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Ong HS, Evans JR, Allan BDS

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[Intervention Review]

Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

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ABSTRACT

Background

Following cataract surgery and intraocular lens (IOL) implantation, loss of accommodation or postoperative presbyopia occurs and remains a challenge. Standard monofocal IOLs correct only distance vision; patients require spectacles for near vision. Accommodative IOLs have been designed to overcome loss of accommodation after cataract surgery.

Objectives

To define (a) the extent to which accommodative IOLs improve unaided near visual function, in comparison with monofocal IOLs; (b) the extent of compromise to unaided distance visual acuity; c) whether a higher rate of additional complications is associated the use of accommodative IOLs.

Search methods

We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library* 2013, Issue 9), Ovid MEDLINE, Ovid MEDLINE in-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily Update, Ovid OLDMEDLINE (January 1946 to October 2013), EMBASE (January 1980 to October 2013), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to October 2013), the *metaRegister* of Controlled Trials (*mRCT*) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrial.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 10 October 2013.

Selection criteria

We include randomised controlled trials (RCTs) which compared implantation of accommodative IOLs to implantation of monofocal IOLs in cataract surgery.

Data collection and analysis

Two authors independently screened search results, assessed risk of bias and extracted data. All included trials used the 1CU accommodative IOL (HumanOptics, Erlangen, Germany) for their intervention group. One trial had an additional arm with the AT-45 Crystallens accommodative IOL (Eyeonics Vision). We performed a separate analysis comparing 1CU and AT-45 IOL.

Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery (Review)

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Main results

We included four RCTs, including 229 participants (256 eyes), conducted in Germany, Italy and the UK. The age range of participants was 21 to 87 years. All studies included people who had bilateral cataracts with no pre-existing ocular pathologies. We judged all studies to be at high risk of performance bias. We graded two studies with high risk of detection bias and one study with high risk of selection bias.

Participants who received the accommodative IOLs achieved better distance-corrected near visual acuity (DCNVA) at six months (mean difference (MD) -3.10 Jaeger units; 95% confidence intervals (CI) -3.36 to -2.83, 2 studies, 106 people, 136 eyes, moderate quality evidence). Better DCNVA was seen in the accommodative lens group at 12 to 18 months in the three trials that reported this time point but considerable heterogeneity of effect was seen, ranging from 1.3 (95% CI 0.98 to 1.68; 20 people, 40 eyes) to 6 (95% CI 4.15 to 7.85; 51 people, 51 eyes) Jaeger units and 0.12 (95% CI 0.05 to 0.19; 40 people, binocular) logMAR improvement (low quality evidence). The relative effect of the lenses on corrected distant visual acuity (CDVA) was less certain. At six months there was a standardised mean difference of -0.04 standard deviations (95% CI -0.37 to 0.30, 2 studies, 106 people, 136 eyes, low quality evidence). At long-term follow-up there was heterogeneity of effect with 18-month data in two studies showing that CDVA was better in the monofocal group (MD 0.12 logMAR; 95% CI 0.07 to 0.16, 2 studies, 70 people, 100 eyes) and one study which reported data at 12 months finding similar CDVA in the two groups (-0.02 logMAR units, 95% CI -0.06 to 0.02, 51 people) (low quality evidence).

The relative effect of the lenses on reading speed and spectacle independence was uncertain. The average reading speed was 11.6 words per minute more in the accommodative lens group but the 95% confidence intervals ranged from 12.2 words less to 35.4 words more (1 study, 40 people, low quality evidence). People with accommodative lenses were more likely to be spectacle-independent but the estimate was very uncertain (risk ratio (RR) 8.18; 95% CI 0.47 to 142.62, 1 study, 40 people, very low quality evidence).

More cases of posterior capsule opacification (PCO) were seen in accommodative lenses but the effect of the lenses on PCO was uncertain (Peto odds ratio (OR) 2.12; 95% CI 0.45 to 10.02, 91 people, 2 studies, low quality evidence). People in the accommodative lens group were more likely to require laser capsulotomy (Peto OR 7.96; 95% CI 2.49 to 25.45, 2 studies, 60 people, 80 eyes, low quality evidence). Glare was reported less frequently with accommodative lenses but the relative effect of the lenses on glare was uncertain (RR any glare 0.78; 95% CI 0.32 to 1.90, 1 study, 40 people, and RR moderate/severe glare 0.45; 95% CI 0.04 to 4.60, low quality evidence).

Authors' conclusions

There is moderate-quality evidence that study participants who received accommodative IOLs had a small gain in near visual acuity after six months. There is some evidence that distance visual acuity with accommodative lenses may be worse after 12 months but due to low quality of evidence and heterogeneity of effect, the evidence for this is not clear-cut. People receiving accommodative lenses had more PCO which may be associated with poorer distance vision. However, the effect of the lenses on PCO was uncertain.

Further research is required to improve the understanding of how accommodative IOLs may affect near visual function, and whether they provide any durable gains. Additional trials, with longer follow-up, comparing different accommodative IOLs, multifocal IOLs and monofocal IOLs, would help map out their relative efficacy, and associated late complications. Research is needed on control over capsular fibrosis postimplantation.

Risks of bias, heterogeneity of outcome measures and study designs used, and the dominance of one design of accommodative lens in existing trials (the HumanOptics 1CU) mean that these results should be interpreted with caution. They may not be applicable to other accommodative IOL designs.

PLAIN LANGUAGE SUMMARY

Accommodative intraocular lenses compared with monofocal intraocular lenses in cataract surgery

Background

Accommodation is the ability of the eye to focus on both distant and near objects.

Accommodation is achieved through the contraction of ciliary muscles, which results in an increase in curvature and a forward shift of the natural lens in the eye. Accommodation declines with increasing age due to a decrease in lens elasticity and a reduction in ciliary muscle contraction, resulting in difficulty in near vision (presbyopia). This is a problem for most people in their 40s or 50s.

For best optical performance, the lens must be transparent. Cataract is the clouding of the human lens. It is more common with increasing age, and is a common cause of visual impairment. Fortunately, cataract is treatable by a surgical procedure in which the natural lens is removed through a small incision. Once all lens material is removed, an artificial lens, known as an intraocular lens (IOL) is implanted into the eye to lie in the original position of the removed natural lens.

All functions of the natural lens are preserved by an IOL, with the exception of accommodation. Standard IOLs, known as monofocal IOLs, allow only distant objects to be focused and seen clearly. Patients require spectacles for near vision. This problem after cataract surgery remains a challenge for ophthalmologists. To overcome the loss of accommodation after cataract surgery, various strategies have been tried with variable success.

Accommodative IOLs have been designed to restore accommodation. The aim of this systematic review is to help define the extent to which accommodative IOLs improve near vision in comparison with standard monofocal IOLs.

Study characteristics

This review looked at four studies that enrolled 229 people (256 eyes) and compared the use of accommodative IOLs to the use of monofocal IOLs in cataract surgery. We last searched for evidence in October 2013.

Key findings

The results of the review showed that participants who received accommodative IOLs had improvements in near vision at six months and at 12 months after surgery compared to those who received monofocal IOLs. However, such improvements were small and reduced with time. Low-quality evidence also showed that more than 12 months after surgery, there was a compromise in distance vision for people with accommodative IOLs. This may be related to the finding that those who received accommodative IOLs also appeared to have a higher rate of posterior capsular opacification (thickening and clouding of the tissue behind the IOL). However, these findings were uncertain. Further research on accommodative IOLs is required before we can draw conclusions on their effectiveness and safety compared to monofocal IOLs.

Quality of the evidence

Overall the quality of the evidence was low or very low with the exception for the findings on near vision at six months.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Accommodative intraocular lens compared with monofocal intraocular lens in cataract surgery						
<p>Patient or population: Participants over age of 21 years undergoing cataract surgery Settings: Ophthalmology centres performing cataract surgery Intervention: Accommodative intraocular lens (IOL) implantation Comparison: Monofocal IOL implantation</p>						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect	No of participants (studies)	Quality of the evidence (GRADE)	Comment
	Assumed risk	Corresponding risk				
	Monofocal IOL	Accommodative IOL				
Distance-corrected near visual acuity at 6 months [Jaeger units]	Mean visual acuity was 9.3 Jaeger units and 8.53 Jaeger units in the two studies	Visual acuity was 3.10 Jaeger units better (95% CI 3.36 better to 2.83 better) [Favours Accommodative IOL]		106 people, 136 eyes including 60 eyes pair-matched (2)	⊕⊕⊕○ ¹ moderate	
Distance-corrected near visual acuity at 12 months or more [Jaeger units and logMAR units]	See comments	See comments	See comments	111 people, 131 eyes including 40 eyes pair-matched	⊕⊕○○ ² low	In all three studies reporting this outcome, people receiving an accommodative IOL had a better distance-corrected near visual acuity at 12 months but there was substantial heterogeneity in effect ($I^2 = 96%$): one study found a mean difference of 1.33 Jaeger units; 95% CI 0.98 to 1.68; 20 people, 40 eyes all pair-matched; one study found a mean

						difference of 6.00 Jaeger units; 95% CI 4.15 to 7.85, 51 people, 51 eyes; one study found a mean difference of 0.12 logMAR; 95% CI 0.05 to 0.19; 40 people, binocular
Corrected distant visual acuity at 6 months [standard deviations]	Mean visual acuity was -0.1 (SD 0.1) logMAR units in one study and 0.93 (SD 0.18) Snellen lines in the other	Visual acuity was 0.04 standard deviations better (95% CI 0.37 better to 0.30 worse)		106 people, 136 eyes including 60 eyes pair-matched (2)	⊕⊕○○ ³ low	
Corrected distant visual acuity at 12 months or more [logMAR units]	Mean visual acuity ranged from -0.1 to 0.04	Visual acuity was 0.12 logMAR worse (95% CI 0.07 worse to 0.16 worse) [Favours Monofocal IOL]		70 people, 100 eyes including 60 eyes pair-matched (2)	⊕⊕○○ ² low	Pooled results for follow-up at 18 months. One additional study with follow-up at 12 months found no difference -0.02 logMAR units [95% CI -0.06, 0.02], 51 people
Reading speed [words per minute]	Mean reading speed was 161.4 words per minute	Reading speed was 11.6 words more (95% CI 12.2 words less to 35.4 words more).		40 people (1)	⊕⊕○○ ³ low	
Spectacle independence	0 per 1000	190 per 1000 (1 to 1000)	RR 8.18; 95% CI 0.47 to 142.62	40 people (1)	⊕○○○ ⁴ very low	
Reported complications Laser capsulotomies for posterior capsule opacification (PCO)	50 per 1000	295 per 1000 (116 to 573)	Peto OR 7.96; 95% CI 2.49 to 25.45	60 people, 80 eyes including 20 eyes pair-matched (2)	⊕⊕○○ ³ low	More cases of PCO were seen in accommodative lenses but the effect of the lenses on PCO was uncertain (Peto OR 2.12; 95% CI 0.45 to 10.02, 91 people, 2 studies)

		Glare was reported less frequently in accommodative lenses but the effect of the lens of glare was uncertain (RR any glare 0.78; 95% CI 0.32 to 1.90, 40 people, 1 study). (RR moderate/severe glare 0.45; 95% CI 0.04 to 4.60, 40 people)
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*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹Downgraded for risk of bias

²Downgraded for risk of bias and inconsistency

³Downgraded for risk of bias and imprecision

⁴Downgraded for risk of bias, imprecision and indirectness.

BACKGROUND

Description of the condition

The normal crystalline lens of the eye is a biconvex transparent and elastic structure with the primary function of focusing images onto the retina. It is the second most powerful refractive structure in the human eye, after the cornea.

The ability of the eye to focus sharp retinal images from distant to near objects by increasing its refractive power is known as accommodation. This increase in refractive power is achieved through the contraction of ciliary muscles, which results in an increase in curvature and a forward shift of the human crystalline lens.

Accommodation declines with increasing age due to a decrease in lens elasticity (Glasser 1999) and a reduction in ciliary muscle contraction (Croft 2001), resulting in difficulty in near vision. This is presbyopia and usually begins in the fifth decade of life.

For optimal optical abilities, the crystalline lens must be transparent. Cataract is the pathological opacification of the crystalline lens. It is derived from the word *cataracta*, Latin for waterfall. Cataracts can be congenital or acquired.

Acquired causes of cataracts include the following:

- age-related (senile);
- drugs (corticosteroids, chlorpromazine, amiodarone, aspirin, topical glaucoma medications, pilocarpine);
- trauma;
- secondary to systemic diseases (diabetes mellitus, myotonic dystrophy, Wilson's disease, atopic dermatitis, neurofibromatosis Type 2, Fabry's disease);
- secondary to other ocular diseases (uveitis, myopia, acute angle closure glaucoma, retinal dystrophies).

Cataract is a common cause of visual impairment in both developed and developing nations. The World Health Organization (WHO) estimates that age-related cataract accounts for 48% of world blindness, which represents about 18 million people (WHO 2011). In many countries where surgical services are inadequate, cataract remains the leading cause of blindness (WHO 2011).

Description of the intervention

Acquired cataract is a treatable and thus a reversible cause of visual impairment. Modern treatment of cataracts is performed by small-incision phacoemulsification of the opacified crystalline lens and implantation of an intraocular lens (IOL). Phacoemulsification has been considerably refined since its first introduction in 1967. All functions of the natural crystalline lens can be restored except accommodation. Standard monofocal IOLs correct only vision at a distance and patients require spectacle correction for near vision. Postoperative presbyopia remains a challenge for ophthalmologists.

To overcome the loss of accommodation after cataract surgery, various strategies have been used, including monovision (Boerner 1984; Greenbaum 2002), myopic astigmatism (Datiles 1990), scleral expansion techniques (Mathews 1999), implantation of corneal inlays (Keates 1995), and multifocal laser-assisted in-situ keratomileusis (LASIK) (Alió 2006). These methods are generally referred to as apparent accommodation, or pseudoaccommodation, as they potentially allow for preservation of near vision without changing the focal length of the eye (Menapace 2007). However, these approaches all involve some compromise in distance vision. Several studies have shown that good functional vision without spectacle dependence can be achieved with bifocal and multifocal IOLs (Avitabile 2001; Leyland 2003; Nijkamp 2004; Pineda-Fernandez 2004), but both refractive and diffractive multifocal IOLs are known to cause decreased contrast sensitivity, glare disability, and higher order aberrations (Chandhrasi 2006; Javitt 2000; Leyland 2003).

Accommodative IOLs have been designed to restore accommodation by transmitting ciliary muscular contractions into a change of refractive power of the eye. They aim to restore good near vision with no compromise for distance vision and fewer optical side-effects.

How the intervention might work

Different accommodative IOLs have been developed. Single-optic accommodative IOLs such as the Ring-haptic Bio-ComFold IOL (Morcher GmbH, Stuttgart, Germany), 1CU IOL (HumanOptics, Erlangen, Germany), CrystaLens (Eyeonics, Aliso Viejo, California, USA), and KH 350 IOL (Lenstec Inc, St Petersburg, Florida, USA), have flexible supporting elements (haptics) that are thought to allow an anterior displacement of the lens optic, increasing the dioptric power of the eye (Menapace 2007). Dual-optic accommodative IOLs such as the Synchrony accommodating IOL (Visiogen, Irvine, California, USA), consist of two separate optics coupled by a spring haptic mechanism. A high powered plus anterior optic of fixed dioptric power is connected to a minus posterior optic. As the lens completely occupies the capsular bag, capsular tension causes a change in the distance between the anterior and posterior lens. During relaxation of the capsule following ciliary muscular contraction, anterior displacement of the positive lens causes an increase in dioptric power of the eye. Other approaches to restore accommodation involve altering the shape and thus refractive power of the IOL. An example is the NuLens accommodating IOL (NuLens Ltd, Herzliya Pituah, Israel). This IOL is made of a soft silicone gel with a piston-like central lens. It uses the capsular bag and zonules as a dynamic diaphragm that transmits forces from contracting ciliary muscles to the attached piston. With ciliary muscular contraction or relaxation, the pressurised silicone gel is displaced through a round hole in the anterior chamber wall to form a lens-shaped bulge which is con-

tinuously changing in its curvature, altering the refractive power of the eye.

Why it is important to do this review

Several randomised controlled trials (RCTs) have been published comparing accommodative IOLs and monofocal IOLs in cataract surgery with varying outcomes. This systematic review of RCTs will help to define the extent to which accommodative IOLs may improve unaided near visual function in comparison with monofocal IOLs and the extent of any compromise to other measures of visual function associated with their use.

OBJECTIVES

To define (a) the extent to which accommodative IOLs improve unaided near visual function, in comparison with monofocal IOLs; (b) the extent of compromise to unaided distance visual acuity; c) whether a higher rate of additional complications is associated the use of accommodative IOLs.

METHODS

Criteria for considering studies for this review

Types of studies

We only included randomised controlled trials (RCTs) in this systematic review.

We included a trial if, on the basis of the best available information, we judged that the individuals followed in the trial were definitely or possibly assigned prospectively to one of two of the interventions using a) random allocation or b) some quasi-random method of allocation.

Types of participants

We included trials in which the participants were over the age of 21 years with cataract. We excluded a) participants with other ocular co-morbidities such as glaucoma, diabetes mellitus, age-related macular degeneration, myopic retinopathy; or b) participants who had previous ocular surgery or ocular trauma.

Types of interventions

We included studies in which implantation of accommodative IOLs was compared with implantation of monofocal IOLs in cataract surgery.

Types of outcome measures

Primary outcomes

Amplitude of accommodation at six months post-treatment. To assess the stability of intervention effect, we analysed amplitude of accommodation after 12 months.

Current trials use both subjective and objective methods to assess accommodative amplitude. Subjective methods include near point of accommodation (the distance from the eye at which blur is first noticed for a standard letter size), defocus curves (corrected distance visual acuity plotted against increasing myopic spherical addition), and distance-corrected near visual acuity (DCNVA). Objective methods includes dynamic retinoscopy, and other objective measures of accommodative responses (e.g. SRW-5000 and interferometry). We studied outcomes for both subjective and objective methods of assessing amplitude of accommodation in the meta-analysis.

Secondary outcomes

- corrected distant visual acuity (CDVA);
- reading speed;
- contrast sensitivity;
- change in anterior chamber depth on accommodation;
- spectacle independence;
- reported complications.

Search methods for identification of studies

Electronic searches

We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) 2013, Issue 9, part of *The Cochrane Library*. www.thecochranelibrary.com (accessed 10 October 2013), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to October 2013), EMBASE (January 1980 to October 2013), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to October 2013), the *metaRegister* of Controlled Trials (*mRCT*) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 10 October 2013.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), LILACS (Appendix 4), *mRCT* (Appendix 5), ClinicalTrials.gov (Appendix 6) and the ICTRP (Appendix 7).

Searching other resources

We searched the reference lists of the studies included in the review for information about further trials. We contacted experts in the field for further information. We used the Science Citation Index to search for papers that cited any studies included in this review. We searched the Food and Drugs Administration (FDA) trials database. We did not handsearch journals or conference proceedings specifically for this review.

Data collection and analysis

Selection of studies

Two review authors (HSO/BA) examined the titles and abstracts resulting from the searches, removed duplicate records and clearly irrelevant reports. We retrieved full-text copies of potentially relevant reports and assessed these against the 'Criteria for considering studies for this review'. We contacted study authors for clarification as needed and linked multiple reports of the same studies. For all these tasks (apart from contacting authors), both review authors worked independently and then compared results. We resolved disagreements by discussion.

Data extraction and management

Two review authors (HSO/JE) extracted data independently using a standard data collection form. We compared the results and resolved any disagreements by discussion. One review author entered data into Review Manager 5 (Review Manager 2012) and then both review authors independently checked the data entered. We extracted the following details from the studies: methods, participants, interventions, outcomes and notes. Where we were unable to extract all the information we were interested in from published reports, both with regard to the details of the study and its numerical results, we requested the missing data from the original investigators.

Assessment of risk of bias in included studies

Two review authors (HSO/BA) assessed studies that met the inclusion criteria for risk of bias using Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2011). We considered the following domains for potential risk of bias: random sequence generation (to determine whether the sequence allocation was adequately generated), allocation concealment, masking (blinding) of outcome assessors and participants (to determine whether knowledge of the allocated intervention was adequately prevented during the study), incomplete outcome data, selective outcome reporting, and other sources of bias. We graded each domain of trial as 'low risk' of bias, 'high risk' of bias or 'unclear risk'. The assessments considered the risk of material bias. We define material bias as bias of sufficient magnitude to have a notable

impact on the results or conclusions of the trial, recognising that subjectivity is involved in any such judgement. We resolved any disagreements between the review authors by discussion. We contacted the trial authors for clarification on any domain assessed as unclear.

Measures of treatment effect

All outcome measures stated were continuous data except 'spectacle independence', posterior capsular opacification (PCO) and numbers of laser capsulotomies, where the outcome measure were dichotomous data. For dichotomous outcomes, we calculated a risk ratio (RR) or odds ratio (OR) (or Peto OR) when the outcome was rare (or very rare). Mean differences (MDs) were calculated for continuous data. We used standardised mean differences (SMDs) in meta-analysis when studies assessed similar outcomes but measured them in a variety of ways or used different scales. The SMD method does not correct for differences in the direction of the scale. If some scales increased with disease severity whilst others decreased, we multiplied the mean values from one set of studies by -1 to ensure that all the scales point in the same direction.

Where possible, we assessed skewness of data of included studies in accordance with Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). Except for one outcome measure, namely, distance-corrected visual acuities, all other continuous data had a low degree of skewness. For this outcome measure, we reported means and standard deviations with the assumption that methods for the meta-analysis are quite robust to some degree of skewness.

Unit of analysis issues

The preferred unit of analysis was outcomes for eyes rather than individuals, since some individuals had unilateral treatment or different treatments in each eye. We included paired-eye studies, where one eye was randomised to one intervention and the second eye had by default gone on to receive the other intervention, as carry-over and period effects were not thought likely to be significant. Similarly we included studies where both eyes were randomised to the same intervention.

Dealing with missing data

Where we were unable to extract all the information we were interested in from published reports, both with regard to the details of the study and its numerical results, we requested the missing data from the original investigators.

Assessment of heterogeneity

We identified differences between the studies which were likely to introduce heterogeneity. As some degree of heterogeneity existed due to the clinical and methodological diversity of the studies,

we employed the results of the Chi² test as well as the I² statistic (Higgins 2003) to quantify inconsistencies across studies.

Assessment of reporting biases

We investigated whether our review was subject to reporting biases. We did not create funnel plots for signs of asymmetry, due to the small number of included trials in this review. We aim to do this when we have 10 or more trials contributing to our meta-analysis.

Data synthesis

We performed the data analysis according to Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). We used a fixed-effect model for our analysis, as we believe the true effect of the intervention is fixed, based on the assumption that the true effect of the interventions had the same resultant effect in every study. In addition, meta-analyses in this review only included three or fewer trials. Where we could not conduct a meta-analysis due to lack of quantitative data, we presented a narrative synthesis regarding the direction of effect, size of effect, and consistency of effect across studies as well as the strength of evidence.

Subgroup analysis and investigation of heterogeneity

As per the protocol for this review, we performed a global analysis of all accommodative IOLs with monofocal IOLs. Given that all studies included in our meta-analysis used the 1CU accommodative IOL for their intervention group, we have not conducted a subgroup analysis.

We endeavoured to identify differences between the studies which were likely to introduce heterogeneity. As some degree of heterogeneity always exists due to the clinical and methodological diversity of the studies, we employed the results of the Chi² test as

well as the I² statistic to quantify inconsistencies across studies. We defined substantial heterogeneity as an I² statistic value of 50% or more combined with a Chi² test value of less than 0.1. If all the results are in the same direction, then we considered pooling to be justified even in the presence of heterogeneity.

Sensitivity analysis

Due to the small number of trials included in the review, we did not perform planned sensitivity analyses to evaluate how robust the results of the review were relative to decisions and assumptions made in the process of conducting the review. There were too few RCTs included to make this worthwhile, and only one of the four trials was not graded at high risk of bias for a least one domain.

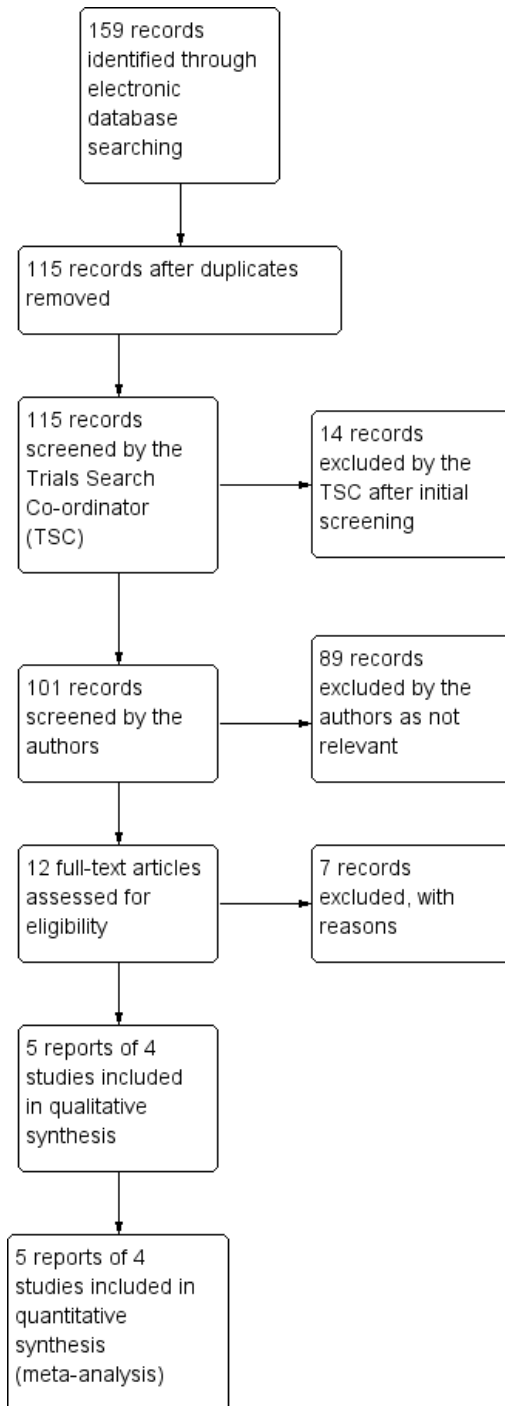
RESULTS

Description of studies

Results of the search

The electronic searches yielded a total of 159 records (Figure 1). After deduplication the Trials Search Co-ordinator scanned 115 records and discarded 14 records as they were not relevant to the scope of the review. The review authors screened the remaining 101 records and rejected a further 89 records as not relevant to the review. We obtained and screened full-text copies of 12 references. We included five reports of four studies in the review, and excluded seven studies that did not meet the inclusion criteria. Two of the five included reports presented different outcome measures from the same trial (Heatley 2005/Hancox 2006).

Figure 1. Results from searching for studies for inclusion in the review.



Included studies

The following summarises the characteristics of the four randomised controlled trials (RCTs) that met the review inclusion criteria (Harman 2008; Heatley 2005/Hancox 2006; Marchini 2007; Sauder 2005). Further details can be found in the 'Characteristics of included studies' table.

Types of participants

The four RCTs included a total of 256 eyes of 229 participants. The age range of all included participants was 21 to 87 years. All studies included people with bilateral cataracts with no pre-existing ocular pathologies. One study only included participants over 21 years of age (Harman 2008). Two studies only included participants between 40 and 80 years of age (Marchini 2007; Sauder 2005). One study only included participants with axial length of less than 25 mm (Harman 2008).

All studies excluded participants with other ocular co-morbidities such as amblyopia, corneal opacity, glaucoma, macular disease, diabetic retinopathy, myopic retinopathy, previous ocular trauma; and history of previous ocular surgery. One study excluded people with mature cataract or anterior segment pathology (pseudoexfoliation and zonular dialysis) (Harman 2008). One study excluded people with preoperative corneal astigmatism of more than 2 dioptres (D) in either eye (Harman 2008) and another excluded people with preoperative corneal astigmatism of more than 1.5 D in either eye (Heatley 2005/Hancox 2006). One study excluded people with refractive error in terms of spherical equivalent more than 5 D. (Marchini 2007).

Types of interventions

All four RCTs compared the 1CU accommodative IOL (HumanOptics) with a monofocal IOL. The types of the monofocal IOL used as controls varied between studies but not within individual studies. For all studies, the postoperative refractive aim was emmetropia. One study performed limbus-relaxing incisions on participants who had more than 1 D of corneal astigmatism at the time of surgery, aiming for postoperative astigmatism of less than 1 D (Harman 2008).

One trial was a paired-eye study, comparing 1CU accommodative IOL with the AcrySof MA30 monofocal IOL (Alcon) (Heatley 2005/Hancox 2006) in which one eye was randomised to receive the 1CU IOL and the other, by default, the MA30 IOL. One trial compared the 1CU accommodative IOL with the Array SA40N multifocal IOL (AMO) and the Clariflex monofocal IOL (AMO) (Harman 2008). One trial compared two different types of accommodative IOL with a monofocal IOL (Marchini 2007). The

accommodative IOLs used in this study were the 1CU IOL and AT-45 Crystalens IOL (Eyeonics Vision) and the monofocal IOL used was the ACR6D IOL. One trial compared the accommodative 1CU IOL with the AR40e Sensar IOL (Allergan) (Sauder 2005).

Types of outcome measures

All four RCTs reported data for some of the primary and secondary outcome measures, as well as adverse outcomes, listed above under Methods. No trial reported data for every outcome measure.

One study included glare, subjective masked assessment of posterior capsular opacity in the right eye, and data from a patient satisfaction questionnaire as secondary outcome measures (Harman 2008).

Harman 2008: All participants were examined at one day and two weeks after surgery for each eye, with a full assessment at three and 18 months after second-eye surgery. All examiners were masked at the three- and 18-month reviews. At one day, two weeks, and three months after surgery the following assessments were made: Slit-lamp microscopy of anterior and posterior segments including intraocular pressure measurements by Goldmann tonometry by an additional non-masked ophthalmologist. Measurements at three months and 18 months included subjective refraction, uncorrected and best-corrected binocular distance acuities, near binocular visual acuities, binocular contrast sensitivity, glare disability in the right eye, and binocular subjective amplitude of accommodation using the Royal Air Force rule and defocus spheres. Near visual acuity was determined binocularly, both unaided and best-corrected using the Bailey-Lovie logMAR reading acuity chart at 40 cm in photopic conditions. Measurements at 18 months after second-eye surgery included binocular near visual acuities with full distance correction, MNRead card assessment of reading speed at 40 cm, and subjective masked assessment of posterior capsular opacity in the right eye. Glare and spectacle independence were compared using a standardised questionnaire.

Heatley 2005/Hancox 2006: All participants were examined at one day, and at 1, 3, 6, and 12 months postoperatively. At every visit, each participant underwent a full ophthalmic examination, duochrome refraction, and assessment of distance and near vision. With best distance correction, all participants had Jaeger near vision at 40 cm, MNRead card assessment of reading speed at 40 cm, and subjective amplitude of accommodation using the Royal Air Force rule and defocus spheres.

In addition, participants were also examined at 18 to 24 months postoperatively, where the following measurements were made: subjective refraction, best-corrected distance visual acuity, and IOL shift to an accommodative stimulus following instillation of pilocarpine 4% using an ACMaster(Zeiss). With best-correction,

all participants had Jaeger near vision at 40 cm, MNRead card assessment of reading speed at 40 cm, subjective amplitude of accommodation using defocus spheres.

Marchini 2007: All participants were examined at 1, 6, and 12 months postoperatively. Visual parameters evaluated included: uncorrected far-distance visual acuity, best-corrected far-distance visual acuity (BCDVA), uncorrected near-distance visual acuity, best-corrected near-distance visual acuity, distance-corrected near visual acuity (DCNVA), and near-distance refractive addition (NDRA). Near-distance visual acuity was measured using a Jaeger chart at 40 cm. Pupil size was recorded during DCNVA in standard illumination. Accommodative amplitude was indirectly calculated by fogging where progressively increasing negative spheres (0.25 D) were added to the BCDVA, until four to five letters of the smallest line in the distance viewing were correctly identified. Anterior chamber depth was measured using a 50-MHz transducer probe (Ultrasound biomicroscopy 850, Carl Zeiss).

Sauder 2005: All participants were examined at one month and six months postoperatively. Examination included slit lamp biomicroscopy of the anterior and posterior segment of the eye, gonioscopy, applanation tonometry, keratometry, optical interferometry (IOL Master, Zeiss-Humphrey), and visual acuity measurements.

Accommodation was measured in the following ways: DCNVA at 30 cm using Niden and Jaeger charts, fogging (using distance-correction and determining distance visual acuity, minus lenses were added to the correction until 1 Snellen line in visual acuity

was lost), and defocus spheres. Change in anterior chamber depth was measured using optical interferometry (IOL Master, Zeiss-Humphrey) in medical mydriasis using tropicamide 0.5% eye drops and medical miosis using pilocarpine 2% eye drops.

Excluded studies

See 'Characteristics of excluded studies' table.

We excluded seven studies (Beiko 2013; Findl 2004; Kampeter 2005; Mesci 2010; Wang 2005; Wolffsohn 2006; Xu 2007) after further assessment. Although published as a randomised trial, we excluded Wolffsohn 2006 due to the sequential recruitment of their participants. Participants were first recruited for the intervention group, and the control group was then recruited. This trial was therefore classified as a controlled clinical trial (Lefebvre 2011). We excluded Kampeter 2005, Findl 2004 and Beiko 2013 as the follow-up period for each study was less than six months. We excluded Wang 2005 as the follow-up period was less than six months and the eyes were not randomised to treatments. We excluded Mesci 2010 because the eyes were not randomised to treatments, and Xu 2007 because it compared an accommodative IOL to a multifocal IOL.

Risk of bias in included studies

See 'Risk of bias' graph (Figure 2) and 'Risk of bias' summary table (Figure 3).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

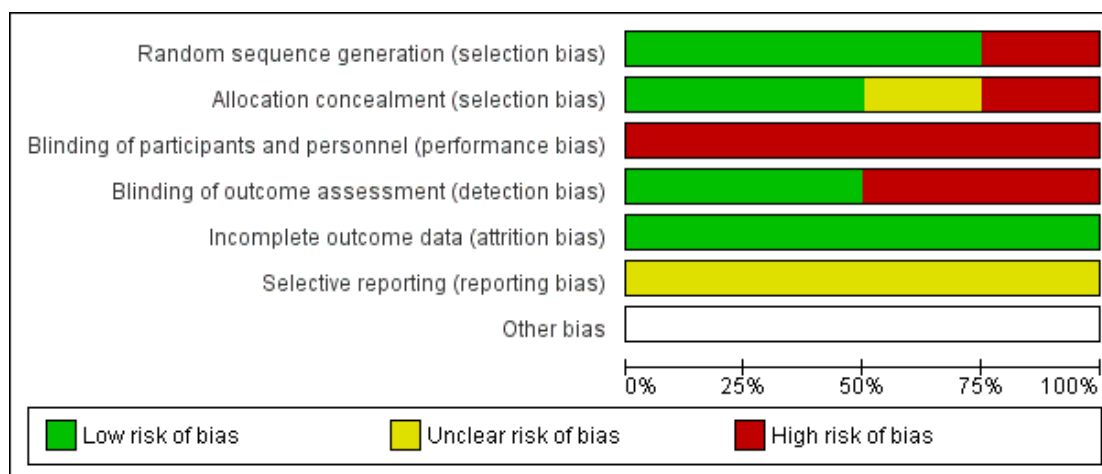


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Harman 2008	+	+	-	+	+	?	
Heatley 2005/Hancox 2006	+	+	-	-	+	?	
Marchini 2007	-	-	-	+	+	?	
Sauder 2005	+	?	-	-	+	?	

One trial ([Heatley 2005/Hancox 2006](#)) used a paired-eye comparison in which one eye was randomised to receive the accommodative IOL and the other eye to receive the monofocal control IOL. As outcome measures were assessed monocularly, eyes were assumed to be independent and thus not to have been influenced by accommodative stimulus to the other eye. We also had no reason to believe that surgery on one eye could influence the outcome of surgery on the other eye.

The other trials randomised people to treatment. This presented a potential problem with regards to the two-eye question. Three trials ([Harman 2008](#); [Marchini 2007](#); [Sauder 2005](#)) were paired-eye studies, where both eyes received either the accommodative or monofocal IOL. Two trials measured outcomes binocularly ([Harman 2008](#); [Sauder 2005](#)). In the [Harman 2008](#) trial, best corrected visual acuities were measured monocularly. For the purposes of our review, we analysed results for the right eye. Another study assumed that independence in both eyes and thus measurements were performed monocularly and considered separately in the analysis ([Marchini 2007](#)). This may represent a source of bias, despite the authors mentioning an assessment of coupled data which showed an even and random distribution. No trials specifically checked for statistical correlation between contralateral eyes.

Allocation

Three trials reported adequate methods of random sequence generation ([Harman 2008](#); [Heatley 2005/Hancox 2006](#); [Sauder 2005](#)). We contacted study investigators for unclear or missing information. Two studies reported adequate methods of allocation concealment ([Harman 2008](#); [Heatley 2005/Hancox 2006](#)). We graded one study at high risk of selection bias. This is due to the consecutive nature of the assignment process ([Marchini 2007](#)). We graded one study as unclear on allocation concealment ([Sauder 2005](#)).

Blinding

As intraocular lenses were inherently different and surgeons knew which intervention they provided for the participants at the time of surgery, masking of providers was not possible and was thus deemed not to have been done in all studies. All studies were therefore graded as having a high risk of performance bias.

In one study, participants were masked as to the nature of the IOL inserted until the three-month postoperative review ([Harman 2008](#)). In addition, all examiners were masked at all postoperative reviews. We thus graded this study as having a low risk of detection bias. All examiners were also masked in another study, which we also graded as having a low risk of detection bias ([Marchini 2007](#)). As masking of outcome assessors to the allocated intervention was not done in two studies, we graded these as having a high risk of detection bias ([Heatley 2005/Hancox 2006](#); [Sauder 2005](#)).

Incomplete outcome data

This was assessed as low risk of bias in all studies. Losses to follow-up were lower at six months compared to after 12 months follow-up (see [Characteristics of included studies](#) table). Losses to follow-up were reported and were equal in all groups for each study. However, an explanation was not always given as to why participants were lost to follow-up ([Heatley 2005/Hancox 2006](#); [Marchini 2007](#); [Sauder 2005](#)).

Selective reporting

All four RCTs reported data for some of the prespecified primary and secondary outcome measures for this review. No trial reported data for every outcome measure and hence not all the trials could be included in each of the outcome analyses. None of the trials provided information on whether the reported methods used in the analysis of outcomes were prespecified or not, and we therefore graded all studies as unclear for selective reporting.

Other potential sources of bias

We did not identify any other potential threats to validity for the included studies.

Effects of interventions

See: [Summary of findings for the main comparison](#)

Participants were randomised to the comparative interventions in four trials. One trial ([Heatley 2005/Hancox 2006](#)) used a paired-eye comparison in which one eye was randomised to receive the accommodative IOL and the other eye to receive the monofocal control IOL. All trials used the 1CU accommodative lens. One trial ([Marchini 2007](#)) had an additional accommodative lens arm with the AT-45 IOL.

1CU accommodative lenses compared to monofocal lenses

Primary outcome

Amplitude of accommodation

People in the accommodative IOL group had a greater amplitude of accommodation at six months. In [Heatley 2005/Hancox 2006](#), for near point of accommodation, there was a mean difference (MD) of 1.43 dioptres (D); 95% confidence interval (CI) 0.79 to 2.07; 30 people, 60 eyes all pair-matched. Two studies reported the results using defocus curves ([Heatley 2005/Hancox](#)

2006; Sauder 2005). There was a pooled mean difference of 0.47 D in favour of accommodative lenses; 95% CI 0.36 to 0.59; 106 people, 136 eyes including 60 eyes pair-matched. (Analysis 1.1) People receiving an accommodative IOL had a better distance-corrected near visual acuity (DCNVA) at six months. Pooled analysis of Heatley 2005/Hancox 2006 and Sauder 2005 showed a mean difference of -3.10 Jaeger units in favour of accommodative IOLs; 95% CI -3.36 to -2.83; 106 people, 136 eyes including 60 eyes pair-matched. (Analysis 1.2)

People in the accommodative IOL group had a greater amplitude of accommodation at 12 months (Harman 2008; Heatley 2005/Hancox 2006; Marchini 2007) with a pooled mean difference of 0.22 D; 95% CI 0.00 to 0.43; 111 people, 131 eyes including 40 eyes pair-matched. Two of these studies provided data at 18 months (Harman 2008; Heatley 2005/Hancox 2006). (Analysis 1.3). Harman 2008 also reported the near point of accommodation (MD 0.46 D; 95% CI -0.33 to 1.25).

People receiving an accommodative IOL had a better DCNVA at 12 months as measured by a Jaeger chart but there was substantial heterogeneity in effect ($I^2 = 96\%$). Heatley 2005/Hancox 2006 found a mean difference of 1.33 Jaeger units (95% CI 0.98 to 1.68) in favour of the accommodative lens (20 people, 40 eyes pair-matched). Marchini 2007 found a mean difference of 6.00 Jaeger units (95% CI 4.15 to 7.85) in favour of the accommodative lens (51 people, 51 eyes). (Analysis 1.4). Harman 2008 reported near visual acuity in logMAR units (MD 0.12 logMAR units; 95% CI 0.05 to 0.19, 40 people, binocular) in favour of accommodative lens.

Secondary outcomes

Corrected distance visual acuity

At six months, data from two trials (Heatley 2005/Hancox 2006; Sauder 2005) suggested that there was similar corrected distance visual acuity (CDVA) in the two groups (standardised mean difference -0.04; 95% CI -0.37 to 0.30, 106 people, 136 eyes including 60 eyes pair-matched (Analysis 1.5)

At 12 months, data from three trials (Harman 2008; Heatley 2005/Hancox 2006; Marchini 2007) showed better CDVA in the monofocal group but there was substantial heterogeneity in effect ($I^2 = 90\%$). Two trials (Harman 2008; Heatley 2005/Hancox 2006) reported fairly similar effects with a pooled mean difference of 0.12 LogMAR; 95% CI 0.07 to 0.16, 70 people, 100 eyes including 60 eyes pair-matched. Marchini 2007 reported no difference between the two groups; mean difference -0.02 logMAR units (95% CI -0.06, 0.02, 51 people, 51 eyes). (Analysis 1.6)

Reading speed

One trial (Harman 2008) reported data for this outcome at 12 months. The effect of the lens on reading speed was uncertain

with wide confidence intervals (mean difference 11.60 words per minute in favour of accommodative lenses, 95% CI -12.15 to 35.35, 40 people). However, when we looked at critical print size (i.e. the smallest print size at which participants can read with their maximum reading speed) the accommodative IOL group performed significantly better than the monofocal IOL group (mean difference 0.12, 95% CI 0.05 to 0.19, 40 people).

Contrast sensitivity

One trial (Harman 2008) reported data for this outcome. In this study, the effect of the lens on contrast sensitivity was uncertain (mean difference -0.10 Pelli-Robson units, 95% CI -1.52 to 1.32, 40 people).

Change in anterior chamber depth on accommodation

One trial (Sauder 2005) reported this outcome at six months. There was a greater reduction in anterior chamber depth on accommodation in the accommodative IOL group (mean difference 0.42 mm, 95% CI 0.28 to 0.56, 76 people, 76 eyes).

At 12 months, data from two trials (Heatley 2005/Hancox 2006; Marchini 2007) showed a greater reduction in mean anterior chamber depth on accommodation in the 1CU accommodative IOL group (mean difference 0.21 mm, 95% CI 0.14 to 0.28, 71 people, 91 eyes (40 eyes pair-matched). (Analysis 1.7).

Spectacle independence

One trial (Harman 2008) reported data for this outcome. At 18 months, 4/21 people in the accommodative group reported that they "did not require glasses for any reading tasks" compared to 0/19 people in the monofocal group. This gives a large risk ratio (8.18) but the small numbers and very wide confidence intervals (95% CI 0.47 to 142.62) mean that the true effect is uncertain. It is worth noting that the participants in this study were unmasked to their lens type by this stage of the study.

Reported complications

Posterior capsule opacification

Three studies reported postoperative PCO and numbers of capsulotomies.

In Heatley 2005/Hancox 2006, there was a decrease in CDVA with the 1CU accommodative IOL group between six and 12 months ($P = 0.019$). This was attributed to PCO by the authors but no data were presented to support this view. The authors reported a trend towards more anterior displacement of IOLs in the post-neodymium:YAG capsulotomy group compared to those who had not received neodymium:YAG capsulotomies, although

this was not statistically significant. [Harman 2008](#) reported a 20% risk of moderate/severe PCO in the accommodative IOL group compared to a 5% risk in the monofocal group (data estimated from a graph). [Marchini 2007](#) reported one case of PCO at 12 months in the 1CU accommodative lens group, no cases in the AT-45 accommodative lens group and one case in the monofocal lens group. The pooled effect was Peto OR 2.12; 95% CI 0.45 to 10.02, 91 people, indicating that although more cases of PCO were seen in the accommodative lens group the relative effect of the lenses on PCO is uncertain ([Analysis 1.8](#)).

Laser capsules

In [Heatley 2005/Hancox 2006](#) 10/20 (50%) of the eyes in the accommodative IOL group required neodymium:YAG capsulotomy by 12 months compared to 0/20 (0%) in the monofocal IOL group. In [Harman 2008](#) two participants in the accommodative IOL group had bilateral and one had unilateral neodymium:YAG capsulotomies by 18 months. One participant had bilateral capsulotomies in the monofocal IOL group. The pooled relative effect was Peto OR 7.96; 95% CI 2.49 to 25.45, 60 people, 80 eyes including 20 eyes pair-matched) ([Analysis 1.9](#)).

Glare

Glare was reported in only one study ([Harman 2008](#)). In this study, 28.6% of the 1CU accommodative IOL group and 36.8% of the monofocal IOL group experienced glare (RR 0.78; 95% CI 0.32 to 1.90, 40 people). In the 1CU group 4.8% experienced moderate to severe glare at 18 months compared to 9.8% of the monofocal group (RR 0.45; 95% CI 0.04 to 4.60, 40 people).

Peri-operative complications

One study ([Sauder 2005](#)) reported intraoperative anterior chamber haemorrhage originating from the anterior chamber angle in one participant from their 1CU accommodative IOL group. No other studies reported any other peri-operative complications.

1CU accommodative IOL versus AT-45 accommodative IOL

As mentioned, one trial ([Marchini 2007](#)) was a three-arm study comparing two accommodative IOLs, namely 1CU IOL and the AT-45 IOL, with a monofocal IOL. For outcomes that included this study, we have made direct comparisons between these two accommodative IOL groups ([Table 1](#))

After 12 months post-treatment, the 1CU IOL group achieved higher amplitude of accommodation and better DCNVA compared to the AT-45 IOL group. However, there was no significant difference between CDVA and reduction in anterior chamber depth on accommodation between the two IOL groups.

DISCUSSION

Summary of main results

(see '[Effects of interventions](#)' and '[Summary of findings for the main comparison](#)')

We included four randomised controlled trials conducted in Germany, Italy and the UK. The age range of participants was 21 to 87 years. All studies included people with bilateral cataracts with no pre-existing ocular pathologies. We judged all studies to be at high risk of performance bias. We graded two studies with high risk of detection bias and one study with high risk of selection bias.

Participants who received the accommodative IOLs achieved better distance-corrected near visual acuity (DCNVA) at six months. Better DCNVA was seen in the accommodative lens group at 12 to 18 months in the three trials that reported this time point but with considerable heterogeneity of effect ranging from 1.3 to 6 Jaeger units and 0.12 logMAR improvement (low-quality evidence). The relative effect of the lenses on corrected distant visual acuity (CDVA) was less certain. At 12 months there was heterogeneity of effect with two studies reporting at 18 months finding better CDVA in the monofocal group and one study finding similar CDVA in the two groups.

The relative effect of the lenses on reading speed and spectacle independence was uncertain. The average reading speed was higher in the accommodative lens group but we could not exclude the possibility that average reading speed was higher in the monofocal group. People with accommodative lenses were more likely to be spectacle-independent but again the estimate was very uncertain. We found more cases of posterior capsule opacification (PCO) in accommodative lenses but with small numbers the results were uncertain with regards to benefit or harm. People in the accommodative lens group were more likely to require laser capsulotomy. Glare was reported less frequently with accommodative lenses, but with wide confidence intervals, the effect of accommodative lenses on glare was uncertain.

Overall completeness and applicability of evidence

The evidence for accommodative lenses in comparison with monofocal lenses cannot be considered complete. We identified only four RCTs with a total of 229 participants (256 eyes). All these trials were conducted in Europe; their results may not apply in different settings and parts of the world. No trial reported data for every outcome measure and hence not all the trials could be included in each of the outcome analyses.

All the trials used 1CU accommodative lenses. The extent to which the findings of this review apply to other types of accommodative lenses is unclear.

The applicability of the evidence and choice of lens will depend on patient preference. This review found that people with accommodative lenses achieved better near vision but there were possible

adverse effects including the possibility of worse corrected distant visual acuity and an increased risk of posterior capsule opacification. Currently there is not enough evidence on patient-relevant outcomes such as reading speed and spectacle independence to make confident judgements on applicability.

Quality of the evidence

The quality of the evidence is summarised in [Summary of findings for the main comparison](#). We downgraded all outcomes because of the risk of bias in the included trials (Figure 2).

The quality of the evidence for most outcomes was low, which means that “further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate”. The exception to this was *DCNVA at six months* for which we judged there to be moderate-quality evidence of an effect. The results for *DCNVA at 12 months or more* and *corrected distant visual acuity at 12 months or more* were additionally downgraded for inconsistency, as we found different results in different studies. We downgraded *corrected distant visual acuity at six months*, *reading speed*, and *reported complications* because the effect estimates were imprecise. We considered the evidence for *spectacle independence* to be very low quality (i.e. we are very uncertain about the estimate) because only one small trial contributed data on this outcome, the trial was unmasked at that stage, and the measurement of the outcome was self-reported and rather unclear.

Potential biases in the review process

The mixture of study designs (unilateral versus bilateral intervention) posed a problem with data synthesis. One trial ([Heatley 2005/Hancox 2006](#)) was included in the review which used a paired-eye comparison, where one eye was randomised to an individual treatment and the other eye received the alternative treatment by default. Similarly, we also included two studies where both eyes were randomised to receive the same intervention ([Harman 2008](#); [Sauder 2005](#)). In one study ([Marchini 2007](#)), most participants received the same intervention to both eyes but some participants only received an intervention to one eye. It must be noted that accommodation reflexes are bilateral and may be influenced by monocular implantation. However, if we had analysed the various paired and unpaired data separately, there would have only been two trials with paired data, one trial with unpaired data, two with data on both eyes, and one with some paired and some unpaired data. Given that not all trials reported on all outcomes and at all time points, it would not otherwise have been possible to combine the studies into an analysis in a meaningful way. As we assessed outcome measures monocularly, measurements should not have been influenced by accommodative stimulus to the other eye. We also assumed that surgery on one eye would not influence the outcome of the surgery on the other eye, and we therefore did

not consider carry-over and period effects to be a problem. The largest prospective non-randomised study that was conducted, investigating the advantages, clinical outcomes, and safety after implantation of the 1CU accommodative IOL in comparison with a conventional monofocal IOL (MCTE, Dr Schmidt), examined this point ([Uthoff 2007](#)). They analysed a subgroup of 90 participants with bilateral 1CU IOL to determine whether there was any additional benefit and found that there were no significant discrepancies between participants implanted in one or both eyes with respect to their accommodative responses.

Agreements and disagreements with other studies or reviews

Our electronic search revealed no meta-analysis of randomised controlled trials comparing accommodative IOL implants with monofocal IOL implants.

The results of this systematic review are in agreement with previous investigations.

Küchle and colleagues ([Küchle 2004](#)) performed one of the earliest studies investigating the properties of accommodative IOLs. In their study, however, they observed a higher accommodative range of approximately 1.55 dioptres (D), a similar increase of anterior chamber depth after cyclopentolate eyedrops of 0.42 mm, and better DCNVA in the 1CU accommodative IOL group relative to the control group. All differences between intervention and control groups in their study were statistically significant ($P < 0.001$). Findl and colleagues published results of a randomised controlled trial, comparing the axial movement of the 1CU accommodative IOL with a monofocal acrylic IOL ([Findl 2004](#)). They assessed anterior chamber depth objectively using partial coherence interferometry, measured before and after topical application of pilocarpine 2%. Near visual acuity was also measured three months after surgery. They found that the accommodative IOL showed a forward movement under pilocarpine with a median amplitude of movement of -314 microns (95% CI -148 to 592), compared with the backward movement of 63 microns (95% CI 161 to -41) for the monofocal IOL. This study did not show a significant difference in distance-corrected near visual acuities between their accommodative group and monofocal group. However, as mentioned by the authors, the number of eyes in each group was too small to achieve sufficient statistical power for this conclusion.

A systematic review of peer-reviewed data of three accommodative IOLs (1CU IOL, AT-45 IOL and BioComFold IOL) was published in 2007 ([Findl 2007](#)). The authors found moderate to no improvement in near visual acuity compared with control IOLs and a statistically significant but small and inter-participant variable anterior shift of the IOL optic after pilocarpine stimulation. This review included both randomised as well as non-randomised studies that were not eligible for inclusion in the current review. Another literature review of accommodative IOLs stated that results from passive-shift accommodative intraocular lenses had

been contradictory (Menapace 2007). The authors concluded that whilst uncorrected reading vision results were initially reported to be favourable with the 1CU accommodative IOL, and excellent with the AT-45 accommodative IOL, distance-corrected near vision did not exceed that encountered with standard monofocal lenses in later studies. The authors of this review concluded that passive-shift accommodative IOL generally fail as capsular fibrosis, which essentially develops during the first three months, stretches and thus immobilises the capsule-IOL diaphragm, preventing adequate anterior optic movement. This was consistent with findings of this review, where a significant difference in both near point of accommodation and amplitude of accommodation using defocus curve in favour of accommodative IOL group at six months post-treatment was not maintained after 12 months. In the included studies of this review, there was also a higher rate of PCO reported in the accommodative IOL groups.

We excluded the largest study that has been conducted investigating the advantages, clinical outcomes, and safety after implantation of the 1CU accommodative IOL (HumanOptics AG) in comparison with a conventional monofocal IOL (Uthoff 2007), as the participants were not randomised to individual treatments. This study compared the results of 553 eyes implanted with the 1CU IOL with 219 eyes in a control group implanted with a monofocal posterior chamber IOL (MCTE, Dr Schmidt). Follow-up was performed at 1, 6, and 12 months postoperatively. The clinical effect for near visual acuity was evaluated by subjective measurements using an accommodometer, defocusing curve, and Niden reading charts. Average DCNVA was better in the 1CU group compared to the control group at 12 months post-treatment ($P < 0.01$). They also found that participants who received 1CU IOLs showed 2.7% excellent DCNVA (Niden 1 - 3), which was not observed in those who received monofocal IOLs. A statistically greater accommodative response of 11 cm ($P < 0.01$) was obtained with the accommodometer at 12 months when comparing the two groups. As with our systematic review, no significant differences were noted in CDVA between the groups. This study also reported post-operative complications not reported in the studies included in our systematic review. Decentration and tilting of the 1CU IOL resulted in explantation of three IOLs. Clinically significant macular oedema was not seen in the control group, whereas a single case was observed in the 1CU group. Posterior capsular opacification resulted in neodymium:YAG capsulotomies in 7.3% of participants in the 1CU group and 5.5% of participants in the monofocal IOL group within one year.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review suggests that implantation of accommodative intraocular lenses (IOLs) in cataract surgery is associated with

small gains in near visual acuity (approximately one Snellen line) as well as gains in some measures of accommodative function (moderate quality of evidence). Size of accommodative function appears to reduce with time. Due to low quality of evidence, the relative effect of accommodative lenses on functional outcomes, such as reading speed and spectacle independence, is uncertain.

There is some evidence that distance visual acuity with accommodative lenses may be worse after 12 months, but currently the evidence for this is not clear-cut. This may be associated with more posterior capsular opacification (PCO) in people receiving accommodative lenses (low quality of evidence). However, the effect of the accommodative lenses on PCO is uncertain.

There was a statistically significant reduction in anterior chamber depth on accommodation in participants who received accommodative IOLs compared to those who received monofocal IOLs at six and after 12 months post-treatment. These reductions of anterior chamber depth on accommodation, typically accounted for by an anterior displacement of IOLs, suggest some validity in the focus shift hypothesis for accommodative IOLs. But the clinical relevance of small changes in anterior chamber depth on accommodative effect observed after 12 months is questionable (mean difference 0.21 mm). Earlier modelling suggests that a forward shift in lens position of approximately 10 times this magnitude (2 mm) would be required to produce 3 dioptres of true pseudophakic accommodation.

Heterogeneity of outcome measures and study designs used, plus the dominance of one design of accommodative lens in existing trials (the HumanOptics 1CU) suggest that the results of our analysis should be interpreted with caution, and may not be applicable to other accommodative IOL designs.

Implications for research

Further trials are required for a definitive evaluation of accommodative IOLs. The mechanisms of any effect through which accommodative IOLs improve near visual function is still poorly understood and, as discussed, may be multifactorial. Further research is required to improve the understanding of such accommodative IOLs. It would also be useful to have more long-term outcome data to monitor sustainability of accommodative and near visual functional capacity of accommodative IOLs. This would also allow detection of any late complications or adverse events. Studies are required that include functionally relevant outcome measures such as unaided reading speed, spectacle dependence and measures of dysphotopsia, to compare accommodative IOLs to multifocal IOLs and monovision strategies for the correction of pseudophakic presbyopia.

A standard framework of outcome measures would facilitate future analyses of combined data.

Future trials should follow CONSORT guidelines (CONSORT 2012) to ensure that reporting of randomised controlled trials is

complete. Variable increase in accommodative function observed in people who received accommodative IOLs suggests the need for improvements in IOL design. Trials comparing accommodative IOLs other than the HumanOptics 1CU with monofocal and multifocal controls are required, to determine the best performing IOL for use in cataract surgery and refractive lens exchange.

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The views expressed in this publication are those of the authors and not necessarily those of the Department of Health.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Harman 2008

Methods	Single-centre, 2 surgeons, prospective randomised, masked trial Duration of study: 18 months
Participants	Setting: Eye Unit, Hillingdon Hospital National Health Service Trust, Uxbridge, United Kingdom Numbers randomised: 90 participants; 30 in each group; 82 participants completed follow-up at 3 months; 64 participants completed follow-up at 18 months Age: Accommodative IOL group (Mean 71.50 ± 10.37 years); Multifocal IOL group (Mean 73.47 ± 10.36 years); Monofocal IOL group (Mean 70.77 ± 11.79 years) Gender: Accommodative IOL group (13 men:17 women); Multifocal IOL group (15 men:15 women); Monofocal IOL group (12 men:18 women) Inclusion criteria: Age over 21 years, bilateral visually significant cataract, and axial length < 25 mm. Axial length limit imposed as the same amount of anterior movement will generate less accommodation in lower-power IOLs than in higher power IOLs Exclusion criteria: Mature cataract, anterior segment pathology such as pseudoexfoliation or zonular dialysis, previous ocular surgery, any ocular pathology that might limit the postoperative VA to < 6/9 (e.g. amblyopia, corneal opacity, macular disease), and preoperative corneal astigmatism of > 2 dioptres (D) in either eye
Interventions	Participants were randomly allocated to 1 of the 3 types of lenses by sealed envelopes opened on the day of surgery, namely, 1CU accommodative IOL (HumanOptics), Array SA40N multifocal IOL (AMO), and Clariflex monofocal IOL (AMO). They received the same IOL in each eye, and the second eye was operated on within 6 weeks of the first Once the allocated IOL type was known, the surgeon calculated the required IOL power using the average of the SRK/T, Hoffer Q and Holladay formulae. The IOL power resulting in predicted postoperative refraction closest to emmetropia was chosen Participants who had > 1 D of corneal astigmatism also underwent limbus-relaxing incisions, using the modified Gills nonogram, at the time of surgery, aiming for postoperative astigmatism of < 1 D
Outcomes	All participants were examined at 1 day and 2 weeks after surgery for each eye, with a full assessment at 3 and 18 months after second-eye surgery. All examiners were masked at the 3- and 18-month reviews At 1 day, 2 weeks and 3 months after surgery: Slit-lamp microscopy of anterior and posterior segments, intraocular pressure measurements by Goldmann tonometry by an additional nonmasked ophthalmologist Measurements at 3 months and 18 months: Subjective refraction, uncorrected and best-corrected binocular distance acuities, near binocular visual acuities (VA), binocular contrast sensitivity, glare disability in the right eye, and binocular subjective amplitude of accommodation using the Royal Air Force rule and defocus spheres. Near VA was determined binocularly, both unaided and best corrected using the Bailey-Lovie logMAR reading acuity chart at 40 cm in photopic conditions Measurements at 18 months after second eye surgery: Binocular near VA with full distance correction, MNRead card assessment of reading speed at 40 cm, subjective masked

	assessment of posterior capsular opacity in the right eye Glare and spectacle independence were compared using a standardised questionnaire	
Notes	Only data from the 1CU accommodative IOL group and the Clariflex monofocal IOL group were used for the systematic review 10 participants had limbus-relaxing incisions at the time of surgery: 5 from the 1CU group, 3 from the multifocal IOL group and 2 from the monofocal IOL group Funding: Financial support from Hillingdon Hospital Research and Development Fund, Uxbridge, United Kingdom Conflict of interest: None declared	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly allocated to 1 of the 3 types of lenses by sealed envelopes opened on the day of surgery" Comment: Probably done
Allocation concealment (selection bias)	Low risk	Investigators used sealed envelopes as the randomisation method. These were opened immediately prior to surgery so there was no selection bias involved Comment: Probably done
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Patients were masked as to the nature of the IOL inserted until the 3-month review, and all were asked to practice reading every day without spectacle correction until this time." Comment: Probably done However, both intraocular lenses are inherently different and surgeons would know which intervention they are providing for participants at the time of surgery
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All examiners were masked at the 3- and 18- month reviews." Comment: Probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	90 participants recruited 8 were lost to follow-up at 3 months; withdrawals were all before second-eye surgery (development of subretinal neovascular membranes n = 2, cystoid macular oedema n = 2, corneal decompensation secondary to undiagnosed Fuchs' endothelial dystrophy n = 1, severe local allergic reac-

		<p>tion to preoperative tropicamide drops n = 1, IOL selection error n = 1, anterior capsule tear at time of surgery n = 1); 2 withdrew from 1CU group and 3 from each of the other groups</p> <p>Further 18 participants were lost to follow-up at 18 months, with 21 participants remaining in the 1CU group, 24 in the multifocal group, and 19 in the monofocal group. No explanation was given as to why participants were lost to follow-up at 18 months</p>
Selective reporting (reporting bias)	Unclear risk	No information on whether reported methods used were prespecified

Heatley 2005/Hancox 2006

Methods	<p>Single-centre, single surgeon, prospective randomised trial, paired-eye study (one eye had been randomised to one intervention and the second eye had by default gone on to receive the other intervention)</p> <p>Duration of study: 12 - 24 months</p>
Participants	<p>Setting: Ophthalmology Department, St Thomas' Hospital, London, United Kingdom</p> <p>Heatley 2005: Numbers randomised: 30 participants (60 eyes) Age: range 29 - 87 years (mean 73 years) Gender: 13 (43.3%) were men Inclusion criteria: bilateral cataracts, < 1.5 D of corneal astigmatism, no concurrent ocular pathology Exclusion criteria: not stated</p> <p>Hancox 2006: Numbers randomised: 30 participants (60 eyes), 20 participants (40 eyes) had complete study data Age: range 31 - 89 years (mean 71 years) Gender: not reported Inclusion criteria: uncomplicated bilateral cataracts, normal eyes, uneventful surgery Exclusion criteria: not stated</p>
Interventions	<p>One eye randomised to either 1CU accommodating IOL (HumanOptics) or AcrySof MA30 IOL (Alcon); the second eye by default went on to receive the other intervention within 4 to 6 weeks</p> <p>Emmetropia was the target refraction in all eyes</p> <p>IOL power calculation was performed using the IOLMaster (Zeiss)</p>
Outcomes	<p>Heatley 2005: All participants were examined at 1 day, and at 1, 3, 6, and 12 months postoperatively At the 1-, 3-, 6-, and 12-month visits, each participant underwent a full ophthalmic examination, duochrome refraction, and assessment of distance and near vision</p>

	<p>With best distance correction, all participants had Jaeger near vision at 40 cm, MNRead card assessment of reading speed at 40 cm, and subjective amplitude of accommodation using the Royal Air Force rule and defocus spheres</p> <p>Hancox 2006: Participants were examined at 18 - 24 months postoperatively All participants had refraction, best corrected distance visual acuity With best distance correction, all participants had Jaeger near vision at 40 cm, MNRead card assessment of reading speed at 40 cm, near point, and defocus spheres IOL shift to an accommodative stimulus following instillation of pilocarpine 4% was measured with an ACMaster (Zeiss)</p>	
Notes	<p>Funding: Information not available Conflict of interest: None declared</p>	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "30 patients who had bilateral cataract surgery with 1CU IOL prospectively randomly allocated to 1 eye and an AcrySof MA30 monofocal IOL to the other were examined." First eyes were allocated to each group by random sequence generation on a computer Comment: Probably done</p>
Allocation concealment (selection bias)	Low risk	<p>The investigator allocated the participants as per the random sequence and was unaware of the sequence prior to allocating treatment groups Comment: Probably done</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Not mentioned but presumably not done Both intraocular lenses are inherently different and surgeon would know which intervention they are providing for participants at the time of surgery</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Not mentioned but presumably not done</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Heatley 2005: All subjects achieved 6 months' follow-up, and 20 have achieved 12 months' follow-up. No explanation was given as to why participants were lost to follow-up at 12 months</p>

		Hancox 2006: Of the 30 participants originally recruited, 20 had complete study data 3 were lost to follow-up (no reasons stated), 2 were too frail to comply with tests, and 1 had a tremor making measurement impossible; in 2 participants, it was not possible to get an ACMaster reading in 1 eye and in another 2 participants, Tracey wavefront readings were unreliable due to errors induced by reflexes from the IOL
Selective reporting (reporting bias)	Unclear risk	No information on whether reported methods used were prespecified

Marchini 2007

Methods	Two-centre, 2 surgeons, prospective randomised, masked trial Duration of study: 12 months
Participants	Setting: Ophthalmology Institute, University of Verona, Verona, Italy and Ophthalmology Institute, University of Parma, Parma, Italy Numbers randomised: 59 participants (80 eyes); 19 participants (30 eyes) Group A, 19 participants (29 eyes) Group B, 21 participants (21 eyes) Group C Age: Mean 66 ± 10 years Gender: 31 (52.5%) were men Inclusion criteria: Subjects aged 40 - 80 years, no pre-existing ocular pathology, any type of cataract considered as the sole cause of a visual decrease of $\leq 20/40$ Exclusion criteria: refractive defect in terms of spherical equivalent > 5 D; glaucoma, diabetic or myopic retinopathy; age-related macular degeneration, either historical or detected preoperative; any previous ocular surgery, including cataract in the other eye
Interventions	Participants were randomly allocated to 2 different types of accommodative IOLs or the monofocal IOL, for the first operated eye. Group A received the accommodative 1CU (HumanOptics), group B received the accommodative AT-45 Crystalens (Eyeonics Vision), and group C received the ACR6D monofocal IOL. They received the same IOL in each eye The IOL power calculation was performed using the SRK/T formula
Outcomes	All participants were examined at 1, 6, and 12 months postoperatively Visual parameters evaluated included: uncorrected far-distance visual acuity; best corrected far-distance visual acuity (BCDVA); uncorrected near-distance visual acuity; best-corrected near-distance visual acuity; distance-corrected near visual acuity (DCNVA); and near-distance refractive addition (NDRA). Near-distance visual acuity was measured using a Jaeger chart at 40 cm. Pupil size was recorded during DCNVA in standard illumination Accommodative amplitude was indirectly calculated by fogging; progressively increasing negative spheres (0.25 D) were added to the BCDVA, until 4 - 5 letters of the smallest

	line in the distance viewing were correctly identified Anterior chamber depth was measured using a 50-MHz transducer probe (Ultrasound biomicroscopy 850, Carl Zeiss)	
Notes	Funding: Information not available Conflict of interest: None declared	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients were randomly allocated to 2 different types of accommodating IOLs or the monofocal IOL, for the first operated eye. Group A received the accommodative 1CU (HumanOptics), group B received the accommodative AT-45 Crystalens (Eyeonics Vision), and group C received the ACR6D monofocal IOL." Comment: Although it was stated that participants were randomly assigned to the 3 treatment groups for the first operated eye, it appeared that participants were actually assigned consecutively to each group, according to the sequence A-B-C in 1 centre and B-A-C in the other centre. Also, it appeared that some participants in Groups A and B then went on to have the same IOL type implanted in the fellow eye, whereas participants in Group C did not
Allocation concealment (selection bias)	High risk	Quote: "Patients were assigned consecutively to each group, according to the sequence A-B-C in 1 centre (Parma) and B-A-C in the other (Verona)." Comment: Due to the consecutive nature of the assignment process, this study is likely to be of high risk in terms of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned but presumably not done Both intraocular lenses are inherently different and surgeon would know which intervention they are providing for participants at the time of surgery In addition, participants were aware that, in case of accommodative implant, no additional lenses for near vision would be prescribed postoperatively for the duration of

Marchini 2007 (Continued)

		the study (1 year)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All visual evaluations and ultrasound biomicroscopy measurements were performed by blinded clinical staff" Comment: Probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "In groups A and C, all the patients completed the 12-month follow-up; in group B, 1 patient (1 eye) was lost to follow-up after 6 months." No explanation was given as to why the participant was lost to follow-up at 6 months
Selective reporting (reporting bias)	Unclear risk	No information on whether reported methods used were prespecified

Sauder 2005

Methods	Single-centre, single surgeon, prospective randomised trial Duration of study: 8 months
Participants	Setting: Germany, setting not reported Numbers randomised: 80 consecutive patients; 40 participants study group, 40 participants control group Age: Study group (Range 62 - 82 years; Mean 73.29 ± 5.89 years); Control group (Range 59 - 80 years; Mean 72.66 ± 4.78 years) Gender: Not reported Inclusion criteria: Subjectes aged 40 - 80 years; advanced cataract for routine cataract surgery Exclusion criteria: Diabetes mellitus, glaucoma, exudative age-related macular degeneration, non-exudative age-related macular degeneration with large soft drusen, history of ocular trauma, previous ocular surgery
Interventions	Study population was randomised into a study group receiving either the accommodative 1CU IOL (HumanOptics) in both eyes or a control group receiving the monofocal AR 40e Sensar IOL (Allergan) in both eyes
Outcomes	All participants were examined at 1 month and 6 months postoperatively Examination included slit lamp biomicroscopy of the anterior and posterior segment of the eye, gonioscopy, applanation tonometry, keratometry, optical interferometry (IOL Master, Zeiss-Humphrey), and visual acuity measurements Accommodation was measured in following ways: Distance-corrected near visual acuity at 30 cm using Niden and Jaeger charts, fogging (using distance-correction and determining distance visual acuity, minus lenses were added to the correction until one Snellen line in visual acuity was lost), and defocus spheres Change in anterior chamber depth was measured using optical interferometry (IOL Master, Zeiss-Humphrey) in medical mydriasis using tropicamide 0.5% eye drops and

	medical miosis using pilocarpine 2% eye drops	
Notes	Funding: Information not available Conflict of interest: None declared	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The total study population was randomised into a study group consisting of 40 patients undergoing standard cataract surgery with implantation of the new foldable monofocal intraocular lens with flexible haptics (IOL 1CU; HumanOptics) in both eyes, and a control group consisting of 40 patients who underwent standard cataract surgery with implantation of a conventional foldable monofocal intraocular lens (IOL AR 40e Sensor; Allergan) in both eyes." Comment: Probably done.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Authors mentioned that this was a non-masked clinical interventional study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned but presumably not done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "At the visit 6 months after surgery, one patient in each group was lost to follow-up". No explanation was given as to why participants were lost to follow-up at 6 months
Selective reporting (reporting bias)	Unclear risk	No information on whether reported methods used were prespecified

Two studies ([Heatley 2005](#)/[Hancox 2006](#)) reported different outcome measures from the same trial.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Beiko 2013	Follow-up period of less than 6 months
Findl 2004	Follow-up period of less than 6 months
Kamppeter 2005	Follow-up period of less than 6 months
Mesci 2010	No randomisation to treatments
Wang 2005	No randomisation to treatments; follow-up period of less than 6 months
Wolffsohn 2006	Sequential recruitment of participants (classified as controlled clinical trial)
Xu 2007	Randomised controlled trial comparing accommodative intraocular lens and multifocal lens; follow up period of less than 6 months

DATA AND ANALYSES

Comparison 1. Accommodative IOL versus monofocal IOL

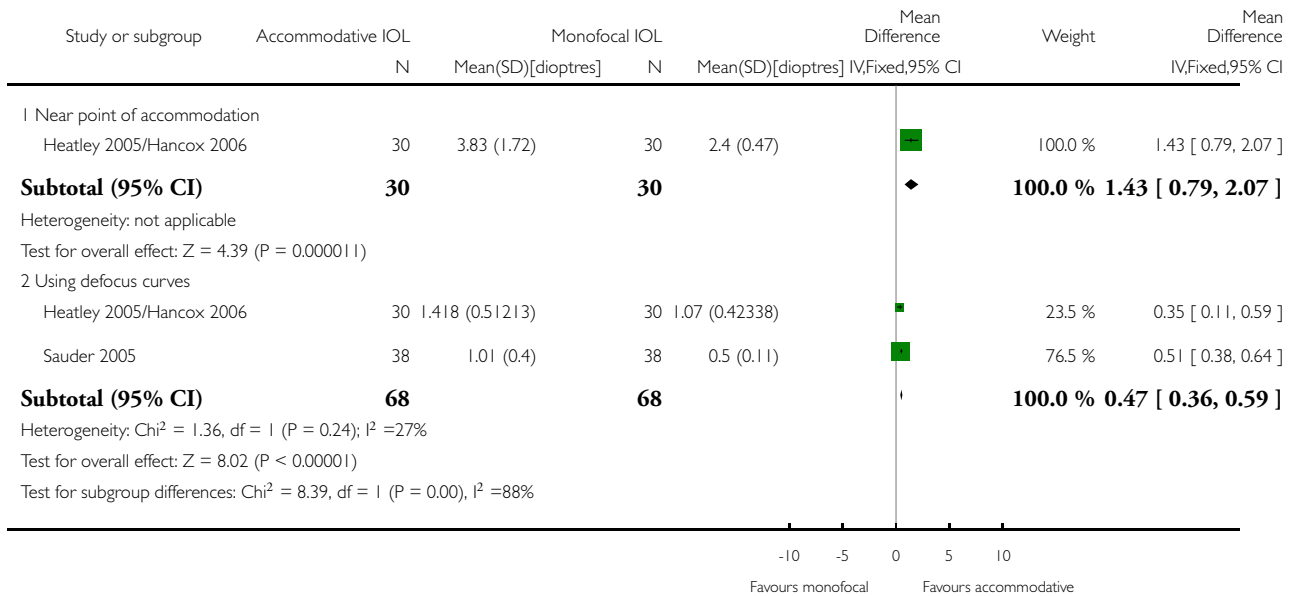
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Amplitude of accommodation at 6 months	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Near point of accommodation	1	60	Mean Difference (IV, Fixed, 95% CI)	1.43 [0.79, 2.07]
1.2 Using defocus curves	2	136	Mean Difference (IV, Fixed, 95% CI)	0.47 [0.36, 0.59]
2 Distance-corrected near visual acuity at 6 months	2	136	Mean Difference (IV, Fixed, 95% CI)	-3.10 [-3.36, -2.83]
3 Amplitude of accommodation at 12 or more months	3	131	Mean Difference (IV, Fixed, 95% CI)	0.22 [-.00, 0.43]
3.1 Using defocus curves	3	131	Mean Difference (IV, Fixed, 95% CI)	0.22 [-.00, 0.43]
4 Distance-corrected near visual acuity 12 months or more	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Corrected distant visual acuity at 6 months	2	136	Std. Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.37, 0.30]
6 Corrected distant visual acuity at 12 months or more	3	151	Mean Difference (IV, Fixed, 95% CI)	0.04 [0.01, 0.07]
6.1 12 months follow-up	1	51	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.06, 0.02]
6.2 18 months follow-up	2	100	Mean Difference (IV, Fixed, 95% CI)	0.12 [0.07, 0.16]
7 Reduction in anterior chamber depth on accommodation at 12 months or more	2	91	Mean Difference (IV, Fixed, 95% CI)	0.21 [0.14, 0.28]
8 Posterior capsule opacification	2	91	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.12 [0.45, 10.02]
9 Laser capsulotomy	2	80	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.96 [2.49, 25.45]

Analysis 1.1. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 1 Amplitude of accommodation at 6 months.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 1 Amplitude of accommodation at 6 months

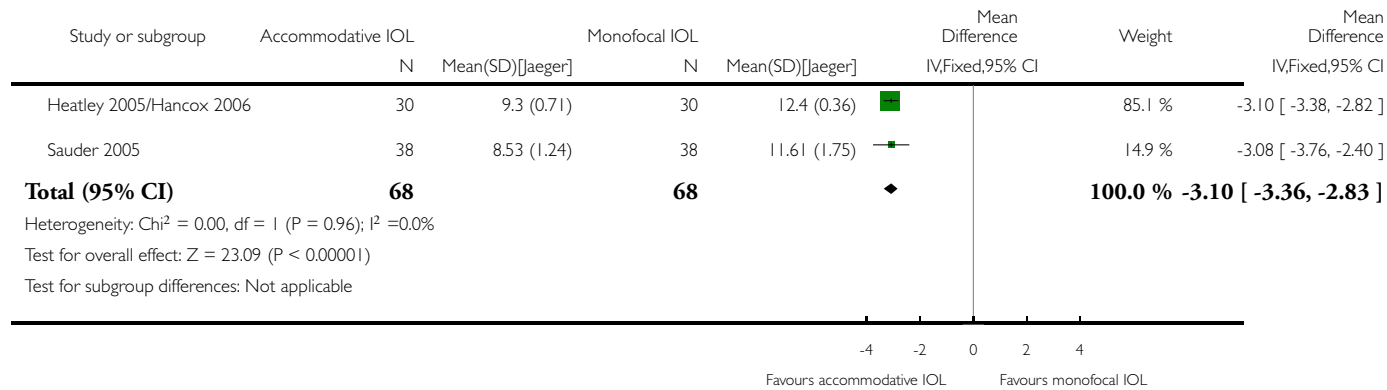


Analysis 1.2. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 2 Distance-corrected near visual acuity at 6 months.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 2 Distance-corrected near visual acuity at 6 months

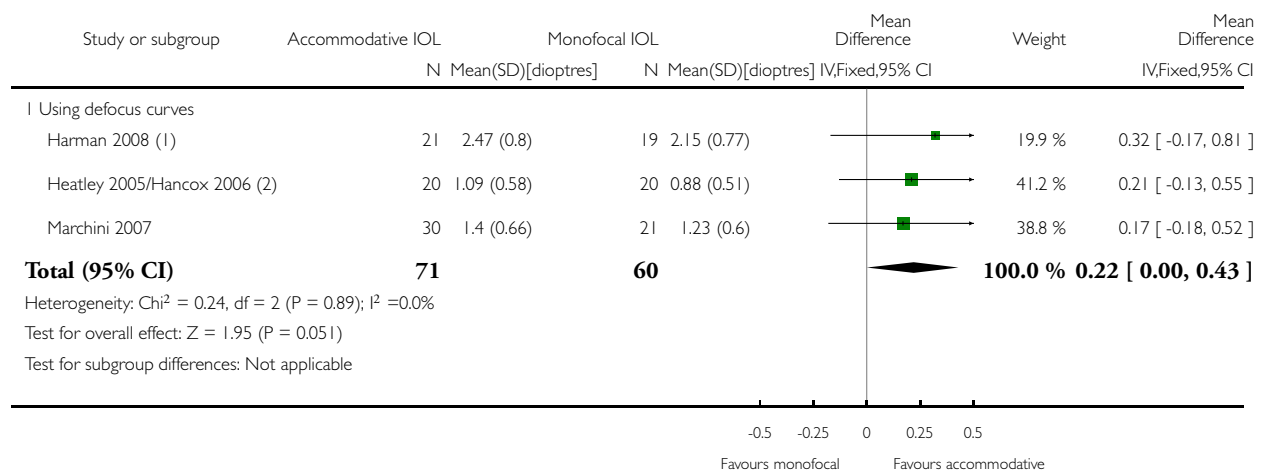


Analysis 1.3. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 3 Amplitude of accommodation at 12 or more months.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 3 Amplitude of accommodation at 12 or more months



(1) 18 months follow up

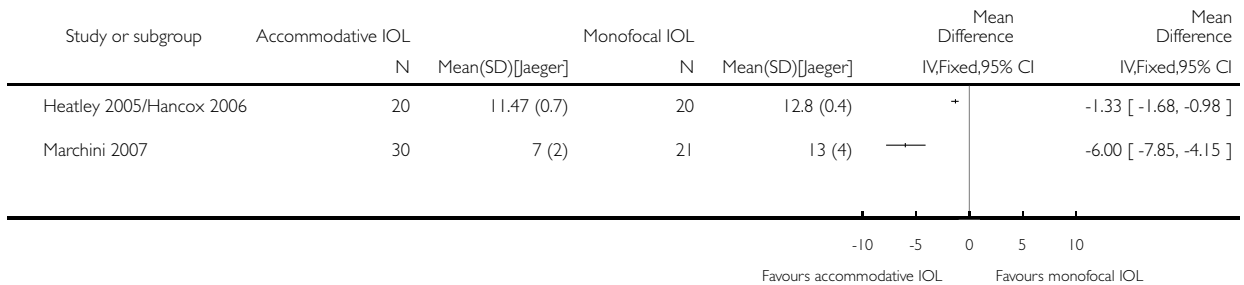
(2) 18 months follow up

Analysis 1.4. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 4 Distance-corrected near visual acuity 12 months or more.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 4 Distance-corrected near visual acuity 12 months or more

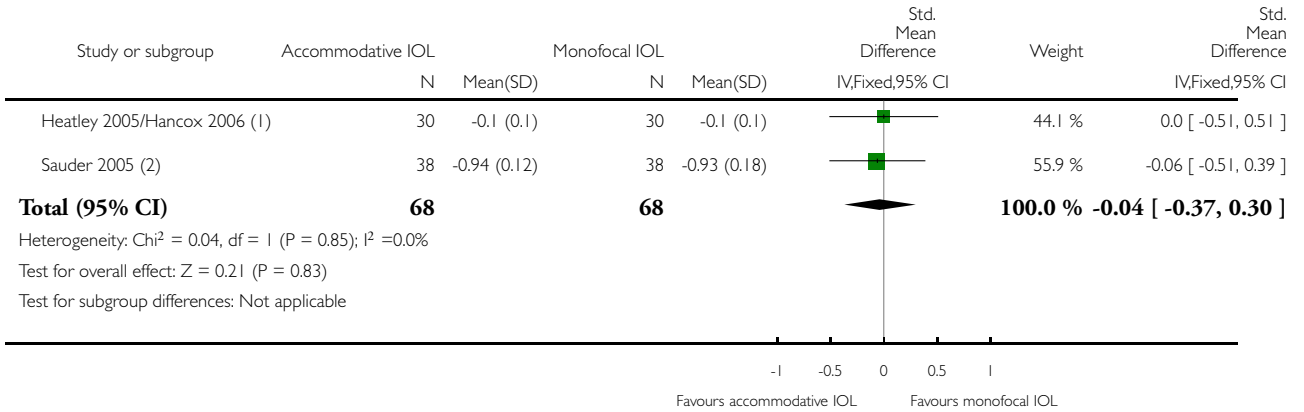


Analysis 1.5. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 5 Corrected distant visual acuity at 6 months.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 5 Corrected distant visual acuity at 6 months



(1) LogMAR

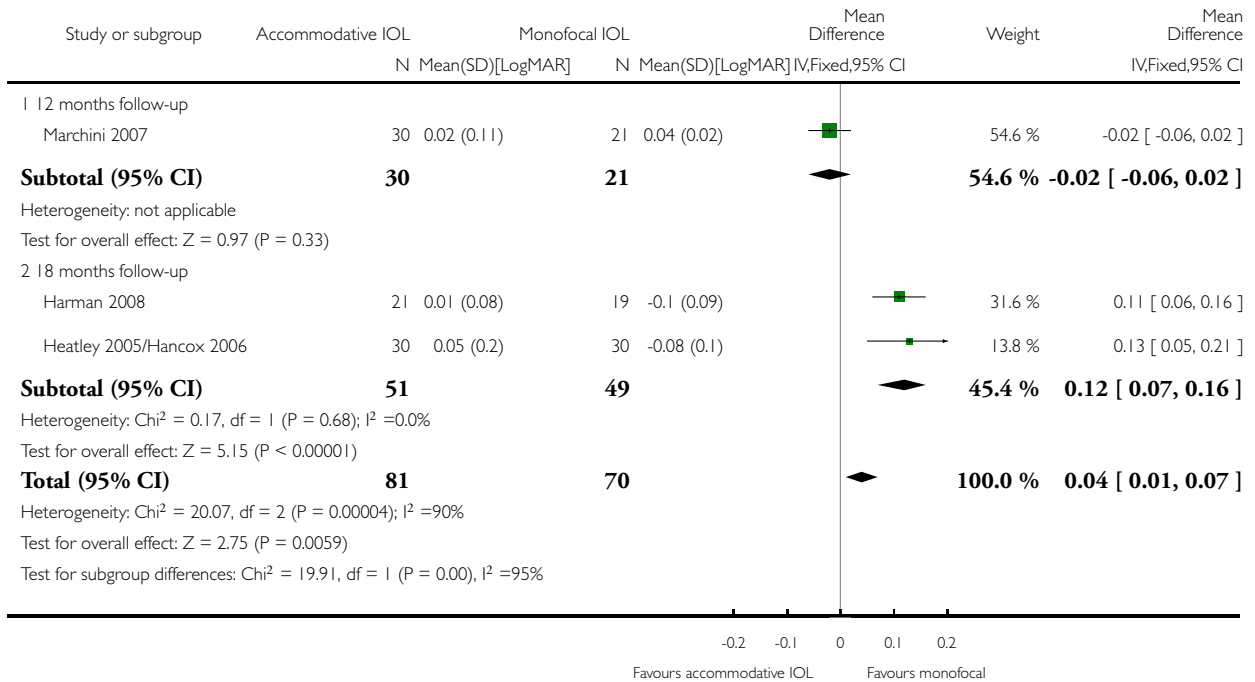
(2) Snellen Lines

Analysis 1.6. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 6 Corrected distant visual acuity at 12 months or more.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 6 Corrected distant visual acuity at 12 months or more

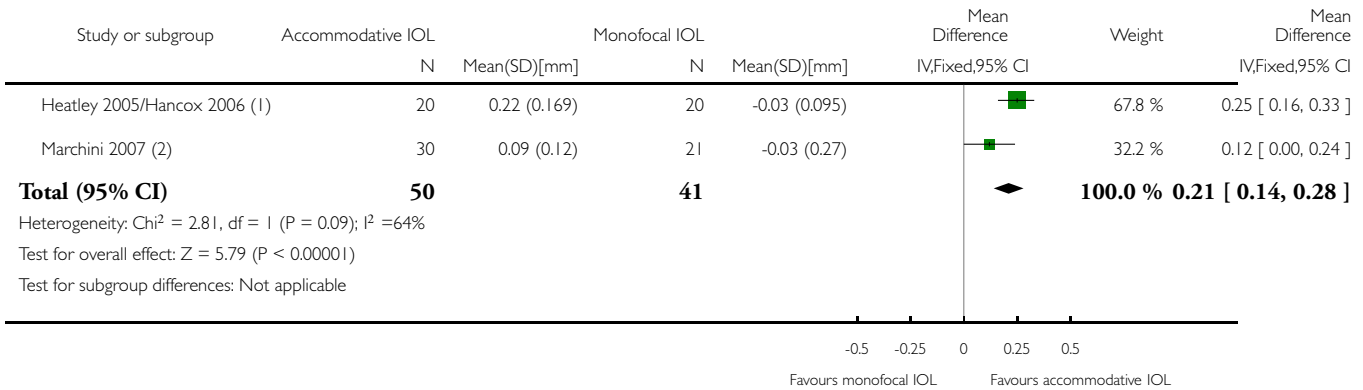


Analysis 1.7. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 7 Reduction in anterior chamber depth on accommodation at 12 months or more.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 7 Reduction in anterior chamber depth on accommodation at 12 months or more



(1) Change in anterior chamber depth was measured using optical interferometry before and after medical miosis using pilocarpine 4% eye drops

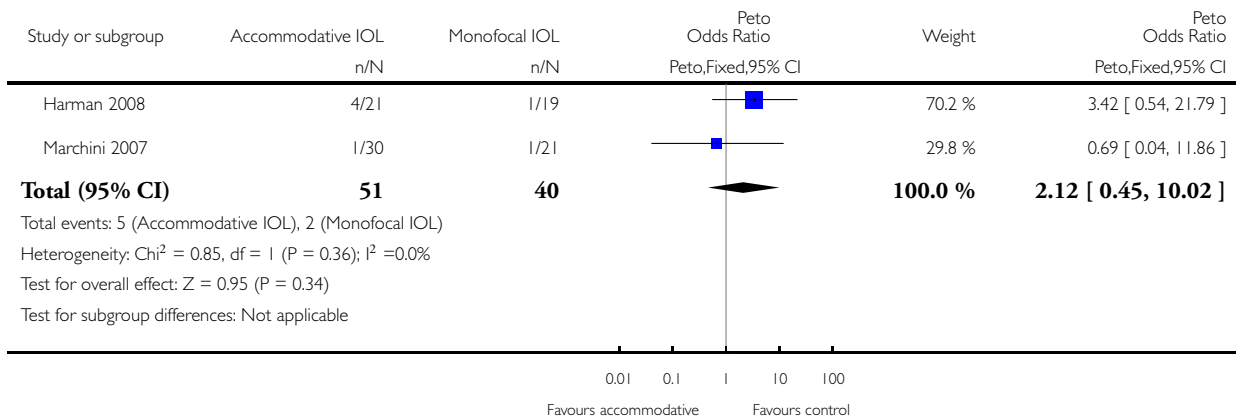
(2) Change in anterior chamber depth was measured using ultrasound biomicroscopy first in an accommodative state and then in an unsolicited state using cyclopentolate 1% eye drops

Analysis 1.8. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 8 Posterior capsule opacification.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 8 Posterior capsule opacification

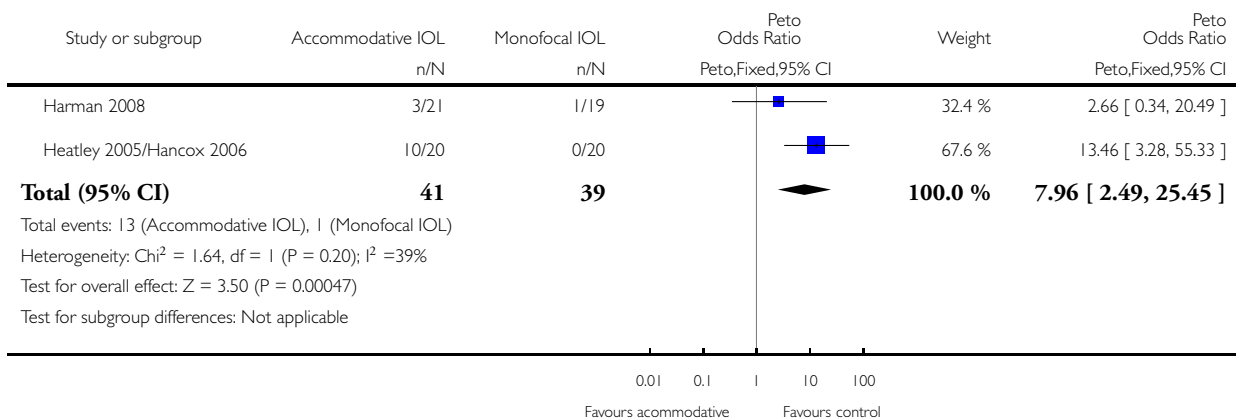


Analysis 1.9. Comparison 1 Accommodative IOL versus monofocal IOL, Outcome 9 Laser capsulotomy.

Review: Accommodative intraocular lens versus standard monofocal intraocular lens implantation in cataract surgery

Comparison: 1 Accommodative IOL versus monofocal IOL

Outcome: 9 Laser capsulotomy



ADDITIONAL TABLES

Table 1. Comparison between 1CU accommodative IOL versus AT-45 accommodative IOL

Data from Marchini 2007	1CU accommodative IOL (n = 30)		AT-45 accommodative IOL (n = 29)		Effect estimate	
	Mean	Standard deviation	Mean	Standard deviation	Mean difference	95% confidence intervals
Amplitude of accommodation using defocus curve \geq 12 months post-treatment	1.4	0.66	0.96	0.44	0.44	0.16 to 0.73
Distance-corrected near visual acuity \geq 12 months post-treatment	7	2	10	4	-3	-4.62 to -1.38
Corrected distant visual acuity \geq 12 months post-treatment	0.02	0.11	0.04	0.07	-0.02	-0.07 to 0.03
Reduction in anterior chamber depth on accommodation \geq 12 months post-treatment	0.09	0.12	0.17	0.27	-0.08	-0.19 to 0.03

APPENDICES

Appendix 1. CENTRAL search strategy

- #1 MeSH descriptor: [Cataract] explode all trees
- #2 MeSH descriptor: [Cataract Extraction] explode all trees
- #3 MeSH descriptor: [Capsulorhexis] explode all trees
- #4 MeSH descriptor: [Phacoemulsification] explode all trees
- #5 pha?oemulsif* or lensectom*
- #6 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*) near (cataract*)
- #7 (extract* or aspirat* or operat* or remov* or surg* or excis* or implant*) near (lens*)
- #8 #1 or #2 or #3 or #4 or #5 or #6 or #7
- #9 MeSH descriptor: [Lenses, Intraocular] explode all trees
- #10 MeSH descriptor: [Lens Implantation, Intraocular] explode all trees
- #11 MeSH descriptor: [Pseudophakia] explode all trees
- #12 #9 or #10 or #11
- #13 (intraocular or intra ocular or intra-ocular or lens* or IOL*) near/4 (accommodative)
- #14 (intraocular or intra ocular or intra-ocular or lens* or IOL*) near/4 (accommodating)
- #15 AIOL*
- #16 #13 or #14 or #15
- #17 #8 and #12 and #16

Appendix 2. MEDLINE (OvidSP) search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. exp cataract/
14. exp cataract extraction/
15. exp capsulorhexis/
16. exp phacoemulsification/
17. (pha?oemulsif\$ or lensectom\$).tw.
18. ((extract\$ or aspirat\$ or operat\$ or remov\$ or surg\$ or excis\$ or implant\$) adj3 cataract\$).tw.
19. ((extract\$ or aspirat\$ or operat\$ or remov\$ or surg\$ or excis\$ or implant\$) adj3 lens\$).tw.
20. or/13-19
21. exp lens, intraocular/
22. Lens Implantation, Intraocular/
23. Pseudophakia/
24. or/21-23
25. ((intraocular or intra ocular or intra-ocular or lens\$ or IOL\$) adj4 accommodative).tw.
26. ((intraocular or intra ocular or intra-ocular or lens\$ or IOL\$) adj4 accommodating).tw.
27. AIOL\$.tw.
28. or/25-27
29. 20 and 24 and 28

30. 12 and 29

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville ([Glanville 2006](#)).

Appendix 3. EMBASE (OvidSP) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random\$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin\$ adj3 trial\$).tw.
14. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw.
15. exp placebo/
16. placebo\$.tw.
17. random\$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control\$ or prospectiv\$ or volunteer\$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp cataract/
34. exp cataract extraction/
35. exp capsulorhexis/
36. exp phacoemulsification/
37. ((extract\$ or aspirat\$ or operat\$ or remov\$ or surg\$ or excis\$ or implant\$) adj3 cataract\$).tw.
38. ((extract\$ or aspirat\$ or operat\$ or remov\$ or surg\$ or excis\$ or implant\$) adj3 lens\$).tw.
39. or/33-38
40. lens implantation/
41. lens implant/
42. pseudophakia/
43. or/40-42
44. ((intraocular or intra ocular or intra-ocular or lens\$ or IOL\$) adj4 accommodative).tw.
45. ((intraocular or intra ocular or intra-ocular or lens\$ or IOL\$) adj4 accommodating).tw.
46. AIOL\$.tw.
47. or/44-46

48. 39 and 43 and 47

49. 32 and 48

Appendix 4. LILACS search strategy

cataract or phacoemulsif\$ and intraocular or intra ocular or intra-ocular or lens\$ or IOL\$ and accommodative or accommodating

Appendix 5. metaRegister of Controlled Trials search strategy

(accommodative or accommodating) AND cataract

Appendix 6. ClinicalTrials.gov search strategy

(Accommodative OR Accommodating) AND Cataract

Appendix 7. ICTRP search strategy

(Accommodative OR Accommodating) AND Cataract

CONTRIBUTIONS OF AUTHORS

HSO and BA conceived the review question, HSO/JE extracted data and did the analysis. All authors wrote drafts of the review and responded to peer review comments and comments from the editorial base.

DECLARATIONS OF INTEREST

None known.

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External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We focused the primary outcome on near vision rather than amplitude of accommodation (to better reflect our objectives) and included an extra outcome - spectacle independence.

INDEX TERMS

Medical Subject Headings (MeSH)

*Accommodation, Ocular; *Cataract Extraction; *Lens Implantation, Intraocular [adverse effects]; *Lenses, Intraocular; Equipment Design; Eyeglasses [utilization]; Randomized Controlled Trials as Topic; Reading; Visual Acuity

MeSH check words

Humans