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Optical aberrations following implantation of multifocal IOLs: a systematic review protocol

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Complete List of Authors:	Henein, Christin; University College London Institute of Ophthalmology; NIHR Moorfields Biomedical Research Centre Fang, Clarissa E H; Manchester Royal Eye Hospital Bokre, Desta; University College London Institute of Ophthalmology Khan, Maaz; University College London Institute of Ophthalmology Adan, Ahmed; University College London Institute of Ophthalmology Bouremel, Yann; University College London Institute of Ophthalmology Nanavaty, Mayank; Sussex Eye Hospital; Brighton and Sussex Medical School
Keywords:	Cataract and refractive surgery < OPHTHALMOLOGY, Ophthalmology < SURGERY, OPHTHALMOLOGY

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3 1 **Optical aberrations following implantation of multifocal IOLs: a systematic review protocol**

4
5 2 **Authors:**

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7 3 **Christin Henein^{1,2}, Clarissa E.H. Fang³, Desta Bokre¹, Maaz Khan¹, Ahmed Adan¹, Yann**

8
9 4 **Bouremel¹, Mayank A. Nanavaty^{4,5}**

10
11 5
12
13 6 **Affiliations**

14 7 ¹UCL, Institute of Ophthalmology, London, UK

15 8 ²NIHR Moorfields Biomedical Research Centre, London, UK

16 9 ³Manchester Royal Eye Hospital, Manchester, UK

17 10 ⁴Sussex Eye Hospital, University Hospitals Sussex NHS Foundation Trust, Eastern Road, Brighton,
18 United Kingdom. BN2 5BF

19 11 ⁵Brighton & Sussex Medical School, University of Sussex, Falmer, Brighton. United Kingdom. BN1
20 12 9PX

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28 16 **Corresponding author***

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49 26 **Authors contribution**

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52 27 MN conceived the idea for the review. CH, MK, AA and DB drafted and revised the protocol with
53 suggestions from YB, CEHF and MN who reviewed the protocol and provided feedback on the draft.
54
55 28 DB constructed the search.
56
57
58
59

60 30 **Conflicts of interest**

1
2
3 31 The authors declare no conflict of interest.
4
5

6 32 **Data sharing statement**
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10 33 No additional data is available.
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13 34 **Patient and Public Involvement**
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16 35 Patients and public were not involved in the development of this protocol. The primary outcome of the
17
18 36 review is patient-centred.
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21 37 **Acknowledgments**
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23

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30

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33

34 41 **Email addresses:**
35
36

37 42 c.henein@ucl.ac.uk, d.bokre@ucl.ac.uk, maaz.khan.20@ucl.ac.uk, ahmed.adan.20@ucl.ac.uk,
38
39 43 y.bouremel@ucl.ac.uk, fangclarissa@gmail.com, mayank.nanavat@nhs.net
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3 454
5 46 **Abstract**

7 47 **Introduction:** Multifocal IOLs are used to restore vision at different focal distances. The technology
8
9 48 of multifocal IOLs is continually advancing. Optical aberrations a property of lenses that causes
10
11 49 spreading of light over a region resulting in a blurred or distorted image. This study aims to
12
13 50 systematically review investigator measured and patient reported optical aberrations following
14
15 51 implantation of multifocal intraocular lenses during phacoemulsification surgery to treat presbyopia in
16
17 52 adults.

18 53 **Methods and Analysis:** We will conduct an electronic database search for randomized controlled
19
20 54 trials, prospective non-randomized studies, observational studies in Ovid MEDLINE, Ovid EMBASE,
21
22 55 Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Scopus, and
23
24 56 ClinicalTrials.gov. Eligibility criteria will include quantitative articles written in English and containing
25
26 57 data on optical aberrations. Two independent reviewers will screen titles and abstracts and extract
27
28 58 data from full texts, reporting outcomes according to Preferred Reporting Items for Systematic
29
30 59 Reviews and Meta-Analyses (PRISMA) guidelines. Data extraction of key characteristics will be
31
32 60 completed using customized forms. Methodological quality will be assessed using Cochrane
33
34 61 Handbook 6.2.

35 62 **Ethics and Dissemination** Ethics approval is not required for this review, as it will only include
36
37 63 published data. Findings will be published in a peer-reviewed journal and disseminated across
38
39 64 ophthalmic networks. We anticipate that the findings of this work will be of interest to multiple
40
41 65 stakeholders: people who have undergone cataract surgery, eye health professionals, ophthalmic
42
43 66 surgeons, device manufacturers and policy makers. It will also inform researchers to where there are
44
45 67 gaps in evidence and identify areas for future research.

46
47 68 **Systematic review registration number:** PROSPERO CRD42021271050
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51 70 **Keywords:** Optics, aberration, intraocular lens, multifocal
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54 71 **Article Summary**55
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57 72 **Strengths and Limitations**
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3 73 • This systematic review protocol follows the Preferred Reporting Items for Systematic
4 Review and Meta-Analysis Protocols guidelines.
5 74
6
7 75 • This systematic review addresses a gap in the current evidence-base by providing a
8 comprehensive assessment of reported optical aberrations following new and older
9 76 generation multifocal IOL
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16 79 **Word count:** 1507
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22 81 **Introduction**

23
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25 82 Traditional monofocal IOLs provide a single point of focus and toric monofocal lenses can correct
26 83 astigmatism. Multifocal IOLs have multiple focal lengths. If they have 2 foci, they are called bifocal,
27 84 three foci, they are trifocal. This enables the patient with a multifocal IOL to see both objects located
28 85 at a distance or near to them. They are three different mechanisms to achieve this: the technology
29 86 can be refractive, diffractive or combined. Moreover, toric multifocal lens also help to correct the
30 87 problem of astigmatism that only toric monofocal lens can do¹.
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37 88 Multifocal IOLs are used to restore vision at different focal distances. It is generally accepted they are
38 89 good for distance and intermediate focal distances. According to the lens design they can be refractive,
39 90 diffractive or combined. The technology of multifocal IOLs is continually advancing. Next generation
40 91 IOLs include rotationally asymmetric segmented multifocal IOL, increase in the central area with the
41 92 aim to improve reading acuity, improved pupil independence and increased depth of focus. Optical
42 93 aberrations a property of lenses that causes spreading of light over a region resulting in a blurred or
43 94 distorted image. Optical aberrations can present as symptoms of glare, holes and stars. This symptoms
44 95 may limit the patient satisfaction achieved with these IOLs and is therefore an important patient-centred
45 96 outcomes to quantify. Spherical aberrations significantly contribute to quality of retinal image and
46 97 subjective refraction. Optical aberrations can be reported subjectively using questionnaires or
47 98 measured objectively by wavefront aberrometry analysis. Contrast sensitivity can be a more useful/
48 99 objective tool to assess visual function. Recent reviews that compared multifocal with monofocal IOLs
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3 100 reported outcomes on spectacle independence, visual acuity and quality of life^{2,3}. To our knowledge
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5 101 this is the first review comparing different multifocal IOLs with optical aberrations as the primary
6
7 102 outcome.

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9
10 103 **Review aim:** We aim to systematically review investigator measured and patient reported optical
11
12 104 aberrations following implantation of multifocal intraocular lenses during phacoemulsification surgery
13
14 105 to treat presbyopia.

16 106 **Methods and analysis**

18 107 **Inclusion and exclusion criteria**

20 108 **Types of studies**

22
23
24
25
26 109 We will include randomised controlled trials (RCTs) and non-randomised interventional studies
27
28 110 (retrospective or prospective studies). Observational studies will allow us to provide real-world
29
30 111 estimates of reported optical aberrations.

32 112 **Types of participants**

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36
37 113 We will include adults aged 18 years and above with presbyopia. We will exclude studies with
38
39 114 participants with history of laser refractive surgery.

41 115 **Intervention(s)**

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46 116 We will include small incision cataract extraction and multifocal lens implantation. All types of refractive
47
48 117 and diffractive multifocal lenses will be included in this review.

49 118 **Comparator(s)**

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55 119 We will include multifocal intraocular lens or alternative type of multifocal IOL as comparators such as
56
57 120 diffractive, refractive and hybrid technologies.

58 59 60 121 **Outcomes**

1
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3 122 *Primary outcome*
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- 6 123 • Participant reported optical aberrations such as but not limited to glare and halos.
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10 124 *Secondary outcomes*
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- 13 125 • Measured optical aberrations with wavefront analysis
14
15 126 • Contrast sensitivity as measured by validated test
16
17 127 • Spectacle independence as determined by the participant or as determined by the
18
19 128 investigator
20
21 129 • Uncorrected near vision acuity
22
23 130 • Uncorrected distance vision acuity
24
25 131 • Mean spherical equivalent within $\pm 0.5D$
26
27 132 • % of eyes seeing 20/20 or better for distance
28
29 133 • % of eyes seeing 20/40 or better for distance
30
31 134 • % of eyes seeing J5 or better for near vision
32
33 135 • YAG laser capsulotomy rates
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36 136 **Search strategy**
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39 137 In collaboration with an information specialist a comprehensive search strategy will be performed using
40
41 138 a combination of controlled vocabulary and free text terms. Searches will be conducted in Ovid
42
43 139 MEDLINE, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of
44
45 140 Science, Scopus and ClinicalTrials.gov bibliographic databases. Other relevant sources will be
46
47 141 searched such as reference lists of existing systematic reviews of multifocal IOLs. Please see appendix
48
49 142 1 for strategy syntax for Ovid Medline 1946 – March 2021 electronic database. We will download
50
51 143 references identified in searches (electronic database and additional searches) into Endnote X9
52
53 144 reference management software and remove duplicate abstracts.
54
55

56 145 **Study selection**
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3 146 The screening process will be undertaken using Endnote X9. Two review authors will independently
4
5 147 assess the titles and abstracts of records and exclude papers that do not meet eligibility criteria. We
6
7 148 will obtain the full text of the remaining papers, and at least two authors will assess the papers against
8
9 149 the inclusion criteria for the review to determine their eligibility for inclusion. Non-English language
10
11 150 papers will be excluded. The review authors will resolve disagreements through mediation with a third
12
13 151 reviewer.

16 152 **Data extraction**

17
18
19 153 Two review authors will extract data independently using Excel. We will pre-pilot the data extraction
20
21 154 template. We will resolve discrepancies by discussion. Two attempts will be made to contact trial
22
23 155 investigators for missing data. Data will be directly imported into Review Manager 5 (RevMan 5); and
24
25 156 the accuracy of the data import will be checked by one author.

26
27
28 157 We will collect the following information on study characteristics:

- 30 158 • Study design: parallel group RCT/within-person RCT/one or both eyes reported
- 31
32
33 159 • Participants: country, total number of participants, age, sex, inclusion and exclusion
34
35 160 criteria
- 36
37
38 161 • Intervention and comparator details: type of multifocal IOL, including number of people
39
40 162 (eyes) randomised to each group
- 41
42 163 • Primary and secondary outcomes as measured and reported in the trials
- 43
44
45 164 • Length of follow-up
- 46
47
48 165 • Date of publication
- 49
50 166 • Date multifocal IOL received market approval (FDA PMA, CE mark)
- 51
52
53 167 • Sample size
- 54
55 168 • Funding and conflicts of interest
- 56
57
58 169 • Trial registration, if available
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60

170 **Data synthesis**

171 We will pool data using a random-effects model in RevMan 5. If there are fewer than three trials in a
172 comparison we will use a fixed-effect model. If there is inconsistency between individual study results
173 such that a pooled result may not be a good summary of the individual trial results — for example, the
174 effects are in different directions or $I^2 > 50\%$ and $P < 0.1$ — we will not pool the data but will describe
175 the pattern of the individual study results. If there is statistical heterogeneity we may pool the data if all
176 the effect estimates are in the same direction, such that a pooled estimate would seem to provide a
177 good summary of the individual trial results.

178 We will extract the following data from each included study for intervention and comparator groups
179 separately.

- 180 • Number of events and number of participants on which outcome data collected for
181 dichotomous variables
- 182 • Mean, standard deviation and number of participants on which outcome measured for
183 continuous variables

184 For multi-arm studies we will use data relevant to our intervention and comparator groups. If two
185 groups contain relevant data we will combine groups using the calculator within RevMan 5. If standard
186 deviation is not available we will use information from confidence intervals and P values, where
187 possible, to estimate it, using the RevMan 5 calculator⁴.

188 **Assessment of risk of bias in included studies**

189 Two review authors will assess independently the risk of bias using Cochrane's 'Risk of bias' tool for
190 assessing risk of bias in each included study according to the following domains selection bias,
191 performance bias, detection bias, attrition bias and selective outcome reporting bias⁵. We will resolve
192 disagreements by discussion. We will specifically consider and report on the following sources of bias.
193 We will grade each domain as low risk of bias, high risk of bias or unclear (lack of information or
194 uncertainty of potential for bias). We will attempt to contact trial investigators for clarification of
195 parameters graded as 'unclear'.

196 **Dealing with missing data**

197 If possible, we will conduct an intention-to-treat (ITT) analysis. We will use imputed data if computed by
198 the trial investigators using an appropriate method, but will not impute missing data ourselves. If ITT
199 data are not available, we will do an available case analysis. This assumes that data are missing at
200 random. We will assess whether this assumption is reasonable by collecting data from each included
201 trial on the number of participants excluded or lost to follow-up and reasons for loss to follow-up by
202 treatment group, if reported.

203 **Assessment of heterogeneity and subgroup analysis**

204 We will examine the overall characteristics of the studies, in particular the type of participants and types
205 of interventions, to assess the extent to which the studies are similar enough to make pooling study
206 results sensible. We will look at the forest plots of study results to see how consistent the results of the
207 studies are, in particular looking at the size and direction of effects. We will calculate I^2 which is the
208 percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error.
209 We will consider I^2 values over 50% to indicate substantial inconsistency but will also consider Chi^2 P
210 value. As this may have low power when the number of studies are few we will consider $P < 0.1$ to
211 indicate statistical significance of the Chi^2 test. If there are sufficient trials we will compare the effect of
212 treatment in the following subgroups; diffractive, refractive and hybrid multifocal IOL and year of market
213 approval.

214 **Sensitivity analysis and assessment of reporting biases**

215 We will examine the impact of excluding studies at high risk of bias in one or more domains. If there are
216 10 trials or more included in a meta-analysis, we will construct funnel plots and consider tests for
217 asymmetry for assessment of publication bias, according to Chapter 8 of the Cochrane Handbook for
218 Systematic Reviews of Interventions⁶.

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5 **Appendix 1. Search strategy**
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8 **Ovid Medline 1946 – March 2021**

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Search Lines	Search Terms	Search Results
1	exp "Optics and Photonics"/	79373
2	(optic* or photonic*).mp.	476463
3	1 or 2	518769
4	exp Refractive Errors/ or exp Refraction, Ocular/ or exp Astigmatism/ or exp Myopia/ or exp Visual Acuity/	108238
5	(aberrat* or diffract* or refract* or HOA).mp.	461904
6	4 or 5	541199
7	exp Lenses, Intraocular/	15452
8	(intraocular lens or Intra-ocular lens or intra ocular lens or IOL or IOLs or lens prosthes* or artificial lens).mp.	18494
9	7 or 8	23720
10	(multifocal or multi focal or multi-focal or bifocal or bi-focal or trifocal or tri-focal or hybrid).mp.	218357
11	3 and 6 and 9 and 10	515

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page Line
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	P1 L1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	P1 L1
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	P3 L62
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	P2 L39
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	P1 L23
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	P2 L35
Sponsor	5b	Provide name for the review funder and/or sponsor	P2 L35
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	P4 L76
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	P4 L87
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	P4 L90
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	P6 L122
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits such that it could be repeated	P6 L22

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	P6 L136
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	P6 L132
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently in duplicate), any processes for obtaining and confirming data from investigators	P6 L137
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	P6 L141
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	P5 L105
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	P8 L147
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	P7 L154
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I ² or Kendall's τ)	P7 L154
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	P9 L208
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	P7 L159
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	P9 L213
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	P9 L217

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite where available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Surgery, Evidence based practice, Ophthalmology
Keywords:	Cataract and refractive surgery < OPHTHALMOLOGY, Ophthalmology < SURGERY, OPHTHALMOLOGY

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5 2 **and meta-analysis protocol**

6
7 3 **Authors:**

8
9 4 **Christin Henein^{*1,2}, Clarissa E.H. Fang³, Desta Bokre¹, Maaz Khan¹, Ahmed Adan¹, Yann**
10 **Bouremel¹, Mayank A. Nanavaty^{4,5}**

11
12
13
14
15 7 *** Correspondence to Dr Christin Henein; c.henein@ucl.ac.uk**

16
17 8 **Affiliations**

18 9 ¹UCL, Institute of Ophthalmology, London, UK

19
20 10 ²NIHR Moorfields Biomedical Research Centre, London, UK

21 11 ³Manchester Royal Eye Hospital, Manchester, UK

22
23 12 ⁴Sussex Eye Hospital, University Hospitals Sussex NHS Foundation Trust, Eastern Road, Brighton,
24 13 United Kingdom. BN2 5BF

25
26 14 ⁵Brighton & Sussex Medical School, University of Sussex, Falmer, Brighton. United Kingdom. BN1
27 15 9PX

28
29
30
31
32 18 **Corresponding author***

33
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43
44
45
46
47
48
49
50
51
52

53 28 **Email addresses:**

54
55
56 29 c.henein@ucl.ac.uk, d.bokre@ucl.ac.uk, maaz.khan.20@ucl.ac.uk, ahmed.adan.20@ucl.ac.uk,
57 30 y.bouremel@ucl.ac.uk, fangclarissa@gmail.com, mayank.nanavaty@nhs.net

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Abstract

Introduction: Multifocal IOLs are used to restore vision at different focal distances. The technology of multifocal IOLs is continually advancing. Optical aberrations a property of lenses that causes spreading of light over a region resulting in a blurred or distorted image. This study aims to systematically review investigator measured and patient reported optical aberrations following implantation of multifocal intraocular lenses during phacoemulsification surgery to treat presbyopia in adults.

Methods and Analysis: We will conduct an electronic database search for randomized controlled trials, prospective non-randomized studies, observational studies in Ovid MEDLINE, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Scopus, and ClinicalTrials.gov in March 2021. Eligibility criteria will include quantitative articles written in English and containing data on optical aberrations. Two independent reviewers will screen titles and abstracts and extract data from full texts, reporting outcomes according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data extraction of key characteristics will be completed using customized forms. Methodological quality will be assessed using Cochrane Handbook 6.2.

Systematic review registration number: PROSPERO CRD42021271050

Keywords: Optics, aberration, intraocular lens, multifocal

Article Summary**Strengths and Limitations**

- This systematic review protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.
- This systematic review addresses a gap in the current evidence-base by providing a comprehensive assessment of reported optical aberrations following new and older generation multifocal IOL

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3 59 • There may be a paucity of RCTs comparing different multifocal IOLs limiting the number of
4
5 60 paired wise meta-analysis that can be done.
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10 62 **Word count:** 1507
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17 64 **Introduction**

19 65 Multifocal intraocular lens (IOLs) have multiple focal lengths; if they have 2 foci, they are called
20
21 66 bifocal, three foci, they are trifocal. This enables the patient with a multifocal IOL to see both objects
22
23 67 located at a distance, intermediate distance or near to them. They are three different mechanisms to
24
25 68 achieve this: the technology can be refractive, diffractive or combined. Moreover, toric multifocal lens
26
27 69 also help to correct the problem of astigmatism [1].
28

29 70 Traditional monofocal IOLs provide a single point of focus. A newer enhanced monofocals and
30
31 71 extended depth-of-focus (EDOF) IOLs which creates a single elongated focal point to enhance the
32
33 72 depth of focus. For the purposes of this study we will assess optical aberrations following the
34
35 73 implantation of different types of multifocal IOL and will exclude enhanced monofocal IOL as well as
36
37 74 EDOF IOLs.
38

39 75 It is generally accepted multifocal IOLs are good for distance and near focal distances. According to
40
41 76 the lens design they can be refractive, diffractive or combined. The technology of multifocal IOLs is
42
43 77 continually advancing. Next generation IOLs include rotationally asymmetric segmented multifocal IOL,
44
45 78 increase in the central area with the aim to improve reading acuity and improved pupil independence.
46
47

48 79 Optical aberrations a property of lenses that causes spreading of light over a region resulting in a blurred
49
50 80 or distorted image. Optical aberrations can present as symptoms of glare, holes and stars. This
51
52 81 symptoms may limit the patient satisfaction achieved with these IOLs and is therefore an important
53
54 82 patient-centred outcomes to quantify. Spherical aberrations significantly contribute to quality of retinal
55
56 83 image and subjective refraction. Optical aberrations can be reported subjectively using questionnaires
57
58 84 or measured objectively by wavefront aberrometry analysis. Contrast sensitivity can be a more useful/
59
60 85 objective tool to assess visual function. Recent reviews that compared multifocal with monofocal IOLs

1
2
3 86 reported outcomes on spectacle independence, visual acuity and quality of life [2, 3]. To our knowledge
4
5 87 this is the first review comparing different multifocal IOLs with optical aberrations as the primary
6
7 88 outcome.
8
9

10 89 **Review aim:** We aim to systematically review investigator measured and patient reported optical
11
12 90 aberrations following implantation of multifocal intraocular lenses during phacoemulsification surgery
13
14 91 to treat presbyopia.
15
16

17 92 **Methods and analysis**

18 19 20 93 **Inclusion and exclusion criteria**

21 22 23 94 **Types of studies**

24
25
26 95 We will include randomised controlled trials (RCTs) and non-randomised interventional studies
27
28 96 (retrospective or prospective studies). Observational studies will allow us to provide real-world
29
30 97 estimates of reported optical aberrations.
31
32

33 34 98 **Types of participants**

35
36
37 99 We will include adults undergoing cataract surgery and desiring correction for anticipated post-operative
38
39 100 presbyopia. We will exclude studies with participants with history of laser refractive surgery.
40
41

42 43 101 **Intervention(s)**

44
45
46 102 We will include small incision cataract extraction and multifocal lens implantation. All types of refractive
47
48 103 and diffractive multifocal lenses will be included in this review.
49
50

51 104 **Comparator(s)**

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53
54
55 105 We will include multifocal intraocular lens or alternative type of multifocal IOL as comparators such as
56
57 106 diffractive, refractive and hybrid technologies.
58
59

60 107 **Outcomes**

1
2
3 108 *Primary outcome*
4
5

- 6 109 • Participant reported optical aberrations such as but not limited to glare and halos.
7
8
9

10 110 *Secondary outcomes*
11
12

- 13 111 • Measured optical aberrations with wavefront analysis
14
15 112 • Contrast sensitivity as measured by validated test
16
17 113 • Spectacle independence as determined by the participant or as determined by the
18
19 114 investigator
20
21 115 • Uncorrected near vision acuity
22
23 116 • Uncorrected distance vision acuity
24
25 117 • Uncorrected intermediate distance
26
27 118 • Mean spherical equivalent within $\pm 0.5D$
28
29 119 • % of eyes seeing 20/20 or better for distance
30
31 120 • % of eyes seeing 20/40 or better for distance
32
33 121 • % of eyes seeing J2 or better for near vision
34
35 122 • YAG laser capsulotomy rates
36
37

38 123 **Search strategy**
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41 124 In collaboration with an information specialist a comprehensive search strategy will be performed using
42
43 125 a combination of controlled vocabulary and free text terms. Searches will be conducted in Ovid
44
45 126 MEDLINE, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of
46
47 127 Science, Scopus and ClinicalTrials.gov bibliographic databases. Other relevant sources will be
48
49 128 searched such as reference lists of existing systematic reviews of multifocal IOLs. Please see
50
51 129 supplementary file 1 for strategy syntax for Ovid Medline 1946 – March 2021 electronic database. We
52
53 130 will download references identified in searches (electronic database and additional searches) into
54
55 131 Endnote X9 reference management software and remove duplicate abstracts.
56
57

58 132 **Study selection**
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1
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3 133 The screening process will be undertaken using Endnote X9. Two review authors will independently
4
5 134 assess the titles and abstracts of records and exclude papers that do not meet eligibility criteria. We
6
7 135 will obtain the full text of the remaining papers, and at least two authors will assess the papers against
8
9 136 the inclusion criteria for the review to determine their eligibility for inclusion. Non-English language
10
11 137 papers will be excluded. The review authors will resolve disagreements through mediation with a third
12
13 138 reviewer.

16 139 **Data extraction**

17
18
19 140 Two review authors will extract data independently using Excel. We will pre-pilot the data extraction
20
21 141 template. We will resolve discrepancies by discussion. Two attempts will be made to contact trial
22
23 142 investigators for missing data. Data will be directly imported into Review Manager 5 (RevMan 5); and
24
25 143 the accuracy of the data import will be checked by one author.

26
27
28 144 We will collect the following information on study characteristics:

- 30 145 • Study design: parallel group RCT/within-person RCT/one or both eyes reported
- 32
33 146 • Participants: country, total number of participants, age, sex, inclusion and exclusion
34
35 147 criteria
- 36
37 148 • Intervention and comparator details: type of multifocal IOL, including number of people
38
39 149 (eyes) randomised to each group
- 40
41 150 • Primary and secondary outcomes as measured and reported in the trials
- 42
43 151 • Length of follow-up
- 44
45 152 • Date of publication
- 46
47 153 • Date multifocal IOL received market approval (FDA PMA, CE mark)
- 48
49 154 • Sample size
- 50
51 155 • Funding and conflicts of interest
- 52
53 156 • Trial registration, if available
- 54
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157 **Data synthesis**

158 We will pool data where there are at least two studies for a particular type of mIOL reporting the same
159 outcome. We will use a random-effects model in RevMan 5. But if there are fewer than three trials in a
160 comparison we will use a fixed-effect model. If there is inconsistency between individual study results
161 such that a pooled result may not be a good summary of the individual trial results — for example, the
162 effects are in different directions or $I^2 > 50\%$ and $P < 0.1$ — we will not pool the data but will describe
163 the pattern of the individual study results. If there is statistical heterogeneity we may pool the data if all
164 the effect estimates are in the same direction, such that a pooled estimate would seem to provide a
165 good summary of the individual trial results.

166 We will extract the following data from each included study for intervention and comparator groups
167 separately.

- 168 • Number of events and number of participants on which outcome data collected for
169 dichotomous variables
- 170 • Mean, standard deviation and number of participants on which outcome measured for
171 continuous variables

172 For multi-arm studies we will use data relevant to our intervention and comparator groups. If two
173 groups contain relevant data we will combine groups using the calculator within RevMan 5. If standard
174 deviation is not available we will use information from confidence intervals and P values, where
175 possible, to estimate it, using the RevMan 5 calculator [4].

176 For the primary outcome a power calculation will made using *metapower* package in R (rstudio.com)
177 to calculate the statistical power for meta-analysis based on Cohen's *d* [5]. We expect to find at least
178 10 studies with sample sizes of at least 40 participants and we anticipate considerable statistical
179 heterogeneity $I^2=50\%$, with an estimated effect size of 0.35. Based on the aforementioned parameters
180 the estimated power for a fixed effects model is 0.93 and a random effects model is 0.69.

181 **Assessment of risk of bias in included studies**

1
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3 182 Two review authors will assess independently the risk of bias using Cochrane's 'Risk of bias' tool for
4
5 183 assessing risk of bias in each included study according to the following domains selection bias,
6
7 184 performance bias, detection bias, attrition bias and selective outcome reporting bias [6]. We will resolve
8
9 185 disagreements by discussion. We will specifically consider and report on the following sources of bias.
10
11 186 We will grade each domain as low risk of bias, high risk of bias or unclear (lack of information or
12
13 187 uncertainty of potential for bias). We will attempt to contact trial investigators for clarification of
14
15 188 parameters graded as 'unclear'.
16
17

18 189 **Dealing with missing data**

19
20
21 190 If possible, we will conduct an intention-to-treat (ITT) analysis. We will use imputed data if computed by
22
23 191 the trial investigators using an appropriate method but will not impute missing data ourselves. If ITT
24
25 192 data are not available, we will do an available case analysis. This assumes that data are missing at
26
27 193 random. We will assess whether this assumption is reasonable by collecting data from each included
28
29 194 trial on the number of participants excluded or lost to follow-up and reasons for loss to follow-up by
30
31 195 treatment group, if reported.
32
33

34 196 **Assessment of heterogeneity and subgroup analysis**

35
36
37
38 197 We will examine the overall characteristics of the studies, in particular the type of participants and types
39
40 198 of interventions, to assess the extent to which the studies are similar enough to make pooling study
41
42 199 results sensible. We will look at the forest plots of study results to see how consistent the results of the
43
44 200 studies are, in particular looking at the size and direction of effects. We will calculate I^2 which is the
45
46 201 percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error.
47
48 202 We will consider I^2 values over 50% to indicate substantial inconsistency but will also consider Chi^2 P
49
50 203 value. As this may have low power when the number of studies are few we will consider $P < 0.1$ to
51
52 204 indicate statistical significance of the Chi^2 test. If there are sufficient trials we will compare the effect of
53
54 205 treatment in the following subgroups; diffractive, refractive and hybrid multifocal IOL and year of market
55
56 206 approval.
57

58 207 **Sensitivity analysis and assessment of reporting biases**

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3 208 We will examine the impact of excluding studies at high risk of bias in one or more domains. If there are
4
5 209 10 trials or more included in a meta-analysis, we will construct funnel plots and consider tests for
6
7 210 asymmetry for assessment of publication bias, according to Chapter 8 of the Cochrane Handbook for
8
9 211 Systematic Reviews of Interventions [7].

12 212 **Limitations of this study**

15 213 Bias such as lack of masking and confounding factors in the studies included will affect the certainty of
16
17 214 the estimate of effect in our study. We will aim to mitigate against this by conducting sensitivity analysis
18
19 215 by assessing the effect of excluding low quality studies. High heterogeneity amongst studies would
20
21 216 reduce the power of this review. One of the reasons for this could be the use of different tools to measure
22
23 217 the prevalence and extent of optical aberrations. Understanding whether the heterogeneity is clinical or
24
25 218 statistical will be important and, in some instances, pooling of the data in a meta-analysis may not be
26
27 219 appropriate. Publication bias could lead to overestimation of the true effect size, so clinical trial registries
28
29 220 will be searched to identify unpublished results where possible. Furthermore, industry sponsored
30
31 221 studies with conflicts of interests amongst investigators could introduce bias which would need to be
32
33 222 evaluated.

36 223 **Patient and Public Involvement**

38
39 224 Patients and public were not involved in the development of this protocol. The primary outcome of the
40
41 225 review is patient centered.

43 226 **Ethics and Dissemination** Ethics approval is not required for this review, as it will only include
44
45 227 published data. Findings will be published in a peer-reviewed journal and disseminated across
46
47 228 ophthalmic networks. We anticipate that the findings of this work will be of interest to multiple
48
49 229 stakeholders: people who have undergone cataract surgery, eye health professionals, ophthalmic
50
51 230 surgeons, device manufacturers and policy makers. It will also inform researchers to where there are
52
53 231 gaps in evidence and identify areas for future research.

56 232 **Authors contribution**

1
2
3 233 MN conceived the idea for the review. CH, MK, AA and DB drafted and revised the protocol with
4
5 234 suggestions from YB, CEHF and MN who reviewed the protocol and provided feedback on the draft.
6
7 235 DB constructed the search.
8
9

10 236 **Conflicts of interest**

11
12
13 237 The authors declare no conflict of interest.
14
15

16 238 **Funding**

17
18
19 239 CH receives support from the National Institute for Health Research CL 2020-18-009
20
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23 240 **Data sharing statement**

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26 241 No additional data is available.
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33 243 **References**

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58 262 *February 2021).* 2021.
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Appendix 1. Search strategy

Ovid Medline 1946 – March 2021

Search Lines	Search Terms	Search Results
1	exp "Optics and Photonics"/	79373
2	(optic* or photonic*).mp.	476463
3	1 or 2	518769
4	exp Refractive Errors/ or exp Refraction, Ocular/ or exp Astigmatism/ or exp Myopia/ or exp Visual Acuity/	108238
5	(aberrat* or diffract* or refract* or HOA).mp.	461904
6	4 or 5	541199
7	exp Lenses, Intraocular/	15452
8	(intraocular lens or Intra-ocular lens or intra ocular lens or IOL or IOLs or lens prosthes* or artificial lens).mp.	18494
9	7 or 8	23720
10	(multifocal or multi focal or multi-focal or bifocal or bi-focal or trifocal or tri-focal or hybrid).mp.	218357
11	3 and 6 and 9 and 10	515

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page Line
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	P1 L1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	P1 L1
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	P3 L62
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	P2 L39
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	P1 L23
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	P2 L35
Sponsor	5b	Provide name for the review funder and/or sponsor	P2 L35
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	P4 L76
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	P4 L87
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	P4 L90
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	P6 L122
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits such that it could be repeated	P6 L22

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	P6 L136
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	P6 L132
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently in duplicate), any processes for obtaining and confirming data from investigators	P6 L137
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	P6 L141
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	P5 L105
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	P8 L147
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	P7 L154
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I ² or Kendall's τ)	P7 L154
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	P9 L208
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	P7 L159
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	P9 L213
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	P9 L217

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite where available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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BMJ Open

Optical aberrations following implantation of multifocal intraocular lenses: a systematic review and meta-analysis protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-059350.R2
Article Type:	Protocol
Date Submitted by the Author:	25-Jul-2022
Complete List of Authors:	Henein, Christin; University College London Institute of Ophthalmology; NIHR Moorfields Biomedical Research Centre Fang, Clarissa E H; Manchester Royal Eye Hospital Bokre, Desta; University College London Institute of Ophthalmology Khan, Maaz; University College London Institute of Ophthalmology Adan, Ahmed; University College London Institute of Ophthalmology Bouremel, Yann; University College London Institute of Ophthalmology Nanavaty, Mayank; Sussex Eye Hospital; Brighton and Sussex Medical School
Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Surgery, Evidence based practice, Ophthalmology
Keywords:	Cataract and refractive surgery < OPHTHALMOLOGY, Ophthalmology < SURGERY, OPHTHALMOLOGY

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3 1 **Optical aberrations following implantation of multifocal intraocular lenses: a systematic review**
4 **and meta-analysis protocol**

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6
7 3 **Authors:**

8
9 4 **Christin Henein^{*1,2}, Clarissa E.H. Fang³, Desta Bokre¹, Maaz Khan¹, Ahmed Adan¹, Yann**
10 **Bouremel¹, Mayank A. Nanavaty^{4,5}**

11
12
13
14
15 7 *** Correspondence to Dr Christin Henein; c.henein@ucl.ac.uk**

16
17 8 **Affiliations**

18 9 ¹UCL, Institute of Ophthalmology, London, UK

19
20 10 ²NIHR Moorfields Biomedical Research Centre, London, UK

21 11 ³Manchester Royal Eye Hospital, Manchester, UK

22
23 12 ⁴Sussex Eye Hospital, University Hospitals Sussex NHS Foundation Trust, Eastern Road, Brighton,
24 United Kingdom. BN2 5BF

25
26 14 ⁵Brighton & Sussex Medical School, University of Sussex, Falmer, Brighton. United Kingdom. BN1
27 15 9PX

28
29
30
31
32 18 **Corresponding author***

33
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52

53 28 **Email addresses:**

54
55
56 29 c.henein@ucl.ac.uk, d.bokre@ucl.ac.uk, maaz.khan.20@ucl.ac.uk, ahmed.adan.20@ucl.ac.uk,
57 30 y.bouremel@ucl.ac.uk, fangclarissa@gmail.com, mayank.nanavaty@nhs.net

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For peer review only

32

Abstract

Introduction: Multifocal IOLs are used to restore vision at different focal distances. The technology of multifocal IOLs is continually advancing. Optical aberrations a property of lenses that causes spreading of light over a region resulting in a blurred or distorted image. This study aims to systematically review investigator measured and patient reported optical aberrations following implantation of multifocal intraocular lenses during phacoemulsification surgery to treat presbyopia in adults.

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Ethics and Dissemination Ethics approval is not required for this review, as it will only include published data. Findings will be published in a peer-reviewed journal and disseminated across ophthalmic networks. We anticipate that the findings of this work will be of interest to multiple stakeholders: people who have undergone cataract surgery, eye health professionals, ophthalmic surgeons, device manufacturers and policy makers. It will also inform researchers to where there are gaps in evidence and identify areas for future research.

Systematic review registration number: PROSPERO CRD42021271050

Keywords: Optics, aberration, intraocular lens, multifocal

Article Summary

61 **Strengths and Limitations**

- 62 • This systematic review protocol follows the Preferred Reporting Items for Systematic
63 Review and Meta-Analysis Protocols guidelines.
- 64 • This systematic review addresses a gap in the current evidence-base by providing a
65 comprehensive assessment of reported optical aberrations following new and older
66 generation multifocal IOL
- 67 • There may be a paucity of RCTs comparing different multifocal IOLs limiting the number of
68 paired wise meta-analysis that can be done.

69
70 **Word count:** 1507

71 72 **Introduction**

73 Multifocal intraocular lens (IOLs) have multiple focal lengths; if they have 2 foci, they are called
74 bifocal, three foci, they are trifocal. This enables the patient with a multifocal IOL to see both objects
75 located at a distance, intermediate distance or near to them. They are three different mechanisms to
76 achieve this: the technology can be refractive, diffractive or combined. Moreover, toric multifocal lens
77 also help to correct the problem of astigmatism [1].

78 Traditional monofocal IOLs provide a single point of focus. A newer enhanced monofocals and
79 extended depth-of-focus (EDOF) IOLs which creates a single elongated focal point to enhance the
80 depth of focus. For the purposes of this study we will assess optical aberrations following the
81 implantation of different types of multifocal IOL and will exclude enhanced monofocal IOL as a well as
82 EDOF IOLs.

83 It is generally accepted multifocal IOLS are good for distance and near focal distances. According to
84 the lens design they can be refractive, diffractive or combined. The technology of multifocal IOLs is
85 continually advancing. Next generation IOLs include rotationally asymmetric segmented multifocal IOL,
86 increase in the central area with the aim to improve reading acuity and improved pupil independence.

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2
3 87 Optical aberrations a property of lenses that causes spreading of light over a region resulting in a blurred
4
5 88 or distorted image. Optical aberrations can present as symptoms of glare, holes and stars. This
6
7 89 symptoms may limit the patient satisfaction achieved with these IOLs and is therefore an important
8
9 90 patient-centred outcomes to quantify. Spherical aberrations significantly contribute to quality of retinal
10
11 91 image and subjective refraction. Optical aberrations can be reported subjectively using questionnaires
12
13 92 or measured objectively by wavefront aberrometry analysis. Contrast sensitivity can be a more useful/
14
15 93 objective tool to assess visual function. Recent reviews that compared multifocal with monofocal IOLs
16
17 94 reported outcomes on spectacle independence, visual acuity and quality of life [2, 3]. To our knowledge
18
19 95 this is the first review comparing different multifocal IOLs with optical aberrations as the primary
20
21 96 outcome.

22
23 97 **Review aim:** We aim to systematically review investigator measured and patient reported optical
24
25 98 aberrations following implantation of multifocal intraocular lenses during phacoemulsification surgery
26
27 99 to treat presbyopia.

30 100 **Methods and analysis**

33 101 **Inclusion and exclusion criteria**

36 102 **Types of studies**

37
38
39
40 103 We will include randomised controlled trials (RCTs) and non-randomised interventional studies
41
42 104 (retrospective or prospective studies). Observational studies will allow us to provide real-world
43
44 105 estimates of reported optical aberrations.

46 106 **Types of participants**

47
48
49
50
51 107 We will include adults undergoing cataract surgery and desiring correction for anticipated post-operative
52
53 108 presbyopia. We will exclude studies with participants with history of laser refractive surgery.

54 55 56 109 **Intervention(s)**

1
2
3 110 We will include small incision cataract extraction and multifocal lens implantation. All types of refractive
4
5 111 and diffractive multifocal lenses will be included in this review.
6
7

8 112 **Comparator(s)**
9

10
11
12 113 We will include multifocal intraocular lens or alternative type of multifocal IOL as comparators such as
13
14 114 diffractive, refractive and hybrid technologies.
15

16
17 115 **Outcomes**
18

19
20 116 *Primary outcome*
21

- 22
23
24 117 • Participant reported optical aberrations such as but not limited to glare and halos.
25
26

27 118 *Secondary outcomes*
28

- 29
30 119 • Measured optical aberrations with wavefront analysis
31
32 120 • Contrast sensitivity as measured by validated test
33
34 121 • Spectacle independence as determined by the participant or as determined by the
35
36 122 investigator
37
38 123 • Uncorrected near vision acuity
39
40 124 • Uncorrected distance vision acuity
41
42 125 • Uncorrected intermediate distance
43
44 126 • Mean spherical equivalent within $\pm 0.5D$
45
46 127 • % of eyes seeing 20/20 or better for distance
47
48 128 • % of eyes seeing 20/40 or better for distance
49
50 129 • % of eyes seeing J2 or better for near vision
51
52 130 • YAG laser capsulotomy rates
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55 131 **Search strategy**
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3 132 In collaboration with an information specialist a comprehensive search strategy will be performed using
4
5 133 a combination of controlled vocabulary and free text terms. Searches will be conducted in Ovid
6
7 134 MEDLINE, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of
8
9 135 Science, Scopus and ClinicalTrials.gov bibliographic databases. Other relevant sources will be
10
11 136 searched such as reference lists of existing systematic reviews of multifocal IOLs. Please see
12
13 137 supplementary file 1 for strategy syntax for Ovid Medline 1946 – March 2021 electronic database. We
14
15 138 will download references identified in searches (electronic database and additional searches) into
16
17 139 Endnote X9 reference management software and remove duplicate abstracts.

140 **Study selection**

141 The screening process will be undertaken using Endnote X9. Two review authors will independently
142 assess the titles and abstracts of records and exclude papers that do not meet eligibility criteria. We
143 will obtain the full text of the remaining papers, and at least two authors will assess the papers against
144 the inclusion criteria for the review to determine their eligibility for inclusion. Non-English language
145 papers will be excluded. The review authors will resolve disagreements through mediation with a third
146 reviewer.

147 **Data extraction**

148 Two review authors will extract data independently using Excel. We will pre-pilot the data extraction
149 template. We will resolve discrepancies by discussion. Two attempts will be made to contact trial
150 investigators for missing data. Data will be directly imported into Review Manager 5 (RevMan 5); and
151 the accuracy of the data import will be checked by one author.

152 We will collect the following information on study characteristics:

- 153 • Study design: parallel group RCT/within-person RCT/one or both eyes reported
- 154 • Participants: country, total number of participants, age, sex, inclusion and exclusion
155 criteria
- 156 • Intervention and comparator details: type of multifocal IOL, including number of people
157 (eyes) randomised to each group

- 1
2
3 158 • Primary and secondary outcomes as measured and reported in the trials
4
5
6 159 • Length of follow-up
7
8 160 • Date of publication
9
10
11 161 • Date multifocal IOL received market approval (FDA PMA, CE mark)
12
13 162 • Sample size
14
15
16 163 • Funding and conflicts of interest
17
18
19 164 • Trial registration, if available
20
21

22 165 **Data synthesis**
23
24

25 166 We will pool data where there are at least two studies for a particular type of mIOL reporting the same
26 167 outcome. We will use a random-effects model in RevMan 5. But if there are fewer than three trials in a
27 168 comparison we will use a fixed-effect model. If there is inconsistency between individual study results
28 169 such that a pooled result may not be a good summary of the individual trial results — for example, the
29 170 effects are in different directions or $I^2 > 50\%$ and $P < 0.1$ — we will not pool the data but will describe
30 171 the pattern of the individual study results. If there is statistical heterogeneity we may pool the data if all
31 172 the effect estimates are in the same direction, such that a pooled estimate would seem to provide a
32 173 good summary of the individual trial results.
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42 174 We will extract the following data from each included study for intervention and comparator groups
43 175 separately.
44
45

- 46 176 • Number of events and number of participants on which outcome data collected for
47 177 dichotomous variables
48
49
50
51 178 • Mean, standard deviation and number of participants on which outcome measured for
52 179 continuous variables
53
54

55 180 For multi-arm studies we will use data relevant to our intervention and comparator groups. If two
56 181 groups contain relevant data we will combine groups using the calculator within RevMan 5. If standard
57
58
59
60

1
2
3 182 deviation is not available we will use information from confidence intervals and P values, where
4
5 183 possible, to estimate it, using the RevMan 5 calculator [4].
6

7 184 For the primary outcome a power calculation will made using *metapower* package in R (rstudio.com)
8
9 185 to calculate the statistical power for meta-analysis based on Cohen's *d* [5]. We expect to find at least
10
11 186 10 studies with sample sizes of at least 40 participants and we anticipate considerable statistical
12
13 187 heterogeneity $I^2=50\%$, with an estimated effect size of 0.35. Based on the aforementioned parameters
14
15 188 the estimated power for a fixed effects model is 0.93 and a random effects model is 0.69.
16

17 18 19 189 **Assessment of risk of bias in included studies**

20
21
22 190 Two review authors will assess independently the risk of bias using Cochrane's 'Risk of bias' tool for
23
24 191 assessing risk of bias in each included study according to the following domains selection bias,
25
26 192 performance bias, detection bias, attrition bias and selective outcome reporting bias [6]. We will resolve
27
28 193 disagreements by discussion. We will specifically consider and report on the following sources of bias.
29
30 194 We will grade each domain as low risk of bias, high risk of bias or unclear (lack of information or
31
32 195 uncertainty of potential for bias). We will attempt to contact trial investigators for clarification of
33
34 196 parameters graded as 'unclear'.
35

36 37 197 **Dealing with missing data**

38
39
40 198 If possible, we will conduct an intention-to-treat (ITT) analysis. We will use imputed data if computed by
41
42 199 the trial investigators using an appropriate method but will not impute missing data ourselves. If ITT
43
44 200 data are not available, we will do an available case analysis. This assumes that data are missing at
45
46 201 random. We will assess whether this assumption is reasonable by collecting data from each included
47
48 202 trial on the number of participants excluded or lost to follow-up and reasons for loss to follow-up by
49
50 203 treatment group, if reported.
51

52 53 204 **Assessment of heterogeneity and subgroup analysis**

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55
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57 205 We will examine the overall characteristics of the studies, in particular the type of participants and types
58
59 206 of interventions, to assess the extent to which the studies are similar enough to make pooling study
60

1
2
3 207 results sensible. We will look at the forest plots of study results to see how consistent the results of the
4
5 208 studies are, in particular looking at the size and direction of effects. We will calculate I^2 which is the
6
7 209 percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error.
8
9 210 We will consider I^2 values over 50% to indicate substantial inconsistency but will also consider Chi^2 P
10
11 211 value. As this may have low power when the number of studies are few we will consider $P < 0.1$ to
12
13 212 indicate statistical significance of the Chi^2 test. If there are sufficient trials we will compare the effect of
14
15 213 treatment in the following subgroups; diffractive, refractive and hybrid multifocal IOL and year of market
16
17 214 approval.

20 215 **Sensitivity analysis and assessment of reporting biases**

21
22
23 216 We will examine the impact of excluding studies at high risk of bias in one or more domains. If there are
24
25 217 10 trials or more included in a meta-analysis, we will construct funnel plots and consider tests for
26
27 218 asymmetry for assessment of publication bias, according to Chapter 8 of the Cochrane Handbook for
28
29 219 Systematic Reviews of Interventions [7].

32 220 **Limitations of this study**

33
34
35
36 221 Bias such as lack of masking and confounding factors in the studies included will affect the certainty of
37
38 222 the estimate of effect in our study. We will aim to mitigate against this by conducting sensitivity analysis
39
40 223 by assessing the effect of excluding low quality studies. High heterogeneity amongst studies would
41
42 224 reduce the power of this review. One of the reasons for this could be the use of different tools to measure
43
44 225 the prevalence and extent of optical aberrations. Understanding whether the heterogeneity is clinical or
45
46 226 statistical will be important and, in some instances, pooling of the data in a meta-analysis may not be
47
48 227 appropriate. Publication bias could lead to overestimation of the true effect size, so clinical trial registries
49
50 228 will be searched to identify unpublished results where possible. Furthermore, industry sponsored
51
52 229 studies with conflicts of interests amongst investigators could introduce bias which would need to be
53
54 230 evaluated.

56 231 **Patient and Public Involvement**

232 Patients and public were not involved in the development of this protocol. The primary outcome of the
233 review is patient centered.

234 **Ethics and Dissemination** Ethics approval is not required for this review, as it will only include
235 published data. Findings will be published in a peer-reviewed journal and disseminated across
236 ophthalmic networks. We anticipate that the findings of this work will be of interest to multiple
237 stakeholders: people who have undergone cataract surgery, eye health professionals, ophthalmic
238 surgeons, device manufacturers and policy makers. It will also inform researchers to where there are
239 gaps in evidence and identify areas for future research.

240 **Authors contribution**

241 MN conceived the idea for the review. CH, MK, AA and DB drafted and revised the protocol with
242 suggestions from YB, CEHF and MN who reviewed the protocol and provided feedback on the draft.
243 DB constructed the search.

244 **Conflicts of interest**

245 The authors declare no conflict of interest.

246 **Funding**

247 CH receives support from the National Institute for Health Research CL 2020-18-009

248 **Data sharing statement**

249 No additional data is available.

250

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Ovid Medline

Search Lines	Search Terms
1	exp "Optics and Photonics"/
2	(optic* or photonic*).mp.
3	1 or 2
4	exp Refractive Errors/ or exp Refraction, Ocular/ or exp Astigmatism/ or exp Myopia/ or exp Visual Acuity/
5	(aberrat* or diffract* or refract* or HOA).mp.
6	4 or 5
7	exp Lenses, Intraocular/
8	(intraocular lens or Intra-ocular lens or intra ocular lens or IOL or IOLs or lens prosthes* or artificial lens).mp.
9	7 or 8
10	(multifocal or multi focal or multi-focal or bifocal or bi-focal or trifocal or tri-focal or hybrid).mp.
11	3 and 6 and 9 and 10

Ovid Embase

Search Lines	Search Terms
1	exp optics/
2	(optic* or photonic*).mp
3	1 or 2
4	exp eye refraction/
5	(aberrat* or diffract* or refract* or HOA).mp
6	4 or 5
7	exp lens implant/
8	(intraocular lens or Intra-ocular lens or intra ocular lens or IOL or IOLs or lens prosthes* or artificial lens).mp.
9	7 or 8
10	(multifocal or multi focal or multi-focal or bifocal or bi-focal or trifocal or tri-focal or hybrid).mp
11	3 and 6 and 9 and 10

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page Line
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	P1 L1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	P1 L1
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	P3 L62
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	P2 L39
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	P1 L23
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	P2 L35
Sponsor	5b	Provide name for the review funder and/or sponsor	P2 L35
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	P4 L76
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	P4 L87
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	P4 L90
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	P6 L122
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits such that it could be repeated	P6 L22

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	P6 L136
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	P6 L132
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently in duplicate), any processes for obtaining and confirming data from investigators	P6 L137
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	P6 L141
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	P5 L105
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	P8 L147
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	P7 L154
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I ² or Kendall's τ)	P7 L154
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	P9 L208
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	P7 L159
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	P9 L213
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	P9 L217

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite where available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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