Title: The Royal College of Ophthalmologists' National Ophthalmology Database study of cataract surgery: Report 9, Risk factors for posterior capsule opacification

Authors: Paul HJ Donachie[1,2], Beth L Barnes[1], Martina Olaitan[1], John M Sparrow[1,3] John C Buchan[1,4,5]

1. The Royal College of Ophthalmologists' National Ophthalmology Audit, 18 Stephenson Way, London NW1 2HD, UK

2. Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, GL53 7AN, UK

3. Bristol Eye Hospital, Lower Maudlin Street, Bristol, BS1 2LX, UK

4. International Centre for Eye Health, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT

5. Leeds Teaching Hospitals NHS Trust, Beckett Street, Leeds, LS9 7TF

Corresponding Author:

John C Buchan

International Centre for Eye Health

London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT

Telephone: +44 (0) 7543943933

Email: john.buchan@lshtm.ac.uk

Short Heading:

NOD Posterior Capsule Opacity Risk Factor Analysis

Summary

What was known before:

- Posterior Capsule Opacification (PCO) is the most common long-term post-operative adverse occurrence after cataract surgery
- Factors associated with increased risk of PCO can relate to the patient or their eye, the surgery, or the intra-ocular lens (IOL) material and design, such as the well-established superiority of a square-edged IOL in preventing PCO

What this study adds:

- This is the largest published series investigating risk factors for PCO
- The six month, one, three, five and nine year observed rates of PCO were 2.1%, 4.0%, 18.0%, 31.2% and 43.5% respectively
- Risk factors that increased the risk of developing PCO included hydrophilic IOL material, an axial length >26 mm, high myopia, previous vitrectomy, uveitis/synechiae, younger age and female gender

Key Words: cataract, posterior capsule opacification, Nd YAG laser capsulotomy

Conflict of Interest: No authors have any conflict of interest to declare

Funding: This analysis was funded by an unconditional grant from Alcon (Geneva, Switzerland) in support of the Royal College of Ophthalmologists National Ophthalmology Database cataract audit. The funders did not have any editorial oversight, right of veto or academic input into the analysis or write up of this work.

Word count = 3351

Abstract (words = 233)

Background / Objectives

Posterior Capsule Opacification (PCO) is the most common long-term post-operative adverse occurrence after cataract surgery often requiring treatment with YAG laser posterior capsulotomy. This study aimed to identify potential risk factors, known at the time of cataract surgery, that influence the development of PCO.

Subject / Methods

A retrospective study of publicly funded cataract surgery from The Royal College of Ophthalmologists' National Ophthalmology Database. Eligible for analysis were 601 084 cataract operations performed in 58 participating centres.

Results

The 601 084 operations were performed on 291 411 (48.5%) left eyes and 309 673 (51.5%) right eyes from 448 510 patients by 2 566 surgeons. Post-cataract PCO was recorded for 65 210 (10.9%) eyes and the six month, one, three, five and nine year observed rates of PCO were 2.1%, 4.0%, 18.0%, 31.2% and 43.5% respectively. Different PCO profiles were observed between IOL designs and materials and the identified risk factors that increased the risk of developing PCO included hydrophilic IOL material, axial length >26 mm, the presence of high myopia and implantation of lower IOL powers, previous vitrectomy surgery and uveitis/synechiae, along with younger age and female gender.

Conclusions

Many factors influence the development of PCO relating to the patient, the eye, the lens and the surgery. Some factors are modifiable such as IOL material and design, therefore the opportunity exists to attempt to reduce PCO rates, benefitting patients and the UK NHS.

Introduction

Cataract surgery is the most frequently performed surgical procedure in the UK, with around 472 000 operations funded by the NHS in England and Wales during the 2018-2019 national cataract audit year (www.nodaudit.org.uk/resources/publications-annual-report). Posterior capsule opacification (PCO) is the most frequent long-term adverse occurrence after cataract surgery, often requiring treatment with YAG laser posterior capsulotomy. As a consequence, despite YAG laser being a frequently performed and low risk procedure, posterior capsule rates are of significant public health interest due to the visual impairment they cause prior to treatment, and the resources directed towards their diagnosis and management which could be redeployed if rates were reduced.

PCO rates have been variously reported depending on definitions used and the length of follow-up in different studies. PCO has been linked to patient factors, cataract surgical techniques and implanted intra-ocular lens (IOL) materials or design, such as the established reduction in PCO rates seen with square-edged IOL designs compared to round edge IOL shown by systematic review of randomised controlled trials (RCT).(1, 2). In addition to RCT, real-world PCO rates and risk factors have been reported.(3, 4).

The Royal College of Ophthalmologists (RCOphth) National Ophthalmology Database (NOD) Cataract Audit accesses post-operative records from the majority of UK cataract service providers, and therefore provides the opportunity to explore PCO rates and risk

factors at a scale not previously reported to identify potential targets for interventions to reduce PCO rates nationally.

Subjects and Methods

The RCOphth NOD receives anonymised data from around 70% of centres providing publicly funded cataract surgery in England, Wales and Guernsey as described in other publications(5) and on the audit website (www.nodaudit.org.uk). Only electronic medical record (EMR) enabled centres are included in this analysis due to the in-house data collection systems submitting follow-up data at one fixed time point after surgery, instead of serial postoperative data. Only data from institutions providing a full range of ocular services were included. Centres only providing primarily cataract-related services were excluded as they have limited opportunity to see patients who are PCO-free, hence would generate artificially high PCO rates if they offer YAG laser, or artificially low rates if they do not provide this service. We excluded any centre that did not have records of at least one case of PCO more than one month after cataract surgery, as some institutions have pathways that systematically fail to capture certain outpatient activity on the EMR. Operations with at least one month's follow-up are included, where the follow-up data could be for any post-surgery hospital visit for either clinical assessments or treatments. The study time period concerns operations performed between 01/04/2010 and 31/03/2018 with 31/08/2019 as the last date of any follow-up record, this enabled all operations to have the opportunity for a minimum of one year and five months follow-up. Each IOL was allocated a group based on model, material and IOL design derived from manufacturer specifications.

Excluded from the analysis were;

- where no IOL was inserted
- IOL was not recorded
- IOL's that could not be allocated to the IOL model grouping
- operations with missing patient age at surgery
- operations with missing IOL power as this could indicate the eye was left aphakic
- operations where the recorded IOL power is outside the range of -10 to +40 dioptres (most likely indicative of a data entry error)
- eyes with a recorded axial length measurement <18 mm as these could be abnormal eyes or data entry errors
- centres with fewer than 50 phacoemulsification operations satisfying the above criteria.

The data was recorded on the Medisoft EMR system (Medisoft Ophthalmology, Medisoft Limited, Leeds, UK, www.medisoft.co.uk) or the Open Eyes EMR system (www.openeyes.org.uk). Anonymized database analyses of this type do not require ethical permission due to being viewed as audit or service evaluation (see http://www.hra.nhs.uk/research-community/before-you-apply/determinewhether-your-study-is-research/). This study was conducted in accordance with the declaration of Helsinki, and the UK's Data Protection Act.

PCO definition

Post-cataract PCO was identified from recorded post-operative complications, post-cataract diagnoses or post-cataract surgical records (for YAG posterior capsulotomy) from eight days post-cataract surgery to the date of the last record of any post-cataract assessment for the patient.

The first record of PCO post-cataract surgery is used as the index "event" for PCO, and for non-PCO eyes the last assessment date for the patient is used as a surrogate for final follow-up. As PCO can occur at different points in time, the Kaplan-Meier method with the actuarial adjustment was used to graphically display the PCO ("failure event") rates over time and create PCO rates at specific post-cataract surgery time points representing the cumulative probability of PCO occurring.

PCO risk factor modelling

To identify potential risk factors influencing the development of PCO, an accelerated failure time Loglogistic model was fitted with robust cluster adjustment of the standard error using the patients as clusters to account for patient level correlation.

The covariates considered as potential risk factors are known before cataract surgery starts, except for PCR which occurs during the operation, and in nearly all cases is known by the end of surgery. The idea behind limiting potential risk factors to those known by the end of surgery is that at that point or the post-cataract follow-up assessment, information could be provided to patients regarding their risk of PCO occurring within specific post-cataract time periods. Attempts to account for specific diseases that could

develop between cataract surgery and PCO are not feasible with data currently submitted to the RCOphth NOD.

All candidate covariates were first investigated using the Logrank test, where any covariate significant at the 10% level was considered eligible for the multivariate Loglogistic model, which was fitted using backwards selection from the 'full' model to the 'best fitting' model by removing covariates with a significance level >1%. The use of 1% significance was adopted due to the increased chance of detecting very small significant differences from the large sample size, and to try to minimise negative impacts of possible overfitting. It is feasible this approach does not produce the best model for the sample, but is practical for a very large sample where some covariates are for rare diseases, and to attempt to remove covariates with minimal clinical differences that otherwise could be found statistically significant if using a higher significance level.

Model diagnostics included comparison of the final model with other parametric modelling approaches (Weibull, Lognormal and Exponential) and plotting Cox-Snell residuals against the cumulative hazard where deviations away from the line of identity imply a poorer model fit. All analysis was conducted in STATA 16 (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC).

Results

Patients and operation characteristics

Within the study period 822 568 operations eligible for the national cataract audit were performed from EMR enabled centres offering a full range of ocular services with at least one case of PCO later than one-month post-cataract surgery. It was necessary to exclude 221 484 (26.9%) operations due to: 210 095 with <1 month of follow-up data recorded, 6 176 from one site where there is uncertainty about the IOL information and no follow-up data since November 2016, 3 056 where we were unable to match the recorded IOL to a specific IOL model, 1 291 were recorded as 'no IOL inserted', 413 with a missing IOL power, 340 with no IOL recorded, 97 with IOL powers outside the range of -10 to +40 dioptres, 15 as the recorded axial length was <18 mm and one missing patient age at surgery. The 601 084 cataract operations eligible for this analysis were performed in 58 participating centres, 56 English NHS Trusts, one Welsh Local Health Board and one centre from Guernsey.

The 601 084 operations were performed on 291 411 (48.5%) left eyes and 309 673 (51.5%) right eyes from 448 510 patients by 2 566 surgeons. The operations were performed by surgeons of different grades; 1 105 consultant surgeons performed 364 153 (60.6%) operations, 337 career grade non-consultant surgeons (associate specialists, staff grades and trust doctors) performed 69 054 (11.5%) operations, 1 401 more experienced trainee surgeons (3rd year of training and beyond) performed 143 478 (23.9%) operations and 438 less experienced trainee surgeons (1st and 2nd year of training and foundation doctors) performed 24 399 (4.1%) operations.

First eye surgery was performed in 396 668 patients where 229 447 (57.8%) were female and the median age at surgery was 76.4 years (range 18.1 – 116.6 years). Second eye surgery was performed in 203 782 patients where 120 453 (59.1%) were female and the median age at surgery was 77.4 years (range 18.0 – 112.4 years). Immediate sequential bilateral cataract surgery (ISBCS) was performed in 317 patients. For the 152 257 (34.0%) patients who had surgery to both eyes on separate days during the study period, the median time between the two operations was 4.3 months (range one day to 7.9 years).

Intra-ocular lenses (IOL)

IOL were classified according to their design as one-piece or two-piece, and according to the material used (table 1). Twenty-one specific branded models were used, with two IOL models implanted in >100 000 operations each Figure 1. The number of different IOL models used in contributing centres varied considerably, with two (3.4%) centres using only one IOL model, 12 (20.7%) centres three IOL models, 10 (17.2%) centres four IOL models and 34 (58.6%) centres five or more models with one centre having data for 14 IOL models.

PCO rates

Post-cataract PCO was recorded for 65 210 (10.9%) eyes, with 41 068 (63.0%) of these cases specifically documented as YAG laser being indicated or performed in the same institution that undertook the cataract surgery. The six month, one, three, five and nine year observed rates of PCO were 2.1%, 4.0%, 18.0%, 31.2% and 43.5% respectively.

Different PCO profiles were observed between IOL designs and materials, Table 2 and Figure 2.

PCO modelling

The covariates considered for the risk factor modelling were grouped into factors related to the IOL, patient factors, cataract surgery and ocular factors. For the individual IOL models there was large variation in the hazard of developing PCO, with some models exhibiting similar patterns to overall and others a virtually flat hazard, potentially related to the tendency for certain IOL to be used predominantly in single centres whose post-operative pathways may be less or more effective at documenting PCO. To circumvent this extreme variation, the individual IOL models were not fitted as a covariate in the risk factor model, instead the IOL material was used.

At the univariate level all covariates considered for the post-cataract PCO risk factor modelling showed association at the 10% level except for the patient's ability to cooperate ($p = 0.559$), the presence of corneal pathology ($p = 0.318$), the presence of no fundal view / vitreous opacity ($p = 0.380$) and the presence of optic nerve / CNS disease ($p = 0.676$). The final best fitting PCO risk factor model estimates are shown in Table 3.

Many of the differences for a covariate occur after a period of time has elapsed, for example the statistical difference in PCO rates between the occurrence of PCR and the presence of glaucoma, pseudoexfoliation / phacodenesis or unspecified 'other' ocular co-pathology only becomes apparent after one year post-cataract surgery. The

difference between male and female patients, diabetic status, previous anti-VEGF therapy and a brunescent / white / mature cataract occurs after two years post-cataract surgery. For some covariates the PCO rates diverge within the first year post-cataract surgery, for example patient age, first or second eye surgery, axial length, previous vitrectomy surgery and the presence of high myopia or other macular pathology. The risk of developing PCO for eyes with uveitis / synechiae switched at around four years post-cataract surgery, initially increasing the risk of PCO and then appearing to lower the risk.

The PCO risk factor model was not a perfect fit and the number of significant covariates is a concern regarding possible over-fitting. There was deviation away from the line of identity between the cumulative hazard and the Cox-Snell residuals, although the area of deviation of concern applied to 0.02% of the sample. As a sensitivity analysis the affected operations were removed, the PCO model re-fitted and very similar estimates found for each covariate.

Discussion

From the RCOphth NOD Cataract Audit dataset, 601 084 cataract operations performed by 2 566 surgeons in 58 centres were included in this analysis with overall one-, three-, and five-year PCO rates of 4.0%, 18.0% and 31.2% respectively. These figures resonate with other large published series,(3, 4, 6) and indicate the burden placed on patients and services by PCO which can be expected to grow as demand for cataract surgical

provision grows over the next two decades.(7) Where opportunities exists to reduce PCO rates, there are strong economic arguments for taking these.(3)

The risk factors for PCO identified in this study included an axial length >26 mm, presence of high myopia and implantation of lower IOL powers, previous vitrectomy surgery and uveitis/synechiae, along with younger age and female gender which could be utilised in the informed consent process.

IOL Material

It has been proposed that hydrophilic IOL materials are a risk factor for PCO development. However, a Cochrane collaboration systematic review in 2010 including 66 prospective RCTs dealing with potential factors for PCO after cataract surgery failed to demonstrate statistically significant differences between different IOL optic materials, although they did conclude that silicone IOLs seem to have lower PCO rates in several studies and hydrogel (hydrophilic acrylic) IOLs tend to have higher PCO scores than other materials.(2) In the UK, the weight of evidence was insufficient for NICE, in their 2017 cataract guidelines [NG77], to promote the selection of one IOL material over another, although a meta-analysis from 2017, did report hydrophobic intraocular lenses as associated with lower Nd:YAG laser capsulotomy rates compared to hydrophilic lenses (OR = 0.38, (95% CI 0.16-0.91, P = 0.029)).(8) Subsequent case series have also reported significantly higher rates of PCO for hydrophilic IOL,(4, 9). The findings from our study of significantly higher PCO rates with hydrophilic IOL (coefficient -0.741) compared with hydrophobic IOL is consistent with these. A report from Sweden suggests

the main attraction of hydrophilic IOL may be economic, and whilst less expensive IOL save money for the surgical provider, the increased PCO rate can be shown to make the overall cost of cataract care at population level more expensive.(3)

Age

The association of older age at the time of surgery with progressively lower PCO rates is consistent with other studies.(9, 10) One study estimated that each year of increased age gives an OR for PCO of 0.96 (95% CI 0.92-1.00).(10) The observation that older patients experience less PCO does not, in itself, suggest any potential for reducing PCO rates at population level. However, should interventions that delay the onset of cataract become available, reduced PCO rates promoted by this delay in uptake of surgery may contribute to considerations of their cost-effectiveness.

IOL Design

The differences observed between IOL designs should be interpreted with caution. There is clear selection bias in the evaluation of monofocal multipiece IOL, as these are often employed in cases of PC rupture where visually significant PCO is less likely as the PC is already ruptured. The monofocal toric IOL can be expected to be implanted into a population of patients with greater interest in spectacle independence, who may be more proactive in maintaining optimal vision, and hence present at an earlier stage of PCO development. Conclusions around toric IOL are also hampered by their vastly smaller sample size in NHS practice.

Differential rates of opacification

The variation over time of the impact of various risk factors requires consideration. For some there is an intuitive explanation, such as uveitic eyes could have an increased inflammatory response following cataract surgery, potentially leading to higher initial PCO rates. However, it may be that uveitic eyes which are destined to get PCO are more likely to get it in the first or second year post-surgery and those eyes which have not developed PCO by three years post-operatively are less likely to subsequently, whereas in non-uveitic eyes the annual risk takes longer to migrate towards zero. This acceleration in accumulation of PCO in uveitis has been reported elsewhere.(9)

Variation may be due to differences in the ability of clinicians to diagnose, or willingness to treat PCO. Those with small pupils had lower PCO rates, which is counterintuitive as these eyes might have been expected to have more residual soft-lens material at the end of surgery increasing their chances of PCO. A potential explanation would be that small pupils make PCO less visible to an examining clinician, hence reducing their tendency to refer for, or to offer, capsulotomy. Amblyopia was seen to increase rates of PCO; which could be expected as clinicians are unable to be certain whether maximum visual benefits have been gained and are therefore more likely to consider capsulotomy for levels of PCO that would be ignored in non-amblyopic eyes where both clinician and patient are happy with the acuity. People with diabetes had lower PCO rates than those without diabetes, potentially explained by surgeon reluctance to perform YAG laser surgery on people with diabetes for fear of provoking macular oedema. Equally, this seemingly protective effect of diabetes could be due to retention of otherwise

uncomplicated post-operative cataract patients in eye care services maintaining a larger denominator, an explanation that would serve equally for the association of lower PCO with glaucoma, age-related macular degeneration and other macular pathologies.

The higher PCO rate in eyes with an axial length >26 mm and in high myopia is potentially linked to the larger size of the capsular bag producing a less tight apposition of the square posterior edge of the IOL to the capsule reducing the effectiveness of that square edge in preventing posterior migration of lens epithelial cells. A recent meta-analysis showed clear benefit of capsular tension rings in reducing PCO rates, potentially by mitigating for looser fitting capsules,(11) and it may be the use of these rings that explains the reduced PCO rates in eyes with pseudoexfoliation found in this study.

Study limitations

The use of routinely collected data, without linkage of health records, limits the inclusion of patients to those who subsequently interact with their cataract surgical provider. In some geographic areas, the assumption patients will remain with the same provider is fairly sound, but in other settings patients move freely between providers for different treatments. Patients who have no further interaction with the cataract surgery provider leave the denominator at their last recorded visit. It is not possible to estimate the extent to which either the departure of PCO-free patients from the series creates a systematic bias towards over-estimation of PCO rates, or systematic under-estimation is produced by patients with PCO remaining undiagnosed, untreated or treated elsewhere. These biases could be reduced if the RCOphth is successful in its application

for *section 251 exemption* which will permit repetition of this study with health data linkage between providers and other NHS databases via the NHS number.

The similarity between our estimates and those of other published series, both RCT (2) and real-world case series,(3, 4, 6) suggests the extent of bias in either direction is acceptable for the purpose of risk factor evaluation, although the caveats need to be considered when citing PCO rates or absolute risks at given time points.

Conclusions

Quality in cataract service delivery is a multi-faceted concept. Reducing PCO rates feeds into most of the domains of quality suggested by the WHO (effectiveness, safety, people-centredness, timeliness, equity, integration and efficiency), as well as contributing to the proposed additional domain of planetary health.(12) Whilst the variation in observed PCO rates between centres, coupled with the tendency of many centres to adopt single IOL models for predominant use, prevented conclusions being drawn about individual IOL models, important inferences are still possible.

Centres should be strongly encouraged to undertake comparison of PCO rates for the different IOL they use, and opt for lenses that minimise the visual loss caused by PCO and the need for subsequent capsulotomy. The cost of YAG laser capsulotomy to the NHS is estimated at £132 per case on average, and it therefore represents a false economy for NHS providers to opt for less expensive IOL with higher PCO rates. Where the purchaser provider split exists, the perverse incentive to ignore PCO rates when

procuring IOL needs to be resisted. It may be that commissioners could opt for lowering PCO rates as one aspect of quality on which they base remuneration, or even combine cataract and YAG laser capsulotomy services, such that no independent tariff is associated with the treatment of PCO. The incentive to lower PCO rates would then be universally felt. Future research might involve economic analyses of interventions to reduce PCO rates such as capsule tension ring usage or adoption of IOL designs or models that perform particularly well in subsequent evaluations.

Acknowledgments

It is with deep regret that we note the death of our friend and colleague Robert Johnston, who sadly died in September 2016. Without his inspirational vision, determination and career long commitment to quality improvement in ophthalmology this work would not have been possible.

We acknowledge the support of the hospitals that participated in this National Ophthalmology Database Audit study and thank our medical and non-medical colleagues for the considerable time and effort devoted to data collection.

The 58 centres with data in this analysis are listed in alphabetical order below separated into the region they are located in.

English NHS Trusts:

Barking, Havering and Redbridge University Hospitals NHS Trust; Barts Health NHS Trust; Bolton NHS Foundation Trust; Bradford Teaching Hospitals NHS Foundation Trust;

Calderdale and Huddersfield NHS Foundation Trust; Chesterfield Royal Hospital NHS Foundation Trust; County Durham and Darlington NHS Foundation Trust; East Kent Hospitals University NHS Foundation Trust; East Sussex Healthcare NHS Trust; Epsom and St Helier University Hospitals NHS Trust; Frimley Health NHS Foundation Trust; Gloucestershire Hospitals NHS Foundation Trust; Great Western Hospitals NHS Foundation Trust; Hampshire Hospitals NHS Foundation Trust; Harrogate and District NHS Foundation Trust; Imperial College Healthcare NHS Trust; Isle of Wight NHS Trust; King's College Hospital NHS Foundation Trust; Leeds Teaching Hospitals NHS Trust; Liverpool University Hospitals NHS Foundation Trust; Manchester University NHS Foundation Trust; Mid Cheshire Hospitals NHS Foundation Trust; Mid and South Essex NHS Trust; Moorfields Eye Hospital NHS Foundation Trust*; Norfolk and Norwich University Hospitals NHS Foundation Trust; North Middlesex University Hospital NHS Trust; North West Anglia NHS Foundation Trust; Northern Devon Healthcare NHS Trust; Nottingham University Hospitals NHS Trust; Oxford University Hospitals NHS Foundation Trust; Portsmouth Hospitals NHS Trust; Royal Berkshire NHS Foundation Trust; Royal Cornwall Hospitals NHS Trust; Royal Free London NHS Foundation Trust; Royal United Hospitals Bath NHS Foundation Trust; Salisbury NHS Foundation Trust; Sandwell and West Birmingham Hospitals NHS Trust; Sheffield Teaching Hospitals NHS Foundation Trust; Shrewsbury and Telford Hospital NHS Trust; South Tees Hospitals NHS Foundation Trust; South Warwickshire NHS Foundation Trust; The Hillingdon Hospitals NHS Foundation Trust; The Mid Yorkshire Hospitals NHS Trust; The Newcastle upon Tyne Hospitals NHS Foundation Trust; The Princess Alexandra Hospital NHS Trust; University Hospitals Dorset NHS Foundation Trust; Torbay and South Devon NHS Foundation Trust;

University Hospital Southampton NHS Foundation Trust; University Hospitals Birmingham NHS Foundation Trust; University Hospitals Bristol and Weston NHS Foundation Trust; University Hospitals Coventry and Warwickshire NHS Trust; University Hospitals Plymouth NHS Trust; Warrington and Halton Teaching Hospitals NHS Foundation Trust; Wirral University Teaching Hospital NHS Foundation Trust; Wrightington, Wigan and Leigh NHS Foundation Trust; Yeovil District Hospital NHS Foundation Trust;

Welsh Local Health Boards:

Cardiff & Vale University Local Health Board;

Guernsey:

Medical specialists group Guernsey;

*Includes data from Bedfordshire Hospitals NHS Foundation Trust and Croydon Health Services NHS Trust as the ophthalmology services for these two NHS Trusts are part of Moorfields Eye Hospital NHS Foundation Trust.

Table and Figure legends

Table 1:

Use of IOL design and materials in centres, for operations, surgeons, time period of use and median age of patients

*Excluding simultaneous bilateral cataract surgery as some patients had different IOL's from different IOL design and IOL material used in each eye. For patients who have had both eyes operated on different dates, their age at each surgery is considered as separate events. N = 600

450 operations from 448 193 patients, where 152 257 patients had surgery to both eyes on different dates.

480 **Table 2:**

481 Observed PCO rates at specified post-cataract surgery for the IOL design and material

482

483

Table 3:

PCO risk factor model estimates

*When the covariate coefficient is negative this implies a higher risk of PCO, and when the covariate coefficient is positive this implies a lower risk of PCO. Each covariate has a reference category with a coefficient of zero, thus the closer a covariate category coefficient is to zero, the less difference there is between this category and the reference category, for example increasing age implies lower risk of PCO as can be seen from the larger positive coefficients for each successive older age group.

Figure 1:

The number of operations in the sample where each IOL model was used. N = 601 084 cataract operations performed by 2 566 surgeons from 58 centres

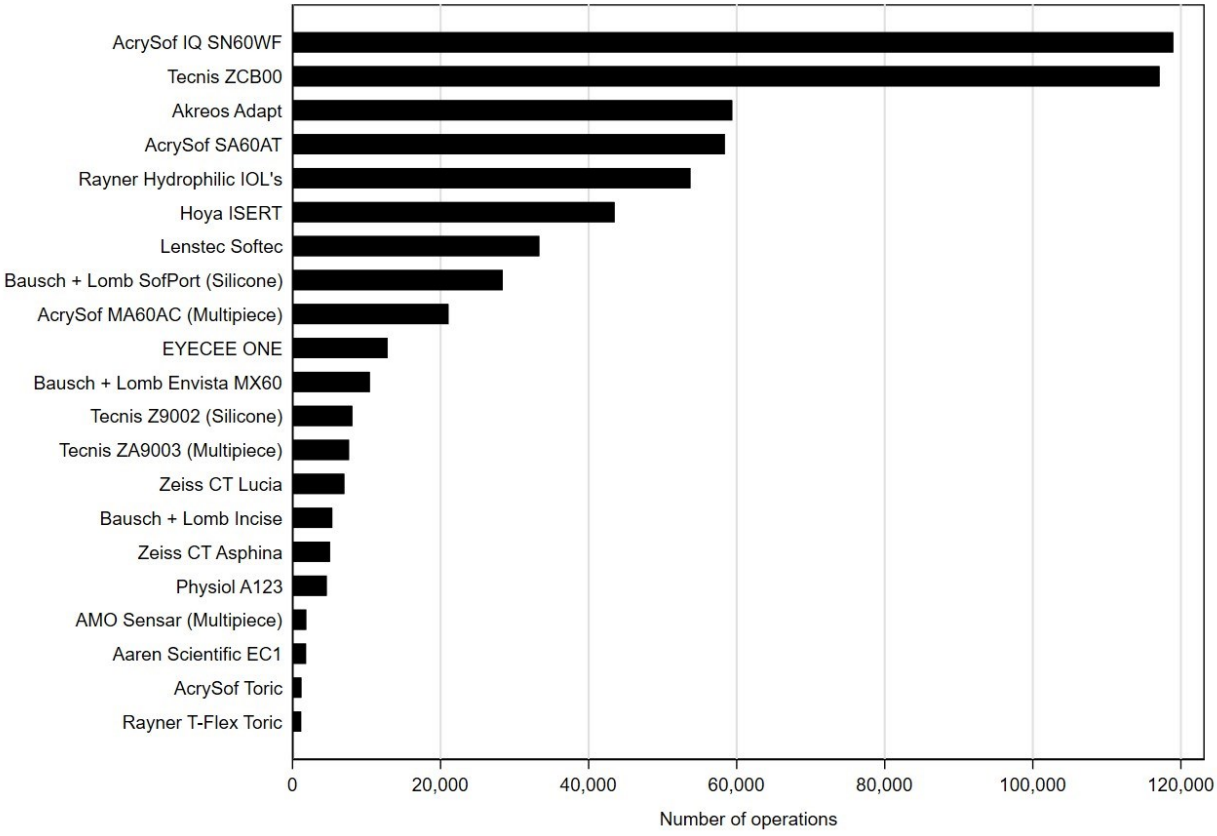
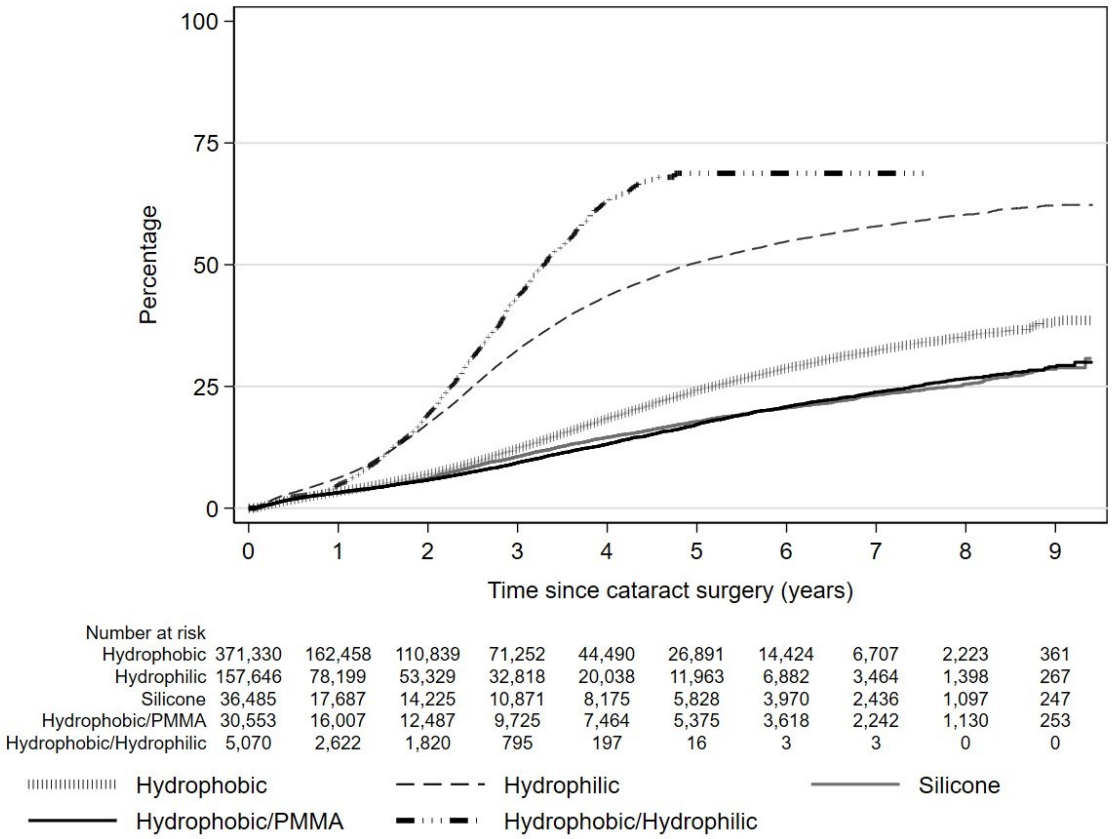


Figure 2:

Kaplan-Meier failure plot of time to post-cataract PCO for the IOL material. N = 601 084 cataract operations performed by 2 566 surgeons from 58 centres



References

1. Maedel S, Evans JR, Harrer-Seely A, Findl O. Intraocular lens optic edge design for the prevention of posterior capsule opacification after cataract surgery. The Cochrane database of systematic reviews. 2021;8:CD012516.

2. Findl O, Buehl W, Bauer P, Sycha T. Interventions for preventing posterior capsule opacification. The Cochrane database of systematic reviews. 2010(2):CD003738.

3. Cullin F, Busch T, Lundstrom M. Economic considerations related to choice of intraocular lens (IOL) and posterior capsule opacification frequency - a comparison of three different IOLs. Acta Ophthalmol. 2014;92(2):179-83.

4. Ursell PG, Dhariwal M, Majirska K, Ender F, Kalson-Ray S, Venerus A, et al. Three-year incidence of Nd:YAG capsulotomy and posterior capsule opacification and its relationship to monofocal acrylic IOL biomaterial: a UK Real World Evidence study. Eye (Lond). 2018;32(10):1579-89.

5. Buchan JC, Donachie PHJ, Cassels-Brown A, Liu C, Pyott A, Yip JLY, et al. The Royal College of Ophthalmologists' National Ophthalmology Database study of cataract surgery: Report 7, immediate sequential bilateral cataract surgery in the UK: Current practice and patient selection. Eye (Lond). 2020;34(10):1866-74.

6. Johansson B. Clinical consequences of acrylic intraocular lens material and design: Nd:YAG-laser capsulotomy rates in 3 x 300 eyes 5 years after phacoemulsification. Br J Ophthalmol. 2010;94(4):450-5.

7. Buchan JC, Amoaku W, Barnes B, Cassels-Brown A, Chang BY, Harcourt J, et al. How to defuse a demographic time bomb: the way forward? Eye (Lond). 2017;31(11):1519-22.

8. Zhao Y, Yang K, Li J, Huang Y, Zhu S. Comparison of hydrophobic and hydrophilic intraocular lens in preventing posterior capsule opacification after cataract surgery: An updated meta-analysis. Medicine (Baltimore). 2017;96(44):e8301.

9. Tokko HA, Hussain F, Al-Awadi A, Mei F, Zeiter JH, Kim C, et al. Factors Associated with the Development of Posterior Capsule Opacification Requiring Yttrium Aluminum Garnet Capsulotomy. Optometry and vision science : official publication of the American Academy of Optometry. 2019;96(7):492-9.

10. Prajna NV, Ellwein LB, Selvaraj S, Manjula K, Kupfer C. The madurai intraocular lens study IV: posterior capsule opacification. Am J Ophthalmol. 2000;130(3):304-9.

11. Zhang K, Dong Y, Zhao M, Nie L, Ding X, Zhu C. The effect of capsule tension ring on posterior capsule opacification: A meta-analysis. PLoS One. 2021;16(3):e0246316.

12. Yoshizaki M, Ramke J, Zhang JH, Aghaji A, Furtado JM, Burn H, et al. How can we improve the quality of cataract services for all? A global scoping review. Clinical & experimental ophthalmology. 2021;49(7):672-85.

543

544 **Table 1: Use of IOL design and materials in centres, for operations, surgeons, time**

545 **period of use and median age of patients**

546

	Number of centres	Number of operations	Number of surgeons	Time span of use (years)	Median age of patients*
IOL design					
Monofocal Single Piece	58	568 162	2 536	8.0	76.8
Monofocal Multipiece	49	30 553	1 560	8.0	76.2
Monofocal Toric	20	2 369	435	8.0	73.1
IOL material					
Hydrophobic	54	371 330	2 065	8.0	76.8
Hydrophilic	40	157 646	1 368	8.0	76.7
Silicone	24	36 485	609	8.0	77.1
Hydrophobic / PMMA	49	30 553	1 560	8.0	76.2
Hydrophobic / Hydrophilic	9	5 070	70	6.2	77.5
Overall	**58**	**601 084**	**2 566**	**8.0**	**76.7**

547

548 *Excluding simultaneous bilateral cataract surgery as some patients had different IOL's

549 from different IOL design and IOL material used in each eye. For patients who have had

550 both eyes operated on different dates, their age at each surgery is considered as

551 separate events.

552

553

554 Table 2: Observed PCO rates at specified post-cataract surgery for the IOL design and

555 material

556

	6 months	1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 yea
k	601 084	355 189	276 973	192 700	125 461	80 364	50 073	28 897	14 8
w PCO cases since previous time point	9 947	6 383	14 444	15 195	9 811	5 223	2 492	1 127	44
N = 601 084)	2.1	4.0	9.7	18.0	25.4	31.2	35.4	38.6	41
gle Piece PCO (N = 568 162)	2.1	4.1	10.0	18.6	26.3	32.2	36.5	39.8	42
ltipiece PCO (N = 30 553)	1.8	3.1	5.7	9.2	13.0	17.0	20.7	23.7	26
ic PCO (2 369)	2.3	3.8	10.1	19.2	30.2	40.6	51.3	58.4	61
CO (N = 371 330)	1.7	3.3	6.8	12.0	18.0	23.7	28.3	31.9	34
O (N = 157 646)	3.1	6.0	17.0	31.9	43.0	50.0	54.3	57.4	59
N = 36 485)	1.7	3.0	6.0	10.4	14.4	17.6	20.4	23.0	25
PMMA PCO (N = 30 553)	1.8	3.1	5.7	9.2	13.0	17.0	20.7	23.7	26
Hydrophilic PCO (N = 5 070)	2.1	4.6	18.8	42.5	61.0	67.4	67.4	67.4	-

557

558

559 Table 3: PCO risk factor model estimates

560

PCO risk factor model covariate*	Coefficient	Standard error	p-value	95% Confidence Interval
Gamma	0.707	0.002	<0.001	0.702 to 0.711
Constant	1.946	0.050	<0.001	1.848 to 2.044
IOL material				
Hydrophobic	0.000	Reference	Reference	Reference
Hydrophilic	-0.741	0.008	<0.001	-0.756 to -0.726
Silicone	0.235	0.017	<0.001	0.201 to 0.269
Hydrophobic / PMMA	0.246	0.018	<0.001	0.210 to 0.281
Hydrophobic / Hydrophilic	-0.927	0.024	<0.001	-0.974 to -0.880
IOL power (dioptres)				
<15	-0.155	0.020	<0.001	-0.194 to -0.115
15 to 19.5	-0.042	0.009	<0.001	-0.060 to -0.025
20 to 28.5	0.000	Reference	Reference	Reference
29 to 40	-0.034	0.026	0.192	-0.085 to 0.017
Age at surgery (years)				
<40	0.000	Reference	Reference	Reference
40 – 49	0.354	0.052	<0.001	0.252 to 0.456
50 – 89	0.630	0.046	<0.001	0.540 to 0.720
≥90	0.718	0.051	<0.001	0.619 to 0.818
Gender				
Female	0.000	Reference	Reference	Reference
Male	0.099	0.007	<0.001	0.084 to 0.114
Diabetic status				
No diabetes	0.000	Reference	Reference	Reference
Diabetic	0.144	0.009	<0.001	0.127 to 0.162
Grade of operating surgeon				
Consultant surgeon	0.000	Reference	Reference	Reference
Career grade non-consultant surgeon	-0.030	0.010	0.003	-0.050 to -0.010
More experienced trainee surgeon	0.025	0.008	0.002	0.009 to 0.041
Les experienced trainee surgeon	-0.024	0.017	0.155	-0.057 to 0.009

First / second eye surgery				
First eye surgery	0.000	Reference	Reference	Reference
Second eye surgery	-0.137	0.006	<0.001	-0.149 to -0.126
PCR occurring during surgery				
No	0.000	Reference	Reference	Reference
Yes	0.384	0.038	<0.001	0.309 to 0.458
Pupil size				
Small	0.000	Reference	Reference	Reference
Medium	-0.091	0.018	<0.001	-0.127 to -0.055
Large	-0.034	0.018	0.055	-0.069 to 0.001
Missing	1.519	0.093	<0.001	1.335 to 1.702
Axial length (mm)				
<26	0.000	Reference	Reference	Reference
≥26	-0.079	0.022	<0.001	-0.122 to -0.036
Missing	0.410	0.018	<0.001	0.375 to 0.445
Anti-VEGF therapy				
No previous Anti-VEGF therapy	0.000	Reference	Reference	Reference
Anti-VEGF therapy	0.121	0.020	<0.001	0.083 to 0.160
The presence of any of the following				
Age-related macular degeneration	0.046	0.011	<0.001	0.024 to 0.069
Brunescent / white / mature cataract	0.065	0.019	0.001	0.028 to 0.103
Glaucoma	0.298	0.011	<0.001	0.278 to 0.319
High myopia	-0.076	0.019	<0.001	-0.113 to -0.040
Other macular pathology	-0.128	0.019	<0.001	-0.166 to -0.091
Pseudoexfoliation / Phacodenesis	0.206	0.034	<0.001	0.140 to 0.272
Previous vitrectomy surgery	-0.621	0.020	<0.001	-0.662 to -0.581
Uveitis / synechiae	-0.083	0.030	0.006	-0.143 to -0.024
Unspecified ‘other’ co-pathology	-0.088	0.013	<0.001	-0.112 to -0.063

*When the covariate coefficient is negative this implies a higher risk of PCO, and when the covariate coefficient is positive this implies a lower risk of PCO. Each covariate has a reference category with a coefficient of zero, thus the closer a covariate category

565 coefficient is to zero, the less difference there is between this category and the
566 reference category, for example increasing age implies lower risk of PCO as can be seen
567 from the larger positive coefficients for each successive older age group.
568
569