Recommendations for Senile Cataracts Evidence Base

Developed by Asia-Pacific Center for Evidence-Based Health Care, 2016
Last Searched May 2016

INTRODUCTION

Aside from these next few paragraphs, the rest of the document is the product of the Asia-Pacific Center for Evidence-Based Healthcare. The contents of this report was provided to the CPG Panelists before the conference. It is reproduced here in its entirety with permission of the PAO to provide interested readers and the stakeholders the bases for the deliberations and the final recommendations of the CPG.

The GRADE methodology, the references selected, and the Forest Plots can be independently verified and analyzed. This unprecedented transparency in the development of the CPG on Senile Cataracts emphasizes the Steering Committee's commitment to eliminating bias and doubt, and, should set the bar for the formulation of future CPGs by the PAO.

HOW TO APPRECIATE THE EVIDENCE BASE

1. Each individual question was searched for evidence until February 29, 2016 and summarized. If possible, the data from several clinical studies were pooled to come up with single estimate or the treatment effect. This was done by conducting a meta-analysis or basing it on an existing meta-analysis.
2. The first 2 sections are guides on how to interpret the results and how the GRADE approach in grading the level of quality of evidence is used.
3. The evidence for each question is presented in 3 parts:
    1. Summary of Evidence in simplified text format (including table on the interpretation of the evidence for some questions).
    2. GRADE Evidence Tables showing the assessment of the quality of evidence and summary statistics
    3. Forest Plots depicting the pooled effect.

I. QUICK GUIDE ON HOW TO INTERPRET THE EVIDENCE

Table 1. Ways of expressing effectiveness

Outcome	Summary of result within each group	Comparison of results between two groups
Dichotomous (e.g. lived or died, BP controlled or not)	Proportion (e.g. deaths per 100 patients)	Relative risk reduction, **absolute risk reduction, relative risk** (see Table 2)
	Rate = e.g. deaths per 100 patients per year	Hazard ratio = rate in treatment/rate in control group
Continuous (e.g. blood pressure in mmHg, quality of life on a scale of 0 to 1)	Mean (e.g. mean blood pressure)	**Mean difference** = mean in control − mean in treatment group

Table 2. Interpreting 95% Confidence Intervals (CIs)

Instructions: When researchers express the effect of treatment using the relative risk reduction, absolute risk reduction, or relative risk, they often give us a range of possibilities rather than a single estimate. This range of possibilities is called a '95% Confidence Interval (95% CI)' to mean 'we are 95% sure that the true effect of a drug lies in this range'. Go through this tackle box in rows, to discover how helpful 95% CIs are.

Measure of effectiveness and interpretation of estimates.	Interpretation of 95% CIs			
	Superior (treatment surely better than control)	**Inferior** (treatment surely worse than control)	**Inconclusive** (we need more studies)	**Equivalent** (the treatments are equal)¶
Relative Risk (RR) = Rt/Rc	Both ends of 95% CI <1.0	Both ends of 95% CI >1.0	95% CI wide; straddles 1.0	95% CI narrow; straddles 1.0
<1.0 Treatment beneficial =1.0 Treatment no effect >1.0 Treatment harmful	Example: RR = 0.7 [95% CI: 0.6, 0.8]	Example: RR = 2.4 [95% CI: 1.8, 3.2]	Example: RR = 1 [95% CI: 0.2, 5.3]	Example: RR = 1 [95% CI: 0.9, 1.1]
Absolute Risk Reduction (ARR) = Rc – Rt	Both ends of 95% CI >0%	Both ends of 95% CI <0%	95% CI straddles 0%; either end is far from 0%	95% CI straddles 0%; either end is close to 0%
(usually in percent) >0% Treatment beneficial =0% Treatment no effect <0% Treatment harmful	Example: ARR = 2% [95% CI: 1%, 3%]	Example: ARR =−3% [95% CI: -7%, -1%]	Example: ARR = 1% [95% CI: –20%, 32%]	Example: ARR = 0.2% [95% CI: –0.1%, 0.5%]

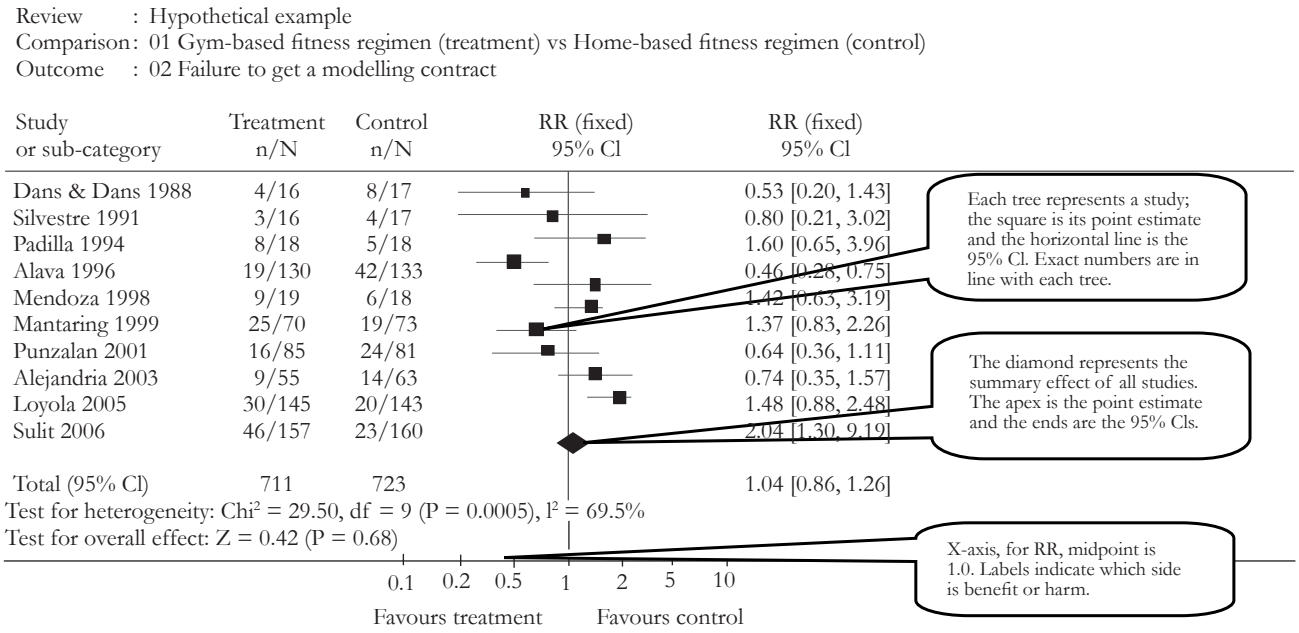
¶ In both inconclusive and equivalent results, the 95% CI interval straddles the point of no effect (ARR=0% or RR=1.0). One end reflects the worst possible harm, while the other end reflects the best possible benefit. The only difference is that, in equivalence, either end is close to "no effect" (i.e. any benefit is ignorable and any harm is ignorable too). Consider the ends of the 95% CI to make sure you agree that the benefits and harms are ignorable.

Rc is the rate of the outcomes in the Control group
Rt is the rate of the outcome in the Treatment group

Note: The interpretations in this table only hold if the dichotomous events are expressed as adverse rather than desirable events, e.g. death rather than survival, treatment failure rather that cure, or disease rather than disease-free. When dichotomous outcomes are expressed as desirable events, the interpretation of benefit and harm is reversed. We feel researchers should standardize reporting and use adverse events in order to avoid confusion. Unfortunately, nobody cares what we think.

Table 3. How to interpret forest plots

Instructions: The balloons below label the most important parts of the forest plot. Go through these labels and familiarize yourself with the anatomy of the graph. Once you feel sufficiently familiar with the anatomy, go through the notes below on what the forest plot can signify.



II. GRADE Approach in assessing the level of quality of evidence

(GRADE: Grading of Recommendations Assessment, Development and Evaluation; modified from WHO Handbook in Guideline Development, 2014).

These quality ratings apply to the body of evidence assessed for the research question, not to individual studies.

Evidence based on randomized controlled trials is initially given a high-quality rating and evidence from observational studies is given a low-quality rating. The level is then adjusted according to the following criteria:

Box 1. Standard criteria for grading of evidence[1]

Domain	Grade	Characteristics
STUDY DESIGN	0	All randomized controlled trials
	-1	All observational studies
STUDY DESIGN LIMITATIONS	0	Most of the pooled effect provided by studies, with low risk of bias ("A")
	-1	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs <40%
	-2	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs ≥40%
	Note	Low risk of bias (no limitations or minor limitations) - "A" Moderate risk of bias (serious limitations or potentially very serious limitations including unclear concealment of allocation or serious limitations, excluding limitation on randomization or concealment of allocation) - "B" High risk of bias (limitations for randomization, concealment of allocation, including small blocked randomization (<10) or other very serious, crucial methodological limitations) - "C"

[1] Adapted from: Schunemann H, Brozek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group. Available at: <http://ims.cochrane.org/revman/gradepro>. (This document is contained within the "Help" section of the GRADE profiler software version v.3.2.2.)

Box 1 (cont.). Standard criteria for grading of evidence[1]

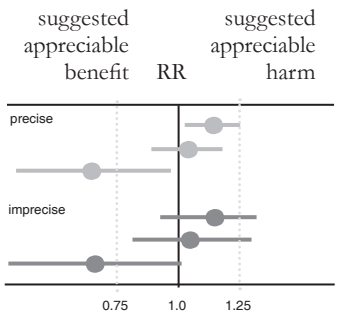
Domain	Grade	Characteristics
INCONSISTENCY	0	No severe, heterogeneity (I^2 <60% or χ^2 ≥0.05)
	-1	Severe, non-explained, heterogeneity (I^2 ≥60% or χ^2 <0.05) If heterogeneity could be caused by publication bias or imprecision due to small studies, downgrade only for publication bias or imprecision (i.e. the same weakness should not be downgraded twice)
INDIRECTNESS	0	No indirectness
	-1	Presence of indirect comparison, population, intervention, comparator, or outcome.
IMPRECISION	0	The confidence interval is precise according to the figure below. The total cumulative study population is not very small (i.e. sample size is more than 300 participants) and the total number of events is more than 30. 
	-1	One of the above-mentioned conditions is not fulfilled.
	-2	The two above-mentioned are not fulfilled.
	Note: If the total number of events is less than 30 and the total cumulative sample size is appropriately large (e.g. above 3000 patients, consider not downgrading the evidence). If there are no events in both intervention and control groups, the quality of evidence in the specific outcome should be regarded as very low.	
PUBLICATION BIAS	0	No evident asymmetry in the funnel plot or less than five studies to be plotted
	-1	Evident asymmetry in funnel plot with at least five studies.

Table 4. Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Q1. AMONG PATIENTS WITH SENILE CATARACTS, HOW EFFECTIVE IS MANUAL SMALL INCISION CATARACT SURGERY (MSICS) VS. PHACO-EMULSIFICATION IN IMPROVING VISION AND IN TERMS OF ADVERSE OUTCOMES/COMPLICATIONS?

SUMMARY OF EVIDENCE

Evidence for MSICS versus phacoemulsification for the outcome of good functional vision at 3 months (uncorrected acuity 6/18 or better from 6-8 weeks of follow-up) showed significant benefit in favor of phacoemulsification with a relative risk (RR) of 0.90 (95% CI 0.84, 0.96) based on 3 randomized controlled trials (RCTs).[1-3]

Other evidence summarized and combined from 13 RCTs[1-13] and 3 meta-analysis[14-16] failed to show significant difference in the following:

1. Good functional vision at 6 months (uncorrected acuity 6/18 or better) based on 1 RCT, with an RR of 1.07 (95% CI 0.91, 1.26).[10]
2. Good functional vision at 3 months (best-corrected acuity 6/18 to 6/12 or better) based on 6 RCTs, with an RR of 0.99 (95% CI 0.98, 1.01).[1-3,5-7]
3. Good functional vision at 6 months (best-corrected acuity) based on 1 RCT, with an RR of 1.0 (95% CI 0.94, 1.06).[10]
4. Poor visual outcome at 3 months (best corrected acuity worse than 6/60), OR 2.48 (95% CI 0.74, 8.28).[1-3,5-7]
5. Poor visual outcome at 6 months (best-corrected acuity worse than 6/18) based on 1RCT is 1.9% in both groups with a computed RR of 1.0 (95% CI 0.06, 16).[10]
6. Uncorreced visual acuity in 1 week after surgery, RR 1.0 (95% CI 0.97, 1.03)[2,4,9,12,13.]

Furthermore neither surgical techniques showed clear benefit in preventing any of the complications such as posterior capsular rupture,[1-3,5-14] corneal edema postoperatively,[1-3,6-9,11-14] endothelial cell loss,[5,7] and astigmatism.[2,3,5,7,11]

In light of the evidence, it seems that phaco-emulsification still has an edge over MSICS in terms of visual acuity improvement. Although astigmatism may be a problem, it has not been clearly established with the current evidence.

Table Q1. Summary of Results (please refer to appendix to view forest plots of combined studies).

OUTCOMES	Measure of Treatment Effect	95% Confidence Interval	Interpretation	Basis
Good functional vision at 3 months (uncorrected acuity 6/18 or better) **(Fig. Q1.1)**	RR 0.90	0.84-0.96	Favors Phacoemulsification	3 RCTs
Good functional vision at 6 months (uncorrected acuity 6/18 or better)	RR 1.07	0.91-1.26	Not significant	1 RCT
Good functional vision at 6 months (best-corrected acuity) **(Fig. Q1.2)**	RR 1.0	0.94-1.06	Not significant	6 RCTs
Poor visual outcome at 3 months (best corrected acuity worse than 6/60) **(Fig. Q1.3)**	OR 2.48	0.74-8.28	Not significant	6 RCTs
Poor visual outcome at 6 months (best-corrected acuity worse than 6/18)	RR 1.0	0.06-16	Not significant	1 RCT
Uncorrected VA in 1 week after surgery **(Fig. Q1.4)**	RR 1.0	0.97-1.03	Not significant	5 RCTs
Posterior capsular rupture **(Fig. Q1.5)**	RR 1.09	0.80-1.48	Not significant	13 RCTs
Corneal edema postoperatively **(Fig. Q1.6)**	RR 0.82	0.65-1.04	Not significant	11 RCTs
Endothelial cell loss in percentage **(Fig. Q1.7)**	SMD - 0.09	-0.33-0.16	Not significant	2 RCTs
Astigmatism **(Fig. Q1.8)**	SMD 0.48	-0.04-0.99	Not significant	5 RCTs

DRAFT RECOMMENDATION

Among patients with senile cataracts, phacoemulsification is favored over MSICS due to good functional vision at 3 months with uncorrected visual acuity of 6/18 or better. Adverse events have shown to be insiginificant for both procedures. Level of Evidence: Very Low to Moderate. Strength of Recommendation: Weak.

REFERENCES

1. Cook C, Carrara H, Myer L. Phacoemulsification versus manual small-incision cataract surgery in South Africa. *S Afr Med J* 2012;102:537-40.
2. Gogate PM, Kulkarni SR, Krishnaiah S, et al. Safety and efficacy of phacoemulsification compared with manual small-incision cataract surgery by a randomized controlled clinical trial: six-week results. *Ophthalmology* 2005;112:869-74.
3. Venkatesh R, Tan CS, Sengupta S, et al. Phacoemulsification versus manual small-incision cataract surgery for white cataract. *J Cataract Refract Surg* 2010;36:1849-54.
4. Fu JM, Ying TR, Zheng HH. Clinical study of senile cataract surgical treatment. *Zhong Guo Xian Dai Yi Sheng* 2012;5036-38.
5. George R, Rupauliha P, Sripriya AV, et al. Comparison of endothelial cell loss and surgically induced astigmatism following conventional extracapsular cataract surgery, manual small-incision surgery and phacoemulsification. *Ophthalmic Epidemiol* 2005;12:293-7.
6. Ghosh S, Roy I, Biswas PN, et al. Prospective randomized comparative study of macular thickness following phacoemulsification and manual small incision cataract surgery. *Acta Ophthalmol* 2010;88:e102-6.
7. Gogate P, Ambardekar P, Kulkarni S, et al. Comparison of endothelial cell loss after cataract surgery: phacoemulsification versus manual small-incision cataract surgery: six-week results of a randomized control trial. *J Cataract Refractive Surg* 2010;36:247-53.
8. Ji Z. Efficacy comparison between small incision ECCE and phacoemulsification surgery in cataract patients. *Zhong Guo Yi Shi Jin Xiu Za Zhi* 2011;34:26-28.
9. Lin RJ, Li LJ. Study on small-incision sutureless cataract extraction and intraocular lens implantation surgery. *Zhong Guo Yi Shi Jin Xiu Za Zhi* 2007;30:21-23.
10. Ruit S, Tabin G, Chang D, et al. A prospective randomized clinical trial of phacoemulsification vs manual sutureless small-incision extracapsular cataract surgery in Nepal. *Am J Ophthalmol* 2007;143:32-8.
11. Singh SK, Winter I, Surin L. Phacoemulsification versus small-incision cataract surgery (SICS): which one is a better surgical option for immature cataract in developing countries?. *Nepal J Ophthalmol* 2009;1:95-100.
12. Zhang L, Liu L. Small-incision sutureless cataract surgery. *Yan Wai Shang Zhi Ye Bing Za Zhi* 2006;28:346-348.
13. Zhang SH, Liao RB, Cai SH. The clinical efficacy of nuclear techniques broken small-incision cataract surgery. *Guang Dong Yi Xue* 2011;32:2305-2307.
14. Zi Y, Shou-Zhi H, Zhao-Hui Li. Efficacy comparison between manual small-incision cataract surgery and phacoemulsification in cataract patients: a meta-analysis. *Int J Clin Exp Med.* 2015;8:8848-8853.
15. Gogate P, Optom JJB, Deshpande S, Naidoo K. Meta-analysis to compare the safety and efficacy of manual small incision cataract surgery and phacoemulsification. *Middle East Afr J Ophthalmol* 2015;22:362-369.
16. Riaz Y, de Silva SR, Evans JR. Manual small incision cataract surgery (MSICS) with posterior chamber intraocular lens versus phacoemulsification with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2013;10:CD008813.

Author(s): Abat M; Sulit MVV
Date: 20 June 2016
Question: MSICS compared to PHACO for Senile Cataracts
Setting: Cook 2012 - South Africa; George 2005, Ghosh 2010, Gogate 2005a/2010 & Venkatesh 2010 - India; Ruit 2007 & Singh 2009 - Nepal; Lin 2007, Zhang 2006, Xu 2007, Ji 2011, Zhang SH 2011, Fu 2012 - China
Bibliography:*

1. Gogate P, Optom JJB, Deshpande S, Naidoo K. Meta-analysis to compare the safety and efficacy of manual small incision cataract surgery and phacoemulsification. *Middle East Afr J Ophthalmol 2015; 22(3): 362-369.*
2. Riaz Y, de Silva SR, Evans JR. Manual small incision cataract surgery (MSICS) with posterior chamber intraocular lens versus phacoemulsification with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2013;10:CD008813.
3. Zi Y, Shou-Zhi H, Zhao-Hui Li. Efficacy comparison between manual small-incision cataract surgery and phacoemulsification in cataract patients: a meta-analysis. *Int J Clin Exp Med.* 2015;8:8848-8853.

***Note:** Only the meta-analysis references are listed here. Please refer to the Evidence Summary for a complete list of references.

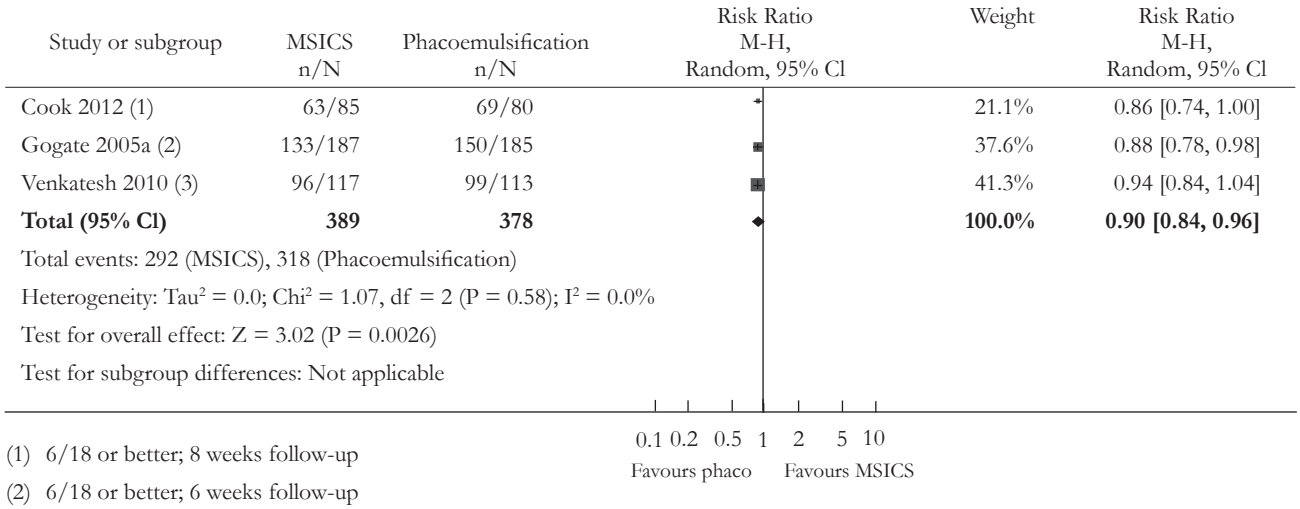
Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**MSICS**	**PHACO**	**Relative (95% CI)**	**Absolute (95% CI)**		
Good functional vision at 3 months (uncorrected acuity) 6/18 or better from 6-8 weeks follow-up												
3	randomised trials	serious[1]	not serious	not serious	not serious	none	292/389 (75.1%)	318/378 (84.1%)	**RR 0.90** (0.84 to 0.96)	**84 fewer per 1,000** (from 34 fewer to 135 fewer	⊕⊕⊕○ MODERATE	
Good functional vision at 6 months (uncorrected acuity)												
1	randomised trials	serious[1]	not serious	not serious	serious[2]	none	41/46 (89.1%)	40/48 (83.3%)	**RR 1.07** (0.91 to 1.26)	**Not Applicable**	⊕⊕○ LOW	
Good functional vision at 3 months (best-corrected acuity) 6/18 to 6/12 or better at 6-8 weeks follow-up												
6	randomised trials	very serious[3]	not serious	not serious	not serious	none	597/617 (96.8%)	596/606 (98.3%)	**RR 0.99** (0.98 to 1.01)	**Not Applicable**	⊕⊕○ LOW	
Good functional vision at 6 months (best-corrected acuity)												
1	randomised trials	serious[1]	not serious	not serious	serious[2]	none	45/46 (97.8%)	47/48 (97.9%)	**RR 1.00** (0.94 to 1.06)	**Not Applicable**	⊕⊕○ LOW	
Poor visual outcome at 3 months (best-corrected acuity worse than 6/60												
6	randomised trials	very serious[3]	not serious	not serious	serious[2]	none	8/617 (1.3%)	3/606 (0.5%)	**OR 2.48** (0.74 to 8.28)	**Not Applicable**	⊕⊕○ VERY LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Incon-sistency**	**Indirect-ness**	**Impreci-sion**	**Other considerations**	**MSICS**	**PHACO**	**Relative (95% CI)**	**Absolute (95% CI)**		
Poor visual outcome at 6 months (best-corrected acuity worse than 6/60)												
1	randomised trials	serious[1]	not serious	not serious	serious[2]	none	BCVA <6/18 1.9% participants in both groups computed as an RR = 1.0 (0.06-16)				⨁⨁◯◯ LOW	
Uncorrected Visual Acuity 1 week After Surgery												
6	randomised trials	very serious[1]	not serious	not serious	not serious	none	1012/1120 (90.4%)	1064/1168 (91.1%)	RR 1.00 (0.97 to 1.03)	**Not Applicable**	⨁⨁◯◯ LOW	
Posterior Capsular Rupture												
13	randomised trials	very serious[3]	not serious	not serious	serious[2]	none	84/1986 (4.2%)	81/2035 (4.0%)	RR 1.09 (0.80 to 1.48)	**Not Applicable**	⨁◯◯◯ VERY LOW	
Corneal Edema Postoperatively												
11	randomised trials	very serious[3]	not serious	not serious	serious[2]	none	173/1870 (9.3%)	214/1919 (11.2%)	**RR** 0.82 (0.65 to 1.04)	**Not Applicable**	⨁◯◯◯ VERY LOW	
Endothelial Cell Loss												
2	randomised trials	very serious[1]	not serious	not serious	serious[4]	none	N=128	N=131	SMD -0.9 (-3.4, 1.6)	**Not Applicable**	⨁◯◯◯ VERY LOW	
Astigmatism												
5	randomised trials	very serious[1]	serious[5]	not serious	serious[6]	none	521	522	SMD - 0.48 (-0.04, 0.99)	**Not Applicable**	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference; **SMD:** Standardised mean difference

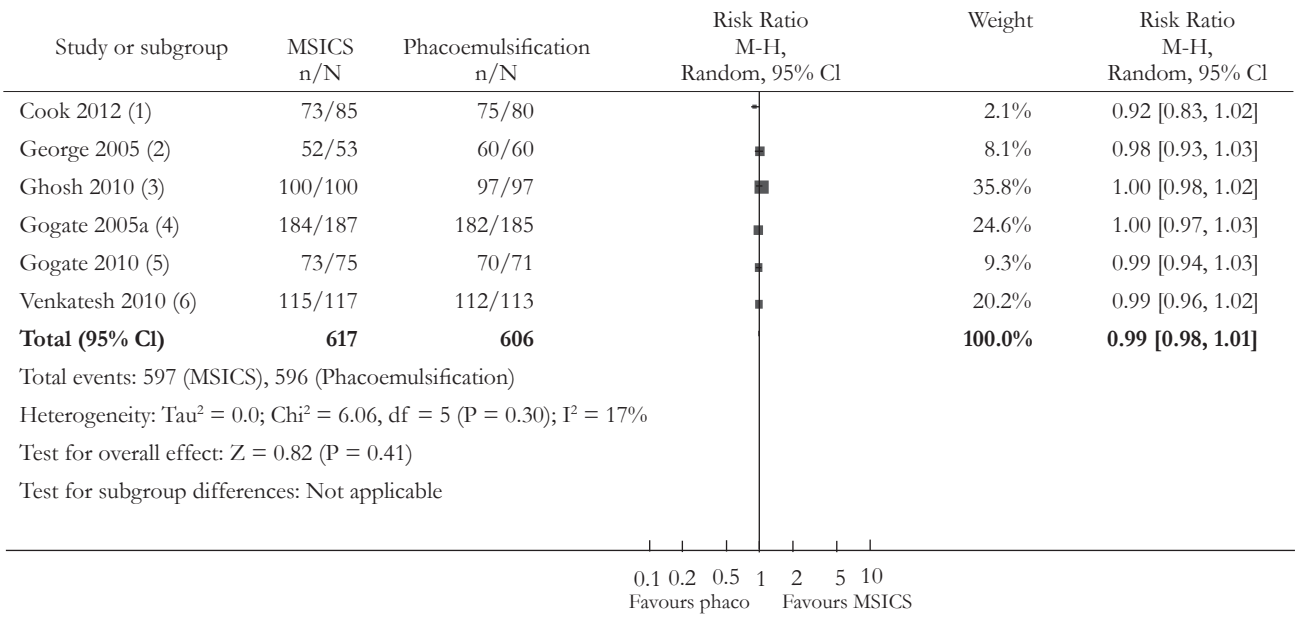
1. unclear risk of bias noted on 1 or more criteria in all included studies.
2. confidence interval straddles 1.0, larger sample size may move the interval to either harm or benefit.
3. unclear risk of bias noted in all included studies with high risk of bias for selective reporting in Ghosh 2010
4. confidence interval may still be affected by an increase in sample size; consider also that the result may be affected by serious risk of bias.
5. Chi^2 test for heterogeneity p value is less than 0.01 and I^2 test more than 50%
6. confidence interval shows only a trend which may be affected by a serious risk of bias

APPENDIX Q1



(1) 6/18 or better; 8 weeks follow-up
(2) 6/18 or better; 6 weeks follow-up
(3) 6/18 or better; 6 weeks follow-up

Figure Q1.1 Good functional vision at 3 months

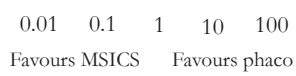


(1) 6/18 or better; 8 weeks follow-up
(2) better than 6/18; 6 weeks follow-up
(3) 6/12 or better; 6 weeks follow-up
(4) 6/18 or better; 6 weeks follow-up
(5) 6/18 or better; 6 weeks follow-up
(6) 6/18 or better; 6 weeks follow-up

Figure Q1.2 Good functional vision at 3 months (best-corrected acuity 6/18 to 6/12 or better)

APPENDIX Q1

Study or subgroup	MSICS n/N	Phacoemulsification n/N	Peto Odds Ratio Peto, Fixed, 95% Cl	Peto Odds Ratio Peto, Fixed, 95% Cl
Cook 2012 (1)	7/85	2/80		3.02 [0.79, 11.54]
George 2005 (2)	1/53	0/60		8.43 [0.17, 428.18]
Ghosh 2010 (3)	0/100	0/97		0.00 [0.0, 0.0]
Gogate 2005a (4)	0/187	1/185		0.13 [0.00, 6.75]
Gogate 2010 (5)	0/75	0/71		0.0 [0.0, 0.0]
Venkatesh 2010 (6)	0/117	0/113		0.0 [0.0, 0.0]
Total (95% Cl)	**617**	**606**		**2.48 [0.74, 8.28]**
Total events: 8 (MSICS), 3 (Phacoemulsification)				
Heterogeneity: $Chi^2 = 2.59$, df = 2 (P = 0.27); $I^2 = 23\%$				
Test for overall effect: Z = 1.47 (P = 0.14)				
Test for subgroup differences: Not applicable				



(1) worse than 6/60, 8 weeks follow-up

(2) worse than 6/18, 6 weeks follow-up

(3) all patients achieved BCVA 6/12 or better; 6 weeks follow-up

(4) worse than 6/60, 6 weeks follow-up

(5) worse than 6/60, 6 weeks follow-up

(6) Follow-up; 6 weeks

Figure Q1.3 Poor visual outcome at 3 months (best corrected acuity worse than 6/60)

Study or Subgroup	MSICS Events	MSICS Total	Phaco Events	Phaco Total	Weight	Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl
Fu 2012	26	30	23	30	1.7%	1.13 [0.89, 1.44]	
Gogate 2005a	117	191	131	192	4.3%	0.90 [0.77, 1.04]	
Lin 2007	725	747	777	806	63.0%	1.01 [0.99, 1.03]	
Zhang L 2006	68	70	67	70	18.9%	1.01 [0.95, 1.08]	
Zhang SH 2011	76	82	66	70	12.1%	0.98 [0.90, 1.07]	
Total (95% Cl)		**1120**		**1168**	**100.0%**	**1.00 [0.97, 1.03]**	
Total events	1012		1064				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.03$, df = 4 (P = 0.28); $I^2 = 21\%$							
Test for overall effect: Z = 0.15 (P = 0.88)							

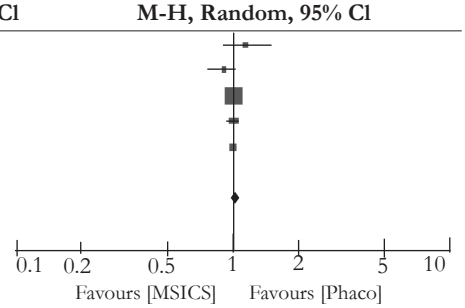


Figure Q1.4 Uncorrected visual acuity in 1 week after surgery

APPENDIX Q1

Study or Subgroup	MSICS Events	MSICS Total	Phaco Events	Phaco Total	Weight	Risk Ratio M-H, Random, 95% CI
Cook 2012	10	100	4	100	7.3%	2.50 [0.81, 7.71]
George 2005	0	62	0	62		Not estimable
Ghosh 2010	1	112	4	112	2.0%	0.25 [0.03, 2.20]
Gogate 2005a	12	201	7	199	11.2%	1.70 [0.68, 4.22]
Gogate 2010	4	100	6	100	6.1%	0.67 [0.19, 2.29]
Ji 2011	6	180	8	180	8.6%	0.75 [0.27, 2.12]
Lin 2007	42	747	38	806	50.9%	1.19 [0.78, 1.83]
Ruit 2007	0	54	1	54	0.9%	0.33 [0.01, 8.01]
Singh 2009	0	89	2	93	1.0%	0.21 [0.01, 4.29]
Venkatesh 2010	2	137	3	133	3.0%	0.65 [0.11, 3.81]
Xu 2007	1	52	1	56	1.2%	1.08 [0.07, 16.78]
Zhang L 2006	4	70	3	70	4.4%	1.33 [0.31, 5.74]
Zhang SH 2011	2	82	4	70	3.3%	0.43 [0.08, 2.26]
Total (95% CI)		**1986**		**2035**	**100.0%**	**1.09 [0.80, 1.48]**
Total events	84		81			

Heterogeneity. $Tau^2 = 0.00$; $Chi^2 = 9.35$, df = 11 (P = 0.59); $I^2 = 0\%$
Test for overall effect: Z = 0.55 (P = 0.58)

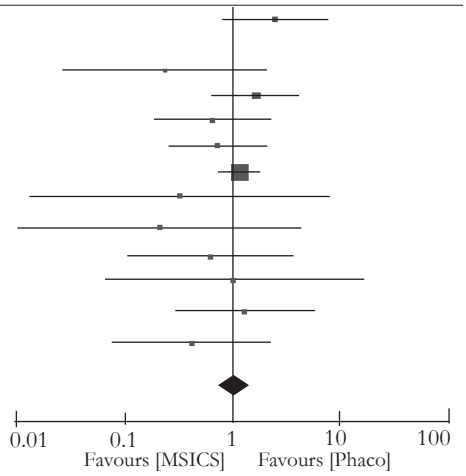
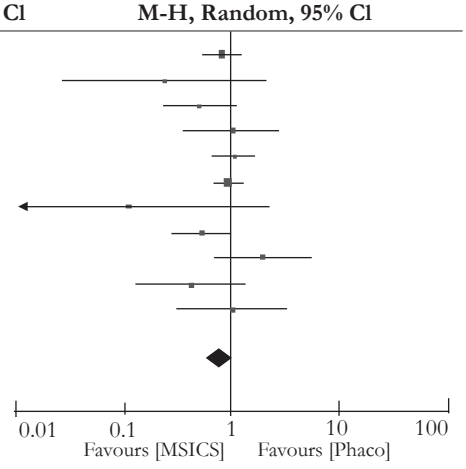


Figure Q1.5 Posterior Capsular Rupture

Study or Subgroup	MSICS Events	MSICS Total	Phaco Events	Phaco Total	Weight	Risk Ratio M-H, Random, 95% CI
Cook 2012	29	100	35	100	19.9%	0.83 [0.55, 1.24]
Ghosh 2010	1	112	4	112	1.1%	0.25 [0.03, 2.20]
Gogate 2005a	9	201	18	199	7.6%	0.50 [0.23, 1.08]
Gogate 2010	7	100	7	100	4.7%	1.00 [0.36, 2.75]
Ji 2011	31	180	29	180	16.9%	1.07 [0.67, 1.70]
Lin 2007	64	747	74	806	26.2%	0.93 [0.68, 1.28]
Singh 2009	0	89	4	93	0.6%	0.12 [0.01, 2.12]
Venkatesh 2010	14	137	25	133	11.2%	0.54 [0.30, 1.00]
Xu 2007	9	52	5	56	4.6%	1.94 [0.69, 5.41]
Zhang L 2006	4	82	8	70	3.7%	0.43 [0.13, 1.36]
Zhang SH 2011	5	70	5	70	3.5%	1.00 [0.30, 3.30]
Total (95% CI)		**1870**		**1919**	**100.0%**	**0.82 [0.65, 1.04]**
Total events	173		214			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 12.29$, df = 10 (P = 0.27); $I^2 = 19\%$
Test for overall effect: Z = 1.66 (P = 0.10)



Q1.6 Corneal Edema Postoperatively

APPENDIX Q1

Study or Subgroup	MSICS Mean	MSICS SD	MSICS Total	Phaco Mean	Phaco SD	Phaco Total	Weight	Mean Difference IV, Random, 95% CI
George 2005	4.21	10.29	53	5.41	10.99	60	40.6%	-1.20 [-5.13, 2.73]
Gogate 2010	17.7	10	75	18.4	10	71	59.4%	-0.70 [-3.95, 2.55]
Total (95% CI)			**128**			**131**	**100.0%**	**-0.90 [-3.40, 1.60]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.04$, df = 1 (P = 0.85); $I^2 = 0\%$
Test for overall effect: Z = 0.71 (P = 0.48)

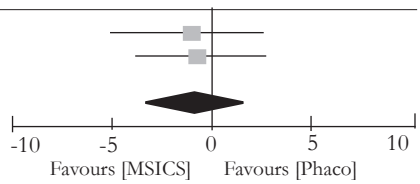


Figure Q1.7 Endothelial Cell Loss Figure

Study or Subgroup	MSICS Mean	MSICS SD	MSICS Total	Phaco Mean	Phaco SD	Phaco Total	Weight	Std. Mean Difference IV, Random, 95% CI
George 2005	1.5	0.77	53	1.38	0.77	60	19.3%	0.15 [-0.22, 0.52]
Gogate 2005a	1.2	1.1	187	1.1	0.9	185	20.8%	0.10 [-0.10, 0.30]
Gogate 2010	0.95	0.7	75	0.48	0.3	71	19.6%	0.86 [0.52, 1.20]
Singh 2009	0.09	0.82	89	0.11	0.74	93	20.1%	-0.03 [-0.32, 0.27]
Venkatesh 2010	1.2	0.36	117	0.8	0.24	113	20.2%	1.30 [1.01, 1.58]
Total (95% CI)			**521**			**522**	**100.0%**	**0.48 [-0.04, 0.99]**

Heterogeneity: $Tau^2 = 0.32$; $Chi^2 = 63.55$, df = 4 (P <0.00001); $I^2 = 94\%$
Test for overall effect: Z = 1.82 (P = 0.07)

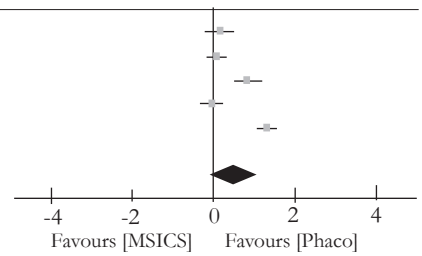


Figure Q1.8 Astigmatism

Q2. AMONG PATIENTS WITH SENILE CATARACTS, HOW EFFECTIVE IS PHACOEMULSIFICATION VERSUS EXTRACAPSULAR CATARACT EXTRACTION (ECCE), IN IMPROVING VISION AND IN TERMS OF ADVERSE OUTCOMES/COMPLICATIONS?

SUMMARY OF EVIDENCE

These findings were derived from 6 randomized controlled trials (RCT)[1-6] and 1 meta-analysis.[7] In the combined analysis, it was noted that good functional vision at 3 months (uncorrected visual acuity and best corrected visual acuity) significantly favored phacoemulsification.[1-4] Good functional vision at 12 months, in terms of uncorrected visual acuity, also significantly favored phacoemulsification.[2] However, at 12 months, measured by best corrected visual acuity, the difference between phacoemulsification and ECCE was insignificant.[2]

Poor visual outcome at 3 months, in terms of best corrected acuity of 6/60 or worse, was significantly lower in phacoemulsification.[1-3] However, after 12 months, this outcome was insignificant between phacoemulsification and ECCE.[2]

Adverse events or complications that did not show any significant difference between the 2 techniques were capsular rupture,[2,3,5] retinal detachment[2] and endothelial cell loss.[2,3,6] However, posterior capsular opacification,[2,5] cystoid macular edema,[2,5] and iris prolapse[2] are complications that were significantly lower with phacoemulsification.

The studies generally had an unclear risk of bias due to poorly reported trial methods and although the quality per outcome ranged from low to moderate, overall quality was deemed low for this question.

DRAFT RECOMMENDATION

Among patients with senile cataracts, phacoemulsification is favored over ECCE because of significant benefit and lower complications. Level of Evidence: Low to Moderate. Strength of Recommendation: Weak.

Table Q2. Summary of Results (please refer to appendix to view forest plots of combined studies).

OUTCOMES	Measure of Treatment Effect	95% Confidence Interval	Interpretation	Basis
Good functional vision at 3 mos (uncorrected visual acuity) **(Fig. Q2.1)**	RR 1.81	1.36-2.41	Favors Phacoemulsification	2 RCTs
Good functional vision at 3 mos (best-corrected visual acuity) **(Fig. Q2.2)**	RR 1.12	1.03-1.22	Favors Phacoemulsification	4 RCTs
Good functional vision at 12 mos (uncorrected visual acuity)	RR 1.99	1.45-2.73	Favors Phacoemulsification	1 RCT
Good functional vision at 12 mos (best corrected visual acuity)	RR 1.06	0.99-1.14	Not significant	1 RCT
Poor visual outcome at 3 mos (best corrected acuity of 6/60 or worse) **(Fig. Q2.3)**	RR 0.33	0.2-0.55	Significantly lower and Favors Phacoemulsification	3 RCTs
Poor visual outcome at 3 mos (best corrected acuity of 6/60 or worse)	RR 0.62	0.36-1.05	Not significant	1 RCT
Capsular Rupturen **(Fig. Q2.4)**	OR 0.56	0.26, 1.22	Not significant	3 RCTs
Retinal detachment	OR 7.04	0.44, 112.93	Not significant	1 RCT
Endothelial Cell loss (%) **(Fig. Q2.5)**	MD 1.0	-0.88, 2.89	Not significant	3 RCTs
Posterior capsular opacification **(Fig. Q2.6)**	OR 0.38	0.22, 0.66	Significantly lower in phacoemulsification	2 RCT
Cystoid macular edema **(Fig. Q2.7)**	OR 0.29	0.29, 0.86	Significantly lower in phacoemulsification	2 RCT
Iris Prolapse	OR 0.12	0.05, 0.32	Significantly lower in phacoemulsification	1 RCT

REFERENCES

1. Chee SP, Ti SE, Sivakumar M, Tan DT. Postoperative inflammation: extracapsular cataract extraction versus phacoemulsification. *J Cataract Refract Surg* 1999;25:1280-5.
2. Bourne RR, Minassian DC, Dart JK, et al. Effect of cataract surgery on the corneal endothelium: modern phacoemulsification compared with extracapsular cataract surgery. *Ophthalmology* 2004;111:679-85.
3. George R, Rupauliha P, Sripriya AV, et al. Comparison of endothelial cell loss and surgically induced astigmatism following conventional extracapsular cataract surgery, manual small-incision surgery and phacoemulsification. *Ophthalmic Epidemiol* 2005;12:293-7.
4. Laurell CG, Zetterstrom C, Philipson B, Syrén-Nordqvist S. Randomized study of the blood-aqueous barrier reaction after phacoemulsification and extracapsular cataract extraction. *Acta Ophthalmol Scand* 1998;76:573-8.
5. Katsimpris JM, Petropoulos IK, Apostolakis K, Feretis D. Comparing phacoemulsification and extracapsular cataract extraction in eyes with pseudoexfoliation syndrome, small pupil, and phacodonesis. *Klin Monbl Augenheilkd*. 2004;221:328-33.
6. Díaz-Valle D, Benítez del Castillo Sánchez JM, Castillo A, et al. Endothelial damage with cataract surgery techniques. *J Cataract Refract Surg* 1998;24:951-5.
7. de Silva SR, Riaz Y, Evans JR. Phacoemulsification with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2014;1:CD008812.

Author(s): Abat M
Date: 2016-04-06
Question: Should Phacoemulsification with posterior chamber intraocular lens vs extracapsular cataract extraction with posterior chamber intraocular lens be used for age-related cataract?
Settings: Chee 1999 – Singapore; Diaz-Valle 1998 – Spain; George 2005 – India; Katsimpris 2004 – Greece; Laurell 1998 – Sweden; MEHOX 2004 – UK
Bibliography:* 1. de Silva SR, Riza Y, Evans JR. Phacoemulsification with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2014;1:CD008812.

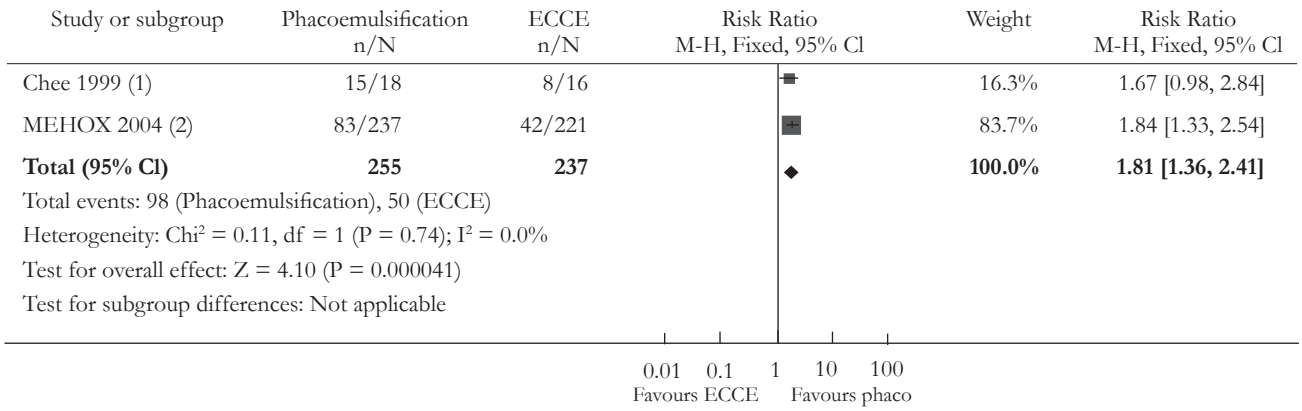
***Note:** Only the meta-analysis is listed here as reference. Please refer to the Evidence Summary for a complete list of references.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phacoemulsification with posterior chamber intraocular lens	Extracapsular cataract extraction with posterior chamber intraocular lens	Relative (95% CI)	Absolute		
good functional vision at 3 months (UCVA) (follow-up 2-3 months; assessed with: uncorrected visual acuity)												
2	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none[3]	98/255 (38.4%)	50/237 (21.1%)	RR 1.81 (1.36 to 2.41)	171 more per 1000 (from 76 more to 297 more)	ÅÅÅO MODERATE	
good functional vision at 3 months (CVA) (follow-up 6-12 weeks; assessed with: corrected visual acuity)												
4	randomised trials	serious[2,4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	313/336 (93.2%)	248/309 (80.3%)	RR 1.12 (1.03 to 1.22)	96 more per 1000 (from 24 more to 177 more)	ÅÅÅO MODERATE	
good functional vision at 12 months (UCVA)[5] (follow-up mean 12 months; assessed with: uncorrected visual acuity)												
1[5]	randomised trials[1]	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	87/224 (38.8%)	42/215 (19.5%)	RR 1.99 (1.45 to 2.73)	193 more per 1000 (from 88 more to 338 more)	ÅÅÅO MODERATE	
good functional vision at 12 months (CVA) (follow-up mean 12 months; assessed with: corrected visual acuity)												
1[5]	randomised trials[1]	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	204/224 91.1%)	184/215 (85.6%)	RR 1.06 (0.99 to 1.14)	Not applicable	ÅÅÅO MODERATE	
poor visual outcome at 3 months (CVA) (follow-up mean 3 months; assessed with: best corrected visual acuity)												
3	randomised trials	very serious[2,8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/315 (5.4%)	49/289 (17%)	RR 0.33 (0.2 to 0.55)	114 fewer per 1000 (from 76 fewer to 136 fewer)	ÅÅOO LOW	
poor visual outcome at 12 months (CVA) (follow-up mean 12 months; assessed with: best corrected visual acuity)												
1[5]	randomised trials	serious[2,8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/224 (8.9%)	31/215 (14.4%)	RR 0.62 (0.36 to 1.05)	Not applicable	ÅÅÅO MODERATE	
capsular rupture (follow-up 2-12 months; assessed with: incidence of capsule rupture)												
3	randomised trials	very serious[7,8,9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/353 (2.8%)	17/335 (5.1%)	OR 0.56 (0.26 to 1.22)	Not applicable	ÅÅOO LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phaco-emulsification with posterior chamber intraocular lens	Extracapsular cataract extraction with posterior chamber intraocular lens	Relative (95% CI)	Absolute		
posterior capsular opacification (follow-up 12-14 months; assessed with: incidence of posterior capsular opacification)												
2	randomised trials	very serious[7,9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/292 (5.8%)	40/279 (14.3%)	OR 0.38 (0.22 to 0.66)	84 fewer per 1000 (from 44 fewer to 108 fewer)	ÅÅOO LOW	
retinal detachment (follow-up mean 12 months; assessed with: incidence of retinal detachment)												
1	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/245 (0.82%)	0/232 (0%)	OR 7.04 (0.44 to 112.93)	Not applicable	ÅÅÅO MODERATE	
cystoid macular edema (follow-up 12-14 months; assessed with: incidence of cystoid macular edema)												
2	randomised trials	very serious[7,9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	3/292 (1%)	11/279 (3.9%)	OR 0.29 (0.1 to 0.8)	28 fewer per 1000 (from 8 fewer to 35 fewer)	ÅÅOO LOW	
iris prolapse[5] (follow-up mean 12 months; assessed with: incidence of iris prolapse)												
1	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/246 (0%)	17/236 (7.2%)	OR 0.12 (0.05 to 0.32)	63 fewer per 1000 (from 48 fewer to 68 fewer)	ÅÅÅO MODERATE	
Endothelial Cell Loss												
3	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none			MD??		ÅÅÅO MODERATE	

[1] all studies included were RCTs
[2] Chee 1999 had unclear risk for bias for random sequence generation, concealment, and blinding of participants, personnel and outcome assessment. MEHOX 2004 had unclear risk for bias for incomplete outcome data
[3] pooled RR 1.81 (CI 95% 1.36-2.41)
[4] George 2005 had unclear risk for bias for allocation concealment, blinding, and incomplete outcome data. Laurell 1998 had unclear risk for bias for blinding of participants and personnel, and selective reporting
[5] MEHOX 2004
[6] No explanation was provided
[7] MEHOX 2004 had unclear risk for bias for incomplete outcome data
[8] George 2005 had unclear risk for bias for allocation concealment, blinding, and incomplete outcome data.
[9] Katsimpris 2004 had unclear risk for bias for random sequence generation, concealment, and blinding

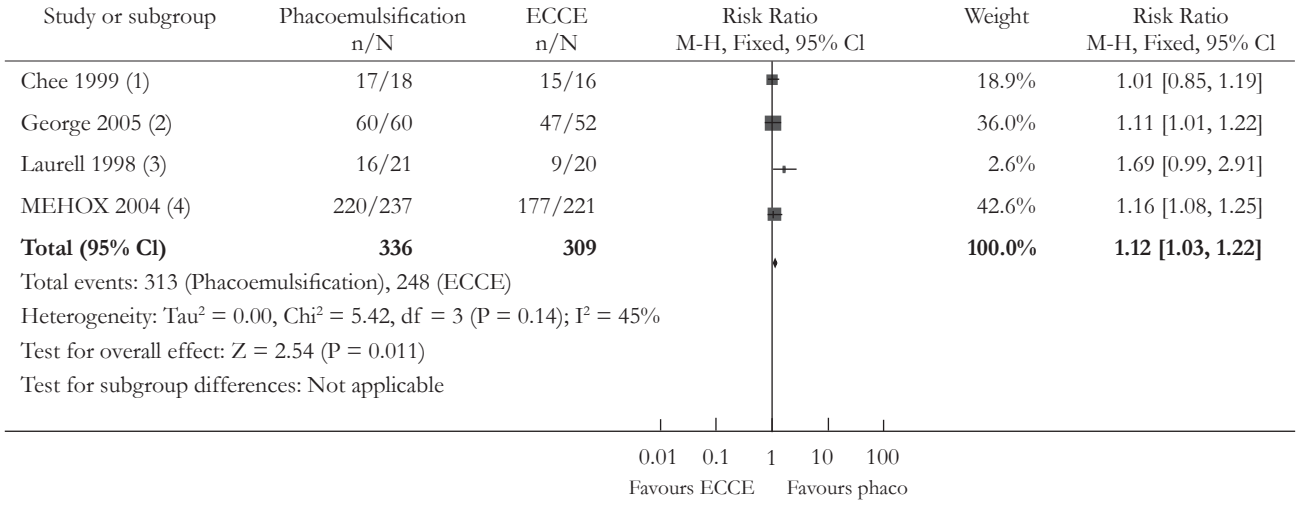
APPENDIX Q2



(1) 6/12 or better; 2 months follow-up

(2) 6/9 or better; 3 months follow-up

Figure Q2.1 Good functional vision at 3 months (uncorrected visual acuity)



(1) 6/12 or better; 2 months follow-up

(2) 6/12 or better; 6 weeks follow-up

(3) better than 6/6; 3 months follow-up

(4) 6/9 or better; 3 months follow-up

Figure Q2.2 Good functional vision at 3 months (best-corrected visual acuity)

APPENDIX Q2

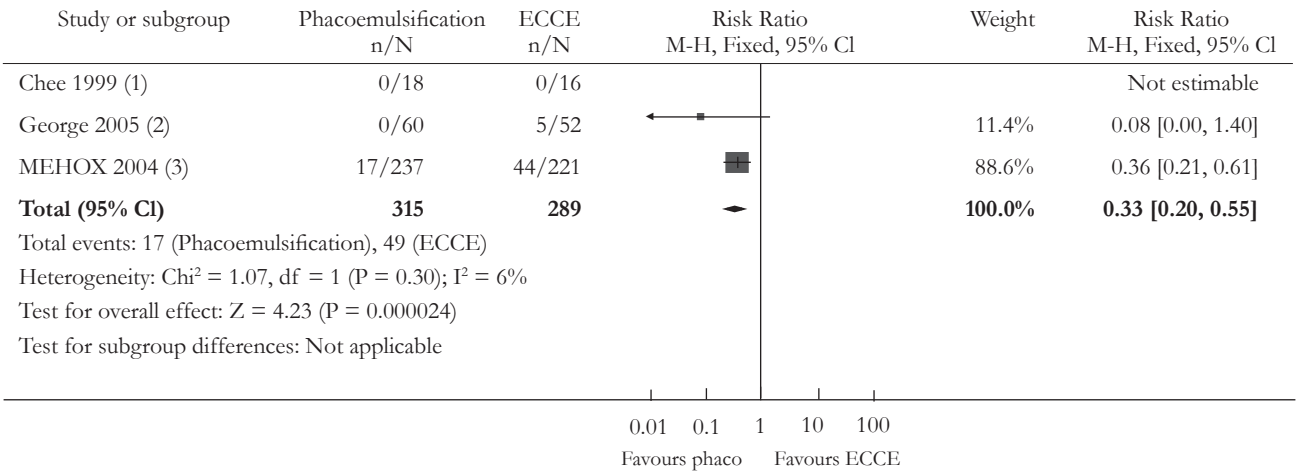


Figure Q2.3 Poor visual outcome at 3 months (best corrected acuity of 6/60 or worse)

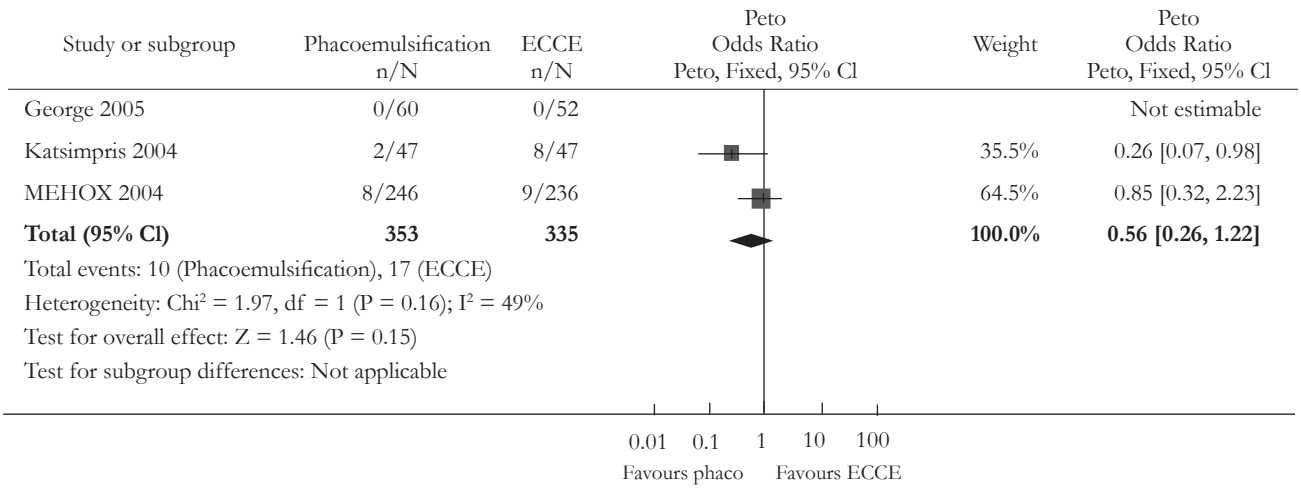


Figure Q2.4 Capsular Rupture

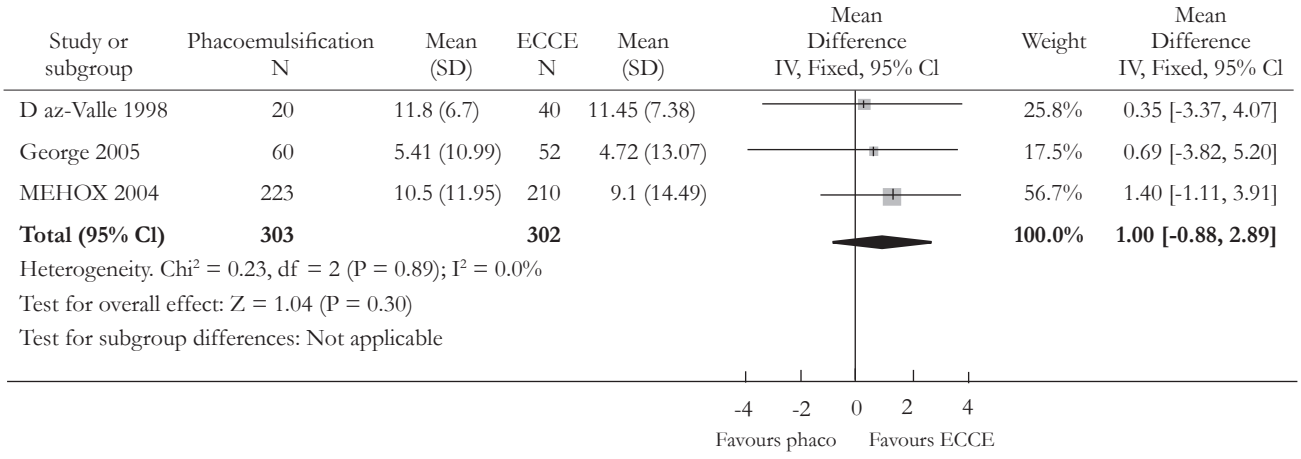


Figure Q2.5 Endothelial Cell loss (%)

APPENDIX Q2

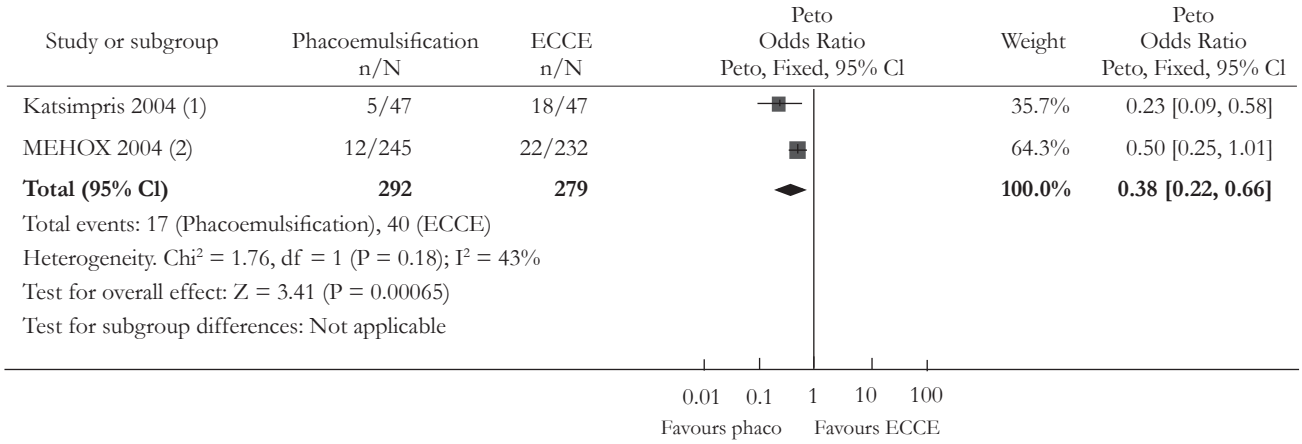


Figure Q2.6 Posterior capsular opacification

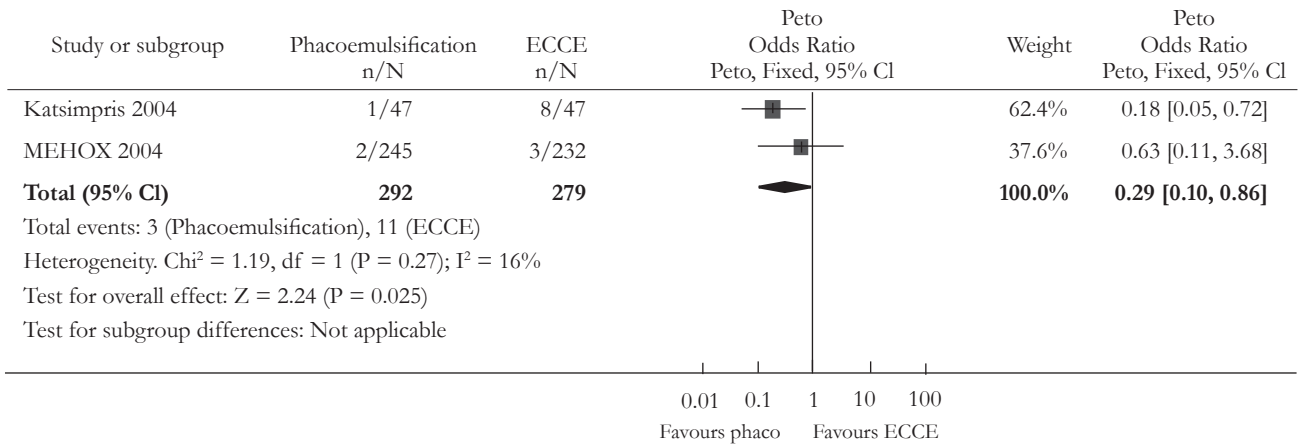


Figure Q2.7 Cystoid macular edema

Q3. AMONG PATIENTS WITH SENILE CATARACTS, HOW EFFECTIVE IS MANUAL SMALL INCISION CATARACT SURGERY (MSICS) VERSUS EXTRA-CAPSULAR CATARACT EXTRACTION (ECCE) IN IMPROVING VISION AND IN TERMS OF ADVERSE OUTCOMES/ COMPLICATIONS?

SUMMARY OF EVIDENCE

Evidence from 2 randomized controlled trials (RCTs) showed that there was no significant difference in terms of improvement of visual acuity at 6-8 weeks between MSICS and ECCE with a relative risk (RR) of 1.57 (95% CI 0.88, 2.8) [Figure Q3.1 in Appendix Q3].[1,2] However the data presented in these 2 RCTs reporting poor visual outcome were not combined due to difference on how the measurements were made. Both RCTs reported an insignificant difference between the 2 procedures with regards to poor visual outcomes at 6-8 weeks. One study reported an RR of 1.58 (95% CI 0.45,5.0) supporting the insignificant findings.[1]

Surgically-induced astigmatism was significantly less for MSICS. One study reported a mean induced astigmatism in diopters of 1.77±1.65 for ECCE vs 1.1±0.95 for MSICS, p=0.012.[3] In another study, the incidence of astigmatism of ≥2D had a relative risk of 0.49, (95% CI 0.32-0.74) indicating less astigmatism in the MSICS technique.[2]

Intraoperative and postoperative complications based on 1 RCT, were significantly higher with MSICS, with relative risks of 1.83 (95% CI 1.02-3.26), and 1.38 (95% CI 1.1-1.73), respectively.[1] Both intraoperative and postoperative complications reported in the RCT were graded and scored as described by the Oxford Cataract Treatment and Evaluation Team (OCTET). Please refer to Appendix Q3 for the list of complications monitored. This list does not include astigmatism.

There were limited number of studies with issues on allocation and concealment. It was unfortunate that most of the data could not be combined due to differences in reporting of outcomes.

DRAFT RECOMMENDATION

There is still inadequate evidence that MSICS showed improved visual acuity (VA) compared to ECCE. MSICS has less surgically-induced astigmatism, but significantly more complications compared to ECCE. Strength of Recommendation: Weak. Level of Evidence: Low--Moderate.

REFERENCES

1. Gogate PM, Deshpande M, Wormald RP, et al. Extracapsular cataract surgery compared with manual small incision cataract surgery in community eye care setting in Western India: a randomised controlled trial. *Br J Ophthalmol* 2003;87:667-72.
2. Gurung A, Karki DB, Shrestha S, Rijal AP. Visual outcome of conventional extracapsular cataract extraction with posterior chamber intraocular lens implantation versus manual small-incision cataract surgery. *Nepal J Ophthalmol* 2009;1:13-9.
3. George R, Rupauliha P, Sripriya AV, et al. Comparison of endothelial cell loss and surgically induced astigmatism following conventional extracapsular cataract surgery, manual small-incision surgery and phacoemulsification. *Ophthalmic Epidemiol* 2005;12:293-7.
4. Ang M, Evans JR, Mehta JS. Manual small incision cataract surgery (MSICS) with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2014;11:CD008811.

Author(s): Abat M
Date: 2016-04-06
Question: Should manual small incision cataract surgery (MSICS) with posterior chamber intraocular lens vs extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens be used for age-related cataract?
Settings: George 2005, Gogate 2003 – India; Gurung 2009 – Nepal
Bibliography:* Ang M, Evans JR, Mehta JS. Manual small incision cataract surgery (MSICS) with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2014;11:CD008811

***Note:** Only the meta-analysis was listed here as reference. Please refer to Evidence Summary for complete reference list.

Quality assessment							No. of patients		Effect			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**MSICS with posterior chamber intraocular lens**	**ECCE with posterior chamber intraocular lens**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
improved visual outcome (follow-up 6-8 weeks; assessed with: visual acuity)												
2[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	182/394 (46.2%)	142/412 (34.5%)	RR 1.57 (0.88, 2.80)	-	⍰⍰OO LOW	
poor visual outcome (best-corrected visual acuity < 6/60)												
1[3]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/344 (1.7%)	4/362 (1.1%)	RR 1.58 (0.45, 5.0)	-	⍰⍰OO LOW	
surgically-induced astigmatism/SIA (follow-up mean 6 weeks; measured with: mean induced astigmatism in diopters; range of scores: 0.12-3.42; Better indicated by lower values)												
1[3]	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	62	62	-	mean 1.77 ± 1.65 diopters in ECCE versus 1.1 ± 0.95 in MSICS; SIA greater in the ECCE group	⍰⍰OO LOW	
surgically-induced astigmatism (follow-up 6-8 weeks; assessed with: astigmatism >= 2D)												
1[5]	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/48 (35.4%)	35/48 (72.9%)	RR 0.49 (0.32 to 0.74)	372 fewer per 1000 (from 190 fewer to 496 fewer)	⍰⍰OO LOW	
intraoperative complications (assessed with: incidence)												
1[7]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29/358 (8.1%)	17/383 (4.4%)	RR 1.83 (1.02 to 3.26)	37 more per 1000 (from 1 more to 100 more)	⍰⍰⍰O MODERATE	
postoperative complications (follow-up mean 6 weeks; assessed with: incidence)												
1[7]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	121/358 (33.8%)	94/383 (24.5%)	RR 1.38 (1.1 to 1.73)	93 more per 1000 (from 25 more to 179 more)	⍰⍰⍰O MODERATE	

[1] Gogate 2003, Gurung 2009
[2] Gogate 2003 had unclear risk for bias for selective reporting and other bias (some surgeons performed more surgeries of one kind if the operating list was more, compared to the other technique). Gurung 2009 had unclear risk of bias for all criteria
[3] George 2005
[4] George 2005 had unclear risk for bias for allocation concealment blinding and selective reporting
[5] Gurung 2009
[6] Gurung 2009 had unclear risk of bias for all criteria
[7] Gogate 2003
[8] Gogate 2003 had unclear risk for bias for selective reporting and other bias (some surgeons performed more surgeries of one kind if the operating list was more, compared to the other technique).

APPENDIX Q3

Study or Subgroup	MSICS Events	MSICS Total	ECCE Events	ECCE Total	Weight	Risk Ratio M-H, Random, 95% CI
Gogate 2003	165	344	135	362	68.8%	1.29 [1.08, 1.53]
Gurung 2009	17	50	7	50	31.2%	2.43 [1.10, 5.34]
Total (95% CI)		**394**		**412**	**100.0%**	**1.57 [0.88, 2.80]**
Total events	1.82		142			

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 2.41$, df = 1 (P = 0.12): $I^2 = 59\%$
Test for overall effect: Z = 1.52 (P = 0.13)

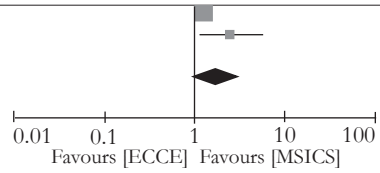


Figure Q3.1 Improvement of visual acuity at 6-8 weeks

INTRAOPERATIVE COMPLICATIONS BY OCTET GRADE AND SCORE*

Intraoperative complications	Grade	Score
Descement's membrane tear	0	0
Shallow AC	0	0
Iris prolapse	0	0
Remnants of cortex	0	0
Failure to implant	0	0
Iridodialysis	1	1-4
Sphincter tear	1	1-4
Nucleus dislocated into vitreous	3	9-13
Rupture of posterior capsule without vitreous loss	2	5-8
Rupture of posterior capsule with vitreous loss	3	9-13
Zonular dialysis/rupture without vitreous loss	2	5-8
Zonular dialysis/rupture with vitreous loss	3	9-13
Large remnants of viscoelastic material	2	5-8

POSTOPERATIVE COMPLICATIONS BY OCTET GRADE AND SCORE*

Postoperative complications	Grade	Score
Pain	0	0
Eyelid swelling	0	0
Chemosis	0	0
External/subconjunctival swelling	0	0
Descement's membrane folds <10	1	1-4
Descement's membrane folds >10	1	1-4
Descement's membrane tear >1/3 of cornea	2	5-8
Transient corneal oedema	1	1-4
Epithelial bullae or defect	1	1-4
Shallow AC iris touches cornea	2	5-8
Wound leak	1	1-4
Hypaema <3 mm blood in AC	1	1-4
Hypaema >3 mm blood in AC	2	5-8
Mild iritis <50 cells in 2 x 1 slit beam	1	1-4
Severe iritis >50 cells in 2 x 1 slit beam	2	5-8
Hypopyon	3	9-13
Decentred pupil	1	1-4
Residual cortex	1	1-4
Vitreous in AC not touching cornea	1	1-4
Vitreous in AC touching cornea	2	5-8
Pupillary block glaucoma	3	9-13
Choroidal effusion	2	5-8
Endophthalmitis	3	9-13
Pupillary capture	1	1-4
Malposition of haptic	1	1-4
Deposits on implant	1	1-4
Decentred implant	2	5-8
Posterior capsule opacification	1	1-4

* Taken from: Gogate PM, Deshpande M, Wormald RP, Deshpande R, Kulkarni SR. Extracapsular cataract surgery compared with manual small incision cataract surgery in community eye care setting in Western India: a randomised controlled trial. *Br J Ophthalmol* 2003;87:667-72.

Q4. AMONG PATIENTS WITH SENILE CATARACTS, HOW EFFECTIVE IS FEMTOSECOND LASER-ASSISTED CATARACT SURGERY (FLACS) VS. CONVENTIONAL PHACOEMULSIFICATION IN IMPROVING VISION AND IN TERMS OF ADVERSE OUTCOMES/COMPLICATIONS?

SUMMARY OF EVIDENCE

There was no significant difference between FLACS and conventional phacoemulsification in the overall result, in terms of improvement in vision, measured by uncorrected distance visual acuity.[1,2] It was also insignificant when sub-grouped by follow-up time (at 1 week, 1 month and 6 months).

As for improvement in vision (measured by corrected distance visual acuity), there was a significant difference favoring FLACS when looking at the overall result, with a mean difference of -0.03 LogMAR units.* (Please refer to Appendix Q4 for the Snellen equivalent). This implies a significant improvement of visual acuity by 0.03 using the LogMAR chart favoring FLACS. The difference is also significant at 1 week and at 6 months postoperatively.[1-3]

However, among the adverse outcomes, the differences were insignificant between FLACS and conventional phacoemulsification in the rates of anterior capsule tear,[4,5] elevated intraocular pressure,[4,6] and macular edema.[4,6]

One study showed that based on the *simulated* complication rates of phacoemulsification and FLACS and assuming resultant visual acuity outcome improvement of 5% in uncomplicated cases of FLACS, the cost-effectiveness (dollars spent per QALY) gained from FLACS was not cost-effective at AUD $92,862.[7]

There were 7 RCTs[1-7] and 1 meta-analysis[2] that showed these findings. Unfortunately there was unclear to high risk for bias for the included studies. These were mainly from issues with randomization and allocation concealment. The studies were also at high risk for performance and detection bias. Consistency issues were seen in the primary outcomes, but not evident in the complications.

DRAFT RECOMMENDATION

Among patients with senile cataracts, FLACS is better over conventional phacoemulsification, in terms of corrected distance visual acuity. Level of Evidence: Very Low. Strength of Recommendation: Weak.

Table Q4.1 Summary of Results (please refer to appendix to view forest plots of combined studies).

OUTCOMES	Measure of Treatment Effect	95% Confidence Interval	Interpretation	Basis
Improvement of Vision (uncorrected distance visual acuity) **(Fig Q4.1)**	MD -0.04	-0.09 to 0.02	Not significant	3 RCTs
Improvement of Vision (corrected distance visual acuity) **(Fig. Q4.2)**	MD -0.03	-0.05 to -0.01	Significant favoring FLACS	4 RCTs
Anterior capsule tear **(Fig. Q4.3)**	OR 0.63	0.08 to 4.83	Not significant	2 RCTs
Elevated intraocular pressure **(Fig. Q4.3)**	OR 0.8	0.21 to 3.01	Not significant	2 RCTs
Macular edema **(Fig. Q4.3)**	OR 0.49	0.14 to 1.65	Not significant	2 RCTs

*Logarithm of the Minimum Angle of Resolution (LogMAR) chart is developed to come up with a standardized and more accurate way of measuring visual acuity compared to other charts such as the Snellen chart. The LogMAR chart comprises the same number of test letters in each line.

REFERENCES

1. Kránitz K, Miháltz K, Sándor GL, et al. Intraocular lens tilt and decentration measured by Scheimpflug camera following manual or femtosecond laser-created continuous circular capsulotomy. *J Refract Surg* 2012;28:259-263.
2. Mastropasqua L, Toto L, Mattei PA, et al. Optical coherence tomography and 3-dimensional confocal structured imaging system-guided femtosecond laser capsulotomy versus manual continuous curvilinear capsulorhexis. *J Cataract Refract Surg.* 2014;40:2035-2043.
3. Filkorn T, Kovács I, Takács A, et al. Comparison of IOL power calculation and refractive outcome after laser refractive cataract surgery with a femtosecond laser versus conventional phacoemulsification. *J Refract Surg* 2012;28:540-544.
4. Conrad-Hengerer I, Al Juburi M, Schultz, T., et al. Corneal endothelial cell loss and corneal thicknessin conventional compared with femtosecond laser-assisted cataract surgery: three-month follow-up. *J Cataract Refract Surg* 2013;39:1307-1313.
5. Reddy KP, Kandulla J, Auffarth GU. Effectiveness and safety of femtosecond laser-assisted lens fragmentation and anterior capsulotomy versus the manual technique in cataract surgery. *J Cataract Refract Surg* 2013;39:1297-1306.
6. Conrad-Hengerer I, Hengerer FH, Al Juburi M, et al. Femtosecond laser-induced macular changes and anterior segment inflammation in cataract surgery. *J Refract Surg* 2014;30:222-226.
7. Abell RG, Vote BJ. Cost-effectiveness of femtosecond laser-assisted cataract surgery versus phacoemulsification cataract surgery. *Ophthalmology.* 2014;121:10-16.
8. Chen X, Xiao W, Ye S, et al. Efficacy and safety of femtosecond laser-assisted cataract surgery versus conventional phaco-emulsification for cataract: a meta-analysis of randomized controlled trials. *Sci Rep* 2015;5:13123.

Author(s): Abat M
Date: 2016-04-09
Question: Should Femtosecond laser-assisted cataract surgery vs Phacoemulsification be used for cataracts?
Settings: Kranitz 2012 – Hungary; Filkorn 2012, Hengerer 2013 & 2014 – Germany; Reddy 2013 – India; Leonardo 2014 - Italy
Bibliography:* Chen X, Xiao W, Ye S, et al. Efficacy and safety of femtosecond laser-assisted cataract surgery versus conventional phaco-emulsification for cataract: a meta-analysis of randomized controlled trials. *Sci Rep* 2015;5:13123.

Note: *Only the meta-analysis is listed here as reference. Please refer to the Evidence Summary for a complete list of references.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Femtosecond laser-assisted cataract surgery	Phaco-emulsification	Relative (95% CI)	Absolute		
improved vision UDVA (follow-up 1-24 weeks; measured with: uncorrected distance visual acuity; Better indicated by lower values)												
3	randomised trials	very serious[1,2]	very serious[3]	no serious indirectness	no serious imprecision	none	310	200	-	MD 0.04 lower (0.09 lower to 0.02 higher)	ÅOOO VERY LOW	
improved vision CDVA (follow-up 1-24 weeks; measured with: corrected distance visual acuity; Better indicated by lower values)												
4	randomised trials	very serious[1,4]	very serious[5]	no serious indirectness	serious[6]	none	387	287	-	MD 0.03 lower (0.05 to 0.02 lower) Favoring FLACS	ÅOOO VERY LOW	
anterior capsular tear (follow-up 1-84 days; assessed with: incidence)												
2	randomised trials	very serious[2,7]	no serious inconsistency	no serious indirectness	very serious[6,8]	none	1/129 (0.78%)	2/136 (1.5%)	OR 0.63 (0.08 to 4.83	5 fewer per 1000 (from 14 fewer to 53 more)	ÅOOO VERY LOW	
elevated intraocular pressure (follow-up 12-24 weeks; assessed with: incidence)												
2	randomised trials	very serious[2,9]	no serious inconsistency	no serious indirectness	very serious[6,8]	none	4/177 (2.3%)	5/177 (2.8%)	OR 0.8 0.221 to 3.01)	6 fewer per 1000 (from 22 fewer to 52 more)	ÅOOO VERY LOW	
macular edema (follow-up 12-24 weeks; assessed with: incidence)												
2	randomised trials	very serious[2,9]	no serious inconsistency	no serious indirectness	very serious[6,8]	none	4/177 (2.3%)	8/177 (4.5%)	OR 0.49 (0.14 to 1.65)	23 fewer per 1000 (from 39 fewer to 27 more)	ÅOOO VERY LOW	

[1] Kranitz 2012 had low risk for bias for selection bias, attrition bias and other biases. Leonardo 2014 had low risk for bias for attrition and other biases. Leonard 2014-2 was low risk for bias for selection, attrition, detection and other biases
[2] all studies at high risk for blinding
[3] I2=92%
[4] Filkorn 2012 was low risk for bias for selection, attrition and other biases
[5] I2=86%
[6] wide CIs
[7] Hengerer 2013 was low risk for bias for allocation, attrition and other bias only. Reddy 2013 was low risk for bias for attrition and other bias
[8] crossed unity
[9] Hengere 2013 and 2014 were low risk for bias for allocation, attrition bias and other biases

APPENDIX Q4

The Snellen Equivalent of LogMAR Units

Visual acuity scales

Foot	Metre	Decimal	LogMAR
20/200	6/60	0.10	1.00
20/160	6/48	0.125	0.90
20/125	6/38	0.16	0.80
20/100	6/30	0.20	0.70
20/80	6/24	0.25	0.60
20/63	6/19	0.32	0.50
20/50	6/15	0.40	0.40
20/40	6/12	0.50	0.30
20/32	6/9.5	0.63	0.20
20/25	6/7.5	0.80	0.10
20/20	6/6	1.00	0.00
20/16	6/4.8	1.25	-0.10
20/12.5	6/3.8	1.60	-0.20
20/10	6/3	2.00	-0.30

Postoperative UDVA	Femtosecond laser			Conventional phaco				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 1 week									
Kinga Kŕanitz, 2012	0.23	0.05	20	0.29	0.09	25	15.5%	-0.06 [-0.10, -0.02]	
Leonardo M, 2014	0.41	0.15	30	0.35	0.15	30	13.0%	0.06 [-0.02, 0.14]	
Leonardo M, 2014-2	0.08	0.08	60	0.18	0.05	0		Not estimable	
Subtotal (95% CI)			**110**			**55**	**28.5%**	**-0.00 [-0.12, 0.11]**	
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 7.39$, df = 1 (P = 0.007); $I^2 = 86\%$									
Test for overall effect: Z = 0.07 (P = 0.94)									
1.1.2 1 month									
Kinga Kŕanitz, 2012	0.16	0.03	20	0.21	0.06	25	16.3%	-0.05 [-0.08, -0.02]	
Leonardo M, 2014	0.35	0.23	30	0.28	0.13	30	11.5%	0.07 [-0.02, 0.16]	
Leonardo M, 2014-2	0.1	0.1	60	0.21	0.09	30	15.6%	-0.11 [-0.15, -0.07]	
Subtotal (95% CI)			**110**			**85**	**43.4%**	**-0.04 [-0.11, 0.03]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 13.51$, df = 2 (P = 0.001); $I^2 = 85\%$									
Test for overall effect: Z = 1.23 (P = 0.22)									
1.1.3 6 months									
Leonardo M, 2014	0.13	0.21	30	0.08	0.15	30	11.6%	0.05 [-0.04, 0.14]	
Leonardo M, 2014-2	0.1	0.06	60	0.25	0.05	30	16.5%	-0.15 [-0.17, -0.13]	
Subtotal (95% CI)			**90**			**60**	**28.1%**	**-0.06 [-0.25, 0.14]**	
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 16.93$, df = 1 (P <0.0001); $I^2 = 94\%$									
Test for overall effect: Z = 0.55 (P = 0.58)									
Total (95% CI)			**310**			**200**	**100%**	**-0.04 [-0.09, 0.02]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 71.22$, df = 6 (P = <0.00001); $I^2 = 92\%$									
Test for overall effect: Z = 1.32 (P = 0.19)									
Test for subgroup differences: $Chi^2 = 0.36$, df = 2 (P = 0.83); $I^2 = 0\%$									

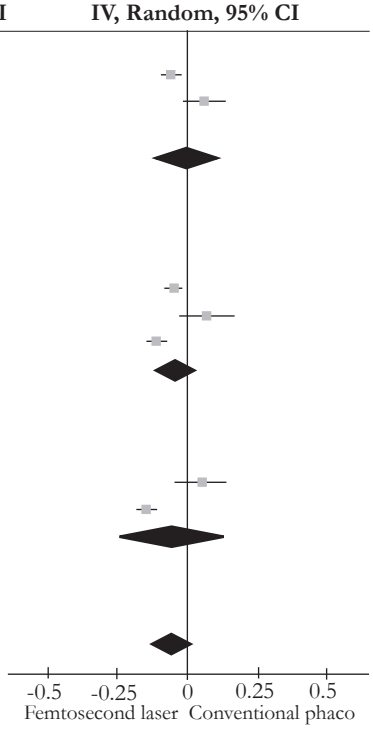


Figure Q4.1 Improvement of Vision (uncorrected distance visual acuity)

APPENDIX Q4

Postoperative CDVA	Femtosecond laser			Conventional phaco				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
1.2.1 1 week								
Kinga Kŕanitz, 2012	0.05	0.01	20	0.11	0.03	25	16.6%	-0.06 [-0.07, -0.05]
Leonardo M, 2014	0.19	0.15	30	0.19	0.15	30	4.9%	0.00 [-0.08, 0.08]
Leonardo M, 2014-2	-0.03	0.08	60	0.01	0.07	30	12.1%	-0.04 [-0.07, -0.01]
Subtotal (95% CI)			**110**			**85**	**33.6%**	**-0.05 [-0.07, -0.03]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.43$, df = 2 (P = 0.18); $I^2 = 42\%$								
Test for overall effect: Z = 4.13 (P <0.0001)								
1.2.2 1-3 months								
Kinga Kŕanitz, 2012	0.03	0.003	20	0.08	0.01	25	17.7%	-0.05 [-0.05, -0.05]
Leonardo M, 2014	0.18	0.18	30	0.16	0.12	30	4.7%	0.02 [-0.06, 0.10]
Leonardo M, 2014-2	-0.08	0.7	60	-0.06	0.1	30	10.3%	-0.02 [-0.06, 0.02]
Tamás Filkom, 2012	0.03	0.06	77	0.02	0.04	57	15.8%	0.01 [-0.01, 0.03]
Subtotal (95% CI)			**187**			**142**	**48.5%**	**-0.01 [-0.06, 0.03]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 49.92$, df = 3 (P <0.00001); $I^2 = 94\%$								
Test for overall effect: Z = 0.66 (P = 0.51)								
1.2.3 6 months								
Leonardo M, 2014	-0.08	0.09	30	-0.03	0.12	30	7.7%	-0.05 [-0.10, 0.00]
Leonardo M, 2014-2	-0.09	0.07	60	-0.06	0.1	30	10.3%	-0.03 [-0.07, -0.01]
Subtotal (95% CI)			**90**			**60**	**17.9%**	**-0.04 [-0.07, -0.01]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.34$, df = 1 (P =0.56); $I^2 = 0\%$								
Test for overall effect: Z = 2.27 (P = 0.02)								
Total (95% CI)			**387**			**287**	**100.0%**	**-0.03 [-0.05, -0.01]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 56.56$, df = 8 (P <0.00001); $I^2 = 86\%$								
Test for overall effect: Z = 3.00 (P = 0.003)								
Test for subgroup differences: $Chi^2 = 2.00$, df = 2 (P = 0.37); $I^2 = 0.1\%$								

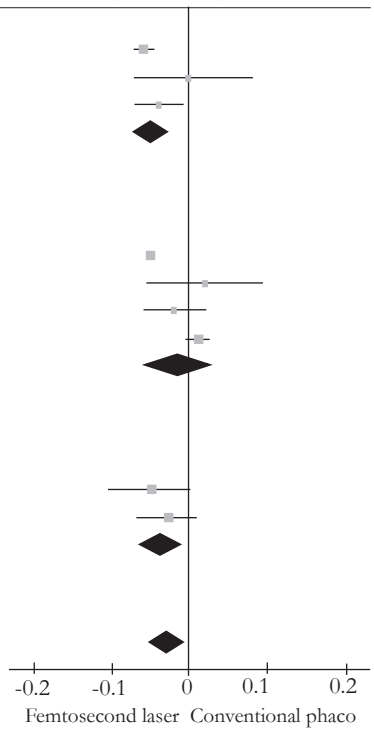


Figure Q4.2 Improvement of Vision (corrected distance visual acuity)

APPENDIX Q4

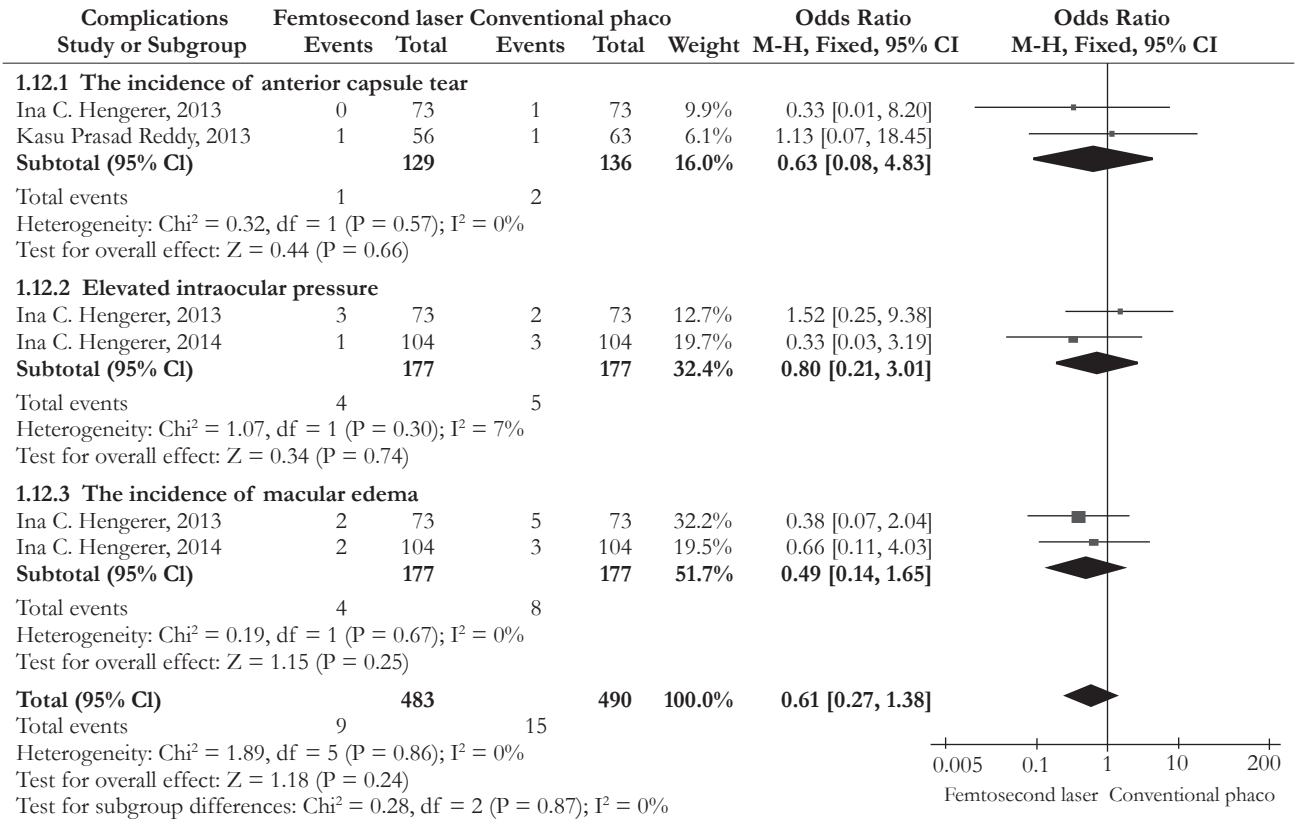


Figure Q4.3 Anterior capsule tear, elevated intraocular pressure & macular edema

Q5. AMONG PATIENTS WITH SENILE CATARACTS SCHEDULED FOR SURGERY, WILL ROUTINE MEDICAL PRE-OPERATIVE TESTING VERSUS NO ROUTINE TESTING REDUCE MORTALITY, MORBIDITY, AND ADVERSE EVENTS?

SUMMARY OF EVIDENCE

Based on moderate level of evidence, there was no significant difference in the rates of intraoperative or postoperative ocular and medical adverse events between routine medical preoperative testing and no routine medical preoperative testing.

A meta-analysis of 3 randomized controlled trials that included 21,531 cataract surgeries done under local anesthesia showed that overall risk for adverse medical events from cataract surgery was low (3 out of 100 surgeries).[1] The rate of adverse events was similar between the routine preoperative testing group (353 events out of 10,764 surgeries) and the no routine testing group (354 events out of 10,766 surgeries). Adverse events were mostly cardiovascular in nature (e.g. half were blood pressure elevations requiring treatment) and occurred intraoperatively. The rate of postponement or cancellation of surgery was also similar in the 2 groups (161 out of 10,287 surgeries in the routine testing group vs. 166 out of 10,295 surgeries in the no testing group).[2,3] Cost was evaluated in one study, which estimated that the cost was 2.5 times higher in those who underwent preoperative testing than those who did not.[2]

Only one study reported rates of myocardial infarction, stroke, and hypoglycemia within 7 days of cataract surgery separately.[3] There was no difference between routine testing and no testing for these outcomes, however confidence intervals for the

results were wide, because event rates were very low (less than 10 in 10,000 in both groups). None of these events occurred intraoperatively.

Majority of the participants enrolled in the included studies were patients with mild to severe, non-incapacitating systemic diseases (e.g. hypertension, diabetes, congestive heart failure, and bleeding disorders). Routine preoperative tests included ECG, CBC, blood sugar, serum electrolytes, BUN and creatinine. Outcomes evaluated were ocular complications, medical adverse events requiring treatment, and postponement or cancellation of surgery.

The results of the meta-analysis were driven mainly by the largest study in the meta-analysis, which included a total of more than 19,000 surgeries[3]. However, this trial was methodologically sound, and the results were consistent across all the studies included in the meta-analysis.

Given these findings, routine medical pre-operative testing is not recommended for patients with senile cataracts scheduled for surgery.

DRAFT RECOMMENDATION

Among patients with senile cataracts scheduled for cataract surgery under local anesthesia, routine medical pre-operative testing is NOT recommended. Level of Evidence: Moderate-high Strength of Recommendation: Strong.

REFERENCES

1. Keay L, Lindsley K, Tielsch J, et al. Routine preoperative medical testing for cataract surgery. *Cochrane Database Syst Rev* 2012;3:CD007293.
2. Lira RP, Nascimento MA, Moreira-Filho DC, et al. Are routine preoperative medical tests needed with cataract surgery? *Rev Panam Salud Publica*. 2001;10:13-7.
3. Schein OD, Katz J, Bass EB, et al. The value of routine preoperative medical testing before cataract surgery. Study of medical testing for cataract surgery. *N Engl J Med* 2000; 342:168-175.
4. Cavallini GM, Saccarola P, D'Amico R, et al. Impact of preoperative testing on ophthalmologic and systemic outcomes in cataract surgery. *Eur J Ophthalmol* 2004;14:369-74.

Table Q5. Summary of Results (please refer to appendix to view forest plots of combined studies).

OUTCOMES	Measure of Treatment Effect	95% Confidence Interval	Interpretation	Basis
Total intraoperative medical adverse events **(Fig. Q5.1)**	OR 1.02	0.85-1.22	Not significant	3 RCTs
Total postoperative medical adverse events **(Fig. Q5.2)**	OR 0.96	0.74-1.24	Not significant	2 RCTs
Total intraoperative ocular adverse events **(Fig. Q5.3)**	OR 0.99	0.71-1.38	Not significant	2 RCTs
Postoperative ocular adverse events **(Fig. Q5.4)**	OR 1.11	0.74-1.67	Not significant	2 RCTs
Total postoperative deaths **(Fig. Q5.5)**	OR 0.5	0.05-5.52	Not significant	2 RCTs
Myocardial infarction within 7 days of surgery	RR 1.67	0.40-6.97	Not significant	1 RCT
Stroke within 7 days of surgery	RR 2.00	0.37-10.91	Not significant	1 RCT
Hypoglycemia within 7 days of surgery	RR 0.20	0.01-4.17	Not significant	1 RCT

Author(s): Palileo-Villanueva LM
Date: 5 April 2016
Question: Among patients for cataract surgery, does routine preoperative medical testing reduce mortality, morbidity (MI, stroke, diabetic complications) and adverse events compared to no preoperative testing?
Setting: Lira 2001 - Brazil; Shein 2000 - US & Canada; Cavallini 2014 - Italy
Bibliography:* Keay L, Lindsley K, Tielsch J, et al. Routine preoperative medical testing for cataract surgery. *Cochrane Database Syst Rev* 2012;3:CD007293.

***Note:** Only the meta-analysis is listed as reference here. Please refer to the Evidence Summary for a complete list of references

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Routine preoperative medical testing**	**No preoperative testing**	**Relative (95% CI)**	**Absolute (95% CI)**		
Myocardial Infarction within 7 days of surgery												
1	randomised trials	not serious	not serious	not serious	serious		5/9624 (0.1%)	3/9626 (0.0%) (0.40 to 6.97)	**RR 1.67**	**Not Applicable**	moderate*	
Stroke within 7 days of surgery												
1	randomised trials	not serious	not serious	not serious	serious		4/9624 (0.0%)	2/9626 (0.0%) (0.37 to 10.91)	**RR 2.00**	**Not Applicable**	moderate*	
Hypoglycemia within 7 days of surgery												
1	randomised trials	not serious	not serious	not serious	serious		0/9624 (0.0%)	2/9626 (0.0%) (0.01 to 4.17)	**RR 0.20**	**Not Applicable**	moderate*	
Total intraoperative medical adverse events												
3	randomised trials	not serious	not serious	not serious	not serious		242/10764 (2.2%)	238/10767 (2.2%) (0.85 to 1.22)	**OR 1.02**	**Not Applicable**	high	
Total postoperative medical adverse events												
2	randomised trials	not serious	not serious	not serious	not serious		116/10262 (1.1%)	121/10264 (1.2%)	**OR 0.96** (0.74 to 1.24)	**Not Applicable**	high	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Routine preoperative medical testing**	**No preoperative testing**	**Relative (95% CI)**	**Absolute (95% CI)**		
Total postoperative deaths												
2	randomised trials	not serious	not serious	not serious	not serious		1/10262 (0.0%)	2/10264 (0.0%)	**OR 0.50** (0.05 to 5.52)	**Not Applicable**	high	
Intraoperative ocular adverse events												
2	randomised trials	not serious	not serious	not serious	serious		78/1140 (6.8%)	79/1141 (6.9%)	**OR 0.99** (0.71 to 1.38)	**Not Applicable**	moderate*	
Postoperative Ocular Adverse Events												
2	randomised trials	not serious	not serious	not serious	serious		54/1140 (4.7%)	49/1141 (4.3%)	**OR 1.11** (0.74 to 1.67)	**Not Applicable**	moderate*	

CI: Confidence interval; **RR:** Relative risk (computed using an online calculator, https://www.medcalc.org/calc/relative_risk.php); **OR:** Odds ratio

*Quality of evidence was downgraded because of imprecision of results.

APPENDIX Q5

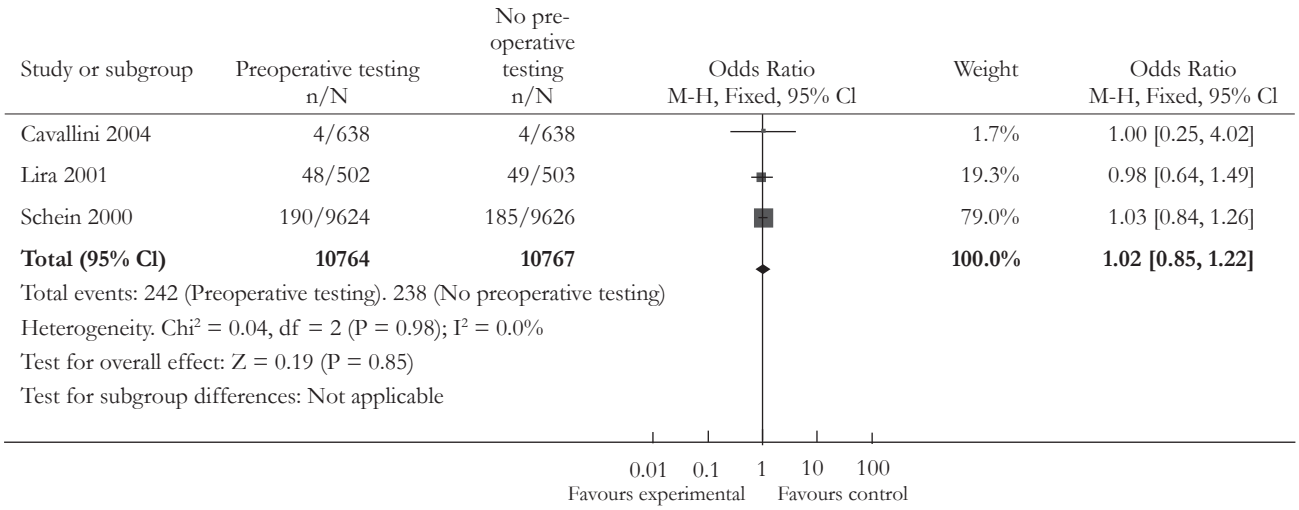


Figure Q5.1 Total intraoperative medical adverse events

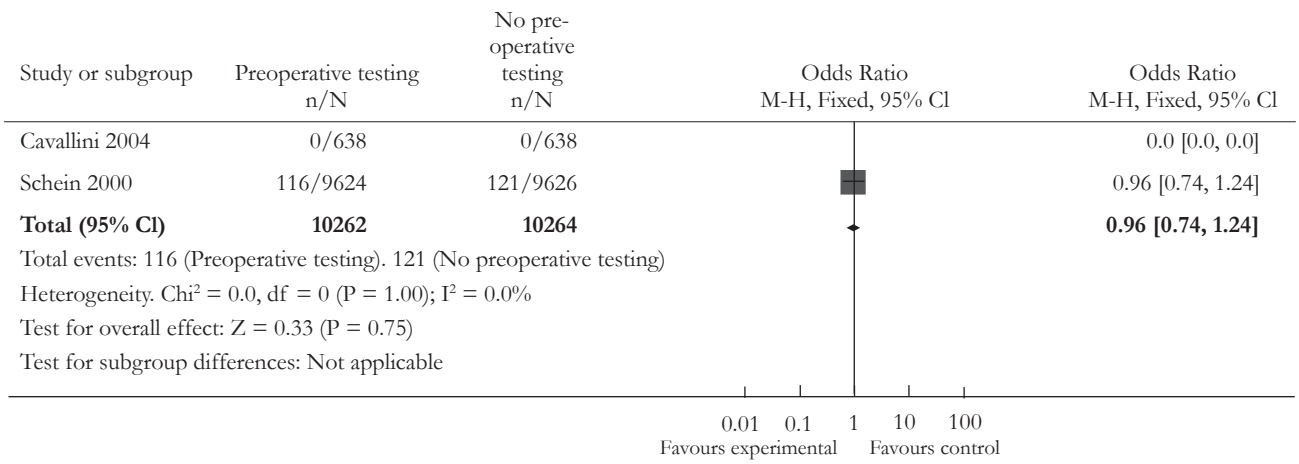


Figure Q5.2 Total postoperative medical adverse events

APPENDIX Q5

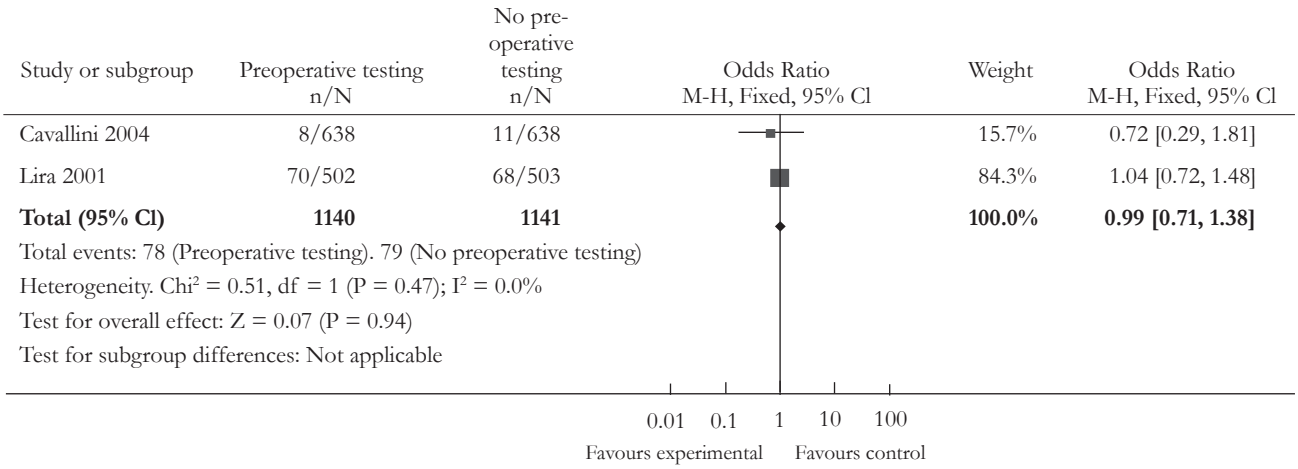


Figure Q5.3 Total intraoperative ocular adverse events

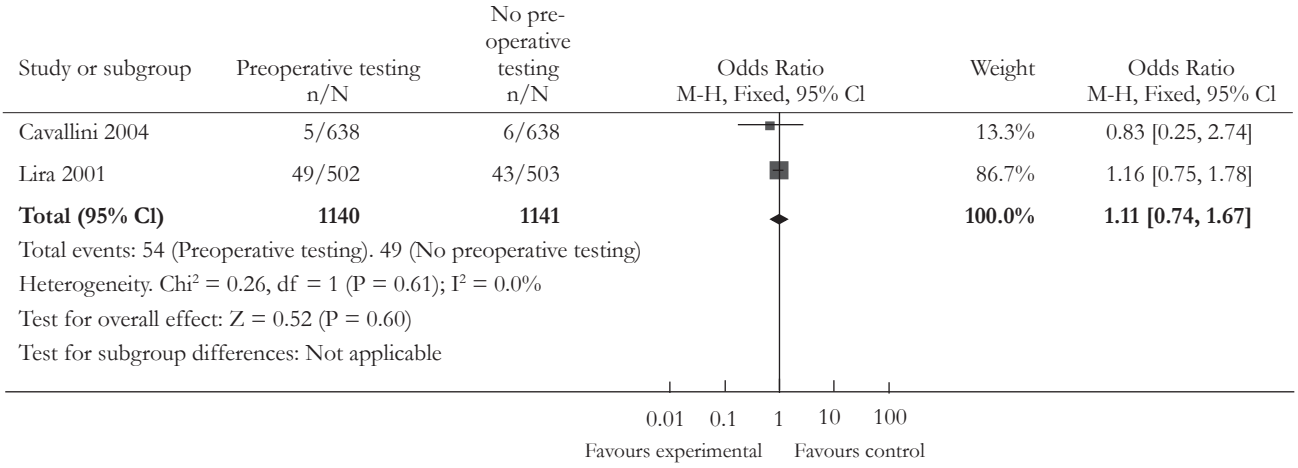


Figure Q5.4 Postoperative ocular adverse events

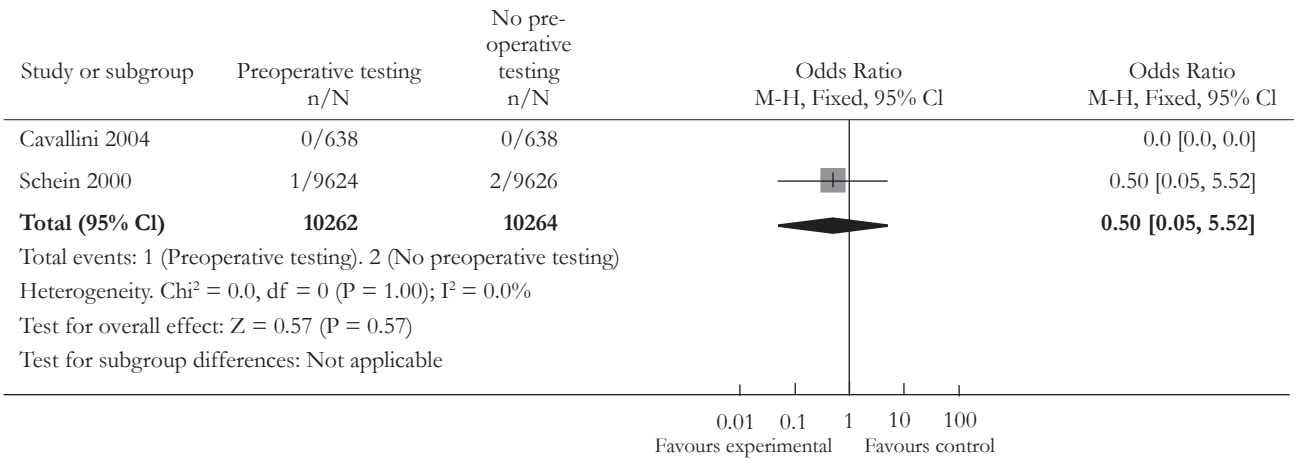


Figure Q5.5 Total postoperative deaths

Q6. AMONG PATIENTS WITH SENILE CATARACTS FOR CATARACT SURGERY, WILL ROUTINE LACRIMAL DUCT IRRIGATION REDUCE POST-OPERATIVE ENDOPHTHALMITIS AND ADVERSE EFFECTS?

SUMMARY OF EVIDENCE

There is no randomized trial found in the literature search to answer the research question. Instead, a prospective cohort study is available where 282 (40%) patients who received no lacrimal system irrigation nor topical antibiotic prior to surgery was compared to 418 (60%) patients who received lacrimal system irrigation with or without neomycin eye drops.[1] No patient developed postoperative endophthalmitis in both groups. Although the overall bacterial contamination was reported at 14.1%, the actual number of patients per group was not mentioned.

DRAFT RECOMMENDATION

There is still inadequate evidence for or against recommending routine lacrimal duct irrigation. Level of Evidence: Very Low. Strength of Recommendation: Weak.

REFERENCE

1. Mistlberger A, Ruckhofer J, Raithel E, et al. Anterior chamber contamination during cataract surgery with intraocular lens implantation. *J Cataract Refract Surg* 1997;23:1064-9.

Author(s): Tabula JA
Date: 19 June 2016
Question: Among patients with senile cataracts for cataract surgery, will routine lacrimal duct irrigation reduce postoperative endophthalmitis and adverse effects?
Bibliography: Mistlberger A, Ruckhofer J, Raithel E, et al. Anterior chamber contamination during cataract surgery with intraocular lens implantation. *J Cataract Refract Surg* 1997;23:1064-9.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine nasolacrimal duct irrigation	No irrigation	Relative (95% CI)	Absolute (95% CI)		
Anterior chamber bacterial contamination												
1	observational	serious[1]	only one study	serious[2]	Unappreciable		?/282 (%)[3]	?/418 (%)	not estimable	Cannot be computed	Very low[4]	
Acute postoperative endophthalmitis												
1	observational	serious	only one study	not serious	unappreciable	Sparse data Not a primary outcome, only observed	0/282 (0.0%)	0/418 (0.0%)	not estimable	0	Very low	

Overall quality: very low
Balance between benefits and harm: Uncertain net benefits
Appropriate recommendation: No recommendation
Previous guidelines did not mention any recommendation about nasolacrimal duct irrigation.

[1] Pretreatment is chosen by the surgeons (retrospective analysis), incomplete outcome data.
[2] Outcome of anterior chamber bacterial contamination is not the outcome in the question.
[3] Actual data not available in the article.
[4] Reporting bias (actual data not available).

Q7. AMONG PATIENTS WITH BILATERAL CATARACTS ABOUT TO UNDERGO CATARACT SURGERY, HOW EFFECTIVE IS SAME SITTING VS DELAYED OPERATION IN PREVENTING INFECTION AND REDUCING COSTS?

SUMMARY OF EVIDENCE

Based on a low-quality cohort study, the risk of infection in delayed sequential bilateral cataract surgery (DSBCS) with intracameral prophylactic antibiotics is very small (1 in 29,582). A non-significant 2 fold increase in the risk of infection was observed among immediate sequential bilateral cataract surgery (ISBCS) patients who were given prophylactic intracameral antibiotics.[1]

The subjective improvement in visual function is not significantly different in ISCBS and DSCBS patients based on a meta-analysis[2] of 2 randomized studies.[3,4] The two trials had conflicting results for this outcome and were significantly very dissimilar. There is also no statistically significant difference in the risk of any intra- and post-operative complications (capsule tears, vitreous loss, iridectomy, sphincterotomy, sutures in wound, intraocular pressure >30 mmHg, wound leak IOL decentration or deplacement, anterior chamber flare, capsular fibrosis, capsule opacification, foreign body sensation, dry eyes and more serious complications such as corneal edema, macular edema, wound leak, or iris prolapse) between patients who underwent ISCBS and DSCBS.[3,4] Likewise, there is no statistically significant difference in the risk of serious post-operative complications (corneal edema, macular edema, wound leak, or iris prolapse) between the aforementioned groups.[3,4]

Canadian estimates of crude cost savings from ISCBS over DSCBS is pegged at US$1,606 (valued in 2013) per patient with adjusted estimates pegged at US$1,431 per quality-adjusted life-year gained.[5] Converting these based on 2013 average peso-dollar exchange rate, crude cost savings amount to Php 68,202 per patient while adjusted cost savings is Php 60,746 per QALY gained. Considering the number of patients needing cataract surgery, the cost savings can potentially add up even if we consider cost variation in different countries. In the Philippines, it is also important to consider the opportunity cost for the caregiver or watcher (*bantay*) of the patient. Often, patients will come for consultations and procedures with a handful of *bantays*. The collective lost earnings of these people are substantial and may confer additional cost savings in favor of ISCBS.

Aside from benefits in terms of costs, ISCBS confers additional benefits to patients: rapid visual recovery and functional advantage in the short term. ISCBS patients tend to regain visual functions earlier than their DSCBS counterparts. Unfortunately, among patients who underwent ISCBS, the very short interval between the surgeries of the two eyes precludes adjustments in surgical plans based on the result of the first eye surgery.[6]

DRAFT RECOMMENDATION

The technique of immediate sequential bilateral cataract surgery (also called same sitting bilateral cataract surgery) cannot be routinely offered to patients at this time. Despite the significant cost savings, the attendant risk for serious bilateral eye complications cannot be discounted with confidence. Level of Evidence: Very Low to Low. Strength of Recommendation: Weak.

Table Q7. Summary of Results (please refer to appendix to view forest plots of combined studies).

OUTCOMES	Measure of Treatment Effect	95% Confidence Interval	Interpretation	Basis
Endophthalmitis with IC Antibiotics	OR 2.06	0.24-17.64	Not significant	1 Cohort
Any intraoperative or postoperative complications **(Fig Q7.1)**	RR 0.76	0.91-1.26	Not significant	2 RCTs
Serious postoperative complications **(Fig Q7.2)**	RR 1.63	0.94-1.06	Not significant	2 RCTs
Subjective Visual Function Test (VF-7 or VF-14 questionnaire) **(Fig Q7.3)**	SMD -0.01 SD higher (0.47 lower to 0.48 higher)	0.74-8.28	Not significant	2 RCTs

REFERENCES

1. Arshinoff SA, Bastianelli PA. Incidence of postoperative endophthalmitis after immediate sequential bilateral cataract surgery. *J Cataract Refract Surg* 2011;37:2105-2114.
2. Kessel L, Andresen J, Erngaard D, et al. Immediate sequential bilateral cataract surgery: a systematic review and meta-analysis. *J Ophthalmology.* 2015;912481.
3. Serrano-Aguilar P, Ramallo-Fariña Y, Cabrera-Herńandez JM, et al.. Immediately sequential versus delayed sequential bilateral cataract surgery: safety and effectiveness. *J Cataract Refract Surg.* 2012;38:1734-1742.
4. Sarikkola AU, Uusitalo RJ, Hellstedt T, et al. Simultaneous bilateral versus sequential bilateral cataract surgery: Helsinki simultaneous bilateral cataract surgery study report 1. *J Cataract Refract Surg.* 2011;37:992-1002.
5. Malvankar-Mehta MS, Filek R, Iqbal M, et al. Immediately sequential bilateral cataract surgery: a cost-effective procedure. *Can J Ophthalmol.* 2013;48:482-488.
6. American Academy of Ophthalmology Cataract and Anterior Segment Panel. Preferred Practice Pattern Guidelines. Cataract in the Adult Eye. San Francisco CA: American Academy of Ophthalmology; 2011. (Accessed at www.aao.org/ppp on June 20, 2016).

Author(s): Loyola A; Sulit MV
Date: 20 June 2016
Question: ISBCS compared to DSBCS in Adult patients with Bilateral Cataract
Setting: Arshinoff et al - Canada; Kessel et al - Europe
Bibliography:* Arshinoff SA, Bastianelli PA. Incidence of postoperative endophthalmitis after immediate sequential bilateral cataract surgery. *J Cataract Refract Surg* 2011;37:2105-2114.
Kessel L, Andresen J, Erngaard D, et al. Immediate sequential bilateral cataract surgery: a systematic review and meta-analysis. *J Ophthalmology.* 2015;912481.

***Note:** Only the meta-analysis is listed here as reference. Please refer to Evidence Summary for a complete list of references.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ISBCS**	**DSBCS**	**Relative (95% CI)**	**Absolute (95% CI)**		
Endophthalmitis (+) IC Antibiotics (assessed with: Rates of Infection)[1]												
1	observational studies	serious[2]	not serious	serious[3]	serious[4]	all plausible residual confounding would reduce the demonstrated effect	5/71759 (0.0%)	1/29582 (0.0%)	**OR 2.06** (0.24 to 17.64)	**Not Applicable**	Very low	
Any postoperative complications												
2	randomised trials	serious[5]	serious[6]	not serious	serious[7]		145/1327 (10.9%)	183/1286 (14.2%)	**RR 0.76** (0.55 to 1.07)	**Not Applicable**	Very low	
Serious postoperative complications												
2	randomised trials	serious[5]	not serious	not serious	serious[4]		19/1327 (1.4%)	12/1286 (0.9%)	**RR 1.63** (0.55 to 4.78)	**Not Applicable**	Low	
Subjective Visual Function Test (VF-7 or VF-14 questionnaire)												
2	randomised trials	serious[5]	serious[8]	not serious	serious[4]		N=1068	N=1028	- **SMD 0.01 SD higher** (0.47 lower to 0.48 higher)		Very low	

CI: Confidence interval; **OR:** Odds ratio; RR: Risk ratio; **SMD:** Standardised mean difference

1. Not explicitly stated
2. Investigators relied heavily on self-reported data which may compromise objectivity in outcome reporting
3. The study was conducted in Canada which has a very different Health System. Likewise, microbial flora, antibiotic sensitivity, patient characteristics, and environmental factors may differ significantly with those in the Philippine setting.
4. Has a very wide 95% CI ranging from Benefit to No Effect to Harm
5. Studies were not blinded to outcome measures
6. Slight variability observed with I squared equal equal to 57%
7. Overall result shows only trend towards ISBCS; not conclusive
8. Chi2 test for heterogeneity $p<0.00001$ with $I^2 = 95\%$

APPENDIX Q7

Study or subgroup	Same-day surgery Events	Total	Different-day surgery Events	Total	Weight	Risk ratio M-H, random, 95% Cl
Sarikkola et al. 2011	106	493	124	506	60.7%	0.88 [0.70, 1.10]
Serrano-Aguilar et al. 2012	39	834	59	780	39.3%	0.62 [0.42, 0.92]
Total (95% Cl)		**1327**		**1286**	**100.0%**	**0.76 [0.55, 1.07]**
Total events	145		183			

Heterogeneity: $r^2 = 0.04$; $\chi^2 = 2.31$, df = 1 (p = 0.13); $I^2 = 57\%$
Test for overall effect: Z = 1.56 (p = 0.12)

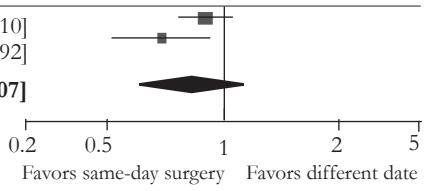


Figure Q7.1 Any intraoperative and postoperative complications

Study or subgroup	Same-day surgery Events	Total	Different-day surgery Events	Total	Weight	Risk ratio M-H, random, 95% Cl
Sarikkola et al. 2011	9	493	9	506	58.5%	1.03 [0.41, 2.56]
Serrano-Aguilar et al. 2012	10	834	3	780	41.5%	3.12 [0.86, 11.29]
Total (95% Cl)		**1327**		**1286**	**100.0%**	**1.63 [0.55, 4.78]**
Total events	19		12			

Heterogeneity: $r^2 = 0.30$; $\chi^2 = 1.92$, df = 1 (p = 0.17); $I^2 = 48\%$
Test for overall effect: Z = 0.89 (p = 0.38)

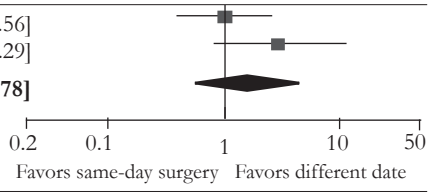


Figure Q7.2 Any serious postoperative complications

Study or subgroup	Same-day surgery Mean	SD	Total	Different-day surgery Mean	SD	Total	Weight	Std. mean difference IV, random, 95% Cl
Sarikkola et al. 2011	24.3	21	234	19.2	19.2	248	48.7%	0.25 [0.07, 0.43]
Serrano-Aguilar et al. 2012	93.3	12.8	834	95.8	8.5	780	51.3%	-0.23 [-0.33, -0.13]
Total (95% Cl)		**1068**				**1028**	**100.0%**	**0.01 [-0.47, 0.48]**

Heterogeneity: $r^2 = 0.11$; $\chi^2 = 21.37$, df = 1 (p <0.00001); $I^2 = 95\%$
Test for overall effect: Z = 0.03 (p = 0.98)

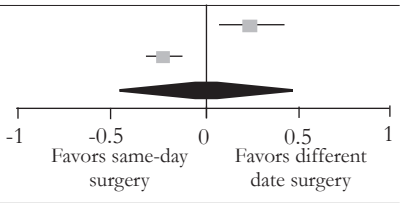


Figure Q7.3 Subjective Visual Function Test (VF-7 or VF-14 questionnaire)

Q8. AMONG ADULTS WITH SENILE CATARACT SCHEDULED FOR CATARACT SURGERY, WILL ROUTINE PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS REDUCE POSTOPERATIVE ENDOPHTHALMITIS?

SUMMARY OF EVIDENCE

There were 3 randomized controlled trials (RCTs) found in the literature search to answer the research question but investigated different kinds of antibiotics. One RCT compared topical regimen (chloramphenicol-sulphadimidine ointment) plus periocular penicillin at the time of surgery with topical regimen alone.[1] This study done in northern Pakistan found significant reduction of endophthalmitis with topical regimen plus periocular penicillin (RR 0.33, 95% CI 0.12–0.92) during surgery compared with topical regimen alone. In another RCT conducted in Turkey, balanced salt solution (BSS) irrigation with vancomycin and gentamycin was compared to BSS alone showed no benefit from vancomycin and gentamycin (RR 0.20, 95% CI 0.01–4.15).[2] The last RCT of high quality evidence was based on a 2 x 2 factorial design, with intracameral cefuroxime and topical perioperative levofloxacin resulting in 4 treatment groups.[3] This was conducted by the European Society of Cataract & Refractive Surgeons (ESCRS) involving 16,603 eyes of 16,603 patients from multiple sites in Europe and Turkey. The results of this study showed that intracameral cefuroxime alone (RR 0.20, 95% CI 0.04–0.91) and combined intracameral cefuroxime with topical levofloxacin (RR 0.10, 95% CI 0.27–0.78) showed significant reduction in endophthalmitis as compared to no antibiotic prophylaxis. However, the reduction of endophthalmitis with topical levofloxacin alone as compared to no antibiotics was not statistically significant (RR 0.70, 95% CI 0.27–1.84). Other comparisons such as intracameral cefuroxime vs topical levofloxacin, combined intracameral cefuroxime and topical levofloxacin vs intracameral cefuroxime, intracameral cefuroxime and topical levofloxacin vs topical levofloxacin did not result in significant reduction in endophthalmitis. There was also no statistically significant reduction in the final visual acuity following endophthalmitis among patients given intracameral cefuroxime with/without topical levofloxacin as compared to no intracameral cefuroxime with/without topical levofloxacin.

Despite this reduction in endophthalmitis, a number of case reports and case series have been published on harm of intracameral and intravitreal cefuroxime. Anterior and posterior segment inflammation were reported in six patients with high doses of intracameral cefuroxime.[4] All six patients in this series had satisfactory final visual outcome even without surgical intervention. Inadvertent overdose of cefuroxime caused hemorrhagic retinal infarction in four patients[5] and macular infarction and associated cystoids macular edema.[6] Two patients developed anaphylactic reactions from intracameral[7] and intravitreal[8] cefuroxime.

DRAFT RECOMMENDATION

Intracameral cefuroxime with or without topical levofloxacin may be recommended for prophylaxis against endophthalmitis (Level of Evidence: High), although there is possibility of serious adverse events. (Level of Evidence: Very Low). Strength of recommendation: Weak. Topical regimen (chloramphenicol-sulphadimidine ointment) plus periocular penicillin may also be recommended over topical regimen alone. Level of Evidence: Moderate. Strength of Recommendation: Strong.

REFERENCES

1. Christy NE, Sommer A. Antibiotic prophylaxis of postoperative endophthalmitis. *Ann Ophthalmol.* 1979;11:1261-5.
2. Sobaci G, Tuncer K, Taş A, et al. The effect of intraoperative antibiotics in irrigating solutions on aqueous humor contamination and endophthalmitis after phacoemulsification surgery. *Eur J Ophthalmol.* 2003;13:773-8.
3. Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.
4. Delyfer MN, Rougier MB, Leoni S, et al. Ocular toxicity after intracameral injection of very high doses of cefuroxime during cataract surgery. *J Cataract Refract Surg.* 2011;37:271-8.
5. Çiftçi S, Çiftçi L, Dağ U. Hemorrhagic retinal infarction due to inadvertent overdose of cefuroxime in cases of complicated cataract surgery: retrospective case series. *Am J Ophthalmol.* 2014;157:421-425.
6. Qureshi F, Clark D. Macular infarction after inadvertent intracameral cefuroxime. *J Cataract Refract Surg.* 2011;37:1168-9.
7. Moisseiev E, Levinger E. Anaphylactic reaction following intracameral cefuroxime injection during cataract surgery. *J Cataract Refract Surg.* 2013;39:1432-4.
8. Villada JR, Vicente U, Javaloy J, Alió JL. Severe anaphylactic reaction after intracameral antibiotic administration during cataract surgery. *J Cataract Refract Surg.* 2005;31:620-1.

Author(s): Tabula JA
Date: 21 June 2016
Question: Among adults with senile cataract scheduled for cataract surgery, will routine perioperative antibiotic prophylaxis reduce postoperative endophthalmitis?
Question 5a1: Routine balanced salt solution (BSS) irrigation vs BSS with vancomycin and gentamycin for cataract surgery
Bibliography: Sobaci G, Tuncer K, Taş A, et al. The effect of intraoperative antibiotics in irrigating solutions on aqueous humor contamination and endophthalmitis after phacoemulsification surgery. *Eur J Ophthalmol.* 2003;13:773-8.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	BSS with vancomycin gentamycin irrigation	BSS alone	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Unclear[1], Serious	Only one study	not serious	serious[2]	Sparse data	0/322 (0%)	2/322 (0.62%)	RR 0.20 (0.01 to 4.15)	Not applicable	Very low	

Question 5a2: Routine chloramphenicol-sulphadimidine ointment plus periocular penicillin vs ointment alone for cataract surgery
Bibliography: Christy NE, Sommer A. Antibiotic prophylaxis of post-operative endophthalmitis. *Ann Ophthalmol.* 1979;11:1261-5.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Chlorampenicol-sulphadimidine ointment plus per ocular penicilline	Chlorampenicol-sulphadimidine ointment alone	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Unclear[3]	Only one study	serious	not serious[2]	none	5/3309 (0.15%)	15/3309 (0.45%)	**RR 0.330 (0.12 to 0.92)**	0.30%	Moderate	

Question 5a3: Routine intracameral cefuroxime vs no antibiotics for cataract surgery

Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intracameral cefuroxime[4]**	**No prophylactic antibiotics**	**Relative (95% CI)**	**Absolute (95% CI)**		
Postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	not serious	none	2/4056 (0.05%)	10/4054 (0.25%)	RR 0.20 (0.04 to 0.91)	0.20%	High	
Adverse events												
Anterior and posterior segment inflammation (1)	Case reports/ series						6				Very low	
Hemorrhagic retinal infarction (1)							4					
Macular infarction and cystoids macular edema (1)							1					
							2[5]					
Anaphylactic reactions (2)												

Question 5a4: Routine topical levofloxacin vs no prophylactic antibiotics for cataract surgery
Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical levofloxacin[6]	No prophylactic antibiotics	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	serious[2]	none	7/4049 (0.17%)	10/4054 (0.25%)	RR 0.70 (0.27 to 1.84)	Not applicable	High	

Question 5a5: Routine intracameral cefuroxime with topical levofloxacin vs no prophylactic antibiotics for cataract surgery
Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intracameral cefuroxime plus topical levofloxacin	No prophylactic antibiotics	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	not serious	Very strong evidence of association	2/4052 (0.05%)	10/4054 (0.25%)	RR 0.10 (0.27 to 0.78)	0.23%	High	

Question 5a6: Routine intracameral cefuroxime vs topical levofloxacin for cataract surgery
Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intracameral cefuroxime	Topical levofloxacin	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	serious[2]	Very strong evidence of association	2/4056 (0.05%)	7/4049 (0.17%)	RR 0.29 (0.06 to 1.37)	Not applicable	High	

Question 5a7: Routine intracameral cefuroxime plus topical levofloxacin vs topical levofloxacin alone for cataract surgery
Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intracameral cefuroxime plus topical levofloxacin	Topical levofloxacin alone	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	serious[2]	none	2/4052 (0.05%)	7/4049 (0.17%)	RR 0.14 (0.02 to 1.16)	Not applicable	High	

Question 5a8: Routine intracameral cefuroxime plus topical levofloxacin vs intracameral cefuroxime alone for cataract surgery
Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intracameral cefuroxime plus topical levofloxacin	Intracameral cefuroxime alone	Relative (95% CI)	Absolute (95% CI)		
Postoperative endophthalmitis												
1	randomized	Not	Only one	not	serious[2]	none	2/4052	2/4056	RR 0.50	Not	High	
	trial	serious	study	serious			(0.05%)	(0.05%)	(0.05 to 5.52)	applicable		

Question 5a9: Routine intracameral cefuroxime ± topical levofloxacin vs no intracameral cefuroxime ± topical levofloxacin for cataract surgery

Bibliography: Endophthalmitis Study Group, European Society of Cataract & Refractive Surgeons. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. *J Cataract Refract Surg.* 2007;33:978-88.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intracameral cefuroxime ± topical levofloxacin**	**No intracameral cefuroxime ± topical levofloxacin**	**Relative (95% CI)**	**Absolute (95% CI)**		
Visual acuity after postoperative endophthalmitis												
1	randomized trial	Not serious	Only one study	not serious	serious[2]	Sparse data	Final VA >20/40 1/3 (33.3%) Final VA >20/200 0/3 (0%)	Final VA >20/40 10/17 (58.1%) Final VA >20/200 4/17 (23.5%)	Final VA >20/40 RR 0.57 (0.11 to 2.95) Final VA >20/200 RR 0.50 (0.03 to 7.54)	Not applicable Not applicable	Very low[7]	

CI: Confidence interval; **RR:** Risk ratio

[1]Unclear for random sequence generation; allocation concealment; and blinding of participants, physicians, clinical care providers, and outcome assessors; serious for incomplete data outcome
[2]confidence intervals are wide
[3]Unclear risk of bias on random sequence generation and allocation concealment
[4]Cefuroxime injected into the anterior chamber at the end of surgery as 1 mg in 0.1 mL normal saline
[5]1 intravitreal, 1 intracameral cefuroxime
[6]Levofloxacin 0.5% administered 1 drop 1 hour before surgery, 1 drop 30 minutes before surgery, and 3 drops at 5-minute intervals commencing immediately after surgery
[7]Sparse data and indirectness

Q9. AMONG PATIENTS WITH SENILE CATARACTS FOR CATARACT SURGERY, WILL ROUTINE 5% POVIDONE-IODINE SOLUTION REDUCE POSTOPERATIVE ENDOPHTHALMITIS AND ADVERSE EFFECTS?

SUMMARY OF EVIDENCE

There is one randomized controlled trial (RCT) and one prospective cohort study found in the literature search to answer the research question. The RCT however does not specify the concentration of Povidone-Iodine (PI) solution used.[1] A total of 4,111 eyes underwent cataract surgery and were included in this study. There was no significant difference between the PI group and the control (silver protein) group (RR 1.17, 95% CI 0.57 – 2.42). The prospective cohort study including 8,083 eyes showed significant difference between 5% PI and no 5% PI ($p < 0.03$).[2] However, on rechecking, it turned out that this is not significant (RR 0.24, 95% CI0.57 – 1.08). Pooled analysis of these two studies (PI vs control) showed a trend of benefit toward PI with an RR of 0.61 (95% CI 0.13 – 2.86, I^2 72%). These two studies are both low quality.

In several case reports, conjunctival irritation is seen in 0.4%.[3] Contact dermatitis is less common (0.04%); however, the risk increases tenfold in the presence of allergy to shellfish or iodine.[4] Despite the increased risk for allergy, patients are still recommended to receive PI prior to surgery.[5] Keratoconjunctivitis sicca has also been reported.[5] Hyperemia of conjunctiva, superficial punctate epitheliopathy and epithelial defect, corneal symptoms (edema or Descemet's membrane folds, and mild to moderate Tyndall were seen in randomized trial comparing different concentrations of PI solutions.[4]

DRAFT RECOMMENDATION

Routine pre-operative 5% PI solution is not recommended because of lack of evidence of effectiveness but also the possibility of adverse events. Level of Evidence: Low-Very Low. Strength of Recommendation: Weak.

REFERENCES:

1. Mørk P. Polyvinylpyrrolidone-iodine as a disinfectant in eye surgery for five years. *Acta Ophthalmol (Copenh)*. 1987;65:572-4.
2. Speaker MG, Menikoff JA. Prophylaxis of endophthalmitis with topical povidone-iodine. *Ophthalmology*. 1991;98:1769-75.
3. Zamora JL. Chemical and microbiologic characteristics and toxicity of povidone-iodine solutions. *Am J Surg*. 1986;151:400-6.
4. Li B, Nentwich MM, Hoffmann LE, et al. Comparison of the efficacy of povidone-iodine 1.0%, 5.0%, and 10.0% irrigation combined with topical levofloxacin 0.3% as preoperative prophylaxis in cataract surgery. *J Cataract Refract Surg*. 2013;39:994-1001.
5. Gills JP. Effective concentration of betadine. *J Cataract Refract Surg*. 1999;25:604.

Author(s): Tabula JA
Date: 21 June 2016
Question: Among patients with senile cataracts for cataract surgery, will routine 5% povidone-iodine solution reduce postoperative endophthalmitis and adverse effects?
Bibliography:

1. Speaker MG, Menikoff JA. Prophylaxis of endophthalmitis with topical povidone-iodine. *Ophthalmology.* 1991;98:1769-75.
2. Mørk P. Polyvinylpyrrolidone-iodine as a disinfectant in eye surgery for five years. *Acta Ophthalmol (Copenh).* 1987;65:572-4.
3. Li B, Nentwich MM, Hoffmann LE, et al. Comparison of the efficacy of povidone-iodine 1.0%, 5.0%, and 10.0% irrigation combined with topical levofloxacin 0.3% as preoperative prophylaxis in cataract surgery. *J Cataract Refract Surg.* 2013;39:994-1001.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Routine prophylactic PI 5%**	**No prophylactic PI 5% (or other concentration**	**Relative (95% CI)**	**Absolute (95% CI)**		
Postoperative endophthalmitis												
5% PI vs silver protein solution (1)	observational	Not serious	Only one study	not serious	Not precise	none	2/34889 (0.06%)	11/4594 (0.24%)	RR 0.24 (0.05 to 1.08)1	0.18%	Low	
PVP-iodine eye drops[2] vs 2.5% iodine on skin (1)	randomised trial	serious[3]	Only one study	unclear[4]	Not precise	None	21/2550 (0.8%)	11/1561 (0.7%)	RR 1.17 (0.57 to 2.42)	-0.1%	Low[5]	
Hyperemia of conjunctiva												
5% PI vs 1% or 10% (1)	randomised trial	very serious[6]	Only one study	not serious	unappreciable	none	64/70 (91%)	1% 52/62 (85%) 10% 61/66 (92%)	RR 1.07 RR 0.99	6% increase 1% decrease	Very low[7]	
Superficial punctate epitheliopathy and epithelial defect												
5% PI vs 1% or 10% (1)[8]	randomised trial	very serious[9]	Only one study	not serious	unappreciable	none	29/70 (41%)	1% 17/66 (26%) 10% 40/66 (60%)	RR 1.58 RR 0.68	15% increase 19% decrease	Very low	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine prophylactic PI 5%	No prophylactic PI 5% (or other concentration	Relative (95% CI)	Absolute (95% CI)		
Corneal symptoms (edema or Descemet's membrane folds)												
5% PI vs 1% or 10% (1)	randomised trial	very serious[9]	Only one study	not serious	unappreciable	none	8/70 (11%)	1% 10/62 (16%) 10% 12/66 (18%)	RR 0.69 RR 0.61	5% decrease 7% decrease	Very low	
Mild to moderate Tyndall												
5% PI vs 1% or 10% (1)	randomised trial	very serious[9]	Only one study	not serious	unappreciable	none	69/70 (98%)	1% 61/62 (98%) 10% 64/66 (97%)	RR 1.00 RR 1.01	0% no change 1% increase	Very low	

CI: Confidence interval; **RR:** Risk ratio

Overall quality: Very low
Balance between benefits and harm: Uncertain tradeoffs
Appropriate recommendation: Do not recommend
Its routine application has been part of the recommendations in at least two CPGs.

[1] Reported to be statistically significant but on rechecking, it was not significant
[2] Polyvinylpyrrolidone-iodine, no concentration available
[3] Unclear risk: only abstract available
[4] Concentration of PI not reported
[5] From high to low because of unclear risk of bias
[6] High dropout rate
[7] High dropout rate: from 271 patients to 198 patients evaluated for side-effects
[8] No table of outcome numbers, have to extract from bar graphs
[9] High dropout rate

Q10. AMONG PATIENTS WHO DEVELOP POSTERIOR CAPSULAR OPACIFICATION (PCO) AFTER CATARACT SURGERY, HOW SAFE IS LESS THAN 6 MONTHS VERSUS 6 MONTHS AND BEYOND LASER (ND:YAG) CAPSULOTOMY IN PREVENTING MACULAR EDEMA, RETINAL DAMAGE, ANTERIOR CHAMBER REACTIONS AND OTHER ADVERSE EVENTS?

SUMMARY OF EVIDENCE

Three studies were identified addressing the adverse effects of Nd:YAG laser capsulotomy in patients with PCO but none of these studies compared the less than 6 months versus 6 months and beyond timing of the capsulotomy. One study however compared different time durations from 6 months up to greater or equal to 37 months[3]. The sample sizes were 23[1], 31[2] and 314[3] adult patients, with follow-up observations ranging from as early as immediately after the procedure to three months post-capsulotomy.

From the very low quality evidence from the two studies with small sample sizes, the limited available data does not seem to show any statistically significant differences ($p < 0.05$) between the anterior chamber depth, intraocular pressure, macular foveal thickness and endothelial cell loss before and after the capsulotomy.[1,2]

However, the cohort study by Shaikh et al.[3] in 2010 demonstrates that laser capsulotomy may induce potential complications, prevalence rates of which are summarized below in this table:

DRAFT RECOMMENDATION

There is no evidence to recommend performing Nd:YAG laser capsulotomy less than 6 months versus 6 months and beyond after the cataract surgery for those who develop PCO. Evidence only shows that Nd:YAG laser capsulotomy performed at least 6 months from cataract surgery may lead to potential complications. Level of Evidence: Very Low. Strength of Recommendation: Weak.

REFERENCES

1. Ozkurt YB, Sengör T, Evciman T, Haboğlu M. Refraction, intraocular pressure and anterior chamber depth changes after Nd:YAG laser treatment for posterior capsular opacification in pseudophakic eyes. *Clin Exp Optom* 2009;92:412-415.
2. Ruiz-Casas D, Barrancos C., Alio JL, et al. Effect of posterior Neodymium:YAG capsulotomy. Safety evaluation of macular foveal thickness, intraocular pressure and endothelial cell loss in pseudophakic patients with posterior capsule opacification. *Arch Soc Esp Oftalmol* 2013; 88:415-422.
3. Shaikh A, Shaikh F, Adwani JR, Shaikh ZA. Prevalence of different Nd:YAG laser induced complication in patients with significant posterior capsule opacification and their correlation with time duration after standard cataract surgery. *Int J Med & Med Sci.* 2010;2:012-017.

Table Q10.1 Post Nd:YAG Laser Capsulotomy Complications

Timing after cataract surgery	AC reactions n (%)	IOP n (%)	IOL damage n (%)	Retinal detachment n (%)	Macular edema n (%)	Vitreous hemorrhage n (%)
Grp. 1 6--12 mos. N=178	14 (7.9)	15 (8.4)	8 (4.5)	0	0	0
Grp. 2 13-24 mos. N=97	8 (8.2)	10 (10.3)	4 (4.1)	0	0	0
Grp. 3 25-36 mos. N=24	1 (4.2)	16 (66.7)	6 (25)	0	0	1 (4.1)
Grp. 4 ≥37 mos. N=15	4 (26.7)	15 (100)	3 (20)	0	1 (6.7)	1 (6.7)

Author(s): Daez ML; Sulit MVV
Date: 20 June 2016
Question: Capsulotomy >6 mos compared to Capsulotomy <6 mos for PCO after Cataract Surgery
Setting: Pakistan
Bibliography: Shaikh A, Shaikh F, Adwani JR, Shaikh ZA. Prevalence of different Nd:YAG laser induced complication in patients with significant posterior capsule opacification and their correlation with time duration after standard cataract surgery. *Int J Med & Med Sci.* 2010;2:012-017.

Quality assessment							Impact	Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
AC Reactions									
1	observational study	very serious[1]	Unable to assess	not serious	Unable to assess		Only the prevalence rates at specified time periods were described that will give an idea of complications over time. Refer to table 1 below.	Very low	

CI: Confidence interval

1. There was no control group; only prevalence rates were presented at different time periods.

Table 1. Post Nd:YAG Laser Capsulotomy Complications

Timing after cataract surgery	AC reactions n (%)	IOP n (%)	IOL damage n (%)	Retinal detachment n (%)	Macular edema n (%)	Vitreous hemorrhage n (%)
Grp. 1 6-12 mos. N=178	14 (7.9)	15 (8.4)	8 (4.5)	0	0	0
Grp. 2 13-24 mos. N=97	8 (8.2)	10 (10.3)	4 (4.1)	0	0	0
Grp. 3 25-36 mos. N=24	1 (4.2)	16 (66.7)	6 (25)	0	0	1 (4.1)
Grp. 4 ≥37 mos. N=15	4 (26.7)	15 (100)	3 (20)	0	1 (6.7)	1 (6.7)

Delphi Results

After three rounds of discussions and voting during the CPG panel conference, there was one issue that could not be resolved, that is, the majority consensus of 70% could not be reached. The issue was whether to recommend ECCE over MSICS or MSICS over ECCE. The matter was then shelved and slated for resolution via the Delphi technique through e-mail.

The panelists were reminded that they would receive email and be expected respond promptly to continue the discussion on ECCE and MSICS in the following weeks. Voting would be conducted also by email for three successive rounds again or until a consensus is reached. No new evidence would be presented but the panelists were allowed more time to ponder on the evidence and the panel discussion.

The first round yielded the results illustrated in Figure 1 with comments in Table 1.

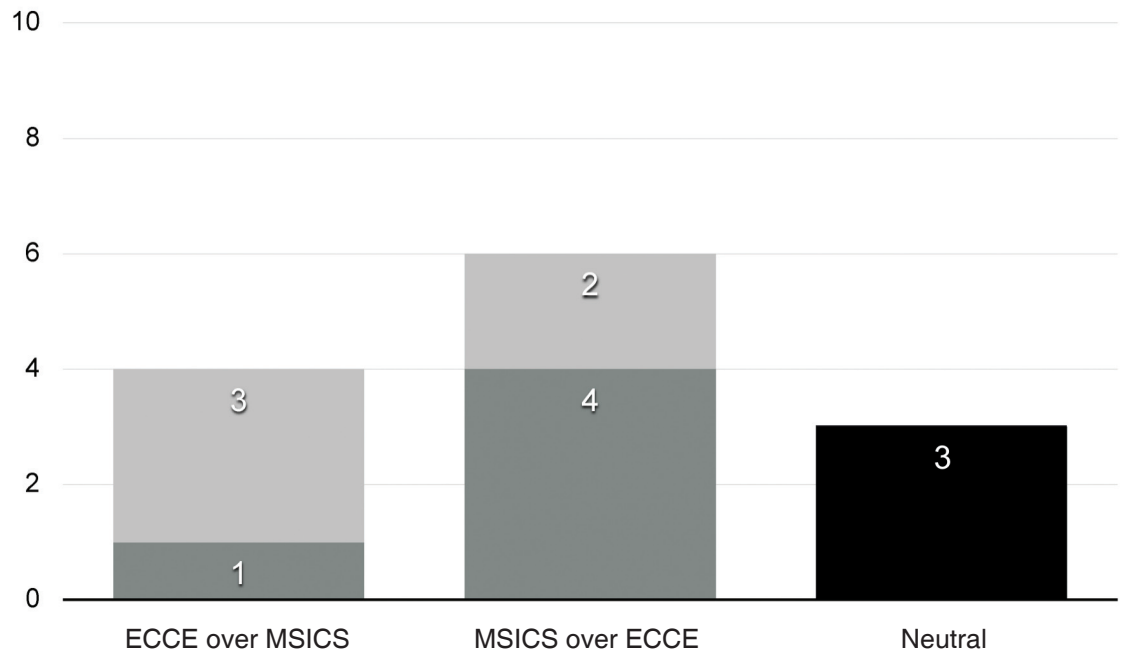


Figure 1. Results of the first round of Delphi protocol. [Gray-Strong Recommendation; Light Gray-Weak Recommendation]

Table 1. Summary of Comments Delhi Round 1

Issue	Recommend ECCE over MSICS	Recommend MSICS over ECCE	Neutral/Undecided
Round 1	**4/13 = 31%**	**6/13 = 46%**	**3/13 = 23%**
Comments Note: These are reproduced faithfully from unedited responses, except for truncated phrases that already appear in the title. Within a column, a different bullet is used per panelist; hence, responses from the same panelist will have the same bullet.	✦ Based on the statement in the attached Summary of Evidence that "MSICS has ... significantly more complications compared to ECCE…As Dr. Carino's response mentions that MSICS requires a smaller incision and is much quicker to do, and that cost-wise they are about the same. ★ Even though there are only limited evidence showing improve vision as outcome with the use of MSICS vs ECCE, evidence available showed MSICS to have more adverse outcomes vs ECCE. Please note that evidence per cost of MSICS and ECCE not considered since it was not provided. ✳ Although both are equivalent in results, practically speaking -- very few know MSICS. Teaching institutions will need to teach MSICS to the residents before it can be recommended. ✓ ECCE has less complications, MSICS has more harms based on reported quality evidence. The predominant astigmatism complication in ECCE is not blinding and can be easily corrected. Although the preference in our setting would be a sutureless small incision, the benefit from a larger less complicated ECCE incision is worth the cost of the surgery.	❖ ECCE is a bigger incision than MSICS and with the trend smaller is better. Secondly though it was not written in the manuscripts, aside from a smaller incision, MSICS is much quicker to do than ECCE. In a surgeon adept at both ECCE and MSICS, the surgeon will finish the surgery much quicker thus making him more efficient. Cost-wise it is essentially the same cost. ⦿ MSICS is my choice since it involves use of small incision resulting in faster visual recovery and rehab, lesser astigmatism and better post-operative results. It also involves use of lesser instruments than ECCE. It is a more useful transition step on learning to perform phaco. Most complications arise from improper techniques done in performing the procedure. MSICS is thoroughly discussed and illustrated in Chapter 14 of the Basic Principle/Technique of Ophthalmic Surgery of the American Academy of Ophthalmology latest edition. ❖ It (MSICS) seems to have greater potential in our setting especially in the provinces and have an important role later on particularly, if there is more dedicated training here (as seen in other 3rd world nations like India and Nepal). ➔ From the panel discussion last 09 July 2016, ophthalmologists relayed that students are basically trained in MSICS from residency and are more oriented on this method than ECCE. Also, compared to ECCE, the incision in MSICS is smaller. Although this means there is a risk of more trauma during cataract extraction because of the narrow incision, this only means faster recovery for trauma during cataract extraction because of the narrow incision, this only means faster recovery for the patient in spite of the risk. - I have been performing MSICS for almost 10 years and find my outcomes to be better than ECCE. We can also have faster and shorter recovery times with MSICS. Like any surgical procedure, skill is the most important factor so training	• I choose to abstain from making a recommendation because I can neither recommend MSICS over ECCE nor ECCE over MSCICS due to insufficiency of evidence that one surgical technique is better than the other for improving vision. While the incidence of surgically induced astigmatism was shown by a single study to be lower for the MSICS group, the incidence of at least one intra-operative and post-operative complications were both higher for the MSICS group. As a lay person, I am not in a position to make recommendations on what should be given more value, absence of astigmatism or non-occurrence of surgical complications. Besides, I also do not know the comparative costs, let alone the cost-benefit of these two surgical procedures ✳ Based on current findings, (though inadequate) MSICS has more postoperative complications; (but has less surgically induced astigmatism) ★ I would like to know if the post-operative complications in MSICS are temporary or permanent, and if those could be resolved? ★ Should surgically-induced astigmatism occurs as a result of ECCE, how could this be resolved or treated? ★ As a patient, I expect my doctor to explain what is "best". Also, is it affordable to most people in the Philippine society ✦ Evidences are insufficient to recommend one versus the other: MSICS or ECCE. We cannot also conclude at this point that the two have the same rate of outcomes even if "no significant difference" were obtained in some studies. Also, results of studies cannot be pooled to come up with summary stats where a decision can be based on combined results.

Issue	Recommend ECCE over MSICS	Recommend MSICS over ECCE	Neutral/Undecided
Round 1	**4/13 = 31%**	**6/13 = 46%**	**3/13 = 23%**
		for MSICS should be as intensive as that for ECCE and Phaco. ▶ Being a closed system unlike an open one in ECCE, the surgery is lesser prone to catastrophic complications like vitreous loss, choroidal detachment and worse, expulsive hemorrhage which can lead irreversible vision loss ▶ The incision architecture is better in terms of wound stability and having less sutures causes little unwanted astigmatism compared to what one gets with ECCE	✓ I believe cost implications (i don't know the cost of these procedures) should be considered, as well as the effect of complications on patients be considered in identifying the current recommendations on this aspect.
Round 2			
Your vote	☐ I recommend ECCE over MSICS ☐ Weak ☐ Strong	☐ I recommend MSICS over ECCE ☐ Weak ☐ Strong	☐ I recommend neither procedure over the other

Because a consensus was not reached after the first round, the summary of email posts were sent (see Table 1) to initiate the second round. After the second round voting, the final recommendation was in favor of MSICS over ECCE (10/13 = 77%, Figure 2). This ended the Delphi proceedings.

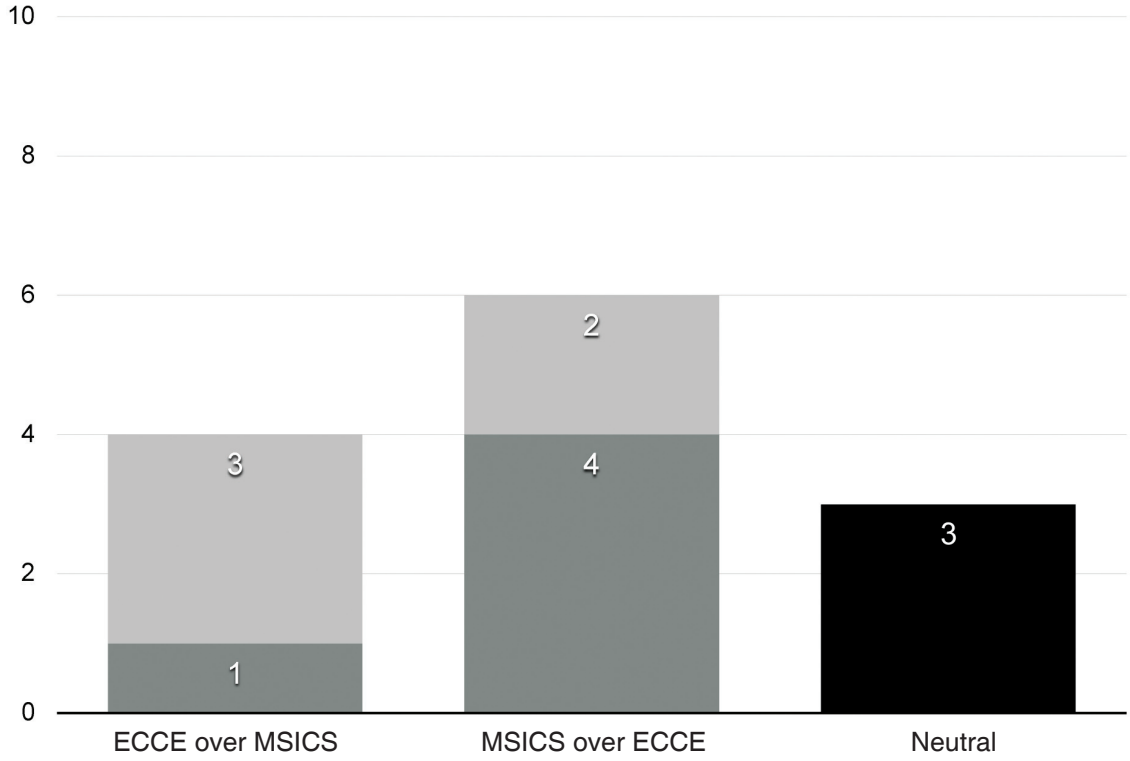


Figure 2. Tallied votes for the respondents of the second Delphi round. [Gray-Strong Recommendation; Light Gray-Weak Recommendation]