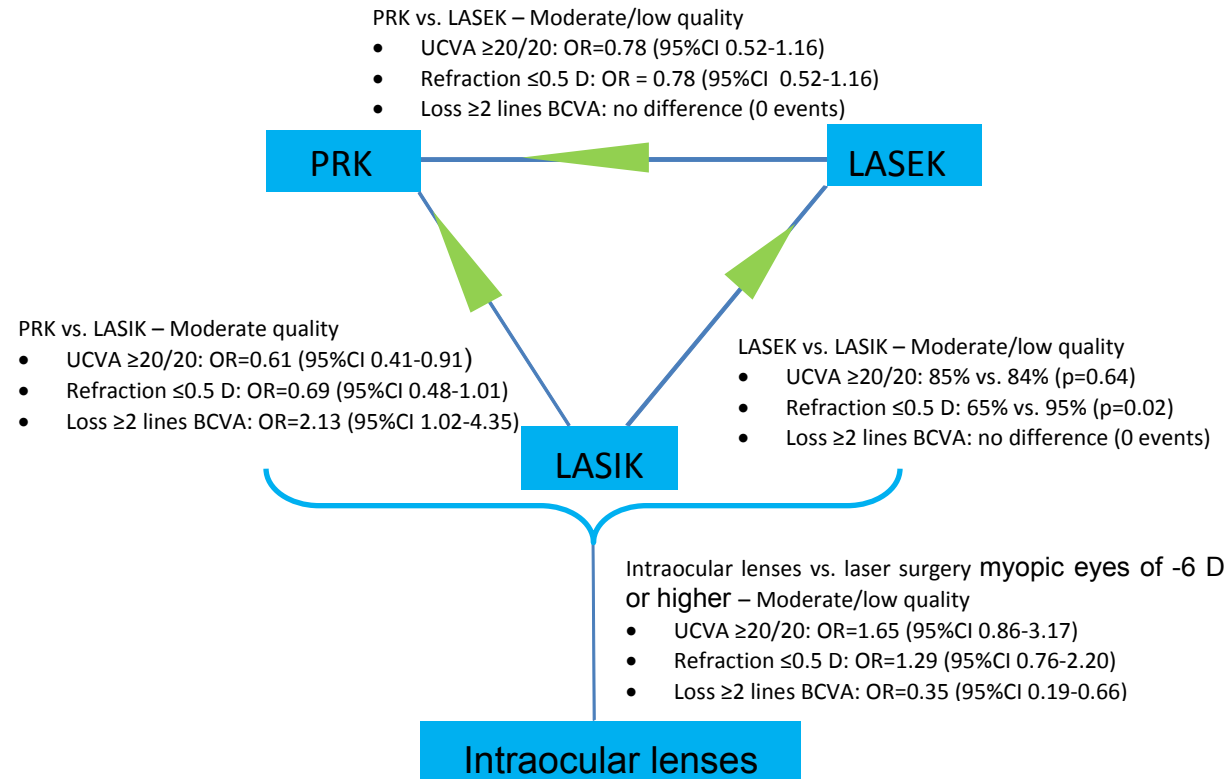
#### 2.6.1.1 *Visual acuity (UCVA $\geq 20/20$ and $\leq 0.5 D$ ) and loss $\geq 2$ lines BCVA*

Direct comparisons of refractive surgery with 'usual care' (spectacles or contact lenses) were not identified, nor were data on spectacle independency available.



## Myopic eyes

**Figure 2 – Myopic eyes - refractive surgery techniques directly compared**





For myopic eyes, with regard to the main outcomes on visual acuity (UCVA  $\geq 20/20$  or refraction  $\leq 0.5$  D of target refraction) and loss of  $\geq 2$  lines BCVA:

- LASEK and LASIK dominated PRK for myopic eyes,
- LASIK dominated LASEK in terms of the proportion of patients that was within 0.5 D of their target refraction, but only one study evaluated this outcome;

In eyes with myopia of at least -6 D laser surgery was less effective than intraocular lenses; more patients lost  $\geq 2$  lines of their BCVA after laser surgery compared to intraocular lens implant (see figure 2).

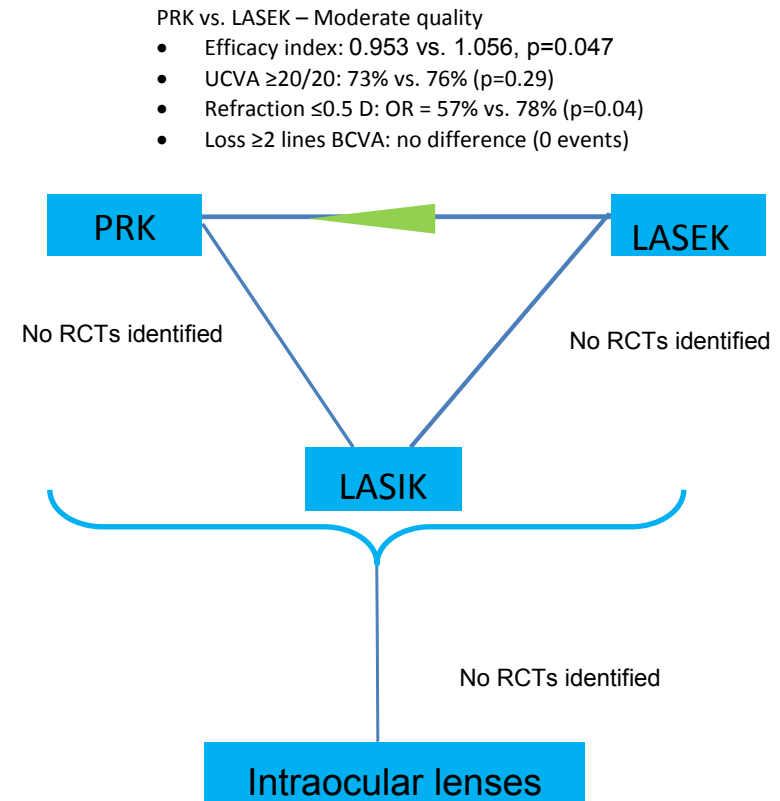
All outcomes were downgraded because of risk of bias and/or imprecision to 'moderate' or 'low' quality evidence. This means that further research is likely - or very likely for low quality evidence - to have an important impact on our confidence in the estimates and may change - or is very likely to change - the estimates.

### Hyperopic eyes

The only RCTs identified in this study were comparisons between PRK and LASEK (see figure 3). No comparisons were found for more recent techniques and for intraocular lenses.

LASEK dominated PRK in terms of the efficacy index and the proportion of patients that was within 0.5 D of their target refraction.

**Figure 3 – Hyperopic eyes - refractive surgery techniques directly compared**



#### 2.6.1.2 Further safety data from direct comparisons

The evaluation of safety data (other than loss of  $\geq 2$  lines BCVA) was hampered by the non-standardised reporting of such events in direct comparisons. As a consequence, it is unclear which treatment is the safest.



The sparse available information from direct comparisons is summarised in Table 1 that shows the global lack and/or inconsistency of safety data reporting.

**Table 1 – Further major safety data from direct comparisons in myopic patients**

	PRK vs. LASEK	PRK vs. LASIK	LASEK vs. LASIK	Intraocular lenses vs. laser surgery
Keratitis/infection	0 vs. 0%	NR	NR	NR
Halo	1.71 vs. 1.62 (ns) \$	5 out of 6 reporting RCTs found no difference	NR	More in laser surgery
Glare	1.83 vs. 1.79 (ns) \$	5 out of 6 reporting RCTs found no difference	NR	More in laser surgery
Haze	0.09 higher in PRK (ns) #	2.1% vs. NR †	35 vs. 0% (s) ‡	NR
Dry eyes	0 vs. 0	NR	NR	21.7% vs. 56.6% artificial tear use at 12 months, p=0.06
(Epithelial) complications	Flap NA	NA vs. 5% ¶	9.4 vs. 9.5% †	NA vs. 2.2% ¶
Raised intraocular pressure	NR	NR	1.6% vs. NR	NR
Epithelial in growth	NR	NR	NR vs. 0.5%	NR
Re-treatment	NR	NR	NR	2.3% ‡ vs. NR
Pain	0.26 (ns) £	More in PRK (s)	NR	NR

Abbreviations: NA: not applicable; NR: not reported on in selected studies; ns: not significant; s: significant

\$ Mean halo/glare score

# Mean corneal haze score

£ (Weighted mean difference) mean post-operative pain score

† Median sub-epithelial haze grade 2

¶ Median

‡ Haze grade ≥2

† Figures from two different trials

‡ Median

¶ Flap/interface/de-centred ablation/haze related complications



## 2.6.2 Summary of findings: observational data

### 2.6.2.1 Visual acuity (UCVA $\geq 20/20$ and $\leq 0.5$ D)

A summary of the main visual acuity data from observational studies is presented in table 2.

Data on spectacle-independency were not available. The comparison of these data has to be done with caution as data stem from different series of eyes, from patients with various characteristics, with the use of different techniques, by different surgeons and in different time periods.

The available data do show somewhat better results in myopic eyes, compared to hyperopic eyes. Better results obtained with laser surgery than with intraocular lenses can be explained by the fact that lenses are mainly implanted in eyes with more severe refractive error.

Still direct comparisons between laser surgery and intraocular lenses in eyes with myopia of -6 D or worse (see section on RCTs above) showed better visual acuity results in eyes treated with intraocular lenses (see figure 2).

**Table 2 – Main visual acuity data from observational studies (median of study outcomes)**

Outcome	PRK	LASEK	LASIK	Intraocular lenses
Mean efficacy index				
• Myopia	• NR	• 1.03-1.13	• NR	• 0.85 § - 0.99 #
• Myopic astigmatism	• NR	• NR	• NR	• NR
• Hyperopia	• NR	• NR	• NR	• 0.73 §
Median % UCVA $\geq 20/20$				
• Myopia	• 76.0%	• 64%	• 64%	• 33%§ - 58.5%#
• Myopic astigmatism	• 62.6%	• NR	• NR	• NR
• Hyperopia	• 59%	• NR	• 51.5%	• 22.7% §
Median % $\leq 0.5$ D target refraction				
• Myopia	• 69.4%	• 82%	• 76.0%	• NR
• Myopic astigmatism	• 55.3%	• NR	• NR	• NR
• Hyperopia	• 60.8%	• NR	• 62%	• NR

Abbreviations: NR: not reported on by selected studies

§ Iris-fixated lenses

# Posterior chamber lenses



### 2.6.2.2 Loss of $\geq 2$ lines BCVA and further safety data

The main safety data from observational studies are presented in Table 3.  
The main conclusions are that:

- There is a lack of data for many safety outcomes;
- Hyperopic eyes are at greater risk of loss of  $\geq 2$  lines of BCVA than myopic eyes;
- Side effects depend on the laser technique: LASIK and LASEK techniques share risks of flap complications, LASEK and PRK cause more pain;
- Potentially serious complications are more frequently reported with intraocular lenses (retinal detachment, choroidal neovascularisation, cataract) than in series of eyes treated with laser surgery. Still indications for both treatments differ and patients with intraocular lenses are usually patients with more severe refractive error.

**Table 3 – Main safety data from observational studies (median of study outcomes)**

Outcome	PRK	LASEK	LASIK	Intraocular lens
Median % $\geq 2$ lines BCVA lost				
• Myopia	• 0.3%	• 0%	• 0.62%	• 0.6-0.7%
• Myopic astigmatism	• 0.6%	• NR	• NR	• NR
• Hyperopia	• 2.1%	• NR	• 3.4%	• 0%
Keratitis/infection				
• Myopia	• 0%	• 0.6% #	Mixed populations:	• NR
• Myopic astigmatism	• 0.1%	• NR	0%	• NR
• Hyperopia	• 0%	• NR		• NR
Corneal ectasia				
• Myopia	• 0.015%	• 0%	Mixed populations:	• NR
• Myopic astigmatism	• NR	• NR	0.25%	• NR
• Hyperopia	• NR	• NR		• NR
Retinal detachment				
• Myopia	• 0.18%	• NR	Mixed populations:	• 2.2%



Outcome	PRK	LASEK	LASIK	Intraocular lens
• Myopic astigmatism	• 0.13%	• NR	0.19%	• NR
• Hyperopia	• NR	• NR		• NR
Choroidal neovascularisation				
• Myopia	• 0.02%	• NR	Mixed populations:	• 2.3%
• Myopic astigmatism	• NR	• NR	0.33%	• NR
• Hyperopia	• NR	• NR		• NR
Cataract				
• Myopia	• NR	• NR	Mixed populations:	• 2%
• Myopic astigmatism	• NR	• NR	0.3%	• NR
• Hyperopia	• NR	• NR		• NR
Halos				
• Myopia	• 17% £	• NR	†	Mixed populations: 8.77%, 5.93% T£
• Myopic astigmatism	• 38%	• NR		
• Hyperopia	• 12% £	• NR		
Glare				
• Myopia	• 17% £	• NR	†	Mixed populations: 8.77%, 5.93% T£
• Myopic astigmatism	• 27%	• NR		
• Hyperopia	• 12% £	• NR		
Haze				
• Myopia	• 0% \$	• 0% \$	Mixed populations: 0%	• NR
• Myopic astigmatism	• NR	• NR	corneal haze #	• NR
• Hyperopia	• NR	• NR		• NR
Drye eyes				
• Myopia	• 41.1% H	• 3.0% #	†	• NR
• Myopic astigmatism	• NR	• NR		• NR
• Hyperopia	• NR	• NR		• NR
(Epithelial) flap complications				
• Myopia	• NA	• 2% #	Mixed populations: different	NA
• Myopic astigmatism	• NA	• NR	flap complications in 0.1-1.2%	





Outcome	PRK	LASEK	LASIK	Intraocular lens
• Hyperopia	• NA	• NR	#	
Raised intraocular pressure				
• Myopia	• 1.9% #	• 1.2%	Mixed populations: 0.14% #	Mixed populations: 4.24%, 4.80 †
• Myopic astigmatism	• 0.6%	• NR		
• Hyperopia	• 8.6%	• NR		
Epithelial in growth				
• Myopia	• 0.6%	• NR	Mixed populations: 1.4% #	• NR
• Myopic astigmatism	• NR	• NR		• NR
• Hyperopia	• NR	• NR		• NR
Re-treatment				
• Myopia	• 1.5% #	• 1.15 #	Mixed populations: 10.7% #	Mixed populations: 3.43%, 3.28% †
• Myopic astigmatism	• 26% ‡	• NR		
• Hyperopia	• 0.6%	• NR		
Pain				
• Myopia	• 28% ¥	• 4.0% ¤	†	• NR
• Myopic astigmatism	• NR	• NR		• NR
• Hyperopia	• NR	• NR		• NR

Abbreviations: NA: not applicable; NR: not reported on by selected studies

£ Haloes and/or glare

\$ Median haze grade 2

# Median

¥ Distressing to excruciating pain 4-5 days post-operatively

¤ Strong-severe post-operative pain

† Iris-fixated lenses, posterior chamber lenses

‡ Single study

§ Data from a single Turkish study from 2000, with a follow-up of 24 months

† Results were reported as 'better' or 'worse' compared to pre-operatively, however, it is unclear how pre-operative problems should be interpreted



## 2.7 Quality-of-life and patient satisfaction

### 2.7.1 No generic quality-of-life data

A search in the peer-reviewed literature did not reveal studies measuring generic quality-of-life in the domain of refractive error correction. This might be explained by the fact that generic quality-of-life instruments are not expected to be very sensitive to discriminate the small differences in health status for the different eye correction methods:

- The commonly used generic EQ-5D questionnaire measures five dimensions in health status: mobility (walking about), self care (washing or dressing), usual activities, pain/discomfort and anxiety/depression. It includes five levels of severity in each of the dimensions. Refractive eye surgery is not expected to have an impact on the mobility or, self care dimensions. It may have a minor impact on discomfort and usual activities, especially on the short term during the recovery period after surgery.
- The SF-36 measure measures vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. Similarly, refractive eye surgery is not expected to have a large impact on any of the dimensions.

Given the lack of generic quality-of-life data, uncertainty remains about the direction, the magnitude and the evolution over time of the impact of eye surgery on overall quality-of-life. It is known however that generic quality-of-life measured for people using conventional correction, is already quite high and thus does not leave much room for improvement. One study measuring general utility values in a myopic population, using conventional correction (i.e. glasses or lenses) in Singapore resulted in utilities from 0.97 to 0.99, according to method used, on a scale from 0 to 1<sup>50</sup>.

### 2.7.2 Vision-related outcomes

According to the KCE guidelines for economic evaluations, scenarios with disease-specific measures for health-related quality of life are not acceptable in the reference case but can be presented as complementary analyses. Given that no generic quality-of-life data are available, we further looked for vision specific outcomes, such as correction independency and vision-related quality-of-life instruments.

#### Decreased dependence on corrective eyewear

A main goal of undergoing refractive surgery is to get rid of glasses or contact lenses. Unfortunately this outcome is only rarely reported. Although UCVA  $\geq 20/20$  may be a good clinical measure for efficacy and be considered as a proxy for spectacle independency; it has shortcomings. It is possible that a person with UCVA  $\geq 20/20$  still needs glasses in dusk or at night or even in daytime. Or vice versa a person not achieving UCVA  $\geq 20/20$  may be correction independent. Furthermore UCVA only measures visual acuity in one eye.

Given the lack of reporting on correction dependence, we further looked for vision related quality-of-life. The following sections analyse in detail the quality-of-life instruments developed specifically for refractive errors.



### Three validated vision-related quality-of-life instruments specific for refractive error correction

A number of quality-of-life questionnaires have been developed specifically for patients with refractive error correction<sup>51</sup> to analyse the benefits of refractive surgery. The three main questionnaires validated by traditional psychometric methods are:

- the National Eye Institute Refractive Quality of Life (NEI-RQL)<sup>52</sup>,
- the Refractive Status and Vision Profile (RSVP)<sup>53</sup>,
- the Quality of Life Impact of Refractive Correction (QIRC) questionnaire<sup>54</sup>.

The sections below detail their content.

Other instruments have been developed as well e.g. the Myopia Specific Quality of Life Questionnaire and the Canadian Refractive Surgery Research Group questionnaire. These questionnaires have also been validated and shown to be responsive to refractive surgery<sup>51</sup>.

The three main questionnaires have been shown sensitive to visual functioning; they reported improved quality-of-life after refractive surgery<sup>53, 55, 56</sup>. Interventions studied were PRK<sup>53</sup>, LASIK<sup>55</sup> or undefined<sup>56</sup>.

The following paragraphs briefly present the items measured by each of the main questionnaires.

- **The National Eye Institute Refractive Quality of Life (NEI-RQL)<sup>52</sup>**

The questionnaire includes 13 subscales and 42 questions:

- Clarity of vision
- Expectations
- Near vision
- Far vision
- Diurnal fluctuations
- Activity limitations
- Glare symptoms
- Dependence on correction
- Worry

- Suboptimal correction
- Appearance
- Satisfaction with correction

The instrument was developed using traditional techniques. McAlinden 2011<sup>57</sup> investigated the psychometric properties of the questionnaire using Rasch analysis and revealed a number of psychometric deficiencies, including response categories not performing as expected, questions that did not fit with the trait represented by a subscale, and poor precision.

This NEI-RQL questionnaire is the only one (out of the 3 validated questionnaires) that includes questions on correction dependency. Questions posed in this questionnaire relate to brief reading (like directions, a menu or a recipe), long reading (like a book, a magazine article, or the newspaper), driving at night and driving at dusk. The categorical answers are scored a number of points (0, 33, 50, 66 or 100) and consequently averaged.

- **The Refractive Status and Vision Profile (RSVP)<sup>53</sup>**

The RSVP consists of 8 subscales:

- Concern
- Expectations
- Physical functioning
- Driving
- Symptoms
- Optical problems
- Glare
- Trouble with corrective lenses

The RSVP was developed predominantly on a refractive surgery population and therefore is considered only valid for refractive surgery. The RSVP was developed using traditional techniques. Its psychometric properties were assessed and re-evaluated using Rasch analysis by Garamendi<sup>58</sup>.



- **Quality of Life Impact of Refractive Correction (QIRC)** <sup>59</sup>

This instrument consists of a 20- item questionnaire including:

- visual function
- symptoms
- convenience
- cost
- health concerns
- well-being

The QIRC questionnaire was validated by both standard psychometric techniques and Rasch analysis <sup>51</sup>.

- **Overview of results of studies using the National Eye Institute Refractive Quality of Life (NEI-RQL) questionnaire**

As the NEI-RQL questionnaire includes explicit questions on correction dependency, we performed an additional literature search on this questionnaire in MEDLINE (Ovid) in September 2013 (see search strategy in appendix 8.3.6). Seven studies were selected:

1. Hays 2003 <sup>60</sup> (1 154 patients) compared the subgroups "no correction" (emmetropes), 'postsurgery—no correction', 'glasses', 'multifocal glasses' and 'contact lenses'. The postsurgery group obtained a score of 84.80 on spectacle dependency, but no further details were reported. Given the scoring rules and averaging (reported above), it is not clear how to decompose this figure.
2. McDonnell 2003 <sup>61</sup> (185 patients) compared myopes and hyperopes before and after keratorefractive surgery (PRK, LASIK) and found statistically significant improvements in scores for 11 of 13 scales. Dependence on correction increased from 26 (before surgery) to 84 (after surgery). No further details on the decomposition of these scores were given.
3. Nichols 2005 <sup>55</sup> (131 patients) compared myopes not seeking surgery with emmetropes and myopes seeking surgery both before and after LASIK. Quality-of-life was compared between natural emmetropes and emmetropes after surgery. Out of 59 patients undergoing surgery, 50 patients were considered emmetrope and were included in the analysis. As it concerned only emmetropes, the subscale on correction

dependency was considered non applicable and consequently not filled out. 9 of the surgery patients did not meet the criteria for emmetropia after surgery as the spherical equivalent in the worse eye was greater than +1 D or less than -1 D. Persons who underwent surgery scored equally on quality-of-life as persons wearing glasses or contact lenses when it came to clarity of vision, near vision, far vision, diurnal fluctuations and clinical measures of visual function. Yet, persons who underwent surgery reported significantly better appearance and greater satisfaction <sup>55</sup>.

4. Toker 2008 <sup>62</sup> (95 patients) compared persons with spectacles, contact lenses and no correction, but no one treated by surgery.
5. Djadi-Prat 2011 <sup>63</sup> and Saragoussi 2011 <sup>64</sup> (307 patients) studied LASIK only in a French population. An average score on correction dependence of 90.8 was scored by the full population, 96.1 by light myopic patients and 72.7 by severely hypermetropic patients. This study also provided some details on the subscale: 83% of the total patient group did not need correction for near sight, whereas 94.1% of the patient group did not need correction for far sight. 17% occasionally or always needed correction for near sight and 6% occasionally or always needed correction for far sight. Furthermore quality-of-life after LASIK overall was lower for strong hypermetropic patients than for weak myopic patients <sup>63</sup>.
6. Queiros 2012 <sup>65</sup> (217 patients) compared spectacles, contact lenses, emmetropes, LASIK and orthokeratology in a myopic population. They found an average decrease in quality of life compared with emmetropes of -7.1% for LASIK, -13.0% for orthokeratology, -15.8% for spectacles, and -17.3% for soft contact lenses. LASIK patients obtained a score of 87 on correction dependence. No details on composition of this score were provided.
7. Uthoff 2013 <sup>66</sup> (167 patients) compared LASIK and orthokeratology. No score on correction dependency was reported.

In conclusion, no studies were detected comparing surgical techniques other than LASIK and PRK. Study populations were heterogeneous and in most cases small. Details on correction dependency were rarely provided. As this search did not yield robust data, we continued our search on patient satisfaction questionnaires.



### 2.7.3 Numerous patient satisfaction questionnaires

Numerous patient satisfaction questionnaires have been developed as well. Solomon 2009<sup>67</sup> et al. performed a systematic review (years 1988 to 2008) for patient satisfaction questionnaires after LASIK surgery. They selected 19 articles but most studies used non validated questionnaires (84.2%). Many questionnaires have been developed on "ad hoc" basis and lacked evidence of their psychometric properties.

The authors pooled the results of the articles. They labelled as "satisfied patients" those who were "very" to "somewhat" satisfied. They further eliminated the answers "undecided", "not sure", or "neutral" from the total number of patients for each study. The resulting pooled patient satisfaction rates were of 95.3% (1 811 of 1 901 patients) after myopic LASIK and 96.3% after hyperopic LASIK. These results however need to be interpreted with caution given the grouping performed by the authors and possible loss of information. Furthermore, patient satisfaction measurement might have been subject to response bias according to the design of the interviews.

## 2.8 Summary and discussion

### 2.8.1 Data on myopic eyes

In direct comparisons, there was moderate to low quality evidence that LASIK provided a better visual acuity than PRK and LASEK. Intraocular lenses provided a better visual acuity than laser surgery in myopic patients with myopia equal or worse than -6 D (low quality evidence).

### 2.8.2 Few data on hyperopic eyes

Most of the selected studies dealt with myopic eyes. Only few data on hyperopic eyes were available.

In the available studies refractive eye surgery seemed somewhat less effective in hyperopic eyes compared to myopic eyes, and less safe.

Direct comparisons between refractive surgery techniques for hyperopic eyes were scarce and only provided moderate quality evidence that LASEK was more effective than, and as safe as PRK.

According to experts, better results for long term stability in myopia than in hyperopia could be partly explained by the worsening of hyperopia with age (no data on longsightedness were available in selected studies).

### 2.8.3 Heterogeneous studies, low evidence

The results summarized above rely on heterogeneous studies: patient populations differed considerably between studies in terms of, for instance, degree of refraction and age. The results of the various studies are therefore neither always comparable nor amenable to pooling.

### 2.8.4 Unknown conflicts of interest

The conflicts of interests and financial support of the studies raise questions. None of the systematic reviews on RCTs reported on funding or potential conflicts of interest of the primary studies and only two of the selected systematic reviews on observational studies reported on potential conflicts of interest of the included primary studies. In the NICE 2005 review, two thirds of the 132 selected studies did not declare their source of funding and 9% of the studies declared a funding by the manufacturer.

### 2.8.5 Success of refractive surgery: difficult to assess on the basis of clinical outcomes only

The primary goal of the patients undergoing refractive surgery is to reduce their dependency on glasses or contact lenses. Yet the most commonly reported effectiveness measures in the scientific literature are visual acuity (e.g. UCVA  $\geq 20/20$ ) and the residual refractive error (e.g. correction within  $\pm 0.5$  D). These clinical parameters respectively measure the efficacy and precision of the correction technique. They can be proxies for glasses/contact lenses dependency after surgery although they do not perfectly distinguish between patients who still need a (partial) correction or not. Some patients with good clinical outcomes may still need correction after surgery - be it mostly on occasional basis, e.g. for driving at night or reading subtitles on television.

As proxies, some clinical outcomes may be too severe (i.e. 20/20, variations within 0.5 D) and some thresholds for safety (i.e. loss 2 lines BVCA) might decrease the sensitivity of safety issues.



### 2.8.6 Success of refractive surgery: patient selection is crucial

Not every patient is a candidate for each type of refractive surgery. Age, severity and type of refractive error, comorbidity may influence the results of surgery. Eyes with a milder degree of myopia are more likely to achieve the intended refractive correction and adverse effects may occur more frequently in patients with contraindications to a treatment (see also below).

A number of consensus-based guidelines have been published on the recommended range of applications of the different types of refractive surgery, including patient selection criteria referring to the range in which a procedure is considered eligible and for which side effects are rare<sup>68, 69</sup>. Such guidelines are needed to standardise practice and ensure patient safety.

### 2.8.7 Evidence on older practices: the techniques and indications evolve

This review includes older series of eyes that underwent refractive surgery: medical practice in some series may not be congruent with today's medical practice. For instance, older laser studies included patients with high myopia up to -14 D, while today's practice limits the indication for laser surgery to -10 D. However, the majority of studies - or the majority of eyes included in studies - were on mild to moderate myopia.

Not only the indications but also the techniques evolve rapidly. Illustrations are the current use of Femtolaser techniques that aim to decrease the occurrence of flap-related complications and the development of flexible iris-fixated intraocular lenses.

According to some experts, the results for PRK and LASEK could have been merged in a single intervention group, given the similarity of the techniques. Because a number of studies did compare PRK and LASEK, we nonetheless opted to keep the two interventions separate. In addition, the experts and one validator stated that PRK is a technique that can be sometimes used in corneas that are not candidates for LASIK.

### 2.8.8 Safety is a major topic

Safety remains a concern for a treatment that is used in otherwise healthy eyes.

#### 2.8.8.1 Limited data, difficult interpretation

Safety data from RCTs and observational studies showed heterogeneous reports except for the loss of  $\geq 2$  lines of BCVA. This hampers a comparison between techniques. Reliable data on rare but potentially sight-threatening harms such as infections after intraocular lenses were not available. Furthermore, many studies were small sized and not well suited to evaluate rare but serious safety events, in particular after intraocular surgery. These findings call for standardised, systematic safety monitoring of large patient series.

#### 2.8.8.2 Importance of appropriate patient selection

The most serious complication in laser surgery, notably corneal ectasia, is rare but has been reported. The NICE 2005 report reviewed the cases of ectasia and found the majority of patients to have a contraindication to LASIK or to have received inappropriate treatment. This confirms the importance of appropriate patient selection and treatment.

#### 2.8.8.3 Safety of laser surgery

The safety results of PRK, LASEK and LASIK reflect their technical differences:

- Flap problems occur with LASEK and LASIK.
- PRK and LASEK are associated with more pain.

Glare and halos are frequently reported with laser treatments.

Dry eyes are frequently reported as well and this side effect may necessitate the use of artificial tears. Experts reported that dry eyes may be the leading adverse effect after LASIK, though mean symptoms and severity return to pre-operative levels at 6 months after surgery<sup>70, 71</sup>. However, some patients may experience a worsening of dry eyes, compared to pre-surgery, whereas others may experience that their dry eyes improve<sup>21</sup>.





#### 2.8.8.4 *Safety of intraocular lenses*

The safety profile of intraocular surgery differs from that of laser surgery: inserting a lens implant involves operating inside the eye and carries a number of sight-threatening risks not present in laser surgery. Since intraocular lenses are a more invasive technique, they are generally only considered when laser treatment is not the best option.

### 3 REFRACTIVE EYE SURGERY: ECONOMIC CONSIDERATIONS

The aim of this chapter is to present an economic analysis of refractive eye surgery in comparison with alternative correction methods:

- The first section summarizes the peer-reviewed economic literature on refractive eye surgery.
- The second section aims at evaluating costs against outcomes; however given the lack of robust outcome data it essentially consists of a long term cost comparison of different correction methods.
- Finally a short section gives an overview of the reimbursement policies in other countries.

#### 3.1 Review of the economic literature on refractive surgery

This part provides a summary of the peer-reviewed economic literature on refractive eye surgery.

##### 3.1.1 *Methods*

An overview of the search strategy is provided in Appendix 8.1.1. The literature search followed standard methods.

- the HTA database of the Centre for Reviews and Dissemination (CRD) of the UK's National Health Service (NHS) was first searched for recent economic reviews;
- consequently the websites of HTA agencies were searched through the KCE Google custom search engine<sup>72</sup>.
- These searches did not find any economic reviews; therefore a search was performed in Ovid MEDLINE® and EMBASE (from 2002 to March 2013).





### 3.1.2 Results

#### 3.1.2.1 Overview of studies

The search yielded partial and full economic evaluations. Studies are considered partial economic evaluations when they assess only one alternative (e.g. LASIK) without comparator, or when they examine only costs but no outcomes. Table 4 provides a brief overview of the identified studies, including study type, comparators and the perspective taken in the analysis. In total 5 relevant studies were found.

- Three studies compared costs of LASIK and/or PRK with classical eyewear<sup>73,74,75</sup>.
- Two studies focused on LASIK only without comparator<sup>14 15</sup>.

Three studies calculated a cost per gained refractive unit for LASIK and/or PRK<sup>14 74 75</sup>. One study focused on the incidence and costs of LASIK's complications<sup>15</sup>.

No economic evaluations were found on phakic intraocular lenses.

**Table 4 – Overview of partial economic evaluations**

Study	Study type	Comparators	Perspective
Lamparter et al. (2007)	Cost description: cost of complications and intervention	LASIK only – no comparator	Health care payer (government and patient)
Lamparter et al. (2005)	Cost-outcome: cost per gained refractive unit	LASIK only – no comparator	Health care payer (government and patient)
Jesper et al. (2004)	Cost-minimisation / Cost-outcome: <ul style="list-style-type: none"> <li>• cost per year to avoid glasses</li> <li>• cost per year per gained refractive unit</li> </ul>	LASIK, PRK, lenses and eyeglasses	Societal
Krummenauer et al. (2003)	Cost-outcome: cost per gained refractive unit	LASIK and eyeglasses	Patient
Berdeaux et al. (2002)	Cost comparison	LASIK, lenses and eyeglasses	Societal



### 3.1.2.2 Costs

Table 26 in appendix provides an overview of the included cost items and cost results for each of the studies. The included cost items varied according to the perspective and the time horizon considered. All studies included a cost estimation of the surgery price and if considered, of eyeglasses and/or contact lenses.

#### Cost of complications

Lamparter 2007<sup>15</sup> provided the most detailed analysis on complication costs associated with surgery. This study combined a worst case scenario for each complication treatment cost with average incidence data.

The complications considered by Berdeaux<sup>73</sup> were the risk of still needing eyeglasses and keratitis for contact lenses.

#### Societal costs

Three studies only took the perspective of the patient or the health care payer and did not include indirect costs.

Two studies took a societal perspective<sup>73,74</sup>: they added indirect costs linked to productivity losses. Berdeaux<sup>73</sup> included costs related to the time spent to care for cleaning and fitting contact lenses, and multiplied it by the average hourly earnings. The Danish CEMT report<sup>74</sup> included costs related to the inability to work during the recovery period.

#### Sensitivity of costs

All but one studies (Lamparter 2007<sup>15</sup>) studied the sensitivity of cost data (e.g. age or time horizon, hospital centre, delay for glass renewal). Two studies reported different costs for two hospital locations<sup>74,75</sup>. Berdeaux<sup>73</sup> performed elaborate sensitivity analyses and assessed the impact of different time horizons, eyeglass change delays and discount rates.

### 3.1.2.3 Outcome items and outcome results

Table 27 in appendix summarizes the sources used for outcomes, the patient characteristics and outcome results for each study. The outcomes considered in Lamparter 2007 were restricted to complication rates. The other studies considered outcomes such as refractive gain, predictability of refractive gain and being free of glasses. Berdeaux 2002 did not include any clinical outcome.

### 3.1.2.4 Cost-outcome results

Table 22 in appendix presents the cost–outcome results per study.

- The Danish study<sup>74</sup> calculated the incremental cost to avoid glasses. This can be considered a meaningful ratio since being free from glasses is in most cases the ultimate objective of the patient.
- Krummenauer<sup>75</sup> and Lamparter<sup>14</sup> considered refractive gain (in D) as outcome measure: they calculated a cost per gained refractive benefit unit. However this ratio may not be meaningful since a higher refractive gain does not necessarily result in a better outcome for the patient (e.g. overcorrection).
- Lamparter<sup>14</sup> considered predictability of refractive gain as outcome and calculated a cost per percentage predictability. Predictability of refractive gain was defined as the proportion of eyes that attained a post operative deviation of <0.5 D from the target refraction. This predictability can be considered as a useful outcome since a higher predictability is in all cases preferable to a lower predictability.

The cost description and comparison studies did not consider non-monetary outcomes. They focused on the cost side without assessing their relation to clinical benefits.



### 3.1.2.5 Conclusions of the economic studies

The cost comparison of Berdeaux 2002 showed a cost-saving potential for LASIK on a long term horizon when compared to contact lenses. The authors analysed time horizons of 10, 20 and 30 years. They found LASIK to be cost-saving compared to lenses in all three time horizon scenarios, at least when the time for cleaning and fitting of lenses was incorporated in the costs. When the time for cleaning and fitting of lenses was not taken into account, LASIK was only cost-saving compared to lenses in the longest, 20 and 30 years, horizon scenarios. Eyeglasses appeared to be less costly than LASIK in all three time horizon scenarios.

The Danish study found LASIK and PRK to be cost-saving in patients wearing glasses younger than 27 years.

The results of the studies calculating a cost per gained refractive unit did not allow drawing solid conclusions. Lamparter 2005 concluded that LASIK showed an encouraging cost-effectiveness range. It is not clear however on what basis this conclusion could be drawn since no data are available for comparison. Krummenauer 2003 concluded that the resulting "cost-benefit" ratio could serve for comparison with other alternative treatments for myopia.

Table 5 summarizes the conclusions stated in each of the studies.

**Table 5 – Conclusions of the reviewed studies**

Study	Conclusion
Lamparter (2007)	"At least the worst case scenario introduced into this investigation demonstrated an economically relevant order for the expectable LASIK complications and the associated additional costs for complication treatment."
Lamparter (2005)	"The conventional LASIK procedures showed an encouraging cost effectiveness range in the correction of myopia; the estimate may serve as a rationale for future allocation discussions in ophthalmology."
Danish CEMT study (2004)	"Refractive surgery is a cost-saving alternative in patients below 27 years of age. In patients around 35 years of age, surgery is associated with additional costs."
Krummenauer (2003)	"German LASIK patients face a median investment of € 667-831 per gained refractive unit" This incremental cost-benefit ratio can be regarded as a surrogate parameter for comparison with alternative surgical or conservative treatment strategies in myopia."
Berdeaux (2002)	"LASIK was less costly than contact lenses and more expensive than eyeglasses, although the potential non-monetary benefit of LASIK over eyeglasses was not taken into account."



### 3.1.3 Conclusion economic literature search

- **There are few peer-reviewed economic evaluations on refractive error correction.**
- **The research did not identify any economic evaluation on phakic intraocular lenses; the economic evaluations only focused on LASIK and PRK.**
- **These studies show a cost-saving potential for PRK and LASIK especially for contact lens wearers and young eyeglasses wearers.**
- **One study reports a significant cost associated with retreatments and complications after LASIK.**
- **In the attempt of balancing costs and clinical outcomes, several cost-outcome ratios were calculated:**
  - incremental cost for being free of glasses
  - incremental cost per gained refractive unit (D)
  - incremental cost per percentage predictability (post operative deviation of < 0.5 D from target refraction)
- **The outcome data however are based on small studies; not all calculated ratios do allow meaningful interpretation.**

## 3.2 Economic evaluation

This section compares the costs at long term of various correction methods i.e. eye surgery, glasses and contact lenses.

### 3.2.1 Methods

A simple Markov simulation model was developed in Excel in order to assess these long term costs and outcomes.

#### 3.2.1.1 Model structure

The cost model structure for each intervention is depicted in Figure 4. The long term costs for the surgery groups consist of the initial surgery cost, including the cost of a potential re-operation and complications, followed by a discounted monthly cost of wearing glasses for those people still needing correction after surgery. Retreatment for most complications was assumed included in the initial surgery price. See appendix 8.3.3 for details.

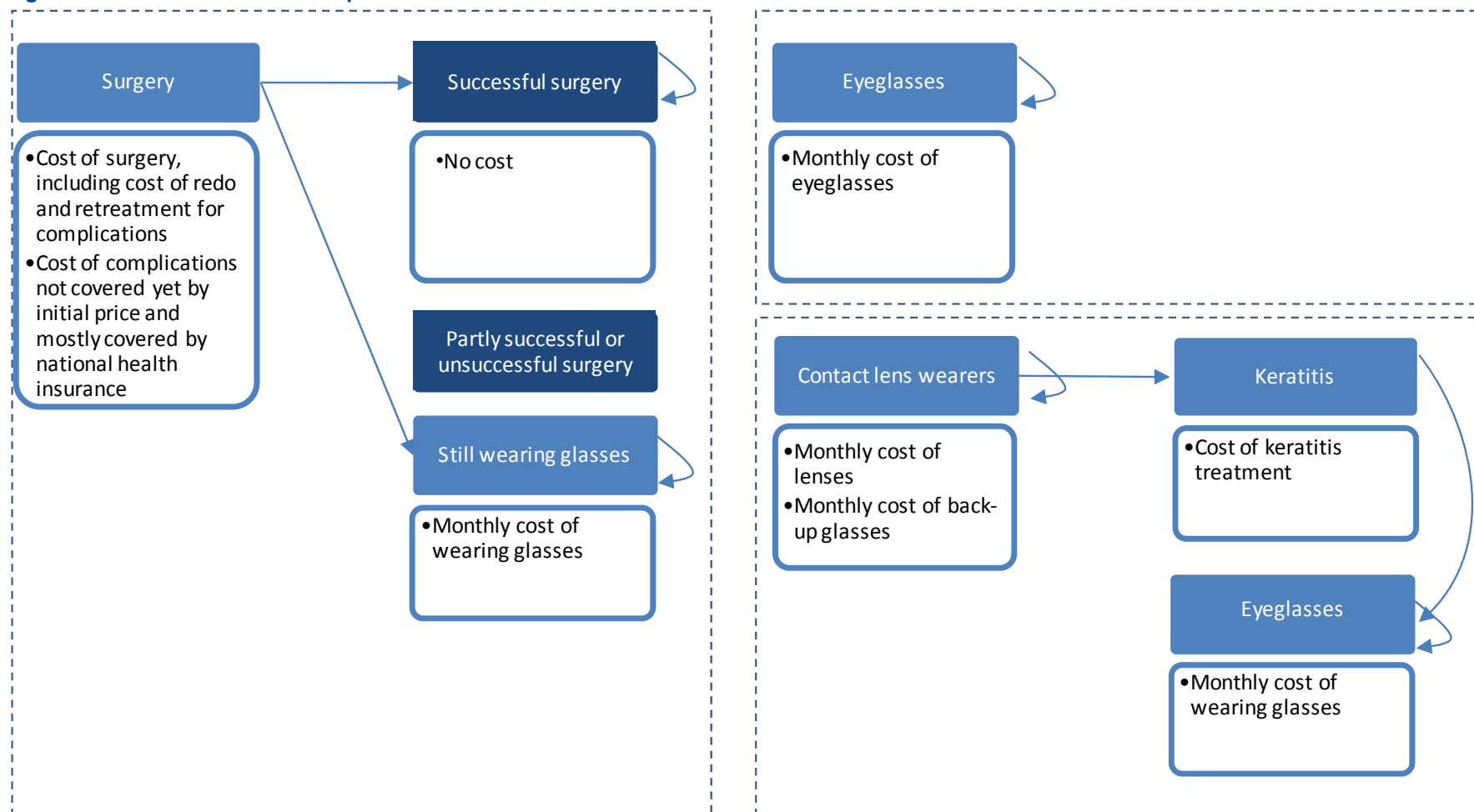
The long term costs for eyeglass wearers consist of the discounted monthly costs of wearing glasses. Patients wearing eyeglasses are not at risk of any specific complication. The long term costs for contact lens wearers consist of the discounted monthly costs of contact lenses and a pair of back-up glasses. People in the lens group run a small monthly risk of keratitis. We added this complication in the cost model and assumed people with keratitis moved to the glass wearers group after one month or lost vision all completely and needed a transplant in a small number of cases.

For sake of simplicity we made a number of assumptions in the possible movements between cost states. We assumed contact lens wearers to continue wearing lenses until the end of the time horizon, although some may switch to eyeglasses after certain time. We assumed patients with correction need after surgery wear glasses, although some of them may still wear contact lenses.

#### 3.2.1.2 Perspective

In accordance with the Belgian pharmaco-economic guidelines, the analysis includes direct health care costs from the perspective of the health care payer. Health care related payments made by patients as well as by the statutory, complementary and private insurance are included. This evaluation of refractive correction is atypical as the patient himself is the most important payer.

Transport costs are not included since the distance in Belgium to an ophthalmologist or optician is considered relatively small. Neither income loss due to incapacity to work nor income compensation for sick leave and invalidity are considered.

**Figure 4 – Cost model structure per intervention**



### 3.2.1.3 Population and subgroups

The model simulates a hypothetical cohort of 1 000 patients for each intervention group and each age group. Patient's start age is set at 20 to 40 years with intervals of 5 years. The calculation is done for a cohort rather than for a single patient, as for each patient, random variables are drawn from the distributions defined for the different input parameters. Note that people in reality may undergo surgery after the age of 40, however since we stop the cost comparison at the age of 45 we limit the age of patients at 40 to maintain a minimum time horizon of 5 years.

- **The hypothetical patient cohorts consist of patients with any correction error: myopia, hyperopia and/or astigmatism.**
- **Patients were not differentiated in terms of indication and severity of error, although these factors influence both costs and success rates.**

### 3.2.1.4 Interventions and comparators

The correction methods compared are the following.

#### **Eyeglass correction**

- unifocal eyeglasses and lenses, i.e. for myopia and hyperopia

#### **Contact lenses**

- hard
- soft daily, monthly and yearly

#### **Surface ablation surgery**

- PRK
- LASEK

EpiLASIK also is part of this category, however it was not considered in this analysis.

#### **Deep ablation surgery**

- LASIK

Femto LASIK and SMILE also are part of this category, however, they are not considered in this analysis.

#### **Monofocal phakic intraocular lenses**

Toric correction (toric eyeglasses, toric contact lenses or toric intraocular lenses) for myopia and hyperopia with astigmatism are not considered in this analysis. In general and regardless of correction method, toric correction is more expensive than correction for pure myopia or hyperopia.

Likewise, neither multifocal correction (also called "progressive" correction and comprising bi-, tri- and multifocal correction) nor accommodative correction for myopia and hyperopia with presbyopia are considered.

Also clear lens extraction (CLE) was not considered, as this intervention does correct cataract conditions with or without refractive error: this inclusion would therefore require the inclusion of other comparators as well.

### 3.2.1.5 Time horizon

Refractive eye surgery may reduce costs related to the wear of eyeglasses or contact lenses over a long period. Therefore, a long term cost horizon is mandatory. While for hyperopic patients, long term stability is less certain than for myopic patients, we assumed for this analysis long term stability for both myopic and hyperopic patients until the age of presbyopia.

#### **Start age - end age**

In this theoretical analysis, costs were accumulated from the time of surgery at 20-25-30-35-40 years until the age of 45 where people typically need correction for presbyopia. Due to presbyopia, expenditure patterns change and become less predictable as

- unoperated people with myopia/hyperopia and presbyopia may need progressive (i.e. bi-, tri or multifocal) correction or choose for monovision strategies;



- people who underwent surgery also need reading glasses but no progressive glasses. Their need for reading glasses may be delayed. Their need for toric correction in case of astigmatism may be permanently solved by surgery.

Stopping the comparison at 45 years is therefore considered a conservative time horizon. Expanding it beyond 45 years would likely result in more favourable cost outcomes for the surgical options.

### **Presbyopia**

Presbyopia is an age-related condition in which the lens of the eye loses its ability to focus, making it difficult to see objects at close.

### **Discount rate**

Future costs are first recalculated to their present value and then summed. Future costs are discounted to their current value in order to account for time preference of money. The time preference rate reflects the fact that even in a world with zero inflation and no bank interest, people prefer a euro in hand today than a euro in the future. In the base-case analyses, future costs are discounted at a rate of 3% conform to the Belgian KCE guidelines.

Assuming that the discount rate is the real discount rate and does not allow yet for the effect of inflation, future costs are also accounted in real terms and not inflated.

### **3.2.2 Cost inputs**

#### **3.2.2.1 Surgery costs**

##### **Data were retrieved from 3 sources**

- a database of the Alliance Nationale des Mutualités Chrétiennes - Landsbond der Christelijke Mutualiteiten (ANMC–LCM);
- a search on the websites of Belgian eye surgery centres;
- data from the telephone survey of the KCE report 202 on refractive errors.

### **Data from ANMC–LCM**

The ANMC-LCM database contains data from members of three local sickness funds in the province of Occidental Flanders who received partial reimbursement for laser eye treatment. The dataset covers the period end September 2007 to end November 2011. It comprises the price paid by the patient and the number of eyes treated but data on specific type of treatment are missing. After cleaning the dataset, 498 observations (patients) were left.

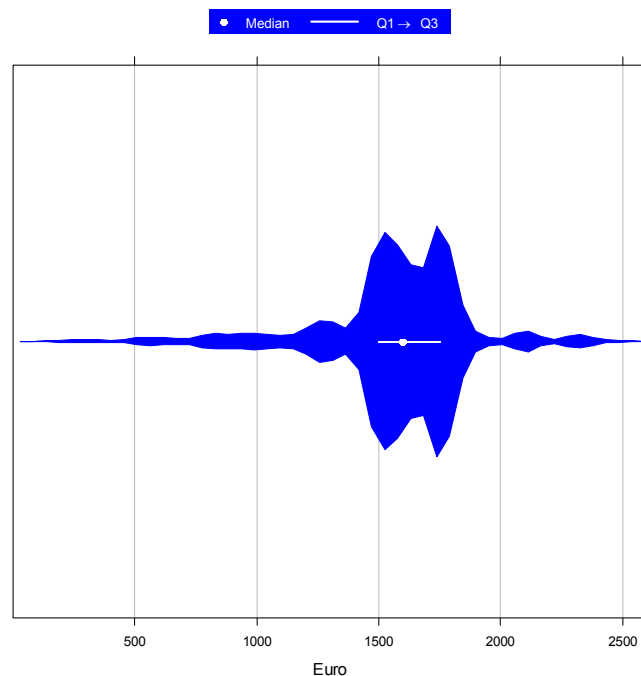
- **Data cleaning**

The initial database comprised 867 files on 788 patients. For some patients there were two or more files as a separate file was entered for each new intervention. The database also included a number of regularization (negative) files. The patients with a total amount paid of zero were discarded (n=240). For patients with two or more files, there was uncertainty about whether the amounts were the total amounts paid or the amounts per eye. Therefore patients with multiple files were discarded as well, except when the amounts entered were different (n=40). Finally, patients with an amount paid per eye of € 100 were discarded given that likely the amount indicated the reimbursed amount rather than the amount actually paid (n=10). A total of 498 patients were kept and a price per eye was calculated for these patients.

- **Results**

The median amount paid per eye is €1600. For 50% of the patients a payment was registered between €1500 and €1750 (Q1 and Q3). The registered minimum was €175 and the maximum €2500. A violin plot of the data is depicted in Figure 5. The expert group however agreed that amounts as low as €175 were clearly outliers and likely due to incorrect registrations.



**Figure 5 – Price per eye of laser correction based on ANMC-LCM data**

Line is delimited by the 1st and 3rd quartiles. Median is represented by a dot. Violin is drawn from the first to the last observation, depicting the probability density function of the data. Based on data from Alliance Nationale des Mutualités Chrétiennes – Landsbond der Christelijke Mutualiteiten

**Data from websites of 14 Belgian eye centres**

These centres were located in Flanders (n=10) and in Wallonia (n=4). An overview of the price for laser correction of one eye is given in Table 6. The prices indicated are sometimes minimum prices, not yet including cost of preoperative consultation. In most cases, prices included cost of a reoperation within a restricted time period of 1 to 2 years and a number of postoperative consultations. The prices for phakic intraocular lenses were in most cases not further detailed according to the type of lens i.e. posterior chamber lenses (ICL) versus iris-claw anterior chamber phakic intraocular lens (Artiflex, Artisane, Verisys).

**Table 6 – Price per eye of laser correction and lens implant based on website of 14 Belgian centers**

Treatment category	n	Average price per eye (€)	Min price (€)	Max price (€)
PRK	10	1 163	950	1 430
LASEK	6	1 190	995	1 300
LASIK	14	1 300	1 000	1 850
pIOL – monofocal	8	1 844	1 250	2 250
pIOL – toric	4	2 275	2 000	2 500

Table 24 provides an overview of the finally used surgery cost inputs and the assumed distributions.



Table 7 – Surgery cost inputs

Costs of surgery	Assumed distribution	Mean	Source
Cost of preoperative consultation	Uniform (Min: €90; Max: €150)	€ 120	Website search
Cost of surgery (both eyes) and postoperative consultations			
• PRK	Uniform (Min: 1 900; Max: 2 860)	€ 2 380	Website search
• LASEK	Uniform (Min: 1 990; Max: 2 600)	€ 2 295	Website search
• LASIK	Uniform (Min: 2 000; Max: 3 700)	€ 2 850	Website search
• pIOL monofocal	Uniform (Min: 2 500; Max: 4 500)	€ 3 500	Website search
• pIOL toric	Uniform (Min: 4 000; Max: 5 000)	€ 4 500	Website search
Cost of complications after surgery not included in surgery price, weighted by incidence	Constant (11)	€ 11	Both incidence and costs are based on results for LASIK from Lamparter (2007) <sup>15</sup>
• PRK			Costs for all surgeries assumed equal (for cost analysis solely)
• LASEK			
• LASIK			
• pIOL monofocal and pIOL toric			



### 3.2.2.2 Eyeglass and contact lens costs

Data on costs of eyeglasses and lenses were based on 2 sources:

- KCE telephone survey from published in the KCE report 202<sup>1</sup>;
- APOOB survey (Belgian Association of opticians and optometrists): These data are based on published data from optical retail chains, on data from UNAMEC/contact lenses (federation for wholesale and producers of contact lenses), on EUROMCONTACT (European Federation of National Associations and International Companies of contact lens and lens care manufacturers and on a survey (2011) on the average cost of eyewear (distinguishing between mono focal and multifocal eyeglasses).

In accordance with the guidelines on pharmaco-economic evaluations<sup>76</sup> only direct health care costs are considered for this evaluation.

Table 9 and Table 10 provide an overview of the eyeglasses and contact lens cost inputs respectively.

### 3.2.2.3 Surgery complications

Although there are clear differences in complications and complication rates between the different types and especially between the intra- and extra-ocular procedures, we assumed an equal complication cost. Since complications constitute a small component, we applied the Pareto principle and did not focus our efforts on it. Lamparter 2007<sup>15</sup> (see previous section on review of economic evaluations) reported in detail costs and incidence of complications after LASIK.

This cost analysis assumed that most of the complications were covered by the initial surgery price. Table 8 reports the cost of keratectasia and retinal detachment with incidence as reported by Lamparter: these were added on top of initial surgery price. Note that these costs are mostly born by national health insurance.

Some complications cannot be treated as such, e.g.  $\geq 2$  lines BCVA lost.

**Table 8 – Complication cost inputs not included in initial surgery price, based on Lamparter (2007)<sup>15</sup>**

Lamparter (2007)	Worst case costs	Incidence
<b>Keratectasia</b>	€8 600.15	0.1%
<b>Retinal detachment</b>	€2 682.79	0.1%

**Table 9 – Glasses: cost inputs**

Cost of glasses	Mean	Assumed distribution	Source
Frequency of purchasing new glasses	Every 3.5 years		see footnote <sup>a</sup>
Cost of unifocal glasses	€300		see footnote <sup>b</sup>
Cost of maintenance products	€ 15 / year		APOOB
Resulting monthly cost	€8.4/month	Gamma ( $\alpha=4.2$ ; $\beta=2$ )	

<sup>a</sup> APOOB estimated the mean delay between 4 to 5 years. The majority of respondents from the telephonic survey in the first part of this study<sup>1</sup> answered they did not know the expected renewal term. About 22% of the respondents who bought glasses 1 to 2 years ago estimated to renew their glasses in 1 to 2 years. The mean from a Dutch survey from 2005 on monofocal glasses was 3.23 years.<sup>77</sup>

<sup>b</sup> APOOB estimated the cost of unifocal glasses at €280. The first part of this study<sup>1</sup> reported 19% of telephonic respondents spent € 300 to € 500 and about an equal percentage spent € 200 to € 300.

**Table 10 – Contact lenses: cost inputs**

Cost of lenses	Mean	Distribution	Source
Cost of soft lenses including maintenance products		-	
• Soft day	€36.7/month (€ 440/year)	Gamma(18.35;2)	APOOB
• Soft month	€18.3/month (€ 220/year)	Gamma(9.15;2)	APOOB
• Soft year	€16.3/month (€ 195/year)	Gamma(8.15;2)	APOOB
Proportion day lenses (within soft lenses)	23%	-	Euromcontacts 2011 (via APOOB)
Proportion month lenses (within soft lenses)	76%	-	Euromcontacts 2011 (via APOOB)
Proportion year lenses (within soft lenses)	1%	-	Euromcontacts 2011 (via APOOB)
Yearly cost of hard lenses including maintenance products		-	
• Hard lenses cost per 2 years	€14.4/month (€ 345/year)	Gamma(7.2;2)	APOOB
• Proportion soft lens users	95%	-	APOOB

#### 3.2.2.4 Keratitis in contact lens wearers

The assumption for the cost of contact lens-induced keratitis included 4 consultations and 2 basic antibiotic treatments for outpatients. For hospitalised cases we included the cost of a hospital stay, a daily consultation in-hospital, a microbiologic examination and antibiotic treatment, 4 outpatient consultations and, if applicable, a corneal transplant.

- An ophthalmologist consultation was accounted at €24.15 (RIZIV-INAMI code 102535).
- A first line antibiotic treatment was approximated at €10.
- The study by Verhelst 2006<sup>78</sup> showed a mean hospital length of 9.4 days for hospitalized contact lens-related corneal ulcers. This translates into a mean cost for the hospital stay alone of €3 467.

- The microbiologic examination and antibiotic treatments for hospitalized patients were accounted at €120 per patient, based on indexed data from Cheng 1999<sup>79</sup>.
- The fee for corneal transplant was accounted at €489.97 (RIZIV-INAMI codes 246212-246223).

For the incidence on keratitis we refer to the section 3.2.3 on transition probabilities.

**Table 11 – Keratitis cost**

Keratitis	Mean	Assumed distribution	Source
First line treatment for keratitis	€116	Gamma(11.6;10)	Estimate
Hospital length of stay for keratitis	9.4 days		Verhelst 2006 <sup>78</sup>
National average 100% hospital cost per day in acute beds	388		KCE
Corneal transplant procedure	€ 489.97		RIZIV–INAMI code 246212-246223
Average cost of hospitalised treatment for keratitis (including corneal transplant in 15% of cases)	€ 4 210	Gamma(210.5;20)	Estimate

### 3.2.2.5 Back-up glasses and sunglasses

It is assumed that all lens wearers have back-up glasses but they renew twice less frequently than regular eyeglass wearers.

Costs of sunglasses with vision correction were not taken into account.

### 3.2.2.6 Ophthalmologic visits

There are no strict recommendations or precise data on consultation frequency, therefore we made assumptions. For people who underwent pIOL we assumed one extra consult per year. For the other correction methods, we did not include consult costs, thereby implicitly assuming an equal frequency of consults in these groups.

- **Cost inputs were retrieved from various sources.**
- **Expenditures on glasses, contact lenses and surgery vary widely. Unlike for typical economic evaluations these costs could not be based on reimbursement data.**
- **As there is no national tariff setting for refractive surgery, prices vary considerably. Costs of glasses and lenses are partly determined by the indication and partly by the person him/herself.**
- **Data for glasses and contact lenses were based on a telephone survey. For contact lenses in particular this survey resulted in poor quality data as cost calculation is complex.**
- **Costs linked to complications for both surgery and contact lenses were weighted by their incidence.**
- **Distributions were used rather than point estimates to take into account the large variation in cost inputs.**



### 3.2.3 Transition probabilities

The transition rates determine the probability of moving from one state to another. People in the surgery state move either to the “successful surgery” state, either to a “partly successful or unsuccessful surgery” state where people still need glasses or contact lenses. People in the contact lenses state either stay in this state or move to the keratitis one.

#### 3.2.3.1 Success rate: correction independency

For the cost evaluation we are interested in the percentage of people still needing any type of correction after surgery. So if people with UCVA >20/20 still need glasses occasionally, they are out of the successful surgery group, as they continue to bear the cost of glasses.

The evidence search in chapter 2 did not yield any study that reported correction independency, neither as a separate outcome measure, nor as part of a broader questionnaire on quality-of-life or patient satisfaction.

#### Data source

The success rate is therefore based on the results from Djadi-Prat et al. 2011<sup>63</sup> (as further detailed) in a group of 307 LASIK treated patients (France). Most patients (83%) did not need any correction for near sight and 94.1% of the patient group did not need it for far sight. 17% occasionally or always needed correction for near sight and 6% occasionally or always needs correction for far sight.

Assuming a considerable overlap in both groups, we assumed that 17% of treated patients needed correction either occasionally or permanently. There is much uncertainty however around this outcome. The results section analyses the sensitivity of the results with regard to this parameter.

### Success depends on surgery type and indication

In reality, the success rate depends on surgery type. However, no comparative data from large studies are available and we assumed therefore equal success rates for the purposes of this cost analysis.

Furthermore, success rate varies not only between surgery types but also between indications (myopia – hyperopia – astigmatism) and in function of the severity (D). Given the lack of data, we also assumed an undifferentiated average success rate equal for all indications. It is furthermore assumed that people with “successful surgery” stayed in that state until the end of the model i.e. short term results were assumed to remain stable in the long run.

- **Differentiated costs were imputed for the different correction methods (eyeglasses - contact lenses – laser techniques - pIOL).**
- **Success rates however were assumed to be equal (for the cost analysis only).**



**Table 12 – Success and complication rates used for the cost calculation**

	Mean	Distribution	Source
Success rate - not needing correction after surgery	- PRK - LASEK - LASIK - pIOL monofocal - pIOL toric	83%	Djadi- Prat 2011 <sup>63</sup>
Yearly incidence of keratitis in lens wearers	1.1 per 10 000 for hard lenses 3.5 per 10 000 for soft lenses	Beta (1.1;9 998.9) Beta (3.5; 9 96.5)	Cheng 1999 <sup>79</sup>
Yearly incidence of keratitis requiring hospitalization	0.34 on 10 000 contact lens wearers	Beta (0.34; 9 999.66)	Verhelst 2006 <sup>78</sup>
Yearly incidence of keratitis requiring corneal transplant	15% of keratitis hospitalizations		

### 3.2.3.2 Keratitis in contact lens wearers

The most serious complication related to contact lenses is microbial keratitis. A lot of research has been done on the incidence of ulcerative keratitis. We selected a large Dutch study executed in 1996 (Cheng 1999 <sup>79</sup>). This study covered 379 ophthalmologists in a 3-month period. Frequency of lens wear was based on a telephonic interview of 20 000 persons of 12 years and older. This study was considered a reliable source for keratitis incidence by the expert group.

The yearly incidence was estimated at 1.1 per 10 000 wearers of hard lenses and 3.5 per 10 000 wearers of soft lenses. The incidence was highest for users of permanent soft lenses (20 per 10 000 wearers). This type of lenses is not commonly used in Belgium.

In a small number of cases, keratitis led to hospitalization and sometimes a corneal transplant. Incidence of contact lens-related corneal ulcers requiring hospitalization were based on a study by Verhelst 2006 <sup>78</sup>. This source was considered a reliable source for hospitalization incidence after keratitis. In 2003, this study registered 22 cases in all Belgian university hospitals. On an estimated population of 650 000 contact lenses wearers, this translates into an incidence of 0.34 on 10 000 contact lens wearers. Over a 7-year period (1997 to 2003), 15% of the hospitalised cases underwent corneal transplant and 1% underwent evisceration of an eye.

The Dutch study by Cheng 1999 indicated that 5.4% of all keratitis cases led to severe loss of vision, amongst which nearly two third of the cases required corneal transplants.





### 3.2.4 Weighing costs against outcomes

Chapter 2 highlighted the need for tailoring the technique to the indication. Still a patient or ophthalmologist may face a choice between techniques. In the evaluation of health care interventions, it is common to determine whether one technique dominates the other, in the sense that it is both cheaper and more effective, or whether a more expensive technique is cost-effective, meaning that it is worth the extra cost.

All dimensions should be considered to assess the relation of the different benefits and risks to costs. A well known summary measure used in health economic evaluations is the number of quality-adjusted life years (QALY) which measures the impact of an intervention on both the quality of life and length of life. New interventions that have a favourable cost-effectiveness ratio, in terms of cost per QALY, are considered to provide good value for money.

- **As there is a lack of robust comparative data on generic quality-of-life, as well as on correction dependency and vision related quality-of-life after surgery, the health economic evaluation was limited to a long term cost comparison.**

### 3.2.5 Results

#### 3.2.5.1 Spread of total costs per correction method

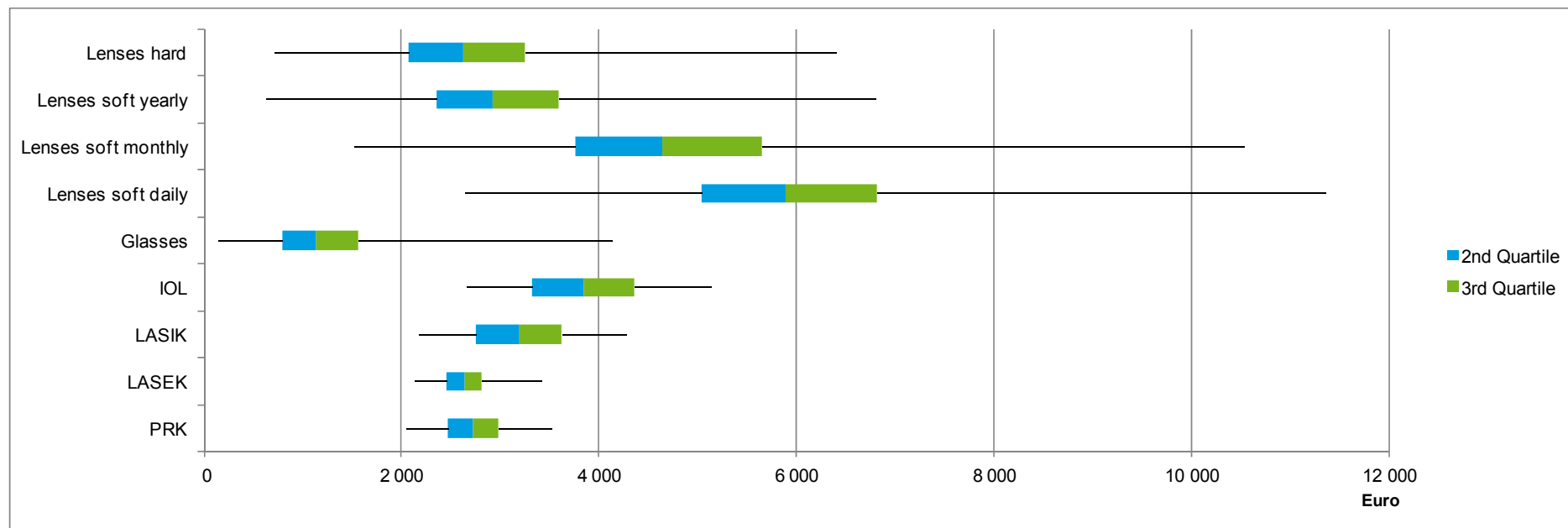
The largest parts of the total costs for each surgical correction method are the price of surgery itself and the costs related to potential complications. An extra cost is added to account for eyeglasses in case of un- or partly successful surgery.

Figure 6 shows the spread in total costs, for the age group of 30 years, reflecting the distributions assumed for the input parameters. Contact lenses and eyeglasses have the largest spread in total costs. This matches the large variance in purchase price and renewal term described in the KCE report 202. Surgical interventions have a smaller spread in total costs.

- **Contact lenses and eyeglasses have the largest spread in total costs. This reflects the variance in purchase price and renewal term.**
- **Surgical interventions have a smaller spread in terms of total costs.**
- **For a person aged 30, based on average data, glasses are the least costly option. Soft daily lenses appear the most costly option. Laser surgery and pIOL are neither the most nor the least costly option. There is however a large overlap in the long term cost distributions and therefore the cost balance may differ from one case to another.**



**Figure 6 – Spread in total long term costs per correction method (at the age of 30)**



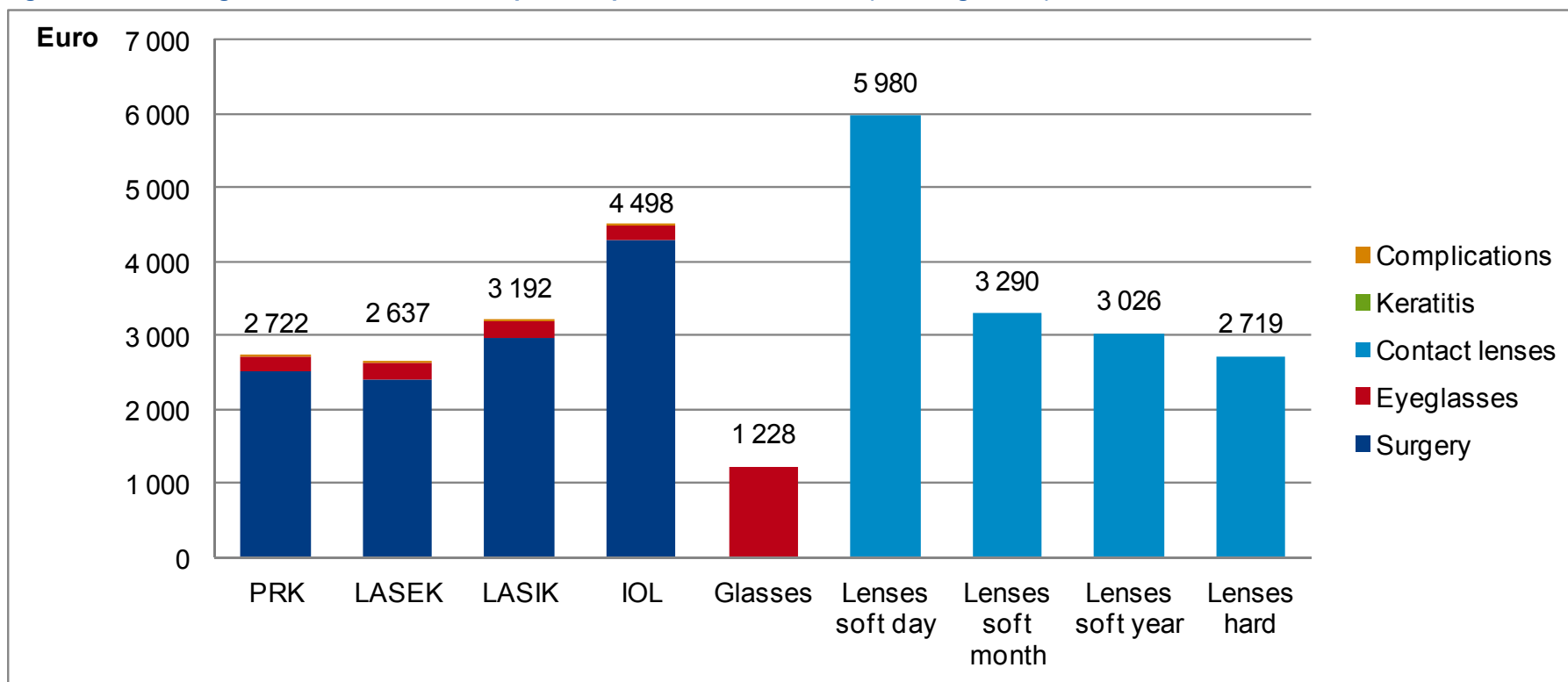
### 3.2.5.2 Cost composition for each correction method

Figure 7 shows the total costs and cost composition for each correction method for a 30-year-old patient considering surgery.

- Total costs for eyeglass correction consist of an accumulated monthly cost of eyeglasses.
- Total costs for lens correction consist of an accumulated monthly cost of lenses, cleaning products, back-up glasses and a very small cost related to treatment of potential keratitis.
- Costs of surgical complications and keratitis are invisible on the chart. Although treatment cost of these complications can be very high, their incidence is low, resulting in a low expected cost.



Figure 7 – Total long term costs and cost composition per correction method (at the age of 30)





### 3.2.5.3 Impact of age

The graph on next page depicts the average total cost results per age category. The younger the patient at the time of surgery, the more cost savings he or she can make compared to eyeglasses or contact lenses.

Total costs for surgical interventions vary slightly in function of the age of the patient, as they predominantly consist of the initial surgery cost. In contrast, total costs for eyeglasses and lenses decline for older persons, as the period of cost accumulation gets shorter. The largest decline in cost is observed for soft daily contact lenses, since these have the highest yearly cost.

### 3.2.5.4 Impact of success rate

The results presented are based on a success rate of 83% for surgery.

If the success rate increases to 90%, total surgery costs, at the age of 20, decrease by about 3 to 4%.

If the success rate increases to 95%, total surgery costs decrease by about 6 to 8%.

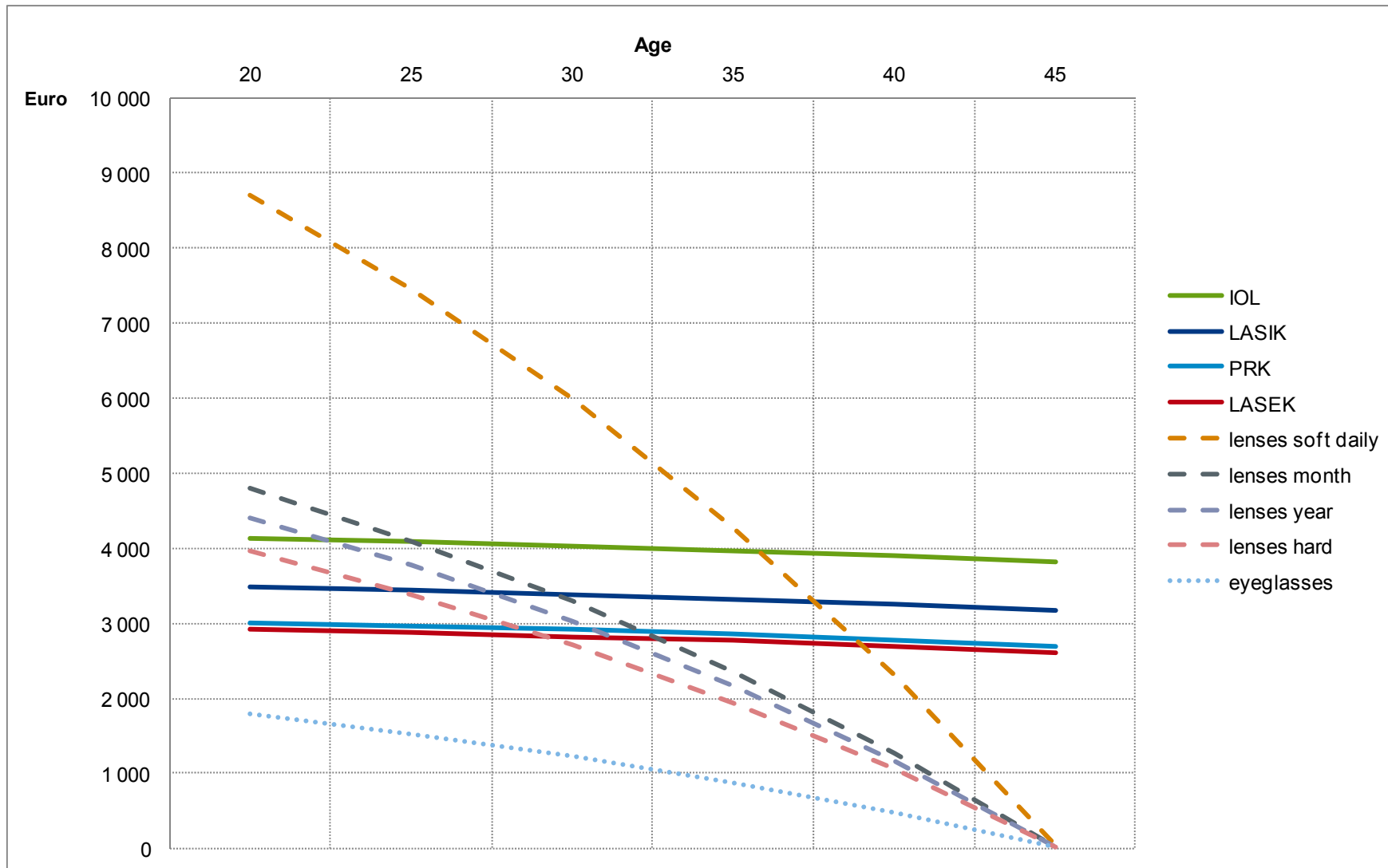
If the success rate decreases to 75%, total surgery costs increase by about 4 to 5%.

The financial impact of the success rate diminishes as the age increases. A higher success rate obviously makes surgery more attractive and makes it more competitive in comparison with lenses, also at higher age.

- **For all age categories, eyeglasses are on average the least costly option.**
- **Surgery shows cost-saving potential compared to all types of contact lenses for persons aged 20.**
- **For persons aged 25-30, surgery has still cost-saving potential compared to daily contact lenses, but its cost comes in the range of cheaper types of lenses.**
- **From the age of 40 onwards, surgery appears the most expensive option.**
- **These averages are based on many hypotheses. A time period until the age of 45 was considered and the success rate for surgery was based on an estimate. A higher success rate makes surgery more competitive with lenses, also at higher age. Glasses however remain in all cases on average the least expensive option.**



Graph 1 – Total long term costs according to start age





### 3.2.6 Discussion

This cost analysis focused on direct health care costs i.e. costs directly related to the correction of refractive error. They include cost of surgery, glasses, lenses, cleaning products and complications. Non-health care and indirect costs were not included e.g. travel expenses to and from the ophthalmologist, productivity losses due to time spent on any of the correction methods or complications. These costs were not included as they are difficult to measure on one hand and to value on the other hand. Furthermore keeping the focus narrow already resulted in large cost variability.

#### **The financial balance varies on an individual basis**

A patient will weigh the benefits and risks when opting for surgery. The qualitative part revealed that costs can be both a motivation (to make savings) and a barrier for undergoing surgery. Indeed, surgery can be either an investment or an expensive option, depending on the comparator (glasses or contact lenses), the age, the indication, individual spending behaviour - these are factors known *ex ante* - and the successfulness of the operation, only known *ex post*. Given the large variation in costs in all options, the eventual financial balance varies on an individual basis. Obviously, the balance turns out less positive for surgery when people spend few on glasses or contact lenses or when the surgery gets more expensive.

#### **Many assumptions made in this analysis**

As contact lenses may not be worn permanently, most — if not all — contact lens wearers also have back-up glasses. The cost of one pair of back-up glasses was accounted for in this analysis.

Still many glass wearers have also back-up glasses, especially in case of high diopters. The cost of an extra pair of glasses was not accounted for in this analysis. Furthermore, prices of glasses vary largely and the same holds for lenses. There may also be variability in frequency of ophthalmologic visits and also here we made assumptions.

In order not to put too much emphasis on average results, we modelled the long term costs probabilistically by imputing distributions reflecting the variability in the cost input parameters. This resulted in large variability in end results as well, showing large overlap between the different options.

#### **Importance of indication**

The indication may influence the final balance in several ways. More severe refractive errors are more costly to correct with glasses or lenses. However, surgery of severe errors is on average less successful than for low or moderate errors. Astigmatism is more expensive to correct than pure refractive errors. However, in the long run, patients who surgically corrected their astigmatism may benefit from savings as they do not require toric correction anymore. Success rates of surgery and long term stability also differ for myopic versus hyperopic patients.

These are factors which ideally should be accounted for in the analysis.

#### **No robust data available on the need for correction after surgery**

Multiple criteria can be used to evaluate the success of refractive error correction. The most commonly reported measures in the clinical literature are uncorrected visual acuity (UCVA) and the magnitude of residual refractive error (in D). The use of these metrics alone, however, fails to distinguish accurately between successful and less successful treatment for the purpose of cost analyses. Some patients with seemingly good clinical outcomes may still need correction occasionally or continuously.

For the cost calculation we were interested in the percentage of people still needing any type of correction after surgery. So even people who obtain clinically good outcomes (e.g. UCVA>20/20) but still need glasses occasionally, are considered not part of the successful surgery group, as they continue to bear the cost of glasses. The independency of postoperative correction is unfortunately a rarely reported outcome. We therefore used data from a small French study on LASIK and assumed equal results for the other techniques. As this assumption of equal successfulness likely may not hold in reality, it is clear that different success rates of surgery by intervention will also impact the cost balance.



### 3.2.7 Conclusions

- Surgery can be either a profitable investment or an expensive option, depending on the correction methods compared, the age, personal spending behavior (factors known ex ante) and the successfulness of the operation, which is only known ex post.
  - The financial balance also depends on the type and severity of correction but given the lack of detailed data, no subgroup analyses could be done to assess the impact of this.
  - In this theoretical analysis, costs were accumulated from the time of surgery at 20-25-30-35-40 years until the age of 45 where people typically need correction for presbyopia. Due to presbyopia expenditure patterns change and become less predictable as:
    - unoperated people with myopia/hyperopia and presbyopia may need progressive (i.e. bi, tri or multifocal) correction or choose for monovision strategies;
    - people who underwent surgery also need reading glasses but no progressive glasses. Their need for reading glasses may be delayed.
  - Stopping the comparison at 45 years is considered a conservative time horizon. Expanding it beyond 45 years likely results in more favourable cost outcomes for the surgical options.
  - This health economic evaluation is an atypical one as the health care payer is the patient for the largest part. Cost data could not be retrieved from reimbursement data. They are subject to particularly large variation.
  - Average results of a long term cost calculation, considering a time horizon until the age of 45, show:
    - For all age categories, eyeglasses are on average the least costly option;
    - Surgery shows cost-saving potential compared to all types of contact lenses for persons aged 20.
- For persons aged 25-30, surgery shows cost-saving potential compared to daily contact lenses. In this age group, surgery costs fall in the range of cheaper lens types.
  - From the age of 40 onwards, surgery appears the most expensive option.
  - Given the large variation in costs in all categories, the eventual financial balance varies on an individual basis. Clearly, the balance turns out less positive for surgery when people spend few on glasses or contact lenses or when the surgery gets more expensive.





### 3.3 Reimbursement of eyewear and refractive surgery: description of six countries

The reimbursement of refractive surgery was out of scope of this report. However a brief overview of reimbursement policies of refractive error surgery is informative as it shows similarities between the six countries under study: Belgium, France, United Kingdom, the Netherlands, Germany and Denmark.

The overview is based on information retrieved through a search on the websites of the national insurance agencies, complemented with e-mail correspondence with experts from Denmark and the Netherlands (see the details of the search in appendix 8.4). We classified the types of insurances into national compulsory and complementary insurance. The national statutory insurance organisations are listed in the table below.

**Table 13 – List of included countries and their national statutory insurance**

National Statutory Insurance	
Belgium	Rijksinstituut voor Ziekte en Invaliditeitsverzekering - Institut National d'Assurance Maladie Invalidité (RIZIV-INAMI)
France	Sécurité Sociale - Couverture Maladie Universelle
United Kingdom	National Health Service (NHS)
The Netherlands	College van zorgverzekeringen (CVZ)
Germany	Gesetzliche Krankenversicherung (GKV)
Denmark	Sundhedsstyrelsen

#### 3.3.1 Eyeglasses and lenses

##### 3.3.1.1 National statutory insurance

Five out of 6 countries provide partial reimbursement for eyeglasses and lenses under certain conditions that relate to age and number of diopters. Only in one country, Denmark, eyeglasses or lenses are not covered by national statutory insurance.

The reimbursement is partial and usually varies in function of e.g. number of diopters. In the Netherlands there is no variation in function of diopters but a fixed annual lump-sum reimbursement.

The Belgian, French, English and German reimbursement schemes differentiate reimbursement for eyeglasses and lenses according to age. The Belgian national reimbursement however is the only one having a separate category for the elderly.

##### Children and teenagers

Children and teenagers demand more frequent eyeglass change in order to suit their sight evolution. The upper age limit for children reimbursement varies between countries. For Belgium, France and Germany this limit is set at 18 years, 16 years in the United Kingdom.

Beyond the age threshold, the coverage may be restricted by diopter criterion. However, the majority of these countries did not set any diopter limit.

The reimbursed amount for children and teenagers is generally higher than for adults, often covering both eyeglasses and frame. In addition, it allows more frequent renewals of eyewear.

For medical reasons, lenses are not advised for children and therefore not covered in any of the countries.

**Table 14 – Comparison of national reimbursement schemes for eyewear in children**

Country	Belgium	France	England	Germany	The Netherlands	Denmark
Age limit	18	18	16	18	See adult scheme	n.a.
- Eyewear	€43 - €315	60% of a fixed tariff of €12 - €67	€42 - €215	€10 - €112	See adult scheme	n.a.
- Frame	2 x €28	60% of a fixed tariff of €30				

### Adults and elderly

All statutory insurances have a reimbursement scheme conditioned on diopter criteria, except in the United Kingdom. The level of this criterion influences the size of the population covered. The combination of population coverage and extent of reimbursement determines the broadness of the coverage. Germany and the Netherlands target the severely visually impaired while France and England provide reimbursement for all diopeters. The reimbursed amounts in France are however small.

In most countries, the adult scheme applies to the elderly. However Belgium has a specific scheme where bifocal and multifocal eyewear is covered from a minimum of  $\pm 4.25$  D, ranging from €90 to €315.

**Table 15 – Comparison of national reimbursement schemes for eyeglasses in adults**

Country	Belgium	France	The Netherlands	England	Germany	Denmark
Diopter threshold	$\geq \pm 8,25$ D $\geq 3$ D if anisometropia, irregular astigmatism	-	$> 10$ D $\geq 4$ D if anisometropia, astigmatism	/	Severely visually impaired	n.a.
Reimbursement range	€ 78 - € 362	60% of a fixed tariff of € 2 - € 24	€ 53 /eyeglass	€ 43 - € 240	20% of the costs	n.a.



The reimbursement schemes for lenses are very similar to those for eyeglasses in terms of age and diopter threshold. The reimbursed amount however may differ slightly. As an illustration the French “Assurance Maladie” reimburses contact lenses in specific severe conditions as for example myopia of at least 8 D or anisometropia of at least 3 D between eyes.

**Table 16 – Comparison of national reimbursement schemes for lenses in adults**

Country	Belgium	France	The Netherlands (coverage starts when charge is above threshold)	England	Germany	Denmark
Reimbursement range	60€ - 550€	Idem eyeglasses plus exceptions for severe eye conditions	Max coverage conditional on the length of use: - > 1 year : € 52.2/lens - < 1 year : € 105/year	€ 43 - € 240	Idem eyeglasses	n.a.

### 3.3.1.2 Complementary insurance

Complementary insurance offers heterogeneous packages. This coverage is financed by its subscribers or for instance by the employers. Complementary insurance for refractive error correction exists in all countries selected. Given the large variety of coverage choices and packages in all countries, no summary table is presented here.

### 3.3.2 Refractive eye surgery

#### 3.3.2.1 National statutory insurance

Only Denmark includes a possible reimbursement of this type of surgery. While the Danish national statutory insurance covers neither eyewear, nor contact lenses, treatment by refractive surgery is reimbursed for patients on the following conditions:

- From 18 to 55 year old;
- Myopia et hyperopia of at least  $\pm 6$  D or/and of  $\pm 3$  D in anisometropia; or

- Difference in refractive power between both eyes of more than  $\pm 3$  D; or
- Astigmatism in one or both eyes with more than 3 D.

Both laser refractive surgery and intraocular lenses are covered at a rate of 100%.

#### 3.3.2.2 Complementary insurance

Complementary insurance either covers eyewear or surgery by two separate reimbursement fees or covers both in a single fixed fee. In the majority of countries, complementary insurance covers surgery partially. Still a 100% refund exists in France (extensive package).



**Table 17 – Comparison of complementary reimbursement schemes for eyeglasses, lenses and refractive eye surgery**

Country	Belgium	France	The Netherlands	England	Germany	Denmark
<b>Eyewear /lenses</b>						
• <b>Adults</b>	€ 50 every two year with min 1 D.	€ 50 / 3 years For progressive eyewear: up to € 250	€ 100- € 150 per 2-3 calendar year	£ 35 - £ 150 100% up to £ 250	up to € 150 in two consecutive calendar years.	frame : kr 420-kr 1 500 glasses: kr 210-kr 750
• <b>Children</b>			€ 200/3 years			
<b>Complementary</b>	€ 200- € 250 for both eye laser refractive surgery	€ 50 - 100%	Lump sum € 100-€ 500 - € 750			

### 3.3.3 Conclusions: reimbursement of eyeglasses, contact lenses and refractive surgery in six countries

#### Reimbursement of glasses and contact lenses

- Eyewear is reimbursed partially and under certain conditions by the national statutory insurance in five out of six countries studied. Denmark is the only exception, where there is no national statutory reimbursement.
- National statutory insurance typically distinguishes between children and adults. Children are entitled to more frequent and higher reimbursement fees than adults. Belgium is the only country providing a separate scheme for the elderly.
- Complementary reimbursement for glasses and contact lenses exist in all countries.

#### Reimbursement of refractive surgery

- Complementary insurance schemes may reimburse surgery but five of the six national statutory insurance do not.
- Laser surgery and intraocular lenses are only reimbursed by the Danish national statutory insurance, under the following conditions:

- age from 18 to 55 year;
- myopia et hyperopia of at least  $\pm 6$  D or/and of  $\pm 3$  D in anisometropia; or
- difference in refractive power between both eyes of more than 3 D; or
- astigmatism in one or both eyes with more than 3 D.



## 4 REFRACTIVE EYE SURGERY: THE PERCEPTIONS OF THE PATIENTS

### 4.1 Introduction and objectives

The two previous chapters analysed the effectiveness and the economic aspects of refractive surgery. This last chapter focuses on the patients. It reports their perception after a refractive surgery procedure.

This chapter is part of a larger qualitative study that analysed the perception of the population who have a refractive error to gain insights into the determinants of the choice of their correction method. The Ipsos team conducted this qualitative study with three main objectives <sup>1</sup>:

- To identify the drivers and inhibitors to opt for specific refractive error corrections (including refractive eye surgery);
- To gain opinion on reimbursement of the different refractive error correction options;
- To evaluate the satisfaction of the patients after refractive eye surgery.

The sections below present the results of this last point. The two first ones have been published in a previous report <sup>1</sup> dedicated to refractive errors.

### 4.2 Methodology

The researchers opted for a qualitative methodology to collect information on the experience of refractive surgery and to understand the patients' motivations, inhibitors and choice criteria.

#### 4.2.1 Data collection

Individual semi-structured face-to-face interviews allow to analyse in depth the respondent's perception and to avoid influence from other participants. Semi-structured interviews ensure a good compromise between attaining the research objectives and the respondents' natural story telling.

#### 4.2.1.1 Sample

We targeted to build a purposive sample in order to carry out 36 face-to-face individual interviews which people having considered, planned or underwent a refractive surgery.

#### Inclusion and exclusion criteria

Relevant criteria used to select participants were:

- age ( $\geq 20$  years),
- suffering from myopia or hyperopia, whether or not in combination with other eye disorders such as astigmatism,
- having considered, planned or undergone refractive surgery less than 4 years ago

Medical conditions such as cataract, glaucoma, prebyopia alone and eye injuries were excluded from this assessment.

#### Criteria to build purposive sample

- Respondents who had considered surgery, but had not been further in this project (not planned or undergone the surgery): in order to gain insight in the main inhibitors.
- Respondents who had either planned or undergone surgery – where respondents who had planned surgery are those who decided to undergo the intervention after having collected information and/or have made the appointment for the surgery. They were included in order to gain insight in the main drivers towards surgery, the role of costs in the decision making process. and for those who have effectively undergone surgery, the patient satisfaction.

For respondents who have undergone refractive surgery, we recruited patients who had undergone surgery less than 4 years ago to ensure that the decision making process and the experience were recent in their mind.



- Socio economic status:

We used the ESOMAR social grades (A, B, C1, C2, D, E1, E2 & E3) for the recruitment. ESOMAR is an organization for encouraging, advancing and elevating market research worldwide. The ESOMAR social grades are commonly used for market research across countries and cultures: they are based on the final education level and on the occupation of the main income earner (see previous report). For this research, we opted to include social grades A, B, C1, C2 and D to ensure that respondents were sufficiently fluent and able to provide a clear argumentation on their reasons behind eye care choice and perception of refractive surgery. These categories are briefly described here.

**Table 18 – Description of social grades categories A, B, C1, C2 and D**

A	'well educated top managers and professionals': well-educated top to middle level managers with responsibility for more extensive personnel, well-educated independent or self-employed professional people;
B	'middle managers': well educated non-manual employees, skilled workers and business owners, smaller middle level managers; well educated non-manual employees, supervisors/skilled manual workers and small business owners; less well educated managers;
C1	'well educated non-manual employees, skilled workers and business owners': smaller middle level managers; well educated non-manual employees, supervisors/skilled manual workers and small business owners; less well educate managers;
C2	'skilled workers and non-manual employees': better educated supervisors/skilled manual workers; moderately well educated non-manual employees and small business owners;
D	'skilled and unskilled manual workers and poorly educated people in non-manual/managerial positions': less well educated supervisors/skilled and unskilled manual workers and poorly educated non-manual workers; poorly educated top/middle managers or smaller business owners; From higher non university education to primary school job seeker and unemployed.

### Participants' characteristics

The researchers built a theoretical grid to recruit participants in order to guarantee a good spread of the opinions (see previous report). Moreover, they did strive to include various diopters problems in the sample to understand whether or not the severity influences the eye care choice in general and the choice for refractive surgery in particular.

### Recruitment and selection of participants

The respondents were recruited by telephone. A part of the respondents were recruited from the sample of telephone survey participants: respondents who mentioned surgery were asked if they agreed to participate in a qualitative interview. Other interviewees were recruited from a free database of Ipsos. A snowball recruiting method was also applied, starting from both lists.

The respondents were screened by means of a selection questionnaire in which all sample criteria were included, such as sex, age, visual acuity disorder and considering (screener available in Dutch and French upon request). The screener was used during the recruitment call to ensure that a potential respondent was eligible for the survey. The topic of the survey was presented as related to public health and visual acuity disorders.

#### 4.2.1.2 Data collection tool

The interviews were moderated on basis of the semi-structured interview guide including all topics to be discussed. This interview guide was developed during an interactive process, in consultation with KCE.

The following topics were covered in the interview guide (available upon request):

- Introduction of research, moderator and respondent;
- Exploration of the experience of having refractive error(s);
- Exploration of the choice process for refractive error solutions with a specific focus on:
  - Choice drivers, influencers and inhibitors for refractive surgery for those who had considered refractive surgery but not undergone;



- Choice drivers, influencers, doubts and expectations for refractive surgery for those who had planned refractive surgery;
- Choice drivers, influencers, experience and satisfaction of refractive surgery for those who had undergone refractive surgery;
- Exploration of the perception of reimbursement for glasses, lenses and refractive surgery.

Three pilot interviews were conducted to enable the research team to observe the first interviews and to fine tune the methodology, terminology and interview guide.

We included the following to fine tune the interview guide:

- Adjusted timings;
- Exploration of the conversation between patient and physician on refractive surgery;
- Experience before and during refractive surgery;
- Pain experience during and after refractive surgery;
- For those who had not undergone or planned refractive surgery: what are the expectations on the process of refractive surgery (duration, type of anaesthesia) and criteria to choose a hospital or extramural centre.

The revised interview guide used for all interviews. It was used as a guideline, ensuring all research objectives were covered but leaving sufficient flexibility for the respondent to tell his/her story. Priority was given to the natural process of the conversation over the interview guide structure.

The interviews were conducted at respondent's best convenience – in home or on location. They were foreseen to last 1 hour each. Moderation was led by an experienced qualitative researcher in the native language.

All interviews were audio-recorded and written out at a later stage.

#### 4.2.2 Data analysis

The data analysis was an interactive process. After all interviews were conducted, an internal debriefing was organized by Ipsos with all moderators involved and the account directors. In this debriefing, initial ideas were shared from the Flemish and French speaking interviews by the moderators and challenged by the account directors. Each moderator also challenged the other moderator to discover similarities or differences based on language. After this debriefing meeting, the project leader read the transcripts from all interviews and made general comments and comments per specific target group in Word. The analysis is based on the information from the transcripts as well as the audio files since non verbal communication is also very important.

The project leader started building the flow of the report and the main overall findings. After the key findings have been elaborated, the project leader focused on detecting specific differences between target groups and highlighting this in the report. A second meeting was organized between moderators and account directors to go through the report and challenge the findings.

A random selection of transcripts was shared with the KCE team and a first debriefing meeting was organized between KCE and Ipsos to share the main findings and discuss the report structure and outline. Ipsos then further developed the report and sent for input and validation to KCE. The final report is the result of an interactive process between KCE and Ipsos.





## 4.3 Results

### 4.3.1 Description of achieved sample

The findings in this report are based on the analysis of 36 qualitative interviews with patients who have at least considered refractive surgery (or planned/underwent it).

Tables in Appendix 9.2 show the final achieved sample of participants that finally counts:

- 9 patients aged 20-30 years, 16 patients aged 31-40 years and 12 patients older than 40 years;
- 22 women and 14 men;
- 16 persons who considered surgery (but decided not to do it after thorough information), 7 persons who planned an operation and 13 persons who had refractive surgery.

### 4.3.2 Perceptions related to refractive eye surgery

This section summarizes the findings detailed in the previous report on refractive errors and correction methods<sup>1</sup>.

#### 4.3.2.1 General perceptions

The following perceptions of refractive surgery emerged from the interviews:

- refractive eye surgery is expensive;
- refractive eye surgery is in particular luxury surgery because it is indicated for a non life threatening condition;
- refractive eye surgery, using Laser technology, is considered to still be fairly recent and new;
- other perceptions included:
  - After refractive surgery, you will probably have to wear sooner eye glasses for presbyopia;
  - If you have worn soft lenses for a long time, you can no longer undergo refractive surgery;
  - After a certain age, you are no longer qualify for refractive surgery;

- Once you have undergone refractive surgery, you can not have additional refractive surgery;
- If you are too near sighted, refractive surgery can not fully correct the refractive error.

#### 4.3.2.2 Perception of reimbursement for refractive surgery

The position of respondents regarding reimbursement of eye correction follows the idea that luxury surgery does not have to be reimbursed by health insurance but eye correction should be reimbursed according to the severity of the refractive error, as a 'recognition' and a support of the individual's problem.

Refractive surgery should not be 100% reimbursed because it would be too heavy for the tax payer: it is not a life threatening condition and it would be unfair since other solutions exist. A reimbursement could be considered according to medical criteria, social criteria or for practically insurmountable issues.

In this sample, the cost of refractive surgery seems to have relatively more influence on the moment of the surgery rather than on the choice for surgery. This finding is not valid for the respondents who consider refractive surgery as a "no go": in this case, fear and insecurity seem to influence the decision more than the cost of surgery.

#### 4.3.2.3 Motivation to undergo surgery

These motivations have been explored in depth in the report mentioned above. They are summarized as follows:

- Functional drivers towards surgery are related to the quality of the vision achieved. It is a last resort when lenses are no option anymore. It is comfortable, aesthetical, practical (sport, time saving, etc.). Refractive surgery allows to acces to some professions. On an economical point of view, surgery is perceived as a long term investment;
- Emotional drivers are regain of identity, even a reborn, peace of mind, freedom and carefreeness.



#### 4.3.2.4 *Inhibitors towards surgery*

The inhibitors are also from two types:

- The functional inhibitors to undergo refractive eye surgery relate to the gravity or the stabilization of the refractive error; the price of the surgery, the complex and time consuming process and the absence of guarantee that the correction will be complete with long-term effect.
- The emotional inhibitors relate to the fear of the consequences and anxiety towards surgery. The perception that refractive surgery is a luxury surgery can provoke feelings of guilty or selfishness.

#### 4.3.2.5 *Profile of patients interviewed in this study*

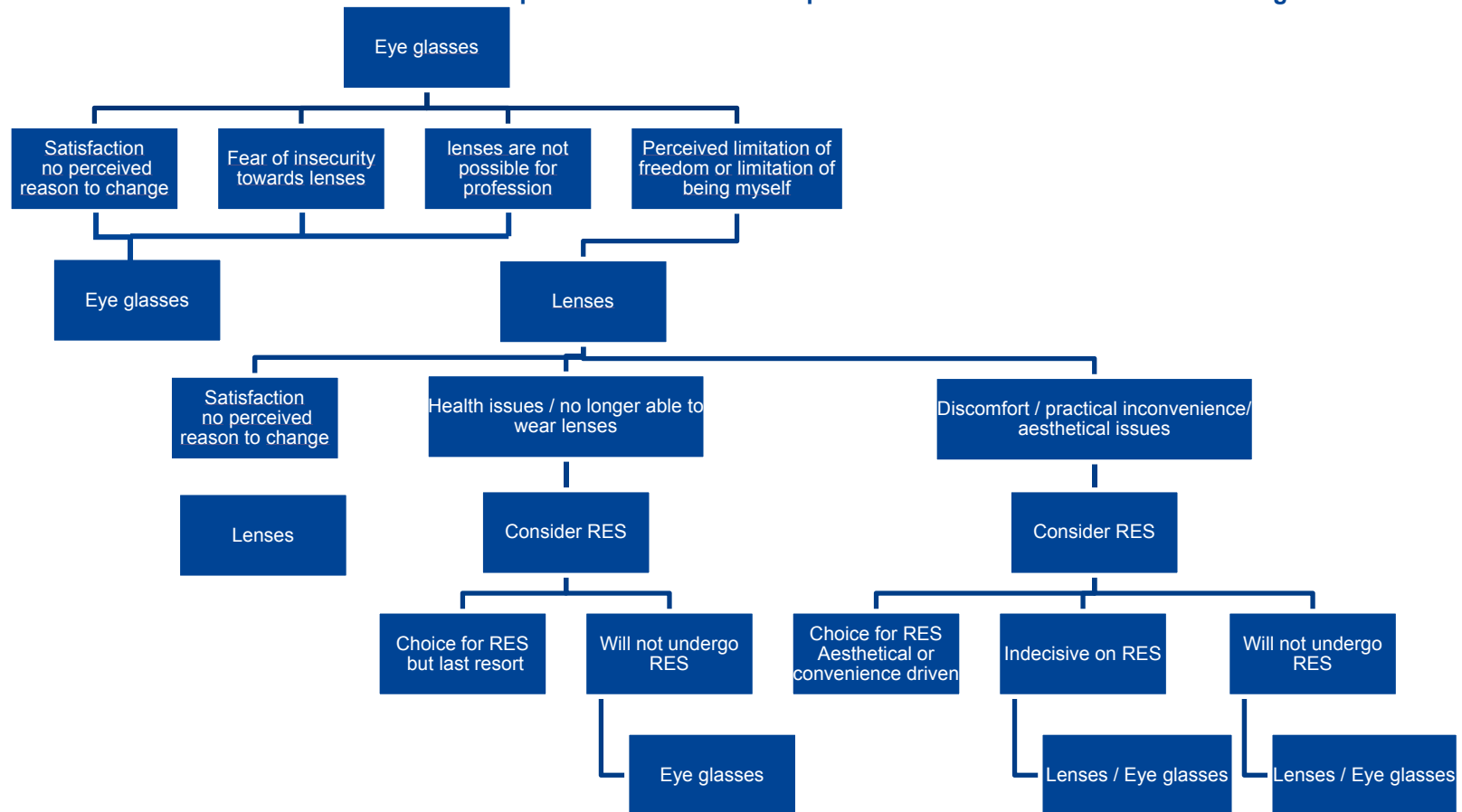
All respondents considered refractive surgery but the final sample included three types of patients:

- Some patients will not opt for refractive surgery: either they are not eligible or they will not plenty benefit from this intervention.
- The indecisive patients are still waiting for practical reasons: the cost of surgery, the need for more guarantee and/or their relative satisfaction with their current eye correction.
- A last group underwent refractive surgery either because they clearly chose it or because they had no other solution apart from continuing to wear glasses.

The steps from glasses error to possible refractive surgery have been schematically represented as follows:



Figure 8 – Overview of the identified consecutive steps in the search for the optimal refractive error treatment or management



For more explanation on this figure please consult KCE report 202 <sup>1</sup>



### 4.3.3 The process of undergoing refractive surgery

The following sections discuss the decisions taken by the patient before undergoing the operation and the experience of surgery.

#### 4.3.3.1 Choice for a surgeon/place of surgery

The patients consider refractive surgery as a very delicate and potentially dangerous surgery. The most crucial elements in the choice of the surgeon are therefore:

- A feeling of trust and confidence in the surgeon;
- The surgeon's reputation.

Their first choice for performing the refractive surgery was usually their usual ophthalmologist. If not, respondents would opt for a surgeon recommended by:

- Their ophthalmologist;
- 'Experts by experience'.

*"Je suis allée chez l'ophtalmologue d'avant mais qui n'opérait pas elle, donc elle m'avait renseigné un confrère chirurgien, que j'avais été voir une première fois pour les informations et alors une deuxième pour l'opération, et une troisième fois pour le postopératoire. Chez la première ophtalmologue, elle m'avait fait des petits schémas et tout" (female, 34 years old, myopia + astigmatism, -2,25 & -2,50, underwent refractive surgery)*

*"Ik heb een heel goede dokter gevonden, via een collega. Ik wist dat ik bij hem wilde gaan. Ik had zoiets van 'dat wordt het, mijn redding'. Ik was ook al op consultatie geweest bij andere dokters waar ik niet zo'n goed gevoel bij had. Het gaat natuurlijk wel over je ogen, dat is heel delicaat." (female, 35 years old, myopia, -6, underwent refractive surgery)*

Some respondents mentioned the fact that certain sickness funds only offered partial reimbursement of the refractive surgery if it was performed by specific surgeons. However, convenience and trust are more important drivers for the choice of a surgeon.

*"De mutualiteit waar ik bij zit, die zijn alleen aangesloten bij 1 kliniek in de Kempen, dus... Ik ga ook niet helemaal naar de Kempen rijden om dan nog naar een dokter te gaan die ik niet ken, om het daar te laten doen. Dus ik krijg niets terugbetaald." (female, 27 years old, myopia, -4,5, underwent refractive surgery)*

The interviews show that the choice of the surgeon determines the choice between hospital or extramural centre: the person who performs the surgery is more important than the setting.

The perceived differences between hospital and extramural centre are mentioned in the table below.

**Table 19 – Overview of perceived differences between hospital and extramural centre for refractive surgery**

Hospital	Extramural centre
More 'routine' approach	More personal approach
More linked with the idea of surgery - safer Better equipped in case of emergency	Specialized in refractive surgery – experienced
Standardized price	Potentially more expensive
Equipment might not always be up to date	Modern, up to date equipment

**Patients choose their surgeon according to their feeling of trust and confidence in him/her or in his/her reputation. The choice of the surgeon will determine if the patient will be operated in a hospital or in an extramural centre.**



#### 4.3.3.2 Choice for refractive surgery technique

Not all respondents who underwent refractive surgery were able to state which technique was used. It also appears that the ophthalmologist is very decisive in the choice of the technique. Respondents stated to follow the physician's recommendation without questioning it. Influencing elements in the ophthalmologist's choice were practice of sports, oversensitivity to pain, work related issues.

Interviewees have limited knowledge of the different surgery techniques. On a first level, they make the distinction between the older technology ('krasjes'/'incisions au bistouri') and laser surgery. Within laser surgery, they mostly distinguish between surface procedures (PRK) and flap procedures (LASIK).

The following comparisons (Table 20) were made between surface and flap procedures (based on respondents' perception).

**Table 20 – Overview of perceived differences between surface versus flap procedures for refractive surgery**

Surface procedures	Flap procedures
Longer recovery period	Short recovery period (48 hours)
More painful & uncomfortable	Less painful
Less risky on the long term	Possibility of accidental traumatic flap displacement years after the surgery Potential scar tissue (permanent and embarrassing)
One eye at a time (some answers)	Both eyes at the same time (some answers)

Respondents preferred to have both eyes operated at the same time but stated that they followed the ophthalmologist's recommendation. Recommendation for both eyes at the same time was based on a shorter recovery period.

Operating one eye at a time was based on:

- To check whether infection would appear,
- Perceived risk – at least one eye would function,
- Convenience – still being able to see (e.g. taking care of kids).

Respondents who had the refractive surgery in two phases (usually with one or two weeks in between) experienced this rather negatively. For the second eye, they knew what was coming. Most felt more afraid for the second surgery. Most also found that the recovery period of the second eye was more painful. Having refractive surgery in two phases also meant having to go through the pain and discomfort of the recovery period twice.

**The patient leaves the surgeon to decide upon the technique and if one or both eyes will be operated at the same time.**

#### 4.3.3.3 Preparation phase

##### Emotional status

Refractive eye surgery always involves risk and fear. The respondents who underwent refractive surgery had two strategies in order to deal with this insecurity:

- Master the insecurity: Some respondents did extensive research in order to prepare for the surgery. They wanted to know every detail of the surgery, so that they knew what to expect:
  - Anaesthesia: type ? duration?
  - Technical description of the surgery technique
  - Duration of the surgery
- Denial: Other respondents did not want to know anything about the process of the surgery. They even got upset when the surgeon explained what would happen during the operation. At this point, they had to lie still and could not react.



*“Je n’ai pas réfléchi longtemps parce que si j’avais réfléchi longtemps, je ne l’aurais pas faite. Je n’ai pas voulu aller voir sur Internet comment l’opération se passait ni rien parce que sinon je pense que je ne l’aurais pas fait. Et je n’ai pas spécialement voulu avoir de détails par rapport à l’opération; j’ai su le jour même, j’étais installée, c’était trop tard.” (female, 32 years old, myopia + astigmatism, -2,25 & -2,75, underwent refractive surgery)*

The evening/night before refractive surgery, respondents experienced a sense of nervousness and anxiety, but also excitement (‘it is finally happening’).

*“De dag voor de operatie was ik wel bezorgd, ik dacht van wat als ik nooit meer in mijn leven kan zien, het is een risicovolle operatie, een operatie met je ogen, ik had veel schrik.” (female, 31 years old, myopia, -2,5, underwent refractive surgery)*

### Practical aspects

Respondents thought that they could not wear lenses for one month before the surgery: this was not considered as an important hindrance.

Respondents had to undergo preliminary examinations to check whether their eyes fitted the indication for surgery (e.g. cornea thickness).

Some respondents had to take medication (sedative) the evening before the refractive surgery and the morning of the surgery.

Respondents stated that they received eye drops that sedated the area of the eyes.

Respondents were always accompanied by a friend, partner or relative because they could not drive back after the surgery.

**Some patients prepare themselves by seeking information on the procedure, other ones prefer to know as little as possible. There are however practical aspects to consider (e.g. how to drive back).**

### 4.3.3.4 Positive and negative experiences during surgery

Respondents mentioned the following positive experiences of refractive surgery:

- The surgery itself lasted surprisingly short (5 to 15 minutes per eye);
- There was no pain experienced, only an uncomfortable feeling when the eye is pulled open (retractor).

*“Ze doen druppels in je ogen en dat verdooft je eigenlijk helemaal. Het reactievermogen van het signaal dat je ogen doorsturen naar je hersenen ligt dan helemaal lam. Je ziet dus helemaal niets en je voelt eigenlijk ook helemaal niets. Het is gewoon zwart voor je ogen. Daar was ik dus wel heel blij om. Dan was ik wel wat gerustgesteld, want zo’n scalpel, stel dat je dat allemaal ziet dat ze in je ogen beginnen te snijden...” (female, 27 years old, myopia, -4,5, underwent refractive surgery)*

Respondents mentioned the following negative experiences of refractive surgery, causing a feeling of fear and anxiety during the surgery:

- The experienced smell of burned flesh during the surgery

*“Il m’a dit qu’il allait brûler la première couche de l’œil et qu’avec son appareil, il allait corriger. Je ne sais pas comment ils font. Et que la sensation, l’odeur de brûler que j’allais sentir, il ne fallait pas trop en tenir compte. Effectivement, c’est l’odeur qui est la plus désagréable...C’est désagréable et ça fait peur quand-même, on se demande si son œil n’est pas en train de brûler, parce que effectivement on le sent chauffer. C’est comme un cochon brûlé, c’est vraiment ça.” (female, 32 years old, myopia + astigmatism, -2,25 & -2,75, underwent refractive surgery)*

- The noise made by the surgery equipment
- The fear of moving one’s head and causing the laser to hurt the eye



*“On m’avait mis des gouttes, une heure dans la salle d’attente le temps que ça agisse. Là, le médecin vient, le cœur bat à mille à l’heure. Lui m’a mis les gouttes pour que ça soit endormi. Il expliquait tout ce qu’il faisait, c’est rassurant. Mais mon cœur ne s’est pas arrêté. Je n’osais vraiment pas bouger ! Stressée vraiment. Boule au ventre... et ne pas respirer presque pour éviter un faux mouvement qui l’empêcherait de faire son travail”. (female, 34 years old, myopia, -5,5 & -6, underwent refractive surgery)*

#### 4.3.3.5 Recovery phase

The recovery phase did cause some physical and emotional discomforts.

##### Physical discomfort:

- Painful eyes: irritated, watery, burning sensation,
- Pain when removing the pressure bandage,
- Need to wear sunglasses because eyes are very light sensitive,
- Fear of touching the eyes or of dirt getting into the eyes,
- Fear of infection,
- Insert eye drops every few hours for a few days after surgery,
- No make-up until one month after the surgery.

##### Emotional impact:

- Feeling like a prisoner – not being able to work, watch TV or read. Need to sit in the dark and sleep a lot.
- Feeling dependent on others – not being able to drive, do groceries, prepare food or look after the kids.

Respondents were unable to work for a period ranging from 2 days to one week, exceptionally two weeks. This is something they were prepared for. However, unexpected side-effects happen caused feelings of irritation.

**The operation is very rapid and painless while the recovery period is uncomfortable because of pain, fear of adverse events and feelings of limited freedom or dependence.**

#### 4.3.3.6 Elements of (dis)satisfaction following refractive surgery

Any discomfort appeared to be outweighed by the satisfaction of being able to see without any correction. The interviewees describe the following positive emotions after the surgery

- Feeling reborn:

*“(na operatie) Een paradijs. Je ogen gaan open en je voelt je goed in je vel. Je zit veilig en op je gemak. Je voelt je beter. Je voelt je thuis.” (female, 35 years old, myopia, -6, underwent refractive surgery)*

- Feeling normal, just like everyone else;
- Feeling like I am again, no longer handicapped:

*“Première réaction (après l’opération), c’est ‘je suis dans un rêve, ce n’est pas possible’. On se rend compte après qu’on était vraiment handicapé. Pour celui qui a moins 2, je ne sais pas, mais moi là, ça change la vie.” (female, 34 years old, myopia + astigmatism, -5,5 & -6, underwent refractive surgery)*

- Freedom:

*“(voor operatie) Het is onzeker frustrerend, niet erg gelukkig en beetje onveiligheid gevoel en bedreigd als je niet goed ziet. Dat wordt echt onderschat want het is echt een belemmering, je leeft echt in een waas, ik vind het zo beangstigend dat je van zo’n bril afhangt, je moet altijd zien dat je een reserve hebt anders ben je verloren. (na operatie) Alles is veel zonniger, het is een totaal ander leven, je voelt je zoveel vrijer, ik voelde mij vollediger en echt heel veel beter. Herboren.” (female, 51 years old, hyperopia, 0,75, underwent refractive surgery)*

*“Je suis hyper content. J’ai toujours été quelqu’un de sportif. J’en reviens toujours au sport car c’est vraiment là que l’opération a été un apport. Dans certains sports extérieurs, j’étais obligé de jouer à certaines places à cause de mes lunettes. Depuis que j’en ai plus, je peux jouer aux places où j’ai toujours voulu jouer. C’est plus de liberté, moins de contraintes. Une facilité!” (male, 37 years old, myopia + astigmatism, -2,75 & -3, underwent refractive surgery)*





- Comfort

*“Het is een last minder. Het is bevrijdend en relaxter. Het is gewoon veel leuker nu. Het heeft mijn leven gemakkelijker gemaakt.” (male, 23 years old, myopia, - 3,5, underwent refractive surgery)*

The interviewees mentioned the following issues in relation to complications or side-effects of the surgery:

- Lengthy recovery due to slow healing,
- Additional correction needed,
- Over-correction.

A certain fear of relapse remains after the surgery. Some respondents mentioned that they felt that their eye sight was deteriorating slightly and went for a check-up.

*“Ik was op de autosnelweg en had het gevoel dat ik een bord niet kon lezen. Dan ben ik het gaan controleren en dat was een 10 op 10, misschien was het mijn inbeelding omdat ik er steeds mee bezig was, het blijft wel in je achterhoofd.” (female, 31 years old, myopia, -2,5, underwent refractive surgery)*

**The patients interviewed in this study were usually positive about the outcomes, at least at the short term (operation since a maximum of 4 years). Some of them mentioned complications.**

#### 4.4 Discussion: patient issues

The findings in this report are based on the analysis of 36 qualitative interviews with patients who have at least considered refractive eye surgery (RES) (or planned/underwent it). A major limitation is the limited number of patients who experienced the surgery (with 9 women and 3 men only, few respondents with low socio economic status). This is an inherent limitation to the methodology and findings cannot be generalized to the whole population.

We collected their perceptions and stories. Their statements reflect their own view and are respected as such. However, confronting these beliefs with the clinical literature and expertise of ophthalmologists we can identify true and false beliefs, therefore what information could be given more precisely to patients about refractive eye surgery (see Table 21 below).



Table 21 – True and false beliefs of the respondents (classified according to clinicians' opinion and/or literature)

Beliefs	True beliefs	Partly true/false beliefs	False beliefs
Indications of RES	<ul style="list-style-type: none"> <li>Eye-sight has to be <b>stabilized</b> to pretend to RES. This stabilization has to be effective for one year at least.</li> <li>The <b>feature of the eyes</b> is an important aspect of the indication for RES by laser: the cornea should be thick enough, the pupil has to be not too big.</li> </ul>	<ul style="list-style-type: none"> <li>RES may not be indicated because of <b>the age</b> of the patient. The expected presbyopia means that laser surgery is not an absolute long term solution for people who wish to get rid of glasses.</li> <li>The <b>quality of the eye sight</b> is not a contra indication as such for the RES but will limit the quality of the results of the surgery.</li> </ul>	<ul style="list-style-type: none"> <li>Some people reported that they are not eligible for RES because they are <b>wearing soft lenses for a long time</b>.</li> <li>A patient told that <b>if you have already had RES</b>, you cannot do it anymore. The fact is that it is always possible to have RES again but the technique will vary according to the previous surgery and the delay since it.</li> </ul>
Surgical options (Flap of surface procedure)	<ul style="list-style-type: none"> <li><b>Recovery period</b> is shorter for flap procedures than for surface procedures.</li> <li>Flap procedure is less <b>painful</b> than surface procedure.</li> <li><b>Risk of incidents</b> differs according to the procedure but these are rare. Scar tissue comes rather after surface procedure than after flap procedure. In general, laser techniques are less risky.</li> </ul>	<ul style="list-style-type: none"> <li>The technique of the surgery partly depends of the feature of the eye. If all parameters are good, the <b>patients have theoretically the choice of the technique</b>. The choice of the technique also depends on the risk of complication: the surgeon will not advise a policeman or a boxer to resort to flap procedure because of the risk in the event of blow to the head.</li> </ul>	
Preparation phase before surgery	<ul style="list-style-type: none"> <li><b>The patient cannot wear his/her lenses before surgery</b>. The time period is about one week before the treatment. Nevertheless, soft lenses have to be retracted 2</li> </ul>	<ul style="list-style-type: none"> <li><b>One eye will be operated at one time</b>: this was the case before but today both eyes are generally operated the same day.</li> </ul>	



Beliefs	True beliefs	Partly true/false beliefs	False beliefs
	<p>days before the examination aiming at taking the measures before the surgery and hard lenses, 2 months before.</p> <ul style="list-style-type: none"> <li>• <b>Medication (sedative)</b> can be given to anxious and stressed patients.</li> <li>• <b>Sedative drops</b> will be put in the eye just before the surgery. Drops against infections will be prescribed before and after the surgery.</li> <li>• <b>Driving is not allowed the D day</b> and not recommended during the week after the operation.</li> </ul>		
<b>Expected results</b>	<ul style="list-style-type: none"> <li>• The results depend on the <b>severity</b> of the refractive error.</li> <li>• <b>There is no guarantee on complete correction and long term effects.</b> RES is a medical act, as any other one: there is no absolute guarantee. Moreover, the results depend on the quality of the material and personal healing process. The results improve with new techniques and it is possible to repeat the operation if necessary.</li> </ul>		<ul style="list-style-type: none"> <li>• People reported that <b>patients who undergo RES will wear eye glasses sooner for presbyopia</b>. Actually, they will wear these glasses at the same time than somebody else with a normal eyesight, not sooner...but well sooner than if they had not corrected their myopia by RES.</li> </ul>
<b>Side-effects/complications</b>	<ul style="list-style-type: none"> <li>• <b>Additional correction need</b> can occur</li> <li>• <b>Over-correction</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Lengthy recovery / slow healing</b></li> </ul>	



In conclusion, the perceptions of the respondents regarding indications of RES, surgical options, preparation phase before surgery and expected results are globally accurate but there are a few misunderstandings or missing details. Regarding side-effects or complications, while the perceptions are accurate, the potential negative outcome list reported is very short compared to what has been identified in the literature. For example, glares and halos are frequently reported in the clinical studies but have not been mentioned by respondents. This could be explained because none of them has experienced it (but they were few to have been interviewed) and/or because they do not remind it or because they were not aware of it,

All of this highlights the need for more and more accurate information before interventions, at least for the more frequent side-effects.

Operated patients are generally satisfied: this can be partly influenced by the recent nature of the surgery (maximum 4 years). They use emotionally strong words such as 'feeling reborn'.

Yet this sample is not representative of the operated population and we cannot draw any conclusion about the satisfaction of operated patients in general.

## 5 GENERAL DISCUSSION AND SYNTHESIS

The general discussion and the synthesis of these findings are published in a separate document (synthesis) on the KCE website.



## ■ APPENDICES

### APPENDIX 1. DETAILED SEARCH STRATEGIES

#### Appendix 1.1. Medline (through Pubmed) search systematic reviews and meta-analyses

Searched on March 11, 2013; 35 citations retrieved

((("Epithelium, Corneal"[Mesh] OR (cornea\* AND epithelium\*)) AND laser\*) OR "Corneal Surgery, Laser"[Mesh] OR (laser\* AND cornea\* AND surger\*) OR photokeratectom\* OR "Keratectomy, Subepithelial, Laser-Assisted"[Mesh] OR lasek OR ((subepitheli\* OR sub-epitheli\*) AND surger\* AND laser\*) OR "Keratomeileusis, Laser In Situ"[Mesh] OR lasik OR keratomeileusis OR "Photorefractive Keratectomy"[Mesh] OR prk OR keratectom\* OR "Lens Implantation, Intraocular"[Mesh] OR ((implantat\* OR intraocular) AND lens\*) OR iol\* OR (eximer AND laser\*) OR "Refractive Surgical Procedures"[Mesh])

AND

((refracti\* AND error\*) OR ametropia OR (refracti\* AND disorder\*) OR "Myopia"[Mesh] OR myopia\* OR nearsightedness\* OR shortsightedness\* OR "Hyperopia"[Mesh] OR hyperopia\* OR hypermetropia\* OR farsightedness\* OR longsightedness\* OR "Astigmatism"[Mesh] OR astigmat\*)

AND

("meta-analysis" [pt] OR "meta-anal\*" [tw] OR "metaanal\*" [tw] OR ("quantitativ\* review\*" [tw] OR "quantitative\* overview\*" [tw]) OR ("systematic\* review\*" [tw] OR "systematic\* overview\*" [tw]) OR ("methodologic\* review\*" [tw] OR "methodologic\* overview\*" [tw]) OR ("review" [pt] AND "medline" [tw])<sup>80</sup>



## Appendix 1.2. Embase (through OVID®) search systematic reviews and meta-analyses

Searched on March 11, 2013; 58 citations retrieved

- 1 exp Meta Analysis/ (69377)
- 2 ((meta adj analys\$) or metaanalys\$.tw. (65672)
- 3 (systematic adj (review\$1 or overview\$1)).tw. (51027)
- 4 or/1-3 (129094)
- 5 cancerlit.ab. (669)
- 6 cochrane.ab. (29731)
- 7 embase.ab. (26848)
- 8 (psychlit or psyclit).ab. (960)
- 9 (psychinfo or psycinfo).ab. (6617)
- 10 (cinahl or cinhal).ab. (9037)
- 11 science citation index.ab. (1944)
- 12 bids.ab. (432)
- 13 or/5-12 (45591)
- 14 reference lists.ab. (8824)
- 15 bibliograph\$.ab. (14080)
- 16 hand-search\$.ab. (4085)
- 17 manual search\$.ab. (2351)
- 18 relevant journals.ab. (742)
- 19 or/14-18 (27143)
- 20 data extraction.ab. (10837)
- 21 selection criteria.ab. (19687)
- 22 20 or 21 (29165)
- 23 review.pt. (1937907)
- 24 22 and 23 (17266)
- 25 letter.pt. (815742)
- 26 editorial.pt. (426842)
- 27 animal/ (1820198)
- 28 human/ (14143417)
- 29 27 not (27 and 28) (1362573)
- 30 or/25-26,29 (2591438)
- 31 4 or 13 or 19 or 24 (160852)
- 32 31 not 30 (154914)
- 33 refraction error/ (9860)
- 34 (refracti\$ and (error\$ or disorder\$)).tw. (8181)
- 35 ametrop\$.tw. (1101)
- 36 exp myopia/ or exp high myopia/ or exp degenerative myopia/ (18325)
- 37 myop\$.tw. (43294)
- 38 ((short or near or long or far) adj3 sight\$).tw. (381)
- 39 exp hypermetropia/ (4521)
- 40 (hyperop\$ or hypermetrop\$).tw. (4524)
- 41 exp astigmatism/ (8905)
- 42 astigmat\$.tw. (8247)
- 43 or/33-42 (65698)
- 44 refractive surgery/ (1708)
- 45 (cornea epithelium/ or (cornea\$ and \$epitheli\$).tw.) and laser\$.tw. (1693)
- 46 (cornea surgery/ or (cornea\$ and surger\$).tw.) and laser\$.tw. (2689)
- 47 keratectomy/ (2612)
- 48 exp photorefractive keratectomy/ (1872)
- 49 exp keratomileusis/ (5765)
- 50 exp laser epithelial keratomileusis/ (512)
- 51 keratectom\$.tw. (3768)
- 52 keratomileusis.tw. (3450)
- 53 LAS?K.tw. (4416)
- 54 PRK.tw. (2152)



55 (laser\$ adj3 refractive adj3 surg\$).tw. (448)  
 56 (laser\$ adj3 \$epithel\$ adj3 surg\$).tw. (8)  
 57 (excimer adj3 laser\$).tw. (4881)  
 58 exp lens implant/ (17262)  
 59 exp lens implantation/ (5181)  
 60 (lens\$ or IOL\$).tw. (75017)  
 61 or/44-60 (91829)  
 62 32 and 43 and 61 (58)

### Appendix 1.3. Cochrane Database of Systematic Reviews (through [www.cochrane.org](http://www.cochrane.org))

Searched on March 11, 2013, through health topics -> eyes and vision -> refractive errors (search result: 6)

### Appendix 1.4. Database of Abstracts of Reviews of Effects (through the Cochrane library)

DARE searched on March 11, 2013

#1 MeSH descriptor: [Lens Implantation, Intraocular] explode all trees 812  
 #2 MeSH descriptor: [Corneal Surgery, Laser] explode all trees 392  
 #3 MeSH descriptor: [Photorefractive Keratectomy] explode all trees 190  
 #4 MeSH descriptor: [Keratectomy, Subepithelial, Laser-Assisted] explode all trees 28  
 #5 MeSH descriptor: [Keratomeileusis, Laser In Situ] explode all trees 225  
 #6 MeSH descriptor: [Refractive Surgical Procedures] explode all trees 2762  
 #7 (laser\* and cornea\* and surger\*) or photokeratectom\* or lasek or ((subepitheli\* or sub-epitheli\*) and surger\* and laser\*) or lasik or keratomileusis or prk or keratectom\* or ((implantat\* or intraocular) and lens\*) or iol\* or (eximer and laser\*) (Word variations have been searched) 3535  
 #8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 4571  
 #9 MeSH descriptor: [Myopia] explode all trees 585  
 #10 MeSH descriptor: [Hyperopia] explode all trees 55

#11 MeSH descriptor: [Astigmatism] explode all trees 329

#12 ((refracti\* and error\*) or ametropia or (refracti\* and disorder\*) or myopia\* or nearsightedness\* or shortsightedness\* or hyperopia\* or hypermetropia\* or farsightedness\* or longsightedness\* or astigmat\*) (Word variations have been searched) 2334

# 13 #9 OR #10 OR #11 OR #12 161116

#14 #8 AND #13 1659, of which 17 DARE abstracts

### Appendix 1.5. Medline (through Pubmed) search RCTs

Searched on April 5, 2013; 1 352 citations

((("Epithelium, Corneal"[Mesh] OR (cornea\* AND epithelium)) AND laser\*) OR "Corneal Surgery, Laser"[Mesh] OR (laser\* AND cornea\* AND surger\*) OR photokeratectom\* OR "Keratectomy, Subepithelial, Laser-Assisted"[Mesh] OR lasek OR ((subepitheli\* OR sub-epitheli\*) AND surger\* AND laser\*) OR "Keratomeileusis, Laser In Situ"[Mesh] OR lasik OR keratomileusis OR "Photorefractive Keratectomy"[Mesh] OR prk OR keratectom\* OR "Lens Implantation, Intraocular"[Mesh] OR ((implantat\* OR intraocular) AND lens\*) OR iol\* OR (eximer AND laser\*) OR "Refractive Surgical Procedures"[Mesh])

AND

((refracti\* AND error\*) OR ametropia OR (refracti\* AND disorder\*) OR "Myopia"[Mesh] OR myopia\* OR nearsightedness\* OR shortsightedness\* OR "Hyperopia"[Mesh] OR hyperopia\* OR hypermetropia\* OR farsightedness\* OR longsightedness\* OR "Astigmatism"[Mesh] OR astigmat\*)

AND

(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals[mh] NOT (animals[mh] AND humans [mh]))<sup>81</sup>

Searches limited to studies published from 2004 onwards, in Dutch, English, French or German.





## Appendix 1.6. Embase (through OVID®) search RCTs

Searched on April 5, 2013

- 1 Clinical trial/ (880865)
- 2 Randomized controlled trial/ (342198)
- 3 Randomization/ (61098)
- 4 Single blind procedure/ (17193)
- 5 Double blind procedure/ (116395)
- 6 Crossover procedure/ (36574)
- 7 Placebo/ (228195)
- 8 Randomi?ed controlled trial\$.tw. (85332)
- 9 Rct.tw. (11212)
- 10 Random allocation.tw. (1266)
- 11 Randomly allocated.tw. (18779)
- 12 Allocated randomly.tw. (1894)
- 13 (allocated adj2 random).tw. (798)
- 14 Single blind\$.tw. (13415)
- 15 Double blind\$.tw. (141791)
- 16 ((treble or triple) adj blind\$.tw. (333)
- 17 Placebo\$.tw. (192256)
- 18 Prospective study/ (229453)
- 19 or/1-18 (1337754)
- 20 Case study/ (19129)
- 21 Case report.tw. (250873)
- 22 Abstract report/ or letter/ (882240)
- 23 or/20-22 (1147218)
- 24 19 not 23 (1301123)
- 25 refraction error/ (9910)
- 26 (refracti\$ and (error\$ or disorder\$)).tw. (8230)
- 27 ametrop\$.tw. (1106)
- 28 exp myopia/ or exp high myopia/ or exp degenerative myopia/ (18380)
- 29 myop\$.tw. (43445)
- 30 ((short or near or long or far) adj3 sight\$.tw. (383)
- 31 exp hypermetropia/ (4542)
- 32 (hyperop\$ or hypermetrop\$).tw. (4551)
- 33 exp astigmatism/ (8947)
- 34 astigmat\$.tw. (8278)
- 35 or/25-34 (65932)
- 36 refractive surgery/ (1721)
- 37 (cornea epithelium/ or (cornea\$ and \$epitheli\$).tw.) and laser\*.tw. (1699)
- 38 (cornea surgery/ or (cornea\$ and surger\$).tw.) and laser\$.tw. (2700)
- 39 keratectomy/ (2615)
- 40 exp photorefractive keratectomy/ (1882)
- 41 exp keratomileusis/ (5785)
- 42 exp laser epithelial keratomileusis/ (514)
- 43 keratectom\$.tw. (3779)
- 44 keratomileusis.tw. (3465)
- 45 LAS?K.tw. (4428)
- 46 PRK.tw. (2157)
- 47 (laser\$ adj3 refractive adj3 surg\$).tw. (448)
- 48 (laser\$ adj3 \$epithel\$ adj3 surg\$).tw. (8)
- 49 (excimer adj3 laser\$).tw. (4889)
- 50 exp lens implant/ (17318)
- 51 exp lens implantation/ (5222)
- 52 (lens\$ or IOL\$).tw. (75230)
- 53 or/36-52 (92093)
- 54 24 and 35 and 53 (1969)

55 limit 54 to ((dutch or english or french or german) and yr="2004 - Current") (1021)

### Appendix 1.7. Food and Drug Administration search

Searched on April 22, 2013

MedWatch ([www.fda.gov/Safety/default.htm](http://www.fda.gov/Safety/default.htm)). Search terms used: PRK (1 result), LASEK (0 results), LASIK (11 results), intraocular lens (20 results)

MedSun, site browsed and MedSun reports searched (2002-2013). Search terms used: PRK (0 results), LASEK (0 results), LASIK (2 results), intraocular lens (43 results)

([www.fda.gov/MedicalDevices/Safety/MedSunMedicalProductSafetyNetwork/ucm223427.htm](http://www.fda.gov/MedicalDevices/Safety/MedSunMedicalProductSafetyNetwork/ucm223427.htm))

FDA LASIK web page, site browsed

([www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/default.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/default.htm))

Phakic IOLs web page, site browsed

([www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/PhakicIntraocularLenses/default.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/PhakicIntraocularLenses/default.htm))

### Appendix 1.8. TOXNET search performed

Searched on April 22, 2013 (toxnet.nlm.nih.gov/)

PRK: prk OR photorefractive (394 citations)

LASEK and LASIK: (lasek OR lasik OR (laser AND refractive))

NOT (prk OR photorefractive) (431 citations)

Intraocular lenses: "intraocular lens" OR "intraocular lens" OR "intra ocular lens" (804 citations)

### Appendix 1.9. Medline (through Pubmed) search observational studies

Searched on July 3, 2013; 5196 citations retrieved

((("Epithelium, Corneal"[Mesh] OR (cornea\* AND epithelium)) AND laser\*) OR "Corneal Surgery, Laser"[Mesh] OR (laser\* AND cornea\* AND surger\*) OR photokeratectom\* OR "Keratotomy, Subepithelial, Laser-Assisted"[Mesh] OR lasek OR ((subepitheli\* OR sub-epitheli\*) AND surger\* AND laser\*) OR "Keratomileusis, Laser In Situ"[Mesh] OR lasik OR keratomileusis OR "Photorefractive Keratectomy"[Mesh] OR prk OR keratectom\* OR "Lens Implantation, Intraocular"[Mesh] OR ((implantat\* OR intraocular) AND lens\*) OR iol\* OR (eximer AND laser\*) OR "Refractive Surgical Procedures"[Mesh])

AND

((refracti\* AND error\*) OR ametropia OR (refracti\* AND disorder\*) OR "Myopia"[Mesh] OR myopia\* OR nearsightedness\* OR shortsightedness\* OR "Hyperopia"[Mesh] OR hyperopia\* OR hypermetropia\* OR farsightedness\* OR longsightedness\* OR "Astigmatism"[Mesh] OR astigmat\*)

Searches limited to studies published from 2004 onwards, in Dutch, English, French or German.



### Appendix 1.10. Embase (through OVID®) search observational studies

Searched on July 3, 2013; 6742 citations retrieved

- 1 refraction error/ (10085)
- 2 (refracti\$ and (error\$ or disorder\$)).tw. (8411)
- 3 ametrop\$.tw. (1123)
- 4 exp myopia/ or exp high myopia/ or exp degenerative myopia/ (18651)
- 5 myop\$.tw. (44115)
- 6 ((short or near or long or far) adj3 sight\$).tw. (391)
- 7 exp hypermetropia/ (4611)
- 8 (hyperop\$ or hypermetrop\$).tw. (4622)
- 9 exp astigmatism/ (9123)
- 10 astigmat\$.tw. (8428)
- 11 or/1-10 (66965)
- 12 refractive surgery/ (1759)
- 13 (cornea epithelium/ or (cornea\$ and \$epitheli\$).tw.) and laser\*.tw. (1720)
- 14 (cornea surgery/ or (cornea\$ and surger\$).tw.) and laser\$.tw. (2742)
- 15 keratectomy/ (2630)
- 16 exp photorefractive keratectomy/ (1915)
- 17 exp keratomileusis/ (5866)
- 18 exp laser epithelial keratomileusis/ (523)
- 19 keratectom\$.tw. (3810)
- 20 keratomileusis.tw. (3508)
- 21 LAS?K.tw. (4500)
- 22 PRK.tw. (2176)
- 23 (laser\$ adj3 refractive adj3 surg\$).tw. (455)
- 24 (laser\$ adj3 \$epithel\$ adj3 surg\$).tw. (8)
- 25 (excimer adj3 laser\$).tw. (4930)
- 26 exp lens implant/ (17524)
- 27 exp lens implantation/ (5342)
- 28 (lens\$ or IOL\$).tw. (76006)
- 29 or/12-28 (93104)
- 30 11 and 29 (15665)
- 31 limit 30 to ((dutch or english or french or german) and yr="2004 - Current") (6742)



## APPENDIX 2. STUDIES EXCLUDED ON FULL-TEXT REVIEW

### Appendix 2.1. Studies from the search for systematic reviews and meta-analyses excluded on full text review

Reference	Reasons for exclusion
Chen L, Ye T, Yang X. Evaluation of the long-term effects of photorefractive keratectomy correction for myopia in China. <i>Eur J Ophthalmol</i> . 2011;21(4):355-62.	Only Chinese/Korean studies included
Daoud YJ, Hutchinson A, Wallace DK, Song J, Kim T. Refractive surgery in children: treatment options, outcomes, and controversies. <i>Am J Ophthalmol</i> . 2009;147(4):573-82 e2.	On children
Donnenfeld E. A review of randomized controlled trials of penetrating keratoplasty techniques. <i>Evidence-Based Ophthalmology</i> . 2006;7(4):174-5.	Abstract of a systematic review that was evaluated full text
Farid M, Steinert RF. Patient selection for monovision laser refractive surgery. <i>Current Opinion in Ophthalmology</i> . 2009;20(4):251-4.	Narrative review
Guell JL, Morral M, Kook D, Kohnen T. Phakic intraocular lenses: Part 1: Historical overview, current models, selection criteria, and surgical techniques. <i>Journal of Cataract and Refractive Surgery</i> . 2010;36(11):1976-93.	Narrative review
Lee NR, Choi J, Jang EJ, Jung SY, Lee EJ, Joo CK. Long-term clinical effectiveness and stability of lasik and surface ablation in Korea: A systematic review approach. <i>Value in Health</i> . 2011;14 (3):A86.	Only Chinese/Korean studies included

Olson RJ, Werner L, Mamalis N, Cionni R. New intraocular lens technology. <i>Am J Ophthalmol</i> . 2005;140(4):709-16.	Narrative review
Packard R. Refractive lens exchange for myopia: A new perspective? <i>Current Opinion in Ophthalmology</i> . 2005;16(1):53-6.	Narrative review
Qian ZG, Ke M, Huang G, Zou J. Laser in situ keratomileusis (LASIK) versus laser epithelial keratomileusis (LASEK) for correction of myopia: A systematic review. <i>Chinese Journal of Evidence-Based Medicine</i> . 2011;11(5):565-9.	Chinese with an English abstract
Rapuan CJ. Meta-analysis: Clinical outcomes of laser-assisted subepithelial keratectomy and photorefractive keratectomy in myopia. <i>Evidence-Based Ophthalmology</i> . 2011;12(2):72-3.	Abstract of a systematic review that was evaluated full text
Shapiro DR. A comparison of modern incisional keratotomies and photorefractive keratectomy. <i>International Ophthalmology Clinics</i> . 1997;37(1):65-81.	Narrative review
Siddiqui MK, Mann K, Vonmaltzahn R, Ternouth AM, Verboven Y, Berdeaux G. Risks and benefits of acrysof cachet implantation in high myopia (<-6 diopter): A systematic literature review. <i>Value in Health</i> . 2011;14 (7):A261.	Systematic review in abstract form
Winkler von Mohrenfels C, Salgado JP, Khoramnia R. [Keratectasia after refractive surgery]. <i>Klin Monbl Augenheilkd</i> . 2011;228(8):704-11	Narrative review



## Appendix 2.2. HTA-reports excluded on full text review

Reference	Reasons for exclusion
AHTA. Implantable Collamer lens for the correction of myopic vision. AHTA	No systematic search or selection reported
CADTH. Sharp and round optic edges of intraocular lenses: a review of the clinical and cost-effectiveness. CADTH	Other comparison
Hjortdal JØ, Ehlers N, Møller-Pedersen T, Ehlers L, Kjellberg J. [Refractive surgery]. Copenhagen: Sundhedsstyrelsen	In Danish with English abstract
IECS. [Usefulness of intraocular lenses in severe myopia]. Buenos Aires: IECS	In Spanish with English abstract
IECS. [Wavefront analysis in refractive surgery]. Buenos Aires: IECS	In Spanish with English abstract
IECS. [Thoracic intraocular lenses]. Buenos Aires: IECS	In Spanish with English abstract
SBU. [Laser eye surgery for the correction of refractive errors]. SBU	In Swedish with English abstract

## Appendix 2.3. RCTs excluded after full text review

Reference	Reasons for exclusion
Auffarth GU. Phakic intraocular lenses. [German] Phake Intraokularlinsen. Der Ophthalmologe : Zeitschrift der Deutschen Ophthalmologischen Gesellschaft. 2004;101(3):229-31.	Narrative review
Camellin M, Wyler D. Epi-LASIK versus epi-LASEK. J Refract Surg. 2008;24(1):S57-63.	Compares two types of LASIK
Fernandes M, Reddy P, Shah SG. One-year outcome of bilateral randomized prospective clinical trial comparing photorefractive keratectomy (PRK) with mitomycin C (MMC) and laser in situ keratomileusis (LASIK). Br J	Letter

Ophthalmol. 2011;95(3):433.	
Hondur A, Bilgihan K, Hasanreisoglu B. A prospective bilateral comparison of epi-LASIK and LASEK for myopia. Journal of Refractive Surgery. 2008;24(9):928-34.	Non-randomized study
Kim TW, Wee WR, Lee JH, Kim MK. Contrast sensitivity after LASIK, LASEK, and wavefront-guided LASEK with the VISX S4 laser. J Refract Surg. 2007;23(4):355-61.	Non-randomized study
Manche EE, Haw WW. Wavefront-guided laser in situ keratomileusis (Lasik) versus wavefront-guided photorefractive keratectomy (Prk): a prospective randomized eye-to-eye comparison (an American Ophthalmological Society thesis). Trans Am Ophthalmol Soc. 2011;109:201-20.	Already included in a selected systematic review
Meidani A, Tzavara C, Dimitrakaki C, Pesudovs K, Tountas Y. Femtosecond laser-assisted LASIK improves quality of life. J Refract Surg. 2012;28(5):319-26.	Non-randomized study
Mostafaei A, Sedgipour MR, Sadeghi-Bazargani H. Contralateral eye comparison on changes in visual field following laser in situ keratomileusis vs photorefractive keratectomy for myopia: a randomized clinical trial. Pak J Biol Sci. 2009;12(23):1521-5.	Other outcomes
Schallhorn S, Tanzer D, Sanders DR, Sanders M, Brown M, Kaupp SE. Night driving simulation in a randomized prospective comparison of Visian toric implantable collamer lens and conventional PRK for moderate to high myopic astigmatism. J Refract Surg. 2010;26(5):321-6.	Other outcomes
Sia RK, Coe CD, Edwards JD, Ryan DS, Bower KS. Visual outcomes after Epi-LASIK and PRK for low and moderate myopia. Journal of	Non-randomized study



Refractive Surgery. 2012;28(1):65-71.

Sun Y, Deng YP, Wang L, Huang YZ, Qiu LM. Compares two types of LASIK. Comparisons of morphologic characteristics between thin-flap LASIK and SBK. Int J Ophthalmol. 2012;5(3):338-42.

Vignat R, Tanzer D, Brunstetter T, Schallhorn S. [Scattered light and glare sensitivity after wavefront-guided photorefractive keratectomy (WFG-PRK) and laser in situ keratomileusis (WFG-LASIK)]. J Fr Ophthalmol. 2008;31(5):489-93.

#### Appendix 2.4. TOXNET retrieved studies excluded after full text review

Reference	Reasons for exclusion
Alio JL, Javaloy J. Corneal inflammation following corneal photoablative refractive surgery with excimer laser. Surv Ophthalmol. 2013 Jan-Feb;58(1):11-25	Narrative review (no systematic selection criteria, narrative presentation)
Randleman JB, Shah RD. LASIK interface complications: etiology, management, and outcomes. J Refract Surg. 2012 Aug;28(8):575-86	Narrative review (no systematic selection criteria: 'The references included in this review are therefore not all-inclusive; rather, they represent the majority of major citations, regardless of publication date, and the majority of the most recent references on the topics covered in this review')
Taneri S, Heiligenhaus A. [Infections after intraocular lens surgery: implications for refractive surgery]. Klin Monbl Augenheilkd. 2012 Sep;229(9):910-6	Narrative review (no systematic selection criteria, narrative presentation)

#### Appendix 2.5. Observational studies excluded after full text review

Reference	Reasons for exclusion
Phakic intraocular lens implant surgery. Clin Privil White Pap. 2005(226):1-8.	Too few eyes included or not an observational study
Surgical refractive correction. Optometry. 2009;80(11):662-7.	Too few eyes included or not an observational study
Photorefractive keratectomy. Clin Privil White Pap. 2012(71):1-16.	Unavailable
Akar S, Dogan M, Kucuksumer Y, Kaya V, Bayraktar S, Gokyigit B, et al. Long-term results of phakic anterior chamber intraocular lens implantation in myopic eyes. Saudi Med J. 2010;31(8):939-41.	Too few eyes included or not an observational study
Albelda-Valles JC, Martin-Reyes C, Ramos F, Beltran J, Llovet F, Baviera J. Effect of preoperative keratometric power on intraoperative complications in LASIK in 34,099 eyes. J Refract Surg. 2007;23(6):592-7.	Follow-up <6 months
Alio JL, El Aswad A, Vega-Estrada A, Javaloy J. Laser in situ keratomileusis for high hyperopia (>5.0 diopters) using optimized aspheric profiles: efficacy and safety. J Cataract Refract Surg. 2013;39(4):519-27.	Too few eyes included or not an observational study
Asbell PA. Quality of vision with corneal refractive therapy. Eye and Contact Lens. 2004;30(4):234-5.	Too few eyes included or not an observational study
Auffarth GU. [Phakic intraocular lenses]. Ophthalmologe. 2004;101(3):229-31.	Too few eyes included or not an observational study
Awwad ST, McCulley JP. Wavefront-guided LASIK: recent developments and results. Int	Too few eyes included or not an observational study





Ophthalmol Clin. 2006;46(3):27-38.		
Berdahl JP, Hardten DR. Residual astigmatism after toric intraocular lens implantation. J Cataract Refract Surg. 2012;38(4):730-1; author reply 1-2.	Too few eyes included or not an observational study	
Binder PS. Risk factors for ectasia after LASIK. J Cataract Refract Surg. 2008;34(12):2010-1.	Too few eyes included or not an observational study	
Bitzer M. Clear lens extraction (CLE): Correction of ametropia with multifocal lens. [German] Clear lens extraction (CLE): Korrektur der fehlsichtigkeit mit multifokallinse. Klinische Monatsblätter für Augenheilkunde. 2008;225(1):4-5.	Too few eyes included or not an observational study	
Brown SM. PRK for myopic anisometropia. Ophthalmology. 2005;112(3):525; author reply -6.	Too few eyes included or not an observational study	
Brown SM. PRK and Amblyopia. Ophthalmology. 2007;114(9):1792.	Too few eyes included or not an observational study	
Carifi G. Rotationally asymmetric multifocal intraocular lens. Journal of Cataract and Refractive Surgery. 2012;38(6):1116-7.	Too few eyes included or not an observational study	
Caster AI, Friess DW, Schwendeman FJ. Incidence of epithelial ingrowth in primary and retreatment laser in situ keratomileusis. J Cataract Refract Surg. 2010;36(1):97-101.	(Mainly) femto-laser	
Chan CC, Holland EJ. Management of astigmatism: toric intraocular lenses. Int Ophthalmol Clin. 2012;52(2):21-30.	Too few eyes included or not an observational study	
Chan CC, Moshegov CN. Amadeus microkeratome: experience with the first 2000 cases and lessons learned. Clin Experiment Ophthalmol. 2005;33(4):356-9.	Follow-up <6 months	
Chang JS. Complications of sub-Bowman's	Too few eyes included or	
keratomileusis with a femtosecond laser in 3009 eyes. J Refract Surg. 2008;24(1):S97-101.	not an observational study	
Chang GC, Pineda R, 2nd. Phakic intraocular lenses. Int Ophthalmol Clin. 2010;50(1):119-28.	(Mainly) femto-laser	
Cheng AC, Yuen KS, Lam DS. Long-term results of implantation of phakic posterior chamber IOLs. J Cataract Refract Surg. 2006;32(1):4; author reply	Too few eyes included or not an observational study	
Cheng AC. Wavefront-guided versus wavefront-optimized treatment. J Cataract Refract Surg. 2008;34(8):1229-30.	Too few eyes included or not an observational study	
Craig JP, Shah S, Wolffsohn JS. Clinical evaluation of the Softec HD aberration-free aspheric intraocular lens. Clinical and Experimental Ophthalmology. 2011;39(3):281-3.	Too few eyes included or not an observational study	
D'Arcy FM, Kirwan C, O'Keefe M. Ten year follow up of laser in situ keratomileusis for all levels of myopia. Acta Ophthalmol. 2012;90(4):e335-6.	Too few eyes included or not an observational study	
Das M, Garg P. LASIK infectious keratitis. Ophthalmology. 2011;118(2):425; author reply e1.	Too few eyes included or not an observational study	
Davison JA, Johnson SC. Intraoperative complications of LASIK flaps using the IntraLase femtosecond laser in 3009 cases. J Refract Surg. 2010;26(11):851-7.	(Mainly) femto-laser	
de Oliveira GC, Solari HP, Ciola FB, Lima AL, Campos MS. Corneal infiltrates after excimer laser photorefractive keratectomy and LASIK. J Refract Surg. 2006;22(2):159-65.	Follow-up <6 months	





de Ortueta D, Pavlidis M. LASIK treatment of mixed astigmatism. <i>J Refract Surg.</i> 2007;23(4):328-9; author reply 9.	Too few eyes included or not an observational study	Ghoreishi M, Attarzadeh H, Tavakoli M, Moini HA, Zandi A, Masjedi A, et al. Alcohol-assisted versus Mechanical Epithelium Removal in Photorefractive Keratectomy. <i>J Ophthalmic Vis Res.</i> 2010;5(4):223-7.	Likely same patients as included study by same author
Eleftheriadis H. Potential complications of phakic IOLs. <i>Br J Ophthalmol.</i> 2004;88(11):1480-1.	Too few eyes included or not an observational study	Henderson BA. Accommodating IOLs. <i>Ophthalmology.</i> 2008;115(10):1850-1.	Too few eyes included or not an observational study
Fares U, Otri AM, Al-Aqaba MA, Faraj L, Dua HS. Wavefront-optimized excimer laser in situ keratomileusis for myopia and myopic astigmatism: refractive outcomes and corneal densitometry. <i>J Cataract Refract Surg.</i> 2012;38(12):2131-8.	Too few eyes included or not an observational study	Ibrahim AI, Sharif KW. Evaluation of haze formation after thin-flap microkeratome LASIK for myopia. <i>J Refract Surg.</i> 2012;28(11):749-50.	Too few eyes included or not an observational study
Fechner PU. [The status of follow-up treatment for patients with refractive anterior chamber IOLs in phakic eyes]. <i>Klin Monbl Augenheilkd.</i> 2010;227(3):228.	Too few eyes included or not an observational study	Javadi MA, Mirbabaei-Ghafghazi F, Mirzade M, Yazdani S, Yaseri M. Steroid induced ocular hypertension following myopic photorefractive keratectomy. <i>J Ophthalmic Vis Res.</i> 2008;3(1):42-6.	Too few eyes included or not an observational study
Feki J, Trigui A, Chaabouni M, Ben Salah S, Bouacida B, Chechia N, et al. [Retinal detachment after Excimer laser (myopic LASIK or PRK). A retrospective multicentric study: 15 cases]. <i>J Fr Ophtalmol.</i> 2005;28(5):509-12.	Too few eyes included or not an observational study	Joesse MV, Snoek C, van Minderhout HM. Comparison of wavefront-guided photorefractive keratectomy and foldable iris-fixated phakic intraocular lens implantation for low to moderate myopia. <i>J Cataract Refract Surg.</i> 2011;37(2):370-7.	Too few eyes included or not an observational study
Fernandes M, Reddy P, Shah SG. One-year outcome of bilateral randomized prospective clinical trial comparing photorefractive keratectomy (PRK) with mitomycin C (MMC) and laser in situ keratomileusis (LASIK). <i>Br J Ophthalmol.</i> 2011;95(3):433.	Too few eyes included or not an observational study	Kamburoglu G, Ertan A. Epithelial ingrowth after femtosecond laser-assisted in situ keratomileusis. <i>Cornea.</i> 2008;27(10):1122-5.	(Mainly) femto-laser
Fernandes M, Goyal J, Shah S. Phakic intraocular collamer lens. <i>Ophthalmology.</i> 2012;119(1):201; author reply -2.	Too few eyes included or not an observational study	Karthikappallil J. Induced astigmatism after laser in situ keratomileusis. <i>J Cataract Refract Surg.</i> 2004;30(5):940-1; author reply 1.	Too few eyes included or not an observational study
Friedlaender MH. Phakic intraocular lens for myopia. <i>Ann Ophthalmol (Skokie).</i> 2006;38(1):9-11.	Too few eyes included or not an observational study	Kermani O, Schmiedt K, Oberheide U, Gerten G. Topographic- and wavefront-guided customized ablations with the NIDEK-EC5000CXII in LASIK for myopia. <i>J Refract Surg.</i> 2006;22(8):754-63.	Too few eyes included or not an observational study



Kim JH, Lim T, Lee HG, Kim JY, Kim MJ, Tchah H. Bilateral comparison of conventional epithelial laser in situ keratomileusis and lamellar epithelial debridement for moderate to high myopia. <i>Cornea</i> . 2010;29(8):853-7.	Too few eyes included or not an observational study	Mohamed TA, Hoffman RS, Fine IH, Packer M. Post-laser assisted in situ keratomileusis epithelial ingrowth and its relation to pretreatment refractive error. <i>Cornea</i> . 2011;30(5):550-2.	Follow-up <6 months
Kowal L. LASIK for hyperopia. <i>Ophthalmology</i> . 2005;112(10):1847; author reply	Too few eyes included or not an observational study	Mohammadpour M. Risk for ectasia with LASIK. <i>J Cataract Refract Surg</i> . 2008;34(2):181-2; author reply 2-3.	Too few eyes included or not an observational study
Kuo IC, Lee SM, Hwang DG. Late-onset corneal haze and myopic regression after photorefractive keratectomy (PRK). <i>Cornea</i> . 2004;23(4):350-5.	Too few eyes included or not an observational study	Mohammadpour M, Jabbarvand M. Risk factors for ectasia after LASIK. <i>J Cataract Refract Surg</i> . 2008;34(7):1056.	Too few eyes included or not an observational study
Kushner BJ. PRK and Amblyopia. <i>Ophthalmology</i> . 2006;113(6):1063-4.	Too few eyes included or not an observational study	Naeser K. Evaluating toric implants. <i>J Cataract Refract Surg</i> . 2011;37(12):2234-5; author reply 5.	Too few eyes included or not an observational study
Lawless M, Hodge C. LASIK. <i>Int Ophthalmol Clin</i> . 2013;53(1):111-28.	Too few eyes included or not an observational study	Nawa Y, Ishibashi H, Ueda T, Kawasaki K, Masuda K, Hara Y. Incidence and pattern of iron deposit after LASIK for hyperopia. <i>J Refract Surg</i> . 2004;20(6):836-8.	Unavailable
Leccisotti A, Bartolomei A, Greco G, Manetti C. Incidence of bacterial keratitis after photorefractive keratectomy [4]. <i>Journal of Refractive Surgery</i> . 2005;21(1):96.	Unavailable	Netto MV, Wilson SE. Flap lift for LASIK retreatment in eyes with myopia. <i>Ophthalmology</i> . 2004;111(7):1362-7.	Retreatment eyes only
Leffler C, Pradhan S, Nguyen N. Refraction after IOL exchange. <i>Ophthalmology</i> . 2008;115(4):754- e1; author reply 5.	Too few eyes included or not an observational study	Paciuc M. Posterior corneal surface changes after H-LASIK. <i>J Cataract Refract Surg</i> . 2006;32(10):1593-4.	Too few eyes included or not an observational study
Llovet F, Galal A, Benitez-del-Castillo JM, Ortega J, Martin C, Baviera J. One-year results of excimer laser in situ keratomileusis for hyperopia. <i>J Cataract Refract Surg</i> . 2009;35(7):1156-65.	Too few eyes included or not an observational study	Packer M, Fine IH, Hoffman RS, Piers P. Aberrations after intraocular lens implantation. <i>J Cataract Refract Surg</i> . 2006;32(2):184-5; author reply 5-6.	Too few eyes included or not an observational study
Llovet F, de Rojas V, Interlandi E, Martin C, Cobo-Soriano R, Ortega-Usobiaga J, et al. Infectious keratitis in 204 586 LASIK procedures. <i>Ophthalmology</i> . 2010;117(2):232-8 e1-4.	Follow-up <6 months	Packer M, Hoffman RS, Fine IH, Dick HB. Refractive lens exchange. <i>Int Ophthalmol Clin</i> . 2006;46(3):63-82.	Too few eyes included or not an observational study
		Parmar DN, Claoue C. Keratectasia following excimer laser photorefractive keratectomy [2]. <i>Acta Ophthalmologica</i>	Too few eyes included or not an observational study



Scandinavica. 2004;82(1):102-5.

Pelit A, Akova YA. One surgeon's experience with hydrophilic and hydrophobic intraocular lens implantation using the Monarch II injector. Canadian Journal of Ophthalmology. 2008;43(2):249.

Follow-up <6 months

Peng C, Zhao JY, Zhang JS. Aspheric multifocal intraocular lens. Ophthalmology. 2012;119(2):423- e2.

Too few eyes included or not an observational study

Prasad S. Clear lens extraction for myopia. Ophthalmology. 2004;111(6):1263.

Too few eyes included or not an observational study

Randleman JB, Lynn MJ, Banning CS, Stulting RD. Risk factors for epithelial defect formation during laser in situ keratomileusis. J Cataract Refract Surg. 2007;33(10):1738-43.

Follow-up <6 months

Randleman JB, White AJ, Jr., Lynn MJ, Hu MH, Stulting RD. Incidence, outcomes, and risk factors for retreatment after wavefront-optimized ablations with PRK and LASIK. J Refract Surg. 2009;25(3):273-6.

Too few eyes included or not an observational study

Rao SK, Shome D, Iyer GK, Fogla R, Padmanabhan P. Bilateral epithelial defects after laser in situ keratomileusis. Clinical features, management and outcome. Indian J Ophthalmol. 2005;53(1):37-42.

Too few eyes included or not an observational study

Reinstein DZ, Threlfall WB, Cook R, Cremonesi E, Sutton HF, Archer TJ, et al. Short term LASIK outcomes using the Technolas 217C excimer laser and Hansatome microkeratome in 46,708 eyes treated between 1998 and 2001. Br J Ophthalmol. 2012;96(9):1173-9.

Follow-up <6 months

Riese J, Gerding H. [Cataract development following posterior chamber phakic

Too few eyes included or not an observational study

intraocular lens implantation in eyes with high myopia]. Klin Monbl Augenheilkd. 2013;230(4):342-3.

Sanders DR, Doney K, Poco M. United States Food and Drug Administration clinical trial of the Implantable Collamer Lens (ICL) for moderate to high myopia: three-year follow-up. Ophthalmology. 2004;111(9):1683-92.

Already included in OTHAS 2009

Scerrati E, Gualdi M, Gualdi L. Correction of myopia and myopic astigmatism with customized ablation using the Nidek NAVEX system. J Refract Surg. 2004;20(5 Suppl):S676-7.

Unavailable

Schein OD, Katz J. Comparing contact lens and refractive surgery risks. Arch Ophthalmol. 2007;125(6):853-4; author reply 4-5.

Too few eyes included or not an observational study

Sekundo W. Phototherapeutic keratectomy (PTK). [German] Phototherapeutische Keratektomie (PTK). Der Ophthalmologe : Zeitschrift der Deutschen Ophthalmologischen Gesellschaft. 2006;103(7):561-2.

Too few eyes included or not an observational study

Simpson MJ. Refractive outcomes for toric intraocular lenses. Arch Ophthalmol. 2012;130(7):945-6; author reply 8-9.

Too few eyes included or not an observational study

Spadea L, Mosca L. Topographically guided LASIK. Ophthalmology. 2006;113(7):1251 e1-2.

Too few eyes included or not an observational study

Spraul CW, Muller A, Lang GK. [Vision loss after LASIK]. Ophthalmologe. 2004;101(7):726-8.

Too few eyes included or not an observational study

Sun L, Liu G, Ren Y, Li J, Hao J, Liu X, et al. Efficacy and safety of LASIK in 10,052 eyes

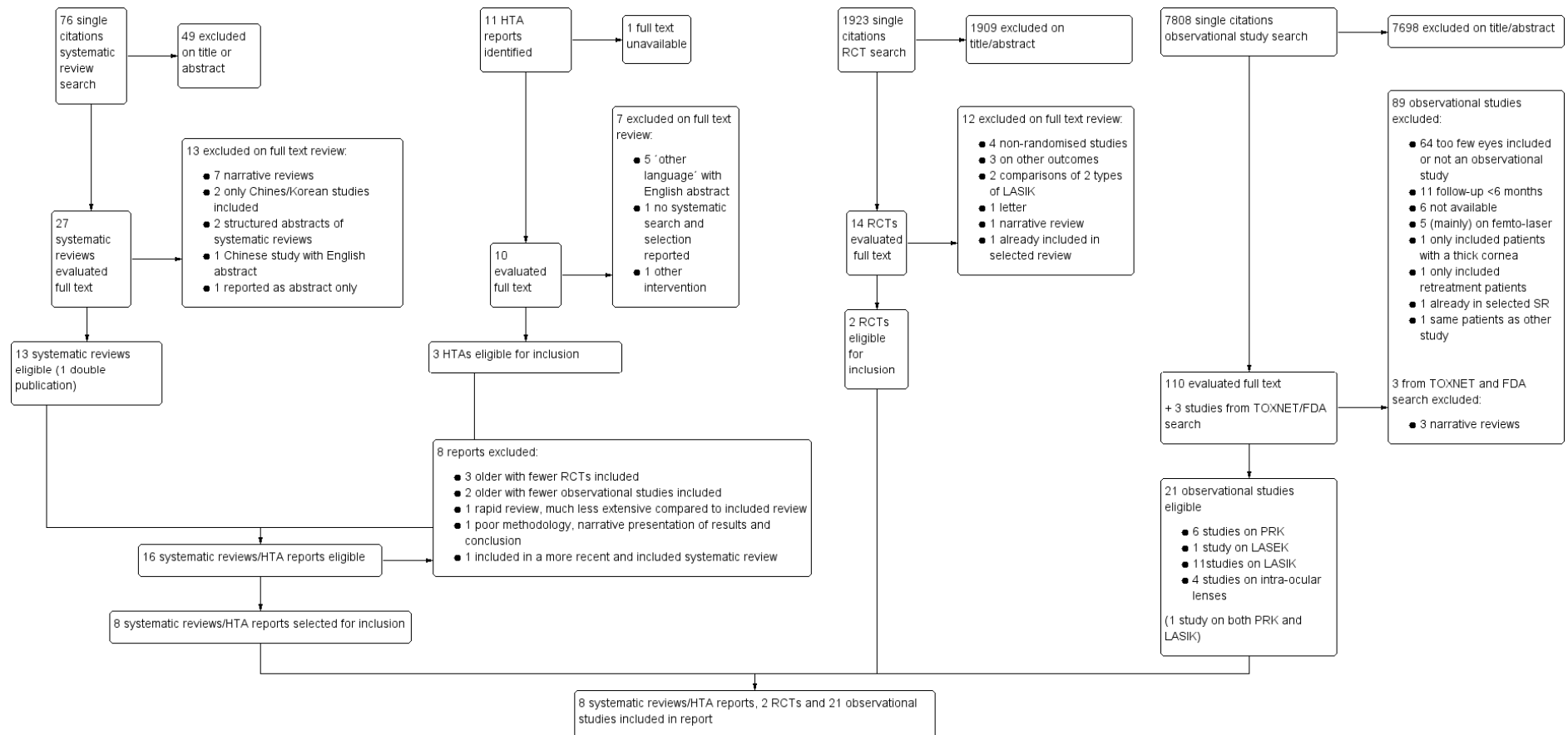
Unavailable



of 5081 myopic Chinese patients. J Refract Surg. 2005;21(5 Suppl):S633-5.	
Sutton G, Hodge C. Accuracy and precision of LASIK flap thickness using the Intralase femtosecond laser in 1000 consecutive cases. J Refract Surg. 2008;24(8):802-6.	(Mainly) femto-laser
Tanna M, Schallhorn SC, Hettinger KA. Femtosecond laser versus mechanical microkeratome: a retrospective comparison of visual outcomes at 3 months. J Refract Surg. 2009;25(7 Suppl):S668-71.	Follow-up <6 months
Thomas R, Nirmalan P. LASIK versus PRK. Ophthalmology. 2007;114(11):2099-100; author reply 100.	Too few eyes included or not an observational study
Titcomb L. Laser surgery for refractive errors. Pharmaceutical Journal. 2006;276(7398):511-4.	Unavailable
Torii H, Negishi K, Dogru M, Saiki M, Yamaguchi T, Watanabe K, et al. Inflammation after phakic implants. Ophthalmology. 2011;118(12):2518 e1-2.	Too few eyes included or not an observational study
Watson SL, Bunce C, Allan BD. Improved safety in contemporary LASIK. Ophthalmology. 2005;112(8):1375-80.	Follow-up <6 months
Wilson SE. Use of lasers for vision correction of nearsightedness and farsightedness. New England Journal of Medicine. 2004;351(5):470-5+517.	Too few eyes included or not an observational study
Wykoff CC, Pineda R, 2nd. Myopic laser in situ keratomileusis in eyes with thick corneas. J Cataract Refract Surg. 2006;32(5):900-1.	Eyes with thick cornea only
Yuen LH, Chan WK, Koh J, Mehta JS, Tan DT. A 10-year prospective audit of LASIK outcomes for myopia in 37,932 eyes at a single institution in Asia. Ophthalmology. 2010;117(6):1236-44 e1.	Follow-up <6 months
Zhang ZY, Zhang XR. Prevention of ectasia for laser in situ keratomileusis with simultaneous corneal crosslinking. J Cataract Refract Surg. 2012;38(12):2206-7; author reply 7-8.	Too few eyes included or not an observational study



## APPENDIX 3. SEARCH AND SELECTION FLOW DIAGRAM





## APPENDIX 4. LIST OF ELIGIBLE SYSTEMATIC REVIEWS, PER TYPE OF COMPARISON OR INTERVENTION

Comparison (SRs on RCTs)	SRs selected: reason	SRs excluded: reason
Refractive surgery vs. spectacles or contact lenses		
• For myopia with or without astigmatism	• None, none identified	• None, none identified
• For hyperopia with or without astigmatism	• None, none identified	• None, none identified
PRK vs. LASEK		
• For myopia with or without astigmatism	<ul style="list-style-type: none"> <li>• Zhao 2010<sup>28</sup>: recent SR, 11 RCTs included</li> <li>• NICE 2005<sup>21</sup>: older SR, 10 RCTs included of which 6 also included by Zhao 2010, 4 abstracts not reported by Zhao included here; no meta-analysis of efficacy data: safety data used for those items not reported on by Zhao</li> </ul>	• Cui 2008 <sup>11</sup> : older SR, 7 RCTs included (all included in Zhao 2010)
• For hyperopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SR identified	• None, none identified
PRK vs. LASIK		
• For myopia with or without astigmatism	• Shortt 2013 <sup>27</sup> : recent SR, 13 RCTs included	<ul style="list-style-type: none"> <li>• Yang 2003<sup>13</sup>: older SR, 5 RCTs included (three of which included by Shortt 2013; two of which excluded by Shortt 2013 because (a) no randomization was used; and (b) data were duplicate of another, included RCT)</li> <li>• DAHTA 2003<sup>12</sup>: older SR, 6 RCTs included (all included in Shortt 2013)</li> <li>• NICE 2005<sup>21</sup>: older SR, 2 RCTs included (all included in Shortt 2013)</li> </ul>
• For hyperopia with or without astigmatism	• Settas 2012 <sup>25</sup> : recent SR, 0 RCTs identified	• NICE 2005 <sup>21</sup> : older SR, 0 RCTs included
LASEK vs. LASIK		
• For myopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SRs identified	• None, none identified
• For hyperopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SRs identified	• None, none identified
Intraocular lenses vs. laser refractive surgery		
• For myopia with or without astigmatism	• Barsam 2012 <sup>7, 23</sup> : recent SR, 3 RCTs identified	• NICE 2008 <sup>16</sup> : overview based on a rapid review,



Comparison (SRs on RCTs)	SRs selected: reason	SRs excluded: reason
		much less extensive than Barsam 2012; 2 RCTs included (all included in Barsam 2012)
		• Othas 2009 <sup>22</sup> : only 1 RCT included (also included in Barsam 2012)
• For hyperopia with or without astigmatism	• OTHAS 2009 <sup>22</sup> : 0 RCTs included	• None, none identified
<b>Intervention (SRs on observational studies, for visual acuity and safety data only)</b>		
<b>PRK</b>		
• For myopia with or without astigmatism	• NICE 2005 <sup>21</sup> : most recent SR, 36 studies included	• DAHTA 2003 <sup>12</sup> : older SR, 20 studies included
• For hyperopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SRs identified	• None, none identified
<b>LASEK</b>		
• For myopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SRs identified	• None, none identified
• For hyperopia with or without astigmatism	• NICE 2005 <sup>21</sup> : no other relevant SRs identified	• None, none identified
<b>LASIK</b>		
• For myopia with or without astigmatism	<ul style="list-style-type: none"> <li>• NICE 2005 <sup>21</sup>: with quality appraisal, 33 studies included; inclusion criteria: either <math>\geq 300</math> eyes for prospective series or <math>\geq 500</math> eyes for retrospective series</li> <li>• Schallhorn 2008 <sup>26</sup>: no quality appraisal, 16 studies included on visual acuity or safety; all include less than 300 eyes</li> </ul>	<ul style="list-style-type: none"> <li>• DAHTA 2003 <sup>12</sup>: older SR, 7 studies included</li> <li>• Lamparter 2005 <sup>14, 15</sup>: no quality appraisal, 30 studies included on safety</li> </ul>
• For hyperopia with or without astigmatism	• NICE 2005 <sup>21</sup> : good methodology, with quality appraisal and summary estimates (e.g. median)	• Varley 2005 <sup>17</sup> : poor methodology, no quality appraisal, no summary estimates, narrative conclusions
<b>Intraocular lenses</b>		
• For myopia with or without astigmatism	<ul style="list-style-type: none"> <li>• Othas 2009 <sup>22</sup></li> <li>• Huang 2009 <sup>24</sup></li> </ul>	<ul style="list-style-type: none"> <li>• NICE 2008 <sup>16</sup>: overview based on a rapid review, much less extensive than OTHAS 2009</li> <li>• Chen 2008 <sup>18</sup>: included in OTHAS 2009</li> </ul>
• For hyperopia with or without astigmatism	• Othas 2009 <sup>22</sup>	<ul style="list-style-type: none"> <li>• NICE 2008 <sup>16</sup>: overview based on a rapid review, much less extensive than OTHAS 2009</li> <li>• Chen 2008 <sup>18</sup>: included in OTHAS 2009</li> </ul>

Abbreviations: RCT: randomized controlled trial; SR: systematic review





## APPENDIX 5. SELECTION STRATEGY OF NEWER RCTS

Comparison	Subgroup of patients	Include RCTs published from
PRK vs. LASEK	Myopia	July 2008
	Hyperopia	December 2004
PRK vs. LASIK	Myopia	November 2012
	Hyperopia	February 2012
LASEK vs. LASIK	Myopia	December 2004
	Hyperopia	December 2004
Intraocular lenses vs. laser refractive surgery	Myopia	November 2011
	Hyperopia	January 2009



## APPENDIX 6. QUALITY APPRAISAL OF INCLUDED STUDIES

Table 22 – Quality appraisal of the selected systematic reviews with the AMSTAR checklist

	Barsam 2012 <sup>7, 23</sup>	Huang 2009 <sup>24</sup>	NICE 2005 <sup>21</sup>	OTHAS 2009 <sup>22</sup>	Settas 2012 <sup>25</sup> #	Schallhorn 2008 <sup>26</sup>	Shortt 2013 <sup>27</sup>	Zhao 2010 <sup>28</sup>
Was an 'a priori' design provided?	Y	N	N	N	Y	N	Y	N
Was there duplicate study selection and data extraction?	Y	N	N	N	Y	N	Y	Y
Was a comprehensive literature search performed?	Y	Y	Y	Y	Y	Y	Y	Y
Was the status of publication (i.e. grey literature) NOT used as an inclusion criterion?	Y	?	Y	N	?	?	?	Y
Was a list of studies (included and excluded) provided?	Y	N	N	N	Y	N	Y	N
Were the characteristics of the included studies provided?	Y	N	Y	Y	NA	N	Y	Y
Was the scientific quality of the included studies assessed and documented?	Y	Y	Y	Y	NA	N	Y	Y
Was the scientific quality of the included studies used appropriately in formulating conclusions?	Y	N	Y	N	NA	N	Y	N
Were the methods used to combine the findings of studies appropriate?	Y	NA	Y	NA	NA	NA	Y	Y
Was the likelihood of publication bias assessed?	N	N	N	N	NA	N	N	N
Was the conflict of interest stated?	N	N	Y	Y	Y	N	N	N

Abbreviations: N: no; NA: not applicable; Y: Yes; ?: unclear

#: this review did not select any RCTs and therefore some of the AMSTAR questions were not applicable



Table 23 – Risk of bias of selected randomized controlled trials

Bias Albarran-Diego 2012	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Computer randomization
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants & personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	Unclear if all patients were accounted for, no randomization schedule provided
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Other bias	Low risk	No other sources of bias identified

Bias Gamaly 2007	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Randomization schedule generated by a biostatistician
Allocation concealment (selection bias)	Unclear risk	Unclear if biostatistician was blinded to allocation
Blinding of participants & personnel (performance bias)	Unclear risk	Patients were blinded, but unclear if personnel was blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias)	High risk	Unclear how many patients were actually randomized (no schedule provided); 75% follow-up available after 6 months
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Other bias	Low risk	No other sources of bias identified



Table 24 – Quality appraisal of the 21 selected observational studies with the McHarm (part 1)

	Abdallat 2011 <sup>29</sup>	Al- Mezaine 2009 <sup>30</sup>	Arevalo 2012 <sup>31</sup>	Bamashmus 2010 <sup>32</sup>	Clare 2011 <sup>33</sup>	Ghoreishi 2009 <sup>34</sup>	Jian 2012 <sup>35</sup>	Kulkarni 2013 <sup>36</sup>	Leccisotti 2007 <sup>37</sup>	Lee 2005 <sup>38</sup>	Lee 2006 <sup>39</sup>	Lee 2011 <sup>40</sup>
1. Were the harms PRE-DEFINED using standardized or precise definitions?	N	N	N	N	N	N	N	N	Y	N	N	N
2. Were SERIOUS events precisely defined?	N	N	N	N	N	N	N	N	N	N	N	N
3. Were SEVERE events precisely defined?	N	N	N	N	N	N	N	N	N	N	N	N
4. Were the number of DEATHS in each study group specified OR were the reason(s) for not specifying them given?	N	N	N	N	N	N	N	N	N	N	N	N
5. Was the mode of harms collection specified as ACTIVE?	U	U	N	N	Y	Y	N	Y	N	Y	U	N
6. Was the mode of harms collection specified as PASSIVE?	U	U	U	N	N	N	Y	N	Y	N	U	Y
7. Did the study specify WHO collected the harms?	N	N	N	N	Y	N	N	N	N	N	N	N
8. Did the study specify the TRAINING or BACKGROUND of who ascertained the harms?	N	N	N	N	Y	N	N	N	N	N	N	N
9. Did the study specify the TIMING and FREQUENCY of collection of the harms?	Y	N	Y	N	Y	Y	N	Y	N	N	N	N
10. Did the author(s) use STANDARD scale(s) or	N	N	N	N	N	N	N	Y	N	N	N	N


**checklist(s) for harms  
collection? \$**
**11. Did the authors specify if  
the harms reported  
encompass ALL the events  
collected or a selected  
SAMPLE? #**

Y N N N N Y N N N N N N

**12. Was the NUMBER of  
participants that withdrew or  
were lost to follow-up  
specified for each study  
group?**

Y N Y N N N N Y N Y N N

**13. Was the TOTAL NUMBER  
of participants affected by  
harms specified for each  
study arm?**

Y Y Y Y Y N Y N Y N Y Y

**14. Did the author(s) specify  
the NUMBER for each TYPE  
of harmful event for each  
study group?**

Y Y Y Y Y Y Y Y Y Y Y Y

**15. Did the author(s) specify  
the type of analyses  
undertaken for harms data?**

Na Y N Na Y N Y Y Na N N Na

Abbreviations: N: no; Na: not applicable; Y: yes; U: unsure

\$ If BCVA loss of  $\geq 2$  lines was the only harm reported this question was assessed as: 'Y'

# If authors specified all events collected this question was assessed as: 'Y', if events were a selected sample this question was assessed as: 'N'



Table 25 – Quality appraisal of the 21 selected observational studies with the McHarm (part 2)

	Qin 2007 <sup>41</sup>	Ruiz- Moreno 2006 <sup>42</sup>	Ruiz- Moreno 2006 <sup>43</sup>	Sanders 2006 <sup>44</sup>	Sanders 2008 <sup>45</sup>	Schraepen 2005 <sup>46</sup>	Sia 2012 <sup>47</sup>	Spadea 2012 <sup>48</sup>	Wroblewski 2006 <sup>49</sup>
1. Were the harms PRE-DEFINED using standardized or precise definitions?	N	N	N	N	Y	Y	N	N	N
2. Were SERIOUS events precisely defined?	N	N	N	N	N	N	N	N	N
3. Were SEVERE events precisely defined?	N	N	N	N	N	N	N	N	N
4. Were the number of DEATHS in each study group specified OR were the reason(s) for not specifying them given?	N	N	N	N	N	N	N	N	N
5. Was the mode of harms collection specified as ACTIVE?	N	Y	Y	N	Y	Y	Y	N	N
6. Was the mode of harms collection specified as PASSIVE?	Y	N	N	Y	N	N	N	U	Y
7. Did the study specify WHO collected the harms?	N	N	N	N	N	N	N	N	N
8. Did the study specify the TRAINING or BACKGROUND of who ascertained the harms?	N	N	N	N	N	N	N	N	N
9. Did the study specify the TIMING and FREQUENCY of collection of the harms?	Y	Y	Y	Y	N	Y	Y	N	Y
10. Did the author(s) use STANDARD scale(s) or checklist(s) for harms collection? \$	N	N	N	Y	Y	Y	N	N	N
11. Did the authors specify if the harms reported encompass ALL the events collected or a selected SAMPLE? #	N	N	N	Y	N	Y	Y	N	N
12. Was the NUMBER of participants that withdrew or were lost to follow-up specified for each study group?	N	Y	Y	Y	Y	N	Y	Y	N
13. Was the TOTAL NUMBER of participants affected by harms specified for each study arm?	Y	Y	Y	N	Y	N	N	Y	Y



14. Did the author(s) specify the NUMBER for each TYPE of harmful event for each study group?	Y	Y	Y	Y	Y	Y	N	Y	Y
15. Did the author(s) specify the type of analyses undertaken for harms data?	Na	Y	Y	Y	Y	Na	Y	N	Na

Abbreviations: N: no; Na: not applicable; Y: yes; U: unsure  
\$ If BCVA loss of  $\geq 2$  lines was the only harm reported this question was assessed as: 'Y'  
# If authors specified all events collected this question was assessed as: 'Y', if events were a selected sample this question was assessed as: 'N'

## APPENDIX 7. EVIDENCE TABLES: SEE SUPPLEMENT





## APPENDIX 8. ECONOMIC CONSIDERATIONS

### Appendix 8.1. Economic literature review

#### Appendix 8.1.1. Search strategy

	2011-23
<b>Project name</b>	HTA Refractive Eye Surgery
<b>Structured search question(s)</b>	
<b>P (atient)</b>	Patients suffering from refractive errors (i.e. patients with myopia, hyperopia and/or astigmatism)
<b>I (ntervention)</b>	Most common surgical methods in refractive eye surgery: <ol style="list-style-type: none"><li>1. Laser treatments:<ul style="list-style-type: none"><li>• photorefractive keratectomy (PRK)</li><li>• laser-assisted sub-epithelial keratomileusis (LASEK)</li><li>• laser in situ keratomileusis (LASIK)</li></ul></li><li>2. Intraocular (contact) lenses</li></ol>
<b>C (omparison)</b>	Either the most common surgical methods in refractive eye surgery mentioned above, or eyeglasses or contact lenses
<b>Design</b>	Economic evaluation
<b>Results</b>	9
<b>Date</b>	18-02-2013; 20-02-2013; 07-03-2013
<b>Database</b>	<b>HTA Database NHS Centre for Reviews &amp; Dissemination</b>
<b>Search strategy</b>	'surgery' AND 'refractive' 'surgery' AND 'refractive' limited for HTA 'eye' AND 'surgery' (intraocular) AND (lens) Lasik Lasek



<b>Results</b>	6
<b>Date</b>	20-02-2013
<b>Database</b>	<b>KCE Google custom search engine</b> ( <a href="http://kce.docressources.info/opac/index.php?lvl=notice_display&amp;id=2566">http://kce.docressources.info/opac/index.php?lvl=notice_display&amp;id=2566</a> )
<b>Search strategy</b>	"eye" AND "surgery" "eye" AND "surgery"+ HTA 'eye' AND 'surgery' "intraocular" AND "lens" "Lasik" "Lasek" "refractive" AND "error" "Intra" AND "ocular" AND "lens"
<b>Results</b>	8
<b>Database</b>	<b>Custom search engine HTAi</b> ( <a href="http://vortal.htai.org/?q=search_websites">http://vortal.htai.org/?q=search_websites</a> )
<b>Date</b>	20-02-2013
<b>Search Strategy</b>	"eye" AND "surgery" "eye" AND "surgery"+ HTA "intraocular" AND "lens" "Lasik" "Lasek" "refractive" AND "error" "Intra" AND "ocular" AND "lens"
<b>Results</b>	118
<b>Date</b>	19/03/2013
<b>Database</b>	<b>Embase</b>



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**Search Strategy**

Refractive AND 'surgery'/exp AND [embase]/lim AND [2000-2013]/py  
OR ('cornea'/exp AND 'epithelium'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (cornea\* AND \$epitheli\* AND [embase]/lim AND [2000-2013]/py)  
OR ('cornea'/exp AND 'epithelium'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (cornea\* AND \$epitheli\* AND [embase]/lim AND [2000-2013]/py) AND [embase]/lim AND [2000-2013]/py)  
OR (cornea\* AND surger\* AND [embase]/lim AND [2000-2013]/py)  
OR ('cornea'/exp AND 'surgery'/exp  
OR (cornea\* AND surger\* AND [embase]/lim AND [2000-2013]/py) AND [embase]/lim AND [2000-2013]/py)  
OR ('cornea'/exp AND 'surgery'/exp  
OR (cornea\* AND surger\* AND [embase]/lim AND [2000-2013]/py)  
AND  
laser\* AND [embase]/lim AND [2000-2013]/py)  
OR ('keratectomy'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (photorefractive AND 'keratectomy'/exp AND [embase]/lim AND [2000-2013]/py)  
OR ('laser'/exp AND epithelial AND 'keratomileusis'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (keratectom\* AND [embase]/lim AND [2000-2013]/py)  
OR ('keratomileusis'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (las?k AND [embase]/lim AND [2000-2013]/py)  
  
OR (prk AND [embase]/lim AND [2000-2013]/py)  
OR (laser\* AND \$epithel\* AND surg\$ AND [embase]/lim AND [2000-2013]/py) OR (laser\* AND refractive AND surg\* AND [embase]/lim AND [2000-2013]/py)  
OR (excimer AND laser\* AND [embase]/lim AND [2000-2013]/py)  
OR ('lens'/exp AND 'implant'/exp AND [embase]/lim AND [2000-2013]/py)  
OR ('lens'/exp AND 'implantation'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (lens\* OR iol\* AND [embase]/lim AND [2000-2013]/py)  
AND  
(refraction AND 'error'/exp AND [embase]/lim AND [2000-2013]/py  
OR (refracti\* AND [embase]/lim AND [2000-2013]/py)  
OR (error\* OR disorder\* AND [embase]/lim AND [2000-2013]/py)  
OR (refracti\* AND (error\* OR disorder\*) AND [embase]/lim AND [2000-2013]/py)

---



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OR (ametrop\$ AND [embase]/lim AND [2000-2013]/py)  
OR (ametrop\* AND [embase]/lim AND [2000-2013]/py)  
OR ('myopia'/exp OR high AND 'myopia'/exp OR degenerative AND 'myopia'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (myop\* AND [embase]/lim AND [2000-2013]/py)  
OR (shortsight\* AND [embase]/lim AND [2000-2013]/py)  
OR (nearsight\* OR longsight\* OR farsight\* AND [embase]/lim AND [2000-2013]/py)  
OR ('hypermetropia'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (hyperop\* OR hypermetrop\* AND [embase]/lim AND [2000-2013]/py)  
OR ('astigmatism'/exp AND [embase]/lim AND [2000-2013]/py)  
OR (astigmat\* AND [embase]/lim AND [2000-2013]/py))  
AND  
cost\*:ab,ti  
AND  
([article]/lim OR [article in press]/lim)  
AND [humans]/lim AND [2000-2013]/py AND [embase]/lim  
AND  
[ophthalmology]/lim AND [medline]/lim AND [2002-2013]/py

---

<b>Results</b>	68
<b>Database</b>	<b>Medline Ovid</b>
<b>Date</b>	19/03/2013

<b>Search Strategy</b>	1 exp Economics/ 2 cost\$.ab,ot,ti. 3 pric\$.ab,ot,ti. 4 Econom\$.ab,ot,ti 5 Epithelium, Corneal/ 6 (corneal and epithelium).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier 7 laser\$.mp.
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8 Corneal Surgery, Laser/  
9 (laser and corneal and surger\$).mp.  
10 (laser and keratectom\$).mp.  
11 photokeratectom\$.mp.  
12 Keratectomy, Subepithelial, Laser-Assisted/  
13 lasek.mp.  
14 (subepithelial and keratomileusis and laser\$).mp.  
15 (subepithelial and photorefractive and keratectomy\$).mp.  
16 (laser\$ and photorefractive and keratectomy\$).mp.  
17 Keratomileusis, Laser In Situ/  
18 lasik.mp.  
19 (laser\$ and keratomileusis).mp.  
20 Photorefractive Keratectomy/  
21 prk.mp.  
22 (photorefractive and Keratectom\$).mp.  
23 Lens Implantation, Intraocular/  
24 (implantation and intraocular and lens\$).mp.  
25 (excimer and laser).mp.  
26 (refractive and error\$).mp.  
27 ametropia.mp.  
28(refractive and disorder\$).mp.  
29 Myopia/  
30 myopia\$.mp.  
31 nearsightedness\$.mp.  
32 Hyperopia/  
33 hyperopia\$.mp.  
34 hypermetropia\$.mp  
35 farsightedness\$.mp.  
36 Astigmatism/

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37 astigmat \$.mp.  
38 Editorial.pt.  
39 historical article.pt.  
40 38 OR 39 OR 40  
41 animals/  
42 human/  
43 42 not (42 and 43)  
44 1 OR 2 OR 3 OR 4  
45 5 OR 6  
46 7 AND 45  
47 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19  
OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 46  
48 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR  
37  
49 47 AND 48  
50 44 AND 49  
51 50 NOT 40  
52 51 NOT 43

---

**Results**

8

**Database****ECONLIT****Date**

02-04-2013

**Search Strategy**

"eye" AND "surgery"  
"intraocular" AND "lens"  
"Lasik"  
"Lasek"  
"refractive"  
"Intra" AND "ocular" AND "lens"

---

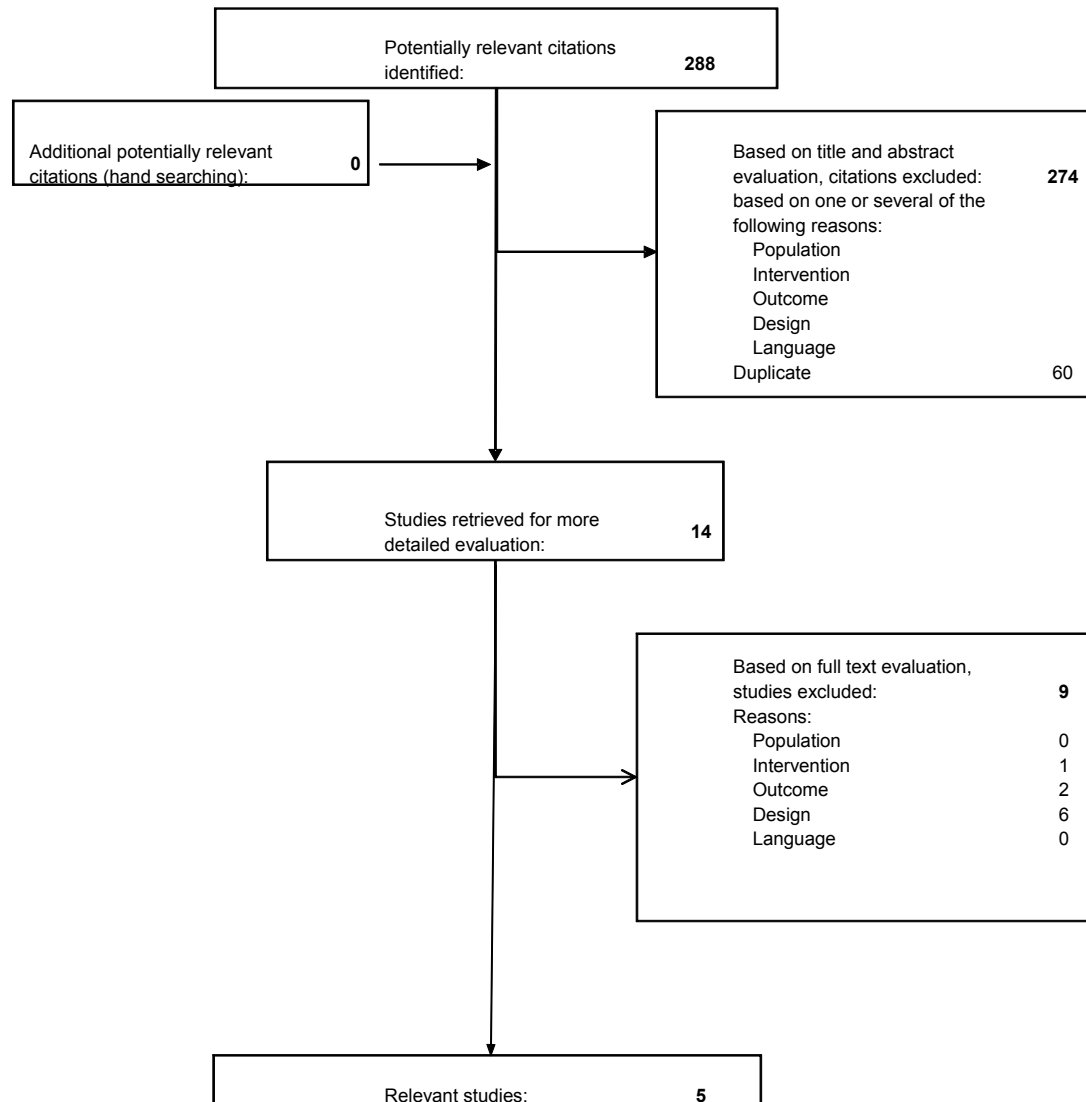


### *Appendix 8.2.1. Study selection criteria and selection process*

The inclusion and exclusion criteria in terms of patients, interventions and comparators were identical to those for the review of clinical effectiveness. In terms of design and outcomes, both partial and full economic evaluations were included.

All retrieved references were assessed against the selection criteria in a two-step procedure: initial assessment of the title, abstract and keywords, followed by a full-text assessment of the selected references. Study selection was done by 2 reviewers (ND and CO).







### Appendix 8.2.2. Details of the economic studies

**Table 26 – Cost items, cost results and scenario/sensitivity analyses per study**

Study	Cost items	Cost results	Scenario and sensitivity analysis
Lamparter (2007) and Lamparter (2005)	<ul style="list-style-type: none"> <li>• Primary LASIK intervention</li> <li>• Complications               <ul style="list-style-type: none"> <li>○ central islands, overcorrection, undercorrection, regression</li> <li>○ haze</li> <li>○ buttonhole, free flap, thin/thick/irregular flap, incomplete/irregular cut, decentration</li> <li>○ foreign body in the interface</li> <li>○ dry eyes</li> <li>○ inflammation</li> <li>○ striae</li> <li>○ erosion corneae</li> <li>○ keratectasia</li> <li>○ retinal detachment</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Surgery cost: € 2 426 per eye</li> <li>• Weighted complication cost: € 648.30               <ul style="list-style-type: none"> <li>○ Incidence: based on meta analysis</li> <li>○ Cost: based on worst case therapy need</li> </ul> </li> </ul> <p>€ 448.91 out of this cost is linked to complications needing retreatment</p>	<ul style="list-style-type: none"> <li>• Sensitivity analysis               <ul style="list-style-type: none"> <li>○ Cost variation of <math>\pm 10\%</math></li> <li>○ Within <math>\pm 0.5</math> D versus <math>\pm 1</math> D target refraction outcome</li> </ul> </li> </ul>
CEMT (2004)	<ul style="list-style-type: none"> <li>• LASIK/PRK surgery</li> <li>• Eyeglasses</li> <li>• Direct cost for municipality and patient (e.g. transport)</li> <li>• Indirect costs (productivity losses)</li> </ul>		Scenarios for <ul style="list-style-type: none"> <li>• Degrees of myopia</li> <li>• Technique (LASIK, PRK)</li> <li>• Patient age (27 or 35 years)</li> <li>• Cost source (Aarhus Universitetshospital or DRG data)</li> </ul>
Krummenauer (2003 <sup>c</sup> )	<ul style="list-style-type: none"> <li>• LASIK surgery</li> <li>• Eyeglasses</li> </ul>	<ul style="list-style-type: none"> <li>• Median cost surgery               <ul style="list-style-type: none"> <li>○ € 3 000 (Mainz)</li> </ul> </li> </ul>	2 scenarios for <ul style="list-style-type: none"> <li>• Cost source (Mainz en Mannheim)</li> </ul>

<sup>c</sup> Based on the English abstract



	o € 3 910 (Mannheim)	hospital)
Berdeaux (2002)	<ul style="list-style-type: none"> <li>• LASIK surgery and hotel expenses linked to the LASIK procedure</li> <li>• glasses/contact lenses, including glasses for 5% of LASIK patients</li> <li>• cleaning products</li> <li>• visits to ophthalmologist/ optometrist/ optical center</li> <li>• transportation cost to the LASIK and optical centers</li> <li>• keratitis for contact lens wearers (incidence of 1 in 1000)</li> <li>• time spent to care for LASIK/eyeglasses/lenses</li> </ul>	<ul style="list-style-type: none"> <li>• Various results presented for different scenarios</li> </ul>
		Scenarios for <ul style="list-style-type: none"> <li>• Time horizon (10, 20, 30 years)</li> <li>• Discount rate (0; 2.5; 5.0; 7.5; 10.0%)</li> <li>• Eyeglass change delay (36, 48; 60; 72 months)</li> <li>• Probability of needing glasses after LASIK (0;5;10;15;20%)</li> </ul>

**Table 27 – Sources used for outcomes, patient characteristics and outcome results per study**

Study	Sources used for outcomes and patient characteristics	Outcome results
Lamparter (2007)	<ul style="list-style-type: none"> <li>• Complications: 30 studies (1994-2004)</li> <li>• Pre-operative refraction: between -1 D and -14 D</li> </ul>	Complication incidence rates: <ul style="list-style-type: none"> <li>• Most frequent “light sensation” (meta incidence of 46%)</li> <li>• Clinical retreatment (meta incidence 24%) [more detailed results in the report]</li> </ul>
Lamparter (2005)	<ul style="list-style-type: none"> <li>• LASIK outcome predictability :15 studies (1994-2004)</li> <li>• Complications: 30 studies</li> <li>• Mean pre-operative refraction -6.31 D</li> </ul>	<ul style="list-style-type: none"> <li>• Mean-refractive gain: 5.93 D</li> <li>• Predictability of refractive gain: 67%</li> </ul>
CEMT (2004)	<ul style="list-style-type: none"> <li>• 227 patients from Aarhus University Hospital</li> <li>• Average age: 33</li> <li>• Pre-operative refraction: &lt;6 D and &gt;6 D (2 groups)</li> </ul>	<ul style="list-style-type: none"> <li>• Being free of glasses</li> <li>• Average refractive gain               <ul style="list-style-type: none"> <li>o &lt;6 D : 4 D gain</li> <li>o &gt;6 D: ±8 D gain</li> </ul> </li> </ul>



Krummenauer (2003)	<ul style="list-style-type: none"> <li>• 178 patients (45 (Mainz), 133 (Mannheim))</li> <li>• Pre-operative mean D</li> <li>• Left eye: -5.1 (Mainz), -4.1 (Mannheim)</li> <li>• Right eye: -5,0 (Mainz) ; -3,9 (Mannheim)</li> </ul>	Refractive gain: 5.6 D (Mainz) , 4.2 D (Mannheim) No longer need of eyeglasses after surgery: 71% (Mainz); 73% (Mannheim) Patients undergoing a LASIK re-treatment: 31% (Mainz); 13% (Mannheim)
Berdeaux (2002)	n.a.	Non-monetary outcomes not considered

**Table 28 – Cost-outcome results**

Study	Cost-outcome results
Lamparter (2007) <sup>d</sup>	No cost-outcome results
Lamparter (2005)	<u>Direct cost</u> <ul style="list-style-type: none"> <li>• € 409 per D (sensitivity range € 351- € 473)</li> <li>• € 36 per gained percentage point in predictability (€ 27-56)</li> </ul> <u>Total costs</u> (include complication costs) <ul style="list-style-type: none"> <li>• € 519 per D (sensitivity range € 445-600)</li> <li>• € 45.89 per gained percentage point in predictability (€ 33.79-71.51/%)</li> </ul>
CEMT (2004)	Additional cost <u>per year free of glasses</u> attributable to LASIK: <ul style="list-style-type: none"> <li>• &lt;6 D               <ul style="list-style-type: none"> <li>○ At 27 years: - (LASIK is cheaper)</li> <li>○ At 35 years: kr 860 (approx. € 115 <sup>e</sup>)</li> </ul> </li> <li>• &gt;6 D               <ul style="list-style-type: none"> <li>○ At 27 years: /</li> <li>○ At 35 years: kr 1 538 (approx. € 205)</li> </ul> </li> </ul> Additional cost <u>per year per gained refractive unit</u> attributable to LASIK: <ul style="list-style-type: none"> <li>• &lt;6 D               <ul style="list-style-type: none"> <li>○ At 27 years: - (LASIK is cheaper)</li> <li>○ At 35 years: kr 239 per D (approx. € 32)</li> </ul> </li> </ul>

<sup>d</sup> Based on the English abstract

<sup>e</sup> Exchange rate of April 2012



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	<ul style="list-style-type: none"><li>• &gt;6 D<ul style="list-style-type: none"><li>○ At 27 years: - (LASIK is cheaper)</li><li>○ At 35 years: kr 275 per D (approx. € 37)</li></ul></li></ul> <p>(For results on PRK we refer to the report)</p>
Krummenauer (2003 <sup>f</sup> )	Incremental cost of <ul style="list-style-type: none"><li>• € 667 per gained refractive unit (Mainz)</li><li>• € 831 per gained refractive unit (Mannheim)</li></ul>
Berdeaux (2002)	No cost-outcome results

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### Appendix 8.3. Long term cost calculation

#### Appendix 8.3.1. Analytic technique

The @Risk adds-on tool is used for probabilistic modelling and probabilistic sensitivity analyses. The cycle duration is 1 month.

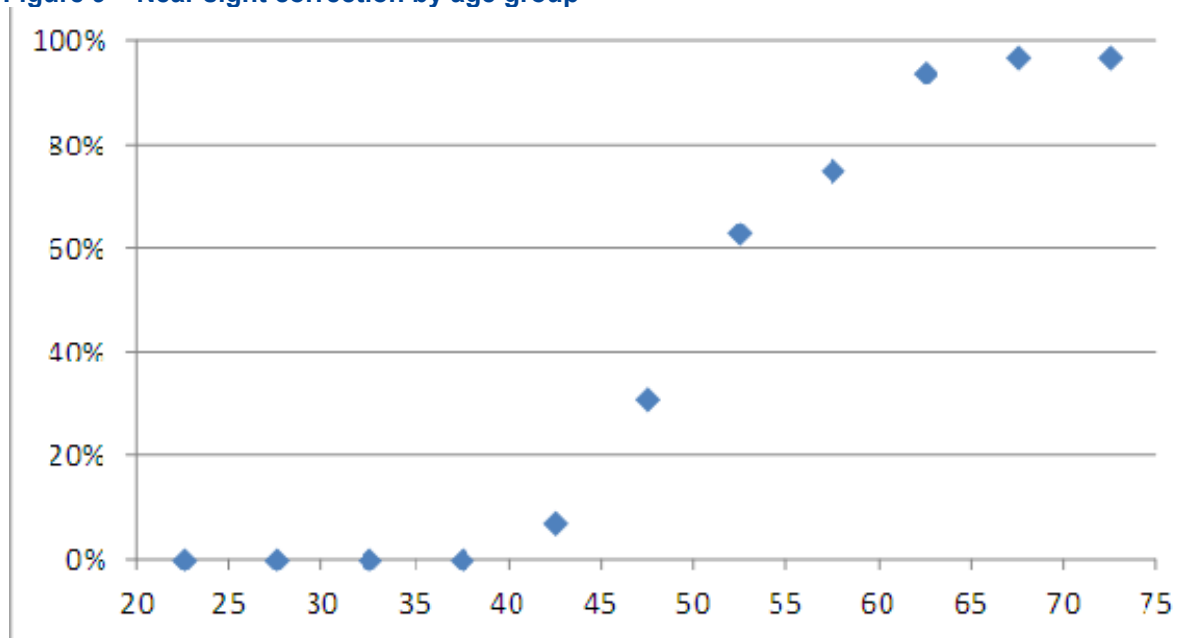
#### Appendix 8.3.2. Data on presbyopia correction

Data were retrieved from research by Jos Rozema (Department of Ophthalmology, Antwerp University Hospital-University Antwerp) in a sample of 443 persons. In the age group between 45 and 49 years, nearly a third of the people use correction for presbyopia whereas in the age group 50-54 years, nearly two thirds of the people (63%) use presbyopia correction. This data is also in line with data found in for instance Pointer 1995<sup>82</sup>.

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<sup>f</sup>

Based on the English abstract

**Figure 9 – Near sight correction by age group**

Source: based on data from Jos Rozema (Department of Ophthalmology, Antwerp University Hospital – University Antwerp)

#### **Appendix 8.3.3. Success and complication rates**

All probabilities were modelled as beta distributions, except for the complication rates. Given that the imputed costs for complications are already weighted by incidence, we modelled a 100% probability.

#### **Appendix 8.3.4. Uncertainty**

The impact of uncertainty and variability in the model's input parameters on the results was modelled probabilistically. The used distributions and parameters are mentioned above. 1 000 Latin Hypercube simulations were performed.

#### **Appendix 8.3.5. Balancing costs with outcomes**

##### **Search strategy for NEI-RQL**

Database: Journals@Ovid Full Text <August 30, 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

1 NEI-RQL.mp. [mp=ti, ab, tx, ct, sh, ot, nm, hw, kf, ps, rs, an, ui] (58)



## Appendix 8.4. Data sources for international comparison

The listed websites were consulted in February 2013.

### Appendix 8.4.1. France

<http://www.ameli.fr/assures/soins-et-remboursements/combien-serez-vous-rembourse/optique-et-audition/les-lunettes-et-les-lentilles/le-remboursement-des-lunettes.php>  
<http://www.ameli.fr/assures/soins-et-remboursements/combien-serez-vous-rembourse/optique-et-audition/les-lunettes-et-les-lentilles/le-remboursement-des-lentilles.php>  
<http://www.ameli.fr/assures/soins-et-remboursements/cmu-et-complementaires-sante/cmu-complementaire/la-prise-en-charge-de-vos-soins-a-100.php>  
[http://www.cmu.fr/fichier-utilisateur/fichiers/CIRCULAIRE\\_DSS\\_2A\\_2000\\_240%20du%2027%20avril%202000%281%29.pdf](http://www.cmu.fr/fichier-utilisateur/fichiers/CIRCULAIRE_DSS_2A_2000_240%20du%2027%20avril%202000%281%29.pdf)  
<http://www.sante-repere.fr/remboursement-chirurgie-refractive-Remboursement-optique-Remboursement-mutuelle/p/3/593/0/>  
[http://www.medicaltourisme.com/index.php?option=com\\_content&view=article&id=29&Itemid=39](http://www.medicaltourisme.com/index.php?option=com_content&view=article&id=29&Itemid=39)

### Appendix 8.4.2. Netherlands

<http://www.cvz.nl/zorgpakket/zvw-kompas/hulpmiddelen/zorg/visuele+hulpmiddelen/visuele+hulpmiddelen.html>  
<http://www.cz.nl/consument/vergoedingen/2013/hulpmiddelen/zien/bijzondere-optische-hulpmiddelen>  
<http://www.menzis.nl/web/Consumenten/Vergoeding/VergoedingenAZ/VergoedingHulpmiddelen/BrillenContactlenzenEnOoglaserbehandelinglensimplantaten.htm>  
<http://www.vgz.nl/sitecollectiondocuments/2013/d0456-vgz-vgoweb.pdf>

### Appendix 8.4.3. Germany

<http://www.brillenkosten.de/2011/02/wird-eine-brille-von-der-krankenkasse-bezahlt/>  
<http://www.refraktives-zentrum.de/fragen-antworten-verfahren.html#c241>  
<http://www.geldsparen.de/sparen/Gesundheit/brille-das-zahlt-die-krankenkasse-2.php>  
[https://www.aok-gesundheitspartner.de/imperia/md/gpp/bund/hilfsmittel/festbeträge/himi\\_estbeträge\\_sehhilfen\\_2008.pdf](https://www.aok-gesundheitspartner.de/imperia/md/gpp/bund/hilfsmittel/festbeträge/himi_estbeträge_sehhilfen_2008.pdf)  
<http://www.ncbi.nlm.nih.gov/pubmed/11130164>  
[http://www.aok-gesundheitspartner.de/imperia/md/gpp/bund/hilfsmittel/festbeträge/himi\\_estbeträge\\_sehhilfen\\_2008.pdf](http://www.aok-gesundheitspartner.de/imperia/md/gpp/bund/hilfsmittel/festbeträge/himi_estbeträge_sehhilfen_2008.pdf)  
<http://www.hdi.de/de/privatkunden/versicherungen/kranken/voll/index.jsp>  
<http://www.ruv.de/de/privatkunden/krankenversicherung/krankenzusatzversicherung/augen-vorsorgeuntersuchung/index.jsp>

### Appendix 8.4.4. UK (England)

<http://www.nhs.uk/chq/Pages/891.aspx?CategoryID=68&SubCategoryID=157>  
<http://www.hsf.co.uk/health-cash-plans/#faq-2>  
<http://www.optometry.co.uk/voucher-values>

### Appendix 8.4.5. Denmark

<http://www.kennedy.dk/default.aspx?id=94>  
<http://www.sygeforsikring.dk/Default.aspx?ID=326>  
<http://www.sygeforsikring.dk/Default.aspx?ID=328>  
<http://www.olce.dk/behandling/tilskud-til-laserbehandling-af-øjne.aspx>  
<http://www.ft.dk/samling/20121/almde/suu/spm/316/svar/1040510/1231737/index.htm>  
e-mail contact with Julie Bay (Københavns Universitet: Det Sundhedsvidenskabelige Fakultet)

### Appendix 8.4.6. Belgium

<http://www.inami.fgov.be/insurer/fr/rate/pdf/last/others/Opti20130101fr.pdf>





## APPENDIX 9. INTERVIEWS ON PATIENTS' PERCEPTIONS

### Appendix 9.1. ESOMAR social grades system

The table below was used to determine the social economic class during recruitment.

**Table 29 – Overview of ESOMAR social grades system to determine social economic status used during recruitment**

Education level of the main income earner (terminal level)				
	University	Higher non university education	Higher secondary education or higher technical	Lower secondary education or lower technical or primary school
Occupation of the main income earner	Profession (physician, lawyer, dentist,...) or higher management, senior official, commanding officer, responsible for at least 5 people	A	A	B
	Middle management, executive official, officer	B	B	B
	Self-employed, trader, craftsman with 5 employees or less	B	B	C1
	Other non-manual labor (office workers, minor official, soldier, education, representative)	B	C1	C1
	Agriculturalist	C1	C1	C2
	Worker	C2	C2	D
	Unemployed, job-seeker	C2	D	D
	Pensioner (calculate based on last occupation and education level)			



## Appendix 9.2. Intended and achieved sample of patients

**Table 30 – Intended sample for patients**

Had considered refractive eye surgery, but had not undergone															Had either planned refractive eye surgery or underwent refractive surgery in the past 4 years																	
Age	20 - 30 years old					31 - 40 years old					more than 40 years old					20 - 30 years old					31 - 40 years old					more than 40 years old						
SEC	A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D				
Language	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N
Number of interviews	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

**Table 31 – Achieved sample for patients**

Considered refractive eye surgery, but did not undergo it															Either planned refractive eye surgery or underwent refractive surgery in the past 4 years																				
Age	20 - 30 years old					31 - 40 years old					more than 40 years old					20 - 30 years old					31 - 40 years old					more than 40 years old									
SEC	A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D			A, B	C1	C2, D							
Language	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N	F	N					
Number of interviews	0	1	1	1	0	0	1	1	1	1	1	2	1	1	1	1	1	1	2	1	1	1	0	3	1	2	1	0	1	1	2	2	0	0	1



Table 32 – Description of the interviewees

## Dutch speaking

Respondent	LEEFTIJD	Geslacht	Socio-economic status	Corrigerende oogoperatie: gepland of ondergaan	Corrigerende oogoperatie overwogen, maar niet ondergaan
1	43 jaar	Vrouw	C1		myopie - oogoperatie overwogen, maar niet ondergaan
2	27 jaar	Vrouw	B	myopie - oogoperatie ondergaan -2 jaar geleden	
3	39 jaar	Man	B		myopie + astigmatisme
4	79 jaar	Vrouw	D	myopie + presbyopie + cataract - oogoperatie ondergaan -2 jaar geleden	
5	64 jaar	Vrouw	D		myopie + presbyopie - oogoperatie overwogen, maar niet ondergaan
6	45 jaar	Man	B		myopie - oogoperatie overwogen, maar niet ondergaan
7	39 jaar	Man	C1		Myopie + astigmatisme aan 1 oog - oogoperatie overwogen, maar niet ondergaan
8	31 jaar	Vrouw	C1	myopie - oogoperatie ondergaan -2 jaar geleden	
9	51 jaar	Vrouw	B	hyperopie - oogoperatie ondergaan -2 jaar geleden	
10	35 jaar	Vrouw	B	myopie + astigmatisme oogoperatie gepland	
11	23 jaar	Man	C1	myopie - oogoperatie ondergaan -2 jaar geleden	
12	41 jaar	Man	C1		myopie + hyperopie - oogoperatie overwogen, maar niet ondergaan
13	39 jaar	Vrouw	C1		hyperopie - oogoperatie overwogen, maar niet ondergaan
14	23 jaar	Vrouw	C2		myopie - oogoperatie overwogen, maar niet ondergaan
15	22 jaar	Man	A		myopie - oogoperatie overwogen, maar niet ondergaan
16	35 jaar	Vrouw	D	myopie - oogoperatie ondergaan -2 jaar geleden	
17	67 jaar	Vrouw	B	hyperopie - oogoperatie ondergaan -2 jaar geleden	
18	29 jaar	Vrouw	B	hyperopie - oogoperatie gepland	



## French speaking

Respondent	AGE	Gender	Socio-economic status	Subi ou prévu une opération des yeux (moins de 2 ans)	Considéré une opération, mais pas subi
1	44	homme	C2		myopie - considéré une opération, mais pas subi
2	32	femme	B	myopie + astigmatisme - subi une opération des yeux	
3	26	femme	C1	myopie + prévu une opération des yeux	
4	34	femme	B	myopie + astigmatisme + subi une opération des yeux	
5	54	homme	B	myopie + subi une opération des yeux	
6	45	femme	B		myopie - considéré une opération, mais pas subi
7	35	homme	C1		hypermétropie + astigmatisme - considéré une opération, mais pas subi
8	35	homme	C2		myopie - considéré une opération, mais pas subi
9	66	homme	C1		myopie + astigmatisme - considéré une opération, mais pas subi
10	27	homme	C2	myopie + prévu une opération	
11	54	femme	C1	myopie + hypermétropie + presbytie + prévu une opération des yeux	
12	34	homme	B		myopie + astigmatisme - considéré une opération, mais pas subi
13	34	femme	B	myopie + prévu une opération des yeux	
14	35	femme	B	myopie - subi une opération des yeux	
15	34	femme	C1	myopie + subi une opération des yeux	
16	27	femme	C1		myopie - considéré une opération, mais pas subi
17	38	homme	C1	myopie + astigmatisme + subi une opération des yeux	
18	43	femme	C1	myopie + astigmatisme + prévu une opération des yeux	



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