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# Comparison of intraocular lens types for cataract surgery in eyes with uveitis

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## Abstract

This is the protocol for a review and there is no abstract. The objectives are as follows:

The aim of this systematic review is to summarize the effects of different IOLs after cataract surgery in uveitis patients. Alternative types of IOLs include PMMA, silicone, acrylic with or without heparin-surface modification.



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Providing general advice on the review: AE, JK, ES, KL
Securing funding for the review: N/A
Performing previous work that was the foundation of the current study: AE, JK

**DECLARATIONS OF INTEREST**

None known

# BACKGROUND

## Description of the condition

Uveitis is a complex intraocular inflammatory disease of the middle eye. A wide variety of causes exist for uveitis, including autoimmune processes, infectious agents, and exposure to toxins (McCannel 1996). Nevertheless, the majority of uveitis cases are not associated with systemic diseases (Munoz-Fernandez 2006). About 1% of the United States population has uveitis (Gritz 2004). This condition appears to increase with age, with the highest incidence rates seen in the elderly (Gritz 2004; Reeves 2006). Uveitis significantly impacts patients' lives. It is thought to be responsible for approximately 5 to 20% of legal blindness in developed countries (Bodaghi 2001). Many uveitis patients may also experience blurred vision, sensitivity to light, eye pain, dark floating spots and redness.

One of the common complications of uveitis is cataract formation (Okhravi 1999). While the incidence rate of cataract varies according to the type of uveitis, it is potentially as high as 50% (Rojas 1997). Unlike the general public, uveitis patients often develop cataract at an earlier stage in life. Prior intraocular inflammation and corticosteroid use are thought to be associated with cataract in individuals with uveitis (Alio 1999).

## Description of the intervention

During the early 1980s, the vast majority of practicing ophthalmologists considered it poor judgement to place an intraocular lens in uveitic eyes (Lichter 1989). It was reasoned that there was not enough experience with intraocular lenses to know whether uveitic eyes would tolerate them over many years. As increasing numbers of implants have been performed, considerable softening of the contraindications occurred (Lichter 1989).

In the past decade, a great deal of discussion has centered on the surgical correction of cataracts in uveitis patients (Alio 1999; Okhravi 1999). Health professionals differ in their opinions of indications and timing of surgery, optimal surgical technique, and pre and post-operative surgical treatment for cataract extraction (Foster 1992). Recently, phacoemulsification with in-the-bag intraocular lens (IOL) implantation has emerged as a preferred surgical procedure for most uveitis patients with cataract (Alio 2002). An IOL is a lens implanted in the eye that replaces the existing (cataractous) crystalline lens. Although IOLs have traditionally been made of poly(methyl methacrylate) (PMMA), this has become superseded by more flexible materials. Some of the more common types of flexible lens are silicone and acrylic (Alio 2002). These lenses as well as the PMMA lens can be modified by adding heparin to the surface of the lens (Tabbara 1998).

## How the intervention might work

Intraocular lens insertion for cataracts is one of the most commonly performed surgical procedures (Woodcock 2004). The surgery is often performed under local anaesthesia with the patient awake. The use of a more flexible IOL has allowed for a smaller incision, avoiding stitches, shortening surgical time, and speeding postoperative recovery. It is believed that utilization of a flexible IOL placed in the intact posterior capsule results in less

surgical trauma and surgically induced inflammation than alternative approaches (Rojas 1996).

In addition, heparin-surface modification of IOLs has been hypothesized to have better outcomes. It has been postulated that an IOL with a heparin surface leads to reduced electrostatic forces and cellular adhesion, consequently preventing the attraction of inflammatory cells and adherence of fibroblasts to the surface of the IOL (Tabbara 1998).

### Why it is important to do this review

The use of flexible IOLs has increased compared to the traditional PMMA lens (Alio 2002). However, it is still unclear which IOL style (PMMA, silicone, acrylic) is optimal for use in cataract surgery for eyes with uveitis, or whether approaches such as heparin-surface modification are beneficial (Alio 2002). It is imperative that health professionals use the IOL type that results in the best health outcomes for their patients. This systematic review will evaluate the safety and effectiveness of various implanted types of IOL with or without heparin-surface modification compared to each other, no treatment or placebo.

## OBJECTIVES

The aim of this systematic review is to summarize the effects of different IOLs after cataract surgery in uveitis patients. Alternative types of IOLs include PMMA, silicone, acrylic with or without heparin-surface modification.

## METHODS

### Criteria for considering studies for this review

**Types of studies—**We will include unpublished and published randomized clinical trials with at least three month follow-up after the cataract surgery.

**Types of participants—**We will include trials that have enrolled adult participants (18 years and older) with cataract developing after uveitis for any indication.

**Types of interventions—**We will include trials comparing any one of the following IOL types(PMMA, silicone, or acrylic) with or without heparin-surface modification with each other, or no treatment.

#### Types of outcome measures

**Primary outcomes:** We will consider that treatment is given to reverse visual impairment. Thus, the primary outcome is the:

- Proportion of people whose vision improved at least five letters on the logMAR chart, or the equivalent changes on the Snellen chart or other scales at least three months postoperatively by lens type.

**Secondary outcomes:** Secondary outcomes at least three months postoperatively include the:

- Proportion of people needing additional interventions in either group.
- Proportion of people with posterior capsule opacification postoperatively by lens type.
- Proportion of people who develop posterior synechiae by lens type.
- Proportion of people with increased inflammation according to lens type.
- Proportion of people who improve their quality of life measured by a validated scale by lens type.

We will consider other time periods of outcome assessment (i.e. six months, 12 months, etc). We will summarize other adverse events reported in the included studies.

## Search methods for identification of studies

**Electronic searches—**We will search the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library*), MEDLINE, EM-BASE, Latin American and Caribbean Literature on Health Sciences (LILACS) and the UK Clinical Trials Gateway (UKCTG). We will search for any ongoing trials that may have pertinent data using the online databases available at www.clinicaltrials.gov, www.controlled-trials.com and www.actr.org.au. There will be no date or language restrictions in the electronic search for trials. See: Appendices for details of search strategies for CENTRAL (*The Cochrane Library*), MEDLINE and EMBASE.

**Searching other resources—**We will search the reference lists of included studies to identify any additional trials. We will also use the Science Citation Index - Expanded database to identify additional trials that may have cited any studies we include in the review.

## Data collection and analysis

**Selection of studies—**Two review authors will independently scan the titles and abstracts (when available) of all reports identified through the electronic searches. For studies appearingto meet the inclusion criteria, or for which there are insufficient data in the title and abstract to make a clear decision, the full text will be obtained. The full texts obtained from all the electronic and other methods of searching will be assessed independently by two review authors to establish whether the studies meet the inclusion criteria or not. Disagreements will be resolved by discussion. Where resolution is not possible, a third review author will be consulted. All studies meeting the inclusion criteria will then undergo a validity assessment and data extraction. Studies rejected at this or subsequent stages will be recorded in the table: 'characteristics of excluded studies', and reasons for exclusion recorded.

**Data extraction and management—**Two review authors will independently extract the data for the primary and secondary outcomes onto paper data collection forms developed in collaboration with the Cochrane Eyes and Vision Group. Discrepancies will be resolved by discussion. Authors of included studies will be contacted for missing data. One review

author will enter all data into RevMan. The second review author will re-enter the data independently, using the double data-entry facility to verify the data entered.

For each trial the following data will be recorded.

- Year of publication, country of origin and source of study funding.
- Details of the participants including demographic characteristics and criteria for inclusion.
- Details of the type of intervention.
- Details of the outcomes reported, including method of assessment, and time intervals.

### Assessment of risk of bias in included studies

**Quality assessment:** The quality assessment of the included trials will be undertaken independently and in duplicate by two or more review authors as part of the data extraction process. We will follow the tools for assessing risk of bias set forth in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008).

Six main quality criteria will be examined:

1. Sequence generation;
2. Allocation concealment;
3. Blinding of participants, personnel and outcome assessors;
4. Incomplete outcome data;
5. Selective outcome reporting; and
6. Other sources of bias.

Each quality criteria will be assessed as:

A. Low risk of bias (plausible bias unlikely to seriously alter the results);
B. Unclear risk of bias (lack of information or uncertainty over the potential for bias); and
C. High risk of bias (plausible bias that seriously weakens confidence in the results).

Additional information will be requested from the authors of the trials if the risk of bias is unclear. Further quality assessments will include sample size calculations, whether there was a clear explanation that final visual acuity took into account differential follow-up, the definition of exclusion/inclusion criteria, adequate definitions of success criteria and comparability of control and treatment groups at entry.

### Measures of treatment effect

**Dichotomous data:** For dichotomous outcomes, the estimates of effect of an intervention will be expressed as risk ratios together with 95% confidence intervals. These will consist of development of posterior capsule opacification, posterior synechiae, inflammation according

to lens type, and adverse events as well as improved vision, better quality of life, and increased need for additional interventions.

**Unit of analysis issues—**The unit of analysis for posterior capsule opacification, additional postoperative interventions, visual acuity and adverse events will be an eye. If any trial randomizes eyes in patients to different types of IOL (paired) versus IOLs randomised to patients, we will refer to Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* as a guide for any intra-person correlation between eyes (Deeks 2008). In addition, for quality of life and specific types of anti-inflammatory medication data the unit of analysis is by person.

**Dealing with missing data—**We will attempt to contact the trial investigators for any missing data. If the investigators do not respond within four weeks, we will extract data as available from the published report. We will refer to guidelines in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008) for handling missing data.

**Assessment of heterogeneity—**We will quantify the proportion of variability within included randomized studies that is explained by heterogeneity using the $I^2$ statistic (Higgins 2008). If the $I^2$ statistic is greater than 50% we will consider it as substantial heterogeneity and will not combine the study results in a meta-analysis. Instead, we will present the studies in a tabulated or narrative summary. Heterogeneity, if present, will be investigated through subgroup analyses.

**Assessment of reporting biases—**Funnel plot will be examined to identify any evidence for publication bias.

**Data synthesis—**Data analysis will follow the guidelines set out in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008). We will calculate a summary risk ratio for dichotomous outcomes. If no significant statistical heterogeneity is detected either statistically or by review or there are a small number of trials in the analysis (three or fewer), the fixed-effect model will be used. If heterogeneity has been detected, we will use the random-effects model.

**Subgroup analysis and investigation of heterogeneity—**If sufficient data are available, we will conduct subgroup analyses. Subgroups of interest include gender, age, and groupings of clinical heterogeneity. Clinical heterogeneity includes the types of participants (i.e. aetiology of uveitis, prior treatment, severity of uveitis, uveitic grading schemes used), interventions and outcomes in each study.

**Sensitivity analysis—**Sensitivity analyses will be conducted to determine the impact of exclusion of studies with lower methodological quality, including exclusion of industry-funded studies and unpublished studies.

## Acknowledgments

The Cochrane Eyes and Vision Group editorial base will prepare and run the electronic searches.

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## Appendix 1. CENTRAL search strategy

#1 MeSH descriptor Uveitis

#2 uveiti*

#3 MeSH descriptor Iritis

#4 iritis

#5 MeSH descriptor Iridocyclitis

#6 iridocyclitis

#7 MeSH descriptor Pars Planitis

#8 pars planitis

#9 MeSH descriptor Choroiditis

#10 retinochoroidit* or choroidit*

#11 MeSH descriptor Behcet Syndrome

#12 MeSH descriptor Uveomeningoencephalitic Syndrome

#13 bechet or Vogt-Koyanagi-Harada or fuch

#14 MeSH descriptor Retinitis

#15 retinitis

#16 MeSH descriptor Ophthalmia, Sympathetic

#17 ophthalmia* sympathetic

#18 MeSH descriptor Arthritis, Juvenile Rheumatoid

#19 juvenile near/2 rheumatoid near/2 arthriti*

#20 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19)

#21 MeSH descriptor Cataract

#22 MeSH descriptor Cataract Extraction

#23 MeSH descriptor Phacoemulsification

#24 MeSH descriptor Capsulorhexis

#25 (cataract* or phacoemulsifcat*)

#26 (#21 OR #22 OR #23 OR #24 OR #25)

#27 MeSH descriptor Lens Implantation, Intraocular

#28 MeSH descriptor Lenses, Intraocular

#29 MeSH descriptor Acrylic Resins

#30 MeSH descriptor Coated Materials, Biocompatible

#31 MeSH descriptor Polymethyl Methacrylate

#32 MeSH descriptor Silicone Elastomers

#33 MeSH descriptor Heparin

#34 (intraocular lens* or IOL*)

#35 lens near/20 (acrylic or silicone or polymethylmethacrylate or PMMA)

#36 IOL* near/20 (acrylic or silicone or polymethylmethacrylate or PMMA)

#37 heparin

#38 (#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37)

#39 (#20 AND #26 AND #38)

* Indicates the major publication for the study

## Appendix 2. MEDLINE 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 uveitis/
14. uveiti$.tw.
15. exp iritis/
16. iritis.tw.
17. exp iridocyclitis/
18. iridocyclitis.tw.
19. exp pars planitis/
20. pars planitis.tw.
21. exp choroiditis/
22. (retinochoroidit$ or choroidit$).tw.
23. exp behcet syndrome/

24. exp Uveomeningoencephalitic Syndrome/
25. (bechet or Vogt-Koyanagi-Harada or fuch).tw.
26. exp retinitis/
27. retinitis.tw.
28. exp ophthalmia, sympathetic/
29. (ophthalm$ adj2 sympathetic).tw.
30. exp arthritis juvenile rheumatoid/
31. (juvenile adj2 rheumatoid adj2 arthriti$).tw.
32. or/13–31
33. exp cataract/
34. exp cataract extraction/
35. exp phacoemulsification/
36. exp capsulorhexis/
37. (cataract$ or phacoemulsificat$).tw.
38. or/33–37
39. exp lens implantation intraocular/
40. exp lenses intraocular/
41. exp acrylic resins/
42. exp coated materials, biocompatible/
43. exp polymethylmethacrylate/
44. exp silicone elastomers/
45. exp heparin/
46. (intraocular lens$ or IOL$).tw.
47. ((acrylic or silicone or polymethylmethacrylate or PMMA) adj20 lens$).tw.
48. ((acrylic or silicone or polymethylmethacrylate or PMMA) adj20 IOL$).tw.
49. heparin.tw.
50. or/39–49
51. 32 and 38 and 50

## Appendix 3. EMBASE 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$).tw.
29. or/25–28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp uveitis/
34. uveiti$.tw.

35. exp iritis/
36. iritis.tw.
37. exp iridocyclitis/
38. iridocyclitis.tw.
39. exp intermediate uveitis/
40. pars planitis.tw.
41. exp choroiditis/
42. (retinochoroidit$ or choroidit$).tw.
43. exp behcet disease/
44. exp Meningoencephalitis/
45. (bechet or Vogt-Koyanagi-Harada or fuch).tw.
46. exp retinitis/
47. retinitis.tw.
48. exp sympathetic ophthalmia/
49. (ophthalm$ adj2 sympathetic).tw.
50. exp Juvenile Rheumatoid Arthritis/
51. (juvenile adj2 rheumatoid adj2 arthriti$).tw.
52. or/33–51
53. exp cataract/
54. exp cataract extraction/
55. exp phacoemulsification/
56. exp capsulorhexis/
57. (cataract$ or phacoemulsificat$).tw.
58. or/53–57
59. exp lens implantation/
60. exp lens implant/
61. exp acrylic acid resin/
62. exp biomaterial/
63. exp polymethylmethacrylate/
64. exp silastic/
65. exp heparin/
66. (intraocular lens$ or IOL$).tw.

**67.** ((acrylic or silicone or polymethylmethacrylate or PMMA) adj20 lens$).tw.

**68.** ((acrylic or silicone or polymethylmethacrylate or PMMA) adj20 IOL$).tw.

**69.** heparin.tw.

**70.** or/59–69

**71.** 52 and 58 and 70

**72.** 32 and 71