Evidence Brief: Intracameral Moxifloxacin For Preventing Endophthalmitis

Supplemental Materials

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APPENDIX A: SEARCH STRATEGY

SYSTEMATIC REVIEWS

Search for current systematic reviews (limited to last 7 years) **Date Searched: 01-31-22**			
A. Bibliographic Databases:	**#**	**Search Statement**	**Results**
MEDLINE: Systematic Reviews Ovid MEDLINE(R) ALL 1946 to January 28, 2022	1	exp Cataract Extraction/ OR Phacoemulsification/ OR ((cataract adj1 (surger* OR extraction)) OR capsulorhexis OR phacoemulsification$1).ti,ab.	45041
	2	Moxifloxacin/ OR (Avelox OR Moxeza OR Vigamox OR moxifloxacin).ti,ab.	5574
	3	1 AND 2	201
	4	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.	498160
	5	3 AND 4	6
	6	limit 5 to english language	6
CDSR: Protocols and Reviews	1	(Cataract Extraction OR Phacoemulsification).kw. OR ((cataract adj1 (surger* OR extraction)) OR capsulorhexis OR phacoemulsification$1).ti,ab.	55

EBM Reviews - Cochrane Database of Systematic Reviews 2005 to January 26, 2022	2	Moxifloxacin.kw. OR (Avelox OR Moxeza OR Vigamox OR moxifloxacin).ti,ab.	6
	3	1 AND 2	0

Search for current systematic reviews (limited to last 7 years) **Date Searched: 01-31-22**		
B. Non-bibliographic databases	**Evidence**	**Results**
AHRQ: evidence reports, technology assessments, U.S Preventative Services Task Force Evidence Synthesis	http://www.ahrq.gov/research/findings/evidence-based-reports/search.html Search: moxifloxacin; cataract surgery	0
CADTH	https://www.cadth.ca Search: moxifloxacin; cataract surgery	0
ECRI Institute	https://guidelines.ecri.org/ Search: moxifloxacin; cataract surgery	0
HTA: Health Technology Assessments (UP TO 2016)	http://www.ohsu.edu/xd/education/library/ See CDSR search above	0
NHS Evidence	http://www.evidence.nhs.uk/default.aspx Search: moxifloxacin; cataract surgery NIHR Alert: Antibiotics by injection into the eye can prevent severe infection following cataract surgery. 2017. NIHR Evidence. https://evidence.nihr.ac.uk/alert/antibiotics-by-injection-into-the-eye-can-prevent-severe-infection-following-cataract-surgery/	1
EPPI-Centre	http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=62 Use browser search function [CNTL + F] for keyword search Search: moxifloxacin; cataract surgery	0
NLM	http://www.ncbi.nlm.nih.gov/books Search: moxifloxacin; cataract surgery	0
VA Products - VATAP, PBM and HSR&D publications	A. http://www.hsrd.research.va.gov/research/default.cfm B. http://www.research.va.gov/research_topics/	0

	C. https://va.dimensions.ai/discover/publication Search: moxifloxacin; cataract surgery	

PRIMARY STUDIES

Search for primary literature **Date searched: 02-04-22**		
MEDLINE [Ovid MEDLINE(R) ALL 1946 to February 03, 2022]		
#	**Search Statement**	**Results**
1	exp Cataract Extraction/ OR Phacoemulsification/ OR ((cataract adj1 (surger* OR extraction)) OR capsulorhexis OR phacoemulsification$1 OR (ophthalmologic surgical procedure) OR ophthalmic surger*).ti,ab.	46325
2	Moxifloxacin/ OR (Avelox OR Moxeza OR Vigamox OR moxifloxacin).ti,ab.	5579
3	1 AND 2	205
4	limit 3 to 2016 and English language	114
CINAHL		
#	**Search Statement**	**Results**
1	(MH "Cataract Extraction+") OR (MH "Phacoemulsification")	8548
2	TI (((cataract N1 (surger* OR extraction)) OR capsulorhexis OR phacoemulsification$1 OR (ophthalmologic surgical procedure) OR ophthalmic surger*)) OR AB (((cataract N1 (surger* OR extraction)) OR capsulorhexis OR phacoemulsification$1 OR (ophthalmologic surgical procedure) OR ophthalmic surger*))	5558
3	1 OR 2	9933
4	TI (Avelox OR Moxeza OR Vigamox OR moxifloxacin) OR AB (Avelox OR Moxeza OR Vigamox OR moxifloxacin)	978
5	3 AND 4	58
6	limit 5 to 2016 and English language	37

APPENDIX B: EXCLUDED STUDIES

Exclude reasons: 1=Ineligible population, 2=Ineligible intervention, 3=Ineligible comparator, 4=Ineligible outcome, 5=Ineligible timing, 6=Ineligible study design, 7=Ineligible publication type, 8=Outdated or ineligible systematic review, 9=Non-English language, 10=Unable to locate.

Citation	Exclude Reason
Anijeet DR, Palimar P, Peckar CO. Intracameral vancomycin following cataract surgery: An eleven-year study. *Clin Ophthalmol.* 2010;4:321-326.	E2
Arbisser LB. Safety of intracameral moxifloxacin for prophylaxis of endophthalmitis after cataract surgery. *J Cataract Refract Surg.* 2008;34(7):1114-1120.	E4
Arshinoff SA, Modabber M. Dose and administration of intracameral moxifloxacin for prophylaxis of postoperative endophthalmitis. *Journal of Cataract & Refractive Surgery.* 2016;42(12):1730-1741.	E3
Arslan OS, Arici C, Unal M, Cicik E, Mangan MS, Atalay E. Safety of prophylactic intracameral moxifloxacin ophthalmic solution after cataract surgery in patients with penetrating keratoplasty. *Int J Ophthalmol.* 2014;7(5):795-799.	E3
Asencio MA, Huertas M, Carranza R, Tenias JM, Celis J, Gonzalez-del Valle F. Impact of changes in antibiotic prophylaxis on postoperative endophthalmitis in a Spanish hospital. *Ophthalmic Epidemiol.* 2014;21(1):45-50.	E2
Ashraf B, Elkhouly S, Nematalla EH, Mostafa A. Safety of Prophylactic Intracameral Moxifloxacin Injection after Uncomplicated Phacoemulsification Surgery. Egyptian Journal of Ophthalmology,(Mansoura Ophthalmic Center). 2022:46-54.	E4
Au CP, White AJ, Healey PR. Efficacy and cost-effectiveness of intracameral vancomycin in reducing postoperative endophthalmitis incidence in Australia. *Clin Exp Ophthalmol.* 2016;44(9):803-811.	E2
Barreau G, Mounier M, Marin B, Adenis JP, Robert PY. Intracameral cefuroxime injection at the end of cataract surgery to reduce the incidence of endophthalmitis: French study. *J Cataract Refract Surg.* 2012;38(8):1370-1375.	E2
Beselga D, Campos A, Castro M, et al. Postcataract surgery endophthalmitis after introduction of the ESCRS protocol: a 5-year study. *Eur J Ophthalmol.* 2014;24(4):516-519.	E2
Cavalcanti Lira RP, Lucena NP, Ferreira KS, Santos BM. Long-term safety of intracameral moxifloxacin after cataract surgery. *Journal of Cataract & Refractive Surgery.* 2017;43(1):139-140.	E4
Colleaux KM, Hamilton WK. Effect of prophylactic antibiotics and incision type on the incidence of endophthalmitis after cataract surgery. *Can J Ophthalmol.* 2000;35(7):373-378.	E2
Coskun M, Altintas AG, Anayol MA, Raza S, Celikbilek N, Simsek S. Evaluation of efficacy of topical povidone-iodine and different types of fluoroquinolones in the sterilization of bacterial flora on the conjunctiva. *J Ocul Pharmacol Ther.* 2011;27(6):589-592.	E2
Espiritu CR, Caparas VL, Bolinao JG. Safety of prophylactic intracameral moxifloxacin 0.5% ophthalmic solution in cataract surgery patients. *J Cataract Refract Surg.* 2007;33(1):63-68.	E3

Citation	Exclude Reason
Feijo ED. Intracameral moxifloxacin after cataract surgery: a prospective study. Response: Intracameral moxifloxacin after cataract surgery: a prospective study. Long-term safety of intracameral moxifloxacin after cataract surgery Intracameral antibiotics during cataract surgery: evidence and barriers. *Arquivos Brasileiros de Oftalmologia.* 2018;81(5):455-456.	E7
Ferreira BG, Cardoso da Silva I, Melega MV, et al. Macular and choroidal thickness after intracameral moxifloxacin for prevention of postcataract endophthalmitis. *Journal of Cataract & Refractive Surgery.* 2021;47(1):40-45.	E4
Group EES. Prophylaxis of postoperative endophthalmitis following cataract surgery: Results of the ESCRS multicenter study and identification of risk factors. *Journal of Cataract & Refractive Surgery.* 2007;33(6):978-988.	E2
Grzybowski A, Koerner JC, George MJ. Postoperative endophthalmitis after cataract surgery: a worldwide review of etiology, incidence and the most studied prophylaxis measures. *Expert Review of Ophthalmology.* 2019;14(4/5):247-257.	E7
Guttman Krader C. Clinical trial suggests safety of unpreserved levofloxacin: Intracameral injection of cefuroxime, moxil oxacin decrease risk of endophthalmitis. *Ophthalmology Times.* 2019;44(11):14-14.	E10
Halachmi-Eyal O, Lang Y, Keness Y, Miron D. Preoperative topical moxifloxacin 0.5% and povidone-iodine 5.0% versus povidone-iodine 5.0% alone to reduce bacterial colonization in the conjunctival sac. *J Cataract Refract Surg.* 2009;35(12):2109-2114.	E2
He L, Ta CN, Hu N, Sinnar S, Miño de Kaspar H. Prospective randomized comparison of 1-day and 3-day application of topical 0.5% moxifloxacin in eliminating preoperative conjunctival bacteria. *J Ocul Pharmacol Ther.* 2009;25(4):373-378.	E2
Inoue Y, Usui M, Ohashi Y, Shiota H, Yamazaki T. Preoperative disinfection of the conjunctival sac with antibiotics and iodine compounds: a prospective randomized multicenter study. *Jpn J Ophthalmol.* 2008;52(3):151-161.	E2
Jabbarvand M, Hashemian H, Khodaparast M, Jouhari M, Tabatabaei A, Rezaei S. Endophthalmitis Occurring after Cataract Surgery: Outcomes of More Than 480 000 Cataract Surgeries, Epidemiologic Features, and Risk Factors. *Ophthalmology.* 2016;123(2):295-301.	E7
Li A, Shao J, Gans R, Bena J, Goshe J. Postoperative Endophthalmitis Before and After Preferred Utilization of Prophylactic Intracameral Antibiotics for Phacoemulsification Cataract Surgeries at Cole Eye Institute. *Eye & Contact Lens: Science & Clinical Practice.* 2019;45(5):306-309.	E2
Li B, Miño de Kaspar H, Haritoglou C, et al. Comparison of 1-day versus 1-hour application of topical neomycin/polymyxin-B before cataract surgery. *J Cataract Refract Surg.* 2015;41(4):724-731.	E2
Linnehan R. Triamcinolone-moxifloxacin stabilizes macular thickness after cataract surgery in DR. *Ocular Surgery News.* 2020;38(19):18-18.	E2
Linnehan R. Optimal dose, concentration of moxifloxacin needed to prevent endophthalmitis. *Ocular Surgery News.* 2021;39(8):15-15.	E7
Lucena NP, Pereira IMS, Gaete MIL, Ferreira KSA, Melega MV, Lira RPC. Intracameral moxifloxacin after cataract surgery: a prospective study. *Arquivos Brasileiros de Oftalmologia.* 2018;81(2):92-94.	E3

Citation	Exclude Reason
Mamalis N. Reducing the risk of endophthalmitis. *Journal of Cataract & Refractive Surgery.* 2019;45(9):1217-1218.	E7
Miño de Kaspar H, Kreutzer TC, Aguirre-Romo I, et al. A prospective randomized study to determine the efficacy of preoperative topical levofloxacin in reducing conjunctival bacterial flora. *Am J Ophthalmol.* 2008;145(1):136-142.	E2
Mitchell W, Tom L, Durai I, et al. The Effectiveness of Intracameral Moxifloxacin Endophthalmitis Prophylaxis for Trabeculectomy. *Ophthalmology Glaucoma.* 2021;4(1):11-19.	E1
Moss JM, Nguyen D, Liu YI, et al. Comparison of one-day versus one-hour application of topical gatifloxacin in eliminating conjunctival bacterial flora. *Ophthalmology.* 2008;115(11):2013-2016.	E2
Myneni J, Desai SP, Jayamanne DG. Reduction in postoperative endophthalmitis with intracameral cefuroxime. *J Hosp Infect.* 2013;84(4):326-328.	E2
Patel SB, Reddy NK, He YG. Toxic Posterior Segment Syndrome after Dropless Cataract Surgery with Compounded Triamcinolone-Moxifloxacin. *Retina.* 2020;40(3):446-455.	E3
Rahman N, Murphy CC. Impact of intracameral cefuroxime on the incidence of postoperative endophthalmitis following cataract surgery in Ireland. *Ir J Med Sci.* 2015;184(2):395-398.	E2
Rathi V, Sharma S, Das T, Khanna R, Rathi VM, Khanna RC. Endophthalmitis Prophylaxis Study, Report 2: Intracameral antibiotic prophylaxis with or without postoperative topical antibiotic in cataract surgery. *Indian Journal of Ophthalmology.* 2020;68(11):2451-2455.	E2
Röck T, Bramkamp M, Bartz-Schmidt K, et al. Using intracameral cefuroxime reduces postoperative endophthalmitis rate: 5 years experience at the University Eye Hospital Tübingen. *Klinische Monatsblatter fur Augenheilkunde.* 2014;231(10):1023-1028.	E9
Rudnisky CJ, Wan D, Weis E. Antibiotic choice for the prophylaxis of post-cataract extraction endophthalmitis. *Ophthalmology.* 2014;121(4):835-841.	E2
Rush SW, Vu D, Rush RB. The Safety and Efficacy of Routine Administration of Intracameral Vancomycin during Cataract Surgery. *J Ophthalmol.* 2015;2015:813697.	E2
Sharma S, Sahu SK, Dhillon V, Das S, Rath S. Reevaluating intracameral cefuroxime as a prophylaxis against endophthalmitis after cataract surgery in India. *J Cataract Refract Surg.* 2015;41(2):393-399.	E2
Shorstein NH, Winthrop KL, Herrinton LJ. Decreased postoperative endophthalmitis rate after institution of intracameral antibiotics in a Northern California eye department. *J Cataract Refract Surg.* 2013;39(1):8-14.	E2
Ta CN, Chan I, Dhatt HS, et al. Prospective comparison of topical moxifloxacin in eliminating conjunctival bacterial flora following a one-day or one-hour application. *J Ocul Pharmacol Ther.* 2008;24(4):427-431.	E2
Ta CN, Egbert PR, Singh K, Shriver EM, Blumenkranz MS, Miño De Kaspar H. Prospective randomized comparison of 3-day versus 1-hour preoperative ofloxacin prophylaxis for cataract surgery. *Ophthalmology.* 2002;109(11):2036-2040; discussion 2040-2031.	E2

Citation	Exclude Reason
Ta CN, Sinnar S, He L, Myung D, Miño De Kaspar H. Prospective randomized comparison of 1-day versus 3-day application of topical levofloxacin in eliminating conjunctival flora. *Eur J Ophthalmol.* 2007;17(5):689-695.	E2
Tan CS, Wong HK, Yang FP. Epidemiology of postoperative endophthalmitis in an Asian population: 11-year incidence and effect of intracameral antibiotic agents. *J Cataract Refract Surg.* 2012;38(3):425-430.	E2
Vidyadevi M, Anuradha A, Rashmi G, Shilpa R, Nishath S. Safety of Fixed drug Combination in Post -Operative Cataract Patients, at Tertiary Care Centre - In South India. *Nepalese Journal of Ophthalmology : A Biannual Peer-reviewed Academic Journal of the Nepal Ophthalmic Society : NEPJOPH.* 2017;9(18):24-29.	E2
Yu-Wai-Man P, Morgan SJ, Hildreth AJ, Steel DH, Allen D. Efficacy of intracameral and subconjunctival cefuroxime in preventing endophthalmitis after cataract surgery. *Journal of Cataract & Refractive Surgery.* 2008;34(3):447-451.	E2

APPENDIX C: EVIDENCE TABLES

CHARACTERISTICS OF INCLUDED PRIMARY STUDIES

Author Year N	Study Design Country	Surgery Type Outcome Timing	Moxifloxacin Concentration and Preparation	Pre- and Postoperative Interventions	Comparator
Arshinoff, 2011[1] N=104,914	Retrospective cohort Global	PE NR	Variable across surgical centers (0.1 to 0.5 mg/01. to 0.2 mL)	Variable	No IC antibiotic or IC cefuroxime
Bhatta, 2021[2] N=11,983	Retrospective cohort Nepal	PE or MSICS 6 weeks	0.5 mg in 0.1 mL direct from vial	Preoperative: 5% PI Postoperative: gentamycin and dexamethasone injection, topical ofloxacin (1 month), topical steroid (prednisone or dexamethasone) (1–2 weeks)	No IC antibiotic
Cetinkaya, 2015[3] N=65	Retrospective cohort Turkey	PE 52.1 weeks	0.1 mL of undiluted 0.5% MOX	Preoperative: 0.5% topical MOX, 10% PI Postoperative: topical MOX 0.5% (1 week) and topical steroid (1 month)	No IC antibiotic
Dave, 2022[4] N=66,967	Retrospective cohort India	PE, MSICS, or ECCE 6 weeks	0.5 mg MOX in 0.1 mL	Preoperative: 5% PI Postoperative: Topical corticosteroid (1 month) and topical antibiotic (1 week)	No IC antibiotic
Ekinci, 2012[5] N=60	Retrospective cohort Turkey	PE 0.43 weeks	0.1 mL of undiluted 0.5% MOX	Preoperative: 5–10% PI Postoperative: 5% PI, topical MOX (5 days until bottle empty), topical prednisolone (3 weeks)	No IC antibiotic

Author Year N	Study Design Country	Surgery Type Outcome Timing	Moxifloxacin Concentration and Preparation	Pre- and Postoperative Interventions	Comparator
Frilling, 2013[6] N=464,755	Retrospective cohort Sweden	PE or "other" 4 weeks	Variable across surgical centers	Variable	No IC antibiotic or IC cefuroxime
Galvis, 2014[7] N=2,674	Retrospective cohort Columbia	PE 2 weeks	0.05 mL of undiluted MOX 0.5%	Preoperative: fluoroquinolone, 5–10% PI Postoperative: fluoroquinolone (8–10 days)	No IC antibiotic
Haripriya, 2016[8] N=75,937	Retrospective cohort India	PE, MSICS, or ECCE 6 weeks	0.5 mg in 0.1 mL or 0.5% MOX	Preoperative: topical ofloxacin, PI Postoperative: topical ofloxacin (15 days), topical gatifloxacin and dexamethasone (42 days)	No IC antibiotic
Haripriya, 2017[9] N=617,453	Retrospective cohort India	PE, MSICS, or ECCE 6 weeks	0.5 mg in 0.1 mL or 0.5% MOX	Preoperative: topical ofloxacin, PI Postoperative: topical ofloxacin (15 days), topical gatifloxacin and dexamethasone (4–6 weeks)	No IC antibiotic
Haripriya, 2019[10] N=2,062,643	Retrospective cohort India	PE, MSICS, or ECCE 6 weeks	0.5 mg in 0.1 mL or 0.5% MOX	Preoperative: topical ofloxacin, PI Postoperative: topical ofloxacin (15 days), topical gatifloxacin and dexamethasone (4–6 weeks)	No IC antibiotic
Herrinton, 2016[11] N=294,649	Retrospective cohort USA	PE 12.9 weeks	NR	NR	Topical antibiotics or IC Cefuroxime

Author Year N	Study Design Country	Surgery Type Outcome Timing	Moxifloxacin Concentration and Preparation	Pre- and Postoperative Interventions	Comparator
Lane, 2008[12] N=57	RCT USA	PE 12.9 weeks	0.25 mg in 0.05 mL of undiluted 0.5% MOX	Preoperative: Topical MOX 0.5%, PI Postoperative: Topical MOX 0.5% (1 week), topical prednisolone acetate (1 month), topical nepafenac (1 month)	Salt solution injection
Matsuura, 2013[13] N=34,755	Retrospective cohort Japan	PE 4.3 weeks	Varied among institutions: 0.05 mg/mL to 0.5 mg/mL MOX	NR	No IC antibiotic
Matsuura, 2014[14] N=138	Retrospective cohort Japan	PE 12.9 weeks	0.15 mg/mL to 0.5 mg/mL of 0.5% MOX	Preoperative: topical levofloxacin, 10% PI plus iodine irrigation Postoperative: topical MOX, topical betamethasone sodium phosphate, and topical bromfenac (1 month)	Salt solution irrigation
Melega, 2019[15] N=3,640	RCT Brazil	PE 6 weeks	0.15 mg in 0.03 mL of undiluted 0.5% MOX	Preoperative: 10% PI Postoperative: 0.5% MOX and 0.1% dexamethasone eyedrops (1 week)	No IC antibiotic
Porwal, 2021[16] N=40392	Retrospective cohort India	MSICS NR	NR	NR	No IC antibiotic
Rathi, 2021[17] N=42,466	Prospective cohort India	PE or MSICS 11 weeks	0.1 mL of MOX at 0.5% weight/volume direct from vial	Preoperative: 5% PI Postoperative: Topical corticosteroids (4-6 weeks). Topical antibiotic prescribed at discretion of surgeon.	IC Cefuroxime

Author Year N	Study Design Country	Surgery Type Outcome Timing	Moxifloxacin Concentration and Preparation	Pre- and Postoperative Interventions	Comparator
Shenoy, 2021[18] N=214,782	Retrospective cohort India	PE or MSICS 25.7 weeks	0.1 mL of 0.5% weight/volume MOX	Preoperative: 5% and 10% PI Postoperative: topical steroid-antibiotic (Ofloxacin and Prednisolone) (2 weeks) and oral Ciprofloxacin was prescribed (3 days)	No IC antibiotic
Shorstein, 2021[19] N=204,655	Retrospective cohort USA	IC Cefuroxime 12.9 weeks	0.1 mL – 1 mL of 0.1% MOX	Variable	IC Cefuroxime
Vieira, 2017[20] N=7,195	Retrospective cohort Brazil	PE 6 weeks	0.05 mL of MOX-hydrochloride at 5.45 mg/mL	Preoperative: 5% PI Postoperative: topical antibiotics (10 days)	No IC antibiotic
Zhou, 2016[21] N=222	Retrospective cohort USA	PE 4.3 weeks	0.5 mg in 0.1 mL of 0.5% MOX	Preoperative: 5% PI, proparacaine, phenylephrine, cyclopentolate, ketorolac, and lidocaine Intraoperative: 5% PI, prednisolone acetate Postoperative: nepafenac, prednisolone acetate drops (2 weeks), 0.5% MOX drops (1 week - no IC group only)	Topical MOX

Abbreviations. ECCE=Extracapsular cataract extraction; IC=Intracameral; MOX=Moxifloxacin; MSICS=Manual small incision cataract surgery; NR=Not reported; PE=Phacoemulsification; PI=Povidone-iodine.
Notes. N=number of eyes.

OUTCOME DATA OF INCLUDED PRIMARY STUDIES

Endophthalmitis

Author Year	Surgery Type	Comparator	N Overall	N MOX	N Comp.	# w/ Endop. MOX	# w/o Endop. MOX	# w/ Endop Comp.	#w/o Endop. Comp.
Arshinoff, 2011[1]	PE	No IC antibiotic (no antibiotic or topical antibiotic)	59,041	35,194	23,847	1	35,193	12	23835
Bhatta, 2021[2]	PE or MSICS	No IC antibiotic	111,983	31,340	80,643	8	31,332	116	80527
Dave, 2022[4]	PE, MSICS, or ECCE	No IC antibiotic	66,967	34,318	32,649	15	34,303	21	32,628
Frilling, 2013[6]	PE or "other"	No IC antibiotic (no antibiotic or topical antibiotic)	9,701	6,897	2804	2	6,895	11	2793
Galvis, 2014[7]	PE	No IC antibiotic	2,674	1,618	1,056	0	1,618	1	1055
Haripriya, 2016[8]	PE, MSICS, or ECCE	No IC antibiotic	75,937	38,160	37,777	6	38,154	30	37,747
Haripriya, 2017[9]	PE, MSICS, or ECCE	No IC antibiotic	617,453	314,638	302,815	64	314,574	214	302,601
Haripriya, 2019[10]	PE, MSICS, or ECCE	No IC antibiotic	2,062,643	1069634	993009	185	1,069,449	692	992,317
Herrinton, 2016[11]	PE	Topical antibiotic	258,859	21,150	237,709	10	21,140	167	237,542

Author Year	Surgery Type	Comparator	N Overall	N MOX	N Comp.	# w/ Endop. MOX	# w/o Endop. MOX	# w/ Endop Comp.	#w/o Endop. Comp.
Matsuura, 2013[13]	PE	No IC antibiotic	34,755	18,797	15,958	3	18,794	8	15,950
Melega, 2019[15]	PE	No IC antibiotic	3,640	1,818	1,822	1	1,817	7	1815
Porwal, 2021[16]	MSICS	No IC antibiotic	40392	19,859	20,533	3	19,856	10	20523
Shenoy, 2021[18]	PE or MSICS	No IC antibiotic	214782	112,967	101,815	92	112,875	179	101636
Vieira, 2017[20]	PE with intraocular implant	No IC antibiotic	7,195	3,680	3,515	1	3,679	8	3507

Abbreviations. Comp=comparator; ECCE=extracapsular cataract extraction; Endop=endophthalmitis; IC=intracameral; MSICS=manual small incision cataract surgery; MOX=moxifloxacin; PE=phacoemulsification; w=with event; w/o=without event.
Notes. N=number of eyes.

Other Adverse Events

Author Year N	Surgery Type	TASS	Corneal or Macular Edema	Other Adverse Events
Arshinoff, 2011[1] N=104,914	PE	NR	Corneal: NR Macular: NR	NR
Bhatta, 2021[2] N=11,983	PE or MSICS	No cases of TASS	Corneal: NR Macular: NR	No adverse reactions to MOX
Cetinkaya, 2015[3] N=65	PE	No cases of TASS	Corneal: Corneal edema: 6% MOX vs 9% control (p=0.623). Macular: NR	Anterior chamber reaction (cells 1 +): 12% MOX vs 9% control (p=0.726)

Author Year N	Surgery Type	TASS	Corneal or Macular Edema	Other Adverse Events
Dave, 2015[4] N=66,967	PE, MSICS, or ECCE	NR	Corneal: Among eyes with endophthalmitis: 33.3% MOX vs 71.4% no MOX (p=0.03) Macular: NR	Lid edema among eyes with endophthalmitis: 40% MOX vs 76.2% no MOX (p=0.03)
Eckinci, 2012[5] N=60	PE	NR	Corneal: There were no corneal edema events in either study group Macular: NR	No study-related adverse events
Friling, 2013[6] N=464,755	PE or "other"	NR	Corneal: NR Macular: NR	NR
Galvis, 2014[7] N=2,674	PE	NR	Corneal: NR Macular: NR	NR
Haripriya, 2016[8] N=75,937	PE, MSICS, or ECCE	No cases of TASS	Corneal: NR Macular: NR	No adverse reactions to MOX, including corneal decompensation
Haripriya, 2017[9] N=617,453	PE, MSICS, or ECCE	No cases of TASS	Corneal: NR Macular: NR	No adverse reactions to MOX, including corneal decompensation
Haripriya, 2019[10] N=2,062,643	PE, MSICS, or ECCE	No cases of TASS	Corneal: Rate of persistent postoperative corneal edema not different between groups (data NR) Macular: NR	No adverse reactions to MOX, including corneal decompensation
Herrinton, 2016[11] N= 294,649	PE	NR	Corneal: NR Macular: Only reported for any IC, not specific to MOX	Only reported for any IC, not specific to MOX
Lane, 2008[12] N=57	PE	2 patients in MOX group excluded from analysis due to TASS	Corneal: Trace (1-5 cells): 1 MOX vs 0 salt solution (p=0.2706) Macular: NR	No study-related adverse events
Matsuura, 2013[13] N=34,755	PE	No cases of TASS	Corneal: NR Macular: NR	No adverse reactions to MOX, including severe corneal damage

Author Year N	Surgery Type	TASS	Corneal or Macular Edema	Other Adverse Events
Matsuura, 2014[14] N=138	PE	No cases of TASS	Corneal: NR Macular: NR	No adverse reactions to MOX, including corneal damage
Melega, 2019[15] N=3,640	PE	NR	Corneal: NR Macular: NR	No ocular or systemic study-related adverse events
Porwal, 2021[16] N=40,392	MSICS	NR	Corneal: NR Macular: NR	NR
Rathi, 2021[17] N=42,466	PE or MSICS	No cases of TASS	Corneal: 2 cefuroxime vs 0 MOX Macular: NR	Any complications (MOX vs cefuroxime): aOR 1.90, 95% CI [0.248–14.583], p=0.536
Shenoy, 2021[18] N=214,782	PE or MSICS	NR	Corneal: NR Macular: NR	NR
Shorstein, 2021[19] N=204,655	NR	NR	Corneal: NR Macular: NR	NR
Vieira, 2017[20] N= 7,195	PE	NR	Corneal: NR Macular: NR	NR
Zhou, 2016[21] N=222	PE	NR	Corneal: 1 day postoperative: 0.188 IC MOX vs 0.083 topical (p=0.069) 1 month postoperative: 0.011 IC MOX vs 0.023 topical (p=0.512) Macular: 0 eyes in MOX vs 2 eyes (1 patient) in the topical group	Anterior chamber reaction (cells 1+): 1 day postoperative: 0.06 IC MOX vs 0.033 topical (p=0.370) 1 month postoperative: 0.011 IC MOX vs 0.023 topical (p=0.512) 2 eyes (1 patient) in MOX vs 1 eye in the topical group developed iritis

Abbreviations. ECCE= extracapsular cataract extraction; IC=Intracameral; MOX=Moxifloxacin; MSICS=Manual small incision cataract; NR=Not reported; OR=Odds ratio; PE=Phacoemulsification, TASS=Toxic anterior segment syndrome.
Notes. N=number of eyes.

QUALITY ASSESSMENT OF INCLUDED PRIMARY STUDIES

Randomized Controlled Trials

Author Year	Risk of Bias from Randomization Process	Risk of Bias from Deviation from Intended Interventions (Assignment)	Risk of Bias from Deviation from Intended Interventions (Adherence)	Risk of Bias from Missing Outcome Data	Risk of Bias in Measurement of Outcome	Risk of Bias in Selection of Reported Result	Overall Bias (High, Low, Unclear)
Lane 2008[12]	Some concerns Unclear how the randomization was done and if allocation was concealed.	Some concerns No blinding of surgeons and no apparent blinding of patients. Unclear if all patients received intervention as assigned.	Some concerns No blinding of surgeons and no apparent blinding of patients. Unclear if there was deviation from intervention in any cases. All patients appear to have received the same co-interventions.	Some concerns ~17% excluded from analysis due to lost to follow-up or unrelated adverse events.	Some concerns Unclear if outcome measurement was blinded. Outcomes of interest are objective.	Some concerns No protocol identified.	Some concerns
Melega 2019[15]	Low Patients randomized and allocated by separate nurses. Allocation in sealed opaque envelopes.	Low All patients received assigned interventions. Patients masked to intervention assignment.	Low Surgeons not blinded, but all patients received allocated intervention. Co-interventions and surgical techniques standardized across groups.	Low <2% lost to follow-up.	Low Outcome assessors were surgeons and thus unblinded, but cases of endo were evaluated by a masked retina specialist.	Low No apparent deviations from protocol.	Low

Observational Studies

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
Arshinoff 2011[1]	High Participants came from different countries reporting different time periods of data. No information on patient or cataract characteristics, and it may have varied across countries.	Unclear Country data was mostly retrospective, unclear how data from the different countries were collected/recorded.	High No information on co-interventions or surgery protocols, which likely differed among the different countries.	Unclear Country data was mostly retrospective, unclear how data from the different countries were collected/recorded.	Unclear No information on patient, cataract, or surgery characteristics. Likely differences among countries. Unclear if there were differences between IC drugs used.	Unclear Unclear level and handling of missing data.	Unclear Many different subgroup analyses reported, unclear how these were chosen.	High
Bhatta 2021[2]	Unclear Patients came from 2 different time periods, but a single institution with similar practice patterns.	Low Clearly defined time point of use of MOX. States all cases received MOX after the time point.	Low All patients after introduction of MOX received intervention. Co-interventions and surgical procedures were standard in single hospital.	Low Standard measurement of endop across patients.	Unclear No information on patient characteristics.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear
Cetinkaya 2015[3]	Unclear Unclear if it	Unclear Unclear why	Low Co-interventions	Unclear No description of	Unclear No differences	Unclear Unclear level	Low No	Unclear

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
	was all patients undergoing surgery during a certain time period or if patients were selected.	certain patients received MOX and other patients did not.	and surgical procedures were standard, performed by a single surgeon.	how outcomes were measured.	in measured baseline patient characteristics, but other potential confounders such as overall health not measured.	and handling of missing data.	indication of selective outcome reporting.	
Dave 2022[4]	Low Appears that all surgery cases during a certain time period were included.	Unclear Unclear why certain patients received MOX and other patients did not.	Low MOX injections and co-interventions standardized, single institution.	Low Standard measurement of endop across patients.	High Significant differences between groups in patient and surgery characteristics, not adjusted for in endop outcome.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	High
Ekinci 2012[5]	Unclear Patients came from 2 different time periods, but a single institution with similar practice patterns.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Low Co-interventions and surgical procedures were standard, performed by a single surgeon.	Unclear Limited information on measurement of endop.	Unclear No detail on baseline characteristics, unclear if there were any differences between groups.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
Friling 2013[6]	Low All patients from surgical database in specific time frame.	Unclear Unclear why certain patients received MOX and other patients did not.	Unclear No information on use of co-interventions, practices may have varied across hospitals.	Low Appears to be standard processes for diagnosis and reporting of endop.	Unclear No data on patient characteristics and why certain patients received MOX. May have differed from those who did not receive MOX.	Low Report only missing data on 1 case for IC antibiotic data and <5% missing for other covariates.	Low No indication of selective outcome reporting.	Unclear
Galvis 2014[7]	Low All patients from surgical database in specific time frame.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Low Co-interventions and surgical procedures were standard, performed by a single surgeon.	Low Standard measurement of endop across patients.	Unclear No detail on baseline characteristics, unclear if there were any differences between groups.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear
Haripriya 2016[8]	Low All patients who underwent cataract surgery during a specific time frame.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Unclear Surgical procedures and co-interventions were standardized across included hospitals, but experience level of surgical staff	Low Standard measurement of endop across patients.	High No control or stratification for surgeon experience and other potentially confounding factors are not reported by	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	High

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
			differed between groups.		intervention group.			
Haripriya 2017[9]	Low All patients who underwent cataract surgery during a specific time frame.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Unclear Surgical procedures and co-interventions were standardized across included hospitals, but experience level of surgical staff and surgery type differed between groups.	Low Standard measurement of endop across patients.	Unclear Results are stratified by surgery type and surgical complications; baseline and patient demographics not reported by group.	Unclear Unclear level and handling of missing data	Low No indication of selective outcome reporting	Unclear
Haripriya 2019[10]	Low All patients who underwent cataract surgery during a specific time frame.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Unclear Surgical procedures and co-interventions were standardized across included hospitals, but experience level of surgical staff differed between groups.	Low Standard measurement of endop across patients.	Unclear Results are stratified by surgery type and surgical complications; baseline and patient demographics not reported by group.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear
Herrinton 2016[11]	Low Includes all eligible	Low Interventions clearly defined and	Unclear Pharmacological co-interventions are well-	Low Standard measurement of	Unclear Some adjustment made for key	Unclear Unclear level and handling	Low No indication of	Unclear

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
	patients during the time frame.	documented in EHR.	documented, but it's unclear whether surgeon experience and/or surgical procedures varied by intervention group.	endop across patients.	confounders, but characteristics not compared between MOX and no MOX groups. Likely residual confounding baseline patient characteristics and surgeon experience levels.	of missing data.	selective outcome reporting.	
Matsuura 2013[13]	Unclear Includes all patients within study period, but unclear if all surgeries were included due to mail survey.	Unclear For cases of endophthalmitis, it's clear whether they did or did not receive IC MOX, but concentration of MOX differed by institution and 1 institution only gave IC MOX to "high risk" patients; unclear if other institutions inconsistently provided IC MOX after introduction.	Unclear Little reporting on co-interventions provided.	Low Standard measurement of endop across patients.	High No information on patient or surgery characteristics and may have differed based on how MOX was administered.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	High

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
Matsuura 2014[14]	Unclear Does not provide info on how patients were selected (*ie* consecutive, random, or convenience), but since patients served as self-controls, it's unlikely selection based on patient characteristics would have mattered.	Low Interventions clearly defined and documented at start of follow-up.	Low Co-interventions well defined and appear to be consistent across intervention categories; single surgeon.	Unclear Endop and other adverse events were not well defined, but also not observed or expected due to small size of study.	Unclear Self-controls in group A, but not in group B. No information about baseline characteristics.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear
Porwal 2021[16]	Unclear Appears to include all patients within study period but does not explicitly state this.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Unclear Little reporting on co-interventions provided.	Unclear Endop was not well defined.	High No information on surgery or patient characteristics and no attempt to stratify or control for confounding.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	High
Rathi 2021[17]	Low All patients	Low Different centers	Low Appears that	Low Standard	Unclear Several	Unclear Unclear level	Low No	Unclear

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
	from included centers during a specific time frame.	selected to use either MOX or cefuroxime.	intervention was adhered to (Fig. 2). Co-interventions and surgical procedures standardized across study sites.	measurement of endop across study sites.	differences between groups at baseline, including factors that could affect endop rates (surgery type, complications). Multivariate analysis conducted, but may be residual confounding.	and handling of missing data.	indication of selective outcome reporting.	
Shenoy 2021[18]	Unclear Patients came from 2 different time periods, but a single institution with similar practice patterns.	Low Clearly defined timepoint of use of MOX. States all cases received or did not receive MOX for the 2 different time frames.	Low Co-interventions and surgical procedures were standard, stated that they did not change over time.	Low Appears to be standard measurement of endop across patients.	Unclear Difference in age between groups at baseline. No adjustment for confounders, but does provide stratified data by surgery type.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	Unclear
Shorstein 2021[19]	Low All patients from health	Low Antibiotic choice left up to	Unclear Mentions that some processes	Low Standard measurement of	Unclear No details on baseline	Unclear Unclear level and handling	Low No indication	Unclear

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
	system receiving surgery in specific time frame.	surgeons, but classified in medical record.	are standard and others are left up to surgeon choice, unclear if co-interventions and surgical techniques are standard.	endop across study sites.	characteristics. IC was selected by surgeon choice, so may have been some systematic differences in patient populations seen by specific surgeons. No adjustment for potential confounding.	of missing data.	of selective outcome reporting.	
Vieira 2017[20]	Low All patients from clinical registry receiving surgery in specific time frame.	Unclear Unclear why certain patients received MOX and other patients did not.	Low Co-interventions and surgical techniques standardized within hospital.	Low Standard measurement of endop across study sites.	High Only age and gender presented, no information on other clinical or surgery characteristics. High risk of confounding, as it is unclear why some patients received antibiotics.	Unclear Unclear level and handling of missing data.	Low No indication of selective outcome reporting.	High

Author, Year	Selection Bias (High, Low, Unclear)	Bias in Classification of Interventions (High, Low, Unclear)	Bias Due to Departures from Intended Interventions (High, Low, Unclear)	Bias Due to Measurement of Outcomes? (High, Low, Unclear)	Bias Due to Confounding? (High, Low, Unclear)	Bias Due to Missing Data? (High, Low, Unclear)	Bias in the Selection of Reported Results (High, Low, Unclear)	Overall Bias (High, Low, Unclear)
Zhou 2016[21]	Unclear Excluded patients with complications during surgery, unclear if this differed between treatment groups.	Unclear Unclear why certain patients received MOX and other patients did not.	Low Co-interventions and surgical techniques standardized within hospital.	Unclear No description of how endop was measured.	High Only age and gender presented, no information on other clinical or surgery characteristics. High risk of confounding, as it is unclear why some patients received antibiotics	Unclear Excluded 162 eyes overall, unclear level of number excluded due to missing follow-up vs surgical complications.	Low No indication of selective outcome reporting.	High

Abbreviations. EHR=electronic health record; Endop=Endophthalmitis; Fig=Figure; IC=Intracameral; MOX=Moxifloxacin.

STRENGTH OF EVIDENCE FOR INCLUDED STUDIES

Strength of Evidence for Endophthalmitis

Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating and Summary of Evidence
14 studies:[1,2,4,6-11,13,15,16,18,20] 1 RCT, 13 cohorts (3,566,022)	Low to high risk of bias	Direct	Consistent	Precise	Not detected	Moderate: Use of intracameral moxifloxacin likely reduced rates of endophthalmitis compared to standard care (OR 0.27, 95% CI [0.19, 0.40]). Limited by study design and methodology.

Abbreviations. CI=Confidence interval; OR=Odds ratio.

APPENDIX D: RESEARCH IN PROGRESS

Status	Study Title	Study Design	Information Resources
Completed (Not published)	Intracameral Moxifloxacin for Prevention of Post cataract Endophthalmitis	Single group assignment	NCT02595359
Completed (Not published)	Postoperative Safety Outcomes of Intraoperative Intracameral Preservative-Free Moxifloxacin Versus Levofloxacin	RCT	NCT04403334
Not yet recruiting	Safety and Efficacy of Intracameral Zimoxin for Prevention of Endophthalmitis After Cataract Surgery	RCT	NCT03244072

Abbreviations. RCT=Randomized controlled trials.

APPENDIX E: PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	1	Yes	*None*
2	2	Yes	*None*
3	3	Yes	*None*
4	4	Yes	*None*
Is there any indication of bias in our synthesis of the evidence?			
5	1	No	*None*
6	2	No	*None*
7	3	No	*None*
8	4	Yes - The authors are biased in favor of moxifloxacin use, perhaps due to standard of care.	*We have addressed the specific comments below.*
Are there any published or unpublished studies that we may have overlooked?			
9	1	No	*None*
10	2	No	*None*
11	3	Yes - Included in my comments below	*Addressed in comments below.*
12	4	Yes - -Mamalis N. Reducing the risk of endophthalmitis. J Cataract Refract Surg 2019;45 (9):1217-1218. -Novack GD, Caspar JJ. Peri-Operative Intracameral Antibiotics: The Perfect Storm? J Ocul Pharmacol Ther 2020;36 (9):668-671.	*We identified both of these studies in our search, and they were not formally included as they are editorials/ commentaries of a study we included (Haripriya). We have added Novack 2020 to the background and discussion sections.*
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.			
13	1	Page 4 line 38: Intracameral antibiotics are given at the end of the case after IOL insertion and viscoelastic removal not "immediately after Cataract removal"	*This has been revised to clarify when intracameral antibiotics are given.*
14	1	Page 4 Line 53: topical or "injectable" - I believe cefuroxime and Vancomycin are injectables not topicals	*We have added "injectable" after topical here.*
15	1	Page 6 line 25: This endophthalmitis rate seems high...is there a range reported and is this only Post-op endophthalmitis	*Thank you, this number was incorrectly reported, and we have revised it to a range of 0.08% to 0.14%.*
16	1	Page 6 line 48: Injected at the end of the case- not "immediately after cataract removal"	*This has been revised to clarify when intracameral antibiotics are given.*
17	1	Page 6 line55: Can we confirm there was an arm of no antibiotics in this study. I believe the fine print * under	*Thank you for pointing this out. We have removed the "no antibiotic use" as the table notes do state that all*

Comment #	Reviewer #	Comment	Author Response
		the table depicting the arms it states all arms received topical antibiotics.	*patients received postoperative topical antibiotics.*
18	1	Page 19 line 4 topical or "injectable"	*We have added "injectable" after topical here.*
19	1	Page 19 line 34 Should this state Intracameral moxifloxacin "alone" versus topical- Just to clarify	*Yes, thank you, this is a good clarification. We have added "alone" after intracameral moxifloxacin.*
20	2	Excellent review of relevant literature, including recent sources.	*Thank you.*
21	3	This is an extremely well written manuscript that is organized and supports its final conclusion. Despite the comprehensive nature of the review, there are a few omissions:	*Thank you, individual comments addressed below.*
22	3	Background: The authors did not include that the current community standard is to concurrently prescribe two medications. A topical antibiotic, most commonly a fluroquinolone, and a topical steroid drop. There is strong evidence within both the ophthalmic and general medical literature that the addition of a second medication dramatically reduces the adherence/compliance with both medications compared to a single prescribed medication.	*Thank you. We have added that steroid drops are also often prescribed with topical antibiotics, and this can also hinder patient adherence.*
23	3	Although the authors did not include the reported cases of TASS due to administering a topically preparation into the eye, they did not include the reported cases of TASS that occurred from compounded formulations.	*Thank you, this is an important point. We have added to the background and discussion the risk of TASS with compounded moxifloxacin.*
24	3	Methods: The methodology utilized is standard for high quality reviews and meta-analyses	*Thank you.*
25	3	Results: In the adverse effects of moxifloxacin use, there is a prospective randomized controlled trial comparing two intracameral doses of moxifloxacin on corneal endothelial cell counts finding no difference in safety. However, it is a recent publication in January of 2022 which may have been after this document was prepared. The ESCRS PRCT has some methodologic flaws preventing FDA acceptance of this data for approval – a	*Thank you for letting us know of this study. We have found Ashraf 2008 "Safety of Prophylactic Intracameral Moxifloxacin Injection after Uncomplicated Phacoemulsification Surgery" and have reviewed it. As the study does not report endophthalmitis rates or moxifloxacin related adverse events, we have formally excluded it.*

Comment #	Reviewer #	Comment	Author Response
		deeper discussion could have been described.	
26	3	Conclusions: The current data is strongly suggestive of the superior efficacy of intracameral moxifloxacin for the prevention of endophthalmitis following cataract surgery. However, only a level 1 PRCT can definitively determine therapeutic superiority and safety.	*We agree and suggest further RCTs in our future research section.*
27	3	This is an excellent review and the minor omissions of information do not materially change the conclusion of the authors.	*Thank you.*
28	4	The authors prepared a "Cochrane review" like document on the issue of use of intracameral moxifloxacin for prevention of endophthalmitis after cataract surgery. At first read, it seems like a very straightforward manuscript, supporting this use. However, on deeper read, several items are not fully described. Other issues, brought up in some recent papers, are seemingly not completely addressed. Thus, I suggest that a reader of this document may come to an inappropriate conclusion about the safety, efficacy and benefit-risk of moxifloxacin by this route.	*Thank you for your comments, we have addressed them individually below.*
29	4	In the executive summary, the authors state: "..Intracameral antibiotics are effective at preventing endophthalmitis." This is arguably not true. Other than a few select studies, there are no randomized trials with concurrent negative controls (e.g., placebo). Without an approved positive control (and there is none in the U.S. – topical or intracameral), a positive-controlled study is not conclusive.	*We have revised discussion of existing research to more accurately describe evidence on intracameral antibiotics in light of methodological limitations of available studies.*
30	4	The authors further state ".there are currently no antibiotics that are approved by the US Food and Drug Administration for intraocular use". The reason for this lack of approved products is simple – there are no publicly submitted applications, presumably due to the lack of the required two concurrent negative controlled trials.	*We agree and discuss in our future research section that further RCTs in the US, including a current ongoing placebo controlled RCT, are needed to impact FDA approval.*
31	4	They state "US surgeons must use repackaged and diluted topical	*We have added further discussion of potential increased risk from using off-*

Comment #	Reviewer #	Comment	Author Response
		solutions off-label. Increased risk, liability, and logistical challenges of using antibiotics off-label has led to less intracameral antibiotic use in the US compared to other countries where commercial intracameral formulations are available". This is exactly the point – but one seemingly not discussed further in the conclusions. These risks must be considered by the surgeon in opting for off-label, compounded intracameral moxifloxacin. Do the authors propose a solution for the VA system – for example, a standard formulation by the pharmacies?	*label compounded moxifloxacin in the US to the discussion of VHA considerations. In the section on considerations for VHA, we discuss the need for either an FDA approved intracameral formulation or standardized VHA pharmacy preparation in order to standardize use within the VHA.*
32	4	The authors state that there is new evidence beyond the cited review papers (Lane 2008; Matsurra 2014 and Melaga 2019). Is it explicitly stated what this new evidence is? Perhaps it is Haripriya 2019? That paper is large – but unfortunately, sequential and not randomized. I suggest the authors asterisk the "new" studies in Table 1.	*We have added a footnote to Table 1 identifying the studies not included in previous reviews, and also cite these studies in the discussion section.*
33	4	The authors blur studies with antibiotics other than moxifloxacin. Just because something was found with one intracameral antibiotic does not mean moxifloxacin is safe and effective.	*Studies included in our synthesis examine intracameral moxifloxacin and we did not include studies of other intracameral antibiotics. Although several of our included studies did compare intracameral antibiotics to another intracameral antibiotic (cefuroxime), we separated this out in a comparative effectiveness analysis.*
34	4	The authors state: "Due to concerns around antibiotic resistance and potential adverse events from use of cefuroxime and vancomycin, moxifloxacin has more recently been investigated." That may be true, however I suggest that the real reason is that marketed topical moxifloxacin is "self-preserved" – i.e., free of a preservative, which would be inappropriate to use by intracameral route.	*We agree that the availability of moxifloxacin without preservatives has likely influenced more recent use. We have added a statement about the availability of moxifloxacin without preservatives.*
35	4	Further, it is essential that the correct formulation of moxifloxacin is used by the pharmacy for preparing the intracameral product. That is, as I understand, Vigamox® rather than Moxeza®.	*We agree. We discuss the brands and dosages used in the studies included in the report in the discussion section and have added a statement about considering potential adverse effects with other brands.*

Comment #	Reviewer #	Comment	Author Response
36	4	Of the many papers excellently reviewed, there are seemingly only two negative controlled trials. -Melage 2019. I suggest that the authors state the findings of this study in the body of the manuscript: "The incidence of endophthalmitis within 6 weeks of follow-up was 1 (0.05%) of 1818 eyes in the moxifloxacin group and 7 (0.38%) of 1822 eyes in the control group (P Z .035). -Lane 2008. This study was not designed nor powered to evaluate endophthalmitis rate.	*We have added the Melaga 2019 findings to the narrative results. We agree that Lane 2008 was not designed to evaluate endophthalmitis and it is not included in our synthesis of endophthalmitis but was included for its assessment of adverse events.*
37	4	The authors may consider reiterating the risk of endophthalmitis (<< 1% without antibiotics). This may help interpret Figure 2. While large Odds Ratios are found – the number needed to treat is very high.	*We have added the low rate of endophthalmitis to the discussion section to contextualize the odds ratio.*
38	4	The authors may consider the antithetical status – while intracameral moxifloxacin is not approved, it may nonetheless be the standard of care, leading to medico-legal issues.	*This is a good point and we have added a statement to the future research section to note this.*
39	4	The authors may consider these two commentaries: -Mamalis N. Reducing the risk of endophthalmitis. J Cataract Refract Surg 2019;45 (9):1217-1218. -Novack GD, Caspar JJ. Peri-Operative Intracameral Antibiotics: The Perfect Storm? J Ocul Pharmacol Ther 2020;36 (9):668-671.	*Thank you for these suggestions. We have added Novack 2020 to the background and discussion sections.*

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