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# Comparative Effectiveness of Multifocal, Accommodative, and Monofocal Intraocular Lenses for Cataract Surgery and Lens Replacement

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## PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the [program website](#).

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at [Nicole.Floyd@va.gov](mailto:Nicole.Floyd@va.gov).

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# ABSTRACT

## INTRODUCTION

The comparative effectiveness of multifocal, accommodative, and monofocal intraocular lenses for cataract surgery and lens replacement remains unclear. This review was requested to assess the evidence.

### Key Questions

1. What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for distance vision in the setting of cataract surgery?
2. What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for near vision in the setting of cataract surgery?
3. What are the harms associated with multifocal or accommodative lenses versus monofocal replacement in the setting of cataract surgery?
4. If feasible, what resources are required to best care for patients who choose multifocal or accommodative lens implants in the setting of cataract surgery?

## METHODS

### DATA SOURCES AND SEARCHES

We conducted searches in PubMed from 1/1/2006 to 4/30/2017.

### STUDY SELECTION

Studies were included if they were randomized trials of a US FDA-approved lens that was either multifocal or accommodative and compared to standard monofocal IOLs (or monovision) in the setting of adult cataract extraction and reported visual acuity outcomes, spectacle independence, or visual function/quality of life.

### DATA SYNTHESIS AND ANALYSIS

Data extraction was completed in duplicate, and included: study design, single versus multi-site study, patient characteristics, intervention lenses, comparison monofocal lens, sample size, duration of follow-up, outcomes, and data needed for the Cochrane Risk of Bias tool.

## RESULTS

### RESULTS OF LITERATURE SEARCH

Our literature searches and reference mining identified 760 potentially relevant citations, of which 93 abstracts were included and obtained as full-text publications. Twelve publications provided some insight into the comparative effectiveness of multifocal, accommodative, and

monofocal intraocular lenses for cataract surgery and lens replacement, and are included in our final sample.

## SUMMARY OF RESULTS FOR KEY QUESTIONS

### Key Question 1

The evidence from 9 RCTs supports a conclusion that there is no difference in uncorrected or corrected distance vision between multifocal or accommodative IOLs and monofocal IOLs. The evidence for accommodative IOLs is restricted to only 1 trial. Two trials comparing multifocal IOLs to monovision found no difference in uncorrected distance vision.

### Key Question 2

Four RCTs support the conclusion that multifocal IOLs are better than monofocal IOLs for uncorrected near vision. This conclusion is also supported by better outcomes for reading accuracy, reading speed, and visual function. In the few studies that have measured visual function or vision-related quality of life, this has been better in patients receiving multifocal IOLs. Data on accommodative IOLs are very sparse. The 2 studies comparing multifocal IOLs to monovision found that multifocal IOLs result in better spectacle independence than monovision.

### Key Question 3

Between 3 and 8 RCTs support the following conclusions: 1) The risks of surgery are no greater for multifocal IOLs than monofocal IOLs in the patient population and lenses included in these trials; 2) Multifocal IOLs may have an increased risk of IOL exchange due to patient dissatisfaction; 3) Multifocal IOLs are associated with worse contrast sensitivity; 4) Multifocal IOLs are associated with greater risk of glare; 5) Multifocal IOLs are associated with a greater risk of halos; 6) Data on accommodative IOLs are too sparse to draw conclusions.

### Key Question 4

No hypothesis-testing study explicitly assessed the need for additional pre-operative or post-operative resources for patients receiving multifocal IOLs. However, several of the included trials used, as exclusion criteria, conditions that would require additional diagnostic tests that may go beyond the standard pre-operative evaluation for monofocal IOLs. Specialty society “best practice” recommendations for multifocal IOL procedures list a number of pre-operative and post-operative best practices that may not be included as part of standard monofocal IOL procedures.

## DISCUSSION

### KEY FINDINGS AND STRENGTH OF EVIDENCE

Moderate-strength evidence supports the conclusion that, compared to monofocal IOLs, multifocal IOLs achieve better outcomes on spectacle independence and uncorrected near visual acuity, without sacrificing uncorrected or corrected distance vision. Low-strength evidence supports the conclusion that multifocal IOLs result in better visual function/ quality of life than monofocal IOLs. More limited data support that multifocal IOLs achieve better spectacle independence than monovision. Moderate-strength evidence supports that multifocal IOLs result

in worse contrast sensitivity and a greater risk of glare, and low-strength evidence supports that they result in a greater risk of halos. Low strength evidence exists that monofocal IOLs result in greater IOL exchange due to dissatisfaction. Data are very limited about accommodative IOLs, consisting of only 1 RCT.

## APPLICABILITY

No studies were performed in VA populations, or even US populations; therefore, the applicability of these results to VA patients with cataracts is uncertain. A limitation is that IOL technology is rapidly changing, and therefore newer lenses may have differences in the benefits and harms we report here for older lenses.

## RESEARCH GAPS/FUTURE RESEARCH

A VA-sponsored multi-site randomized clinical trial would provide higher quality evidence than what currently exists about the benefits, harms, needed pre- and post-operative resources, and costs of multifocal IOLs compared to monofocal IOLs.

## CONCLUSIONS

Multifocal IOLs compared to monofocal IOLs produce better uncorrected near vision and a greater proportion of patients who are spectacle independent, but are associated with worse contrast sensitivity and a greater risk of glare and halos. Current evidence is insufficient to reach conclusions about resource requirements and other outcomes such as additional enhancements or IOL exchange.

## ABBREVIATIONS

AA	Accommodative amplitude
ACD	Anterior chamber depth
BCDVA	Best corrected distance visual acuity
BCIVA	Best corrected intermediate visual acuity
BCNVA	Best corrected near visual acuity
BCVA	Best corrected visual acuity
CDVA	Corrected distance visual acuity
CPD6	6 cycles per degree
DCNVA	Distance-corrected near visual acuity
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IOL	Intraocular Cataract Lenses
LASIK	Laser-assisted in situ keratomileusis
logMAR	Logarithm of the Minimum Angle of Resolution
MD	Mean Difference
MFIOL	Multifocal Intraocular Lens
MTF	Modulation transfer function
NDRA	Near-distance refractive addition
NVA	Near visual acuity
RMS	Root mean square

RMS4	Root mean square four
RMS <sub>h</sub>	RMS high order
RR	Risk Ratio
SCPA	Sclerociliary process angle
SMD	Standardized effective size
TEP	Technical Expert Panel
UCNVA	Uncorrected near visual acuity
UDVA	Uncorrected distance visual acuity
UIVA	Uncorrected intermediate visual acuity
UNVA	Uncorrected near visual acuity
VF7	Visual function index (shortened)
VF11R	Rasch-modified National Eye Institute Visual Function questionnaire
VF14	Visual function index

# EVIDENCE REPORT

## INTRODUCTION

Cataract is an eye condition in which the natural crystalline lens becomes cloudy and can ultimately lead to poor vision. Usually associated with aging, cataract affects more than 24.4 million Americans age 40 and older.<sup>1</sup> It is estimated that half of all Americans over 75 have cataract or have had cataract surgery. Surgical removal of cataract and implantation of a prosthetic lens can lead to improved vision and is one of the most common surgeries performed in the United States. In the past decade, the rate of cataract surgery has risen 20%.

Cataract surgery typically involves placement of a monofocal intraocular lens implant, which has a single focal point and is meant to correct vision at a single distance. For most patients, monofocal lens implants are used to correct far distance vision. However, this results in an inability to focus at near distance without the use of spectacle correction (*ie*, when reading a book or newspaper). More advanced intraocular lens implants involve optics that provide the ability for a patient to focus at distance and near without the use of spectacles correction.

The most commonly used type of advanced intraocular lens implants in the United States is the multifocal lens, which utilizes concentric rings with graduated power to produce multiple focal points at far and near distances. The 2 main types include refractive and diffractive optics, the latter of which is more commonly used. Another advanced design is the accommodative lens, which uses the muscle tone of the ciliary body to move the lens optic either forward or backward within the eye to achieve multiple focal points. More recently, another class of lens implants known as “extended depth of focus” lenses utilize concentric rings to induce improved range and depth of focus rather than distinct focal points.

Additional lens designs are available internationally and are currently under development in the United States.

While there are potential advantages to these newer lenses in terms of improved spectacle independence, there may be downsides including increases in unwanted visual symptoms such as glare, halo, and decreased contrast sensitivity. Also, many pre-existing ocular conditions are considered contraindications to their use.

Another consideration is the added cost of these advanced lens implants. Medicare and other private insurances do not cover the additional cost associated with these lenses. Typically, a patient choosing to have this type of lens would incur the additional cost out of pocket. However, within VA, there is no mechanism for balance billing. Currently, the use of these lenses in VA is limited and approved on a case-by-case basis. This systematic review has been requested to assess the benefits and harms of these types of intraocular lens implants so that further guidance on their use within VA can be provided.

## METHODS

### TOPIC DEVELOPMENT

This topic was developed in response to a nomination by Dr. Donald Higgins, Acting Chief Consultant for Specialty Care Services (10P4E), and Dr. William Gunnar, National Director of Surgery (10NC2). Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

1. What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for distance vision in the setting of cataract surgery?
2. What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for near vision in the setting of cataract surgery?
3. What are the harms associated with multifocal or accommodative lenses versus monofocal replacement in the setting of cataract surgery?
4. If feasible, what resources are required to best care for patients who choose multifocal or accommodative lens implants in the setting of cataract surgery?

The review was submitted to PROSPERO: CRD42017069949

The Technical Expert Panel consisted of the following people: Donald Higgins, MD, Acting Chief Consultant for Specialty Care Services, VA Central Office; William Gunnar, MD, National Director of Surgery, VA Central Office; Amy Chomsky, MD, Chair, Ophthalmology Surgical Advisory Board; Glenn Cockerham, MD, National Program Director, VA Ophthalmology Service; Mary Daly, MD, Chief of Ophthalmology, VA Boston Healthcare System; Martha Farber, MD, Chief of Ophthalmology, Albany VA Medical Center; and Paul Greenberg, MD, MPH, Providence VA Medical Center.

Topic refinement with the TEP established that not all multifocal or accommodative lenses were of interest to VA: only lenses that are FDA-approved for use in the US are of interest. Furthermore, because of the pace of change in technology, priority was given to studies published within the past 10 years. “Effectiveness” was defined as spectacle independence: that is the goal of using a multifocal or accommodative lens. Visual acuity, survey measures of visual function, and quality of life were of also of interest. Harms included both the harms of the surgery itself, but also visual aberrations such as glare, halos, contrast sensitivity, and other optical phenomena. The timing of outcome measures was determined to be not particularly crucial. While 3-month or 6-month outcomes were desirable, earlier time points were considered adequate for the purposes of inclusion.

### SEARCH STRATEGY

We conducted searches in PubMed from 1/1/2006 to 4/30/2017 (see Appendix A for full search strategy). The search in PubMed used a broad set of terms relating to “cataract” or “cataract

extraction” and “lenses, intraocular” or “lens implantation, intraocular” and terms of multifocal or accommodative lenses.

## STUDY SELECTION

Two team members independently screened the titles of retrieved citations. Citations deemed relevant by at least 1 reviewer were then screened at the full-text level by 2 independent reviewers. Any disagreements were resolved by consensus decision after study team discussion. To be included, full texts needed to be randomized controlled trials of adults undergoing cataract extraction and comparing a multifocal or accommodative lens with a standard monofocal lens and reporting an outcome of interest. Included studies had to assess at least one lens that is FDA-approved for use in the VA.

The following PICOTS framework describes our inclusion criteria:

*Participants/population:* Adult patients undergoing cataract surgery with placement of intraocular lenses

*Intervention(s):* Placement of either multifocal or accommodative intraocular lenses

*Comparators:* Standard monofocal lenses

*Outcomes:* The primary outcome was spectacle independence. Additional outcomes were uncorrected and corrected distance vision, uncorrected near vision, validated measures of vision function (such as the VF-14) or quality of life. Harms included the harms of the surgery itself plus effects such as contrast sensitivity and aberrations like glare and halos.

*Timing:* Outcomes measured at any time point following surgery were included. When multiple time points were reported, later time points were preferred to earlier time points.

*Setting:* Cataract surgery

## DATA ABSTRACTION

Data extraction was completed in duplicate. All discrepancies were resolved with full-group discussion. We abstracted data on the following: study design, single versus multi-site study, patient characteristics, intervention lenses, comparison monofocal lens, sample size, duration of follow-up, outcomes, and data needed for the Cochrane Risk of Bias tool.

## QUALITY ASSESSMENT

Included randomized controlled trials were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool.<sup>2</sup> This tool requires an assessment of whether a study is at high or low (or unknown) risk of bias in 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other. We used the “other” category to assess whether authors specifically stated there was no loss to follow-up in studies for which only a single sample size number was reported (for example, a study might say “there were 50 patients in our study” and no additional information is ever given about how many were enrolled versus how

many completed the study). As a study of a surgical procedure, it is impossible or impractical to blind the surgeons to what kind of IOL is being implanted, or to blind the patient about what kind of IOL they are receiving. We did consider it possible to blind the outcome assessor if the outcome required the interpretation of a third party and that third party was kept blinded to treatment assignment.

## DATA SYNTHESIS

The sample size, mean, and standard deviation for each treatment group was extracted from articles that reported visual acuity using Snellen or logMAR measurements. Data that reported visual acuity using Snellen charts were converted into logMAR values. A mean difference (MD) was calculated for each comparison of multifocal and monofocal lenses. Similar data was collected for quality of life measures but since the scales varied, a standardized effect size (SMD) was calculated for each comparison. The sample size and number or percent of patients with spectacle independence was collected and a risk ratio (RR) was calculated for each comparison.

Meta-analyses were conducted for the visual acuity and quality of life outcomes using trials that reported a monofocal lens comparator. Because several trials reported comparisons of more than one intervention, 2-level multilevel random effects models were estimated.<sup>3</sup> For the two trials that reported a monovision comparator, a fixed-effects meta-analysis was performed.<sup>4</sup>

Test of heterogeneity were reported using the  $I^2$  statistic.<sup>5</sup> Values of the  $I^2$  statistic close to 100% represent high degrees of heterogeneity. Begg rank correlation<sup>6</sup> and Egger regression asymmetry test<sup>7</sup> were used to examine publication bias. R version 3.4.1 was used for all statistical analyses.

There was only 1 study that used an accommodative lens, so the results of that study were presented narratively.

## RATING THE BODY OF EVIDENCE

Where possible, a summary of findings and quality of evidence table was used to summarize the existing evidence. Based on the GRADE working group,<sup>8</sup> the quality of the evidence was categorized as follows:

**High:** We are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate:** We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low:** Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

**Very low/Insufficient:** We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

GRADE evaluates the quality of the evidence across all identified studies contributing to the outcome of interest.

## **PEER REVIEW**

A draft version of the report was reviewed by technical experts and clinical leadership. Reviewer comments and our responses are documented in Appendix B.

## RESULTS

### LITERATURE FLOW

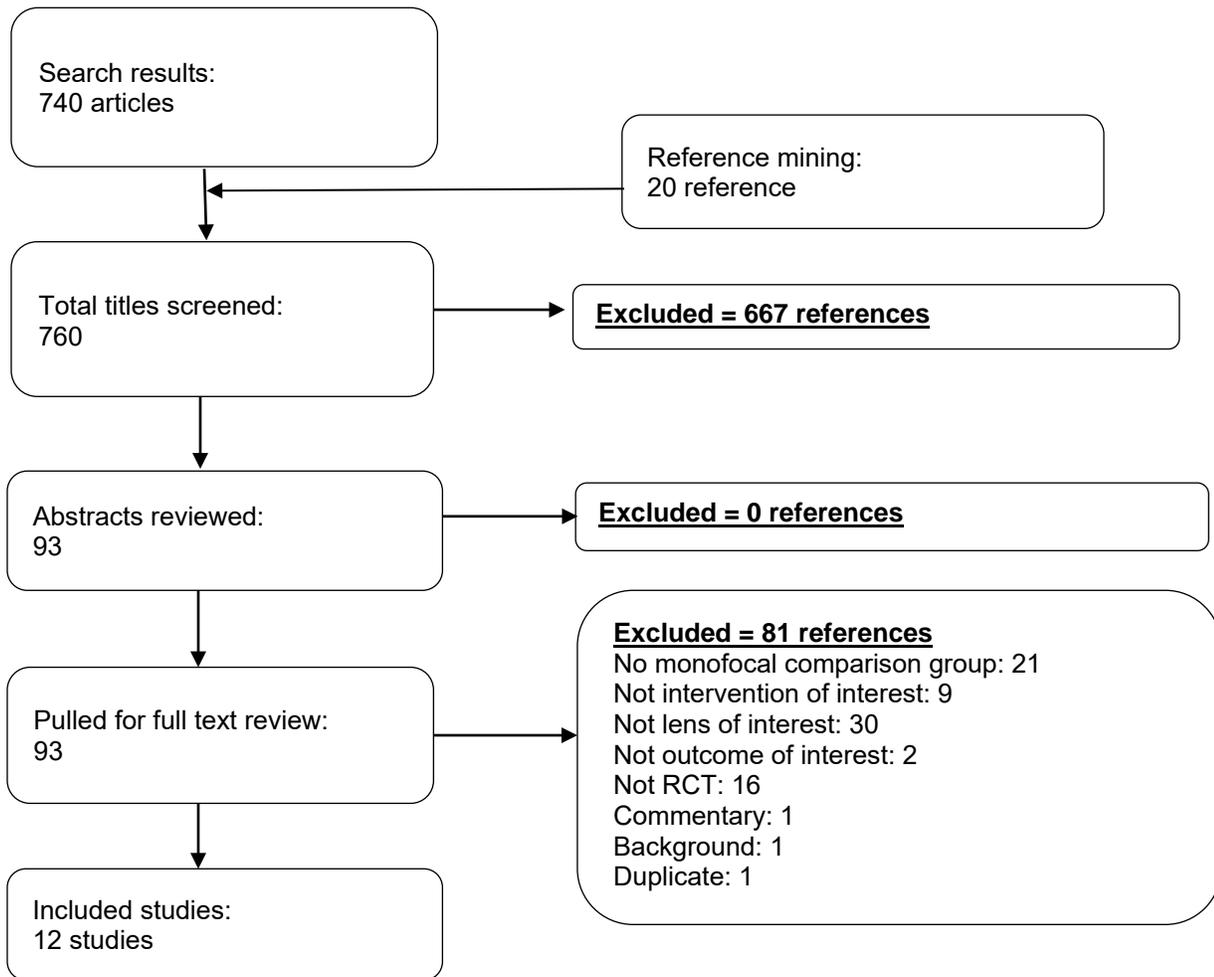
Our literature searches, expert recommendations, and reference mining identified 760 potentially relevant citations, of which 93 were included at the abstract screening. All 93 abstracts were included and obtained as full-text publications. Eighty-one studies were excluded for the following reasons: no monofocal comparison group (n=21); not intervention of interest (n=9); not lens of interest (n=30); not outcome of interest (n=2); not RCT (n=16); commentary (n=1); background (n=1); duplicate (n=1). A total of 12 publications were identified at full-text review as includes that contributed to our final sample (See Figure 1). Details of included studies are provided in the Evidence Table in Appendix C. A full list of these excluded studies from the full-text review is included in Appendix D.

### DESCRIPTION OF THE EVIDENCE

All of the studies were single-site with 3 exceptions.<sup>9-11</sup> No study was performed in the USA; 4 studies were performed in China.<sup>12-15</sup> Sample sizes were modest: 5 studies enrolled 75 patients or less,<sup>11,13,16-18</sup> and only 1 study enrolled more than 200 patients.<sup>9</sup> The mean age of patients enrolled was 60-75 years of age, and patients were 50-60% female. All but one study assessed multifocal IOLs.<sup>11</sup> Two studies compared the interventions lenses to monovision or mini-monovision,<sup>9,18</sup> where the 2 eyes have monofocal IOLs of different focal lengths, such that one eye sees predominantly distance vision and the other eye sees predominantly near vision. Nearly all studies reported visual acuity; 6 studies reported spectacle independence<sup>9,14-16,18,19</sup>; other outcomes were variably reported. We considered the 2 studies by Alio and colleagues<sup>10,17</sup> to potentially have overlapping patients, and for the purposes of statistical pooling only used the results from the study with the larger sample size.

The quality of studies was in general low – no study was judged to be at low risk of bias across all domains, though one study was at low risk of bias in all domains except one.<sup>16</sup> Since only 2 studies were reported as having had their protocol prospectively registered,<sup>9,18</sup> for example on [clinicaltrials.gov](http://clinicaltrials.gov), our ability to assess selective reporting bias is limited.

**Figure 1. Literature Flow Chart**



**Table 1. Quality Assessment for Included Studies**

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Marchini, 2007 <sup>11</sup>	~	-	-	½	~	TM	-
Zeng, 2007 <sup>12</sup>	½	½	-	-	½	TM	-
Cillino, 2008 <sup>16</sup>	TM	TM	½	TM	TM	TM	
Palmer, 2008 <sup>19</sup>	TM	½	½	TM	½	TM	
Zhao,2009 <sup>15</sup>	TM	-	½	TM	TM	TM	
Alio, 2011 <sup>10</sup>	TM	½	-	-	½	TM	-
Alio, 2011 <sup>17</sup>	TM	½	-	-	½	TM	-
Ji, 2012 <sup>13</sup>	½	-	-	-	TM	TM	
Peng, 2012 <sup>14</sup>	TM	-	-	-	½	TM	
Rasp, 2012, <sup>20</sup>	½	-	-	½	~	TM	
Wilkins, 2013 <sup>9</sup>	TM	TM	-	-	TM	TM	TM
Labiris, 2015 <sup>18</sup>	TM	½	-	-	½	TM	-

TM = low risk of bias ~ = risk of bias ½ = unknown

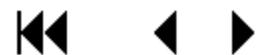
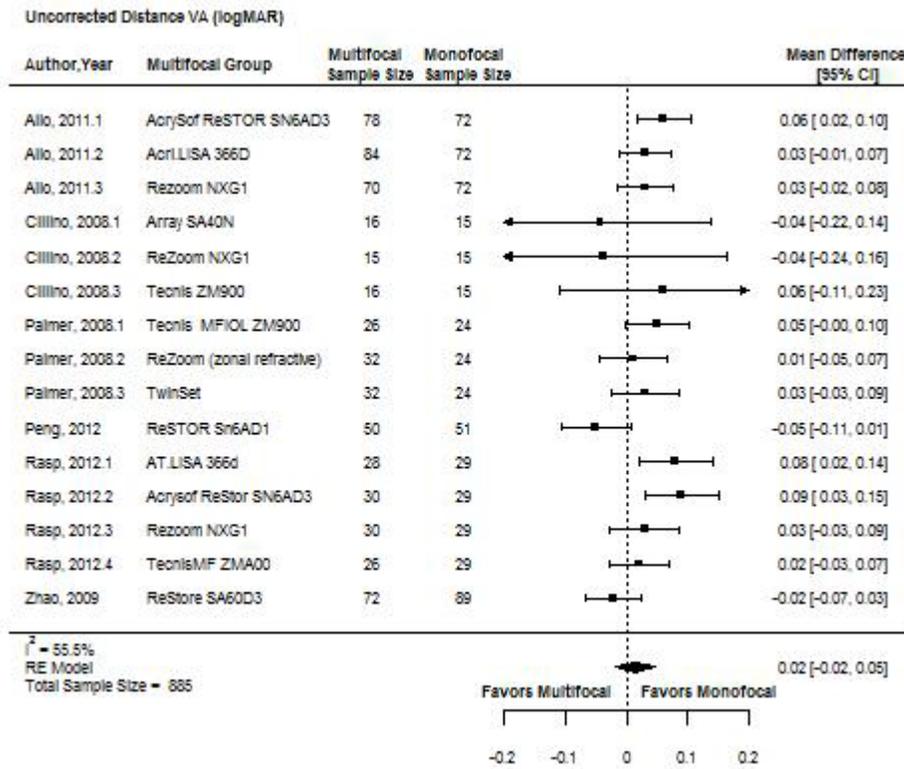
**KEY QUESTION 1: What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for distance vision in the setting of cataract surgery?**

**Multifocal IOLs Compared to Monofocal IOLs**

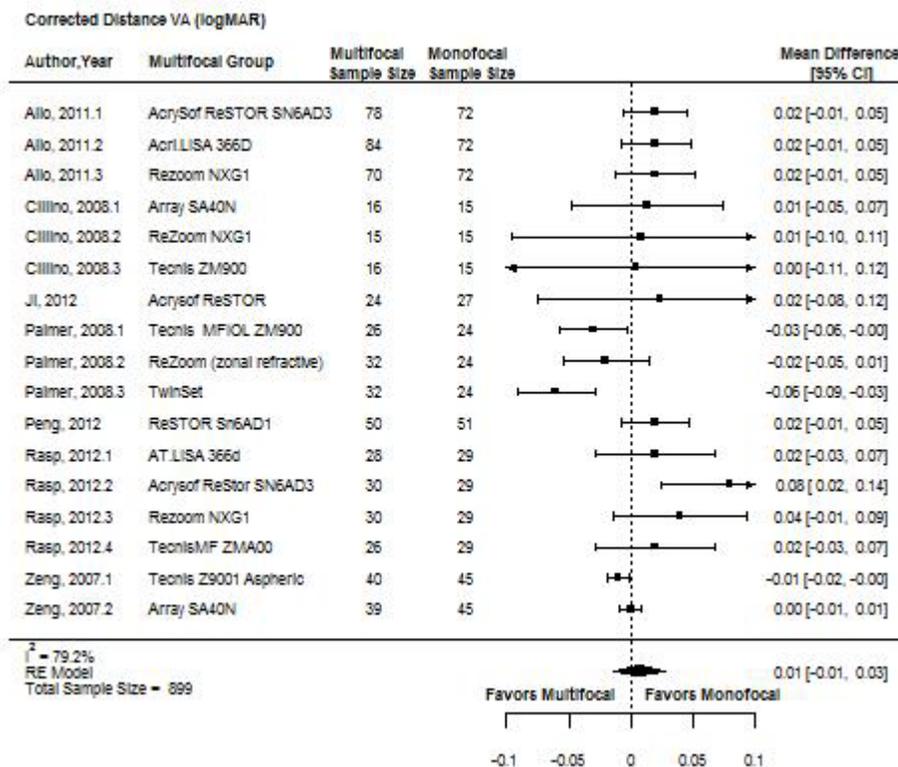
We identified 6 studies (with 15 comparisons and 885 patients) and 7 studies (with 17 comparisons and 899 patients) that reported uncorrected and corrected distance vision, respectively, when comparing multifocal IOLs to monofocal IOLs (that were not used for monovision). Figure 2 presents the data for uncorrected distance vision and figure 3 presents the data for corrected distance vision. For both outcomes, there were no statistically significant differences in vision between the multifocal and monofocal IOLs. There was no statistical evidence for publication bias (Begg’s test p value = 0.55, Eggar’s test p value = 0.78).



**Figure 2. Multifocal IOLs Compared to Monofocal IOLs Uncorrected Distance VA (logMAR)**



**Figure 3. Multifocal IOLs Compared to Monofocal IOLs Corrected Distance VA (logMAR)**

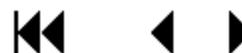


**Multifocal IOLs Compared to Monofocal IOLs as Monovision**

We identified 2 RCTs that compared multifocal IOLs to monofocal IOLs for monovision.<sup>9,18</sup> We pooled these using a fixed effects model. There was no statistically significant difference in uncorrected distance vision (see appendix). Corrected distance vision was not reported. There was no statistical evidence of publication bias.

**Accommodative IOLs Compared to Monofocal IOLs**

One RCT was identified that compared the use of accommodative IOLs to a standard monofocal IOL during routine cataract surgery.<sup>11</sup> This trial was a three-arm comparison of 2 different accommodative IOLs compared to a single monofocal IOL during cataract surgery in patients with visually significant cataract. In group 1, 19 subjects (30 eyes) received the 1CU accommodative IOL (HumanOptics, Erlangen, Germany); in group 2, 19 subjects (29 eyes) received the AT-45 Crystalens accommodative IOL (Eyeonics Vision, Aliso Viejo, CA); and in group 3, 21 subjects (21 eyes) received the ACR6D monofocal IOL (Corneal, Paris, France). Patients were recruited from a single university-based ophthalmology practice and were determined to have any type of cataract as the sole cause of decreased vision less than or equal to 20/40 and no other preexisting ocular comorbidities. The enrolled sample of 59 subjects (80 eyes) was 47.4% female with a mean age of 66 ± 10 years. All subjects underwent pre-operative evaluation including slit-lamp evaluation, indirect funduscopy, applanation tonometry, keratometry, and immersion A-scan biometry. Two surgeons performed all surgeries based on standardized techniques. The authors state that no major surgical complications occurred.



Outcome measures included: uncorrected far-distance visual acuity; best-corrected far-distance visual acuity; uncorrected near-distance visual acuity; best-corrected near-distance visual acuity; distance-corrected near visual acuity; near-distance refractive addition (NDRA); accommodative amplitude (AA); variation in anterior chamber depth (ACD); and variation in sclerociliary process angle (SCPA). Outcomes were measured at post-operative months 1, 6, and 12.

At 12 months, statistically significant differences were found in the following areas:

- The NDRA needed to reach best-corrected near visual acuity was significantly lower in the accommodative IOL groups versus the monofocal IOL group (although no difference was found between the 2 accommodative IOL groups)
- Distance-corrected near visual acuity was significantly better in the accommodative IOL groups versus the monofocal group. DCNVA was better in the 1CU group versus the AT-45 group.
- The variation in anterior chamber depth was significantly greater in the AT-45 group compared to the monofocal group.

No significant differences were found in the following areas: BCDVA; BCNVA; uncorrected near-distance VA; AA variation; and SCPA variation.

## Summary of Findings

From 9 RCTs the evidence supports a conclusion that there is no difference in uncorrected or corrected distance vision between multifocal or accommodative IOLs and monofocal IOLs. The evidence for accommodative IOLs is restricted to only 1 trial. Two trials comparing multifocal IOLs to monovision found no difference in uncorrected distance vision.

## Quality of Evidence for Key Question 1

We judged the evidence for the outcomes of distance vision with multifocal IOLs as moderate (downgraded due to methods limitation in the RCTs), and for accommodative IOLs as low due to sparseness of data (1 RCT).

**Table 2. GRADE Quality of Evidence Table (Outcomes of Distance Vision)**

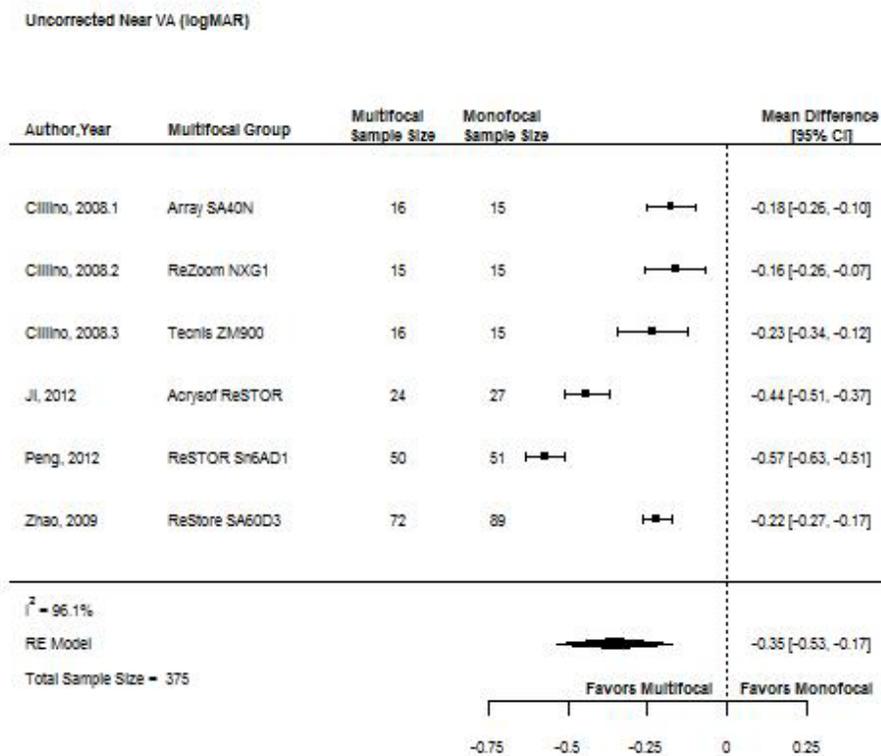
Outcome	Number of Studies and Design	Methodological Quality of Studies	Consistency Across Studies	Directness of Evidence	Other Considerations	Qualitative Description of Effect Size	Quality of Evidence
Multifocal IOLs – Uncorrected distance vision	6 RCTs	Serious limitation	No serious limitations	No serious Limitations	None	No difference	Moderate
Multifocal IOLs – Corrected distance vision	7 RCTs	Serious limitation	No serious limitations	No serious limitations	None	No difference	Moderate
Accommodative IOLs – Uncorrected distance vision	1 RCT	Serious limitation	N/A	No serious limitation	Sparse data	No difference	Low
Accommodative IOLs – Corrected distance vision	1 RCT	Serious limitation	N/A	No serious limitation	Sparse data	No difference	Low

## KEY QUESTION 2. What is the effectiveness of multifocal or accommodative versus monofocal lenses with spectacle correction for near vision in the setting of cataract surgery?

### Multifocal IOLs Compared to Monofocal IOLs

We identified 4 studies (with 6 comparisons and 375 patients) that reported uncorrected near vision comparing multifocal IOLs to monofocal IOLs (that were not used for monovision).<sup>13-16</sup> Figure 4 presents the results. The random effects pooled estimate of effect in logMAR was -0.35 (95% CI -0.93, -0.17) favoring multifocal IOLs. There was significant heterogeneity ( $I^2 = 96.1\%$ ). There was no statistical evidence of publication bias (Begg's test p value = 1, Eggar's test p value = 0.61).

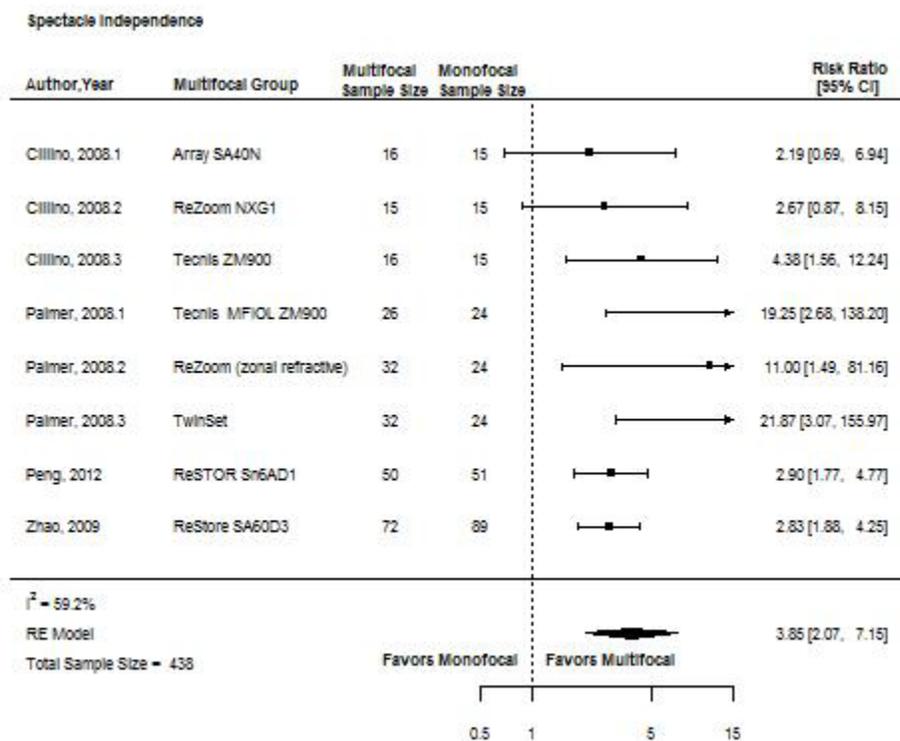
**Figure 4. Multifocal IOLs Compared to Monofocal IOLs Uncorrected Near VA (logMAR)**



We identified 4 studies (with 8 comparisons and 438 patients) that reported spectacle independence comparing multifocal IOLs to monofocal IOLs (that were not used for monovision).<sup>14-16,19</sup> Figure 5 presents the results. The random effects pooled estimate was a relative risk of 3.85 (95% CI 2.07, 7.15) favoring spectacle independence with multifocal IOLs. There was moderate heterogeneity. ( $I^2 = 59.2\%$ ). Begg’s test for publication bias was not statistically significant ( $p = .11$ ); however, Eggar’s test was significant ( $p = 0.008$ ). This was probably due to the results of the study by Palmer showing 5-10 times greater benefits for spectacle independence than the other 3 studies.



**Figure 5. Multifocal IOLs Compared to Monofocal IOLs Spectacle Independence**

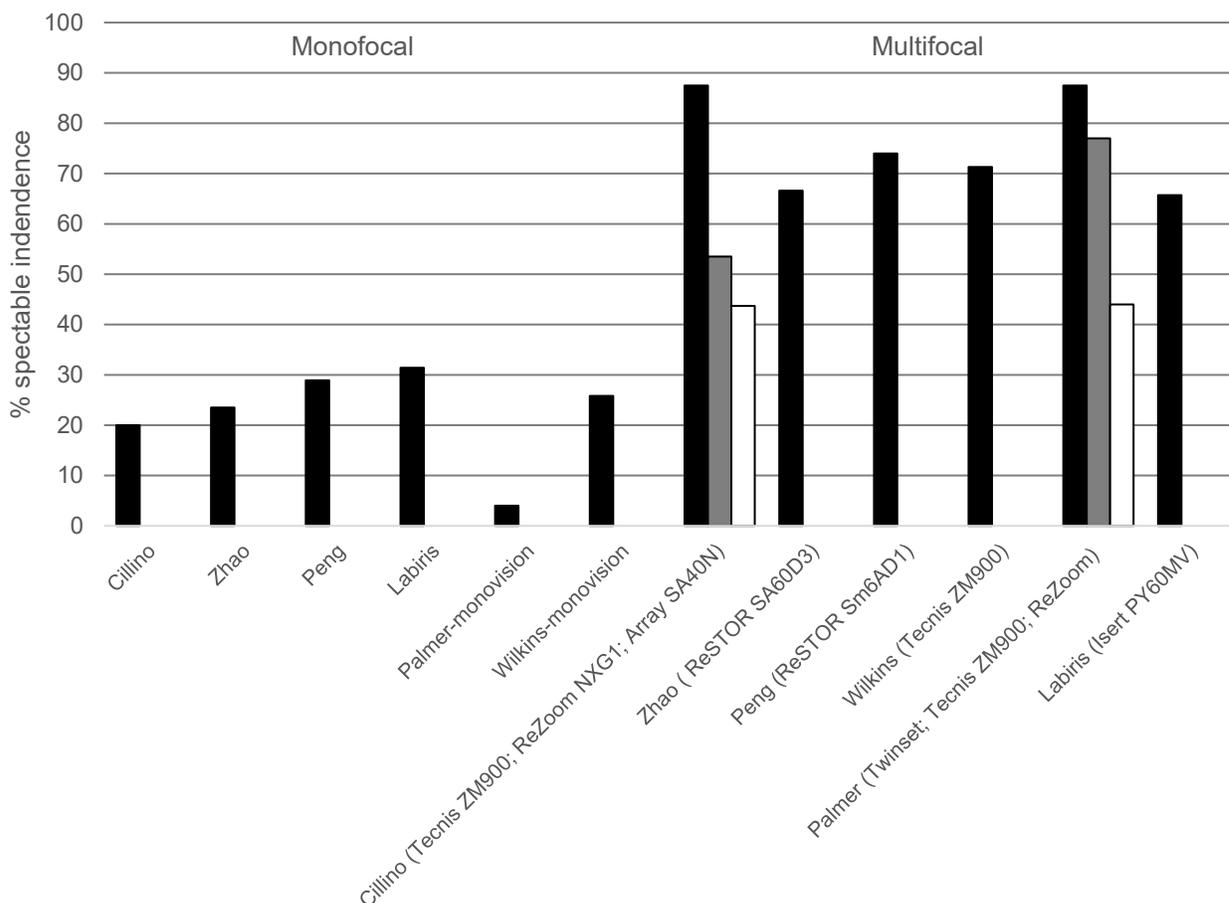


**Multifocal IOLs Compared to Monofocal IOLs as Monovision**

We identified 2 RCTs that compared multifocal IOLs to monofocal IOLs as monovision.<sup>9,18</sup> We pooled these studies with a fixed effect model. The pooled fixed effect logMAR for uncorrected near vision was -0.03 (95% CI -0.07, 0.00) favoring multifocal IOLs (see Appendix E). For spectacle independence, the pooled fixed effect was a risk ratio of 2.52 (95% CI 1.87, 3.41) favoring multifocal IOLs.

As another means of displaying the results for spectacle independence, the bar graph (Figure 6) presents the proportion of patients who achieved spectacle independence in the 6 studies reporting this outcome. On the left is the standard monofocal IOL patients (or monovision patients) and on the right are multifocal IOL patients (some studies tested more than 1 multifocal IOL). The proportion of patients achieving spectacle independence with multifocal IOLs is 2- or 3-fold higher than with monofocal IOLs or monovision.

**Figure 6. Spectacle Independence**



**Accommodative IOLs Compared to Monofocal IOLs**

We identified 1 RCT comparing accommodative IOLs to monofocal IOLs.<sup>21</sup> It is discussed in the prior section. No statistically significant differences were found for uncorrected near visual acuity. However, distance-corrected near visual acuity was significantly better in the accommodative IOL group.

**Other Outcomes**

Two RCTs were identified that evaluated bilateral reading performance after implantation of different types of multifocal IOLs as compared to a control monofocal IOL.<sup>10,20</sup> The authors of both studies contend that reading performance provides a better means of assessing functional near vision after cataract surgery as compared to visual acuity measurements based on single letters.

Rasp et al evaluated 143 patients (286 eyes) undergoing routine bilateral cataract surgery for visually significant cataract randomized to receive 1 of 4 different multifocal IOLs or a control monofocal IOL.<sup>20</sup> Alio et al evaluated 152 patients (304 eyes) undergoing bilateral cataract surgery who received 1 of 3 different multifocal IOLs or a control monofocal IOL.<sup>10</sup> All patients

underwent bilateral implantation of the same IOL model. Exclusion criteria for both studies included any coexisting ocular disease and illiteracy.

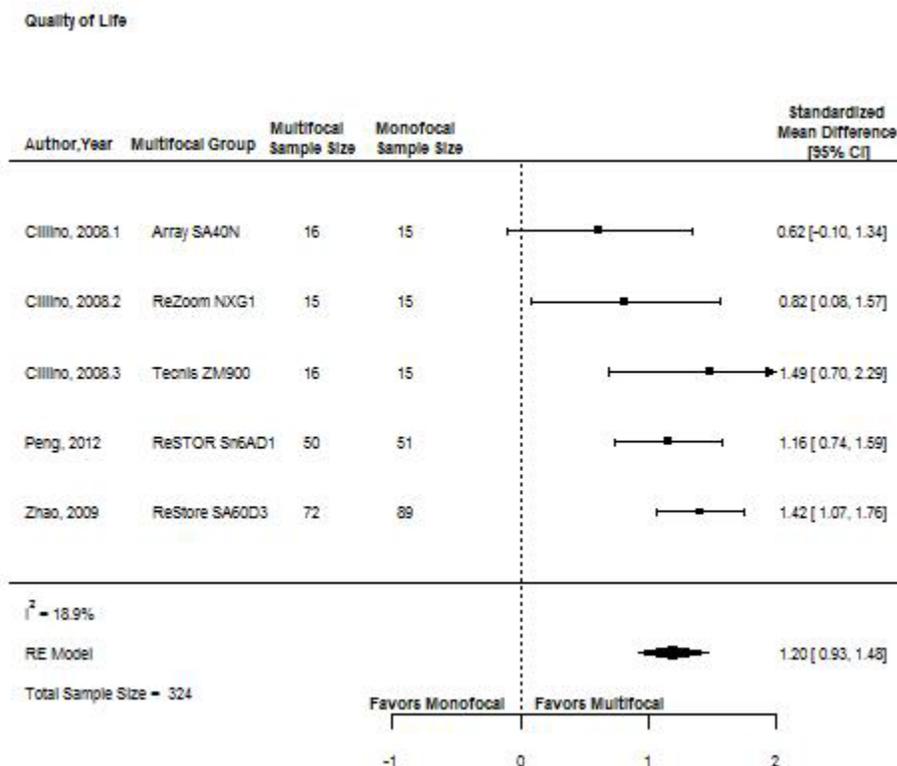
Both studies utilized the Salzburg Reading Desk system to measure reading performance. The Salzburg Reading Desk utilizes a reading desk, computer, and proprietary software to measure various aspects of reading performance including reading acuity, reading distance, reading speed, and smallest print size. This system is automated and provided testing under standardized conditions while simulating a natural reading process.

Rasp et al found significantly improved uncorrected reading acuity and uncorrected smallest print size in the diffractive multifocal IOL groups compared to the monofocal and refractive multifocal IOL groups.<sup>20</sup> Uncorrected reading distance was decreased in the diffractive multifocal IOL groups (32 cm) as compared to the monofocal (38.9 cm) and refractive IOL groups (37.1 cm). One specific diffractive IOL demonstrated the best reading speed values as compared to all other groups. Outcomes were measured at 12 months.

Alio et al found similar outcomes based on their comparison groups followed for 6 months.<sup>10</sup> Uncorrected reading acuity was significantly better in the diffractive multifocal IOL groups as compared to the monofocal and refractive IOL groups ( $p < 0.1$ ). Uncorrected reading speed was significantly worse in the refractive multifocal IOL group than in the monofocal IOL group. Reading distance was significantly worse in the monofocal group as compared to all other multifocal groups.

Three studies presented data on visual function or quality of life for multifocal IOLs compared to monofocal IOLs.<sup>14-16</sup> These studies included 5 comparisons and 324 patients. The pooled random effects standardized mean difference was 1.20 (95% CI 1.07, 1.76) favoring multifocal IOLs (Figure 7). There was no significant heterogeneity ( $I^2 = 18.9\%$ ). There was no statistical evidence for publication bias (Begg's test  $p$  value = 0.82, Egger's test  $p$  value = 0.20).

**Figure 7. Multifocal IOLs Compared to Monofocal IOLs Quality of Life**



**Summary of Evidence**

4 RCTs support the conclusion that multifocal IOLs are better than monofocal IOLs for uncorrected near vision. This conclusion is also supported by better outcomes for reading accurately and speed and visual function. In the few studies that have measured visual function or vision-related quality of life, this has been better in patients receiving multifocal IOLs. Data on accommodative IOLs are very sparse. Two studies found that multifocal IOLs result in better spectacle independence than monovision.

**Quality of Evidence for Key Question 2**

We judged the evidence for the outcomes of uncorrected near vision and spectacle independence with multifocal IOLs as moderate, downgraded due to methods limitations in the RCTs and for accommodative IOLs as low due to sparseness of data.



**Table 3. GRADE Quality of Evidence Table (Outcomes of Uncorrected Near Vision and Spectacle Independence)**

Outcome	Number of Studies and Design	Methodological Quality of Studies	Consistency Across Studies	Directness of Evidence	Other Considerations	Qualitative Description of Effect Size	Quality of Evidence
Multifocal IOLs – Uncorrected near vision	4 RCTs	Serious limitation	No serious limitations	No serious Limitations	None	Multifocal IOLs better	Moderate
Multifocal IOLs – Spectacle independence	4 RCTs	Serious limitation	No serious limitations	No serious limitations	None	Multifocal IOLs better	Moderate
Accommodative IOLs – uncorrected near vision	1 RCT	Serious limitations	N/A	No serious limitations	Sparse data	No difference	Low
Multifocal IOLs – quality of life	3 RCTs	Serious limitations	No serious limitations	No serious limitations	Sparse data	Multifocal IOLs better	Low

### KEY QUESTION 3. What are the harms associated with multifocal or accommodative lenses versus monofocal replacement in the setting of cataract surgery?

#### Surgical Complications

Six of the 10 multifocal IOL studies addressed whether any surgical adverse events occurred in the study with varying degrees of detail.<sup>9,12,14-17</sup> We considered the 2 studies by Alio to have potentially overlapping patients, and so include here only the 1 study by Alio that reported adverse events. The one study of accommodative IOLs only reported “no major surgical complications occurred.”<sup>11</sup> Zeng commented that patients with posterior capsule rupture or suboptical rhexis size were excluded but did not comment on intraoperative or postoperative complications from the included eyes.<sup>12</sup> Peng commented that no intraoperative or postoperative complications occurred.<sup>14</sup> Alio commented no complication occurred intraoperative or postoperative and capsule remained clear until 3 months follow up.<sup>17</sup> Cillino and Zhao excluded intraoperative complications but also specifically commented that no post-operative complications occurred including high pressure, infection, and swelling, as well as IOL decentration and development of posterior capsule opacification in the 6-month follow-up.<sup>15,16</sup> Wilkins described 5 patients randomized to MFIOL who received a monofocal IOL instead due to intraoperative complications or administrative error.<sup>9</sup> The study also described 12.2% of MFIOL cases had an IOL exchange at the time of surgery due to damage of the IOL during injections. The authors add that the injector system was changed after the study following reports of this issue. One patient in each arm needed LASIK for refractive error. More importantly, 6 patients with MFIOL had a second surgery to exchange the lens for a monofocal due to dissatisfaction with the lens.

## Contrast Sensitivity

Eight of the 10 multifocal IOL studies reported contrast sensitivity.<sup>9,12-16,18,19</sup> Zeng showed statistical significant contrast sensitivity issues for the Tecnis multifocal lens (Z9001) compared to the monofocal lens then followed by the second multifocal lens (SA40N).<sup>12</sup> Cillino showed better contrast with the monofocal lens (AR40) and multifocal lens (ZM9000) compared to the Array and ReZoom lenses ( $p=0.038$ ).<sup>16</sup> Palmer showed monofocal IOLs with statistically significant better contrast compared to the ZM9000 and Twin set lens at all frequencies and luminance.<sup>19</sup> Meanwhile the difference was only significant between the monofocal and ReZoom at high frequencies in scotopic conditions.

Ji showed lower contrast sensitivity with the ReSTOR lens compared to monofocal lens under all 6 spatial frequencies with mesopic and photopic conditions.<sup>13</sup> Compared to monovision, multifocal lenses had less contrast sensitivity according to Wilkins.<sup>9</sup> Meanwhile Peng showed worse contrast with the ReSTOR lens at low MTF but no difference at higher MTF.<sup>14</sup> On the other hand, Zhao showed no difference in contrast sensitivity between the ReSTOR lens (SA60AD3) and the monofocal lens (SA60AT).<sup>15</sup> Labiris et al showed no difference in contrast comparing “mini-monovision” with a refractive multifocal lens.<sup>18</sup>

**Table 4. Contrast Sensitivity Results in Studies Comparing Multifocal IOLs to Monofocal IOLs**

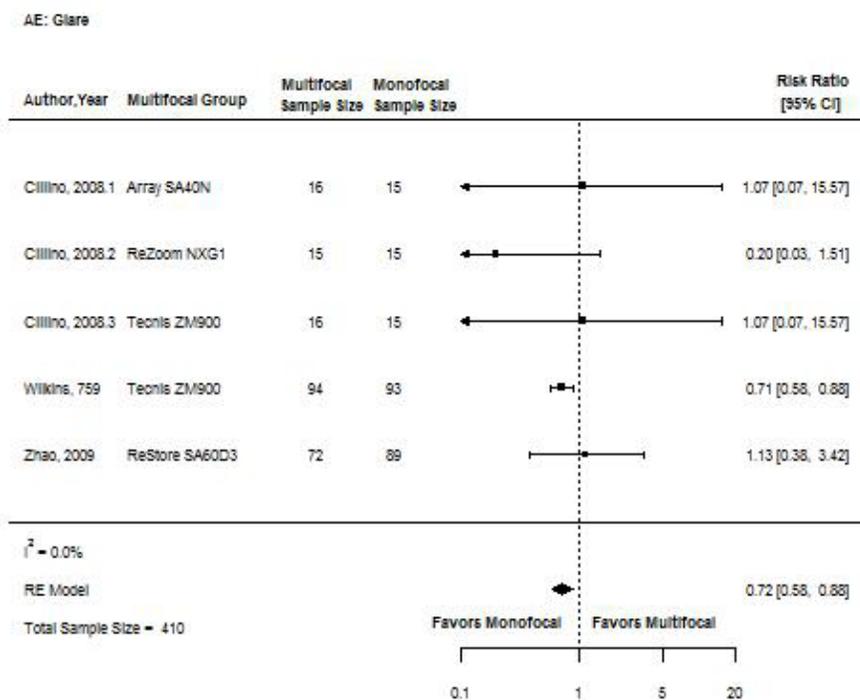
Studies	Favors Multifocal IOLs	No difference	Favors Monofocal IOLs
Zeng, 2007 <sup>12</sup>			x
Cillino, 2008 <sup>16</sup>			x
Palmer, 2008 <sup>19</sup>			x
Zhao, 2009 <sup>15</sup>		x	
Ji, 2012 <sup>13</sup>			x
Peng, 2012 <sup>14</sup>			x
Wilkins, 2013 <sup>9</sup>			x
Labiris, 2015 <sup>18</sup>		x	

## Glare

Six of 10 multifocal IOL studies reported glare following surgery.<sup>9,12,14-16,18</sup> Zeng showed significantly worse glare with the Tecnis multifocal lens (Z9001) compared to the Array multifocal lens (SA40N), followed by the monofocal lens which had the least glare ( $p=0.004$ ).<sup>12</sup> Cillino showed no significantly higher reported cases of glare following surgery amongst the multifocals and monofocal lenses, although the ReZoom had the most cases reported (5 compared to 1 in each other group).<sup>16</sup> Peng et al showed worse reported glare in the ReSTOR lens compared to the monofocal lens on an impact rating score.<sup>14</sup> Wilkins grouped glare with “dazzle” and showed the ReSTOR had more “debilitating” and “annoying” glare following surgery compared to the monovision patients.<sup>9</sup> Labiris showed not statistically significant difference in reported glare on a 4-point scale of a refractive MFIOL compared to mini-monovision.<sup>18</sup> Zhao found 5 cases with glare in the multifocal IOL group compared to 7 cases in the monofocal IOL group.<sup>15</sup>

We pooled the 3 studies reporting binary outcomes for glare which totaled 410 patients.<sup>9,15,16</sup> The random effects pooled estimate was a risk ratio of 0.72 (95% CI 0.58, 0.88) favoring monofocal IOLs. There was no heterogeneity ( $I^2 = 0\%$ ).

**Figure 8. Multifocal IOLs Compared to Monofocal IOLs Glare**



**Halos**

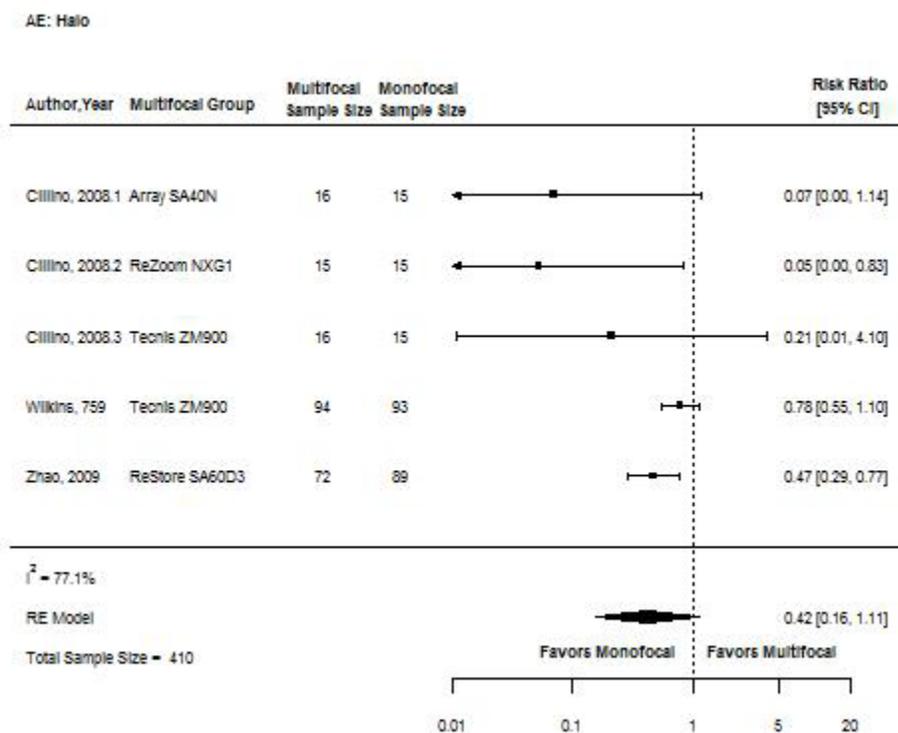
There were 3 of 10 multifocal IOL studies reporting halos following surgery.<sup>14-16</sup> Cillino showed significantly worse reported halos following surgery in the Rezoom and Array compared to monofocal.<sup>16</sup> Zhao determined 43.1% of patients who had a ReSTOR had halos compared to only 20.2% of the monofocal patients ( $p < 0.01$ ).<sup>15</sup> Peng determined the ReSTOR had more halos than the monofocal on its impact rating score.<sup>14</sup> One additional trial reported the outcome, “have you noticed any unwanted images?” and reported about 10% greater occurrence of this in patients receiving multifocal IOLs.<sup>9</sup>

We pooled the 3 studies reporting binary outcomes for halo/unwanted images, which totaled 410 patients.<sup>9,15,16</sup>

The random effects pooled estimate was a risk ratio of 0.42 (95% CI 0.16, 1.11) favoring multifocal IOLs. Heterogeneity was high ( $I^2 = 77\%$ ).



**Figure 9. Multifocal IOLs Compared to Monofocal IOLs Halo**



**Other Visual Phenomena**

Palmer noted that more patients had complaints of dysphotopsias in the ZM900 group (81%) compared to the TwinSet (47%) and ReZoom (53%) and monofocal groups (48%).<sup>19</sup> The authors also point out that no patient in the monofocal group complained on their own about photopsias compared to 16-18% of the MFIOL patients. Labiris commented on complaints of shadows following surgery being higher in the MFIOL group compared to mini monovision.<sup>18</sup> The study also commented there was no difference in stereopsis between MFIOL and mini monovision.

**Summary of Findings**

Between 3 and 8 RCTs support the following conclusions:

1. The intraoperative risks of surgery are probably no greater for multifocal IOLs than monofocal IOLs in the patient population and lenses included in these trials.
2. Multifocal IOLs may increase the risk of IOL exchange due to patient dissatisfaction.
3. Multifocal IOLs are associated with worse contrast sensitivity.
4. Multifocal IOLs are associated with greater risk of glare.
5. Multifocal IOLs are associated with a greater risk of halos.
6. The need for further procedures following multifocal IOL such as corneal refractive surgery or IOL exchange is not addressed in these studies and requires additional research.
7. Data on accommodative IOLs are too sparse to draw conclusions.

### Quality of Evidence for Key Question 3

**Table 5. GRADE Quality of Evidence Table (Harms)**

Outcome	Number of Studies and Design	Methodological Quality of Studies	Consistency Across Studies	Directness of Evidence	Other Considerations	Qualitative Description of Effect Size	Quality of Evidence
Multifocal IOLs – Operative risk	6 RCTs	Serious limitations	No serious limitation	No serious Limitations	None	No difference	Moderate
Multifocal IOLs – IOL exchange	1 RCT	No serious limitations	N/A	No serious limitation	Sparse data	Multifocal IOLs worse	Low
Multifocal IOLs – Contrast sensitivity	8 RCTs	Serious limitations	No serious limitation	No serious limitations	None	Multifocal IOLs worse	Moderate
Accommodative IOLs – glare	6 RCT	Serious limitations	No serious limitation	No serious limitations	None	Multifocal IOLs worse	Moderate
Multifocal IOLs - halo	4 RCTs	Serious limitations	Serious limitation	No serious limitation	None	Multifocal IOLs worse	Low
Accommodative IOLs – all outcomes	1 RCT	Serious limitations	N/A	No serious limitation	Sparse data	None	Very low

### KEY QUESTION 4. If feasible, what resources are required to best care for patients who choose multifocal or accommodative lens implants in the setting of cataract surgery?

None of the 12 studies specifically addressed Key Question 4.

However, 6 out of 12 studies included pre-op corneal astigmatism greater than 1 diopter as an exclusion criterion. Residual refractive error due to uncorrected corneal astigmatism is thought to decrease the effectiveness of multifocal lenses. While these studies did not further elaborate on the method by which corneal astigmatism was measured, this is commonly done with specialized equipment, specifically a corneal topographer.

Residual post-operative astigmatism plays an important role in quality of vision and spectacle independence following cataract surgery. Of the 11 studies looking at multifocal IOLs, 8 excluded patients in whom pre-op corneal astigmatism was “high”. This number ranged from 1 to 3 diopters (D). Another study did not rule out astigmatism cases and instead used coupled incision to treat up to 2D of pre-op astigmatism.

Only 5<sup>9,14,16,17,20</sup> of the 11 multifocal IOL studies reported post-operative astigmatism (cylinder). Although the average residual post-operative astigmatism was reported as 0.4-0.6D, the standard deviations were high and with a range up to 2.5D. The amount of residual astigmatism may contribute to patient satisfaction and vision following cataract surgery, further emphasizing the need for a future trial that addresses post-operative astigmatism.

One study included “age-related macular degeneration” as a specific exclusion criterion, which is often confirmed with additional testing such as ocular coherence tomography (OCT).<sup>11</sup>

The American Society of Cataract and Refractive Surgeons (ASCRS) published a review article outlining best clinical practice for use of multifocal IOLs that included recommended pre-operative diagnostic testing.<sup>22</sup> These tests include:

- Corneal topography to evaluate corneal astigmatism and screen for other ocular surface abnormalities;
- OCT to evaluate macular function; and
- Pupillometry.

These diagnostic tests would require additional resources in terms of equipment, technical support, and interpretation.

The ASCRS article also recommends detailed patient discussion and counseling regarding factors that may influence the perceived outcome of multifocal IOL implantation. These topics include:

- Limitations of multifocals;
- Risk of unwanted visual phenomenon (*ie*, glare/halo);
- Patient temperament; and
- Patient lifestyle considerations.

Such discussion/counseling would also require additional time and resources as compared to monofocal IOL.

Finally, the ASCRS article acknowledges that post-operative refractive error or intolerable visual phenomena may need to be managed with additional surgical intervention such as corneal refractive surgery or IOL exchange.

## Summary of Findings

No hypothesis-testing study explicitly assessed the need for additional pre-operative or post-operative resources for patients receiving multifocal IOLS. However, several of the included trials used as exclusion criteria conditions that would require additional diagnostic tests that may go beyond the standard pre-operative evaluation for monofocal IOLs. Specialty society “best practice” recommendations for multifocal IOL procedures list a number of pre-operative and post-operative best practices that may not be included as part of standard monofocal IOL procedures.

## Quality of Evidence for Key Question 4

As there were no hypothesis-testing studies found for Key Question 4, the evidence is judged as insufficient. However, clinicians wishing to follow the same inclusion/exclusion criteria used in many of the multifocal IOL RCTs will need to do additional pre-operative testing.

## SUMMARY AND DISCUSSION

Moderate-strength evidence supports the conclusion that, compared to monofocal IOLs, multifocal IOLs achieve better outcomes on spectacle independence and uncorrected near visual acuity, without sacrificing uncorrected or corrected distance vision. Low-strength evidence supports the conclusion that multifocal IOLs result in better visual function/ quality of life than monofocal IOLs. More limited data support that multifocal IOLs achieve better spectacle independence than monovision. Moderate-strength evidence supports that multifocal IOLs result in worse contrast sensitivity and a greater risk of glare, and low-strength evidence supports that they result in a greater risk of halos. Low-strength evidence exists that monofocal IOLs result in greater IOL exchange due to dissatisfaction. A limitation of all these conclusions is that IOL technology is rapidly changing, and therefore newer IOLs may have differences in the benefits and harms we report here for older lenses. Data are very limited about accommodative IOLs, consisting of only 1 RCT.

### SUMMARY OF EVIDENCE BY KEY QUESTION

#### Key Question 1

The evidence from 9 RCTs supports a conclusion that there is no difference in uncorrected or corrected distance vision between multifocal or accommodative IOLs and monofocal IOLs. The evidence for accommodative IOLs is restricted to only 1 trial. Two trials comparing multifocal IOLs to monovision found no difference in uncorrected distance vision.

#### Key Question 2

Four RCTs support the conclusion that multifocal IOLs are better than monofocal IOLs for uncorrected near vision. This conclusion is also supported by better outcomes for reading accurately and speed and visual function. In the few studies that have measured visual function or vision-related quality of life, this has been better in patients receiving multifocal IOLs. Data on accommodative IOLs are very sparse. Two studies found that multifocal IOLs result in better spectacle independence than monovision.

#### Key Question 3

Between 3 and 8 RCTs support the following conclusions: 1) The risks of surgery are no greater for multifocal IOLs than monofocal IOLs in the patient population and lenses included in these trials; 2) Multifocal IOLs may have an increased risk of IOL exchange due to patient dissatisfaction; 3) Multifocal IOLs are associated with worse contrast sensitivity; 4) Multifocal IOLs are associated with greater risk of glare; 5) Multifocal IOLs are associated with a greater risk of halos; and 6) Data on accommodative IOLs are too sparse to draw conclusions.

#### Key Question 4

No hypothesis-testing study explicitly assessed the need for additional pre-operative or post-operative resources for patients receiving multifocal IOLs. However, several of the included trials used as exclusion criteria conditions that would require additional diagnostic tests that may go beyond the standard pre-operative evaluation for monofocal IOLs. Specialty society “best practice” recommendations for multifocal IOL procedures list a number of pre-operative and

post-operative best practices that may not be included as part of standard monofocal IOL procedures.

## LIMITATIONS

A limitation of all these conclusions is that IOL technology is rapidly changing, and therefore newer lenses may have differences in the benefits and harms we report here for older lenses.

### Publication Bias

We were not able to test for publication bias and can make no conclusions about its possible existence.

### Study Quality

The principal limitation to this review is the quality of the original RCTs. Most studies had methodologic limitations and were of small size. This contributed to our assessment of the quality of evidence being moderate rather than high.

### Heterogeneity

Heterogeneity was in general not large in most of the pooled analyses.

### Applicability of Findings to the VA Population

No studies were performed in VA populations, or even US populations, therefore the applicability of these results to VA patients with cataracts is uncertain.

## RESEARCH GAPS/FUTURE RESEARCH

A VA-sponsored multi-site randomized clinical trial would provide higher quality evidence than that which currently exists about the benefits, harms, needed pre- and post-operative clinical resources, assessments of pre- and post-operative astigmatism, and costs of multifocal IOLs compared to monofocal IOLs in VA patients, using contemporary IOLs.

## CONCLUSIONS

Multifocal IOLs compared to monofocal IOLs produce better uncorrected near vision and a greater proportion of patients who are spectacle-independent, but are associated with worse contrast sensitivity and a greater risk of glare and halos. Current evidence is insufficient to reach conclusions about resource requirements and other outcomes such as additional enhancements or IOL exchange.

## REFERENCES

1. Institute NE. Cataracts. <https://www.nei.nih.gov/eyedata/cataract>.
2. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
3. Konstantopoulos S. Fixed effects and variance components estimation in three-level meta-analysis. *Res Synth Methods*. 2011;2(1):61-76.
4. Hedges LV, Vevea JL. Fixed-and random-effects models in meta-analysis. *Psychological methods*. 1998;3(4):486.
5. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.
6. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994;50(4):1088-1101.
7. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629-634.
8. GRADE working group. 2014; <http://www.gradeworkinggroup.org/>. Accessed 09/25/15.
9. Wilkins MR, Allan BD, Rubin GS, et al. Randomized trial of multifocal intraocular lenses versus monovision after bilateral cataract surgery. *Ophthalmology*. 2013;120(12):2449-2455 e2441.
10. Alio JL, Grabner G, Plaza-Puche AB, et al. Postoperative bilateral reading performance with 4 intraocular lens models: six-month results. *Journal of cataract and refractive surgery*. 2011;37(5):842-852.
11. Marchini G, Mora P, Pedrotti E, Manzotti F, Aldigeri R, Gandolfi SA. Functional assessment of two different accommodative intraocular lenses compared with a monofocal intraocular lens. *Ophthalmology*. 2007;114(11):2038-2043.
12. Zeng M, Liu Y, Liu X, et al. Aberration and contrast sensitivity comparison of aspherical and monofocal and multifocal intraocular lens eyes. *Clinical & experimental ophthalmology*. 2007;35(4):355-360.
13. Ji J, Huang X, Fan X, Luo M. Visual performance of Acrysof ReSTOR compared with a monofocal intraocular lens following implantation in cataract surgery. *Exp Ther Med*. 2013;5(1):277-281.
14. Peng C, Zhao J, Ma L, Qu B, Sun Q, Zhang J. Optical performance after bilateral implantation of apodized aspheric diffractive multifocal intraocular lenses with +3.00-D addition power. *Acta ophthalmologica*. 2012;90(8):e586-593.
15. Zhao G, Zhang J, Zhou Y, Hu L, Che C, Jiang N. Visual function after monocular implantation of apodized diffractive multifocal or single-piece monofocal intraocular lens Randomized prospective comparison. *Journal of cataract and refractive surgery*. 2010;36(2):282-285.
16. Cillino S, Casuccio A, Di Pace F, et al. One-year outcomes with new-generation multifocal intraocular lenses. *Ophthalmology*. 2008;115(9):1508-1516.
17. Alio JL, Plaza-Puche AB, Pinero DP, Amparo F, Rodriguez-Prats JL, Ayala MJ. Quality of life evaluation after implantation of 2 multifocal intraocular lens models and a monofocal model. *Journal of cataract and refractive surgery*. 2011;37(4):638-648.
18. Labiris G, Giarmoukakis A, Patsiamanidi M, Papadopoulos Z, Kozobolis VP. Mini-monovision versus multifocal intraocular lens implantation. *Journal of cataract and refractive surgery*. 2015;41(1):53-57.

19. Martinez Palmer A, Gomez Faina P, Espana Albelda A, Comas Serrano M, Nahra Saad D, Castilla Cespedes M. Visual function with bilateral implantation of monofocal and multifocal intraocular lenses: a prospective, randomized, controlled clinical trial. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2008;24(3):257-264.
20. Rasp M, Bacherneegg A, Seyeddain O, et al. Bilateral reading performance of 4 multifocal intraocular lens models and a monofocal intraocular lens under bright lighting conditions. *Journal of cataract and refractive surgery*. 2012;38(11):1950-1961.
21. Menant JC, St George RJ, Sandery B, Fitzpatrick RC, Lord SR. Older people contact more obstacles when wearing multifocal glasses and performing a secondary visual task. *Journal of the American Geriatrics Society*. 2009;57(10):1833-1838.
22. Braga-Mele R, Chang D, Dewey S, et al. Multifocal intraocular lenses: relative indications and contraindications for implantation. *Journal of cataract and refractive surgery*. 2014;40(2):313-322.

## APPENDIX A. SEARCH STRATEGIES

### DATABASE SEARCHED & TIME PERIOD COVERED:

PubMed – 2006/1/1 to 2017/4/30

### LANGUAGE:

English

### SEARCH STRATEGY:

lenses, intraocular OR lens implantation, intraocular OR accommodation, ocular OR accommodative lens\* OR accommodating lens\* OR multifocal lens\* OR multifocal intraocular lens\*

AND

cataract extraction OR cataract\*[tiab]

AND

systematic[sb]

Limited to English and 2006-2017

## APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Comment	Response
<p>Conclusions too favorable given all problems with studies on multifocal IOLs.</p>	<p>We have somewhat reduced the favorability.</p>
<p>Page 20 line 48 "independence" is spelled wrong</p> <p>Page 20 line 53 should be "than" not "that"</p> <p>page 29 Line 17 Summary # 1. I don't think you can say the risk of surgery with multifocals is no greater as the undesirable visual issues post-operative- (glare, halos, decreased contrast) are uncorrectable and there is likely an increased risk of need for lens exchange which is a risky procedure. Do the authors mean the intraoperative risk is no greater?</p> <p>Page 32 lines 40-44: As far as the statement "there is no data to support complications or effectiveness of cataract surgery varies by population characteristics". This statement is likely not true. We do know certain characteristics and ocular co-morbidities increase the risk of undesirable visual outcomes (glare, halos, decreased contrast) with multifocals. This would then logically increase the risk of lens exchange and unfavorable visual outcomes. We would need to know what the prevalence of these characteristics such as dry eye and macular changes are in the VA population getting cataract surgery compared to the general population getting cataract surgery.</p> <p>Page 32 line 53-57 Conclusions: I would add the need for additional patient face-to-face or "chair" time and therefore resources and the higher need for lens exchange</p>	<p>Thank you for pointing this out, this has been corrected.</p> <p>Thank you for pointing this out, this has been corrected.</p> <p>The reviewer is correct, we meant interoperative risks. We have made this change.</p> <p>We changed this statement to saying the applicability is uncertain.</p> <p>We made this addition.</p>
<p>This is well written summary of the literature. Unfortunately much of the literature was excluded to answer if multifocal lenses are more effective than monofocal lenses after implantation. I feel the authors made valid conclusions with the limited articles that met criteria for review.</p>	<p>Thank you for your comment.</p>
<p>My primary concern: there should be more of an emphasis in the poor quality of the studies (see page 13—e.g., only two were registered prospectively!), in the Discussion and Conclusions (pages 5-6). In this context, for example, "moderate evidence supports...." is overly optimistic. I really</p>	<p>We have somewhat reduced our conclusions, in terms of applicability and potential for harms, but believe the assessment of quality of evidence as "moderate" for the conclusion that multifocal IOL, produce better uncorrected near vision and spectacle independence is justified. The</p>

<p>think more rigorous studies need to be done to support these IOLs (though this question is probably irrelevant given the significant financial incentives to use them outside the VA) and they should be in US populations (none of the studies in the ESP were done in the US, which I found very surprising and very disheartening). My opinion: much more caution needs to be emphasized in the report!</p> <p>Another concern: the ESP states that the findings are generalizable to the VA population (top of page 6). Given that none of the studies were done in US populations and that VA patients undergoing cataract surgery have much higher burden of illness than their non-VA counterparts in the US, I find this conclusion problematic. We simply do not know.</p>	<p>methodologic limitations of the RCTs are already accounted for in the downgrade of the quality of evidence from high to moderate.</p> <p>This change was already made.</p>
<p>This was a very sound study that examined the outcomes of multifocal and accommodating IOL implantation relative to monofocal IOL implantation in cataract surgery. The methods of paper selection and the key investigational questions were clearly laid out. The statistical methods that were employed were appropriate. Given the data presented, I agree with the conclusions that were drawn with respect to the key questions.</p> <p>The results of the stringent screening process for the included papers highlights the deficiencies in the current literature and the challenges that present themselves when trying to design studies that answer the questions of interest.</p> <p>A weakness of the study (which is beyond the authors' control) is the selection of IOLs that were available for examination in published randomized clinical trials. A few of the IOLs are not available in the US (Acry LISA, TwinSet) or are outdated technology not in current use (Array, ReZoom). Of the remaining IOLs (ReSTOR SN6AD3, Tecnis ZM900/9001, Tecnis ZMB00), their use is being significantly replaced by "lower-add" MF IOLs or extended depth-of-focus IOLs. The newer IOLs may have improved side effect profiles, but unfortunately the available literature is not of sufficient quality for a similar evaluation of their performance. Maybe mention could be made of these issues in the discussion and/or conclusion, if the authors feel it is appropriate.</p> <p>In today's environment, I would be careful with the statement that corneal topography is not needed for "standard" cataract surgery. I believe the consensus that corneal topography is or should be an essential component of any cataract surgery has spread or is spreading beyond subspecialty</p>	<p>Thank you for your comment.</p> <p>Thank you for your comment.</p> <p>We have added this information to the conclusion.</p> <p>We made the change.</p>



## APPENDIX C. EVIDENCE TABLES

Author Year Country	Design (Single or Multi-Center) Prospectively registered	Intervention	Comparison	Sample Size (Patients) Mean Age % Female	Duration of Follow-up	Outcomes
Marchini, 2007 <sup>11</sup> Italy	RCT Multi-site Not reported as registered	1) 1CU (accommodative) 2) Crystalens AT-45	Conventional monofocal IOL	38 Mean age = NR %Female = NR	12 months	<p>VA</p> <ul style="list-style-type: none"> <li>- BCDVA                             <ul style="list-style-type: none"> <li>o 1CU (0.02)</li> <li>o AT-45 (0.04)</li> <li>o ACR6D (0.04)</li> </ul> </li> <li>- UCNVA – just states not sig different (no actual data)</li> <li>- Best-corrected near-distance VA – “excellent and comparable between 3 groups”</li> </ul> <p>Other</p> <ul style="list-style-type: none"> <li>- Change in ACD (mm)                             <ul style="list-style-type: none"> <li>o 1CU (0.09)</li> <li>o AT-45 (0.17)</li> <li>o ACR6D (-0.03)</li> <li>o P = 0.002</li> </ul> </li> <li>- Change in SPCA (mm)                             <ul style="list-style-type: none"> <li>o 1CU (2.78)</li> <li>o AT-45 (2.08)</li> <li>o ACR6D (1.78)</li> <li>o P = 0.816</li> </ul> </li> <li>- NDRA (diopters)                             <ul style="list-style-type: none"> <li>o 1CU (1.29)</li> <li>o AT-45 (1.50)</li> <li>o ACR6D (2.15)</li> <li>o P = 0.002</li> </ul> </li> <li>- AA (diopters)                             <ul style="list-style-type: none"> <li>o 1CU (1.40)</li> <li>o AT-45 (0.96)</li> <li>o ACR6D (1.23)</li> <li>o P = 0.102</li> </ul> </li> <li>- Distance corrected NVA (Jaeger)                             <ul style="list-style-type: none"> <li>o 1CU (7)</li> <li>o AT-45 (10)</li> </ul> </li> </ul>



						<ul style="list-style-type: none"> <li>○ ACR6D (13)</li> <li>○ P = 0.001</li> </ul>
Zeng, 2007 <sup>12</sup> China	RCT Single-site Not reported as registered	Array SA40N	1) AcrySof SA60AT 2) Tecnis Aspherical	124 Mean age = 65.4 %Female = NR	3 months	<p>VA</p> <ul style="list-style-type: none"> <li>- BCVA                             <ul style="list-style-type: none"> <li>○ Z9001 (0.00)</li> <li>○ SA40N (0.01)</li> <li>○ SA60AT (0.01)</li> <li>○ P = 0.303</li> </ul> </li> </ul> <p>Corneal aberrations</p> <ul style="list-style-type: none"> <li>- No sig difference btw IOL groups</li> <li>- Spherical aberration                             <ul style="list-style-type: none"> <li>○ Z9001 (0.24)</li> <li>○ SA40N (0.21)</li> <li>○ SA60AT (0.26)</li> <li>○ P = 0.81</li> </ul> </li> <li>- Coma                             <ul style="list-style-type: none"> <li>○ Z9001 (0.35)</li> <li>○ SA40N (0.33)</li> <li>○ SA60AT (0.32)</li> <li>○ P = 0.54</li> </ul> </li> <li>- RMS                             <ul style="list-style-type: none"> <li>○ Z9001 (1.54)</li> <li>○ SA40N (1.58)</li> <li>○ SA60AT (1.62)</li> <li>○ P = 0.37</li> </ul> </li> </ul> <p>Higher-order aberrations</p> <ul style="list-style-type: none"> <li>- SA40N &gt; SA60AT &gt; Z9001</li> <li>- C12                             <ul style="list-style-type: none"> <li>○ Z9001 (0.05)</li> <li>○ SA40N (0.40)</li> <li>○ SA60AT (0.20)</li> <li>○ P = 0.000</li> </ul> </li> <li>- RMS4                             <ul style="list-style-type: none"> <li>○ Z9001 (0.26)</li> <li>○ SA40N (0.45)</li> <li>○ SA60AT (0.32)</li> <li>○ P = 0.000</li> </ul> </li> <li>- RMSH                             <ul style="list-style-type: none"> <li>○ Z9001 (0.45)</li> <li>○ SA40N (1.02)</li> <li>○ SA60AT (0.69)</li> <li>○ P = 0.000</li> </ul> </li> </ul> <p>Contrast sensitivity</p>



						<ul style="list-style-type: none"> <li>- Measure with and without glare at 4 spatial frequencies</li> <li>- Z9001 &gt; SA60AT &gt; SA40N (P&lt;0.01)</li> <li>- Examples:</li> <li>- Glare Cpd 6                         <ul style="list-style-type: none"> <li>o Z9001 (1.87)</li> <li>o SA40N (1.69)</li> <li>o SA60AT (1.71)</li> <li>o P = 0.004</li> </ul> </li> <li>- Without glare CPD6                         <ul style="list-style-type: none"> <li>o Z9001 (1.97)</li> <li>o SA40N (1.68)</li> <li>o SA60AT (1.72)</li> <li>o P = 0.000</li> </ul> </li> </ul>																
Cillino, 2008 <sup>16</sup> Italy	RCT Single site Not reported as registered	1) Rezoom NXG1 2) Tecnis ZM900 3) Array SA40N	AR40 (US monofocal)	68 Mean age = 62.3 % Female = 53.2	12 months	<p>1) Complete spectacle independence</p> <table border="0"> <tr><td>Tecnis ZM900</td><td>87.5%<sup>+</sup></td></tr> <tr><td>Rezoom NXG1</td><td>53.5%<sup>+</sup></td></tr> <tr><td>Array SA40N</td><td>43.7%<sup>*</sup></td></tr> <tr><td>AR40</td><td>20%<sup>*</sup></td></tr> </table> <p>(<sup>+</sup> p &lt; 0.05; <sup>*</sup> p = 0.53)</p> <p>2) VF7</p> <p>Mean score</p> <table border="0"> <tr><td>Tecnis ZM900</td><td>99.1</td></tr> <tr><td>Rezoom NXG1</td><td>94.6</td></tr> <tr><td>Array SA40N</td><td>93.8</td></tr> <tr><td>AR40</td><td>87.1</td></tr> </table> <p>(p = 0.002)</p> <p>Difficulty reading small print</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 98.9</li> <li>- Rezoom NXG1 – 78.1</li> <li>- Array SA40N – 73.3</li> <li>- AR40 – 56.7</li> <li>- P &lt; 0.0005</li> </ul> <p>Fine handwork</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 94.6</li> <li>- Rezoom NXG1 – 92.2</li> <li>- Array SA40N – 96.7</li> <li>- AR40 – 56.7</li> <li>- P &lt; 0.0005</li> </ul> <p>3) VA (mean Snellen in decimal form)</p>	Tecnis ZM900	87.5% <sup>+</sup>	Rezoom NXG1	53.5% <sup>+</sup>	Array SA40N	43.7% <sup>*</sup>	AR40	20% <sup>*</sup>	Tecnis ZM900	99.1	Rezoom NXG1	94.6	Array SA40N	93.8	AR40	87.1
Tecnis ZM900	87.5% <sup>+</sup>																					
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Tecnis ZM900	99.1																					
Rezoom NXG1	94.6																					
Array SA40N	93.8																					
AR40	87.1																					



						<p>Uncorrected distance VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.69</li> <li>- Rezoom NXG1 – 0.86</li> <li>- Array SA40N – 0.87</li> <li>- AR40 – 0.79</li> <li>- P = 0.134</li> </ul> <p>Best corrected distance VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.99</li> <li>- Rezoom NXG1 – 0.98</li> <li>- Array SA40N – 0.97</li> <li>- AR40 – 1.00</li> <li>- P = 0.958</li> </ul> <p>Uncorrected near VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.72</li> <li>- Rezoom NXG1 – 0.61</li> <li>- Array SA40N – 0.63</li> <li>- AR40 – 0.42</li> <li>- P &lt; 0.0005</li> </ul> <p>Best corrected near VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.84</li> <li>- Rezoom NXG1 – 0.81</li> <li>- Array SA40N – 0.87</li> <li>- AR40 – 0.80</li> <li>- P = 0.501</li> </ul> <p>Best corrected distance near VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.78</li> <li>- Rezoom NXG1 – 0.56</li> <li>- Array SA40N – 0.63</li> <li>- AR40 – 0.39</li> <li>- P &lt; 0.0005</li> </ul> <p>Uncorrected intermediate VA</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.69</li> <li>- Rezoom NXG1 – 0.75</li> <li>- Array SA40N – 0.67</li> <li>- AR40 – 0.61</li> <li>- P = 0.001</li> </ul> <p>Best corrected intermediate VA</p>
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						<ul style="list-style-type: none"> <li>- Tecnis ZM900 – 0.90</li> <li>- Rezoom NXG1 – 0.75</li> <li>- Array SA40N – 0.83</li> <li>- AR40 – 0.77</li> <li>- P = 0.316</li> </ul> <p>4) Contrast sensitivity curve</p> <ul style="list-style-type: none"> <li>- ZM900 and AR40 better than Rezoom and Array (P = 0.038)</li> </ul> <p>5) Glare (# cases)</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 1</li> <li>- Rezoom NXG1 – 5</li> <li>- Array SA40N – 1</li> <li>- AR40 – 1</li> <li>- P &gt; 0.05</li> </ul> <p>6) Halo (# cases)</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 2</li> <li>- Rezoom NXG1 – 9</li> <li>- Array SA40N – 7</li> <li>- AR40 – 0             <ul style="list-style-type: none"> <li>o ZM900 v Rezoom = 0.017</li> <li>o Rezoom v Mono = 0.0007</li> <li>o Array v Mono = 0.007</li> </ul> </li> </ul> <p>7) Overall patient satisfaction</p> <ul style="list-style-type: none"> <li>- Tecnis ZM900 – 4.7</li> <li>- Rezoom NXG1 – 4.5</li> <li>- Array SA40N – 4.4</li> <li>- AR40 – 4.6</li> <li>- P = 0.071</li> </ul>																
Palmer, 2008 <sup>19</sup> Spain	RCT Single site Not reported as registered	1) Tecnis MFIOL ZM900 2) ReZoom (zonal refractive) 3) Twin Set (asymmetric diffractive)	Tecnis Z9000 (monofocal)	114 patients Mean age = 73.7 % Female = 62.5	3 months	<p>Spectacle independence</p> <table border="0"> <tr> <td>Tecnis Z9000</td> <td>4%</td> </tr> <tr> <td>Twinset</td> <td>87.5%</td> </tr> <tr> <td>Tecnis ZM900</td> <td>77%</td> </tr> <tr> <td>Rezoom</td> <td>44%</td> </tr> </table> <p>Visual Acuity</p> <p>Binocular distance UCVA</p> <table border="0"> <tr> <td>Tecnis Z9000</td> <td>0.13</td> </tr> <tr> <td>Twinset</td> <td>0.18</td> </tr> <tr> <td>Tecnis ZM900</td> <td>0.14</td> </tr> <tr> <td>ReZoom</td> <td>0.16</td> </tr> </table>	Tecnis Z9000	4%	Twinset	87.5%	Tecnis ZM900	77%	Rezoom	44%	Tecnis Z9000	0.13	Twinset	0.18	Tecnis ZM900	0.14	ReZoom	0.16
Tecnis Z9000	4%																					
Twinset	87.5%																					
Tecnis ZM900	77%																					
Rezoom	44%																					
Tecnis Z9000	0.13																					
Twinset	0.18																					
Tecnis ZM900	0.14																					
ReZoom	0.16																					



						<p>Binocular CDVA</p> <p>Tecnis Z9000 0.05</p> <p>Twinset 0.08</p> <p>Tecnis ZM900 0.07</p> <p>ReZoom 0.11</p> <p>Binocular CNVA</p> <p>Tecnis Z9000 0.04</p> <p>Twinset 0.01</p> <p>Tecnis ZM900 0.01</p> <p>ReZoom 0.03</p> <p>Photopsia</p> <p>Tecnis Z9000 81%</p> <p>Twinset 47%</p> <p>Tecnis ZM900 48%</p> <p>ReZoom 53%</p>
Zhao, 2010 <sup>15</sup> China	RCT Single site Not reported as registered	ReSTOR SA60D3	Acrysof SA60AT	161 patients Mean age = 66 % Female = 47.2	6 months	<p>Spectacle independence</p> <p>ReSTOR 66.6%</p> <p>Monofocal 23.5%</p> <p>(p &lt; 0.05)</p> <p>VF 7</p> <p>Post-operative score</p> <p>ReSTOR 97.3</p> <p>Monofocal 89.8</p> <p>(p &lt; 0.05)</p> <p>Patient satisfaction score (1 to 5)</p> <p>ReSTOR 4.7</p> <p>Monofocal 4.3</p> <p>(p = not significant)</p> <p>Halos</p> <p>ReSTOR 43.1%</p> <p>Monofocal 20.2%</p> <p>(p &lt; 0.01)</p> <p>Contrast sensitivity: not significant</p>

<p>Alio, 2011<sup>17</sup> Spain</p>	<p>RCT Single site Not reported as registered</p>	<p>1) AcrySof ReSTOR SN6AD3 2) Acri.LISA 366D (Non-US, diffractive MF)</p>	<p>Acri.Smart 48S (Non-US, monofocal)</p>	<p>53 Mean age = 63 % Female = NR</p>	<p>3 months</p>	<p>VA  <ul style="list-style-type: none"> <li>- UDVA (logmar)                             <ul style="list-style-type: none"> <li>o Acri.Smart (0.03)</li> <li>o ReSTOR (0.05)</li> <li>o Acri.LISA (0.05)</li> <li>o Monofocal better (P = 0.01)</li> </ul> </li> <li>- CDVA                             <ul style="list-style-type: none"> <li>o Acri.Smart (0.02)</li> <li>o ReSTOR (0.02)</li> <li>o Acri.LISA (0.00)</li> <li>o No difference (P = 0.24)</li> </ul> </li> <li>- UNVA                             <ul style="list-style-type: none"> <li>o Acri.Smart (0.47)</li> <li>o ReSTOR (0.28)</li> <li>o Acri.LISA (0.19)</li> <li>o Multifocal better (P &lt;0.01)</li> </ul> </li> </ul> </p>
<p>Alio 2011<sup>10</sup> Spain</p>	<p>RCT Multi-site Not reported as registered</p>	<p>1) AcrySof ReSTOR SN6AD3 2) Acri.LISA 366D (Non-US, diffractive MF) 3) ReZoom</p>	<p>Acri.Smart 48S (Non-US, monofocal)</p>	<p>152 Mean age = 71 %Female = NR</p>	<p>6 months</p>	<p>VA  <ul style="list-style-type: none"> <li>- UDVA (logmar)                             <ul style="list-style-type: none"> <li>o Acri.Smart (0.09)</li> <li>o ReSTOR (0.15)</li> <li>o Acri.LISA (0.12)</li> <li>o Rezoom (0.12)</li> <li>o Monofocal better (P = 0.02)</li> </ul> </li> <li>- CDVA                             <ul style="list-style-type: none"> <li>o Acri.Smart (0.04)</li> <li>o ReSTOR (0.06)</li> <li>o Acri.LISA (0.06)</li> <li>o Rezoom (0.06)</li> <li>o No difference (P = 0.25)</li> </ul> </li> <li>- Reading acuity                             <ul style="list-style-type: none"> <li>o Only graphical data</li> <li>o ReSTOR and Acri.LISA better than monofocal (P&lt;0.01)</li> </ul> </li> <li>- Smallest print size                             <ul style="list-style-type: none"> <li>o ReSTOR and Acri.LISA better than monofocal and Rezoom (P&lt;0.01)</li> </ul> </li> <li>- Reading speed and distance Difficult to interpret ? relevant</li> </ul> </p>



<p>Ji, 2012<sup>13</sup> China</p>	<p>RCT Single site Not reported as registered</p>	<p>Acrysof ReSTOR (? Model #)</p>	<p>Acrysof Natural (Monofocal, ? Model #)</p>	<p>51 (64 eyes) Mean age = 63.1 % Female = 56.9</p>	<p>3 months</p>	<p>1) VA Best corrected distance VA Acrysof ReSTOR 0.71 Acrysof Natural 0.75 No significant difference (p = 0.77) Uncorrected near VA Acrysof ReSTOR 0.58 Acrysof Natural 0.21 (p = 0.008)</p> <p>2) Contrast sensitivity Measured mesopic/photopic at 6 spatial frequencies -Multifocal scored lower than monofocal under all conditions all P&lt;0.05 Example: Mesopic, 2.5 spatial freq - ReSTOR 33.46 - Natural 41.67 - P = 0.03 Photopic, 2.5 spatial freq - ReSTOR 15.57 - Natural 22.83 - P = 0.02</p> <p>3) Wavefront analysis RMS 4mm pupil - ReSTOR 0.21 - Natural 0.50 - P = 0.00 6mm pupil - ReSTOR 0.41 - Natural 0.96 - P = 0.02 Not sure if these are useful</p>
<p>Peng, 2012<sup>14</sup> China</p>	<p>RCT Single site Not reported as registered</p>	<p>ReSTOR Sn6AD1</p>	<p>Alcon SN60WF</p>	<p>102 patients Mean age = 66 % Female = 52.4</p>	<p>6 months</p>	<p>Spectacle independence ReSTOR 74% Monofocal 28.9%</p> <p>Visual acuity Uncorrected distance – VA ReSTOR .03</p>



						<p>Monofocal .08 Uncorrected near VA ReSTOR .07 Monofocal .64 Visual Disturbance ReSTOR &gt; Monofocal for glare, night driving, halos Example: problems with night vision 1.2 vs 0.6 on 0 to 7 impact rating scare Monofocal IOL &gt; ReSTOR got blurry near vision</p> <p>Patient satisfaction ReSTOR 8.14 Monofocal 6.23 (P &lt; 0.001)</p> <p>Contrast: MTF 3.0mm ReSTOR worse at 5 – 10 cpd MTF 5.00 – no difference</p>
Rasp, 2012 <sup>20</sup> Austria	RCT Single site	<p>1) Acrysof ReSTOR SN6AD3 2) AT.LISA 366D (Non-US, diffractive MF) 3) Rezoom NXG1 4) Tecnis ZMA00</p>	Acri.Smart 48S (Non-US, monofocal)	143 Mean age = 75.9 % female = NR	12 months	<p>1) VA - Uncorrected distance VA (logMAR) - Acri-Smart (0.08) - Acri.LISA (0.16) - ReSTOR (0.17) - Rezoom (0.11) - ZMA00 (0.10) - No significant difference reported Corrected distance VA (logMAR) - Acri-Smart (0.03) - Acri.LISA (0.05) - ReSTOR (0.11) - Rezoom (0.07) - ZMA00 (0.05) - No significant difference reported</p> <p>2) Reading performance - Uncorrected reading acuity (logRAD) - Acri-Smart (0.47) - Acri.LISA (0.23) - ReSTOR (0.28) - Rezoom (0.40) - ZMA00 (0.27) - All multifocals better than</p>



						<p>monofocal (P &lt; 0.001)</p> <ul style="list-style-type: none"> <li>- Reading speed             <ul style="list-style-type: none"> <li>- Uncorrected (WPM)                 <ul style="list-style-type: none"> <li>- Acri-Smart (148)</li> <li>- Acri.LISA (178)</li> <li>- ReSTOR (147)</li> <li>- Rezoom (152)</li> <li>- ZMA00 (139)</li> <li>- P values:                     <ul style="list-style-type: none"> <li>- Acrismart vs AcriLISA(0.001)</li> <li>- ReSTOR vs AcriLISA (0.003)</li> <li>- Rezoom vs AcriLISA (0.016)</li> <li>- Tecnis vs AcriLISA (0.00)</li> </ul> </li> </ul> </li> <li>- Corrected</li> </ul> </li> <li>- No significant difference (P&gt;0.21)</li> </ul> <p>- Reading distance (cm)</p> <ul style="list-style-type: none"> <li>- Uncorrected             <ul style="list-style-type: none"> <li>- Acri.LISA (31.6), ReSTOR (31.8), and ZMA00 (32.1) better than Acri.Smart (38.9) and Rezoom (37.1)</li> </ul> </li> </ul> <p>P values:</p> <ul style="list-style-type: none"> <li>- Significant difference between AcriSmart vs AcriLISA/ReSTOR/ZMA00 (P=0.00)</li> <li>- Significant difference between Rezoom vs AcriLISA/ReSTOR/ZMA00 (P = 0.04)</li> </ul> <p>- Corrected</p> <ul style="list-style-type: none"> <li>- Acri.LISA (31.3), ReSTOR (31.4), and ZMA00 (30.8) better than Acri.Smart (36.7) and Rezoom (35.5)</li> </ul> <p>P value:</p> <p>Significant difference between AcriSmart vs AcriLISA/ReSTOR/ZMA00 (P = 0.006)</p> <ul style="list-style-type: none"> <li>- Smallest print size (mm)             <ul style="list-style-type: none"> <li>- Acri.LISA (0.74) ReSTOR (0.87) and ZMA00 (0.87) better than Acri.Smart (1.76) and Rezoom (1.38) (P = 0.26)</li> </ul> </li> </ul>
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<p>Wilkins, 2013<sup>9</sup> England</p>	<p>RCT Multi-site Registered on <a href="https://www.clinicaltrials.com">controlled-trials.com</a>, ISRCTN37400841</p>	<p>Tecnis ZM900</p>	<p>Akreos AO with monovision</p>	<p>212 patients Mean age = 67.8 % Female = 56.6</p>	<p>4 months</p>	<p>Spectacle independence (do you wear glasses?)</p> <table border="1"> <thead> <tr> <th></th> <th>Tecnis</th> <th>Monovision</th> </tr> </thead> <tbody> <tr> <td>Always</td> <td>2.1%</td> <td>3.2%</td> </tr> <tr> <td>Sometimes</td> <td>36.6%</td> <td>71%</td> </tr> <tr> <td>Never</td> <td>71.3%</td> <td>25.8%</td> </tr> </tbody> </table> <p>VF -11R (pre to post)</p> <p>TecnisZM900</p> <table border="1"> <tr> <td>Pre</td> <td>2.7</td> </tr> <tr> <td>Post</td> <td>3.4</td> </tr> </table> <p>Monovision</p> <table border="1"> <tr> <td>Pre</td> <td>2.66</td> </tr> <tr> <td>Post</td> <td>3.25</td> </tr> </table> <p>(p = not significant)</p> <p>Visual acuity</p> <p>Binocular UDVA (p = 0.377)</p> <table border="1"> <tr> <td>Monovision</td> <td>0.06</td> </tr> <tr> <td>MFIOL</td> <td>0.08</td> </tr> </table> <p>Binocular UIVA (p = 0.000)</p> <table border="1"> <tr> <td>Monovision</td> <td>0.15</td> </tr> <tr> <td>MFIOL</td> <td>0.22</td> </tr> </table> <p>Binocular UNVA (p=0.037)</p> <table border="1"> <tr> <td>Monovision</td> <td>0.01</td> </tr> <tr> <td>MFIOL</td> <td>-0.03</td> </tr> </table> <p>Contrast</p> <table border="1"> <tr> <td>TecnisZM900</td> <td>1.39</td> </tr> <tr> <td>Monovision</td> <td>1.45</td> </tr> </table> <p>(P=0.009)</p> <p>Glare/Dazzle</p> <table border="1"> <thead> <tr> <th></th> <th>Monovision</th> <th>MFIOL</th> </tr> </thead> <tbody> <tr> <td>None</td> <td>44</td> <td>21</td> </tr> <tr> <td>Barely</td> <td>37</td> <td>36</td> </tr> <tr> <td>Annoying</td> <td>16</td> <td>36</td> </tr> <tr> <td>Debilitating</td> <td>2</td> <td>6</td> </tr> </tbody> </table>		Tecnis	Monovision	Always	2.1%	3.2%	Sometimes	36.6%	71%	Never	71.3%	25.8%	Pre	2.7	Post	3.4	Pre	2.66	Post	3.25	Monovision	0.06	MFIOL	0.08	Monovision	0.15	MFIOL	0.22	Monovision	0.01	MFIOL	-0.03	TecnisZM900	1.39	Monovision	1.45		Monovision	MFIOL	None	44	21	Barely	37	36	Annoying	16	36	Debilitating	2	6
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<p>Labiris, 2015<sup>18</sup> Greece</p>	<p>RCT Single site Registered on <a href="https://www.clinicaltrials.gov">clinicaltrials.gov</a>, NCT81998698</p>	<p>Iserit PY60MV (Non-US, refractive MF)</p>	<p>Mini-monovision with Alcon SN60WF</p>	<p>75 Mean age = 60.4 % female = NR</p>	<p>6 months</p>	<p>Spectacle independence</p> <p>Intervention: 65.7%</p> <p>Comparison: 31.4%</p> <p>VF-14 score</p> <p>Intervention: 90.1</p>																																																			



						<p>Comparison: 91.6 (p=0.11)</p> <p>VF-14 near vision Intervention: 91.4 Comparison: 89.0 (p=0.09)</p> <p>VF-14 distance vision Intervention: 89.1 Comparison: 92.9 (p=.08)</p> <p>VA:</p> <p>UDVA Intervention: 0.92 Comparison: 0.95 (p = 0.15)</p> <p>UNVA Intervention: 1.21 Comparison: 1.87 (p = 0.47)</p> <p>Other visual tests:</p> <p>Contrast sensitivity Intervention: 1.40 Comparison: 1.39 (p = 0.41)</p> <p>Glare (4-point scale) Intervention: 0.21 Comparison: 0.06 (p = 0.08)</p> <p>Shadows Intervention: 0.57 Comparison: 0.21 (p = 0.02)</p> <p>Stereopsis Intervention: 75 Comparison: 71 (p = 0.12)</p>
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## APPENDIX D. CITATIONS FOR EXCLUDED STUDIES

Lens not of interest (n=30)

1. Alio JL, Plaza-Puche AB, Pinero DP. Rotationally asymmetric multifocal IOL implantation with and without capsular tension ring: refractive and visual outcomes and intraocular optical performance. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2012;28(4):253-258.
2. Alio JL, Simonov A, Plaza-Puche AB, et al. Visual Outcomes and Accommodative Response of the Lumina Accommodative Intraocular Lens. *American journal of ophthalmology*. 2016;164:37-48.
3. Allen ED, Burton RL, Webber SK, et al. Comparison of a diffractive bifocal and a monofocal intraocular lens. *Journal of cataract and refractive surgery*. 1996;22(4):446-451.
4. Bournas P, Drazinos S, Kanellas D, Arvanitis M, Vaikoussis E. Dysphotopsia after cataract surgery: comparison of four different intraocular lenses. *Ophthalmologica Journal internationale d'ophtalmologie International journal of ophthalmology Zeitschrift für Augenheilkunde*. 2007;221(6):378-383.
5. Cleary G, Spalton DJ, Gala KB. A randomized intraindividual comparison of the accommodative performance of the bag-in-the-lens intraocular lens in presbyopic eyes. *American journal of ophthalmology*. 2010;150(5):619-627.e611.
6. el-Maghraby A, Marzouky A, Gazayerli E, Van der Karr M, DeLuca M. Multifocal versus monofocal intraocular lenses. Visual and refractive comparisons. *Journal of cataract and refractive surgery*. 1992;18(2):147-152.
7. Haaskjold E, Allen ED, Burton RL, et al. Contrast sensitivity after implantation of diffractive bifocal and monofocal intraocular lenses. *Journal of cataract and refractive surgery*. 1998;24(5):653-658.
8. Hancox J, Spalton D, Heatley C, Jayaram H, Marshall J. Objective measurement of intraocular lens movement and dioptric change with a focus shift accommodating intraocular lens. *Journal of cataract and refractive surgery*. 2006;32(7):1098-1103. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/953/CN-00612953/frame.html>.
9. Hancox J, Spalton D, Heatley C, et al. Fellow-eye comparison of posterior capsule opacification rates after implantation of 1CU accommodating and AcrySof MA30 monofocal intraocular lenses. *Journal of cataract and refractive surgery*. 2007;33(3):413-417.
10. Harman FE, Maling S, Kampougeris G, et al. Comparing the 1CU accommodative, multifocal, and monofocal intraocular lenses: a randomized trial. *Ophthalmology*. 2008;115(6):993-1001 e1002.



11. Henriquez M, Izquierdo L, Mendoza AJ, Suarez P. Comparison of Visual Results in Monofocal (Clariflex) vs. Multifocal (ReZoom) IOLs After Cataract Surgery. *American Academy of Ophthalmology*. 2006:201.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/822/CN-00634822/frame.html>.
12. Javitt J, Brauweiler HP, Jacobi KW, et al. Cataract extraction with multifocal intraocular lens implantation: clinical, functional, and quality-of-life outcomes. Multicenter clinical trial in Germany and Austria. *Journal of cataract and refractive surgery*. 2000;26(9):1356-1366.
13. Javitt JC, Steinert RF. Cataract extraction with multifocal intraocular lens implantation: a multinational clinical trial evaluating clinical, functional, and quality-of-life outcomes. *Ophthalmology*. 2000;107(11):2040-2048.
14. Joshi RS. Diffractive multifocal intraocular lens compared to pseudo-accommodative intraocular lens implant for unilateral cataracts in pre-presbyopic patients. *Middle East African journal of ophthalmology*. 2013;20(3):207-211.
15. Jusufovic V, Sarajlic D, Zvornicanin J, Musanovic Z, Halilbasic M. Comparison of the binocular vision quality after implantation of monofocal and multifocal intraocular lenses. *Acta Medica Saliniana*. 2011;40(2):63-68.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/693/CN-00897693/frame.html>.
16. Kamlesh, Dadeya S, Kaushik S. Contrast sensitivity and depth of focus with aspheric multifocal versus conventional monofocal intraocular lens. *Canadian journal of ophthalmology Journal canadien d'ophthalmologie*. 2001;36(4):197-201.
17. Kaya V, Ozturker ZK, Ozturker C, et al. ThinOptX vs AcrySof: comparison of visual and refractive results, contrast sensitivity, and the incidence of posterior capsule opacification. *European journal of ophthalmology*. 2007;17(3):307-314.
18. Kretz F, Gerl M, Gerl R, Müller M, Auffarth G. Clinical evaluation of a new pupil independent diffractive multifocal intraocular lens with a +2.75 D near addition: a European multicentre study. *British journal of ophthalmology*. 2017;99(12):1655-1659.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/166/CN-01258166/frame.html>.
19. Lau G, Kasthurirangan S, Vargas L. Functional vision with diffractive multifocal and accommodating iols. *American Academy of Optometry*. 2009.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/688/CN-00745688/frame.html>.
20. Leyland MD, Langan L, Goolfee F, Lee N, Bloom PA. Prospective randomised double-masked trial of bilateral multifocal, bifocal or monofocal intraocular lenses. *Eye (London, England)*. 2002;16(4):481-490.

21. Maxwell W, Waycaster C, D'Souza A, Meissner B, Hileman K. A United States cost-benefit comparison of an apodized, diffractive, presbyopia-correcting, multifocal intraocular lens and a conventional monofocal lens. *Journal of cataract and refractive surgery*. 2008;34(11):1855-1861.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/351/CN-00665351/frame.html>.
22. Mojzis P, Kukuckova L, Majerova K, Liehneova K, Pinero DP. Comparative analysis of the visual performance after cataract surgery with implantation of a bifocal or trifocal diffractive IOL. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2014;30(10):666-672.
23. Nijkamp MD, Dolders MG, de Brabander J, van den Borne B, Hendrikse F, Nuijts RM. Effectiveness of multifocal intraocular lenses to correct presbyopia after cataract surgery: a randomized controlled trial. *Ophthalmology*. 2004;111(10):1832-1839.
24. Percival SS, SS. Prospectively randomized trial comparing the pseudoaccommodation of the AMO ARRAY multifocal lens and a monofocal lens. *Journal of cataract and refractive surgery*. 1993;19(1):26-31.
25. Rossetti L, Carraro F, Rovati M, Orzalesi N. Performance of diffractive multifocal intraocular lenses in extracapsular cataract surgery. *Journal of cataract and refractive surgery*. 1994;20(2):124-128.
26. Sen HN, Sarikkola AU, Uusitalo RJ, Laatikainen L. Quality of vision after AMO Array multifocal intraocular lens implantation. *Journal of cataract and refractive surgery*. 2004;30(12):2483-2493.
27. Steinert RF, Post CT, Jr., Brint SF, et al. A prospective, randomized, double-masked comparison of a zonal-progressive multifocal intraocular lens and a monofocal intraocular lens. *Ophthalmology*. 1992;99(6):853-860; discussion 860-851.
28. Tang W, Zhuang S, Liu G. Comparison of visual function after multifocal and accommodative IOL implantation. *Eye science*. 2014;29(2):95-99.
29. Wang M, Corpuz C, Fujiwara M, Tomita M. Visual and optical performance of diffractive multifocal intraocular lenses with different haptic designs: 6 month follow-up. *Clinical ophthalmology (Auckland, NZ)*. 2014;8:919-926.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/876/CN-00992876/frame.html>.
30. Wolffsohn JS, Naroo SA, Motwani NK, et al. Subjective and objective performance of the Lenstec KH-3500 "accommodative" intraocular lens. *The British journal of ophthalmology*. 2006;90(6):693-696.

## No monofocal comparison (n=21)

31. Alfonso JF, Fernandez-Vega L, Puchades C, Montes-Mico R. Intermediate visual function with different multifocal intraocular lens models. *Journal of cataract and refractive surgery*. 2010;36(5):733-739.
32. Barisic A, Dekaris I, Gabric N, et al. Comparison of diffractive and refractive multifocal intraocular lenses in presbyopia treatment. *Collegium antropologicum*. 2008;32 Suppl 2:27-31.
33. Bijaoui S, Milazzo S, Thomas F, Berthout A. Comparison of Visual Results and Quality of Vision Between Two Multifocal Intra Ocular Lenses : Rezoom versus ReSTOR. *Iovs*. 2007;48:ARVO E-Abstract 3122.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/159/CN-00746159/frame.html>.
34. Chiam PJ, Chan JH, Haider SI, Karia N, Kasaby H, Aggarwal RK. Functional vision with bilateral ReZoom and ReSTOR intraocular lenses 6 months after cataract surgery. *Journal of cataract and refractive surgery*. 2007;33(12):2057-2061.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/622/CN-00717622/frame.html>.
35. Gangwani V, Hirschschall N, Findl O, Maurino V. Multifocal toric intraocular lenses versus multifocal intraocular lenses combined with peripheral corneal relaxing incisions to correct moderate astigmatism. *Journal of cataract and refractive surgery*. 2014;40(10):1625-1632.
36. Gil MA, Varon C, Rosello N, Cardona G, Buil JA. Visual acuity, contrast sensitivity, subjective quality of vision, and quality of life with 4 different multifocal IOLs. *European journal of ophthalmology*. 2012;22(2):175-187.
37. Hutz WW, Eckhardt HB, Rohrig B, Grolmus R. Intermediate vision and reading speed with array, Tecnis, and ReSTOR intraocular lenses. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2008;24(3):251-256.
38. Hutz WW, Jackel R, Hoffman PC. Comparison of visual performance of silicone and acrylic multifocal IOLs utilizing the same diffractive design. *Acta ophthalmologica*. 2012;90(6):530-533.
39. Jonker SM, Bauer NJ, Makhotkina NY, Berendschot TT, van den Biggelaar FJ, Nuijts RM. Comparison of a trifocal intraocular lens with a +3.0 D bifocal IOL: results of a prospective randomized clinical trial. *Journal of cataract and refractive surgery*. 2015;41(8):1631-1640.
40. Lane SS, Javitt JC, Nethery DA, Waycaster C. Improvements in patient-reported outcomes and visual acuity after bilateral implantation of multifocal intraocular lenses with +3.0 diopter addition: multicenter clinical trial. *Journal of cataract and refractive surgery*. 2010;36(11):1887-1896.

41. Leydolt C, Neumayer T, Prinz A, Findl O. Effect of patient motivation on near vision in pseudophakic patients. *American journal of ophthalmology*. 2009;147(3):398-405.e393.
42. Mastropasqua R, Toto L, Vecchiarino L, Falconio G, Nicola MD, Mastropasqua A. Multifocal IOL implant with or without capsular tension ring: study of wavefront error and visual performance. *European journal of ophthalmology*. 2013;23(4):510-517.
43. Maurino V, Allan BD, Rubin GS, Bunce C, Xing W, Findl O. Quality of vision after bilateral multifocal intraocular lens implantation: a randomized trial--AT LISA 809M versus AcrySof ReSTOR SN6AD1. *Ophthalmology*. 2015;122(4):700-710.
44. Maxwell WA, Cionni RJ, Lehmann RP, Modi SS. Functional outcomes after bilateral implantation of apodized diffractive aspheric acrylic intraocular lenses with a +3.0 or +4.0 diopter addition power Randomized multicenter clinical study. *Journal of cataract and refractive surgery*. 2009;35(12):2054-2061.
45. Munoz G, Albarran-Diego C, Javaloy J, Sakla HF, Cervino A. Combining zonal refractive and diffractive aspheric multifocal intraocular lenses. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2012;28(3):174-181.
46. Nuijts RM, Jonker SM, Kaufer RA, et al. Bilateral implantation of +2.5 D multifocal intraocular lens and contralateral implantation of +2.5 D and +3.0 D multifocal intraocular lenses: Clinical outcomes. *Journal of cataract and refractive surgery*. 2016;42(2):194-202.
47. Pepose JS, Hayashida J, Hovanesian J, et al. Safety and effectiveness of a new toric presbyopia-correcting posterior chamber silicone intraocular lens. *Journal of cataract and refractive surgery*. 2015;41(2):295-305.
48. Santhiago MR, Netto MV, Espindola RF, et al. Comparison of reading performance after bilateral implantation of multifocal intraocular lenses with +3.00 or +4.00 diopter addition. *Journal of cataract and refractive surgery*. 2010;36(11):1874-1879.
49. Santhiago MR, Wilson SE, Netto MV, et al. Visual performance of an apodized diffractive multifocal intraocular lens with +3.00-d addition: 1-year follow-up. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2011;27(12):899-906.
50. Santhiago MR, Wilson SE, Netto MV, et al. Modulation transfer function and optical quality after bilateral implantation of a +3.00 D versus a +4.00 D multifocal intraocular lens. *Journal of cataract and refractive surgery*. 2012;38(2):215-220.
51. Toto L, Falconio G, Vecchiarino L, et al. Visual performance and biocompatibility of 2 multifocal diffractive IOLs: six-month comparative study. *Journal of cataract and refractive surgery*. 2007;33(8):1419-1425.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/662/CN-00717662/frame.html>.

## Not intervention of interest (n=9)

52. Alio JL, Plaza-Puche AB, Javaloy J, Ayala MJ, Vega-Estrada A. Clinical and optical intraocular performance of rotationally asymmetric multifocal IOL plate-haptic design versus C-loop haptic design. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2013;29(4):252-259.
53. Barisic A, Gabric N, Dekaris I, Romac I, Bohac M, Juric B. Comparison of different presbyopia treatments: refractive lens exchange with multifocal intraocular lens implantation versus LASIK monovision. *Collegium antropologicum*. 2010;34 Suppl 2:95-98.
54. Donnenfeld E, Roberts C, Perry H, Solomon R, Wittpenn J, McDonald M. Efficacy of Topical Cyclosporine versus Tears for Improving Visual Outcomes Following Multifocal IOL Implantation. *Iovs*. 2007;48:ARVO E-Abstract 1066.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/705/CN-00745705/frame.html>.
55. Donnenfeld ED, Solomon R, Roberts CW, Wittpenn JR, McDonald MB, Perry HD. Cyclosporine 0.05% to improve visual outcomes after multifocal intraocular lens implantation. *Journal of cataract and refractive surgery*. 2010;36(7):1095-1100.
56. Fernandez-Vega L, Madrid-Costa D, Alfonso JF, Montes-Mico R, Poo-Lopez A. Optical and visual performance of diffractive intraocular lens implantation after myopic laser in situ keratomileusis. *Journal of cataract and refractive surgery*. 2009;35(5):825-832.
57. Gerten G, Kermani O, Schmiedt K, Farvili E, Foerster A, Oberheide U. Dual intraocular lens implantation: Monofocal lens in the bag and additional diffractive multifocal lens in the sulcus. *Journal of cataract and refractive surgery*. 2009;35(12):2136-2143.
58. Schrecker J, Feith A, Langenbacher A. Comparison of additional pseudophakic multifocal lenses and multifocal intraocular lens in the capsular bag. *The British journal of ophthalmology*. 2014;98(7):915-919.
59. Schrecker J, Langenbacher A. Visual performance in the long term with secondary add-on versus primary capsular bag multifocal intraocular lenses. *Journal of refractive surgery (thorofare, NJ : 1995)*. 2017;32(11):742-747.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/178/CN-01292178/frame.html>.
60. Szigeti A, Kranitz K, Takacs AI, Mihaltz K, Knorz MC, Nagy ZZ. Comparison of long-term visual outcome and IOL position with a single-optic accommodating IOL After 5.5- or 6.0-mm Femtosecond laser capsulotomy. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2012;28(9):609-613.

## Not outcome of interest (n=2)

61. Dolders M, Nijkamp M, Nuijts R, et al. Cost effectiveness of foldable multifocal intraocular lenses compared to foldable monofocal intraocular lenses for cataract surgery. *British journal of ophthalmology*. 2004;88(9):1163-1168.

<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/359/CN-00480359/frame.html>.

62. Varon C, Gil MA, Alba-Bueno F, et al. Stereo-acuity in patients implanted with multifocal intraocular lenses: is the choice of stereotest relevant? *Current eye research*. 2014;39(7):711-719.

Not RCT (n=16)

63. Visual performance and rotational stability of a multifocal toric intraocular lens. *Journal of Refractive Surgery* 32 (7) (pp 444-450), 2016 Date of Publication: July 2016. 2016. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01197299/frame.html>.
64. Alfonso J, Puchades C, Fernandez-Vega L, Montes-Mico R, Valcarcel B, Ferrer-Blasco T. Visual acuity comparison of 2 models of bifocal aspheric intraocular lenses. *Journal of cataract and refractive surgery*. 2009;35(4):672-676. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/810/CN-00754810/frame.html>.
65. Bi H, Cui Y, Ma X, et al. Early clinical evaluation of AcrySof ReSTOR multifocal intraocular lens for treatment of cataract. *Ophthalmologica Journal internationale d'ophtalmologie International journal of ophthalmology Zeitschrift für Augenheilkunde*. 2008;222(1):11-16. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00621916/frame.html>.
66. Chen T, Yu F, Lin H, et al. Objective and subjective visual quality after implantation of all optic zone diffractive multifocal intraocular lenses: a prospective, case-control observational study. *British journal of ophthalmology*. 2017;100(11):1530-1535. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/266/CN-01292266/frame.html>.
67. Greenbaum S. Re: Wilkins et al.: randomized trial of multifocal intraocular lenses versus monovision after bilateral cataract surgery (Ophthalmology 2013;120:2449-55). *Ophthalmology*. 2014;121(7):e34. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/707/CN-01071707/frame.html>.
68. Hantera M, Hamed A, Fekry Y, Shoheib E. Initial experience with an accommodating intraocular lens: controlled prospective study. *Journal of cataract and refractive surgery*. 2010;36(7):1167-1172. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/270/CN-00749270/frame.html>.
69. Knorz MC, Rincon JL, Suarez E, et al. Subjective outcomes after bilateral implantation of an apodized diffractive +3.0 D multifocal toric IOL in a prospective clinical study. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2013;29(11):762-767.

70. Lawless M, Bali S, Hodge C, Roberts T, Chan C, Sutton G. Outcomes of femtosecond laser cataract surgery with a diffractive multifocal intraocular lens. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2012;28(12):859-864.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/599/CN-00917599/frame.html>.
71. Macsai MS, Padnick-Silver L, Fontes BM. Visual outcomes after accommodating intraocular lens implantation. *Journal of cataract and refractive surgery*. 2006;32(4):628-633.
72. Patel S, Alio JL, Feinbaum C. Comparison of Acri. Smart multifocal IOL, crystalens AT-45 accommodative IOL, and Technovision presbyLASIK for correcting presbyopia. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2008;24(3):294-299.
73. Pedrotti E, Mastropasqua R, Passilongo M, Parisi G, Marchesoni I, Marchini G. Comparison of two multifocal intraocular lens designs that differ only in near add. *Journal of refractive surgery (Thorofare, NJ : 1995)*. 2014;30(11):754-760.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/711/CN-01036711/frame.html>.
74. Perea-Milla E, Vidal S, Briones E, et al. Development and validation of clinical scores for visual outcomes after cataract surgery. *Ophthalmology*. 2011;118(1):9-16.e11-13.
75. Sun Y, Zheng D, Song T, Liu Y. Visual function after bilateral implantation of apodized diffractive multifocal IOL with a +3.0 or +4.0 D addition. *Ophthalmic Surgery Lasers and Imaging*. 2011;42(4):302-307.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/105/CN-00890105/frame.html>.
76. Vilupuru S, Lin L, Pepose JS. Comparison of Contrast Sensitivity and Through Focus in Small-Aperture Inlay, Accommodating Intraocular Lens, or Multifocal Intraocular Lens Subjects. *American journal of ophthalmology*. 2015;160(1):150-162.e151.
77. Wang Q, Zhao G, Wang Q, Jia W. Visual quality after AcrySof IQ ReSTOR intraocular lens implantation in eyes with high myopia. *European journal of ophthalmology*. 2012;22(2):168-174. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/578/CN-00972578/frame.html>.
78. Zhang F, Sugar A, Jacobsen G, Collins M. Visual function and patient satisfaction: Comparison between bilateral diffractive multifocal intraocular lenses and monovision pseudophakia. *Journal of cataract and refractive surgery*. 2011;37(3):446-453.  
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00891916/frame.html>.

#### Background (n=1)

79. Silva S, Evans J, Kirthi V, Ziaei M, Leyland M. Multifocal versus monofocal intraocular lenses after cataract extraction. *Cochrane database of systematic reviews (online)*.

2017;2016(12) (no pagination). <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/631/CN-01286631/frame.html>.

Commentary (n=1)

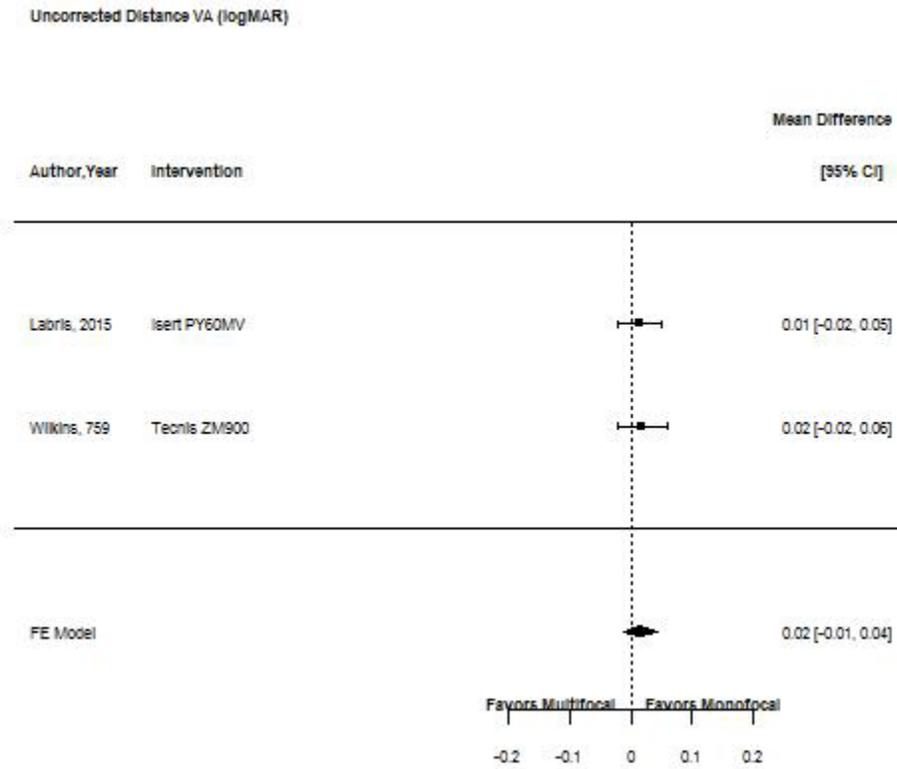
80. Lloyd J. A randomized intraindividual comparison of the accommodative performance of the bag-in-the-lens intraocular lens in presbyopic eyes. *Evidence-Based Ophthalmology*. 2011;12(2):69-71. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/061/CN-00895061/frame.html>.

Duplicate (n=1)

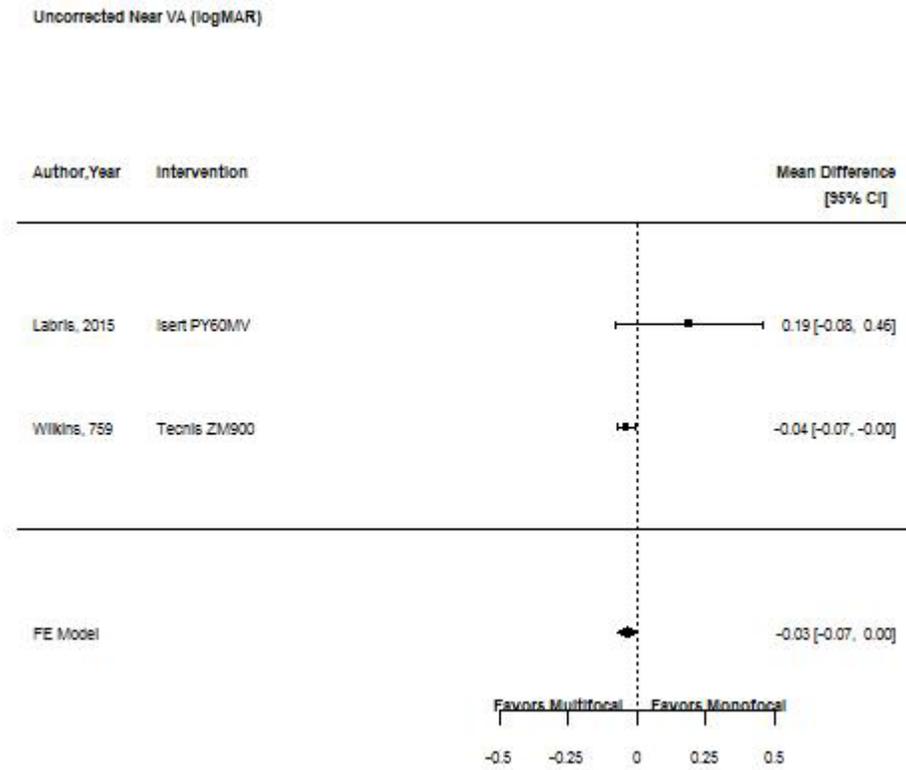
81. Joshi R. Diffractive multifocal intraocular lens compared to pseudo-Accommodative intraocular lens implant for unilateral cataracts in pre-Presbyopic patients. *Middle East African journal of ophthalmology*. 2013;20(3):207-211. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/028/CN-00911028/frame.html>.

## APPENDIX E. RESULTS OF POOLED ANALYSES COMPARING MULTIFOCAL IOLS WITH MONOVISION

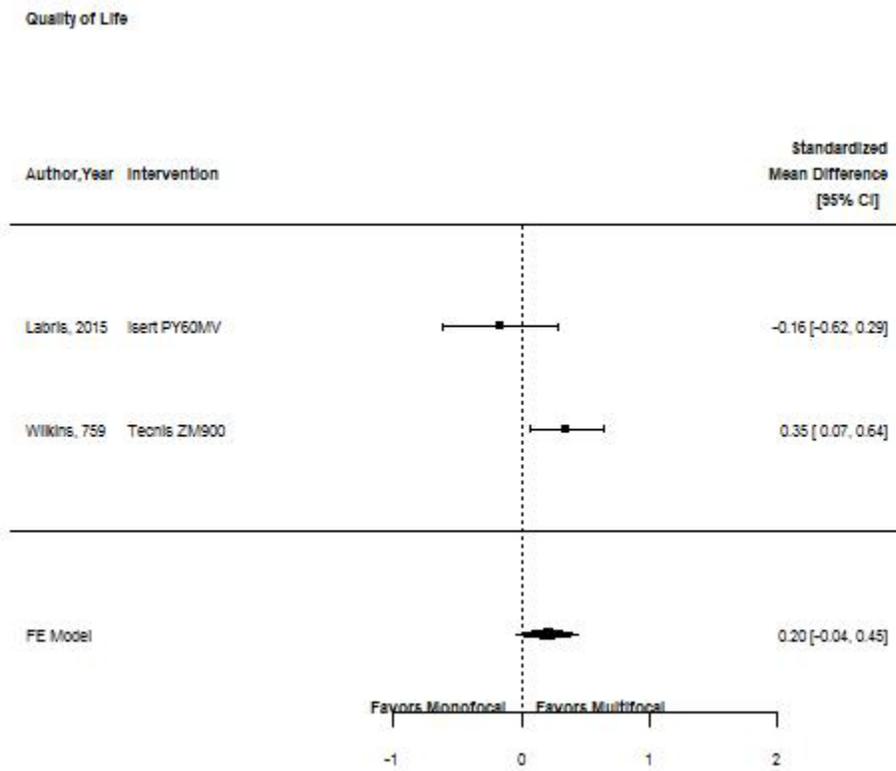
Figure 1. Multifocal IOLs Compared to Monovision Uncorrected Distance



**Figure 2. Multifocal IOLs Compared to Monovision Uncorrected Near**



**Figure 3. Multifocal IOLs Compared to Monovision Quality of Life**



**Figure 4. Multifocal IOLs Compared to Monovision Spectacle Independence**

