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Phakic Intraocular Lenses for the Treatment of Refractive Errors

An Evidence-Based Analysis

Presented to the Ontario Health Technology Advisory Committee in June, 2009

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About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practising medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

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List of Abbreviations

BSCVA	Best spectacle corrected visual acuity
CLE	Clear lens extraction
EI	Efficacy index
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HTA	Health technology assessment
IOL	Intraocular lens
LASIK	Laser-assisted in situ keratomileusis
LASEK	Laser-assisted sub-epithelial keratomileusis
logMAR	Logarithm of the minimum angle of resolution
MRSE	Manifest refraction spherical equivalent
Nd:YAG	Neodymium:yttrium-aluminum-garnet
pIOL	Phakic intraocular lens
PMMA	Polymethyl methacrylate
PRK	Photorefractive keratectomy
RCT	Randomized controlled trial
SI	Safety index
UCVA	Uncorrected visual acuity

Executive Summary

Objective

The objective of this analysis is to review the effectiveness, safety, and cost-effectiveness of phakic intraocular lenses (pIOLs) for the treatment of myopia, hyperopia, and astigmatism.

Clinical Need: Condition and Target Population

Refractive Errors

Refractive errors occur when the eye cannot focus light properly. In myopia (near- or short-sightedness), distant objects appear blurry because the axis of the eye is too long or the cornea is too steep, so light becomes focused in front of the retina. Hyperopia (far sightedness) occurs when light is focused behind the retina causing nearby objects to appear blurry. In astigmatism, blurred or distorted vision occurs when light is focused at two points rather than one due to an irregularly shaped cornea or lens.

Refractive errors are common worldwide, but high refractive errors are less common. In the United States, the prevalence of high myopia (≤ −5 D) in people aged 20 to 39, 40 to 59, and 60 years and older is 7.4% (95% confidence interval [CI], 6.5% – 8.3%), 7.8% (95% CI, 6.4% – 8.6%), and 3.1% (95% CI, 2.2% – 3.9%), respectively. The prevalence of high hyperopia (≥ 3 D) is 1.0% (95% CI, .6% – 1.4%), 2.4% (95% CI, 1.7% – 3.0%), and 10.0% (95% CI, 9.1% – 10.9%) for the same age groupings. Finally, the prevalence of astigmatism (≥ 1 D cylinder) is 23.1% (95% CI, 21.6% – 24.5%), 27.6% (95% CI, 25.8% – 29.3%) and 50.1% (48.2% – 52.0%).

Low Vision

According to the Ontario Schedule of Benefits, low visual acuity is defined by a best spectacle corrected visual acuity (BSCVA) of 20/50 (6/15) or less in the better eye and not amenable to further medical and/or surgical treatment. Similarly, the Ontario Assistive Devices Program defines low vision as BSCVA in the better eye in the range of 20/70 or less that cannot be corrected medically, surgically, or with ordinary eyeglasses or contact lenses.

Estimates of the prevalence of low vision vary. Using the criteria of BSCVA ranging from 20/70 to 20/160, one study estimated that 35.6 per 10,000 people in Canada have low vision. The 2001 Participation and Activity Limitation Survey (PALS) found that 594,350 (2.5%) Canadians had "difficulty seeing ordinary newsprint or clearly seeing the face of someone from 4 m," and the Canadian National Institute for the Blind (CNIB) registry classified 105,000 (.35%) Canadians as visually disabled.

Phakic Intraocular Lenses (pIOL)

A phakic intraocular lens (pIOL) is a supplementary lens that is inserted into the anterior or posterior chamber of the eye to correct refractive errors (myopia, hyperopia, and astigmatism). Unlike in cataract surgery, the eye's natural crystalline lens is not removed when the pIOL is inserted, so the eye retains its accommodative ability. In Canada and the United States, iris-fixated (anterior chamber lenses that are anchored to the iris with a claw) and posterior chamber lenses are the only types of pIOLs that are licensed by Health Canada and the Food and Drug Administration, respectively.

Evidence-Based Analysis Method

Research Questions & Methodology

1. What are the effectiveness, cost-effectiveness, and safety of pIOLs for the treatment of myopia, hyperopia, and astigmatism?
2. Do certain subgroups (e.g. high myopia and low vision) benefit more from pIOLs?
3. How do pIOLs compare with alternative surgical treatment options (LASIK, PRK, and CLE)?

Using appropriate keywords, a literature search was conducted up to January 2009. Systematic reviews, meta-analyses, randomized controlled trials, and observational studies with more than 20 eyes receiving pIOLs were eligible for inclusion. The primary outcomes of interest were uncorrected visual acuity (UCVA), predictability of manifest refraction spherical equivalent (MRSE), and adverse events. The GRADE approach was used to systematically and explicitly evaluate the quality of evidence.

Summary of Findings

The search identified 1,131 citations published between January 1, 2003, and January 16, 2009. Including a health technology assessment (HTA) identified in the bibliography review, 30 studies met the inclusion criteria: two HTAs; one systematic review; 20 pre-post observational studies; and seven comparative studies (five pIOL vs. LASIK, one pIOL vs. PRK, and one pIOL vs. CLE).

Both HTAs concluded that there was good evidence of the short-term efficacy and safety of pIOLs, however, their conclusions regarding long-term safety differed. The 2006 HTA found convincing evidence of long-term safety, while the 2009 HTA found no long-term evidence about the risks of complications including cataract development, corneal damage, and retinal detachment.

The systematic review of adverse events found that cataract development (incidence rate of 9.6% of eyes) is a substantial risk following posterior chamber pIOL implantation, while chronic endothelial cell loss is a safety concern after iris-fixated pIOL implantation. Adverse event rates varied by lens type, but they were more common in eyes that received posterior chamber pIOLs.

The evidence of pIOL effectiveness is based on pre-post case series. These studies reported a variety of outcomes and different follow-up time points. It was difficult to combine the data into meaningful summary measures as many time points are based on a single study with a very small sample size. Overall, the efficacy evidence is low to very low quality based on the GRADE Working Group Criteria.

For all refractive errors (low to high), most eyes experienced a substantial increase in uncorrected visual acuity (UCVA) with more than 75% of eyes achieving UCVA of 20/40 or better at all postoperative time points. The proportion of eyes that achieved postoperative UCVA 20/20 or better varied substantially according type of lens used and the type of refractive error being corrected, ranging from about 30% of eyes that received iris-fixated lenses for myopia to more than 78% of eyes that received posterior chamber toric lenses for myopic astigmatism.

Predictability of manifest refraction spherical equivalent (MRSE) within ± 2.0 D was very high (≥ 90%) for all types of lenses and refractive error. At most time points, more than 50% of eyes achieved a MRSE within ± 0.5 D of emmetropia and at least 85% within ± 1.0 D. Predictability was lower for eyes with more severe preoperative refractive errors. The mean postoperative MRSE was less than 1.0 D in all but two studies.

Safety, defined as a loss of two or more Snellen lines of best spectacle corrected visual acuity (BSCVA), was high for all refractive errors and lens types. Losses of two or more lines of BSCVA were uncommon, occurring in fewer than 2% of eyes that had received posterior chamber pIOLs for myopia, and less than 1% of eyes that received iris-fixated lens implantation for myopia. Most eyes did not experience a clinically significant change in BSCVA (i.e. loss of one line, no change, or gain of one line), but 10% to 20% of eyes gained two or more lines of BSCVA.

The pIOL outcomes for UCVA, predictability, BSCVA, and adverse events were compared with FDA targets and safety values for refractive surgery and found to meet or exceed these targets at most follow-up time points. The results were then stratified to examine the efficacy of pIOLs for high refractive errors. There was limited data for many outcomes and time points, but overall the results were similar to those for all levels of refractive error severity.

The studies that compared pIOLs with LASIK, PRK, and CLE for patients with moderate to high myopia and myopic astigmatism showed that pIOLs performed better than these alternative surgical options for the outcomes of:

- UCVA,
- predictability and stability of MRSE,
- postoperative MRSE,
- safety (measured as clinically significant loss of BSCVA), and
- gains in BSCVA.

Correction of refractive cylinder (astigmatism) was the only outcome that favoured refractive surgery over pIOLs. This was observed for both toric and non-toric pIOLs (toric pIOLs correct for astigmatism, non-toric pIOLs do not).

Common adverse events in the LASIK groups were diffuse lamellar keratitis and striae in the corneal flap. In the pIOL groups, lens repositioning and lens opacities (both asymptomatic and visually significant cataracts) were the most commonly observed adverse events. These studies were determined to be of low to very low evidence quality based on the GRADE Working Group Criteria.

Keywords

Eye, myopia, hyperopia, astigmatism, phakic intraocular lens, LASIK, PRK, uncorrected visual acuity, best corrected visual acuity, refractive errors, clear lens extraction

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Background

Objective of Analysis

The objective of this analysis is to review the effectiveness, safety, and cost-effectiveness of phakic intraocular lenses (pIOLs) for the treatment of myopia, hyperopia, and astigmatism.

Clinical Need and Target Population

Refractive Errors

Refractive errors occur when the eye cannot focus light properly. In myopia (near- or short-sightedness), distant objects appear blurry because the axis of the eye is too long or the cornea is too steep, so light becomes focused in front of the retina. Hyperopia (far sightedness) occurs when light is focused behind the retina causing nearby objects to appear blurry. In astigmatism, blurred or distorted vision occurs when light is focused at two points rather than one due to an irregularly shaped cornea or lens. (1)

Refractive errors are common worldwide. In the United States, they account for almost 80% of the visual impairment in people aged 12 and older. (1) Vitale et al. (1) estimated the prevalence of refractive errors in the United States using the National Health and Nutrition Examination Survey (NHANES). The results from Vitale et al. (Table 1) show the prevalence of myopia, hyperopia, and astigmatism varied by age. (1)

Table 1: Prevalence of Refractive Errors in the United States

Refractive Error	Prevalence (95% CI)		
	20 – 39 years	40 – 59 years	≥ 60 years
Myopia			
≤ −0.5 D MRSE	50.2 (47.8 – 52.7)	50.1 (47.8 – 52.4)	26.5 (24.0 – 29.0)
≤ −5 D MRSE	7.4 (6.5 – 8.3)	7.8 (6.4 – 8.6)	3.1 (2.2 – 3.9)
Hyperopia			
≥ 3 D MRSE	1.0 (.6 – 1.4)	2.4 (1.7 – 3.0)	10.0 (9.1 – 10.9)
Astigmatism			
≥ 1 D cylinder	23.1 (21.6 – 24.5)	27.6 (25.8 – 29.3)	50.1 (48.2 – 52.0)

*CI refers to confidence interval; D, diopter; MRSE, manifest refraction spherical equivalent

Low Vision

A variety of definitions exist for low vision. According to the Ontario Schedule of Benefits, low visual acuity is defined by a best spectacle corrected visual acuity (BSCVA) of 20/50 (6/15) or less in the better eye and not amenable to further medical and/or surgical treatment. (2) The Ontario Assistive Devices Program defines low vision by a BSCVA in the better eye in the range of 20/70 or less that cannot be corrected medically, surgically, or with ordinary eyeglasses or contact lenses. (3) The Canadian Ophthalmology Society defines low vision (partially sighted) as vision less than 20/60 that cannot be improved through medical or surgical means. (4) The World Health Organization and the International Council of Ophthalmology define low vision (referred to as moderate visual impairment) by a BSCVA of less than 20/70 to 20/160. (5)

There are a variety of estimates of the prevalence of low vision in Canada. Using the criteria of a BSCVA between 20/70 and 20/160, Maberley et al. (6) estimated that 35.6 per 10,000 people in Canada have low vision based on a sample of patients attending a physician's office in Prince George, British Colombia. The 2001 Participation and Activity Limitation Survey (PALS) found that 594,350 (2.5%) Canadians had "difficulty seeing ordinary newsprint or clearly seeing the face of someone from 4 m," and the Canadian National Institute for the Blind (CNIB) registry classified 105,000 (.35%) Canadians as visually disabled based on a study conducted between 1996 and 2001. (6) Cataract and visual pathway disease followed by age-related macular degeneration and other retinal diseases are the most common cause of low vision. (6)

Description of phakic intraocular lenses

A pIOL is a supplementary lens that is inserted into the eye to correct refractive errors (myopia, hyperopia, and astigmatism). Unlike in cataract surgery, the eye's natural crystalline lens is not removed when the pIOL is inserted, so the eye retains its accommodative ability. (7)

Phakic IOLs may be inserted in the anterior or posterior chamber of the eye. (7) In Canada and the United States, iris-fixated (anterior chamber lenses that are anchored to the iris with a claw) and posterior chamber lenses are the only types of pIOLs that are licensed by Health Canada.

Design and Materials

Phakic lenses are designed to be permanent but can be exchanged or removed if necessary. The lenses are made of a variety of ultraviolet light absorbing materials including polymethyl methacrylate (PMMA), hydrophilic porcine collagen (< .1%), and hydroxyethyl methacrylate (HEMA). (7;8)

Phakic intraocular lenses may be spheric or toric in design. Spheric pIOLs are indicated for those with myopia or hyperopia with low astigmatism (less than 2.5 Diopters, D). Toric pIOLs are inserted at a specific angle to treat myopia or hyperopia with astigmatism (1.0 to 4.0 D). (9)

Regulatory Status

Canada

Four pIOLs are licensed by Health Canada (described in Table 2). While the Artisan and Verisyse lenses have different license numbers and distributors, they are the same lens. (10)

United States

The Food and Drug Administration (FDA) in the United States approved the Artisan/Verisyse pIOL (Ophtec, B.V.) in September 2004 for the correction of myopia (-3 to -20 D) and myopic astigmatism (astigmatism ≤ 2.5 D at the spectral plane). In December 2005, the FDA also approved the Visian ICL (Implantable Collamer Lens, Staar Surgical Company) to correct myopia (-3 to -20 D) and myopic astigmatism (astigmatism ≤ 2.5 D at the spectral plane). (11) Toric pIOLs for the treatment of astigmatism greater than 2.5 D are not licensed in the United States.

Table 2: Phakic Intraocular Lenses Licensed by Health Canada

Device Name	Device Class	Licence Number	Indication
Staar Surgical Company (Monrovia, California, United States)			
UV-Absorbing Collamer Implantable Contact Lenses	4	30347	Correction of moderate to high myopia or hyperopia
Toric ICL	4	68575	Phakic adults 21 to 45 years of age for treatment of myopia in the range of −3.0 to −20.0 D and astigmatism of 1.0 to 4.0 D
Ophtec B.V. (Groningen, the Netherlands)			
Artisan Myopia Phakic Intraocular Lens	3	65736	Reduction or elimination of axial myopia in adults with myopia requiring lenses from −5.0 to −20.0 D with less than 2.5 of astigmatism
Advanced Medical Optics, Inc. (Santa Ana, California, United States)			
Verisyse Phakic Intraocular Lens			Reduction or elimination of axial myopia in adults with myopia requiring lenses from −5.0 to −20.0 D with less than 2.5 D of astigmatism

D refers to diopter

Alternatives

There are numerous treatments options for refractive errors of which eyeglasses are the least invasive and safest, followed by external contact lenses (hard and soft). More invasive, surgical techniques are also an option including numerous refractive keratoplasty procedures (surgical techniques that alter the shape of the cornea), corneal incision procedures, thermal procedures, intrastromal corneal ring segment implantations, and intraocular refractive surgery (7;12)

Refractive keratoplasty procedures are excimer laser ablation techniques such as laser assisted in-situ keratomileusis (LASIK), photorefractive keratectomy (PRK), laser assisted sub-epithelium keratomileusis (LASEK), and epi-LASIK. There are a number of complications associated with these procedures including surgical complications and problems with wound healing, flap-related complications, loss of BSCVA, unpredictability of refractive correction, severe night glare, excessive corneal thinning, and ectasia. Many of these complications are more common in patients with high refractive errors. (7;12-16)

Less common techniques include corneal incision procedures (e.g. radial keratotomy, arcuate keratotomy, and limbal relaxing incisions), thermal techniques (e.g. noncontact Holmium laser thermokeratoplasty and conductive keratoplasty with a high-frequency electric probe), and intrastromal corneal ring segments. (12)

There are two types of intraocular refractive surgery: pIOLs and clear lens extraction (CLE). Clear lens extraction, or refractive lens exchange, is the removal and replacement of the eye's natural crystalline lens with an IOL for individuals that do not have a visually significant cataract. Disadvantages of this procedure include the loss of the eye's accommodative ability, increased risk of retinal detachment, endophthalmitis, and maculopathy. (7;12)

Evidence-Based Analysis of Effectiveness

Research Questions

- What are the effectiveness, cost-effectiveness, and safety of pIOLs for the treatment of myopia, hyperopia, and astigmatism?
- Do certain subgroups (e.g. high myopia and low vision) benefit more from pIOLs and could they be used as a basis for potentially insurable indications?
- How do pIOLs compare with alternative surgical treatment options (e.g. LASIK, PRK, and CLE)?

Literature Search

The Medical Advisory Secretariat completed a computer-aided search of electronic databases (OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, and International Agency for Health Technology Assessment/Centre for Reviews and Dissemination) to identify evidence related to pIOLs for the treatment of refractive errors published between January 1, 2003, and January 16, 2009. The search strategies are detailed in Appendix 1. Studies meeting the inclusion and exclusion criteria (listed below) were identified from the search results. Additional studies were identified from the reference lists of included studies.

Inclusion Criteria

- English language studies
- HTAs, systematic reviews, meta-analyses, randomized controlled trials (RCTs), and observational studies
- adult patients (≥18 years of age) with myopia, hyperopia, or astigmatism
- primary outcome: UCVA or predictability of refractive correction
- studies with clearly defined design, methods, population of interest and subject characteristics
- studies published from January 1, 2003 to January 16, 2009

Exclusion Criteria

- studies with fewer than 20 eyes for each refractive error type
- pIOLs that are not licensed by Health Canada
- pIOLs in combination with other surgical techniques (i.e., bioptics)
- pIOLs for presbyopia
- non-systematic reviews, letters, editorials, comments, and case reports
- grey literature and abstracts
- duplicate publications (superseded by another publication by the same investigator group with the same objective and data)
- studies with insufficient data for analysis
- animal and *in vitro* studies

Comparisons of Interest

- pIOL versus LASIK
- pIOL versus PRK
- pIOL versus CLE

Outcomes of Interest

Primary Outcomes

- uncorrected visual acuity (UCVA)
- predictability of manifest refraction spherical equivalent (MRSE)
- adverse events

Secondary Outcomes

- Efficacy Index
- MRSE
- stability of MRSE
- predictability of manifest cylinder
- stability of manifest cylinder
- change in Best spectacle corrected visual acuity (BSCVA)
- safety index
- patient satisfaction
- quality of life and vision

Methods of Analysis

Included studies were separated into two categories: pre-post observational case series evidence concerning the efficacy and safety of pIOLs and comparative case series comparing the effectiveness and safety of pIOLs with other refractive keratoplasty techniques. For the pre-post case series, results were stratified by lens type (iris-fixated or anterior chamber pIOL) and refractive error (myopia, hyperopia, and myopic astigmatism), then weighted means were calculated for each outcome. Results were also stratified by severity of myopia to examine the effectiveness of pIOLs in high myopia (myopia ≤−6 D). The results of the comparative case series were used to evaluate the effectiveness of pIOLs compared with LASIK, PRK, and CLE.

The FDA Ophthalmic Devices Panel has developed and recommended safety and effectiveness endpoints and target values for refractive surgery laser applications for investigational device exemptions. (17) These include effectiveness target values for UCVA and predictability of MRSE and safety target values for BSCVA and adverse events. The target values were originally developed for patients with low myopia (≥ −7 D) but were expanded in 1997 to include patients with high myopia (< −7 D), patients with hyperopia, and patients with myopic or hyperopic astigmatism. (18) In this analysis, the results of comparative studies and pre-post observational case series were compared with the FDA effectiveness and safety targets shown in Table 3 (where possible).

Table 3: FDA Effectiveness and Safety Targets for Laser Refractive Surgery

Effectiveness and Safety Target Values	Percentage of Eyes (%)		
	Low to moderate myopia (≥ −7 D) with or without astigmatism	High myopia (< −7 D) with or without astigmatism	Hyperopia with or without astigmatism
UCVA 20/40 or better (BSCVA 20/20 or better preoperatively)	85	75	85
Predictability of the MRSE within ± 2.00 D		90	
Predictability of the MRSE within of ± 1.00 D	75	60	75
Predictability of the MRSE within ± .50 D	50	30	50
Loss of more than 2 lines of BSCVA	<5	<5	<5
Adverse events (per type of event)	<1	<1	<1

*BSCVA refers to best spectacle corrected visual acuity; D, diopters; UCVA, uncorrected visual acuity

Results of Evidence-Based Analysis

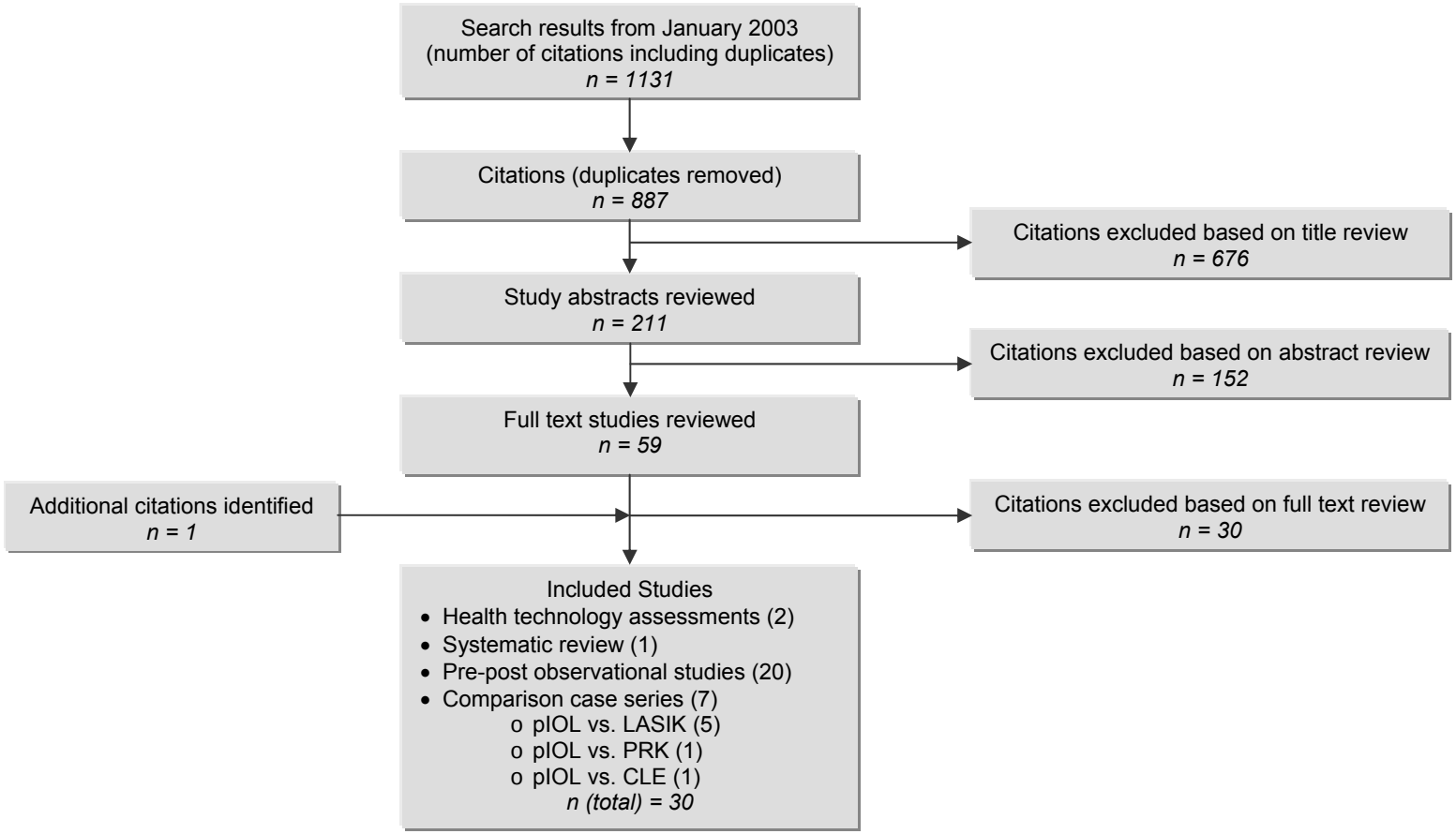
The database search yielded 1,131 citations published between January 1, 2003, and January 16, 2009. One reviewer, who was not blinded to author, institution, or journal of publication, evaluated the eligibility of the identified citations. Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded or included in the analysis.

Two hundred forty-four of the identified citations were duplicates (the same article identified by more than 1 database) and excluded from further review. Twenty-nine studies (1 HTA, 1 systematic review, 20 pre-post observational studies, and 7 comparative studies) met the inclusion criteria. An additional citation (a HTA) was identified from other sources. Table 4 lists the level of evidence and number of studies identified. Characteristics of the included studies were extracted and are described in Tables 5 and 29.

Table 4: Quality of Evidence of Included Studies

Study Design†	Level of Evidence	Number of Eligible Studies: pIOL Efficacy	Number of Eligible Studies: pIOL vs. Refractive Surgery
Large RCT, systematic review of RCTs	1	0	0
Large RCT unpublished but reported to an international scientific meeting	1(g)*	0	0
Small RCT	2	0	1
Small RCT unpublished but reported to an international scientific meeting	2(g)	0	0
Non-RCT with contemporaneous controls	3a	0	0
Non-RCT with historical controls	3b	0	0
Non-RCT presented at international conference	3(g)	0	0
Surveillance (database or register)	4a	0	0
Case series (multisite)	4b	4	4
Case series (single site)	4c	16	2
Retrospective review, modeling	4d	0	0
Case series presented at international conference	4(g)	0	0

* g refers to grey literature; pIOL, phakic intraocular lens; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (19) An additional designation “g” was added for preliminary reports of studies that have been presented at international scientific meetings.



Reasons for exclusion
Abstract review: aphakic eyes (32); not licensed by Health Canada (10); excluded study type (non-systematic review, 9); not relevant (28); N < 20 eyes (21); wrong primary outcome (45); not myopia / hyperopia / astigmatism (5); RCT comparing pIOL brands (1); duplicate (1)

Full text review: excluded study type (non-systematic review, 2; comment, 1); duplicate (1); aphakic eyes (14); unknown N (1); not relevant (3); comparison of brands (2); N < 20 eyes (2); unable to obtain article (1); not myopia/hyperopia/astigmatism (1); non-English language (2)

CLE refers to clear lens extraction; LASIK, laser-assisted in situ keratomileusis; PRK, photorefractive keratectomy

Figure 1: Citation Flow Chart

Summary of Existing Evidence

HTAs

Two international HTAs were identified in the literature. The first was a 2009 recommendation issued by the National Institute for Health and Clinical Excellent (NICE) Interventional Procedures Programme on the use of pIOLs for the correction of refractive errors based on a 'rapid review' of the technology. (20) Literature published up to May 14, 2008 was searched for efficacy and safety data yielding one meta-analysis (safety), two RCTs (pIOL efficacy compared with LASIK and PRK), two non-randomized controlled trials (efficacy), three case series (efficacy and safety), and three case reports (safety) for inclusion in the review. The analysis consisted of descriptive summaries of the studies without summary estimates for efficacy or safety outcomes. NICE concluded that there is good evidence of short-term efficacy and safety based on a large number of patients, but there is no data on the long-term risks of cataracts, corneal damage, or retinal detachment. (21) The second HTA identified was an updated review of implantable contact lenses for the correction of myopia published by the Australian and New Zealand Horizon Scanning Network in 2006. (22) The review included one RCT (pIOL efficacy compared with LASIK) and six case series reports evaluating safety and efficacy of pIOLs. The analysis consisted of descriptive summaries of the studies without summary estimates for efficacy or safety outcomes. They concluded that there is "convincing" long-term data for the safety of pIOLs. (22)

Both HTAs contained several important limitations. Firstly, both were based on rapid or horizon scanning literature reviews (as opposed to systematic reviews) and neither provided a comprehensive examination of the efficacy or safety of pIOLs. Secondly, there were no clear descriptions of the inclusion/exclusion criteria used, making it impossible to determine why the included studies were chosen while other identified studies were not. Finally, both HTAs contained only short qualitative descriptions of the included studies, while none of the data has been synthesized to create summary estimates of effect.

Systematic Reviews

A single systematic review by Chen et al. examined adverse events, particularly cataract development, after pIOL implantation. (23) The review included English language studies identified through Medline (National Library of Medicine, Bethesda, USA) and a bibliography search of materials published between 1966 and December 2006. Studies reporting clinical data or complications after implantation of anterior chamber, iris-fixated, and posterior chamber pIOLs were included in the review. Since there are no anterior chamber pIOLs licensed by Health Canada, results in Chen et al. related to these lenses were not included in the summary of the results in this report.(23) Similarly, a variety of the iris-fixated and posterior chamber lenses included in the systematic review are not licensed by Health Canada. Where possible, results are reported for only those lenses licensed by Health Canada.

Iris-Fixated Lenses

Chen et al. (23) included 50 studies with 2,781 eyes of at least 1,729 patients that received iris-fixated pIOLs, including 2,391 eyes that received lenses licensed by Health Canada. This was comprised of 2,075 Artisan/Verisyse IOL for myopia including the Worst myopic claw lens and the Artisan toric IOL for myopia, and 316 Artisan/Verisyse IOL for hyperopia including the Artisan toric IOL for hyperopia.[1] (23) Figure 2A (on page 20) shows the combined incidence of complications (number of complications divided by total number of pIOLs) for the included studies, including the complications associated with iris-fixated lenses not licensed by Health Canada. The most common complication was glare/halos, which was reported for 244 eyes (8.8%). Ten other adverse events, including cataracts and uveitis, had incidence rates greater than 1%, the FDA safety target for adverse events (Figure 2A, Table 16). (17;18) Ninety-one eyes required additional operations due to complications other than cataract surgery. (23)

[1] The other iris-fixated lenses included in Chen et al. (23) were the first generation Worst-Fechner biconcave iris-claw IOL (318 eyes) and the Artiflex IOL (72 eyes), which are not licensed by Health Canada.

Cataracts were observed in 41 eyes comprising 20 new onset cataracts, 11 pre-existing progressive cataracts, and 10 pre-existing nonprogressive cataracts. Sixteen eyes (10 new onset and six pre-existing progressive cataracts) required pIOL explantation and cataract surgery. The mean time for development of new onset cataracts after pIOL implantation was 37.65 months. (23)

The overall incidence of cataracts (new onset and pre-existing progressive cataracts only) was 1.11%. The incidence of cataracts in eyes that received the Artisan/Verisyse pIOL was 1.1% for myopic eyes and 0.3% for hyperopic eyes. Of the new onset and pre-existing progressive cataracts, 24 occurred in patients that received the Artisan/Verisyse lenses. Nuclear sclerotic cataracts were the most common type of cataract (10/24) followed by cortical opacities (8/24) and posterior subcapsular cataracts (3/24). Three cataracts were of unknown type. The new onset nuclear sclerotic cataracts, however, were not attributed to the pIOL surgery because they occurred so long after occurred pIOL implantation. (23)

Endothelial cell loss due to contact between the pIOL and the cornea and/or chronic subclinical inflammation is another potential safety concern for iris-fixated pIOLs and suggests the need for regular, annual monitoring after pIOL insertion. (23)

Posterior Chamber Lenses

Chen et al. (23) included 49 studies of 2,396 eyes from at least 1,210 patients that received posterior chamber pIOLs. Of these eyes, 1,933 received lenses that are licensed by Health Canada (the Implantable Collamer Lens, ICL, STAAR Surgical Company); however, not all eyes received the current V4 model (589 eyes received an unspecified model and 467 received the V3 or earlier models).[2] (23)

Figure 2B shows the combined incidence of complications for the included studies (including the posterior chamber lenses not licensed by Health Canada). The most common complication was pigment deposits on the pIOL, as reported in 260 eyes (10.85%). New onset or pre-existing progressive cataracts occurred in 230 eyes (9.60%). Glare and halos occurred in 142 eyes (5.93%). The incidence rates of five other adverse events including corneal edema and increased intraocular pressure were greater than 1%, the FDA safety target for adverse events (Figure 2B, Table 16). Additional operations due to complications other than cataract surgery were required for 157 eyes. (23)

Cataracts were observed in 262 eyes comprising 223 new onset cataracts, seven pre-existing progressive cataracts, and 32 pre-existing nonprogressive cataracts. Explantation of the pIOL and cataract surgery was required for 76 eyes with new onset cataracts and 6 eyes with pre-existing progressive cataracts. (23) The mean time for development of new onset cataracts after ICL pIOL implantation was 16.67 months (range, 1 – 44 months). (23)

The overall incidence of cataracts (new onset and pre-existing progressive) in eyes that received posterior chamber pIOLs was 9.60%. The incidence in the ICL group was 8.48% for myopic eyes and 11.05% for hyperopic eyes. Of the new onset and pre-existing progressive cataracts, 164 occurred in patients that received the ICL lens. Anterior subcapsular cataracts[3] were the most common type of cataract observed (144/164), followed by nuclear sclerotic cataracts (6) and cortical opacities (3). Eleven cataracts were of unknown type. (23) Most of the anterior subcapsular cataracts were nonprogressive or slowly progressive, and 31.2% required surgery. (23)

[2] The other posterior chamber lenses included in Chen et al. (23) were the Russian design plate silicone IOL (Fyodorov), the Chiron-Adatomed IOL, and the PRK.

[3] The 144 anterior subcapsular cataracts included 4 eyes with both anterior subcapsular cataracts and cortical opacities, 3 eyes with both anterior subcapsular cataracts and nuclear sclerosis cataracts, and 1 eye with both anterior subcapsular cataracts and posterior subcapsular cataracts. (23)

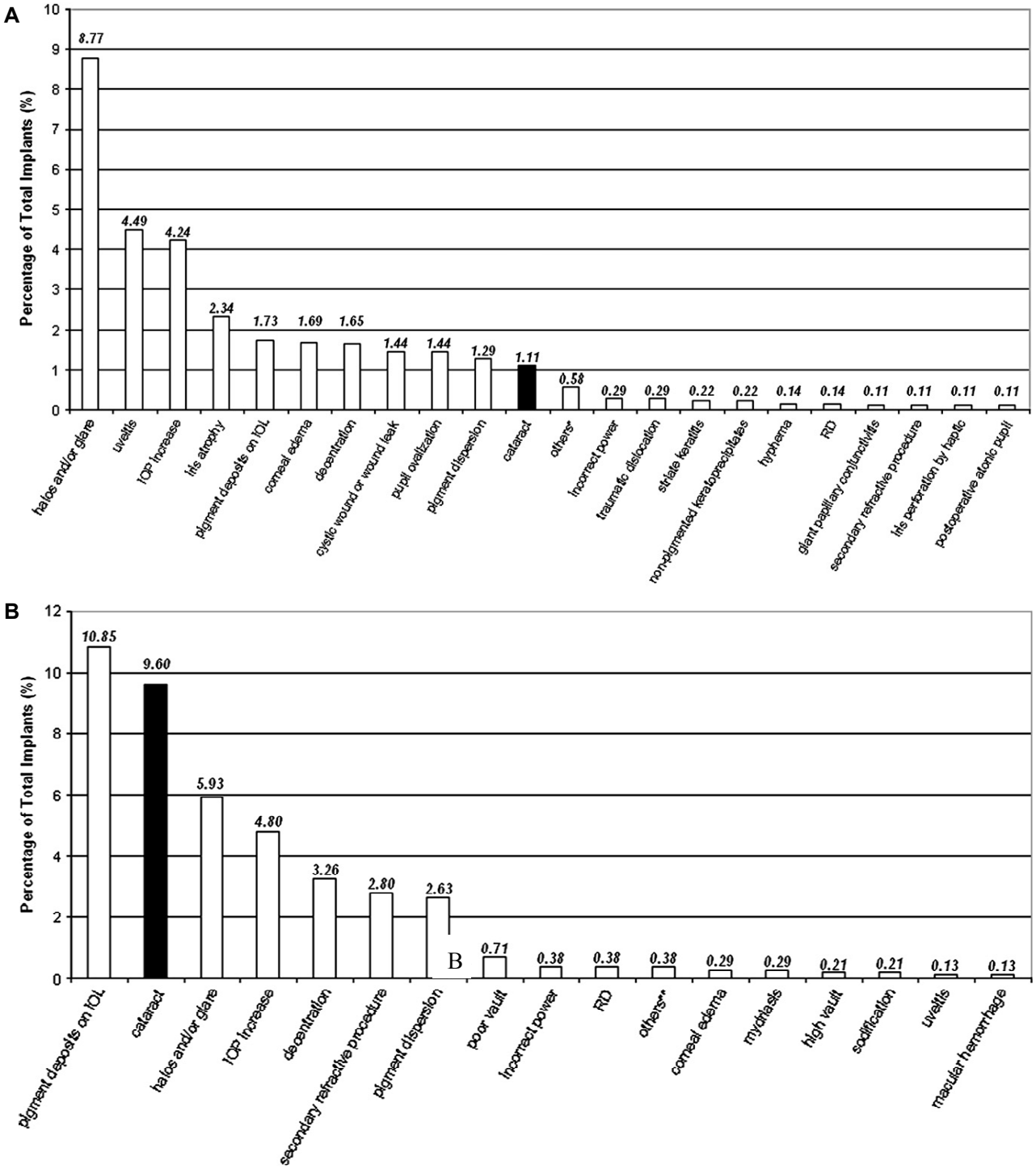


Figure 2: (A) Complications following 2,781 iris-fixated pIOL implantations
(B) Complications following 2,396 posterior chamber pIOL implantations*

IOP refers to intraocular pressure; RD, retinal detachment

Cataract formation was most likely to occur after posterior chamber pIOL surgery. *Includes 7 eyes with IOL replacement (reason unclear), 2 with pIOL removal due to inability to observe endothelium, 2 with diplopia, 1 pIOL removal due to frequent eye rubbing, 1 with wound infection, 1 with a damaged haptic, 1 with iris prolapse, and 1 with retinitis centralis serosa. **Includes 2 eyes with IOL replacement (reason not clear), 1 with iris prolapse, 1 with pupil ovalization, 1 with pupillary entrapment of IOL, 1 with a broken lens, 1 with removal due to aberrant ciliary body anatomy, 1 with progressive dry macular degeneration, and 1 with retinal hole.

Reprinted from Meta-analysis of cataract development after phakic intraocular lens surgery, 34/7, Chen L-J, Chang Y-J, Kuo JC, Rajagopal R, Azar DT, 1181-1200, 2008, with permission from Elsevier.

Risk Factors for Cataract Development

Chen et al. (23) identified numerous risk factors for cataract development including age at time of implantation, high refractive errors, ocular trauma, inflammation (iridocyclitis), pre-existing opacities, inadequate lens vaulting, incompatible lens material, long follow-up duration, excessive postoperative steroid use, and pilocarpine use. The systematic review also found that the risk of cataract development is dependent on the location of the pIOL in the patient's eye. Patients who received posterior chamber pIOLs were more likely to develop cataracts than patients who received iris-fixated pIOLs. This is thought to be because the posterior chamber lens is located closer to the crystalline lens where it is more likely to cause a pressure effect or metabolic imbalance of the lens. (23) Furthermore, different generations or models of a particular pIOL exhibit different rates of cataract development due design differences, particularly those related to adequate vaulting between the pIOL and the natural lens. (23)

While late-onset (≥ 1 year) cataracts are usually attributed to pIOL contact with the crystalline lens and/or repeated microtrauma resulting from IOL movement, surgical trauma (e.g. inadvertent lens touch or repositioning of an inverted pIOL, etc.) during pIOL implantation is the primary cause of new onset cataract development. In the systematic review, 14 of the 17 eyes that developed a cataract within 1 week of pIOL implantation had a history of intraoperative trauma. (23) In addition, several of the included studies observed a steep surgical learning curve, suggesting that surgeon experience may be important for reducing complication rates. (23)

MAS Systematic Review

Efficacy Studies: Low to High Refractive Errors

Twenty[4] pre-post observational case series reporting efficacy and safety data for pIOLs were identified in the literature (summarized in Table 5). Only 19 of the 20 identified studies were included in this analysis. Guell et al. (27) was excluded because 36%[5] (117/315) of eyes received additional refractive surgeries (LASIK, PRK, conductive keratoplasty, or arcuate keratotomy) after pIOL implantation to enhance refractive correction and the refractive results after the additional surgery were included in the reported visual outcomes thereby biasing the results (study details can be found in Appendix 2).

In this section, the results are reported by outcome for each lens type and refractive error. When possible, data were combined to create summary estimates using weighted means (based on the sample size of the case series). It was not, however, always possible to combine data because studies reported a variety of outcomes and not all relevant outcomes were consistently reported in all studies. In addition, many studies reported results at different follow-up time points. For the outcomes or time points when it was not possible to combine the data, the resulting data values were often based on a study with a very small sample size, so these results must be interpreted with caution as they may be less accurate.

Uncorrected Visual Acuity

In the pIOL literature, UCVA is the main criterion for efficacy. (28) The proportion of patients who achieved UCVA of 20/20 or better and 20/40 or better were extracted from each study and used to calculate weighted means (Table 6).

Iris-fixated lenses for myopia

The UCVA results at 5 years were substantially higher than those from other time points. As these results are based on a single study with a small sample size (19 eyes), they must be interpreted with caution. Over the first 3 years, 20% to 34% of eyes achieved an UCVA of 20/20 or better. About 74% to 87% of eyes achieved an UCVA 20/40 or better over 10 years of follow-up after implantation.

Iris-fixated lenses for hyperopia

Only one study with a small number of eyes (22 eyes) reported UCVA results, so these results may be less accurate. (29) About 23% of eyes achieved 20/20 or better and 91% achieved 20/40 or better.

Posterior chamber lenses for myopia

Ninety-two to 94% of eyes achieved an UCVA of 20/40 or better during the first year of follow-up; however, over the next 2 years, this decreased to about 80% of eyes. About 56% of eyes achieved an UCVA of 20/20 or better during the first 2 years of follow-up, which decreased to 41% at 3 years.

Posterior chamber toric lenses for astigmatism

Uncorrected visual acuity results were only available for the first year of follow-up. About 80% of eyes achieved an UCVA of 20/20 or better and 95% achieved 20/40 or better.

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[4] Two of the posterior chamber lens studies (24;25) and two iris-fixated lens studies (13;26) reported results for the same trials/patient populations. These studies were not excluded as duplicates as they report different time points or outcomes. However, results for any outcomes that were reported in 2 or more of these studies were based only on the study that provides the most complete results.

[5] 36% includes only the myopic and hyperopic eyes. The eyes with astigmatism were excluded from this report because they received a lens that is not licensed by Health Canada.

Table 5: Characteristics of Included Pre-Post Efficacy Studies

Author, Year	Study Design	Refractive Error	Country	No. of Sites	No. of Eyes (No. Patients)	Follow-Up Duration (months)
Posterior Chamber Lenses						
Alfonso et al., 2008† (30)	P. case series	myopia	Spain	1 site	25 (16)‡	12
Chang et al., 2007 (31)	P. case series	myopia	Hong Kong	1 site	61 (40)‡	24 (mean, 13.67 ± 8.51 SD, range, 1–32)
ITM, 2004; ITM 2003 (24;25)§	P. case series	myopia	USA	14 sites	526 (294)	36
Lackner et al., 2003 (32)	P. case series	myopia‖	Austria	1 site	65 (40)‡	mean, 21.9 ± 15.94
Shen et al., 2003 (33)	P. case series	myopia	China	1 site	39 (20)	48 (mean, 25.35 ± 12.13 ; range, 6–48)
Sanders et al., 2007 (9)	P. case series	myopic astigmatism (toric lenses)	USA	7 sites	210 (124)	12
Gimbel et al., 2005 (34)	P. case series	myopic astigmatism (toric lenses)	Canada	1 site	58 (32)‡	6
Pesando et al., 2007 (15)	P. case series	hyperopia	Italy	1 site	59 (34)	120 (mean, 46; range, 6–120)
Iris-Fixated Lenses						
Guell et al., 2008 (27)	R. case series	myopia, hyperopia¶	Spain	1 site	315 (173)¶	60 (mean, 48.6; range, 3–60)
Stulting et al., 2008 (26)	P. case series	myopia	USA	22 sites	1179 (684)#	36
Silva et al., 2008 (13)**	P. case series	myopia	USA	1 site	26 (15)‡	60 (mean, 22.4)
Chung et al., 2007 (35)	P. case series	myopia	Korea	1 site	25 (15)	3
Moshirfar et al., 2007 (16)	R. case series	myopia	USA	1 site	85 (56)	24
Tahzib et al., 2007 (36)	R. case series	myopia	The Netherlands	1 site	89 (49) ††	120
Senthil et al., 2006 (37)	R. case series	myopia	India	1 site	60 (36)	24
Asano-Kato et al., 2005 (38)	P. case series	myopia	Japan	1 site	44 (33)	24 (mean, 12.4)
Benedetti et al., 2005 (28)	P. case series	myopia	Italy	1 site	93 (80)	24
Lifshitz et al., 2004 (14)	R. case series	myopia	Israel	1 site	31 (22)‡	3
Saxena et al., 2003 (29)	P. case series	hyperopia	The Netherlands	1 site	26 (13)‡	36 (mean, 22.4)

ITM refers to ICL in Treatment of Myopia Study Group; p, prospective; r, retrospective; SD, standard deviation †Included patients had myopia due to keratoconus
‡Consecutive patients §ITM, 2003 study reports 6, 12, and 24 month data (based on 523 eyes of 291 patients), and ITM, 2004 reports 36 month data.
‖Lackner et al. (32) also report data for 10 eyes of 5 hyperopic patients. These data were excluded from this report based on the exclusion of studies/data with < 20 patients for a specified type of refractive error.
¶Guell et al. (27) also examined 84 eyes of 42 patients with astigmatism, however, the Artisan-Verisyse lens for astigmatism is not licensed by Health Canada, so these results are not included in the analysis. The mean follow-up time reported in the paper includes the patients with astigmatism.
#662 first eyes and 478 second eyes. The efficacy results were reported separately for all first eyes and all second eyes due to potential for correlation data from both eyes.
**Silva et al., 2008 (13) reports results for subsets of eyes/patients (5 year data) reported by Stulting et al. 2008 (26).
††The total sample size was 177 eyes of 89 patients, but the reported results exclude 88 eyes as they have different periods of clinical evaluation.

Table 6: Uncorrected visual acuity weighted mean calculations stratified by lens type and refractive error

Time (months)	UCVA (Snellen VA)	Iris-Fixated Lenses				Posterior Chamber Lenses			
		Myopia		Hyperopia		Myopia		Myopic Astigmatism	
		Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)
3	≥ 20/20	5.0	60 (1)						
	≥ 20/40	81.0	85 (2)			94.4	36 (1)		
4	≥ 20/20	20.4	93 (1)						
	≥ 20/40	79.6	93 (1)						
6	≥ 20/20	17.4	69 (1)	22.7	22 (1)	55.8†	317 (1)	78.8	52 (1)
	≥ 20/40	82.6	69 (1)	90.9	22 (1)	92.1†	317 (1)	94.2	52 (1)
12	≥ 20/20	33.9	554 (2)			58.8†	318 (2)	82.7	186 (1)
	≥ 20/40	87.2	643 (3)			92.1†	318 (2)	96.2	186 (1)
24	≥ 20/20	32.2	394 (2)			57.4†	258 (1)		
	≥ 20/40	86.8	394 (2)			80.2†	258 (1)		
36	≥ 20/20	31.2	231 (1)			40.8	369 (1)		
	≥ 20/40	84.0	231 (1)			81.3	369 (1)		
60	≥ 20/20	73.7	19 (1)						
	≥ 20/40	94.7	19 (1)						
72	≥ 20/20								
	≥ 20/40	78.7	89 (1)						
120	≥ 20/20								
	≥ 20/40	82.0	89 (1)						

no. refers to number; UCVA, uncorrected visual acuity †Includes results from ITM, 2004 (25) for which the UCVA results were only reported for individuals with good visual potential defined as a preoperative BSCVA ≥20/20 (this restricts the results to a cohort of 523 eyes out of the total 662 eyes included in the study).

FDA Targets

As shown in Table 7, iris-fixated lenses for myopia and hyperopia, and posterior chamber lenses for myopia and myopic astigmatism met the FDA effectiveness targets for UCVA for high myopia at all time points through follow-up. The lenses did not meet the criteria for low to moderate myopia at all time points, but as the study populations consist primarily of people with high refractive errors, the high myopia targets are more appropriate. Additionally, the FDA targets were set for eyes with good visual potential, that is, those that have a preoperative BSCVA of 20/20 or better. (39;40) Only 1 study (24) reported UCVA specifically for this cohort of eyes while the other studies included eyes with any preoperative BSCVA.

Table 7: Comparison of UCVA Weighted Mean Results with FDA Targets for Iris-Fixated and Posterior Chamber pIOLs

	Time (months)								
Target UCVA (≥20/40)	**3**	**4**	**6**	**12**	**24**	**36**	**60**	**72**	**120**
Iris-fixated lenses for myopia									
75% of eyes (H)	✓	✓	✓	✓	✓	✓	✓	✓	✓
85% of eyes (L)	×	×	×	✓	✓	×	✓	×	×
Iris-fixated lenses for hyperopia									
Hyperopia			✓						
Posterior chamber lenses for myopia									
75% of eyes (H)	✓		✓	✓	✓	✓			
85% of eyes (L)	✓		✓	✓	×	×			
Posterior chamber toric lenses for myopic astigmatism									
75% of eyes (H)			✓	✓					
85% of eyes (L)			✓	✓					

H refers to FDA target for high myopia; H, FDA target for high myopia; L, FDA target for low to moderate myopia; UCVA, uncorrected visual acuity

Predictability of Manifest Refraction Spherical Equivalent

Predictability of MRSE (attempted versus achieved) is the measured by the percentage of eyes that are corrected within a target range (i.e., ± 0.5 D, ± 1.0 D, and ± 2.0 D) of emmetropia[6], and it is an important measure of pIOL effectiveness. Fourteen studies (9;13;15;16;24-26;28-30;34;36-38) reported predictability, and the results of the weighted mean calculations[7] stratified by lens type and refractive error are presented in Table 8.

Iris-fixated lenses for myopia

The results reported at 5 years postoperatively were based on a single study (Silva et al. (13)), with very few eyes (19 eyes), these results are therefore less accurate and should be considered with caution, especially since the results are substantially higher than all other time points.

Predictability for each target range improved after 1 month follow-up. At each time point over 10 years (except 1 month), more than 90% of eyes were within ± 2.0 D of emmetropia. Predictability within ± 1.0 D ranged from 65 to 95% during the 10 year follow-up, and declined over time: in the first 2 years of follow-up, predictability ranged from 74 to 82%, which decreased to 65% at 6 years and to 69% at 10 years. Predictability within ± 0.5 D was also decreased over time, ranging from 64% at 3 months to 44% at 10 years.

Iris-fixated lenses for hyperopia

At 6 months follow-up, 100% of eyes were within ± 2.0 D of emmetropia, 86% were within ± 1.0 D, and 59% were within ± 0.5 D. These results may not be accurate, however, because they are based on only one study with a small sample size (Saxena et al. (29), 22 eyes) and should thus be interpreted with caution.

Posterior chamber lenses for myopia

Between 6 and 24 months follow-up, at least 96% of eyes were within ± 2.0 D of emmetropia. Over 3 years of follow-up, at least 86% of eyes were within ± 1.0 D of emmetropia, and 51 to 73% of eyes were within ± 0.5 D. While predictability within ± 0.5 D decreased over time (although an increase was reported at 3 years), predictability within ± 2.0 D increased.

Posterior chamber lenses for hyperopia

Predictability data was only available for 10 years postoperatively, with 100% of eyes within ± 2.0 D of emmetropia, 96% within 1.0 D, and 81% within ± 0.5 D. These predictability results are substantially higher than the 10 year postoperative predictabilities for iris-fixated lenses for myopia and the 3 year predictabilities for posterior chamber lenses for hyperopia. These results suggest high predictability of these lenses over time, but as they are based on only one study (Pesando et al. (15), 55 eyes), the results must be considered with caution.

Posterior chamber toric lenses for astigmatism

At 6 and 12 months follow-up, 100% of eyes were within ± 2.0 D of emmetropia, at least 93% were within 1.0 D, and at least 73% were within ± 0.5 D. Predictability appeared to be stable for at least the first year after implantation.

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[6] Emmetropia occurs when parallel rays are focused exactly on the retina and vision is perfect. This corresponds to a MRSE of 0.0 diopters.

[7] Results from Chang et al. (31) and Stulting et al. (26) were excluded from the weighted mean calculations because the sample sizes at the follow-up time point were not provided in the text.

Table 8: Predictability Results Stratified by Lens Type and Refractive Error for Iris-Fixated and Posterior Chamber pIOLs

Time (months)	Predictability (D)	Iris-Fixated				Posterior Chamber					
		Myopia		Hyperopia		Myopia		Hyperopia		Myopic Astigmatism	
		Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)	Weighted mean (% eyes)	N eyes (no. studies)
1	within ± 0.5	28.6	56 (2)								
	within ± 1.0	55.4	56 (2)								
	within ± 2.0	92.9	56 (2)								
3	within ± 0.5	58.6	145 (4)								
	within ± 1.0	82.1	145 (4)								
	within ± 2.0	97.2	145 (4)								
6	within ± 0.5	56.7	104 (2)	59.1	22 (1)	60.3	464 (1)			73.0	226 (2)
	within ± 1.0	81.7	104 (2)	86.4	22 (1)	86.6	464 (1)			92.5	226 (2)
	within ± 2.0	97.1	104 (2)	100.0	22 (1)	95.5	464 (1)			99.6	226 (2)
12	within ± 0.5	50.5	186 (3)			62.8	449 (2)			76.9	186 (1)
	within ± 1.0	80.6	186 (3)			85.5	449 (2)			97.3	186 (1)
	within ± 2.0	96.8	186 (3)			96.9	449 (2)			100.0	186 (1)
24	within ± 0.5	55.9	59 (2)			50.9	165 (1)				
	within ± 1.0	74.6	59 (2)			93.3	165 (1)				
	within ± 2.0	94.9	59 (2)			100.0	165 (1)				
36	within ± 0.5					67.5	NR (1)				
	within ± 1.0					88.1	NR (1)				
	within ± 2.0										
60	within ± 0.5	73.7	19 (1)								
	within ± 1.0	94.7	19 (1)								
	within ± 2.0	94.7	19 (1)								
72	within ± 0.5	50.5	89 (1)								
	within ± 1.0	65.2	89 (1)								
	within ± 2.0	93.3	89 (1)								
120	within ± 0.5	43.8	89 (1)					80.7	57 (1)		
	within ± 1.0	68.8	89 (1)					96.5	57 (1)		
	within ± 2.0	93.3	89 (1)					100.0	57 (1)		

D refers to diopters; no., number; NR, not reported

†3, 6, 12, and 12 month weighted means for myopic iris-fixated lenses include results extracted from a figure in Asano-Kato et al. (38), so percentages may not be completely accurate.

FDA Targets

As shown in Table 9, the predictability of posterior chamber lenses for myopia, hyperopia, and myopic astigmatism, as well as iris-fixated lenses for hyperopia, met or exceeded the FDA effectiveness targets for high and low to moderate myopia at all time points (the FDA targets are summarized in Table 3). Iris-fixated lenses for myopia met or exceeded the targets for high and low to moderate myopia at most time points.

Table 9: Comparison of predictability results with FDA targets

Target predictability	Time (months)								
	1	3	6	12	24	36	60	72	120
Iris-fixated lens, myopia									
30% within ± .5 D (H)	×	✓	✓	✓	✓		✓	✓	✓
50% within ± .5 D (L)	×	✓	✓	✓	✓		✓	✓	×
60% within ± 1.0 D (H)	×	✓	✓	✓	✓		✓	✓	✓
75% within ± 1.0 D (L)	×	✓	✓	✓	✓		✓	×	×
90% within ± 2.0 D (H)	✓	✓	✓	✓	✓		✓	✓	✓
Iris-fixated lens, hyperopia									
50% within ± .5 D			✓						
75% within ± 1.0 D			✓						
Posterior chamber lens, myopia									
30% within ± .5 D (H)			✓	✓	✓	✓			
50% within ± .5 D (L)			✓	✓	✓	✓			
60% within ± 1.0 D (H)			✓	✓	✓	✓			
75% within ± 1.0 D (L)			✓	✓	✓	✓			
90% within ± 2.0 D (H)			✓	✓	✓				
Posterior chamber lens, hyperopia									
50% within ± .5 D									✓
75% within ± 1.0 D									✓
Posterior chamber lens, myopic astigmatism									
30% within ± .5 D (H)			✓	✓					
50% within ± .5 D (L)			✓	✓					
60% within ± 1.0 D (H)			✓	✓					
75% within ± 1.0 D (L)			✓	✓					
90% within ± 2.0 D (H)			✓	✓					

D refers to diopters; H, FDA target for high myopia; L, FDA target for low to moderate myopia

Predictability Stratified by Severity of Myopia

Four studies (24;25;28;37) examined the effect of preoperative myopia severity on predictability. Senthil et al. (37) stratified predictability within ± 1.0 D results for iris-fixated lenses at 3 months using three levels of severity (Table 10), while Benedetti et al. (28) stratified predictability results for iris-fixated lenses for myopia at 4 months by two levels of severity (Table 11). The ICL in Treatment of Myopia Study Group reported 2 and 3 year predictability results from its clinical trial (24;25) for posterior chamber lenses for myopia stratified by 3 levels of severity (Table 12).

Table 10: Predictability of MRSE Stratified by Severity

Severity of Myopia (D)	n/N eyes within ± 1.0 D (%)
−5.0 to −10.0	19/20 (95)
−10.5 to −20.0	33/37 (89)
−20.5 to −24.0	2/3 (66)

D refers to diopters

Table 11: Predictability of MRSE Stratified by Severity

Predictability Target (D)	n/N eyes (%)	
	−6.75 to −15.5 D	−16.0 to −23.0
within ± 0.5	30/68 (44.1)	8/25 (32.0)
within ± 1.0	47/68 (69.1)	13/25 (52.0)
within ± 2.0	63/68 (92.6)	22/25 (88.0)

D refers to diopters.

Source: Benedetti S, Casamenti V, Marcaccio L, Brogioni C, Assetto V. Correction of myopia of 7 to 24 diopters with the Artisan phakic intraocular lens: two-year follow-up. J Refract Surg 2005; 21(2):116-26.

Table 12: Predictability of MRSE Stratified by Severity

Time (months)	Predictability (D)	n/N eyes (%)		
		≤ −7	> −7 to −10	> −10
6	within ± 0.5	67/87 (77.0)	120/162 (74.1)	93/215 (43.3)
	within ± 1.0	85/87 (97.7)	151/162 (93.2)	166/215 (77.2)
	within ± 2.0	87/87 (100.0)	161/162 (99.4)	194/215 (90.2)
12	within ± 0.5	63/84 (75.0)	103/149 (69.1)	95/191 (49.7)
	within ± 1.0	81/84 (96.4)	137/149 (91.9)	141/191 (73.8)
	within ± 2.0	84/84 (100.0)	148/149 (99.3)	178/191 (93.2)
24	within ± 0.5	32/40 (80.0)	62/94 (66.0)	54/124 (43.5)
	within ± 1.0	38/40 (95.0)	84/94 (89.4)	85/124 (68.5)
	within ± 2.0	40/40 (100.0)	94/94 (100.0)	113/124 (91.1)
36	within ± 0.5	84.7%	71.0%	56.9%
	within ± 1.0	97.2%	93.1%	80.0%
	within ± 2.0	100.0%	100.0%	95.6%

D refers to diopters.

Sources: a) Sanders DR, Vukich JA, Doney K, Gaston M, Implantable Contact Lens in Treatment of Myopia Study Group. U.S. Food and Drug Administration clinical trial of the Implantable Contact Lens for moderate to high myopia. Ophthalmology 2003; 110(2):255-66. b) 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.

The stratified results showed that the proportion of eyes within target predictability varied by the preoperative severity of refraction. As preoperative severity of myopia increased, fewer postoperative eyes were within target predictability ranges, but the statistical significance of these differences is unknown. Despite the decreased predictability with severity, each stratified group still met or exceeded the FDA predictability target for high myopia.

Predictability of Manifest Cylinder

Toric lenses are designed to correct astigmatism, so the predictability of the manifest cylinder (similar to predictability of MRSE) is an important outcome for these lens types. As shown in Table 13, at least 85% of eyes were within ± 1.0 D of emmetropia. Predictability within ± 0.5 D was 59% at 6 months, which declined to 48% at 12 months.

Table 13: Predictability of Manifest Cylinder for Posterior Chamber Toric Lenses for Astigmatism

Time (months)	Predictability (D)	Weighted Mean (% Eyes)	N eyes (no. studies)
6	within ± 0.5	59.3	226 (2)
	within ± 1.0	88.5	227 (2)
	within ± 2.0	100.0	228 (2)
12	within ± 0.5	48.4	189 (1)
	within ± 1.0	85.5	190 (1)
	within ± 2.0	NR	n/a

D refers to diopters; no., number

Efficacy Index

The efficacy index (EI) is the ratio of the mean postoperative UCVA to the mean preoperative BSCVA. It is an important measure of pIOL efficacy because it takes into account the severity of patients' refractive error, which can influence the effectiveness of the pIOL. (25) Eleven studies (13;14;26;28-32;34;36;37) reported either EI values or the data needed to calculate the EI.[8] Weighted mean EIs were calculated using study sample sizes as the weights and the results are shown in Table 14.
For all lens types and refractive errors, the weighted mean EIs were less than 1.0. This indicates that the mean UCVA achieved postoperatively was worse than the mean preoperative BSCVA. Thus, patients achieved better vision with glasses or contact lens correction than pIOL insertion.

Iris-fixated lenses for myopia

The weighted mean EI for iris-fixated lenses for myopia ranged from 0.43 to 0.95 over 10 years of follow-up. The 3 and 5 year time points are based on only one study with very few eyes (Silva et al. (13), 19 eyes), thus these values must be interpreted with caution, especially because they are much lower than at the other time points. Excluding the results from Silva et al. (13), overall, the EI increased over the first 2 years then decreased slowly about 6 to 10 years after implantation.

[8]Six studies provided the EI in the reported results. For 3 studies, while the EI was not reported, it was possible to calculate the value using the mean preoperative BSCVA and mean postoperative UCVA provided in the study. However, for 7 studies, there was inadequate data to calculate the EI, so the authors were contacted to ask for the EI or raw data. We were unable to contact 2 authors as the available email addresses were not active. Two authors responded to our request and provided us with the necessary information to include the studies in our analysis (1 of these authors provided us with combined EI data as only stratified results by myopia severity were reported in the paper).

Table 14: Efficacy Index Calculations

Time (months)	Iris-Fixated Lenses				Posterior Chamber Lenses			
	Myopia		Hyperopia		Myopia‡		Astigmatism	
	Weighted mean EI	N eyes (no. studies)	Weighted mean EI	N eyes (no. studies)	Weighted Mean EI	N eyes (no. studies)	Weighted mean EI	N eyes (no. studies)
3	0.95	31 (1)						
6			0.76	22 (1)	0.86‖	65 (1)	0.94	52 (1)
12	0.85†	704 (3)	0.73	17 (1)	0.99§‖¶	101 (2)		
24	0.89†	153 (2)	0.69	15 (1)	0.87§‖¶	102 (3)		
36	0.43‡	20 (1)	0.67	10 (1)	0.69‖¶	65 (1)		
48					0.84‖¶	65 (1)		
60	0.63‡	19 (1)						
72	0.83	89 (1)						
120	0.80	89 (1)						

EI, refers to efficacy index; no., number

† EI calculations include data from Stulting et al. (26) provided by the author for all first eyes enrolled in the study with paired data at 12 months postoperatively (i.e. preoperative BSCVA is based on only the eyes that were examined at 12 month time point or 602 of the total 662 eyes). This group included all eyes regardless of postoperative refractive goal and eyes with various pathologies.

‡ Only 36 and 60 month EIs were included from Silva et al. (13) because the 12 month results was based on a subgroup of patients that were also reported at 12 months in Stulting et al. (26)

§ 12 and 24 month EI results include data from Chang et al. (31) provided by the author for all eyes with paired data at 12 and 24 months postoperatively (i.e., mean preoperative BSCVA was different at 12 and 24 months).

‖6, 12, 24, 36, and 48 month EI calculations included data extracted from a figure in Lackner et al., (32), and so might not be precise due to difficulties identifying the exact postoperative UCVA values in the figure.

¶Sample size weights for the EI calculations for 12, 24, 36, and 48 month time points include data from Lackner et al. (32) which were based on the study's initial sample size (65 eyes) as drop-outs are not reported in the study (the 6 month time point weight reflects the actual sample size at 6 months as all eyes were followed for at least 6 months).

Iris-fixated lenses for hyperopia

Over 3 years of follow-up, the EIs for iris-fixated lenses for hyperopic ranged from 0.67 to 0.76. The results also showed that the EI decreased over time. Compared with iris-fixated lenses for myopia, hyperopic lenses had lower EIs and a faster decline over time. These values are, however, based on only one study, Pesando et al. (15), with few eyes (small initial sample size and > 50% loss to follow-up at 3 years), so these results may be less accurate and the statistical significance of this trend is not known.

Posterior chamber lenses for myopia

For posterior chamber lenses for myopia, EI ranged from 0.69 to 0.99 over 4 years follow-up (all but one value are > 0.84). Overall, EI appears to increase over the first 2 years and then decrease over the subsequent 2 years. The accuracy of the results at 1 and 2 years is questionable, however, as the calculated weighted means include data from Lackner et al. (32), which was to heavily weighted because the preoperative sample size (65 eyes) was used as the weight since loss to follow-up beyond 6 months was not reported in the paper.[9] Lackner et al. also had a larger sample size than the other included studies [n at 2 years was 25 and 12 in Alfonso et al. (30) and Chang et al. (31), respectively], which means that it may have unduly influenced the results. (When the Lackner data is included, the weighted mean EI at 2 years is 0.87, but when it is excluded, the EI is 0.97.)

[9]The 3 and 4 year data were based on the Lackner et al. results, but because no other studies reported results at these time points, weighted means were not used to calculate the EIs, so they are not affected by inflated sample size weights.

Posterior chamber toric lenses for astigmatism

At 6 months follow-up, posterior chamber toric lenses for astigmatism had a high EI (0.94).

An important caveat to consider when examining the EI data is that some studies calculated the EI using the preoperative mean BSCVA for all eyes included in the study, while some studies used the preoperative mean BSCVA for only those eyes with paired data at the postoperative time point. Using paired data could bias the results if the eyes that were followed for longer experienced bigger improvements than those lost to follow-up. For example, in Chang et al. (31), the mean preoperative BSCVA (decimal acuity) for eyes with paired data was 0.84 and 0.75 at 12 and 24 months postoperatively (data from author). Therefore, EI was higher at 24 months than 12 months, but not because of increasing EI over time, but rather the differences between the patients who were followed for 24 months compared to those who were only followed to 12 months.

Manifest Refraction Spherical Equivalent

Table 15 displays the comparison of the preoperative and postoperative MRSE for each study. It was not possible to combine MRSE results into a summary measure, so the results for each study are presented separately. Only two studies had a postoperative MRSE greater than 1 D (Shen et al. (33), −1.79 ± 1.13 D; Lackner et al. (32), −1.77 ± 2.17D). Some patients in these studies, however, were not targeted for emmetropia because their preoperative myopic error exceeded the maximum corrective strength of pIOLs (pIOLs are licensed to correct myopia up to −20 D).

Table 15: Summary of Mean Pre- and Postoperative Manifest Refraction Spherical Equivalent for Iris-Fixated and Posterior Chamber pIOLs

Author, Year	Mean MRSE +/- SD (range) (D)							
	Preoperative	3 mo	6 mo	12 mo	24 mo	36 mo	60 mo	120 mo
Iris-Fixated Lens, Myopia								
Silva et al., 2008 (13)	−12.30 ± 2.62 (−8.25 to −17.25)			−0.44 ± 0.56 (−2.0 to 0.38)	−0.71 ± 0.99 (−4.50 to 2.0)	−0.38 ± 0.78 (−0.5 to −2.63)	−0.37 ± 0.69 (0.84 to 1.11)	
Chung et al., 2007 (35)	−11.03 ± 2.25 (−8.08 to −13.75)	−.77 ± .34 (−2.0 to 0)						
Moshirfar et al., 2007 (16)	−12.20 ± 2.79 (−7.9 to −18.9)		−0.26	−0.40	−0.50			
Tahzib et al., 2007 (36)	−10.37 ± 4.69 (−3.75 to −25.25)			−0.70 ± 0.97 (−4.88 to 1.75)			−0.71 ± 0.99 (−4.50 to 2.0)	−0.70 ± 0.99 (−4.00 to 2.00)
Senthil et al., 2006 (37)	−12.5 ± −4.96							
Asano-Kato et al,, 2005 (38)	−12.80 ± 2.94 (−7.63 to −20.75)		−0.68 ± 0.96 (−3.5 to 0.75)	−0.42 ± 0.41 (−1.38 to 0.0)	−0.71 ± 0.81 (−1.75 to 0.5)			
Benedetti et al., 2005 (28)	Group 1: −11.89 ± 2.4 (−6.75 to −15.5) Group 2: −18.92 ± 2.04 (−16.0 to −23.0)			Group 1: −0.89 ± 0.77 Group 2: −1.14 ± 1.08	Group 1: −0.91 ± 0.77 Group 2: −1.20 ± 1.19			
Lifshitz et al., 2004 (14)	−11.25 ± 3.33 (−5.25 to −23.5)	−.50 ± .36 (−1.25 to 0.0)						
Iris-Fixated Lens, Hyperopia								
Saxena et al., 2003 (29)	6.80 ± 1.97 (3.0 to 11.0)		−0.08 ± 0.74 (−1.50 to 1.38)	−0.03 ± 0.71 (−1.50 to 1.13)	−0.15 ± 0.89 (−2.0 to 1.0)	0.10 ± 0.85 (−1.50 to 1.25)		
Posterior Chamber Lens, Hyperopia								
Pesando et al., 2007 (15)	5.78 ± 2.54 (2.50 to 11.75)							0.07 ± 0.50 (−1.00 to 1.50)
Posterior Chamber Lens, Myopia								
Alfonso et al., 2008 (30)	−8.54 ± 4.15 (−3.00 to −18.00)		−0.32 ± 0.55					
Chang et al., 2006 (31)		−13.42 ± 2.38 (−7.0 to −17.25)				−0.10 ± 0.74 (−2.0 to 2.75) at last follow-up		
Shen et al., 2003 (33)	−16.79 ± 3.37		−1.79 ± 1.13					
Lackner et al., 2003 (32)		−16.23 ± 5.29				−1.77 ± 2.17		
Posterior Chamber Lens, Astigmatism								
Sanders et al., 2007 (9)	−9.36 ± 2.66			0.05 ± 0.46				
Gimbel et al., 2005 (34)	−9.36 ± 3.21 (−3.88 to −19.25)		0.02 ± 0.48 (−1.25 to 1.33)					

D refers to diopter; fup, follow-up; mo, month; MRSE, manifest refraction spherical equivalent; SD, standard deviation.

Safety

Best Spectacle Corrected Visual Acuity

Preservation of BSCVA is a main criterion for assessment of the safety of a refractive surgical procedure. (24) A change in one Snellen line is not clinically significant as it is within the range of normal individual variation for repeated measurements. (41;42) The loss of more than one line of BSCVA is considered the standard for safety, so that after pIOL implantation, a patient will at least retain the same level of vision with spectacle/contact correction. (42) Table 16 and Figures 3 to 7 show the proportion of eyes that gained or lost lines of BSCVA after pIOL implantation. Since change in BSCVA was not reported in all studies and most reported results for different postoperative time points, it was only possible to calculate a weighted mean for the 3 month follow-up for iris-fixated lenses for myopia and 12 month follow-up for posterior chamber lenses for myopia.

Approximately 77% to 90% of eyes did not experience a clinically significant change in BSCVA (loss of one line, no change, or gain of one line). Very few eyes lost two or more lines of BSCVA after pIOL implantation. The highest loss of BSCVA was observed in the posterior chamber lenses for myopia at 24 months follow-up (1.6% of eyes lost ≥2 lines of BSCVA).

Approximately 10% to 20% of eyes gained two or more Snellen lines. Based on the observed trends for iris-fixated lenses for myopia and hyperopia and posterior chamber toric lenses for astigmatism, the number of eyes that gain two or more lines of BSCVA may increase slightly over time. However, given the small increases and limited number of eyes at some time points, this trend must be interpreted with caution.

United States Food and Drug Administration Target Values

The FDA defined safety targets for loss of BSCVA: loss of two or more lines of BSCVA should occur in fewer than 5% of eyes. (17;39;40) All of the lenses met this safety target (Table 17).

Safety Index

The safety index (SI) is the ratio of the mean postoperative BSCVA to the mean preoperative BSCVA. Table 18 shows the weighted mean SI over time after pIOL insertion.

Iris-fixated lenses

The SI for iris-fixated lenses for both myopia and hyperopia declined over time. While the observed decline was more rapid for hyperopic lenses, the statistical significance of this trend is not known. The results for hyperopia data are based on one study with a small sample size (Saxena et al. (29), 22 eyes), so must be considered with caution.

Posterior chamber lenses

The SI for posterior chamber lenses for myopia is also based on only one study with a small sample size (Alfonso et al. (30), 25 eyes). Lackner et al. (32) reported a safety index of 1.31 for posterior chamber myopic lenses, but this SI was averaged over the entire observation period (mean follow-up 21.9 ± 15.94 months), and so could not be included in the weighted mean SI calculations.

Table 16: Safety Measured by Change in Best Spectacle Corrected Visual Acuity for Iris-Fixated and Posterior Chamber pIOLs

Time (months)	N eyes	Change in BSCVA (% of eyes)						
		Loss ≥ 2 Lines	Loss 2 Lines	Loss 1 Line	No Change	Gain 1 Line	Gain 2 Lines	Gain ≥ 2 lines
Iris-fixated lenses for myopia								
3†	91	0.0	0.0	7.7	45.1	24.2	14.3	23.1
4	93	0.0	0.0	0.0	40.9	16.1	20.4	43.0
6	69	0.0	0.0	7.2	30.4	42.0	18.9	18.9
12	493	0.6	NR	6.1	45.0	35.9	11.0	12.4
24	355	0.3	NR	3.7	45.4	37.5	11.5	13.5
36	228	0.9	NR	6.6	38.6	40.4	11.8	13.6
60	19	0.0	0.0	0.0	26.3	57.8	15.8	15.8
Iris-fixated lenses for hyperopia								
6	22	0.0	0.0	13.6‡	68.2	9.1	NR	9.1
36	10	0.0	0.0	40.0	30.0	10.0	NR	20.0
Posterior chamber lenses for hyperopia								
120	57§	0.0	0.0	1.8¶	64.4	15.2	8.3	17.5
Posterior chamber toric lenses for astigmatism								
6	52	0.0	0.0	3.8	50.0	28.8	17.3	17.3
12	186	0.5	1.1	5.9	16.1	57.5	16.7	18.8
Posterior chamber lenses for myopia								
6	464	0.4	0.4	4.1	47.0	36.6	8.8	11.9
12†	452	0.7	0.7	5.5	45.8	38.1	7.3	10.0
24	257	1.6	1.2	7.8	41.2	38.5	7.4	10.9

BSCVA refers to best spectacle corrected visual acuity; NR, not reported. Note, a change in only 1 line is not considered clinically significant (shown in light grey in the table).
†2 studies reported data for this time point, so results were combined into a weighted mean using sample sizes as the weights.
‡The percentage is based on Figure 3 in Saxena et al. (29). The value in Figure 3 and the value reported in the text of the paper were different. The value in the Figure was selected because it corresponds with the correct sample size of 10 eyes at 36 months.
§The sample size of 57 eyes at 10 years was chosen based on information presented in the text, however, the follow-up description was unclear, and the sample size may actually be lower.
¶Percentage is based on Fig. 3 in Pesando et al. (15). The value reported in Figure 3 and in the text were different. The value in the figure was chosen because it makes more sense with the data (i.e., the sum of the percentages reported in the text is > 100%, but the value from the figure adds up to 100%).

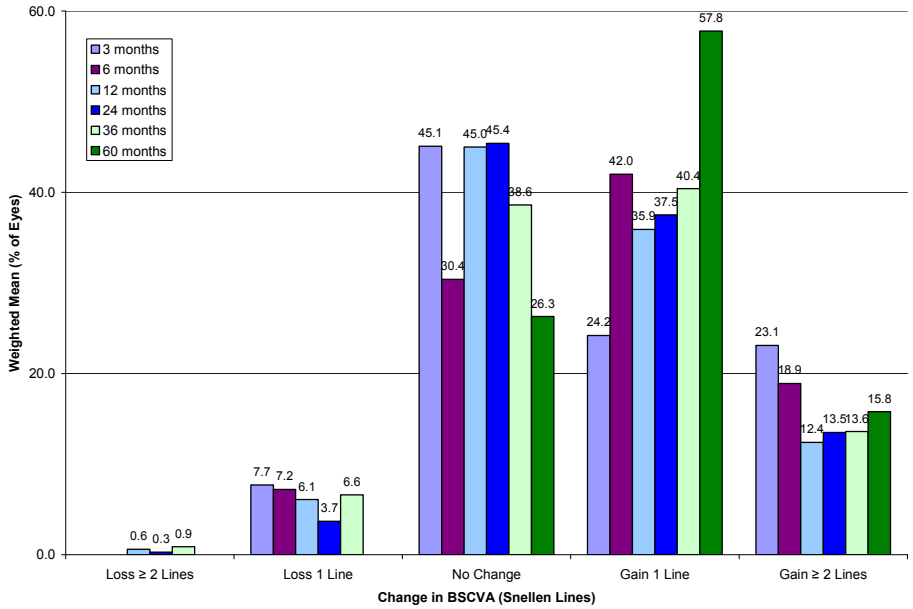

Figure 3: Change in Best Spectacle Corrected Visual Acuity over Time for Iris-Fixated Lenses for Myopia

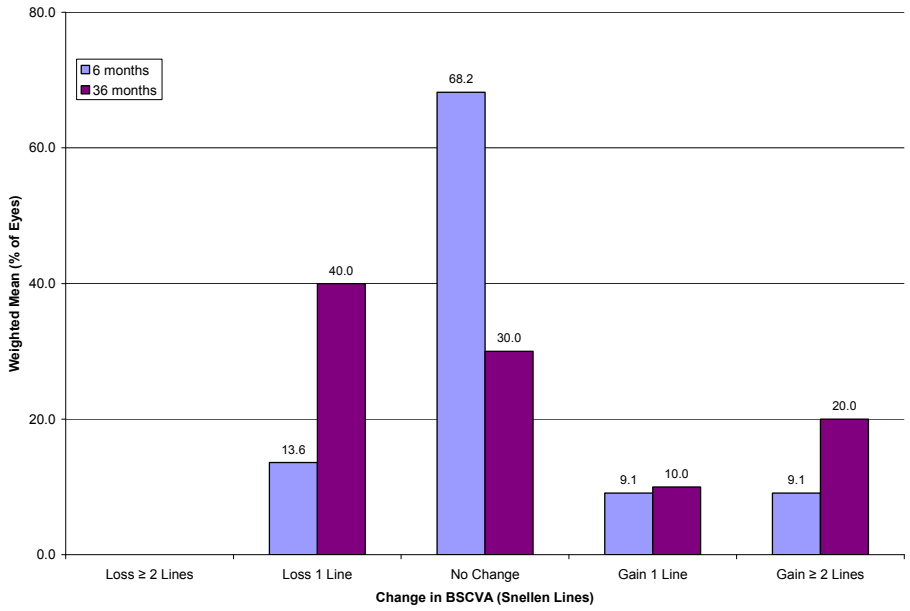

Figure 4: Change in Best Spectacle Corrected Visual Acuity over Time for Iris-Fixated Lenses for Hyperopia

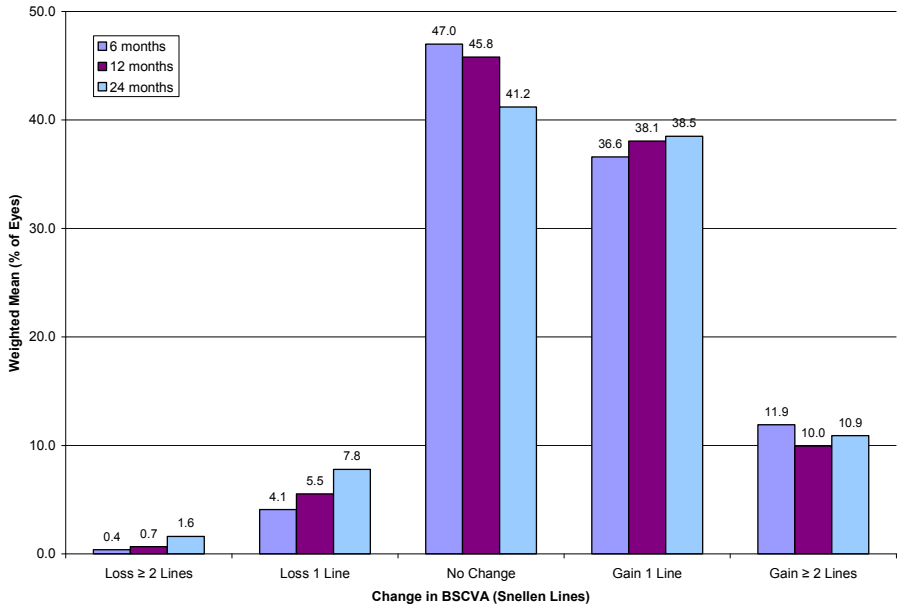

Figure 5: Change in Best Spectacle Corrected Visual Acuity over Time for Posterior Chamber Lenses for Myopia

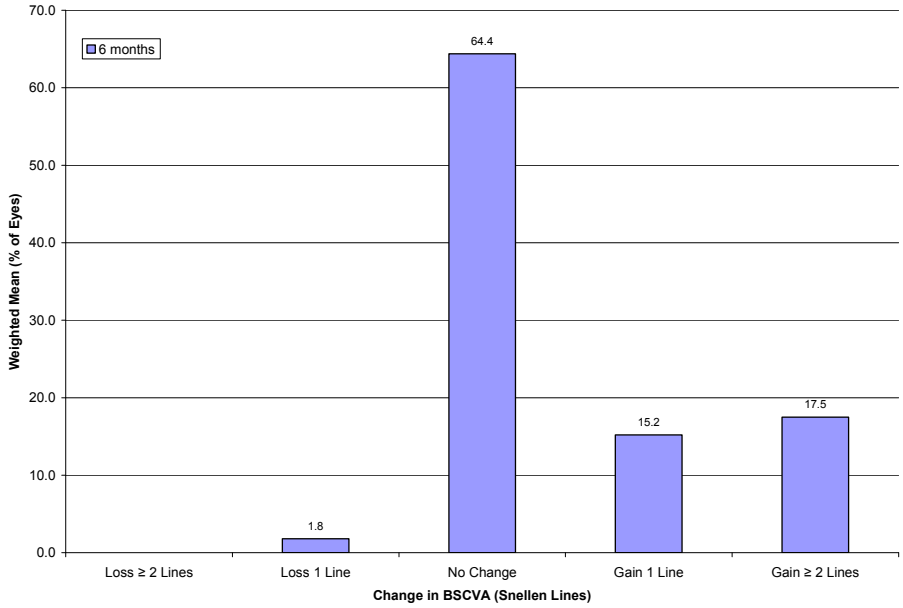

Figure 6: Change in Best Spectacle Corrected Visual Acuity over Time for Posterior Chamber Lenses for Hyperopia

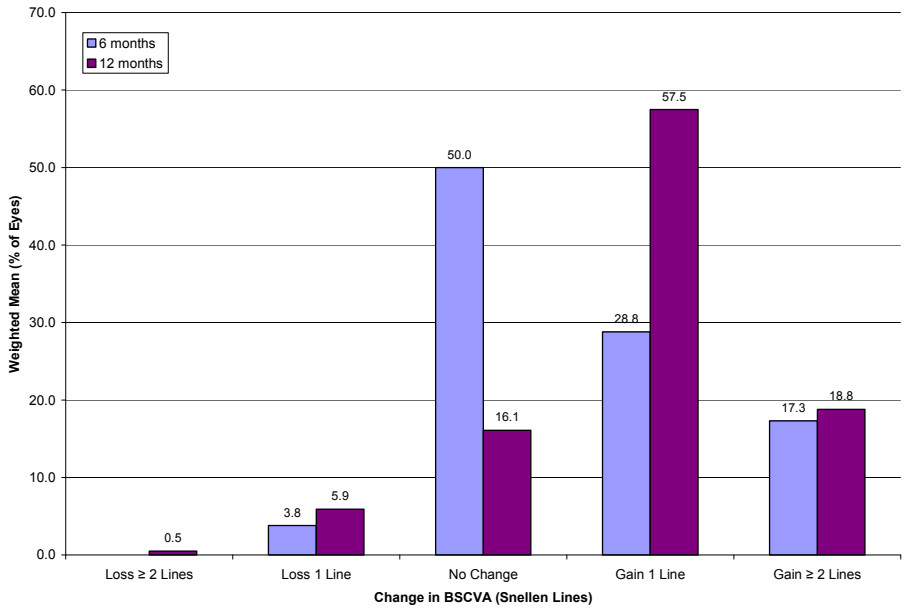

Figure 7: Change in Best Spectacle Corrected Vision over Time for Posterior Chamber Lenses for Myopic Astigmatism

Table 17: Comparison of FDA Targets for Loss of BSCVA with pIOL Results

Lens Type	Time (months)						
	3	6	12	24	36	60	120
Iris-fixated lenses							
for myopia	✓	✓	✓	✓	✓	✓	
for hyperopia		✓			✓		
Posterior chamber lenses							
for myopia		✓	✓	✓			
for hyperopia							✓
for astigmatism		✓	✓				

Table 18: Safety Index Calculations Stratified by Lens Type and Refractive Error

Time (months)	Iris-Fixated Lenses				Posterior Chamber Lenses			
	Myopia†		Hyperopia		Myopia		Astigmatism	
	Weighted Mean SI	N eyes (no. studies)	Weighted mean SI	N eyes (no. studies)	Weighted mean SI	N eyes (no. studies)	Weighted mean SI	N eyes (no. studies)
3	1.29	31 (1)						
4	1.18	93 (1)						
6			1.01	22 (1)			1.13	52 (1)
12	1.20	182 (2)	0.95	17 (1)	1.05	25 (1)		
24	1.19	153 (2)	0.95	15 (1)				
36			0.87	10 (1)				
72	1.10	89 (1)						
120	1.10	89 (1)						

no. refers to number; SI, safety index

†4, 12, and 24 month weighted mean calculations includes data from Benedetti et al. (28) which provided the safety index stratified by severity of myopia. Both safety indexes were included in the calculation and weighted by the size of each group.

Adverse Events

Chen et al. (23) conducted a systematic review of the literature on adverse events associated with pIOLs. Their focus was cataracts but all reported complications were included. Glare/halos were the most common complication reported in the iris-fixated lens group and pigment deposits on the pIOL in the posterior chamber lens group. A summary of the systematic review and incidence of complications are provided in the Summary of Existing Evidence, Systematic Review section of this report.

More than 30 adverse events including cataract development, glare/halos, macular holes, iritis, corneal edema, and increased intraocular pressure were reported in the 19 included pre-post observational case series. As the adverse events were reported differently by each study and the completeness of reporting and examinations varied, the results were not combined into summary rates. A complete list and description of these adverse events can be found in the data tables in Appendix 4. The adverse event data was limited in that some of the serious complications, such as retinal detachment and cataract development, are more common in people with high myopia. Without a control group, it is difficult to determine if these complications are due to the pIOL insertion or the patient's high myopia.

The FDA specified safety targets for adverse events: for each type of adverse event, less than 1% of eyes should experience the event. (17;18) This target applies to myopia (with or without astigmatism) and hyperopia. Twelve complications reported in the systematic review by Chen et al. (23) exceeded this safety target (Table 19).

In the pre-post observational case series, many of the adverse event rates exceeded this safety target as well but rates varied substantially between studies. The highest adverse event rates (those ≥ 10%) were observed for:

- postoperative inflammation (cells and flare) in Stulting et al. (26) (40.3% at 1 day postoperatively),
- pigment deposits on lens in Shen et al. (33) (100% at 1 day),
- iritis in ITM 2003(24)(19.3% at 1 day), lens opacification in Lackner et al. (32) (33%),
- blunt trauma in Moshirfar et al. (16) (11.6%),
- increased intraocular pressure in Senthil et al. (37) (10%),
- persistent iris atrophy in fixation area of hepatic in Saxena et al. (29) (11.8%),
- asymptomatic ovalization of the pupil in Stulting et al. (26)(13% at 1 day), and
- corneal edema in Stulting et al. (26) and ITM 2003 (24) (19.4% and 11.3% at 1 day, respectively).

Higher complication rates were more common in the smaller studies.

Table 19: Adverse Events that Exceed the FDA Safety Target from Chen et al. (23)

Adverse Event	Adverse Event Rate (%)	
	Iris-Fixated Lens	Posterior Chamber Lens
Cataract	1.11	9.60
Corneal Edema	1.69	<1%
Cystic wound/wound leakage	1.44	NR
Decentration	1.65	3.26
Halo/glare	8.77	5.93
Increased IOP	4.24	4.80
Iris atrophy	NR	NR
Pigment deposits on lens	1.73	10.85
Pigment dispersion	1.29	2.63
Pupil ovalization	1.44	NR
Secondary refractive surgery	<1%	2.80
Uveitis	4.49	<1%

IOP refers to intraocular pressure; NR, not reported

Endothelial Cell Density and Loss

The posterior surface of the cornea is covered by a layer of endothelial cells. Adequate endothelial cell density (ECD) is important to maintain a clear cornea. Implantation of IOLs, particularly those that are inserted in the anterior chamber, can result in loss of these endothelial cells, which is an important safety concern. Endothelial cell loss (ECL) has been attributed to contact between pIOLs in the anterior chamber, as well as corneal endothelial remodelling after surgical trauma. (43) Ten studies reported ECD, summarized in Table 20. Preoperative ECD varied substantially across studies, so the results were not combined into a summary weighted mean ECD. Table 21 summarizes the ECL (calculations based on only patients with paired data at the preoperative and postoperative time points) reported by nine studies. Some studies took into account annual physiologic cell loss unrelated to pIOL implantation (loss ranged from 0.5 – 0.6%). Endothelial cell loss also varied substantially between studies.

Learning Curve

In the systematic review, Chen et al. (23) observed that several of the included studies identified higher rates of adverse events when a surgeon first starts to perform the procedure. A learning curve associated with lower complication rates as surgical skills and experience increased was also observed in two of the studies included in this analysis. (26;37)

Patient Satisfaction

Four studies measured postoperative patient satisfaction. (9;24;25;28). Benedetti et al. (28) reported that 100% of patients were satisfied with the results of their pIOL implantation; the other three studies reported satisfaction segmented by three categories (Table 22). Overall, more than 90% of patients were very/extremely satisfied with the results of the pIOL implantation, and satisfaction remained high over time (3 years).

One study covered above (ITM, 2004) also reported satisfaction stratified by preoperative MRSE. The results showed that satisfaction varied by severity of preoperative MRSE: patients with more severe myopia reported less satisfaction with the results (very/extremely satisfied: ≥ -7 D, 95.8%; < -7 to -10 D, 94.3%; < -10 D, 88.4%), and only patients in the most severe group of myopia reported dissatisfaction with their results (2 eyes, 1.4%). (25)

Table 20: Endothelial Cell Density

Author, Year	Endothelial Cell Density (cells/mm^2 ± SD)									
	Preop	3 months	6 months	12 months	24 months	36 months	48 months	60 months	72 months	120 months
Iris-Fixated Lenses, Myopia										
Silva et al, 2008 (13)	2481 ± 291			2325 ± 396		2256 ± 370		2156 ± 495		
Senthil et al., 2006 (37)	2741 ± 313		2598 ± 453	2597 ± 320	2566 ± 315					
Asano-Kato et al., 2005 (38)	2831 ± 304		2875 ± 260	3007 ± 222	2750 ± 284					
Moshirfar et al., 2007 (16)	2713 ± 362		2730 ± 376	2641 ± 361	2534 ± 395					
Benedetti et al., 2005 (28)	2658 ± 360			2554 ± 322	2514 ± 305					
Tahzib et al., 2007 (36)	2817 ± 359			2928 ± 351					2734 ± 360	2800 ± 292
ITM, 2004 (25)	NR					2354	2355			
Lifshitz et al., 2004 (14)	2925 ± 377	2809 ± 414								
Iris-Fixated Lenses, Hyperopia										
Saxena et al., 2003 (29)	2749 ± 348		2858 ± 462	2965 ± 305	2611 ± 472	2471 ± 372				
Posterior Chamber Lenses, Hyperopia										
Pesando et al., 2007 (15)	2696 ± 298									2437 ± 243

Preop refers to preoperative

Table 21: Endothelial Cell Loss

Author, Year	Endothelial Cell Loss (%)							
	3 months	6 months	12 months	24 months	36 months	60 months	72 months	120 months
Iris-Fixated Lenses, Myopia								
Silva et al, 2008 (13)*						14.05		
Stulting et al., 2008 (26)		.36	1.06	2.55	4.76			
Senthil et al., 2006 (37)		5.2	5.25	6.38				
Moshirfar et al., 2007 (16)		.69	3.3	6				
Benedetti et al., 2005 (28)			3.9	5.4				
Tahzib et al., 2007 (36)†			9.39				3.26	8.86
Lifshitz et al., 2004 (14)	3.96							
Iris-Fixated Lenses, Hyperopia								
Saxena et al., 2003 (29)				8.5	11.7			
Posterior Chamber Lenses, Hyperopia								
Pesando et al., 2007 (15)								4.7

*12 and 36 month results for Silva et al. (13) are not included in the table because the patient results are included in Stulting et al. (26) for these time points.
†ECL is adjusted for a 0.5% physiological cell loss per year.

Table 22: Satisfaction with results of pIOL implantation

Author, Year	Lens Type, Refractive Error	Time (years)	Satisfaction with Results (% of patients)		
			Very/Extremely	Moderately/Fairly	Unsatisfied
Sanders et al., 2007 (9)	Posterior Chamber, Astigmatism	1	97.7	2.3	0.0
ITM, 2003 (24)	Posterior Chamber, Myopia	1	92.4	6.7	1.0
ITM, 2004 (25)	Posterior Chamber, Myopia	3	92.1	7.3	0.6

Quality of Life and Vision

The ICL in Treatment of Myopia (ITM) Study Group assessed quality of vision after pIOL implantation using a standardized subjective questionnaire. (25) Changes in postoperative symptoms at 1 and 3 years were compared with preoperative levels. Overall, 76% to 80% of patients did not experience a change in glare, halos, night vision, or night driving symptoms, while more than 97% of patients did not experience a change in double vision. (24;25)

In Benedetti et al. (28), quality of life was assessed using a subjective survey at 4 months postoperatively. Overall, 95% of patients reported increased quality of life after pIOL implantation. Most patients reported improvements in several aspects of their daily lives including reading (87%), watching TV (89%), shopping (81%), playing sports (87%), and driving during the day (88%). However, 17% of patients reported worse night driving and 6.4% reported halos and/or medium intensity nocturnal glare. (28)

Pesando et al. (15) assessed quality of life and vision using a subjective questionnaire before pIOL implantation and at 6 and 12 months postoperatively. Approximately 89% of patients reported good quality of vision and improved quality of life. The number of patients who reported halos under scoptic light decreased over time (6 months, 70%; 1 year, 6%). The two patients who reported halos at 1 year had overly vaulted[10] pIOLs, which the authors believed to be the cause of the decreased quality of vision. (15)

[10]The distance between the eye's natural crystalline lens and the pIOL is called the vault. Vaulting should provide maximal clearance between the pIOL and the eye's lens. However, if the lens is over or under vaulted, then it comes into contact with structures in the eye and can cause problems.

Efficacy Studies for High Refractive Errors

Preoperative severity of myopia, hyperopia, or astigmatism is an important factor that can influence the efficacy and safety of pIOLs. (24;25) The American Academy of Ophthalmology's Preferred Practice Pattern Guidelines: Refractive Errors & Refractive Surgery (12) classify the severity of refractive errors as follows:

Myopia

- Low to moderate: greater than −6.00 D
- High: less than −6.00 D

Hyperopia and Astigmatism

- Low to moderate: less than 3.00 D
- High: greater than 3.00 D.

Except when studies have reported their results stratified by severity (e.g. four studies reported predictability of MRSE stratified by severity of myopia), it was not possible to compare the results for high myopia with moderate and/or low myopia as many of the studies included patients with a wide range of myopia from low to high. To isolate the efficacy of pIOLs for high refractive errors, results were re-examined including only the studies with high myopia (defined as those studies with a preoperative mean MRSE of −6 D or higher) and high hyperopia (defined as preoperative mean MRSE ≥ 3 D) patient populations (Table 23).

Table 23: Summary of Studies with Patient Populations with High Refractive Errors for Iris-Fixated and Posterior Chamber pIOLs

Author, Year	Refractive Error	Mean preoperative MRSE ± SD (range) (D)
Posterior Chamber Lenses		
Chang et al., 2007 (31)	myopia	−14.54 ± 3.61 (−7.00 to −24.75)
Shen et al., 2003 (33)	myopia	−16.79 ± 3.37 (−11.75 to −25.75)
Pesando et al., 2007 (15)	hyperopia	5.78 ± 2.54 (2.50 – 11.75)
Iris-Fixated Lenses		
Silva et al., 2008 (13)	myopia	−12.30 ± 2.69 (−8.25 to −17.25)
Chung et al., 2007 (35)	myopia	−11.03 ± 2.25 (−8.08 to −13.75)
Moshirfar et al., 2007 (16)	myopia	−12.2 ± 2.79 (−7.9 to −18.9)
Asano-Kato et al., 2005 (38)	myopia	−12.8 ± 2.9 (−7.63 to −20.75)
Benedetti et al., 2005 (28)	myopia	−13.7 ± 3.8 (−6.75 to −23.0)
Saxena et al., 2003 (29)	hyperopia	6.80 ± 1.97 (3.00 to 11.00)

D refers to diopters; MRSE, manifest refraction spherical equivalent; SD, standard deviation

Uncorrected Visual Acuity

Weighted means could not be calculated for UCVA for high myopia or hyperopia since not all studies reported this outcome and those that did didn't report for the same follow-up periods, lens type, or refractive error.

Overall, the results for both iris-fixated and posterior chamber lenses exceeded FDA effectiveness targets for UCVA for high myopia[11]. This is particularly impressive as many of the eyes had a preoperative BSCVA worse than 20/20. It was not possible to separate the results for the cohort of eyes with good visual potential from other eyes, except for the ITM, 2003 (24) study in which this data is provided.

Iris-fixated lenses for high myopia

At most of the follow-up visits, 10% to 24% of eyes achieved an UCVA of 20/20 or better. At 5 years, 74% of eyes had UCVA of 20/20 or better, however, this result was based on one study with a small sample size [Silva et al. (13), 19 eyes], so it must be interpreted with caution. Approximately 80% to 95% of eyes achieved UCVA of 20/40 or better over the 5 year follow-up period. The FDA effectiveness target for UCVA for high myopia was exceeded at all time points.

Iris-fixated lenses for high hyperopia

Only one small study (22 eyes) reported UCVA results for high hyperopia. Saxena et al. (29) reported that 23% of eyes achieved an UCVA of 20/20 or better and 91% 20/40 or better at 6 months postoperatively. These results exceed the FDA effectiveness target for UCVA for hyperopia.

Posterior chamber lenses for high myopia

Ninety-four percent of eyes achieved an UCVA of 20/40 or better at 3 months, exceeding the FDA effectiveness target for UCVA for high myopia. This was the only follow-up time point that was reported, and it was based on only one study with a limited sample size [Shen et al. (33), 36 eyes], thus results must be interpreted with caution.

Predictability of Manifest Refraction Spherical Equivalent

Predictability of MRSE was reported in eight studies (13;15;16;24;25;28;29;38). Weighted means were calculated for high myopia (Table 24), but as only one study for each lens type was identified for hyperopia, results could not be pooled for high hyperopia (Table 25).

Iris-fixated lenses for high myopia

The predictability trends for high myopia are similar to those for all myopia. Predictability improved over the first 12 months, especially over the first few months. After 3 months, 56% to 74% of eyes were within ± 0.5 D of emmetropia and almost all eyes were within ± 2.0 D. At all time points beyond 1 month, the results exceeded the FDA effectiveness targets for predictability for high myopia. The results at 60 months are based on a small number of eyes (19 eyes), so these values must be interpreted with caution.

Posterior chamber lenses for high myopia

Fifty percent to 60% of eyes were within ± 0.5 D of the emmetropia at all time points, and almost all eyes (about 95%) were within ± 2.0D. At all time points, the results exceeded the FDA effectiveness target for predictability for high myopia.

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[11] FDA target for UCVA for high myopia (applies to eyes with preoperative BSCVA of 20/20 or better):
- At least 75% of eyes achieve UCVA of 20/40 or better

Table 24: UCVA for Iris-Fixated and Posterior Chamber Lenses for High Refractive Errors

Time (months)	UCVA (Snellen VA)	Iris-Fixated Lenses				Posterior Chamber Lenses	
		High Myopia		High Hyperopia		High Myopia	
		Mean (% eyes)	N eyes (no. studies)	Mean (% eyes)	N eyes (no. studies)	Mean (% eyes)	N eyes (no. studies)
3	≥ 20/20						
	≥ 20/40	80.0	25 (1)			94.4	36 (1)
4	≥ 20/20	20.4	93 (1)				
	≥ 20/40	79.6	93 (1)				
6	≥ 20/20	17.4	69 (1)	22.7	22 (1)		
	≥ 20/40	82.6	69 (1)	90.9	22 (1)		
12	≥ 20/20	24.6	61 (1)				
	≥ 20/40	93.4	61 (1)				
24	≥ 20/20	10.5	38 (1)				
	≥ 20/40	84.2	38 (1)				
60	≥ 20/20	73.7	19 (1)				
	≥ 20/40	94.7	19 (1)				

UCVA refers to uncorrected visual acuity; VA, visual acuity

High Hyperopia

Iris-fixated lenses for high hyperopia

Predictability of MRSE was only available for 6 months postoperatively. One hundred percent of eyes achieved predictability within ± 2.0 D of emmetropia and 60% of eyes were within ± 0.5 D. These results exceeded the FDA effectiveness targets for predictability for hyperopia.

Posterior chamber lenses for high hyperopia

Ten years following implantation of the pIOL, 81% of eyes were within 0.5 D of emmetropia and more 100% within 2.0 D. These results exceeded the FDA effectiveness targets for predictability of hyperopia.

Table 25: Predictability for Iris-Fixated and Posterior Chamber Lenses for High Myopia

Time (months)	Predictability (D)	Iris-fixated lenses for high myopia			Posterior chamber lenses for high myopia		
		Weighted mean (% eyes)	FDA Target for High Myopia	N eyes (no. studies)	Weighted mean† (% eyes)	FDA Target for High Myopia	N eyes (no. studies)
1	within ± 0.5	28.6	×	56 (2)			
	within ± 1.0	55.4	×	56 (2)			
	within ± 2.0	92.9	✓	56 (2)			
3	within ± 0.5	37.0	✓	54 (2)			
	within ± 1.0	68.5	✓	54 (2)			
	within ± 2.0	94.4	✓	54 (2)			
6	within ± 0.5	56.7	✓	104 (2)	56.5	✓	377 (1)
	within ± 1.0	81.7	✓	104 (2)	84.1	✓	377 (1)
	within ± 2.0	97.1	✓	104 (2)	94.2	✓	377 (1)
12	within ± 0.5	61.9	✓	97 (2)	58.2	✓	340 (1)
	within ± 1.0	86.6	✓	97 (2)	81.8	✓	340 (1)
	within ± 2.0	99.0	✓	97 (2)	95.9	✓	340 (1)
24	within ± 0.5	55.9	✓	59 (2)	53.2	✓	218 (1)
	within ± 1.0	74.6	✓	59 (2)	77.5	✓	218 (1)
	within ± 2.0	94.9	✓	59 (2)	95.0	✓	218 (1)
60	within ± 0.5	73.7	✓	19 (1)			
	within ± 1.0	94.7	✓	19 (1)			
	within ± 2.0	94.7	✓	19 (1)			

D refers to D; no., number

†Weighted means were calculated from the ITM 2003 study (24) which provided predictability results stratified into 3 groups (<−7 D, −7 to −10 D, and <−10 D). Values from the latter 2 groups were combined using the group sample size as weights to calculate the values reported in this table.

Note, the rest of the severity stratified analyses use <−6 D as the cut-off for severe and this is <−7 D.

Table 26: Predictability for Iris-Fixated and Posterior Chamber Lenses for High Hyperopia

Time (months)	Predictability (D)	Iris-fixated lenses for high hyperopia			Posterior chamber lenses for high hyperopia		
		Mean (% eyes)	FDA Target for High Myopia	N eyes (no. studies)	Mean (% eyes)	FDA Target for High Myopia	N eyes (no. studies)
6	within ± 0.5	59.1	✓	22 (1)			
	within ± 1.0	86.4	✓	22 (1)			
	within ± 2.0	100.0		22 (1)			
120	within ± 0.5				81.0	✓	57 (1)
	within ± 1.0				96.0	✓	57 (1)
	within ± 2.0				100.0		57 (1)

D refers to D; no., number

Efficacy Index

Weighted mean EIs could not be calculated for high myopia or hyperopia because only a few studies reported this outcome and reported time points did not overlap across studies/lens types.

Iris-fixated lenses for high myopia and hyperopia

The EI for high myopia ranged from 0.43 to .86 over the 5 year follow-up period. The results at 3 and 5 years are based on one study with a small sample size (high myopia: 3 years, 20 eyes; 5 years, 19 eyes; high hyperopia: 3 years, 10 eyes), so results must be interpreted with caution. EI decreased over time from 0.76 at 6 months to 0.67 at 3 years, but the statistical significance of this trend is unknown.

Posterior chamber lenses for high myopia

EI was greater than 0.90 at 1 and 2 years follow-up, but these results are based on one study with a small sample size (12 eyes at 2 years), thus must again be interpreted with caution.

Table 27: Efficacy Index for Iris-Fixated and Posterior Chamber Lenses for High Myopia and Hyperopia

Time (months)	Iris-Fixated Lenses				Posterior Chamber Lenses	
	High Myopia		High Hyperopia		High Myopia	
	EI	N eyes (no. studies)	EI	N eyes (no. studies)	EI	N eyes (no. studies)
6	0.84	93 (1)	0.76	22 (1)		
12	0.86	93 (1)	0.73	17 (1)	0.90	36 (1)
24	0.43	20 (1)	0.69	15 (1)	0.94	12 (1)
36	0.43	20 (1)	0.67	10 (1)		
60	0.63	19 (1)				

Safety: Change in Best Spectacle Corrected Visual Acuity

High Myopia

Weighted means could not be calculated for BSCVA for high myopia because only a few studies reported this outcome, and the reported time points did not overlap across studies. Furthermore, data was only available for iris-fixated lenses for high myopia (see Table 28 and Figure 8).

No eyes lost two or more lines of BSCVA, so the FDA safety target for loss of BSCVA was met. About 80% to 85% of eyes did not experience a clinically significant change in BSCVA, while the other 15% to 20% gained two or more lines of BSCVA. At 4 months, however, 43% of eyes reported a gain in two or more lines of BSCVA, but since the result is substantially higher than the other results, it must be considered with caution.

Table 28: Change in Best Spectacle Corrected Visual Acuity for Iris-Fixated Lenses for High Myopia

Time (months)	N eyes	Change in BSCVA (% of eyes)						
		Loss ≥ 2 Lines	Loss 2 Lines	Loss 1 Line	No Change	Gain 1 Line	Gain 2 Lines	Gain ≥ 2 lines
4	93	0.0	0.0	0.0	40.9	16.1	20.4	43.0
6	69	0.0	0.0	7.2	30.4	42.0	18.9	18.9
60	19	0.0	0.0	0.0	26.3	57.8	15.8	15.8

BSCVA refers to best spectacle corrected visual acuity

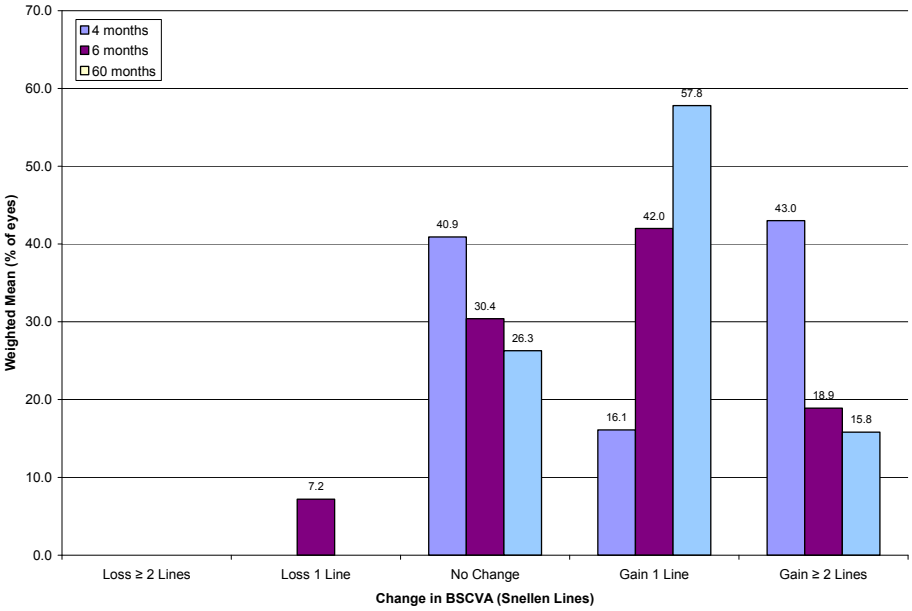

Figure 8: Change in Best Spectacle Corrected Visual Acuity over Time for Iris-Fixated Lenses for High Myopia

High Hyperopia

Weighted means could not be calculated for BSCVA for high hyperopia as only two studies reported this outcome and the reported time points did not overlap (Table 29 and Figures 9 and 10).

No eyes lost 2 or more lines of BSCVA, so the FDA safety target for loss of BSCVA was met. About 80% to 91% of eyes did not experience a clinically significant change in BSCVA[12], while the other 9% to 20% gained 2 or more lines of BSCVA. The results for iris-fixated lenses for based on only one study with a small sample size (10 eyes at 3 years), so these results may be less accurate.

[12] A clinically significant change is defined as a gain or loss of 2 or more Snellen lines of BSCVA. (41)

Table 29: Change in Best Spectacle Corrected Visual Acuity for Iris-Fixated and Posterior Chamber pIOLs for High Hyperopia

Time (months)	N eyes	Change in BSCVA (% of eyes)						
		Loss ≥ 2 Lines	Loss 2 Lines	Loss 1 Line	No Change	Gain 1 Line	Gain 2 Lines	Gain ≥ 2 lines
Iris-fixated lenses								
6	22	0.0	0.0	13.6	68.2	9.1	NR	9.1
36	10	0.0	0.0	40.0	30.0	10.0	NR	20.0
Posterior chamber lenses								
120	57	0.0	0.0	1.8	64.4	15.2	8.3	17.5

BSCVA refers to best spectacle corrected visual acuity; NR, not reported

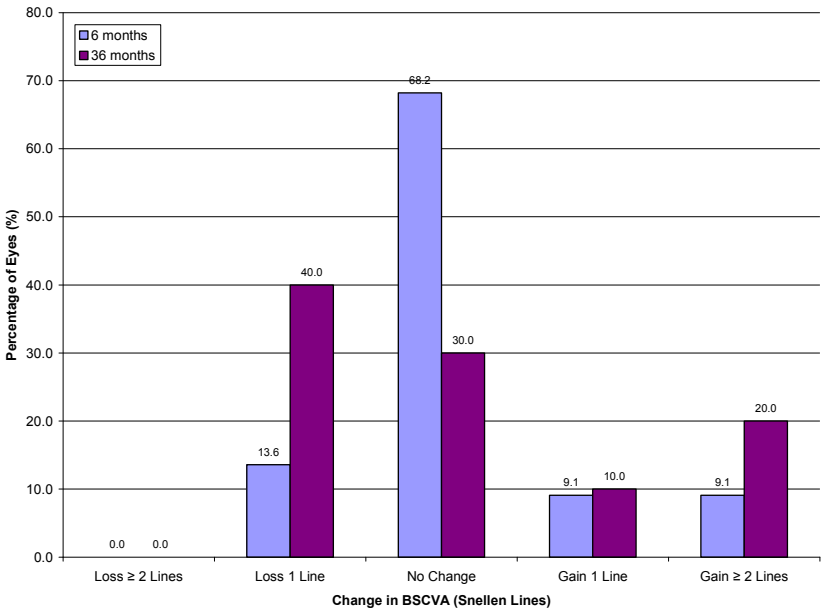

Figure 9: Change in Best Spectacle Corrected Visual Acuity over Time for Iris-Fixated Lenses for High Hyperopia

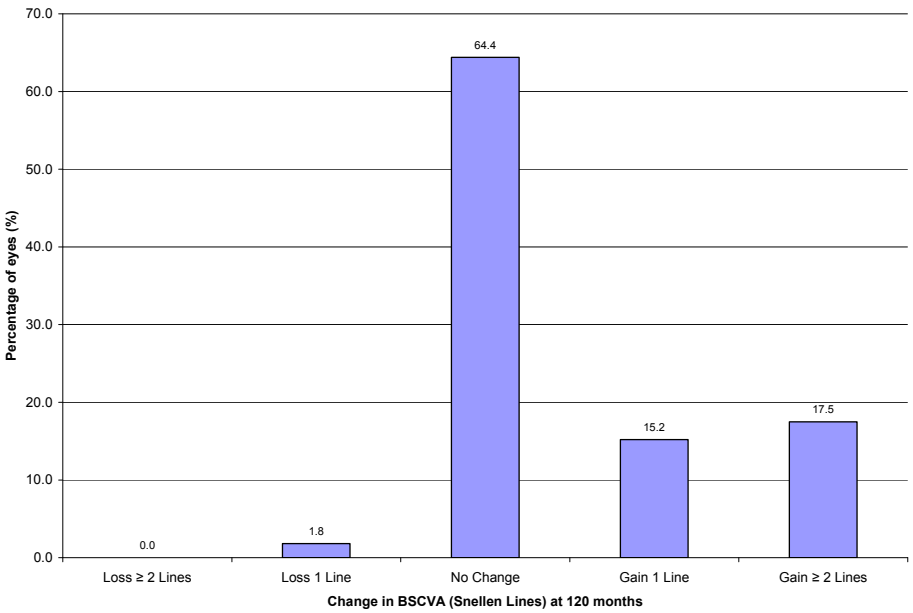

Figure 10: Change in Best Spectacle Corrected Visual Acuity at 120 Months for Posterior Chamber Lenses for High Hyperopia

Safety: Safety Index

High Myopia and Hyperopia

The SI was only reported in two studies, one for high myopia and one for low myopia, thus weighted means could not be calculated (Table 30). Over time, the SI was higher for posterior chamber lenses for high myopia compared with iris-fixated lenses for high hyperopia, but the statistical significance of this trend is unknown. The results for high myopia are based on one study with a very small sample size (10 eyes at 3 years), so these results must be interpreted with caution.

Table 30: Safety Index for High Refractive Errors

Time (months)	Iris-Fixated Lenses for High Hyperopia		Posterior Chamber Lenses for High Myopia	
	SI	N eyes (no. studies)	SI	N eyes (no. studies)
4			1.18	93 (1)
6	1.01	22 (1)		
12	.95	17 (1)	1.12	94 (1)
24	.95	15 (1)	1.19	95 (1)
36	.87	10 (1)		

No. refers to number; SI, safety index

General Limitations: Efficacy Studies

Several limitations apply to most or all of the included case series. First, eyes were used as the unit of analysis rather than the number of patients in all 20 studies. Many of the patients enrolled in the studies received pIOLs in both eyes and the results from each eye are included in the reported results. This resulting study sample sizes may be close to double the number of participating patients. Measurements from two eyes of the same individual are, however, correlated (within-subject correlation), violating the assumption of independent data units on which most standard statistical significance tests are based. Thus, the variability of the data is decreased and the statistical power of the study is increased, which may result in falsely precise confidence intervals and small *P* values. (44-46) Stulting et al. (26) took within-subject correlation into account in their analysis and included results for only the first eye that received the pIOL in the refractive outcomes (data from all eyes were included for safety outcomes). The other 19 studies did not attempt to correct for within-subject correlations. Accordingly, reported results may be falsely precise and some of the observed statistically significant results may be spurious.

Second, many of the studies exhibited high loss to follow-up (> 30%), especially beyond 6 or 12 months. This limits our understanding of long-term outcomes as well our confidence in the results. While some of the retrospective case series had very good follow-up, this was generally because patients were only included in the study if they had a minimum follow-up length. This selection bias could affect the results if patients with poorer outcomes were more likely to have shorter follow-up durations than those with good outcomes, for instance if patients have the pIOLs removed before the minimum time period requirement.

Third, selection bias was a potential concern in some of the studies. Ten studies did not enrol consecutive patients, which could be a concern if the enrolled patients did not represent the average patient seeking pIOL implantation, but rather a subset of patients who were more likely to experience the best outcomes after pIOL implantation.

Finally, the literature is limited by the study design itself. All 20 studies are pre-post case series and do not have a contemporaneous control group, which decreases the quality of evidence. This is addressed more in the next section on the GRADE Quality of Evidence.

GRADE Quality of the Evidence: Efficacy Studies

A summary of the GRADE quality of the evidence for each lens type and refractive error is provided in Table 31. Due to serious limitations in study quality and sparse data for some outcomes (further details can be found in the GRADE tables in Appendix 3), the pIOL efficacy literature was determined to be of low or very low quality.

Table 31: Summary of GRADE Quality of Evidence for Efficacy Studies

Lens Type	Refractive Error	Outcome	Number of Studies	GRADE Quality of Evidence
Iris-fixated pIOLs	Myopia	UCVA	7	Low
		Predictability	7	Very low
		BSCVA	5	Low
		Efficacy Index	5	Low
		Safety Index	4	Very low
		MRSE	8	Low
		Adverse Events	7	Very low
	Hyperopia	UCVA	1	Very low
		Predictability	1	Very low
		BSCVA	1	Very low
		Efficacy Index	1	Very low
		MRSE	1	Very low
		Adverse Events	1	Very low
Posterior chamber pIOLs	Myopia	UCVA	4	Low
		Predictability	2	Very low
		BSCVA	2	Low
		Efficacy Index	3	Low
		Safety Index	2	Very low
		MRSE	4	Low
		Adverse Events	5	Very low
	Hyperopia	Predictability	1	Very low
		BSCVA	1	Very low
		MRSE	1	Very low
		Adverse Events	1	Very low
	Myopic Astigmatism	UCVA	2	Low
		Predictability	2	Very low
		BSCVA	2	Low
		Efficacy Index	1	Very low
		Safety Index	1	Very low
		MRSE	2	Low
		Refractive Cylinder	2	Low
		Adverse Events	2	Very low

BSCVA refers to best spectacle corrected visual acuity; MRSE, manifest refraction spherical equivalent; UCVA, uncorrected visual acuity

Comparative Studies

Seven studies compared *posterior chamber* pIOLs with other surgical techniques (summarized in Table 32). Of note, only one RCT was found to meet the inclusion criteria. Characteristics of these studies are described in Table 32. The results for each study are examined below. Limitations specific to individual studies are included within the study summaries, while those limitations that apply to most or all of the studies are discussed in the General Limitations section (page 75). No studies comparing iris-fixated pIOLs with other surgical techniques that that met the inclusion criteria were identified.

Phakic Intraocular Lenses Compared with LASIK for Myopia

Table 33 provides a summary of the 1 week, 1 month, 6 months, and 12 months postoperative results from the studies which compared pIOLs with LASIK for myopia.

Moderate Myopia: Sanders and Vukich, 2006 (47)

Sanders and Vukich, 2006 (47) conducted a case series that compared pIOLs with LASIK for moderate myopia (−4.00 – −7.88 D). The LASIK group consisted of 1,678 eyes from patients who received their surgery at the Davis Duehr Eye Center in Wisconsin, while the ICL group consisted of 144 eyes from the US FDA multicenter clinical trial of the Implantable Collamer Lens (STAAR Surgical). (47) The study groups were significantly different with respect to a several characteristics including mean age ($P < .001$), preoperative myopia ($P < .001$), cylinder ($P < .001$), and UCVA ($P < .001$).

Uncorrected Visual Acuity

The proportion of eyes that achieved an UCVA of 20/20 or better was significantly greater in the LASIK group at 1 day (LASIK, 38%; pIOL, 28%; $P = .019$). There was no significant difference between the groups at 1 week and 1 month, but at 6 months the proportion of eyes seeing 20/20 or better was significantly higher in the pIOL group. (47)

Beyond the first postoperative day when the proportion of eyes that achieved an UCVA of 20/40 was significantly higher in LASIK group (pIOL, 69%; LASIK, 92%; $P < .001$), there were no significant differences in the proportion of eyes that achieved an UCVA of 20/40 or better between the two groups. The FDA effectiveness targets for UCVA for low and high myopia were met or exceeded in the LASIK group at all time points and in the pIOL group after 1 day. (17;18;47)

Predictability

The proportion of eyes that achieved refraction within ± 0.5 D of emmetropia was similar in both groups at all time points, except for 6 months at which time the pIOL group was significantly higher than the LASIK group. Similarly, predictability within ± 1.0 D was significantly different between the two groups only at the 6 month visit. Predictability of the MRSE within ± 0.5 and 1.0 D met the FDA targets for high myopia in both the LASIK and pIOL groups. (17;18;47)

Manifest Refraction Spherical Equivalent

The preoperative mean MRSE was significantly higher in the pIOL group (pIOL, −6.4 ± .009 D; LASIK, −5.6 ± .03 D; $P < .001$). At 1 week postoperatively, the mean MRSE was significantly lower (closer to emmetropia) in the LASIK group than the pIOL group. At 3 and 6 months, however, the mean MRSE was lower in the pIOL group and this difference was significant at 6 months. (47)

Table 32: Characteristics of Included Comparison Studies

Study	Study Design	Comparison	Refractive Error	Country	Number of Sites	Number of Eyes (Number of Patients)	Follow-Up Duration (months)
Schallhorn et al., 2007 (8)	RCT	pIOL vs. PRK	myopic astigmatism	USA	1 site	pIOL: 43 (23) PRK: 45 (23)	12
Arne, 2004 (48)	Comparative case series†	pIOL vs. CLE	myopia	France	1 site	pIOL: 41 (21) CLE: 36 (18)	12
Kamiya et al., 2008 (49)	Comparative case series†	pIOL vs. wave-front guided LASIK	myopic astigmatism	Japan	1 site	pIOL: 30 (18) LASIK: 24 (17)	6
Sanders and Sanders, 2008 (50)	Retrospective comparative case series	pIOL vs. custom ablation LASIK‡	myopic astigmatism	USA,	pIOL: data from FDA study LASIK: data from FDA premarket approval applications	pIOL: 210 (124) LASIK: ?	6§
Sanders, 2007 (40)	Mixed comparative case series‖	pIOL vs. LASIK	myopia	USA	pIOL: data from FDA study LASIK: 1 site	pIOL: 164 (106) LASIK: 164 (106)	6
Sanders and Vukich., 2006 (47)	Mixed comparative case series‖	pIOL vs. LASIK	myopia	USA	pIOL: data from FDA study LASIK: 1 site	pIOL: 144 (101) LASIK: 1678 (976)	6
Sanders and Vukich, 2003 (39)	Mixed comparative case series‖	pIOL vs. LASIK	myopia	USA	pIOL: data from FDA study LASIK: 1 site	pIOL: 210 (121) LASIK: 559 (358)	12

CLE refers to clear lens extraction; LASIK; laser-assisted in-situ keratomileusis; pIOL, phakic intraocular lens; PRK, photorefractive keratectomy; RCT, randomized controlled trial

†Unable to determine whether it is a prospective or retrospective case series.

‡LASIK data obtained from published Summaries of Safety and Effectiveness for 2 wavefront-guided laser systems. The results for the 2 systems were reported separately.

§ Data for the VISX system for low myopes was only available for the 3 month endpoint.

‖pIOL group was followed prospectively while LASIK group was retrospective

Table 33: Summary of Outcomes from the Studies Comparing pIOLs with LASIK for Myopia

Author, Year	1 wk			1 month			6 months			12 months		
	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value
UCVA ≥ *20/20*, n/N (%)												
Sanders and Vukich, 2006 (47) *Moderate myopia*	66/137 (48)	674/1233 (55)	.150	77/139 (55)	735/1256 (58)	.526	90/134 (67)	688/1210 (57)	.027			
Sanders, 2007 (40) *Moderate to high myopia*	78/159 (49)	60/134 (45)	.483	96/164 (59)	59/136 (43)	.011	102/161 (63)	79/162 (49)	.010			
Sanders and Vukich, 2003 (39) *High myopia*	77/204 (38)	108/420 (26)	.002	87/204 (43)	121/392 (31)	.005	131/376 (35)	98/197 (50)	< .001	96/185 (52)	36/100 (36)	.01
UCVA ≥ *20/40*, n/N (%)												
Sanders and Vukich, 2006 (47)	127/137 (93)	1184/1233 (96)	.076	133/139 (96)	1191/1256 (95)	.839	129/134 (96)	1116/1210 (92)	.114			
Sanders, 2007 (40)	149/159 (94)	123/134 (92)	.650	158/164 (96)	123/136 (90)	.055	159/161 (99)	154/162 (95)	.104			
Sanders and Vukich, 2003 (39)	173/204 (85)	356/420 (85)	1.00	182/204 (89)	320/392 (82)	.02	305/376 (81)	171/197 (87)	.10	87/100 (87)	165/185 (89)	.57
Mean MRSE, D ± SD												
Sanders and Vukich, 2006 (47)	−.24 ± .04	−.01 ± .01	< .001	−.15 ± .03	−.24 ± .03	.89	−.08 ± .03	−.35 ± .02	< .001			
Sanders, 2007 (40)	−.25 ± .43	−.18 ± .67	.093	−.14 ± .38	−.25 ± .69	.579	−.09 ± .31	−.33 ± .65	.001			
Sanders and Vukich, 2003 (39)	−.39	−.06	NR	−.27	−.18	NR	−.27	−..33	NR	−.30	−.30	NR
Predictability within ± .5 D, n/N (%)												
Sanders and Vukich, 2006 (47)	104/134 (78)	982/1236 (79)	.654	109/138 (79)	935/1257 (76)	.462	104/132 (79)	846/1212 (70)	.034			
Sanders, 2007 (40)	123/156 (79)	101/134 (75)	.487	131/163 (80)	99/136 (73)	.131	134/158 (85)	108/162 (67)	< .001			
Sanders and Vukich, 2003 (39)	138/202 (68)	250/420 (60)	.03	143/203 (70)	227/393 (58)	.002	127/196 (65)	200/378 (53)	.007	127/184 (69)	57/100 (57)	.04
Predictability within ± 1.0 D, n/N (%)												
Sanders and Vukich, 2006 (47)	130/134 (97)	1184/1236 (96)	.648	129/138 (93)	1163/1257 (92)	.864	128/132 (97)	1063/1212 (88)	< .001			
Sanders, 2007 (40)	152/156 (97)	124/134 (93)	.059	154/163 (94)	123/136 (90)	.191	154/158 (97)	143/162 (88)	.002			
Sanders and Vukich, 2003 (39)	178/202 (88)	358/420 (85)	.38	183/203 (90)	307/393 (78)	< .001	177/196 (90)	287/378 (76)	< .001	172/184 (94)	79/100 (79)	< .001

Author, Year	1 wk			1 month			6 months			12 months		
	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value
Loss of ≥ Snellen lines of BSCVA, n/N (%)												
Sanders and Vukich, 2006 (47)	1/134 (.7)	69/1142 (6)	.008	0/138 (0)	25/1205 (2)	.101	0/133 (0)	17/1168 (1)	.245			
Sanders, 2007 (40)	1/156 (.6)	13/134 (10)	< .001	0/163 (0)	9/136 (7)	.001	0/157 (0)	2/162 (1)	.499			
Sanders and Vukich, 2003 (39)	5/203 (2)	45/401 (11)	< .001	1/203 (.5)	24/380 (6)	< .001	0/196 (0)	8/361 (2)	.05	0/184 (0)	0/94 (0)	–
Gain of ≥ Snellen lines of BSCVA, n/N (%)												
Sanders and Vukich, 2006 (47)	4/134 (3)	8/1142 (.7)	.029	7/138 (5)	11/1205 (.9)	.001	5/133 (4)	10/1168 (.8)	.013			
Sanders, 2007 (40)	4/156 (3)	2/134 (2)	.690	7/163 (4)	5/136 (4)	1.000	5/157 (3)	4/162 (3)	.747			
Sanders and Vukich, 2003 (39)	11/203 (5)	5/401 (1)	.005	12/203 (6)	10/380 (3)	.07	13/196 (7)	10/361 (3)	.04	9/184 (5)	2/94 (2)	.34
Mean Refractive Cylinder, D ± SD												
Sanders and Vukich, 2006 (47)	.54 ± .05	.25 ± .01	< .001	.54 ± .05	.27 ± .02	< .001	.52 ± .05	.25 ± .01	< .001			
Sanders, 2007 (40)	.56 ± .56	.23 ± .31	< .001	.52 ± .56	.24 ± .36	<.001	.50 ± .53	.25 ± .31	< .001			
Sanders and Vukich, 2003 (39)												
Stability of Refraction (≤ .5 D), n/N (%)	**1 week to 1 month**			**1 to 6 months**			**6 months to 1 year**					
Sanders and Vukich, 2006 (47)	117/128 (91)	737/898 (82)	.008	119/127 (94)	693/849 (82)	< .001						
Sanders, 2007 (40)	140/155 (90)	85/111 (77)	.003	146/157 (93)	110/134 (82)	.006						
Sanders and Vukich, 2003 (39)	171/197 (87)	205/306 (67)	< .001	197/192 (93)	198/275 (72)	< .001	192/197 (98)	268/306 (88)	< .001			
Stability of Refraction (≤ 1.0 D), n/N (%)	**1 week to 1 month**			**1 to 6 months**			**6 months to 1 year**					
Sanders and Vukich, 2006 (47)	126/128 (98)	855/898 (95)	.108	126/127 (99)	812/849 (96)	.050						
Sanders, 2007 (40)	153/155 (99)	102/111 (92)	.009	156/157 (99)	130/134 (97)	.184						
Sanders and Vukich, 2003 (39)	192/197 (98)	268/306 (88)	< .001	192/192 (100)	256/275 (93)	< .001	181/183 (99)	85/93 (91)	.003			

BSCVA refers to best spectacle corrected visual acuity; D, diopters; MRSE, manifest refraction spherical equivalent; NR, not reported; RS, refractive surgery (LASIK in this table); SD, standard deviation; UCVA, uncorrected visual acuity

Stability of Refraction

The stability of refraction (proportion of eyes with ≤ 0.5 change) was significantly greater in the pIOL group than the LASIK group at all time points. Stability of refraction within 1.0 D was high in both groups (≥ 95%) and only significantly better in the pIOL group between 1 and 6 months. (47) Both groups stability within 1.0 D results met or exceeded the FDA effectiveness target for stability for low and high myopia. (17;18;47)

Refractive Cylinder

The preoperative manifest cylinder was significantly higher in the LASIK group (LASIK, .88 ± .02 D; PIOL, .59 ± .05 D; $P < .001$); however, LASIK was more effective at reducing the cylinder. At all postoperative time points, the cylinder was significantly lower in the LASIK group. (47)

Best Spectacle Corrected Visual Acuity

While clinically significant losses of BSCVA (≥ 2 Snellen lines) were higher in the LASIK group than the pIOL group at all time points, the difference was only statistically significant at 1 week ($P = .008$). At 1 week, loss of BSCVA in the LASIK group was higher than the FDA safety value, but was less than 5% at all other time points for both groups. (47)

Clinically significant gains in BSCVA were significantly higher in the pIOL group than the LASIK group at all time points. (47)

Additional Refractive Surgeries

In the LASIK group, 416 eyes (25%) received additional LASIK re-treatments to enhance refractive correction. (47) None of the eyes in the pIOL group received LASIK procedures to enhance vision. (47)

Adverse Events

In the pIOL group, two pIOLs were replaced in the first week because they were too large and one pIOL was repositioned twice. In addition, one asymptomatic lens opacity [LOCS III anterior or posterior subcapsular opacity score ≥ to trace (1+) was observed]. (47)

In the LASIK group, 81 eyes (4.8%) developed diffuse lamellar keratitis. Striae in the corneal flap were observed in 30 eyes (1.8%), which were treated in 24 of these eyes by lifting the flap. One free cap (.06%) was observed, but this was not associated with any loss of BSCVA. (47)

Sanders, 2007 (40)

Sanders (40) also conducted a second case series that compared pIOLs and LASIK for eyes with moderate myopia (−3.0 to −7.88 D). This study is similar to the one described above and includes the same patients; however, the LASIK patients are a subset of the LASIK group (164 eyes) that was selected to match the pIOL group on age, gender, and spherical equivalent refraction. (40) The groups were well matched for age ($P = .85$), gender ($P = .3$), and mean preoperative MRSE ($P = .79$); however, the mean preoperative manifest cylinder was significantly higher in the LASIK group than the pIOL group (LASIK, .74 D; pIOL, .58 D; $P = .037$). (40)

Uncorrected Visual Acuity

The proportion of eyes achieving an UCVA of 20/20 or better was higher at all time points in the pIOL group than the LASIK group (this trend was significant at 1 and 6 months). (40) At all time points beyond 1 day, at least 90% of eyes achieved an UCVA of 20/40 or better in both groups. (40) Both groups exceeded the FDA effectiveness targets for UCVA for high and low myopia at all time points after 1 day.

Predictability of Manifest Refraction Spherical Equivalent

At all time points, predictability of MRSE within ± 0.5 and 1.0 D was higher in the pIOL group than the LASIK group, which reached significance at the 6 month time point. In the LASIK group, under-correction was common, especially in patients with higher myopia (< −6 D). (40) Both groups exceeded the low and high myopia FDA effectiveness targets for predictability within ± 0.5 and 1.0 D at all time points.

Stability of Manifest Refraction Spherical Equivalent

Stability of MRSE (change ≤ .5 D) was significantly higher in the pIOL group at all time points. Stability (change ≤ 1.0 D) was high in both groups (>92%), but significantly better in the pIOL group for the first month. (40) Stability within ± 1.0 D exceeded the high myopia FDA effectiveness target for stability after 1 month in the LASIK group and at all time points in the pIOL group.

Manifest Cylinder

The preoperative manifest cylinder was significantly higher in the LASIK group (LASIK, .74 ± .66 D, pIOL, .58 ± .56 D, $P = .037$). At all postoperative time points, however, the cylinder was significantly lower in the LASIK group compared with the pIOL group. (40)

Manifest Refraction Spherical Equivalent

There was no significant difference in the preoperative MRSE between the two groups (pIOL, −6.01 ± 1.40; LASIK, −6.01 ± 1.33; $P = .794$). While both groups achieved large decreases in MRSE, at 6 months postoperatively the MRSE was significantly lower in the pIOL group. (40)

Defocus Equivalent Refraction[13]

At 6 months, the proportion of eyes with defocus equivalent refraction less than or equal to 0.5, 1.0, or 2.0 D was higher in the LASIK group, but these differences were not significant. In both groups, 100% of eyes achieved a defocus equivalent refraction of less than or equal to 3.0 D. (40)

Best Spectacle Corrected Visual Acuity

Clinically significant losses of BSCVA were higher in the LASIK group at all time points and the difference was statistically significant at 1 week and 1 month, when the losses in the LASIK group exceeded the FDA safety targets. There were no significant differences between the LASIK and pIOL groups in terms of gains in two or more lines of BSCVA, which occurred in 2% to 4% of eyes in both groups at all time points. (40)

Additional Refractive Surgeries

In the LASIK group, 15 eyes (9.1%) received additional LASIK treatments to further enhance the refractive correction. The study protocol did not allow for patients in the pIOL group to receive enhancement procedures. (40)

Adverse Events

In the pIOL group, one lens (0.6%) was replaced during the first week postoperatively as it was too long, while another lens (0.6%) was repositioned twice due to improper placement in the eye. Seven eyes (3.7%) received additional YAG iridotomies, six to treat acute increases in intraocular pressure and one in an eye (0.6%) that did not receive the procedure preoperatively. (40)

[13] The defocus equivalent refraction is a measure of the refractive state of the eye which takes into account residual astigmatism and is calculated as the sphere (respecting the sign) plus half the cylinder (respecting the sign) plus half the cylinder (ignoring the sign). (42)

In the LASIK group, 11 eyes (6.7%) developed diffuse lamellar keratitis and one of these eyes lost two lines of BSCVA. Striae in the corneal flap were observed in three eyes (1.8%) and were treated in two of these eyes by lifting the flap. Very thin flaps were observed in two eyes, while one eye had corneal ectasia. (40)

Limitations

An important limitation in this study is that despite matching the study groups on some variables, significant differences between the groups remained. The mean preoperative refractive cylinder was significantly higher in the LASIK group (cylinder: 0.74 D; range: 0.00 – 2.75 D) than the pIOL group (cylinder: 0.58 D; range: 0.00 – 2.50 D). The age limits for inclusion were also higher in the LASIK group (patients 21 to 50 years of age vs. 21 to 45 years of age) resulting in additional differences between the groups. (40)

High Myopia: Sanders and Vukich, 2003 (39)

Sanders et al. (39) conducted a case series that compared pIOLs with LASIK for high myopia (−8 to −12 D). The LASIK group consisted of 559 eyes from patients who had LASIK performed at the Davis Duehr Eye Center in Wisconsin between December 1998 and June 2001. The pIOL group consisted of 210 eyes from the US FDA Implantable Collamer Lens (STAAR Surgical Company) multicenter trial. The LASIK patients were significantly older (mean age: LASIK, 38.8 ± 9.41 years; pIOL, 36.3 ± 5.96 years; $P = .001$) and had lower myopia (mean preoperative MRSE: LASIK, −9.1 ± 0.97 D; pIOL, −9.8 ± 1.7 D; $P < .001$). (39)

Uncorrected Visual Acuity

The proportion of eyes that achieved an UCVA of 20/20 or better was significantly higher in the pIOL group at all time points. After 1 day, more than 80% of eyes in both groups achieved an UCVA of 20/40 or better. Both groups exceeded the FDA effectiveness target for UCVA for high myopia. (39)

Predictability of Manifest Refraction Spherical Equivalent

The proportion of eyes that achieved refraction within ± .5 D of emmetropia was significantly higher at all time points in the pIOL group. Similarly, after 1 week, the proportion of eyes that achieved refraction within ± 1.0 D of emmetropia was significantly higher at all time points in the pIOL group. (39) Both groups exceeded the low and high myopia FDA effectiveness targets for predictability within ± 0.5 and 1.0 D.

Stability of Manifest Refraction Spherical Equivalent

The stability of refraction was significantly higher in the pIOL group at all time points for changes of less than 0.5 D and 1.0 D. (39) The stability results within 1.0 D exceeded the low and high myopia FDA effectiveness targets for stability of MRSE at all time points in the pIOL group. The LASIK group, however, did not meet the FDA stability targets at any time point.

Best Spectacle Corrected Visual Acuity

Loss of two or more lines of BSCVA was significantly higher in the LASIK group at all time points except at 1 year. (39) At 1 week and 1 month, the LASIK group exceeded the FDA safety target for loss of BSCVA. The proportion of eyes that gained two or more lines of BSCVA was higher in the pIOL group at all time points, and significantly higher at the 1 week and 6 months. (39)

Additional Refractive Surgeries

Eleven eyes (5.2%) in the pIOL group underwent additional refractive surgeries (LASIK or PRK) after pIOL implantation. In the LASIK group, 128 eyes (23%) were received additional LASIK treatments to enhance refractive correction. (39)

Adverse Events

Few adverse events were observed in either group. In the pIOL group, one lens was repositioned at 2 weeks. No clinically significant lens opacities or other adverse events were observed. (39) In the LASIK group, 17 eyes (3%) developed diffuse lamellar keratitis and striae in the corneal flap were observed in 17 eyes and were treated in 12 of these eyes. A single free cap (0.2%) was also observed but not associated with any loss of BSCVA. (39)

Limitations

While patient follow-up was high in the pIOL group (88% at 1 year), it was much lower in the LASIK group (18% at 1 year). (39) Unlike the pIOL group, patients in the LASIK group were not enrolled in a clinical trial and were assessed at routine follow-up visits, which patients frequently missed. The 6 month follow-up for the LASIK group was also actually a combination of the 3, 6, and 9 month follow-up visits (if a patient attended more than one of these visits, the later visit was chosen). (39) Based on comparisons of early postoperative visits, patients lost to follow-up were not significantly different than those who were followed for the entire study with regards to changes in BSCVA, UCVA, and predictability. (39)

Phakic Intraocular Lenses Compared with LASIK for Myopic Astigmatism

Table 34 provides a summary of the 1 week, 1 month, 6 months, and 12 months postoperative results from the studies which compared pIOLs with LASIK for myopic astigmatism.

Kamiya et al. 2008 (49)

Kamiya et al. (49) conducted a case series that compared pIOLs with *wavefront-guided* LASIK. Patient recruitment and inclusion criteria for each group were not described in the paper. Patients in the pIOL group had significantly higher myopia (preoperative mean MRSE: pIOL, −10.8 ± 2.4 D, LASIK, −7.9 ± 1.5 D, $P < .001$) and refractive cylinder (preoperative mean cylinder: pIOL, 2.1 ± 0.8 D, LASIK, 1.3 ± 0.4 D, $P < .001$), and significantly worse preoperative UCVA (logMAR UCVA: pIOL, 1.55 ± 0.14, LASIK, 1.43 ± 0.24, $P = .004$).

Uncorrected Visual Acuity

The proportion of eyes that achieved an UCVA of 20/20 or better was higher in the pIOL group at all time points. Uncorrected visual acuity of 20/40 or better was not reported by the study, but the proportion of eyes seeing 20/20 or better uncorrected exceeded the FDA targets for UCVA of 20/40. (49)

Efficacy Index

The efficacy index at 6 months was higher in the pIOL group than the LASIK group (pIOL, 0.87 ± 0.15, LASIK, 0.83 ± 0.23). (49)

Predictability of Manifest Refraction Spherical Equivalent

The proportion of eyes that achieved refraction within ± 0.5 of emmetropia was higher in the pIOL group at all time points. Similarly, the proportion of eyes within ± 1.0 D of targeted refraction was higher in the pIOL group at all times, but the differences between the 2 groups were much smaller. (49) Both the pIOL and LASIK groups meet the low and high myopic astigmatism FDA effectiveness targets for predictability within 0.5 and 1.0 D at all time points.

Table 34: Summary of Outcomes from the Studies Comparing pIOLs with LASIK for Myopic Astigmatism

Author, Year	1 wk			1 month			6 months		
	pIOL	RS	P value	pIOL	RS	P value	pIOL	RS	P value
UCVA ≥ 20/20, n/N (%)									
Kamiya et al., 2008 (49)	97	79	NR	97	88	NR	100	83	NR
Sanders and Sanders, 2008 (50)									
3.0 to 7.0 D							30/32 (94)	VISX: 105/132 (80) Alcon: 100/123 (91)	VISX: .071 Alcon: .109
7.0 to 11.0 D							91/109 (84)	VISX: 55/77 (71) Alcon: 23/28 (82)	VISX: .069 Alcon: 1.00
UCVA ≥ 20/40, n/N (%)									
Kamiya et al., 2008 (49)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sanders and Sanders, 2008 (50)									
3.0 to 7.0 D							31/32 (97)	VISX: 124/132 (4) Alcon: 119/123 (97)	VISX: 1.00 Alcon: 1.00
7.0 to 11.0 D							106/109 (97)	VISX: 75/77 (97) Alcon: 28/28 (100)	VISX: 1.00 Alcon: 1.00
Mean MRSE, D ± SD									
Kamiya et al., 2008 (49)	−0.10 ± 0.26	0.57 ± 0.67	NR	−0.12 ± 0.24	0.32 ± 0.59	NR	−0.13 ± 0.18	−0.60 ± 0.49	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Predictability of MRSE within ± .5 D, %									
Kamiya et al., 2008 (49)	100	67	NR	97	75	NR	100	71	NR
Sanders and Sanders, 2008 (50)									
3.0 to 7.0 D							26/32 (81)	VISX: 102/132 (77) Alcon: 98/123 (80)	VISX: .812 Alcon: 1.00
7.0 to 11.0 D							85/112 (76)	VISX: 55/77 (71) Alcon: 18/28 (64)	VISX: 1.00 Alcon: .235
Mean Refractive Cylinder, D									
Kamiya et al., 2008 (49)	0.68 ± .37	0.49 ± 0.36	NR	0.65 ± 0.37	0.49 ± 0.24	NR	0.47 ± 0.40	0.42 ± 0.24	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author, Year	1 wk			1 month			6 months		
	pIOL	RS	P value	pIOL	RS	P value	pIOL	RS	P value
Predictability of MRSE within ± 1.0 D, %									
Kamiya et al., 2008 (49)	100	83	NR	100	88	NR	100	92	NR
Sanders and Sanders, 2008 (50)									
3.0 to 7.0 D							32/32 (100)	VISX: 124/132 (94) Alcon: 111/123 (90)	VISX: .357 Alcon: .129
7.0 to 11.0 D							109/112 (97)	VISX: 70/77 (91) Alcon: 23/28 (82)	VISX: .094 Alcon: .008
Predictability of refractive cylinder within ± .5 D, %									
Kamiya et al., 2008 (49)	59	75	NR	63	79	NR	78	88	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Predictability of refractive cylinder within ± 1.0 D, %									
Kamiya et al., 2008 (49)	93	96	NR	93	100	NR	96	100	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mean Postoperative Efficacy Index, EI ± SD									
Kamiya et al., 2008 (49)							0.87 ± 0.15	0.86 ± 0.23	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mean Postoperative Safety Index, SI ± SD									
Kamiya et al., 2008 (49)							1.28 ± 0.25	1.01 ± 0.16	NR
Sanders and Sanders, 2008 (50)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gain of ≥ 2 Snellen lines of BSCVA, %									
Kamiya et al., 2008 (49)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sanders and Sanders, 2008 (50)							20%	VISX: 11% Alcon: 2%	< .001†

BSCVA refers to best spectacle corrected visual acuity; D, diopter; MRSE, manifest refraction spherical equivalent; NR, not reported; RS, refractive surgery (LASIK in this table); SD, standard deviation; UCVA, uncorrected visual acuity
†*P* value for pIOL vs. both excimer lasers combined

Manifest Refraction Spherical Equivalent

The MRSE was substantially reduced in both groups at all postoperative follow-up visits. At 1 week, 1 month, and 3 months, the pIOL group was lower (closer to emmetropia) than the LASIK group. At 6 months, however, the LASIK group was closer to emmetropia than the pIOL group. (49)

Stability of Manifest Refraction Spherical Equivalent

Stability of refraction was higher in the pIOL group: the mean change in MRSE from 1 week to 6 months was −0.04 ± .24 D and −0.60 ± 0.49 D in the pIOL and LASIK groups, respectively. (49)

Refractive Cylinder

The postoperative cylinder was lower at all time points in the LASIK group. (49)

The predictability of refractive cylinder correction was higher in the LASIK group at most follow-up visits. The proportion of eyes within ± 0.5 D of the attempted cylinder correction was higher in the LASIK group at almost all time points. The same trend was observed within ± 1.0 D, but the differences between the predictability of the LASIK and pIOL corrections were smaller. (49)

Best Spectacle Corrected Visual Acuity

A clinically significant loss of two or more lines of BSCVA was not observed in either group. Compared with the LASIK group, more eyes in the pIOL group gained two or more lines of BSCVA (LASIK, 4%, pIOL, 13%). (49) The FDA safety target for loss of BSCVA was not exceeded in either group.

Safety Index

The safety index at 6 months was higher in the pIOL group than the LASIK group (pIOL, 1.28 ± .25, LASIK, 1.01 ± 0.16). (49)

Additional Refractive Surgeries

Two eyes (8.3%) in the LASIK group received an additional LASIK treatment to enhance the refractive correction. No eyes in the pIOL group received additional refractive surgeries (49)

Adverse Events

No adverse events were observed in either group. (49)

Limitations

Except for the demographic characteristics, *P* values were not reported in this paper, so the statistical significance of the results is unknown. In addition, the paper reported only a limited description of participant recruitment and inclusion criteria and no description of loss to follow-up.

Sanders and Sanders, 2008 (50)

Sanders and Sanders (50) conducted a case series comparing pIOLs and *custom ablation* LASIK for the treatment of myopic astigmatism. The pIOL group consisted of 210 eyes from 124 patients that participated in the US FDA multicenter clinical trial of the Toric Implantable Collamer Lens (STAAR Surgical Company). The LASIK data was derived from published Safety and Effectiveness Summaries of the approved Premarket Approval Applications (obtained from the FDA through the Freedom of Information Act) for the VISX CustomVue and Alcon CustomCornea laser systems. (50) Results were compared for patients with moderate (−3 to −7 D) and high (−7 to −11 D) myopia.

Uncorrected Visual Acuity

In the moderate myopia comparison, while more eyes achieved an UCVA of 20/20 or better in the pIOL group, there were no significant differences between the three groups ($P = .109$). Similarly, there were no significant differences in the high myopia groups ($P = 1.00$). (50)

Most eyes (≥ 94% in each group) achieved an UCVA of 20/40 or better, and the proportions were not significantly different between groups. (50) Both the moderate and high myopia groups for LASIK and pIOLs met the FDA effectiveness targets for UCVA of 20/40.

Predictability

While the proportion of eyes that were corrected within ± 0.5 D of emmetropia was slightly higher in the pIOL group for both moderate and high myopia eyes, there was no significant difference between the groups. Predictability within ± 1.0 D was high in all groups (> 82%) and there was no significant difference between the groups with moderate myopia. For the high myopia group, however, predictability was significantly higher in the pIOL group than the Alcon CustomCornea (97% vs. 82%, $P = .008$), but not the VISX CustomVue (97% vs. 91%, $P = .094$). (50) All groups met or exceeded the low and high FDA effectiveness targets for predictability within ± 0.5 and 1.0 D.

Best Spectacle Corrected Visual Acuity

Loss of two or more lines of BSCVA was not reported in the study. The proportion of eyes that gained two or more lines of BSCVA was higher in the pIOL group: 20% in the pIOL group versus 11% in the VISX CustomVue group and 2% in the Alcon CustomCornea group. (50)

Additional Refractive Surgeries and Adverse Events

Additional refractive surgeries and adverse events were not reported in this paper. (50)

Limitations

The LASIK data reported in this study was based on published Safety and Effectiveness Summaries of the approved Premarket Approval Applications for the two laser systems. Like many secondary data sources, the published result summaries did not provide complete information for all outcomes that were examined in this study. In addition, the LASIK data could not be combined into a single comparison group. (50)

Phakic Intraocular Lenses Compared with Photorefractive Keratectomy for Myopic Astigmatism

Table 35 provides a summary of the 1 week, 1 month, 6 months, and 12 months postoperative results from the studies that compared pIOLs with PRK for myopic astigmatism.

Schallhorn et al., 2007 (8)

Schallhorn et al. (8) conducted an RCT to compare pIOLs with PRK *for the treatment of myopic astigmatism*. Patients with moderate to high myopia, astigmatism between 1.0 and 4.0 D cylinder, and BSCVA of 20/40 or better were enrolled in the study. Patients were randomized to receive either the Visian toric implantable collamer lens (STAAR Surgical) or conventional PRK[14] using the VISX Star S3 (VISX Inc, Santa Clara, California) excimer laser combined with mitomycin C[15]. The pIOL and PRK groups were similar with respect to age, gender, preoperative mean MRSE, and preoperative mean cylinder. (8)

[14] PRK custom ablation techniques for high myopia did not exist at the time of the study

[15] Mitomycin C was used to aid in the healing process after PRK

Table 35: Summary of Outcomes from Schallhorn et al. Comparing pIOLs with Photorefractive Keratectomy for Myopic Astigmatism

Outcome	1 wk			1 month			6 months			12 months		
	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value	pIOL	RS	*P* value
UCVA ≥ *20/20*, n/N (%)	36/42 (86)	4/43 (9)	< .001	37/42 (88)	21/46 (46)	< .001	32/33 (97)	32/39 (82)	.063	37/38 (97)	36/44 (82)	.033
UCVA ≥ *20/40*, n/N (%)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mean MRSE, D ± SD	0.23 ± 0.44	0.81 ± 1.42	.013	0.27 ± 0.44	0.66 ± 0.79	.009	0.28 ± 0.41	0.76 ± 0.86	.005	0.27 ± 0.36	0.60 ± 0.75	.541
Predictability of MRSE within ± .5 D, n/N (%)	32/42 (76)	19/43 (44)	.004	32/42 (76)	20/46 (44)	.002	23/33 (70)	16/39 (41)	.019	29/38 (76)	25/44 (57)	.101
Predictability of MRSE within ± 1.0 D, n/N (%)	41/42 (98)	27/43 (63)	< .001	40/42 (95)	32/46 (70)	.002	33/33 (100)	26/39 (67)	< .001	38/38 (100)	35/44 (80)	.003
Mean Refractive Cylinder, D ± SD	0.52 ± 0.39	0.80 ± 0.64	.020	0.58 ± 0.39	0.68 ± 0.58	.338	0.52 ± 0.33	0.46 ± 0.35	.450	0.58 ± 0.31	0.52 ± 0.34	.759
Loss of ≥ 2 Snellen lines of BSCVA	0/42 (0)	8/43 (19)	.006	0/42 (0)	2/46 (4)	.495	0/33 (0)	0/39 (0)	1.00	0/38 (0)	0/44 (0)	1.00
Gain of ≥ Snellen lines of BSCVA	4/42 (10)	0/43 (0)	.055	6/42 (14)	0/46 (0)	.010	0/33 (0)	1/39 (2)	1.00	1/38 (3)	1/44 (2)	1.00
Stability	**1 week to 1 month**			**1 months to 3 months**			**3 months to 6 months**			**6 months to 12 months**		
Stability of MRSE (≤ .5 D), n/N (%)	39/42 (93)	19/43 (44)	< .001	34/40 (85)	25/44 (57)	.008	30/33 (91)	23/39 (59)	.003	31/33 (94)	33/39 (85)	.275
Stability of MRSE (≤ 1.0 D), n/N (%)	41/42 (98)	33/43 (77)	.007	40/40 (100)	36/44 (82)	.006	33/33 (100)	33/39 (85)	.028	33/33 (100)	36/39 (92)	.245
Stability of Refractive Cylinder (≤ .5 D), n/N (%)	41/41 (100)	31/43 (72)	< .001	36/39 (92)	31/44 (71)	.013	33/33 (100)	37/39 (95)	.497	33/33 (100)	39/39 (100)	1.00
Stability of Refractive Cylinder (≤ 1.0 D), n/N (%)	41/41 (100)	38/43 (88)	.055	38/39 (97)	41/44 (93)	.618	33/33 (100)	38/39 (97)	1.00	33/33 (100)	39/39 (100)	1.00

BSCVA refers to best spectacle corrected visual acuity; D, diopter; MRSE, manifest refraction spherical equivalent; NR, not reported; RS, refractive surgery (PRK in this table); SD, standard deviation; UCVA, uncorrected visual acuity

Uncorrected Visual Acuity

The proportion of eyes that achieved an UCVA of 20/20 or better was higher in the pIOL group compared with the PRK group at all time points. This difference was significant at 1 week and 12 months. Uncorrected visual acuity improvements occurred faster in patients who received pIOLs than PRK as evidenced by the significant different at 1 week. Similarly, the proportion of eyes with UCVA 20/12.5 or better and 20/16 or better was significantly higher in the pIOL group at all time points (UCVA ≥ 20/12.5, $P \leq .001$; UCVA ≥ 20/16, $P < 0.005$). (8)

Uncorrected visual acuity of 20/40 or better was not reported by in study, but the proportion of eyes seeing 20/20 or better uncorrected exceeded the FDA targets for UCVA of 20/40.

Predictability of Manifest Refraction Spherical Equivalent

The percentage of eyes that achieved refraction within ± 0.5 D of emmetropia was significantly higher in the pIOL group for all time points except at 12 months ($P <.019$). Predictability within ± 1.0 D was significantly higher in the pIOL group at all time points ($P < .003$), ranging from 98% to 100% of eyes in the pIOL group versus 55% to 80% in the PRK group. In the pIOL group, refraction within ± 0.5 and 1.0 D of emmetropia was achieved within the first week after surgery and remained relatively stable over the 1 year follow-up; more variation was observed over time in the PRK group. (8) The pIOL group exceeded the low and high FDA effectiveness targets for predictability within ± 0.5 and 1.0 D at all time points. The PRK group exceeded the FDA target for high myopia at most time points, but not for low myopia.

Stability of Manifest Refraction Spherical Equivalent

The stability of refraction (proportion of eyes with ≤ 0.5 D change) was significantly better in the pIOL group for the first 6 months ($P < .03$); however, in the last six months, the stability was high in both groups. Similarly, the stability within 1.0 D was significantly higher in the pIOL group in the first 6 months ($P < .028$), but was high in both groups in the final 6 months. (8) The high myopia FDA effectiveness target for stability of MRSE within 1.0 D was exceeded at all time points in the pIOL group, but the PRK group did not meet the target at any time point.

Refractive Cylinder

The refractive cylinder was lower in the pIOL group at 1 week, 1 month, and 3 months, but the difference was only significant at 1 week. At 6 months and 1 year, the refractive cylinder was lower in the PRK group, but these differences were not significant. Stability of manifest cylinder was high in both groups, but the pIOL group achieved significantly better stability in the first few postoperative months. (8)

Manifest Refraction Spherical Equivalent

The MRSE was lower (closer to emmetropia) in the pIOL group at all postoperative time points, and significantly lower from 1 week to 6 months. (8)

Best Spectacle Corrected Visual Acuity

The preoperative mean BSCVA was similar in the pIOL and PRK groups (−0.04 ± 0.09 and −0.04 ± 0.12, respectively). (8) The postoperative mean BSCVA and mean line change were significantly higher in the pIOL group at all follow-up points ($P < .001$ for both outcomes).

Clinically significant losses of BSCVA were observed in the PRK group in the first month after surgery but this declined over time: 19% of eyes at 1 week, 4% at 1 month, and 0% after. The PRK group exceeded the FDA targets for loss of BSCVA at 1 week and 1 month. No eyes lost two or more lines of BSCVA after pIOL implantation. (8) One eye in the PRK group and four to six eyes in the pIOL group gained two or more Snellen lines; however, the increases in BSCVA disappeared after 3 months.

Adverse Events

At 1 month, a visually insignificant anterior lens opacity was observed in one eye in the pIOL group, which was not associated with a significant loss of BSCVA or UCVA. (8) A grade 2 anterior subcapsular cataract was observed in one pIOL patient at 2 years postoperatively. The patient required pIOL removal and cataract extraction, after which, BSCVA was restored to 20/20. No other adverse events were reported. (8)

Quality of Vision

Compared with the pIOL group, 3 to 6 months after surgery, patients in the PRK group experienced significantly more vision fluctuation ($P = .001$), glare symptoms at night ($P = .033$), glare from oncoming car headlights at night ($P = .014$), and problems with dry eyes (increased need for artificial tears) ($P = .002$). At 12 months, problems with dry eyes were the only visual symptom that remained significantly different between groups. (8)

Limitations

The quality of this study was assessed using the Jadad scale which evaluates RCTs based on randomization, blinding, and follow-up. (51) Schallhorn et al. (8) scored 1 out of a possible 5 points and is therefore low quality.

Phakic Intraocular Lenses Compared with Clear Lens Extraction for Myopia

Table 36 provides a summary of the 1 week, 1 month, 6 months, and 12 months postoperative results from the studies that compared pIOLs with CLE for myopia.

Table 36: Summary of Outcomes from Arne et al. Comparing pIOL with Clear Lens Extraction for Myopia

Outcome	12 months		
	pIOL	RS	*P* value
Mean postoperative MRSE, D ± SD (range)	−1.06 ± 0.78 (0.50 to −2.75)	−1.88 ± 0.83 (−1.00 to −3.25)	NR
Predictability of MRSE within ± 1.0 D, n/n (%)†	29/41 (70.7)	17/36 (47.4)	NR
Predictability of MRSE within ± 2.0 D, n/N (%)†	34/41 (82.9)	29/36 (80.5)	NR
BSCVA ≥ 20/40	37/41 (87.8)	21/36 (58.3)	NR

BSCVA refers to best spectacle corrected visual acuity; D, diopter; MRSE, manifest refraction spherical equivalent; SD, standard deviation

†The target MRSE for the pIOL group was 0.0 D, but the target for the CLE group was −2.00 D

Arne, 2004 (48)

Arne (48) conducted a case series comparison of pIOLs with CLE for high myopia. The pIOL group consisted of 41 eyes from 21 patients who received an implantable collamer lens (STAAR Surgical Company). The CLE group was 36 eyes from 18 patients who received phacoemulsification of the crystalline lens and implantation of an AcrySof posterior chamber IOL (Alcon). Patients were allocated based on different enrolment criteria such as recent changes in distance visual acuity, opacification of the crystalline lens, and anterior chamber depth. Emmetropia was the target refraction for the pIOL group, while −2 D was the target for the CLE group.

Predictability

Predictability of MRSE within ± 1.0 and 2.0 D of target refraction was higher in the pIOL group. In the pIOL group, 71% of eyes (29/40) achieved a MRSE within ± 1.0 D of emmetropia and 83% (34/41) within ± 2.0 D. In the CLE extraction group, −2 D was the residual refraction target rather than emmetropia with 47% of eyes (17/36) being within ± 1.0 D of this target and 81% (29/41) within ± 2.0 D. (48) Neither group met the high myopia FDA effectiveness target for predictability within 2.0 D. While the CLE group also did not meet the 1.0 D predictability target, the pIOL group exceeded this target.

Manifest Refraction Spherical Equivalent

Compared with the CLE group, mean postoperative MRSE was closer to emmetropia in the pIOL group.

Best Spectacle Corrected Visual Acuity

Preoperatively, 76% (31/41) of eyes had a BSCVA of 20/40 or better in the pIOL group and 58% (21/36) in the CLE group. This increased in both groups to 88% of eyes in the pIOL group and 81% in the CLE group. There were no clinically significant losses of BSCVA in the pIOL group, but at least two eyes in the CLE group lost two or more lines of BSCVA after retinal detachments. (48)

Additional Refractive Surgeries

No additional refractive surgeries to improve vision were reported in the paper.

Adverse Events

In the pIOL group, three eyes developed lens opacification, which were treated by lens removal and cataract extraction. Inadequate vaulting leading to contact between the lens and the anterior capsule was observed in one of the cataract cases. Visual acuity after phacoemulsification was good: 6 months after cataract removal, all eyes achieved a BSCVA of 20/32 or better. At 2 years, one eye experienced an increase in intraocular pressure, which was well controlled with topical beta-blockers. (48)

In the CLE group, 17 eyes (47.2%) developed posterior capsule opacifications requiring neodymium:YAG capsulotomy, 12 in the first postoperative year and five in years 2 to 4. Retinal detachment occurred in two eyes (5.55%) at 39 and 43 months and re-attachment was unsuccessful in one eye. After detachment, BSCVA was low in both eyes (counting fingers and 20/200, respectively). (48)

Endothelial Cell Loss

The rate of endothelial cell loss was equivalent in both groups[16] (pIOL, 2.0%; CLE, 1.9%). (48)

Satisfaction

As shown in Table 37, satisfaction was higher in the pIOL group.[17] In addition, 7 patients in the CLE group were unsatisfied with their near vision which required spectacle correction post-surgery. (48)

[16]The results did not specify whether the reported endothelial cell loss was at 6 months or 1 year.

[17]It was not specified when the postoperative interview regarding satisfaction and visual disturbances was conducted.

Table 37: Satisfaction with Results

Group	Satisfaction, # eyes (%)		
	Very Satisfied	Moderately Satisfied	Satisfied
pIOL	15 (71.4)	2 (9.5)	4 (19.0)
CLE	10 (55.6)	3 (16.7)	5 (27.8)

CLE refers to clear lens extraction; pIOL, phakic intraocular lens

Limitations

A major limitation to this study was that the enrolment criteria for the pIOL and CLE groups were different, so the resulting study groups were not well matched (e.g. the CLE group was significantly older than the pIOL group, $P = .05$). Thus, differences in outcomes between the groups could be due to preoperative group differences.

Many important outcomes such as UCVA, stability of refraction, and loss of BSCVA were not reported in this paper. As well, the actual complication rate for posterior capsule opacification was difficult to determine because different numbers reported in the paper (47.2% and 41.7%). (48)

Long-term follow-up was limited with loss to follow-up exceeding 20% in both groups after 2 years (all eyes were followed for 2 years). In the pIOL group, 51% of eyes were followed for 4 years and 64% in the CLE group. Reasons for dropouts and withdrawals were not provided.

General Limitations: Comparative Studies

Several limitations applied to most or all of the studies (summarized below and in Table 38). In all seven studies, most of the patients received treatment (pIOL, LASIK, PRK, or CLE) for both eyes and the number of eyes was used as the unit of analysis. As described in the General Limitations section for the efficacy studies, measurements from two eyes of the same individual are correlated (within-subject correlation), which violates the assumption of independent data units on which most standard statistical significance tests are based. Thus, the variability of the data is decreased and the statistical power of the study is increased, which may result in falsely precise confidence intervals and small *P* values. (44-46) None of the studies attempted to correct for within-subject correlations (e.g. analyze data from one eye only or use statistical techniques to correct for correlation). Thus, the reported results may be falsely precise and some of the observed statistically significant results may be spurious.

Selection bias was also a problem. In five of the studies, the patient groups were not well matched with significant differences between the patient populations in regards to important population characteristics such as mean preoperative MRSE, UCVA, age, and refractive cylinder. Furthermore, in Arne (48), the inclusion criteria for the two study groups differed. As these variables were usually worse in the pIOL group (i.e., higher preoperative myopia), the data is probably biased in favour of the LASIK, so the observed benefit of pIOLs may be an underestimate. (39;47-49)

The high attrition rates in the LASIK groups compared to the pIOL groups may also be a source of selection bias. For instance, in Sanders and Vukich, 2006 (47), the LASIK group lost about 30% of patients at 1 week, 1 month, and 6 months. In Sanders and Vukich, 2003, the loss to follow-up in the LASIK group was 31% at 6 months and more than 80% at 1 year.

Table 38: Summary of Major Limitations in the Comparative Studies

Limitation	Kamiya et al., 2008 (49)	Sanders and Sanders, 2008 (50)	Sanders, 2007 (40)	Sanders and Vukich, 2006 (47)	Sanders and Vukich, 2003 (39)	Schallhorn et al., 2007 (8)	Arne, 2004 (48)
Comparator	LASIK	LASIK	LASIK	LASIK	LASIK	PRK	CLE
Both eyes included in results	✓	✓	✓	✓	✓	✓	✓
Potential selection bias	✓†	✓†		✓†‡	✓†‡		✓†
Different fup procedure			✓	✓	✓		
Additional refractive surgeries	✓	NR	✓	✓	✓		
Older LASIK or PRK technique			✓	✓	✓		n/a
Poor study quality	✓	✓	✓	✓	✓	✓	✓

CLE, clear lens extraction; fup, follow-up; LASIK, laser-assisted in-situ keratomileusis; NR, not reported; PRK, photorefractive keratectomy

†Selection bias because the study groups were not well matched on important population characteristics

‡Selection bias because there was high loss to follow-up in one group (attrition bias)

A major reason for higher loss to follow-up in the refractive surgery group compared with the pIOL group is that in most of these studies, the pIOL data was obtained from eyes participating in U.S. FDA clinical trials while the LASIK data was obtained from routine clinical follow-up of patients receiving refractive surgery. In clinical trials, testing procedures and data collection are based on strictly standardized protocols that often lead to more complete, reliable, and precise data. In clinical trials, for example, investigators must ensure patients read the maximum lines of UCVA or BSCVA, but this may not occur in routine clinically follow-up. (40)

In most of the studies, patients in the LASIK groups were allowed to undergo additional refractive surgery procedures to further enhance refractive correction. In one study, patients in the pIOL group were also allowed to receive LASIK or PRK treatments after pIOL insertion. The reported refractive results include the results after the additional corrections, which could bias the results because the vision changes resulting from these enhancement procedures will make the procedure appear more effective.

Another important consideration is that refractive surgery techniques have evolved over time and are becoming increasingly accurate and precise. These comparisons may thus overestimate the benefit of pIOLs compared with LASIK/PRK.

Finally, an important limitation for most of these studies is the study design itself, comparative case series, which downgrades the evidence based on the GRADE Working Group Criteria. The GRADE quality of the evidence is discussed in more depth at the end of this section.

Discussion

Overall, pIOLs performed better than LASIK, PRK, or CLE for many of the examined outcomes. The proportion of eyes that achieved an UCVA of 20/20 or better was higher in the pIOL group compared with the LASIK and PRK[18] groups at all time points, this difference was significant at many time points. (8;39;40;47;49;50) In the studies that reported MRSE, the postoperative result was lower (closer to emmetropia) in the pIOL groups compared with the refractive surgery groups.(8;40)

Predictability within ± 0.5 and ± 1.0 D of emmetropia was higher in the pIOL group compared with the refractive surgery groups (LASIK, PRK, or CLE) in all of the studies, a difference that was often statistically significant. (8;39;40;47-50) This trend was consistent despite higher residual astigmatism in the pIOL group (since LASIK can treat astigmatism, but non-toric pIOLs cannot) and additional refractive enhancement treatments in many eyes in the refractive surgery groups. The decreased predictability of refractive surgery in the LASIK and PRK groups is likely the result of the difficultly associated with accurately ablating tissue that is subject to healing, compared with a lens that is manufactured for an exact correction. (39;40;47)

In addition, stability of manifest refraction (changes ≤ 0.5 and 1.0 D between time points) was higher, an often significantly higher, in the pIOL group compared with the LASIK and PRK groups[19] at all postoperative time points. (8;39;40;47;49) The reduced stability after LASIK and PRK may be due to the time it takes for corneal tissue to heal, which can affect refraction. In contrast, the pIOLs used in these studies (posterior chamber foldable lenses) require only a 3 mm clear corneal incision, similar to that used in cataract surgery, which has been shown to have minimal effect on refraction. (39;40;47;50)

The proportion of eyes that gained of two or more lines of BSCVA was higher in the pIOL groups than the refractive surgery groups. (8;39;47;49;50) These clinically significant gains in BSCVA in the pIOL group have been attributed to increased magnification. It is thought that patients treated with LASIK do

[18] Arne (48) did not report UCVA, so this observation does not include the comparison between pIOLs and CLE.

[19] Arne (48) did not report stability, so this observation does not include the comparison between pIOLs and CLE.

not achieve similar gains in BSCVA because of increased higher order aberrations that degrade retinal images. (9;41;42;51;52)

Compared with the pIOL group, loss of two or more lines of BSCVA (an important safety concern) was much more common in the LASIK, PRK, and CLE groups, especially early on in the healing process (i.e. within the first postoperative month); however, almost all of the reported losses were within the FDA safety targets (loss of ≥ 2 lines of BSCVA in < 5% of eyes).

The only outcome that favoured refractive surgery (LASIK and PRK) over pIOLs was correction of refractive cylinder. In the three studies that reported this outcome, LASIK was more effective at reducing astigmatism than pIOLs at most time points. (9;42;50) Similarly, predictability within ± 0.5 and 1.0 D of targeted refractive cylinder was higher in the LASIK group. (50) While this is result is understandable in the myopic eye populations (as non-toric pIOLs cannot correct astigmatism while LASIK and PRK can), this trend remained true in the comparison between LASIK and toric pIOLs for the treatment of myopic astigmatism. (50)

Finally, the long-term effectiveness and safety of pIOLs compared with refractive surgery is unknown. The identified studies provided only 6 to 12 months of follow-up data and these short-term results were further hampered by high loss to follow-up.

GRADE Quality of the Evidence: Comparative Studies

A summary of the GRADE quality of evidence for each comparison and refractive error is provided in Table 39. Due to serious limitations in study quality, issues with directness, and sparse data (details in Appendix 3), the evidentiary value of the literature comparing pIOLs with refractive surgeries was determined to be of low or very low quality.

Table 39: Summary of GRADE Quality of Evidence

Comparison	Refractive Error	No. of Studies	Type of Study	GRADE Quality of Evidence
pIOL vs. LASIK	myopia	3	case series	very low
pIOL vs. LASIK	myopic astigmatism	2	case series	low/very low
pIOL vs. PRK	myopic astigmatism	1	RCT	low/very low
pIOL vs. CLE	myopia	1	case series	very low

CLE refers to clear lens extraction; LASIK, laser-assisted in situ keratomileusis; no., number; PRK, photorefractive keratectomy

Phakic Intraocular Lenses for Low Vision

Experts in low vision were contacted to discuss the utility of pIOLs in patients with low vision. Low vision cannot be corrected by pIOLs as it is usually the result of more than just a severe refractive error. Implantation of a pIOL in a patient with low vision and myopia would eliminate the eye's natural ability to magnify near objects and make the patient reliant on external magnifiers. For patients with low vision and hyperopia, a pIOL could provide magnification for near vision, but as this can be achieved with plus lenses in head-borne, hand-held, or electronic devices, pIOLs are not recommended for these patients. This is level 5 evidence based on expert opinion.

Summary of Findings

Pre-Post Case Series

Based on the GRADE Working Group Criteria (52), the quality of evidence ranged from low to very low, depending on the outcome, so any estimate of effect is uncertain (as summarized in Table 40).

Table 40: Summary of Findings from the Pre-Post Case Series

Outcome	Findings
UCVA	▪ Substantial increase in UCVA (> 75% of eyes achieved UCVA ≥ 20/40)
Predictability of MRSE	▪ High predictability (at most time points, ≥90% of eyes were within ± 2.0 D of emmetropia, ≥ 80% within ± 1.0 D, and > 50% within ± 0.5 D)
Efficacy Index	▪ EI < 1.0 at all time points ▪ Varied by lens type and refractive error ▪ Declined over time
Change in BSCVA (Snellen lines)	▪ 77% to 90% of eyes did not experience a clinically significant change in BSCVA (gain or loss of < 2 lines) ▪ < 2% of eyes lost ≥ 2 lines ▪ 10% to 20% of eyes gained ≥ 2 lines
Patient Satisfaction and Quality of Life/Vision	▪ > 90% of patients were very/extremely satisfied with the results ▪ ≥ 89% of patients reported improved quality of life
Adverse Events	▪ Adverse event rates vary by lens type ▪ Many adverse events exceed the FDA safety target (< 1% per adverse event) including cataracts, halo/glare, deposits on the lens, increased intraocular pressure, uveitis, etc.

BSCVA refers to best spectacle corrected visual acuity; EI, efficacy index; MRSE, manifest refraction spherical equivalent; UCVA, uncorrected visual acuity

Comparative Studies

Overall, for most outcomes, the results favoured pIOLs compared with LASIK, PRK, and CLE for the treatment of moderate to high myopia and myopic astigmatism (Table 41). However, LASIK, PRK, and CLE result in superior correction of refractive cylinder (astigmatism) compared to both toric and non-toric pIOLs[20]. Based on the GRADE Working Group Criteria (52), the quality of evidence is low to very low, so any estimate of effect is uncertain.

Conclusions

- While pIOLs improve UCVA with high predictability, stability, and patient satisfaction for low to high refractive errors, there is no clinical advantage to using a pIOL as opposed to alternative corrective options.
- Adverse events are a potential concern.
- pIOL use in low vision has not been explored because low vision is caused by a comorbid condition (e.g. macular degeneration) that cannot be corrected by a pIOL.

[20] Toric pIOLs are designed to treat astigmatism, whereas, non-toric pIOLs cannot correct astigmatism.

Table 41: Summary of Findings from the Comparison of pIOLs with LASIK for Myopia and Myopic Astigmatism

Outcome	LASIK					PRK	CLE
	Myopia			Myopic Astigmatism		Myopia	Myopia
	Sanders and Vukich, 2003 (39)	Sanders and Vukich, 2006 (47)	Sanders, 2007 (40)	Kamiya et al., 2008† (49)	Sanders and Sanders, 2008 (50)	Scallhorn et al., 2007 (8)	Arne et al., 2004† (48)
UCVA (≥ 20/20)	pIOL‡	pIOL§	pIOL§	pIOL	pIOL	pIOL§	pIOL
Predictability (± 0.5 D)	pIOL‡	pIOL§	pIOL§	pIOL	pIOL	pIOL§	pIOL
Predictability (± 1.0 D)	pIOL§	pIOL§	pIOL§	pIOL	pIOL§	pIOL‡	
Stability (>0.5D)	pIOL‡	pIOL‡	pIOL‡	pIOL		pIOL§	
Stability (>1.0D)	pIOL‡	pIOL§	pIOL§			pIOL§	pIOL
MRSE		LASIK at 1 wk‡, then pIOL after§	LASIK at 1 wk, then pIOL after§	pIOL		pIOL§	
Refractive cylinder		LASIK‡	LASIK‡	LASIK		pIOL to 6 mo‡, then PRK at 12 mo	CLE
Loss ≥ 2 lines BSCVA	LASIK§	LASIK§	LASIK§	no difference		PRK§	
Gain ≥ 2 lines BSCVA	pIOL§	pIOL‡	pIOL at 1 wk, no difference after	pIOL	pIOL§	pIOL§	

BSCVA refers to best spectacle corrected visual acuity; CLE, clear lens extraction; D, diopters; mo, months; LASIK, laser-assisted in situ keratomileusis; MRSE, manifest refraction spherical equivalent; pIOL; phakic intraocular lens; PRK, Photorefractive keratectomy; UCVA, uncorrected visual acuity; wk, week

†The study did not report the statistical significance of the results.

‡Statistically significant at all time points

§Statistically significant at some time points

Diffusion of pIOL

Diffusion in Ontario

Correction of low to high refractive errors is not insured in Ontario. The Ministry of Health and Long-Term Care Assistive Devices Program does, however, cover specialized glasses and lenses for anyone with *long-term low vision or blindness* that cannot be corrected medically, surgically or with ordinary eyeglasses or contact lenses (e.g. corrected vision in the better eye is in the range of 20/70 or less). (3)

Clear lens extraction is covered by OHIP for people who have vision loss due to a disease of the lens, but refractive errors are not considered a disease of the lens in this policy (Box 1).

It is recommended that clear lens extraction followed by IOL insertion be eligible for payment under OHIP when the patient has:

1. Best corrected vision of worse than 20/40,
2. Visual loss is due to a disease of the lens, and
3. Does not have coexistent conditions, such as amblyopia, which would render the surgery ineffective.

Note: In this context refractive errors are not to be considered a disease of the lens.
The claims should be submitted to the Ministry for prior-approval and paid under R990 at a fee equal to E140 and E950. Information required to assess the prior approval request includes a description of the lens disease, test results and current visual acuity. Where available, previous measurements of visual acuity (to try to demonstrate amblyopia does not exist) should be sought out and reviewed.

Box 1. Ontario Health Insurance Payment Policy for clear lens extraction.

Diffusion in Other Provinces

As of March 2008, pIOLs were not insured by other provinces and territories in Canada (Table 42).

Table 42: Status of Phakic Intraocular Lenses in Canadian Provinces/Territories

Province/Territory	Funding Status
Alberta	Not insured
British Columbia	No reply to date
Manitoba	Not insured
New Brunswick	Not insured
Newfoundland	Not insured
Northwest Territories	No reply to date
Nova Scotia	Not insured
Nunavut	No reply to date
Prince Edward Island	Not insured (considered a cosmetic procedure)
Quebec	Not insured
Saskatchewan	Not insured
Yukon	No reply to date

Diffusion Outside Canada

United States

Visual impairment due to myopia, hyperopia, and astigmatism can be corrected by external contact lenses and eyeglasses, so refractive keratoplasty, and specifically phakic intraocular lenses, for the treatment of refractive errors is not considered medically necessary. Therefore, most of the major insurers in the United States including CIGNA, Aetna, Blue Cross Blue Shield, Excellus Health Plan Inc, and Centers for Medicare and Medicaid Services do not cover phakic intraocular lenses or other refractive keratoplasty procedures. (53-57)

United Kingdom

The National Institute for Health and Clinical Excellence issued the following guidance about pIOLs for refractive errors in February 2009:

Current evidence on intraocular lens (IOL) insertion for correction of refractive error, with preservation of the natural lens is available for large numbers of patients. There is good evidence of short-term safety and efficacy. However, there is an increased risk of cataract, corneal damage or retinal detachment and there are no long-term data about this. Therefore, the procedure may be used with normal arrangements for clinical governance and audit, but with special arrangements for consent.

Clinicians wishing to undertake IOL insertion for correction of refractive error, with preservation of the natural lens should ensure that patients understand the risks of having an artificial lens implanted for visual impairment that might otherwise be corrected using spectacles or contact lenses. They should understand the possibility of cataract, corneal damage or retinal detachment, and the lack of evidence relating to long-term outcomes. Patients should be provided with clear information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG289publicinfo).
Both clinicians and manufacturers are encouraged to collect long-term data on people who undergo IOL insertion, and to publish their findings. NICE may review the procedure on publication of further evidence. (21)

Economic Analysis

Disclaimer: The Medical Advisory Secretariat uses a standardized costing methodology for all of its economic analyses of technologies. The main cost categories and the associated methods from the province's perspective are as follows:

Hospital: Ontario Case Costing Initiative cost data are used for all in-hospital stay costs for the designated International Classification of Diseases-10 (ICD-10) diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may need to be made to ensure the relevant case mix group is reflective of the diagnosis and procedures under consideration. Due to the difficulties of estimating indirect costs in hospitals associated with a particular diagnosis or procedure, the secretariat normally defaults to considering direct treatment costs only.

Nonhospital: These include physician services costs obtained from the Ontario Schedule of Benefits for physician fees, laboratory fees from the Ontario Laboratory Schedule of Fees, device costs from the perspective of local health care institutions, and drug costs from the Ontario Drug Benefit formulary list price.

Discounting: For all cost-effectiveness analyses, a discount rate of 5% is used as per the Canadian Agency for Drugs and Technologies in Health.

Downstream costs: All costs reported are based on assumptions of utilization, care patterns, funding, and other factors. These may or may not be realized by the system or individual institutions and are often based on evidence from the medical literature. In cases where a deviation from this standard is used, an explanation has been given as to the reasons, the assumptions, and the revised approach. The economic analysis represents an estimate only, based on assumptions and costing methods that have been explicitly stated above. These estimates will change if different assumptions and costing methods are applied for the purpose of developing implementation plans for the technology.

Literature Review

A literature review was conducted and no cost-effectiveness (cost-utility) economic analysis on the use of pIOL for refractive errors was identified.

Hospital, Physician and Device Costs of Phakic IOLs

Current clinical guidelines from the Canadian Ophthalmological Society for usual care of refractive errors were used to estimate pre-operative, surgical and post-operative costs associated with pIOL implantation. (58) Hospital and physician costs associated with the current standard of care were estimated using average patient costs from the Ontario Case Costing Initiative, and physician fees from the schedule of medical benefits for health professionals from the Ontario Ministry of Health and Long-Term Care and Alberta Health and Wellness. (59-61)

Hospital day surgery and physician costs and the corresponding procedure and fee codes used in the current analysis are listed in Table 43. As pIOL implantation is not covered by the Ontario Health Insurance Schedule of Benefits, physician costs for surgery were estimated from the fee code E146, associated with the secondary insertion of an intraocular lens prosthesis after cataract removal. (59) Similarly, as pIOL procedures are not publically insured in Ontario, hospital surgery costs are based on 2009 CCI codes for lens implantation (1.CL.53) for ICD-10-CA codes related to myopia (H521). (60;61)

Also note the cost of the phakic lens is non-specific to astigmatism, myopia, or hyperopia and represents the average cost of the different lens as determined through consultations with phakic intraocular lens manufacturers. "Physician" and "Device" surgery costs in Table 43 are listed for refractive error correction of one eye only and were multiplied by two to estimate the average cost per patient.

Table 43: Physician, Hospital and Device costs for Phakic IOL Implantation by Stage of Care

Stage of care	Type of cost	Description	Cost	Reference
Pre-Operative Ophthalmic Testing	Physician	Major Eye Examination	$42.15	OHIP (fee code A115)
		Corneal pachymetry	$5.10	OHIP (fee code G813)
		Corneal topography	$4.80	OHIP (fee code G810)
		Specular photomicroscopy	$4.80	OHIP (fee code G812)
		Biometry (Axial length - A-mode)	$48.75	OHIP (fee code J108)
Surgery	Hospital	Implantation of internal device, lens; Myopia	$682.00	OCCI (CCI code 1.CL.53; ICD-10-CA code H521)
	Physician	Insertion of secondary intraocular lens	$400.00	OHIP (fee code E146)
	Device	Phakic intraocular lens device (CAD)	$1,268.21	IOL lens manufacturers
Post-Operative Care	Physician	Subsequent visits: first 5 weeks	$29.20	OHIP (fee code C232)
		Subsequent visits: 6 to 13 weeks	$29.20	OHIP (fee code C007)

Cases of Refractive Error in Ontario

The prevalence of refractive errors differs by age group and type of error. The number of cases of astigmatism, myopia and hyperopia for people of age 20-59 was estimated by Vitale et al. in 2008. (1) In the United States, the prevalence of refractive errors for people aged 20-39 and 40-59 was approximately:

- 23.1% and 27.6% for astigmatism (≥ 1D cylinder),
- 7.4% and 7.8% for myopia (≤ -5D), and
- 1.0% and 2.4% for hyperopia (≥ 3 D).

In Ontario, these rates of refractive errors imply approximately 1.76 million cases of astigmatism, 520,000 cases of myopia, and 120,000 cases of hyperopia in 2006. The total number of cases of refractive errors is estimated as being 2.40 million.

Estimated Costs for Ontario

To estimate the cost of pIOL implantation for refractive errors in Ontario, the summarized costs were taken to represent the anticipated average cost per case for each stage of care. The total average hospital, physician and device costs were estimated as being $4,200 per case, with stage-specific average costs of approximately $106 for pre-operative ophthalmic testing, $1,477 for surgery and $58 for post-operative care. The total number of cases of refractive errors in Ontario was used to calculate an approximate cost of $10 billion. The cost estimation represents the maximum possible cost to Ontario taking a Ministry of Health perspective to insure pIOL implantation procedures for refractive errors. Limitations of this estimate include: every case of refractive error has a pIOL implant, the physician cost of the pIOL procedure is estimated from current IOL lens removal and replacement fees (after cataract removal), and the prevalence of refractive errors in the United States was used to represent that found in Ontario.

Appendices

Appendix 1: Search Strategy

Search date: January 30, 2009
Databases searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library (all via OVID); CRD/INAHTA

Ovid MEDLINE(R) <1996 to January Week 3 2009>
Search Strategy:

1 exp Vision, Low/ (981)
2 (vision adj2 (low or loss or impaired or reduc* or diminished or sub?normal)).ti,ab. (4168)
3 exp Refractive Errors/ (10007)
4 exp Astigmatism/ (2327)
5 (ametropic or ametropia$ or myopia$ or myopic or astigmatism or hyperopia$ or hyperopic or hypermetropia$ or far?sighted$ or near?sighted$ or long?sighted$ or short?sighted$ or refractive error$).ti,ab. (9944)
6 or/1-5 (17100)
7 exp Lens Implantation, Intraocular/ or exp Lenses, Intraocular/ (7114)
8 (phakic or piol* or p-iol*).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (992)
9 (toric or Artisan or Verisyse or Visian or STAAR or AcrySof).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (843)
10 ((implant* or intraocular) adj2 lens*).mp. (7878)
11 (collamer adj2 lens*).mp. (31)
12 (iol or iols).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (3550)
13 or/7-12 (8672)
14 6 and 13 (2040)
15 limit 14 to (english language and humans and yr="2003 - 2009") (927)
16 limit 15 to (case reports or comment or editorial or letter) (241)
17 15 not 16 (686)

Embase: EMBASE <1980 to 2009 Week 04>
Search Strategy:

1 exp Refraction Error/ or exp Astigmatism/ (17319)
2 (vision adj2 (low or loss or impaired or reduc* or diminished or sub?normal)).ti,ab. (5898)
3 (ametropic or ametropia$ or myopia$ or myopic or astigmatism or hyperopia$ or hyperopic or hypermetropia$ or far?sighted$ or near?sighted$ or long?sighted$ or short?sighted$ or refractive error$).ti,ab. (13770)
4 or/1-3 (25097)
5 exp lens implant/ (9953)
6 exp Lens Implantation/ (2296)
7 (phakic or piol* or p-iol*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1454)
8 (toric or Artisan or Verisyse or Visian or STAAR or AcrySof).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1013)
9 ((implant* or intraocular) adj2 lens*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (12937)
10 (collamer adj2 lens*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (32)
11 (iol or iols).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (4790)
12 or/5-11 (14281)
13 4 and 12 (2771)
14 limit 13 to (human and english language and yr="2003 - 2009") (1001)
15 limit 14 to (editorial or letter or note) (165)
16 Case Report/ (1022358)
17 14 not (15 or 16) (669)

Appendix 2: Results from Guell et al. (27)

Guell et al. (27) conducted a retrospective case series of 399 eyes with myopia, hyperopia, or astigmatism. Results were reported for four groups:

- Group 1, myopia eyes that received lens model 204 (n = 101),
- Group 2, myopic eyes that received lens model 206 (n = 173),
- Group 3, hyperopic eyes that received lens model 203 (n = 41), and
- Group 4, astigmatic eyes that received the toric lens model (n = 84). (27)

Table 1 in Appendix 4 provides a summary of the results from this study for the first three groups. Since the toric model is not licensed by Health Canada, this study group was excluded from the reported results. When possible, results for the two myopic eye groups were combined.

UCVA

At the 3 month follow-up, an UCVA of 20/20 or better was achieved in 1.8% of myopic eyes and 0% of hyperopic eyes. An UCVA of 20/40 or better was achieved in 32.5% and 41.6% of myopic and hyperopic eyes, respectively. (27) These results are very low compared to the FDA target for UCVA of 20/40 (75% of high myopes and 85% of low myopes). (27)

Predictability

At 3 months, 27.4% and 63.4% of myopic eyes achieved a MRSE within ± 0.5 D and 1.0 D of emmetropia, respectively. These results do not meet the FDA targets for predictability (30% of high myopes and 50% of low myopes within ± 0.5 D of emmetropia and 75% of high myopes and 85% of low myopes within ± 1.0 D of emmetropia). (17) Only the 44.5% and 63.4% of hyperopic eyes achieved a MRSE within ± 0.5 D and 1.0 D of emmetropia, respectively. (27) These results do not meet most of the FDA targets for predictability.

Efficacy Index

Compared with the hyperopia group, the EI was higher at almost all time points in the two myopia groups. In myopia group 1, the EI ranged from .61 to 1.157. The EI increased over the first year to its highest value (SI, 1.157) at 1 year and then declined over the next 4 years. In myopia group 2, the EI ranged from 0.74 to 0.95. In the hyperopia group, the EI ranged from 0.58 to 0.71. Like myopia group 1, the EI increased over the first year, and generally decreased over the final 4 years in the second myopia group and the hyperopia group. (27)

Safety Index

The SI was higher in myopia group 1 compared with myopia group 2 and the hyperopia group at all follow-up time points. In myopia group 1, the remained quite stable around 1.40 to 1.41 for the first 3 years and then declined to 1.30 in the final 2 years of follow-up. In the second myopia group, the SI was more variable ranging from 1.17 at 1 year to 0.99 at 5 years. In the hyperopia group, the overall trend was an increase in the SI over time from 0.86 at 3 months to 1.25 (the highest value reported for this group) at 5 years. (27)

Best Spectacle Corrected Visual Acuity

Although a loss of two or more Snellen lines of BSCVA is the primary criterion of safety, it was not reported in the study. The safety index (ratio of the mean postoperative BSCVA to the mean preoperative BSCVA) varied by group and over time. In myopic eyes, the safety index was substantially higher in group 1 than group 2 at all time points (e.g. at 3 months, the safety index was 1.41 and 1.11 in groups 1 and 2, respectively), and it decreased over time in both groups. While the safety index for hyperopic eyes was much lower than both groups 1 and 2 at all time points (e.g. at 3 months the safety index in hyperopic eyes was 0.86), it increased over time. (27)

Complications and Adverse Events

Complications were uncommon and occurred in less than 1% of all eyes. However, three major adverse events were observed during the follow-up period: retinal detachment (1 eye, .25%), macular haemorrhage (1 eye, .25%), and nuclear cataract development (2 eyes, 1 patient, .5%). (27)

Appendix 3: GRADE Tables

Efficacy Studies

Note that when studies were included in the GRADE analysis, three of the iris-fixated lens studies (Stulting, Silva, and Lombardo) were counted as one study because they report the results for the same patients but for different outcomes or at different time points. Similarly, two of the posterior chamber lens studies (ITM 2003 and 2004) were treated as one for the same reason.

Table A1: GRADE Assessment of the Literature for Iris-Fixated Lenses for Myopia

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Uncorrected Visual Acuity							
7	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Predictability							
7	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Best Spectacle Corrected Visual Acuity							
5	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Efficacy Index							
5	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Safety Index							
4	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
8	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Adverse Events							
7	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW

[1]Downgraded due to serious limitations including use of data from both eyes of most patients without correction in analyses for within-subject correlation and high loss to follow-up in most studies.
[2]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A2: GRADE Assessment of the Literature for Iris-Fixated Lenses for Hyperopia

Quality assessment							
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Overall Quality
Uncorrected Visual Acuity							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Predictability							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	⊕OOO VERY LOW
Best Spectacle Corrected Visual Acuity							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Efficacy Index							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Adverse Events							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	⊕OOO VERY LOW

1 Downgraded due to serious limitations including use of data from both eyes of most patients without correction in analyses for within-subject correlation and high loss to follow-up in most studies.

2Downgraded due to sparse data as only one study reported on this outcome.

3Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A3: GRADE Assessment of the Literature for Posterior Chamber Lenses for Myopia

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Uncorrected Visual Acuity							
4	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Predictability							
2	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Best Spectacle Corrected Visual Acuity							
2	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Efficacy Index							
3	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Safety Index							
2	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
4	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Adverse Events							
5	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW

[1]Downgraded due to serious limitations including use of data from both eyes of most patients without correction in analyses for within-subject correlation and high loss to follow-up in most studies.

[2]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A4: GRADE Assessment of the Literature for Posterior Chamber Lenses for Hyperopia

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Predictability							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	⊕OOO VERY LOW
Best Spectacle Corrected Visual Acuity							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
1	Observational studies	Serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕OOO VERY LOW
Adverse Events							
1	Observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	⊕OOO VERY LOW

[1]Downgraded due to serious limitations including use of data from both eyes of most patients without correction in analyses for within-subject correlation and high loss to follow-up in most studies.

[2]Downgraded due to sparse data as only one study reported on this outcome.

[3]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A5: GRADE Assessment of the Literature for Posterior Chamber Lenses for Myopic Astigmatism

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Uncorrected Visual Acuity							
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Predictability							
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Best Spectacle Corrected Visual Acuity							
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Efficacy Index							
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	strong association[2]	⊕OOO VERY LOW
Safety Index							
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
2	observational studies	Serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Refractive Cylinder							
2	observational studies	Serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Adverse Events							
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	No serious imprecision	none	⊕OOO VERY LOW

[1] Downgraded due to serious limitations including use of data from both eyes of most patients without correction in analyses for within-subject correlation and high loss to follow-up in most studies.

[2]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

[3]Downgraded due to sparse data as only one study reported on this outcome.

Comparative Studies

Table A6: GRADE Assessment of the Literature Comparing pIOLs with LASIK for the Treatment of Myopia

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Uncorrected Visual Acuity (% eyes seeing ≥ 20/20 or ≥ 20/40)							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	strong association[3]	⊕OOO VERY LOW
Predictability of Refraction							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	⊕OOO VERY LOW
Stability of Refraction							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
2	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	strong association[3]	⊕OOO VERY LOW
Refractive Cylinder							
2	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	strong association[3]	⊕OOO VERY LOW
Best Spectacle Corrected Vision (Gain/Loss Snellen Lines)							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	strong association[3]	⊕OOO VERY LOW
Additional Refractive Surgeries							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	⊕OOO VERY LOW
Adverse Events							
3	observational studies	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	⊕OOO VERY LOW

[1]Downgraded due to serious limitations including use of data from both eyes of most patients without correcting the analysis for the within-subject correlations, selection bias (unmatched study groups and attrition bias); and inclusion of additional refractive surgeries in results.

[2]Three studies compared pIOLs with older LASIK techniques which may be less accurate and precise than the current wavefront-guided laser systems.

[3]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A7: GRADE Assessment of the Literature Comparing pIOLs with LASIK for the Treatment of Myopic Astigmatism

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
Uncorrected Visual Acuity							
2	observational studies	Very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Predictability of Refraction							
2	observational studies	Very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Stability of Refraction							
1	observational studies	Very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Manifest Refraction Spherical Equivalent							
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Refractive Cylinder							
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Best Spectacle Corrected Vision (Gain/Loss Snellen Lines)							
2	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[2]	⊕⊕OO LOW
Additional Refractive Surgeries							
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW
Adverse Events							
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	⊕OOO VERY LOW

[1] Downgraded due to serious limitations including use of data from both eyes of most patients without correcting the analysis for the within-subject correlations, selection bias (unmatched study groups and attrition bias); no sample size calculations; and inclusion of additional refractive surgeries in results.

[2]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A8: GRADE Assessment of the Literature Comparing pIOLs with PRK for the Treatment of Myopic Astigmatism

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
UCVA, BSCVA, MRSE, Contrast Sensitivity, Refractive Cylinder							
1	Randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	strong association[3]	⊕⊕OO LOW
Predictability, Stability of Refraction, Adverse Events							
1	Randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	⊕OOO VERY LOW

[1]Downgraded due to serious limitations. The study scored 1 out of 5 on Jadad scale (method of randomization not reported, no blinding, no description of reason for dropouts/withdrawals). As well, the study used results for both eyes of most patients, but did not correct for the within-subject correlated data in the analysis.

[2]Downgraded because the evidence is based on only one study of 46 patients (23 in each group).

[3]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Table A9: GRADE Assessment of the Literature Comparing pIOLs with CLE for the Treatment of Myopia

Quality assessment							
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Overall Quality**
All Outcomes (Predictability, Manifest Refraction Spherical Equivalent, Best Spectacle Corrected Visual Acuity, Endothelial Cell Loss, Adverse Events)							
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious (sparse data)[2]	strong association[3]	⊕OOO VERY LOW

[1]Downgraded due to serious limitations including use of data from both eyes of most patients with no correction in the analysis for the within-subject correlation, different enrolment criteria for the study groups, and high loss to follow-up in both groups after 2 years.

[2]Downgraded because the evidence is based on only one study of 39 patients (21 and 18 in the pIOL and CLE groups, respectively)

[3]Upgraded due to a strong association as patients move from being unable to see uncorrected to good uncorrected vision. While there was no control group for comparison, the natural history of refractive errors in the age group included in these studies suggests that visual acuity would remain the same or worsen, but not improve.

Appendix 4: Results of Systematic Review

Table A10: Study Results

Study	Outcome	Results	Comments
Guell et al., 2008 (27) **Artisan Lens** **Myopia, Hyperopia, Astigmatism** N @ preop: 315 (excludes astigmatism group) N @ fup varies by group and time point Fup = 5 years Note: group 1, myopia (lens model 204); group 2, myopia lens model 206; group 3, hyperopia lens model 203; group 4, astigmatism toric lens (not licensed by HC)	UCVA at 3 mo	# eyes (%) Group 1 & 2 Group 3 UCVA ≥ 20/20: 5/274 (1.8) 0/41 (0.0) UCVA ≥ 20/40: 89/274 (32.5) 17/41 (41.5)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Additional Refractive Surgery** To correct remaining refractive errors, many eyes received additional refractive surgery procedures after pIOL implantation, and these results are included in the reported refraction outcomes (Group 1, 61 eyes [60.4%]; Group 2, 34 eyes [19.6%]; Group 3, 17 eyes [41.4%); Group 4, 5 eyes [6.0%]). **Follow-up** Follow-up varied by group and time point. Some patients that missed a follow-up appointment attended the next one. Overall, at most time points, follow-up was ≥ 80%, but in group 1 at 3 years follow-up was only 67% and in group 3 at 5 years it was 68%. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	MRSE	Preop 3 mo 1 yr 3 yr 5 yr Group 1: −19.8 ± 3.23 −2.64 ± 2.24 −1.32 ± 1.01 −.78 ± .88 −.5 ± .89 Group 2: −11.27 ± 3.11 −.98 ± 1.07 −.58 ± .75 −.95 ± 1.06 −.64 ± .8 Group 3: 4.92 ± 1.7 −.51 ± .85 .2 ± .48 −.11 ± .75 .02 ± .51	
	Predictability at 3 mo	# E (%) Group 1 & 2 Hyperopia within ±0.5 D 75/274 (27.4) 14/41 (34.1) within ±1.0 D 122/274 (44.5) 26/41 (63.4) within ±2.0 D NR NR	
	Efficacy Index	3 mo 1 yr 2 yr 3 yr 4 yr 5 yr Group 1 .61 1.16 1.09 1.11 .9 .86 Group 2 .77 .95 .86 .81 .93 .74 Group 3 .58 .79 .77 .81 .71 .74	
	BSCVA	Mean preop BSCVA (range) Group 1: 20/50 ± 20/150 (20/400 – 20/25) Group 2: 20/30 ± 20/90 (20/400 – 20/20) Group 3: 20/35 ± 20/90 (20/60 – 20/20) Preop BSCVA # E (%) Group 1 Group 2 Group 3 BSCVA ≥ 20/20: 0/101 (0) 17/173 (9.8)‡ 7/41 (17.0) BSCVA ≥ 20/40: 32/101 (31.6) 118/173 (68.2) 35/41 (85.3) BSCVA at 3 mo # E (%) Group 1 Group 2 Group 3 BSCVA ≥ 20/20: 0/101 (0.0) 30/173 (17.3) 7/41 (17.1) BSCVA ≥ 20/40: 172/101(71.3) 142/173 (82.1) 31/41 (75.6)	
	Safety Index	3 mo 1 yr 2 yr 3 yr 4 yr 5 yr Group 1 1.41 1.40 1.41 1.40 1.3 1.3 Group 2 1.11 1.17 1.04 .99 1.14 1.04 Group 3 .86 .94 .95 .92 .98 1.25	
	Astigmatism	Preop 3 mo 1 yr 3 yr 5 yr Group 1: −1.71 ± .11 −1.48 ± .94 −.71 ± .26 −.75 ± .3 −.75 ± .27 Group 2: −1.43 ± .2 −.49 ± .67 −.49 ± .67 −.18 ± .51 −.06 ± .26 Group 3: −1.15 ± 1.07 −1.25 ± 1.22 −.81 ± .89 −.27 ± .57 −.55 ± .43	
	Additional Refractive Surgery	Group 1: 61/101 (60.4) Group 2: 34/173 (19.7) Group 3 : 17/41 (41.4)	

Study	Outcome	Results	Comments
Guell et al., 2008 (27) (continued)	ECD/ECL	Endpt. ECD (cells/mm^2 ± SD) Mean Cell Loss (%)	
	Group 1	*Preop* 2836 ± 398 n/a	
		1 yr 2598 ± 350 8.4	
		2 yr 2548 ± 398 10.1	
		3 yr 2625 ± 372 7.4	
		4 yr 2791 ± 246 1.5	
		5 yr 2514 ± 529 11.3	
	Group 2	*Preop* 2755 ± 362 n/a	
		1 yr 2643 ± 414 4.1	
		2 yr 2614 ± 469 5.1	
		3 yr 2519 ± 372 8.6	
		4 yr 2698 ± 576 2.1	
		5 yr 2454 ± 588 10.9	
	Group 3	*Preop* 2735 ± 355 n/a	
		1 yr 2600 ± 442 4.9	
		2 yr 2587 ± 551 5.4	
		3 yr 2505 ± 508 8.4	
		4 yr 2560 ± 335 6.4	
		5 yr n/a n/a	
	Complications	- Lens repositioned: 3/399 (.75%) - pIOL dislodged: 3/399 (.75%), 2 due to ocular contusion, 1 because not enough iris grasped by lens claw - pIOL exchange: 3/399 (.75%) (due to inadequate refractive correction) - pIOL explantation: 3/399 (.75%) due to unacceptable ECL (all occurred in group 1 and likely due to eye rubbing lens) - nuclear cataract development: 2/399 (.5%) (2 eyes of 1 patient) - macular haemorrhage: 1/399 (.25%) at 4 mo (patient from group 1) - retinal detachment: 1/399 (.25%) at 3 yrs (patient from group 1)	

Study	Outcome	Results	Comments
Silva et al., 2008 (13) Artisan lens Myopia (high) This study reports 5 year fup results for a subgroup of patients who are included in the Stulting et al. (26) study, so only results for the 5 year time point are presented, with the exception of results for outcomes that are not reported in the Stulting et al. trial (e.g. efficacy index), for which all time points are reported here N@ preop: 26 N@12 mo: 23 N@36 mo: 20 N@60 mo: 19 Fup = 5 yr	UCVA	Preop UCVA ≤ 20/200 in 26 e (100%) *Snellen ratio* *yr 1* *yr 3* *yr 5* UCVA ≥ 20/20: 15/23 (65.2) 12/20 (60) 14/19 (73.7) UCVA ≥ 20/40: 20/23 (87) 17/20 (85) 18/19 (94.7)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** 7 of 26 eyes were lost to follow-up (5 due to relocation or unavailability and 2 due to complications associated with pIOL implantation. **Study Funding/Conflict of Interest** No financial disclosure reported
	Refraction: mean SE ± SD (range) (D)	*Preop:* −12.30 ± 2.62 (−17.25 to −8.25) *1 yr:* −.44 ± .56 (−2 to −.38) *3 yr:* −.38 ± .78 (−2.63 to −.5) *5 yr:* −.37 ± .69 (.84 to 1.11) No significant difference between yr 1 and 3 (*P* = .89) and yr 1 and 5 (*P* = .65)	
	Predictability of refraction (SE)	*Range* *1 yr* *3 yr* *5 yr* within ± 0.5 D 16 (69.6) 15 (75) 14 (73.7) within ± 1.0 D 21 (91.3) 17 (85) 18 (94.7) within ± 2.0 D 23 (100) 17 (85) 18 (94.7)	
	Astigmatism (Mean cylinder ± SD) (D)	*Preop* *1 yr* *3 yr* *5 yr* .98 ± 1 .61 ± .8 .5 ± .6 .5 ± .4	
	BSCVA	*Snellen ratio* preop *yr 1* *yr 3* *yr 5* BSCVA ≥ 20/20: 19 (73.1) 22 (95.7) 17 (85) 18 (94.7) BSCVA ≥ 20/30: 23 (100) 19 (95) 19 (100) Postop results significantly better than preop results at 1 and 5 yr fup	
	Safety (change in BSCVA, Snellen lines) *at 5 years*	Loss ≥ 2 lines: 0/19 (0) Loss 1 line: 0/19 (0) No change: 5/19 (26.3) Gain 1 line: 11/19 (57.8) Gain 2 lines: 3/19 (15.8)	
	Efficacy index	*yr 1* *yr 3* *yr 5* .80 .43 .63	
	IOP	Mean IOP ± SD (range) (mmHg) Preop: 15.5 ± 1.9 (12 to 20) 1 yr: 15.5 ± 1.6 (12 to 17) 3 yr: 16.1 ± 2.5 (11 to 20) 5 yr: 15.9 ± 1.6 (12 to 18)	
	ECD	*Endpt.* *ECD (cells/mm^2 ± SD)* *Mean Cell Loss (%)* *Annual Cell Loss (%)* Preop 2481 ± 291 (2045 – 3246) n/a n/a 1 yr 2325 ± 396 (1203 – 3018) 7.18 7.18 ± 17.28 3 yr 2256 ± 370 (1086 – 2634) 9.98 1.18 ± 3.83 5 yr 2156 ± 495 (1081 – 2959) 14.05 3.15 ± 7.51 Notes: - No significant difference in mean endothelial cell loss between 6 mm and 5 mm diameter lenses - No correlation between preop anterior chamber depth and endothelial cell change at 5 yr (r^2 = .029) -	
	Complications	- Reported as a part of the Stulting et al. study	

Study	Outcome	Results	Comments
Stulting et al., 2008 (26) Artisan Lens Myopia (high) N@ preop 1179 (662 first e and 478 second e) N@ 1 yr: 493 N@ 2 yr: 355 N@ 3 yr: 228 Fup = 3 yr	UCVA	*Snellen ratio* — *Preop* — *yr 1* — *yr 2* — *yr 3* UCVA ≥ 20/20: 0/662 (0) — 173/493 (35.1) — 123/355 (34.6) — 72/228 (31.2) UCVA ≥ 20/40: 0/662 (0) — 427/493 (86.6) — 310/355 (87.1) — 194/228 (84.0) UCVA < 20/40: 662/662 (100) — 66/493 (13.4) — 46/355 (12.9) — 37/228 (16.0)	Efficacy results are based on 662 first eyes enrolled only. The safety results include 1179 eyes (first eyes, second eyes of same patient, and eyes implanted under compassionate use). 26.9^ of patients were enrolled with protocol deviations including patients over 50, preoperative manifest cylinder > 2.5 D, mesopic pupil size > than optic size, preoperative lens opacities, retinal pathology, and/or a combination. Results for these patients were included in the efficacy analyses. **Follow-up** A total of 64 eyes were lost to follow-up (55 first eyes including 2 deaths and 6 second eyes). In addition, 84 eyes were discontinued (73 and 11 first and second eyes, respectively) including 36 that were recruited for the 2 year study and did not return for the 3rd year. Of 662 first eyes, 232 (35%) completed the 3rd year follow-up, and 357 (53.9%) are ongoing. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Predictability of refraction (SE)	*Range* — *at 6 mo (n unknown at 6 mo)* within ± 0.5 D — 71.7% within ± 1.0 D — 94.7% Mean change in MRSE between consecutive visits (6 mo to 1 yr, 1 to 2 yr, and 2 to 3 yr) within ± 0.5 D for 82.5 to 85.4% of e and within ± 1.0 D for 95.9 to 97.7% of e	
	Safety (change in BSCVA, Snellen lines)	*yr 1* — *yr 2* — *yr 3* Loss ≥ 2 lines: 3/493 (0.6) — 1/355 (0.3) — 2/228 (0.9) Loss 1 line: 30/493 (6.1) — 13/355 (3.7) — 15/228 (6.6) No change: 222/493 (45) — 161/355 (45.4) — 88/228 (38.6) Gain 1 line: 177/493 (35.9) — 132/355 (37.5) — 92/228 (40.4) Gain 2 lines: 54/493 (11) — 41/355 (11.5) — 27/228 (11.8) Gain 3 lines: 6/493 (1.2) — 6/355 (1.7) — 4/228 (1.8) Gain ≥4 lines: 1/493 (0.2) — 1/355 (0.3) — 0/228 (0) Gain > 2 lines: 7/493 (1.4) — 7/355 (1.97) — 4/228 (1.8) Notes: 99 to 100% e had BSCVA ≥ 20.20 in postop from 1 mo to 3 yr fup	
	Astigmatism (cylinder)	- Change in refractive cylinder > 2 D in 2.4% (12/492) of first eyes at *yr 1* and 2% (7/355) at *yr 2*, and 3.5% (8/226) at *yr 3* - 16/230 (6.9%) of eyes had secondary refractive procedures to treat astigmatism	
	EDC (Substudy: 6 mo n = 139, 1 yr n = 134, 2 yr n = 135, 3 yr n = 107)	*Endpt.* — *Mean change (% ± SD)* — *Yearly rate (%)* — *P value* *6 mo* −.36 ± 6.8 — −.72 — >.05 *1 yr* −1.06 ± 6.8 — −1.06 — .395 *2 yr* −2.55 ± 7.4 — −1.27 — .085 *3 yr* −4.76 ± 7.8 — −1.59 — .025 Notes: - 1 site had a consistently greater loss than others at year 2 and 3, but had more staff changes etc., mean % change excluding this site = −1.7% per year (90% CI: −2.3 to 1.1) - Also analyzed cohort with 57 e that had endothelial cell counts at all fup points and estimated change over entire study = −1.7% per year (90% CI: −5.9 to −1.7%) - Study studies had difficulty measuring endothelial cell counts accurately and protocol changed during study	
	IOP	- Mean preop IOP = 14.6 mmHg - 18/1140 e (1.6%) IOP >30 mmHg at initial fup, but decreased by 20 d fup (primarily due to retained viscoelastic or steroid response)	

Study	Outcome	Results	Comments
Stulting et al., 2008 (26) (continued)	Complications N = 1179	- Lens explant: 13 (1.1%) o Cataract: 3 e o Inflammation response: 3 e o Trauma: 4 e o Patient not satisfied: 1 o Patient anxiety: 1 o Pupil size > optic size: 1 - Lens exchange: 12 (1.02%) o Power calculation error: 8 e o Pupil size > optic size: 2 e o Inadequate surgical fixation: 2 e - Lens reattached: 10 (0.85%) o Inadequate surgeon fixation: 5 e o Postop trauma: 5 e - Retinal repair: 6 (0.51%) o Retinal detachment: 4 e o Macular hole: 2 e - Postop inflammation (cells and flare): 266/600 (40.3%) at 1 d and decreased over time to 8.3% at wk 2 and 3 and 3.6% at mo 1 and 2 - Iris pigment precipitation: progressively lower over fup -> 6.8% (45/660) at d 1 and 2, 9% (57/630) at wk 1 and 2, 9.4% (40./581) at mo 4 to 6, no deposits at yr 3 - Corneal edema: 19.4% (128/660) at d 1, 2.2% (14/630) at 2 wk - Asymptomatic oval pupil: 13% (86/660) at d 1, 1.7% (10/581) at 4 to 6 mo, 0.5% at 3 yr	

Study	Outcome	Results	Comments
Moshirfar et al., 2007 (16) Artisan Lens Myopia (high) N@ preop: 85 N@ 6 mo: 69 N@ 12 mo: 60 N@ 24 mo: 38 Fup = 2 yr	UCVA	*# eyes (%)* *at 6 mo* *at 12 mo fup* *at 24 mo* UCVA ≥ 20/20: 12/69 (18) 15/61 (24) 4/38 (10) UCVA ≥ 20/40: 57/69 (83) 57/61 (93) 32/38 (84)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** Lost to follow-up was high: >20% at 1 and 2 years (29% and 55.3%, respectively). **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Refraction (manifest spherical equivalent)	Mean SE ± SD (range) (D) *Preop* = −12.20 ± 2.79 (−7.9 to −18.9) *6 mo* = −.26 *12 mo* = −.40 *24 mo* = −.50	
	Predictability of refraction (SE) # E (%)	*Range* *at 6 mo* *at 12 mo* *at 24 mo* within ± 0.5 D 39/69 (57) 34/60 (57) 21/38 (55) within ± 1.0 D 60/69 (87) 50/60 (83) 32/38 (84) within ± 2.0 D 68/69 (99) 59/60 (98) 35/38 (92)	
	BSCVA	# eyes (%) *at 6 mo* *at 12 mo* *at 24 mo* BSCVA ≥ 20/20: 59/69 (85) 7/60 (78) 32/38 (83) BSCVA ≥ 20/40: 68/69 (99) 60/60 (100) 38/38 (100)	
	Safety (change in BSCVA) *at 6 mo*	# E (%) Loss ≥ 2 lines: 0/69 (0.0) Loss 1 line: 5/69 (7.2) No change: 21/69 (30.4) Gain 1 line: 29/69 (42.0) Gain 2 lines: 13/69 (18.9) Gain ≥ 3 lines: 0/69 (0.0) Note: percentages adjusted slightly for more accuracy based on calculations	
	ECD	Endpt. ECD (cells/mm^2 ± SD) Mean Cell Loss (%) Mean Adjusted Cell Loss (%) *Preop* 2713.2 ± 361.5 n/a n/a *6 mo* 2729.8 ± 376.4 0.69 ± 13.65 0 .99 ± 13.65 *12 mo* 2641.3 ± 361.4 −3.30 ± 7.92 −2.70 ± 7.93 *24 mo* 2534.4 ± 394.7 −6.00 ± 10.75 −4.80 ± 10.7 Adjusted cell loss adjusts for possible basal cell rate loss of 0.5% per year, despite adjustment, still a significant decrease at year 1 (*P* = .05) and year 2 (*P* = .02)	
	Complications	- Inc. IOP: 1 e (due to retained ophthalmic viscosurgical device after implantation) - Cataract: 1 e (anterior subcapsular cataract, in same e with inc IOP, pIOL explanted) - Glare/halos: 6% patients at 1 mo, 2.7% patients at 24 mo - Blunt trauma: 8 e (2 needed pIOL repositioning) - pIOL repositioning: 1 e (due to poor centration from surgeon error) - Lens exchange: 1 e (due to undercorrection - Pupil ovalization: 2 patients - Cornea edema: 2 patients (mild) - Cell and flare: 1 patient (persisted for 1 mo)	

Study	Outcome	Results	Comments
Tahzib et al., 2007 (36) Artisan Lens Myopia (moderate to high) N = 89 at all time points 10 years	UCVA	UCVA (logMAR) *1 yr* = .16 ± .16 (−.08 to .6) *6 yr* = .24 ± .23 (0 to 1.30) *10 yr* = .27 ± .29 (−.08 to 1.3) *Snellen Ratio* *1 yr* *6 yr* *10 yr* UCVA ≥ 20/40: 86.5% 78.7% 82.0%	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. The initial study group consisted of 177 eyes of 89 patients. However, only 89 eyes of 49 patients were evaluated at 1, 6, and 10 years. As the remaining patients were observed at different time points, they were excluded from the analysis. Endothelial cell counts were performed by an independent employee. **Follow-up** Using only the 89 eyes that were included in the analysis, follow-up was 100%. **Study Funding/Conflict of Interest** Dr. Budo (last author) is a medical monitor and consultant to Ophtec BV. No other author has a financial or proprietary interest in any material or method mentioned in the paper.
	Refraction (Mean SE ± SD [range] [D])	*Preop* = −10.37 ± 4.69 (−3.75 to −25.25) *1 yr* = −.70 ± .97 (−4.88 to 1.75) *6 yr* = −.71 ± .99 (−4.50 to 2.0) *10 yr* = −.70 ± 1.00 (−4.00 to 2.0) No significant difference between postop Endpts. (6 yr, *P* = .94; 10 yr, *P* = .71) Note, preop SD 4.69 is based on text value, value in Table 2 is slightly different (4.67)	
	Predictability of refraction (SE)	*Range* *1 yr* *6 yr* *10 yr* within ± 0.5 D 34/89 (38.3) 45/89 (50.5) 39/89 (43.8) within ± 1.0 D 66/89 (74.2) 58/89 (65.1) 61/89 (68.8) within ± 2.0 D 84/89 (94.4) 83/89 (93.3) 83/89 (93.3)	
	BSCVA (Mean BSCVA [logMAR])	*Preop* = .16 ± .23 (o to 1) *1 yr* = .07 ± .09 (−.08 to .30) *6 yr* = .12 ± .17 (−.08 to 1.30) *10 yr* = .12 ± .21 (−.08 to 1.30)	
	BSCVA (Snellen Ratio)	*Snellen Ratio* *1 yr* *6 yr* *10 yr* BSCVA ≥ 20/20: 70.8% 50.6% 52.8% BSCVA ≥ 20/40: 100% 96.6% 93.3%	
	Safety (change in BSCVA)	Safety results cannot be extracted from paper as information in both the text and figure are not clear or interpretable.	
	Efficacy index	*1 yr: 0.96* *6 yr: 0.83* *10 yr*: 0.80 Loss over 10 years believed to be due to development of age and high myopia related changes such as earlier lens opacities and maculopathy	
	ECD	*Endpt.* *ECD (cells/mm^2 ± SD)* *Mean Cell Loss (%)** *P value* *Preop* 2817 ± 359 n/a n/a *1 yr* 2928 ± 351 −9.39 ± 18.56 .002 *6 yr* 2734 ± 360 −3.26 ± 18.96 .494 *10 yr* 2800 ± 292 −8.86 ± 16.01 .001 *mean cell loss adjusted for 0.6% physiologic loss per year Notes: no significant correlation found between preoperative anterior chamber depth and endothelial cell change	
	IOP mean IOP ± SD (range) (mmHg)	Preop: 14.7 ± 2.8 (8 to 19) 1 yr: 15.3 ± 3.3 (9 to 26) 6 yr: 15.6 ± 3.8 (9 to 24) 10 yr: 15.5 ± 3.5 (7 to 25)	

	Complications	- Second surgery for additional SE correction: 1 e
		- Visually significant cataract: 2 e (pIOL explantation and phacoemulsifcation)
		- Glare: mean ± SD (range) (%) [scored from 0 to 5, 0 is high glare, 5 is no glare]
		  - Perception of stars around light: 4.49 ± .65 (3 to 5)
		  - Distortion of detail: 4.69 ± .59 (3 to 5)
		Double outline of images: 4.69 ± (3 to 5)	

Study	Outcome	Results	Comments
Chung et al., 2006 (35) Artisan Lens Myopia N = 25 eyes Fup = 3 mo	UCVA	Preop = 1.58 ± .14 (logMAR) 1 mo = .26 ± .13 3 mo = .22 ± .13 e/E (%) UCVA ≥ 20/40: 20/25 (80)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. Patients with high postoperative astigmatism had the sutures partially cut at 2 weeks. If high astigmatism persisted at 4 to 6 weeks, sutures were completely removed **Follow-up** Follow-up was not reported in the study. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Refraction	Preop MRSE = −11.03 ± 2.25 (range −8.08 to −13.75) D 1 mo = −.99 ± .59 (−2.00 to −.25) 3 mo = −.77 ± .34 (−2.00 to 0)	
	Predictability	*At 1 mo* within ± 0.5 D: 3/20 (15) within ± 1.0 D: 11/20 (55) within ± 2.0 D: 20/20 (100) *At 3 mo* within ± 0.5 D: 4/20 (20) within ± 1.0 D: 16/20 (80) within ± 2.0 D: 20/20 (100)	
	Astigmatism	Preop = 1.6 ± .76 1 mo = 2.3 ± 1.9 (*P* = .02) 3 mo = 1.6 ± .8	
Senthil et al., 2006 (37) Artisan lens Myopia N = 60 at all time points fup 24 mo	UCVA	Mean preop UCVA = 20/384 or 0.05 Mean postop UCVA = 20/41 or 0.49 # eyes (%) at 3 mo fup UCVA ≥ 20/20: 3 (5%) UCVA ≥ 20/30: 34 (56.6%) UCVA ≥ 20/40: 45 (75%)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. 3 months prior to surgery all pts underwent a peripheral pan retinal photocoagulation of the peripheral retina **Follow-up** Follow-up was high as patients were only included if 24 months of data were available. **Study Funding/Conflict of Interest** No conflicts of interest were declared.
	Refraction (SE)	Mean SE ± SD (D) preop = −12.5 ± 4.96 (range, −5 to −24) No significant difference in postop SE (around 0 D) at 1 wk, 3 wk, 3 mo, 6 mo, 12 mo, and 24 mo time points (*P* = .406)	
	Predictability of Refraction (SE) *at 3 mo*	Range # E (%) within ±0.5 D 44/60 (73.3) within ±1.0 D 54/60 (90.0) within ±2.0 D 59/60 (98.3) % e within target predictability varies by severity Severity (D) E within ±1.0 D (%) −5 to −10 19/20 (95) −10.5 to −20 33/37 (89) −20.5 to −24 2/3 (66)	
	Efficacy Index	0.93 at 24 mo	

Study	Outcome	Results	Comments
Senthil et al., 2006 (37) (continued)	BSCVA	Mean preop BSCVA = 20/39 or 0.51 Mean postop BSCVA = 20/32 or 0.63	
	Safety (change in BSCVA) *at 3 mo*	# E (%) Loss ≥ 2 lines: 0/60 (0) Loss 1 line: 7/60 (11.6) No change: 30/60 (50) Gain 1 line: 15/60 (25) Gain 2 lines: 6/60 (10) Gain 3 lines: 2/60 (3.3)	
	Safety Index *at 24 mo*	1.19 at 24 mo fup	
	Endothelial cell density/loss	ECD (cells/mm^2 ± SD), *P* = .406 Preop: 2741 ± 313 6 mo: 2598 ± 453 12 mo; 2597 ± 320 24 mo: 2566 ± 315 Mean cell loss (%) 6 mo: 5.2 12 mo: 5.25 24 mo: 6.38	
	Astigmatism (refractive cylinder)	Mean preop = −1.61 ± 1.07 D Mean postop = −0.4 ± 0.65 D	
	Complications	# e (%) - Anterior uveitis = 2 (3) - pIOL dislocation = 2 (3) → due to trauma, 1 required explantation - Inc. IOP = 6 (10) → 1 e not able to control with antiglaucoma medication and required pIOL explantation and CLE	

Study	Outcome	Results	Comments
Asano-Kato et al., 2005 (38) Artisan Lens Myopia (high) N@ preop: 44 N@6 mo: 35 N@1 yr: 37 N@2 yr: 21 Note: fup numbers provided in figures does not match numbers in text, but numbers from figures used in analysis as they are reported twice and match with the mean fup while the text numbers do not. Fup = 2 yr (mean = 12.4 mo)	UCVA	UCVA logMAR (decimal acuity): Preop = 1.62 (.02) 6 mo = .11 (.78) 12 mo = .01 (.98) 24 mo = .14 (.72)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. Several models of the pIOL were used in the study. **Follow-up** High loss to follow-up in study (>50% at 24 months). **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Safety (change in BSCVA)	Safety data could not be extracted from the paper as the results in the text are for each patient's last follow-up visit which does not provide results at a specific time point and data in the figure showed more eyes than assessed at several time points, so data was excluded from analysis.	
	Refraction (manifest spherical equivalent)	Mean SE ± SD (range) (D) preop = −12.80 ± 2.94 (−20.75 to −7.625) 6 mo = −.68 ± .96 (−3.5 to .75) 12 mo = −.42 ± .41 (−1.375 to 0.0) 24 mo = −.71 ± .81 (−1.75 to .5)	
	Predictability of refraction (SE)	Range — *1 mo* — *3 mo* — *6 mo* — *12 mo* — *24 mo* within ± 0.5 D 13/36 (36.1) 16/34 (47) 20/35 (57) 26/37 (70) 12/21 (57) within ± 1.0 D 20/36 (55.6) 21/34 (62) 25/35 (71) 34/37 (92) 12/21 (57) within ± 2.0 D 32/36 (88.9) 31/34 (91) 33/35 (94) 37/37 (100) 21/21 (100) Note: results for 3, 6, 12, and 24 mo time points are based on figure and may not be exact. Results provided for 1 mo Endpt. and remained relatively stable for rest of postop period At 1 mo, 5 e not within 2 D, but had high postop astigmatism and 1 e had corneal epithelitis	
	ECD (cells/mm^2 ± SD)	*Preop:* 2831 ± 304 *6 mo*: 2875 ± 260 *12 mo:* 3007 ± 222 *24 mo:* 2750 ± 284 No significant difference between endpts.	
	Complications	- Inc IOP: 3 e in wk 1 (resolved with beta-blocker eye drops) - High postop astigmatism: >2 D in 4 e (4 patients) (1 resolved with suture removal, 3 spontaneously decreased at 3 mo) - Pigment precipitation: 2 e (no affect on VA) - Fibrin coagulation in anterior chamber (@ 1 wk): 1 e - Wound leakage in first wk: 1 e (resolved with therapeutic soft contact lens)	

Study	Outcome	Results	Comments
Benedetti et al., 2005 (28) Artisan Lens Myopia (moderate to high) N: 93 (at all time points) N group 1: 68 N group 2: 25 Fup = 24 mo Results presented stratified by severity of myopia: Group 1 (SE −6.75 to −15.5) and Group 2 (SE −16 to −23 D)	UCVA at 4 mo # eyes (%)	Mean preop UCVA: Group 1 = .03 ± .02 (.01 to .075); Group 2 = 01 ± .005 (.01 to .025) *Group 1* *Group 2* *Combined* UCVA ≥ 20/20: 17 (25) 2 (8) 19 (20.4) UCVA ≥ 20/40: 57 (83.8) 17 (68) 74 (79.6)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** Follow-up was excellent (100% at 24 months). **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Refraction (mean SE ± SD [range] [D])	*Group 1* *Group 2* *Preop* −11.89 ± 2.4 (−6.75 to −15.5) −18.92 ± 2.04 (−16.0 to −23) *4 mo* −.80 ± .80 −1.07 ± .94 *12 mo* −.89 ± .77 −1.14 ± 1.08 *24 mo* −.91 ± .77 −1.20 ± 1.19 Refraction stable over time, no significant difference between postop values (group 1, *P* = .6819; group 2, *P* = .9126)	
	Predictability of refraction (SE) # E (%) *At 4 mo*	*Range* *Group 1* *Group 2* *Combined* within ± 0.5 D 30 (44.1) 8 (32) 38 (40.9) within ± 1.0 D 47 (69.1) 13 (52) 60 (64.5) within ± 2.0 D 63 (92.6) 22 (88)	
	BSCVA	Mean preop BSCVA: Group 1 = .86 ± .18 (.2 to 1); Group 2 = .62 ± .19 (.3 to 1) Postop BSCVA significantly better at all visits than preop (*P* < .05) *at 12 mo* *at 24 mo* *Group 1* *Group 2* *Group 1* *Group 2* BSCVA ≥ 20/20: 58 10 60 0 BSCVA ≥ 20/40: 0 0 1 0	
	Safety (change in BSCVA) *at 4 mo*	*Group 1* *Group 2* *Combined* Loss ≥ 2 lines: 0 0 0/93 (0) Loss 1 line: 0 0 0/93 (0) No change: 35 3 38/93 (40.9) Gain 1 line: 11 4 15/93 (16.1) Gain 2 lines: 15 4 19/93 (20.4) Gain 3 lines: 6 7 13/93 (14.0) Gain 4 lines: 1 4 5/93 (5.4) Gain 5 lines 0 2 2/93 (2.2) Gain 6 lines: 0 1 1/93 (1.1) Gain > 2 lines 7 14 21/93 (22.6)	
	Efficacy index	*Group 1* *Group 2* *4 mo* .79 .87 *12 mo* .82 .87 *24 mo* .84 .94	
	Safety index	*Group 1* *Group 2* *4 mo* 1.10 1.40 *12 mo* 1.09 1.42 *24 mo* 1.12 1.39	

Study	Outcome	Results	Comments
Benedetti et al., 2005 (continued)	Astigmatism (cylinder)	*Group 1 (D)* *Group 2 (D)* *Preop* −1.25 ± .9 −1.58 ± .9 *24 mo* −.75 ± .6 −1.17 ± 1.0 Note, in group 1, there was a significant increase in astigmatism observed at the first postop visit and then decreased at subsequent visits	
	ECD	*Endpt.* *ECD (cells/mm^2 ± SD)* *Mean Cell Loss (%)* *Preop* 2658 ± 360 n/a *4 mo* 2583 ± 361 2.8 *12 mo* 2554 ± 322 3.9 *24 mo* 2514 ± 305 5.4 No significant difference in cell loss between the group 1 and 2, but mean postop ECD was significantly lower than the preop ECD (*P* = .0276)	
	Quality of Life	*Outcome* *% of patients* Satisfaction with results: 100 inc quality of life: 95 easier to read: 87 easier to watch TV: 89.2 easier to shop: 80.6 easier to play spots: 87.1 better day driving: 88 worse night driving: 17.2 halos and/or medium intensity nocturnal glare: 6.4 recommend procedure to friend: 96.7	
	Complications	Intraoperative complications - Blood in anterior chamber from iridotomy: 2 (2.1) - Centering or enclavation difficult: 18 (19.5) - Iris prolapse in wound: 5 (5.4) - pIOL damaged during enclavation: 1 (1.1) Postop complications - Inc IOP (> 24 mmHg): 7 (7.5), resolved topically - Glare/halos: 6 e (6.4) (primarily in patients who received 5 mm optic diameter lens) - Persistent iris atrophy in fixation area of hepatic: 11 (11.8) (thought to be due to excessive manipulation of iris during enclavation) - Claw haptic perforated iris leading to slight decentration: 1 (1.1) - Moderate IOL decentration: 5 (5.4) - Pigment deposit on lens: 4 (4.3)	

Study	Outcome	Results	Comments
Lifshitz et al., 2004 (14) Artisan Lens Myopia N = 31 Fup = 3 mo	UCVA	Preop UCVA ≤ 0.05 1 mo = .62 ± .23 3 mo = .69 ± .17 Statistically significant improvement in UCVA from preop to 1 week and between 1 week and 1 month -> maximal UCVA obtained during first postop month UCVA ≥ 20/40: 29/31 (93.5)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** For some outcomes, data were available for 100% of eyes, but for others such as ECD, results were only reported for ~70% of eyes. **Study Funding/Conflict of Interest** The paper did not provide any information on conflicts of interest or study funding.
	MRSE	Preop MRSE = −11.25 ± 3.33 D (range, −5.25 to −23.5)	
	BSCVA Change in BSCVA (Snellen lines) at 3 mo	Preop BSCVA = .80 ± .18 1 mo = .84 ± .19 3 mo = .95 ± .10 Statistically significant difference between BSCVA at 1 week and at 1 month (*P* = .05) and 1 month and 3 months (*P* = .01) Loss 2 lines: 0/31 (0) Loss 1 line: 0/31 (0) No change: 11/31 (35.5) Gain 1 line: 7/31 (22.6) Gain 2 lines: 7/31 (22.6) Gain 3 lines: 1/31 (3.2) Gain 4 lines: 2/31 (6.5) Gain 5 lines: 2/31 (6.5) Gain 6 lines: 1/31 (3.2)	
	Predictability of MRSE	*Range* *3 mo* within ± 0.5 D NR within ± 1.0 D 28/31 (90.4) within ± 2.0 D 31/31 (100.0)	
	Endothelial Cell Density	ECD (cells/mm^2) Mean cell loss (%) Preop 2925 ± 377 n/a 3 mo 2809 ± 414 3.96 Note – these results are only for the 21 eyes with 3 mo endothelial cell counts	
	Complications	No complications observed	

Study	Outcome	Results	Comments
Saxena et al., 2003 (29) Artisan Lens Hyperopia N = 26 (13) Fup = 3 mo (mean, 22.4)	UCVA	*6 mo* *1 yr* *2 yr* *3 yr* .65 ± .65 .63 ± .62 .59 ± .60 .58 ± .57 No significant difference between fup time periods At 6 mo: UCVA ≥ 20/20: 5 (22.7%) UCVA ≥ 20/40: 20 (90.9%)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** Loss to follow-up was high. At 3 years, loss to follow-up was > 50%. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	MRSE	Mean SE ± SD (range) (D) Preop = 6.80 ± 1.97 (3 to 11) 6 mo = −.08 ± .74 (−1.50 to 1.38) 1 yr = −.03 ± .71 (−1.50 to 1.13) 2 yr = −.15 ± .89 (−2.0 to 1.0) 3 yr = .10 ± .85 (−1.50 to 1.25)	
	Predictability of MRSE	*Range* *6 mo* within ± 0.5 D 13/22 (59.1) within ± 1.0 D 19/22 (86.4) within ± 2.0 D 22/22 (100.0) All e within ± 2.0 D at all postop endpts. Notes: - 4 e required stronger correction than available - 5 e would benefit from 0.5D incremental lens not available at time of insertion	
	BSCVA	Mean BSCVA ± SD (range) (D) Preop = .86 ± .59 6 mo = .87 ± .67 1 yr = .82 ± .27 2 yr = .82 ± .59 3 yr = .75 ± .52 *Snellen Ratio* *6 mo* *1 yr* *2 yr* *3 yr* BSCVA ≥ 20/20: 11 (50) 10 (58.5) 9 (60.0) 4 (40.0) BSCVA ≥ 20/40: 21 (95.5) 16 (94.1) 14 (93.3) 8 (80.0)	
	Safety (change in BSCVA, Snellen lines)	*6 mo* *3 yr* Loss 2 lines: 0 0 Loss 1 line: 3 4 No change: 15 3 Gain 1 line: 2 1 Gain ≥ 2 lines: 2 2 Note: Numbers are based on figure and loss 1 line at 6 mo different from text number	
	ECD	*Endpt.* *ECD (cells/mm^2 ± SD)* *Mean Cell Loss (%)* Preop 2749 ± 348 n/a 6 mo 2858 ± 462 NR 1 yr 2965 ± 305 NR 2 yr 2611 ± 472 8.5 3 yr 2471 ± 372 11.7 Significant negative correlation between endothelial cell loss and depth of anterior chamber at 3 mo and 2 yrs, but not comparing preop and postop or any other postop time points	

Study	Outcome	Results	Comments
	Complications	- Posterior synechiae and pigment cell deposits: 2 patients -> 1 patient had pIOL explanted and underwent a clear lens extraction	
Alfonso et al., 2008 (30) ICL Lens Myopia N = 25 e Fup = 12 mo	UCVA	Mean postop UCVA (logMAR) at 12 mo = .17 ± .19 (.7 to 0) UCVA ≥ 20/20: 11 (44) UCVA ≥ 20/40: 22 (88)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. Outcomes were assessed at 12 months by a ophthalmic technician who was unaware of the study objective. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	MRSE	Mean postop SE = −.32 ± .55 D	
	Predictability of refraction (SE)	*Range* within ± 0.5 D: 84% within ± 1.0 D: 100%	
	BSCVA	Mean BSCVA (logMAR) = .12 ± .12 (.4 to 0) BSCVA ≥ 20/20: 11 (44) BSCVA ≥ 20/40: 24 (96) Postop BSCVA was statistically significantly better than preop BSCVA (*P* = .0021)	
	Safety (change in BSCVA, Snellen lines)	At 12 mo: Loss ≥ 2 lines: 0 Loss 1 line: 2 No change: 18 Gain 1 line: 1 Gain 2 lines: 3 Gain > 2 lines: 1	
	Efficacy index	.98 at 12 mo	
	Safety index	1.05 at 12 mo	
	Complications	None observed	
Chang et al., 2006 (31) ICL Lens Myopia (high) N = 61 e Fup = 24 mo (mean fup = 13.67 ± 8.51)	UCVA	Preop UCVA: all e counting fingers or worse	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. 8 eyes had very high preoperative myopia, and so emmetropia (0 D) was not the target refraction for these eyes. **Follow-up** Loss to follow-up was high (> 30%) after 6 months follow-up. At 24 months, loss to follow-up was >80%. **Study Funding/Conflict of Interest** Dr. Chang is an unpaid instructor of ICL. The authors had no financial or
	Refraction	Mean SE ± SD (range) Preop: −13.42 ± 2.38 (−7 to −17.25) Postop (at last fup): −.1 ± .74 (−2.0 to 2.75) Note: only for eyes targeted for emmetropia (51 of 61 e) 8 e underwent bioptics Mean preop SE = −21.52 ± 2.52 Mean postop SE (at last fup) = −2.11 ± 1.10 -> none had further refractive surgery	
	Predictability of refraction	*Range* within ± 0.5 D: 37 (72.5) within ± 1.0 D: 45 (88.2) Note: only for eyes targeted for emmetropia (51 of 61 e)	
	Stability of refraction	Interval / Refractive Change / ≤.5D / ≤1.0D 1 mo to 6 mo: .11 ± .33 / 38/48 (83) / 45/46 (98)	

Study	Outcome	Results	Comments
		6 mo to 1 yr: −.03 ± .57 30/36 (83) 35/36 (97) 1 yr to 2 yr: .17 ± .20 9/12 (75) 12/12 (100)	proprietary interest in any material or method mentioned in the paper.
Chang et al., 2006 (continued)	Astigmatism (manifest cylinder)	Mean preop cylinder (31 e) = 1.83 ± 1.12 D Mean postop cylinder (at last fup) = .97 ± 1.0 D Good stability reached at 3 mo (little difference between 3 mo and 24 mo results)	
	BSCVA	Preop BSCVA ≥ 20/20 = 32 (100) Mean preop BSCVA (logMAR): 0.075	
	Safety (change in BSCVA, Snellen lines) *at last preop visit*	*Change in Snellen Lines (%)* Loss > 1 line: 0% Loss 1 line: 2% No change: 26.2% Gain 1 line: 62.5% Gain ≥ 2 lines: 8%	
	Efficacy index	CALC	
	IOP	Mean preop IOP = 16.8 ± 2.72 (10 to 25) mmHg Mean postop IOP (at last fup) = 16.98 ± 3.19 (12 to 26) mmHg IOP > 21 1 wk: 5 (82) 2 mo: 16 (26.2) 3 mo: 0 (0)	
	Complications	- Glare: 3 patients but resolved quickly for all but 1 eye - Macular haemorrhage: 2 (3.3%) at 1 yr - Retinal detachment: 1 (1.6%) at 15 mo - Late anterior subcapsular opacity: 1 e (1.6%) at 14 mo - Overcorrection by 2.75 D: 1 e (surgeon error) - ICL explantation: 1 patient (due to difficultly reading) - Brow ache: 1 e (resolved after 2 mo)	
ICL in Treatment of Myopia (ITM) Study Group, 2004 (25) ICL Lens Myopia (moderate to high) N@ preop: 526 e N@3 yr: 369 Fup = 3 yr	UCVA	At 3 years ≤−7D > −7 to −10 D >−10D Total UCVA ≥ 20/20: 68.1% 48.9% 21.9% 40.8% UCVA ≥ 20/40: 97.2% 86.3% 70% 81.3% Subset with preop BSCVA ≥ 20/20 where emmetropia targeted ≤−7D > −7 to −10 D >−10D Total UCVA ≥ 20/20: 72.4% 62.7% 37.5% 59.3% UCVA ≥ 20/40: 98.3% 92.8% 93.8% 94.7% Notes: At 3 yr, 57.5% could see uncorrected as well or better than preop BSCVA	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. 9.5% of eyes required correction > 20 D so these eyes were intentionally under corrected as the maximum power of the pIOL is 20 D. This is an additional report on the FDA Clinical Trial for ICL lenses. The FDA recommended the trial be continued for
	Predictability of refraction (SE)	Range ≤−7D > −7 to −10 D >−10D Total within ± 0.5 D: 84.7% 71% 56.9% 67.5% within ± 1.0 D: 97.2% 93.1% 80% 88.1% within ± 2.0 D: 100% 100% 95.6%	

Study	Outcome	Results	Comments
ICL in Treatment of Myopia (ITM) Study Group, 2004 (continued) NOTE – patients same as in ITM 2003 study, but with longer fup, so only extracted updated results	BSCVA	*Preop* *2 yr* *3 yr* BSCVA ≥ 20/20: 67.7% 82.3% 84.8% BSCVA ≥ 20/40: 97.0% 98.2% 98.6% Notes: BSCVA was improved at all fup visits compared with preop values Mean BSCVA improvement ranged from .5 to .6 lines between 1 and 3 yr endpts.	an additional year for the Premarket Approval application. The ITM 2003 study was extended until 350 eyes reached 3 year follow-up visits. **Follow-up** Accountability (accountability = eyes available for analysis divided by (enrolled minus discontinued minus not yet eligible for time interval) was 77.2% at 3 years. **Study Funding/Conflict of Interest** The study was supported by STAAR Surgical, Monrovia, California, and Drs Vukich, Bylsma, Brown, and Sanders are paid consultants to STAAR Surgical.
	ECD (results from a substudy)	- Cumulative cell loss of first 3 years = 8.4 to 9.7% (depending on calculation method used) - 57 e examined at 3 and 4 yr postop: 2354 and 2355 cells/mm^2, respectively → 0.1% (90% CI: −1.4 to −1.6%) gain	
	Patient satisfaction	*≤−7D* *> −7 to −10 D* *>−10D* *Total* Very/extremely satisfied: 95.8% 94.3% 88.4% 92.1% Fairly/moderately satisfied: 4.2% 5.7% 10.2% 7.3% Unsatisfied: 0% 0% 1.4% (2e) 0.6% 97.1% of patients would choose pIOL implantation again	
	Complications (since first report)	- Secondary surgical interventions: 4 o 3 IOL replacements o 1 IOL explantation and cataract extraction - Retinal detachments: 2 - Opacities o Nuclear opacities grade > 2: 5 e (3 patients) or .9%	
	Subjective symptom assessment	Glare Halos Double vis Night vis Night driving Improved 2 cat: 10 (2.8) 8 (2.3) 0 (0) 11 (3.1) 12 (3.6) Improved 1 cat: 32 (9.1) 24 (6.9) 4 (11) 31 (8.9) 34 (10.1) No Change: 275 (78.3) 278 (79.4) 341 (97.2) 266 (76.0) 255 (76.1) Worsen 1 cat: 30 (8.5) 30 (8.6) 6 (1.7) 34 (9.7) 25 (7.5) Worsen 2 cat: 4 (1.1) 10 (2.9) 0 (0) 8 (2.3) 9 (2.7)	
Lackner et al., 2003 (32) ICL Lens Myopia (high) N = 65 (results for myopia eyes included only) Mean fup = 21.9 ± 15.94 mo	UCVA	Mean preop UCVA = .03 ± .03 Mean postop UCVA = .36 ± .36 (decimal acuity)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. This study included a variety of models of the ICL lens, but the primary model was the current V4 model. **Study Funding/Conflict of Interest** The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Refraction (SE)	Mean preop SE = −16.23 ± 5.29 D Mean postop SE = −1.77 ± 2.17 D	
	BSCVA	Mean preop BSCVA = .49 ± .23 (decimal acuity) Mean postop BCVA = .64 ± .25 (decimal acuity) Mean improvement in BSCVA = .17 ± .17 (decimal acuity)	
	Safety index	1.31 (averaged over entire time period)	
	IOP	Mean preop IOP = 14.2 ± 2.7 mmHg Mean postop IOP = 13.46 ± 2.1 Note: mean IOPs include hyperope patients	
	Complications	- Visually nonsignificant lens opacity (nonprogressive): 3 e (suspected due to minimal intraoperative touch of crystalline lens) - Lens opacification: 25 e (33), 14 progressive and 11 stable (includes hyperope eyes) - Cataract surgery: 8 e (6 patients)	

Study	Outcome	Results	Comments
Shen et al., 2003 (33) ICL Lens Myopia (high) N = 39 e Fup = 48 (mean, 25.35 ± 12.13; range, 6 – 48)	UCVA	UCVA ≥ 20/40: 34 e at 3 mo	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** This study had poor follow-up. At 12 and 24 months, loss to follow-up was > 20%. At 48 months, loss to follow-up was > 70%. **Study Funding/Conflict of Interest** The paper did not report study funding or conflicts of interest.
	Refraction (manifest SE)	Mean SE ± SD (range) Preop: −16.79 ± 3.37 (−11.75 to −25.75) 6 mo: −1.79 ± 1.13 No significant difference between postop time periods	
	BSCVA	BSCVA change 6 mo 12 mo 24 mo 0.3 to 0.5 23.7% 25.64% 25.64% 0.4 to 0.6 20.51% 20.51% 23.07% 0.5 to 0.8 38.46% 38.46% 41.03%	
	Complications	- pIOL explantation: 1 e (bend to corneal endothelium due to > diameter than sulcus) - papillary block in 2 e at 1 d - Inc IOP at 2 mo: 2 e (1 patient) (resolved with corticosteroids) - Cataract under anterior subcapsular membrane: 1 e - Lens opacities: 3 e (2 patients) - Pigment disposition: all eyes at 1 day, inc until 3 mo when stable trend occurred - Macular haemorrhage: 1 e	
The Implantable Contact Lens in Treatment of Myopia (ITM) Study Group, 2003 (24) ICL Lens Myopia (moderate to high) N@ preop: 523 e N@ 1 wk: 501 N@1 mo: 505 N@3 mo: 482 N@6 mo: 468 N@12 mo: 428 N@24 mo: 258 Fup = 24 mo	UVCA	Results for cohort with preop BSCVA ≥ 20/20 (e with good visual potential) *Snellen Ratio 6 mo 12 mo 24 mo* UCVA ≥ 20/20: 177/317 (55.8) 176/293 (60.1) 84/165 (50.9) UCVA ≥ 20/40: 292/317 (92.1) 271/293 (92.5) 154/165 (93.3) UCVA ≥ 20/200: 317/317 (100) 293/293 (100) 165/165 (100) Postop mean UCVA at 12 mo = 10.31 Snellen lines	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. 52 eyes (9.9%) were enrolled with pre-existing ocular conditions including myopic retinal degeneration, amblyopia, and early cataracts. 12 eyes had a history of previous ocular surgery. 15 eyes underwent LASIK after pIOL implantation, but their results after LASIK were not included in the reported results. **Follow-up** Accountability > 90% at all time points. Follow-up was >80% up to 12 months postoperatively, but only 50% of patients were seen at the 24 month time period. **Study Funding/Conflict of Interest** The study was funded by STAAR Surgical Company, Monrovia, California, and Drs Sanders and Vukich are paid consultants to STAAR Surgical.
	Refraction (manifest SE)	Preop: −10.046 (−3 to −20)	
	Predictability of refraction (SE)	*Range 6 mo 12 mo 24 mo* within ± 0.5 D: 280/464 (60.3) 261/424 (61.6) 148/258 (57.4) within ± 1.0 D: 402/464 (86.6) 359/424 (84.7) 207/258 (80.2) within ± 2.0 D: 443/464 (95.5) 410/424 (96.7) 247/258 (95.7%)	
	Predictability stratified by preop SE at 6 mo	*Range ≤−7D > −7 to −10 D >−10D* within ± 0.5 D: 67/87 (77) 120/162 (74.1) 93/215 (43.3) within ± 1.0 D: 85/87 (97.7) 151/162 (93.2) 166/215 (77.2) within ± 2.0 D: 87/87 (100) 161/162 (99.4) 194/215 (90.2)	
	Predictability stratified by preop SE at 12 mo	*Range ≤−7D > −7 to −10 D >−10D* within ± 0.5 D: 63/84 (75.0) 103/149 (69.1) 95/191 (49.7) within ± 1.0 D: 81/84 (96.4) 137/149 (91.9) 141/191 (73.8) within ± 2.0 D: 84/84 (100) 148/149 (99.3) 178/191 (93.2)	
	Predictability stratified by preop	*Range ≤−7D > −7 to −10 D >−10D* within ± 0.5 D: 32/40 (80) 62/94 (66) 54/124 (43.5)	

Study	Outcome	Results	Comments
The Implantable Contact Lens in Treatment of Myopia (ITM) Study Group, 2003 (continued)	SE at 24 mo	within ± 1.0 D: 38/40 (95) 84/94 (89.4) 85/124 (68.5) within ± 2.0 D: 40/40 (100) 94/94 (100) 113/124 (91.1)	
	BSCVA N at 6 mo = 464 N at 12 mo = 427 N at 24 mo = 257	*6 mo* *12 mo* *24 mo* BSCVA ≥ 20/20: 67.7% 82.4% NR BSCVA ≥ 20/40: 98.7% 98.1% 98.1% *Snellen lines* *6 mo* *12 mo* *24 mo* Loss > 2 lines: 0 (0) 0 (0) 1 (.4) Loss 2 lines: 2 (.4) 3 (.7) 3 (1.2) Loss 1 line: 19 (4.1) 23 (5.4) 20 (7.8) No change: 218 (47) 189 (44.3) 106 (41.2) Gain 1 line: 170 (36.6) 171 (40.0) 99 (38.5) Gain 2 lines: 41 (8.8) 30 (7.0) 19 (7.4) Gain 3 lines: 14 (3) 11 (2.6) 9 (3.5)	
	Quality of vision: # eyes (%)	Glare Halos Double vis Night driving Quality of Vision Improved 2 cat: 10 (2.5) 12 (2.9) 2 (.5) 17 (4.3) 23 (5.7) Improved 1 cat: 39 (9.6) 29 (7.1) 4 (1.0) 37 (9.4) 105 (25.9) No Change: 325 (79.9) 314 (77.1) 397 (97.5) 309 (78.4) 236 (58.3) Worsen 1 cat: 30 (7.4) 38 (9.3) 4 (1.0) 23 (5.8) 39 (9.6) Worsen 2 cat: 3 (0.7) 14 (3.4) 0 (0) 8 (2.0) 2 (.5)	
	Satisfaction with results at 12 mo	Very/extremely satisfied: 375/406 (92.4%) Unsatisfied: 4/406 (1%)	
	IOP	Acute inc IOP within 1st mo after surgery: 21 (4.0%) -> due to small iridotomies blocked with viscoelastic - received following treatments which resolved IOP inc: 16 received additional iridotomy to enlarge site, 3 had irrigation of anterior chamber, and 2 had surgical iridotomies	
	Complications	**Intraoperative Complications** - pIOL repositioned: 4 - pIOL replaced: 6 (2 too long, 3 too short, 1 not correct power) - pIOL removed for cataract extraction : 2 - pIOL inserted upside down -> removal and reinsertion during surgery or on same day: 11 (2.1%) (6 had early anterior subcapsular lens opacities) - pIOL repositioning during surgery: 1 - surgeon error: 1 e (gave patient preservative containing solution in anterior chamber) **Postop Complications** - Iritis: 101/523 (19.3%) at 1 d, 6/501 (1.2%) at 1 wk - Corneal edema: 59/523 (11.3%) at 1 d, 2/501 @ 1 wk - Retinal detachment: 1/468 (.2%) at 6 mo - Iris prolapse repair: 1/523 (.2%) at 1 d - Acute retinal hole: 1/482 (.2%) at 3 mo - Ovalization of pupil: 1/468 (.2%) at 6 mo	

Study	Outcome	Results	Comments
The Implantable Contact Lens in Treatment of Myopia (ITM) Study Group, 2003 (continued)		**Opacities** (Lens Opacity Classification System III): 3 eyes (%) Nuclear colour — *6 mo* / *12 mo* / *24 mo* Trace 108/468 (23.1) / 103/425 (24.2) / 93/257 (36.2) Mild 0/468 (0) / 0/426 (0) / 0/257 (0) Moderate 1/468 (0.2) / 1/426 (0.2) / 1/257 (0.4) Marked 0/468 (0) / 0/426 (0) / 0/257 (0) Nuclear opalescence Trace 105/468 (22.4) / 95/426 (22.3) / 91/257 (35.4) Mild 2/468 (0.4) / 1/426 (0.2) / 0/257 (0.0) Moderate 1/468 (0.2) / 1/426 (0.2) / 1/257 (0.4) Marked 0/468 (0) / 0/426 (0) / 0/257 (0) Cortical Trace 7/468 (1.5) / 8/426 (1.9) / 0/247 (0) Mild 1/468 (0.2) / 1/426 (0.2) / 0/257 (0) Moderate 1/468 (0.2) / 0/426 (0) / 0/257 (0) Marked 0/468 (0) / 0/426 (0) / 0/257 (0) Posterior subcapsular Trace 1/468 (0.2) / 0/426 (0) / 0/257 (0) Mild 0/468 (0) / 0/426 (0) / 0/257 (0) Moderate 0/468 (0) / 0/426 (0) / 0/257 (0) Marked 0/468 (0) / 0/426 (0) / 0/257 (0) Anterior Subcapsular Trace 15/468 (3.2) / 22/426 (3.2) / 13/257 (5.1) Mild 4/468 (0.9) / 22/426 (0.5) / 4/257 (1.6) Moderate 2/468 (0.4) / 4/426 (0.5) / 2/257 (0.8) Marked 0/468 (0.0) / 0/426 (0) / 0/257 (0)	
Pesando et al., 2007 (15) ICL Lens Hyperopia N = 59 e Fup = 10 yr (mean = 46 mo)	Refraction (manifest SE)	Mean SE ± SD (range) (D) Preop: 5.78 ± 2.54 (2.50 to 11.75) 10 yr: .07 ± .5 (−1.00 to 1.50)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. Inclusion criteria includes certain occupations (e.g. firefighter, snow-skiing instructor, etc.), participation in agnostic sports (e.g. soccer), and certain hobbies. **Follow-up** Actual loss to follow-up unclear as different numbers are provided (both 89% and 96% are stated in the paper). Mean follow-up was 46 months (range, 6 months to 10 years), but paper also states that all patients attended the 2 year and 6 year follow-up visits which does not make sense with the provided range. **Study Funding/Conflict of Interest**
	Predictability of refraction (SE)	*Range* — *10 yr* within ± 0.5 D 81% within ± 1.0 D 96% within ± 2.0 D 100%	
	BSCVA	Preop Mean BSCVA ± SD (range): .58 ± 1.21 (.2 to 10) *Snellen Ratio* — *10 yr* BSCVA ≥ 20/20: 56.45% BSCVA ≥ 20/40: 95.17% BSCVA ≥ 20/70: 100.00%	

Study	Outcome	Results	Comments
Pesando et al., 2007 (continued)	Safety (change in BSCVA, Snellen lines)	*10 yr* Loss ≥ 2 lines: 0% Loss 1 line: 8.3%* No change: 64.4% Gain 1 line: 15.2% Gain 2 lines: 8.3% Gain 3 lines: 8.3% *this % does not match the figure	The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	ECD	*Endpt.* *ECD (cells/mm^2 ± SD)* *Mean Cell Loss (%)* Preop 2696 ± 298 n/a 10 yr 2437 ± 243 4.7%	
	IOP	Mean IOP ± SD (range) (mmHg) Preop: 13.36 ± .53 (9 to 18) 10 yr: 15.16 ± 1.84	

	Quality of Vision	- Good quality of vision and quality of life greatly improved: 29 patients (89%)
		- Most patients would repeat surgery and recommend to a friend
		- Quality of uncorrected vision
		  - Excellent: 4 patients (14%)
		  - Good: 26 patients
		  - Moderate with possibility of improvement: remaining patients
		- Halos under scotopic light
		  - At 6 mo: 23 patients (70%)
		  - At 1 yr: 2 patients (6%) (ICL overly vaulted in these patients)	

	Complications	Group A (patients who received older model ICLs) - Papillary block glaucoma: 1 patient -> ICL explanted - ICL implanted upside down: 1 patient -> ICL explanted and replaced - Anterior paracentral nonprogressive subcapsular opacity: 1 patient (found at 1 d) Group B (patients received current ICL model V4) - Complete anterior subcapsular cataract: 1 patient at 4 yr (inadequate vaulting noticed) - Nuclear subcapsular cataract: both eyes of 1 patient (ICL vaulting inadequate, ICL explanted and phacoemulsification) - Retinal edema and pupil mydriasis: 1 patient (caused by dislocation of haptic footplate due to trauma -> resolved after repositioned lens) - Persistent pain, weight sensation, glare and halos, iris chaffing, pigment mobilization: 2 e (2 patients) (due to excessive vaulting) -> explanted and replaced with shorter ICL	

Study	Outcome	Results	Comments
Sanders et al., 2007 (9) Toric ICL Lens Astigmatism (moderate to high) N@ preop: 210 e N@ 1 wk: 200 N@ 1 mo: 195 N@ 3 mo: 188 N@ 6 mo: 175 N@ 12 mo: 186 Fup = 12 mo	UVCA	At 12 mo: UCVA ≥ 20/20: 83% UCVA ≥ 20/40: 96% 76.5% of e had 12 mo UCVA ≥ preop BSCVA	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** Follow-up was good. 186 eyes (88.5%) were examined at 1 year. **Study Funding/Conflict of Interest** The study was funded by STAAR Surgical Company, Monrovia, California, and Drs Sanders, Slade, and Vukich are consultants to STAAR Surgical.
	Astigmatism (manifest refraction cylinder)	Mean cylinder ± SD (range) (D) Preop: 1.93 ± .84 (1 – 4) 12 mo: .51 ± .48 (0 – 3) *Cylinder* *Preop* *12 mo* Cylinder ≤.25 D 0 (0) 76 (40.9) Cylinder ≤ .50 D 0 (0) 122 (65.6) Cylinder ≤ 1.0 D 39 (21) 170 (91.4) Cylinder ≤ 2.0 D 122 (65.6) 185 (99.5) Cylinder ≤ 4.0 D 186 (100) 186 (100)	
	Predictability of cylinder	*Range* *6 mo* *12 mo* within ± 0.5 D 93 (53.4) 90 (48.4) within ± 1.0 D 150 (86.2) 159 (85.5)	
	Accuracy of cylinder	*6 mo* *12 mo* Attempted change 1.55 ± .66 D 1.56 ± .69 D Achieved change 1.50 ± .75 D 1.53 ± .82 D	
	Stability of cylinder	- Mean difference in cylinder between fup time points ranged from −.03 to .04 D - 88.2 to 99.4% e changed ≤1 D at all time points and 84.3 to 89.6% changed ≤.5 D at all time points	
	Refraction	Manifest SE: Preop: −9.36 ± 2.66 12 mo: .05 ± .46	
	Predictability of refraction (SE) N at 6 mo = 174 N at 12 mo = 186	*Range* *6 mo* *12 mo* within ± 0.5 D 124 (71.3) 143 (76.9) within ± 1.0 D 159 (91.4) 181 (97.3) within ± 2.0 D 173 (99.4) 186 (100)	
	BSCVA	*Snellen Ratio* *Preop* *12 mo* BSCVA ≥ 20/20: 83% 97% BSCVA ≥ 20/40: 100% 99%	
	Safety (change in BSCVA, Snellen lines)	*12 months* Loss ≥ 2 lines: 0.5% Loss 2 lines: 1.1% Loss 1 line: 5.9% No change: 16.1% Gain 1 line: 57.5% Gain 2 lines: 16.7% Gain > 2 lines: 2.2% Mean change in BSCVA: .88 lines of improvement at 12 mo	
	Patient Satisfaction with results	Very/extremely satisfied: 97.7% Moderately/fairly satisfied: 2.3% Unsatisfied: 0%	
	Complications	- ICL explantation: 4 e -> 1 had shorter ICL put in - ICL repositioned: 1 e - Transient iritis: 2 patients - Retinal detachment: 1 (0.5%) - Anterior subcapsular opacities of trace or more: 6 e (2.9%); 5 asymptomatic	

Study	Outcome	Results	Comments
Gimbel et al., 2005 (34) ICL Lens Myopia Astigmatism N@ preop: 58 e N@ 6 mo: 52 e Fup = 6 mo	UCVA at 6 mo	UCVA ≥ 20/20: 41/52 (78.8) UCVA ≥ 20/40: 49/52 (94.2)	Most patients received pIOLs in both eyes. Both eyes are included in the analysis with no attempt to correct for within-subject correlations. **Follow-up** 52 eyes (89.7%) were accountable for 6 months follow-up. 1 eye was excluded from the refractive outcomes analyses because the pIOL was explanted 1 week after surgery (no reason given). **Study Funding/Conflict of Interest** Dr.Halkiadakis was financially supported by Lilian Voudouri Foundation, Athens, Greece. The authors had no financial or proprietary interest in any material or method mentioned in the paper.
	Refraction (manifest SE)	Mean preop SE: −9.36 ± 3.21 (−3.88 to −19.25) Mean postop SE: .02 ± .48 (−1.25 to 1.33)	
	Predictability of refraction (SE) at 6 mo (n = 52)	*Range* within ± 0.5 D: 41 (78.8) within ± 1.0 D: 50 (96.2) within ± 2.0 D: 52 (100)	
	Astigmatism	Preoperative cylinder: −2.33 ± 1.04 (−0.75 to −5.25) Preoperative sphere: -8.20 ± 3.46 (−2.00 to −18.75)	
	Stability of	UCVA and BSCVA stabilized at 1 wk fup visit with little change at subsequent visits	
	BSCVA	Mean preop BSCVA = .999 Mean postop BSCVA = 1.125	
	Safety (change in mean BSCVA, Snellen lines) at 6 mo	Loss 2 lines: 0 (0) Loss 1 line: 2 (3.8) No change: 26 (50) Gain 1 line: 15 (28.8) Gain 2 lines: 9 (17.3)	
	Efficacy index	At 6 months: 0.94	
	Safety index	At 6 months: 1.126	
	Complications	- Acute angle closure: 1 e (lead to pIOL removal) o Excessive vaulting: 1 e (oversized lens used -> led to blurry vision and pressure sensation, required explantation and refractive lens exchange chosen instead) Note, this patient's results were excluded from the analysis - Anterior subcapsular lens opacities (trace to +1): 2 e (1 occurred in eye with prolonged anterior chamber inflammation and other in eye after pIOL removal and replacement) - Prolonged postop inflammation: 2 e - pIOL rotation off axis: 4 e o 2 off axis by ≥20 degrees (pIOL repositioned) o 2 off axis by < 10 degrees (no further action taken) - Unsatisfactory targeted SE: 1 (pIOL replaced) - Inc IOP at 1 d: 5 e (8.6%) (1 e required enlarging of iridotomy, 2 required anti-glaucoma meds)	

BSCVA refers to best spectacle corrected visual acuity; cat, category; CI, confidence interval; ECD, endothelial cell density; endpt, endpoint; e, eyes; fup, follow-up; HC, Health Canada; inc, increase; ICL, implantable collamer lens; IOP, intraocular pressure; mo, months; NR, not reported; preop, preoperative, postop, postoperative; SD, standard deviation; SE, spherical equivalent; UCVA, uncorrected visual acuity; VA, visual acuity; vis, vision; wk, week; yr, year

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