# Journal of Cataract & Refractive Surgery


## Biometric description of 34 589 eyes undergoing cataract surgery: sex differences.

--Manuscript Draft--

| | |
|---|---|
| **Manuscript Number:** | JCRS-23-817 |
| **Article Type:** | Full Length Article |
| **Section/Category:** | Cataract |
| **Full Title:** | Biometric description of 34 589 eyes undergoing cataract surgery: sex differences. |
| **Corresponding Author:** | Marta Jiménez-García, MSc.<br>Universitair Ziekenhuis Antwerpen<br>Zaragoza, Zaragoza SPAIN |
| **First Author:** | Marta Jiménez-García, MSc. |
| **Order of Authors:** | Marta Jiménez-García, MSc. |
| | Francisco Javier Segura-Calvo |
| | Martin Puzo |
| | Francisco Javier Castro-Alonso |
| **Abstract:** | Purpose<br>To describe gender differences in the biometric parameters of a large sample of cataract patients. Cataract surgery has evolved from a vision restoration to a refractive procedure, and population-based studies are vital to optimise normative databases and post-surgical outcomes.<br>Setting<br>Miguel Servet University Hospital, Zaragoza, Spain.<br>Design<br>Retrospective single-centre observational study.<br>Methods<br>The study included 34589 eyes (20004 cataract patients). Biometric data was obtained from IOL Master 700 and Pentacam HR. Linear mixed models were used to account for inter-eye correlation. HofferQST formula was used to calculate the hypothetical distribution of IOL power (arbitrary lens; A=119.2).<br>Results<br>Most biometric variables showed significant differences between sexes (p<0.0001), such as 0.53mm shorter eyes found in females, of which 0.16mm are explained by shorter aqueous depth. Steeper anterior keratometries (~0.75D) were found in females, to end up in no difference on anterior astigmatism magnitude, but different orientation (p<0.0001). The distribution of IOL power differed between sexes (p<0.001), with the interquartile range shifting one dioptre towards more powerful lenses in females and odds ratio (power>26D) = 2.26, p<0.0001 (Fisher's).<br>Conclusions<br>Large sample size studies provide smaller margin of error, higher power, and controlled risk of reporting false (negative or positive) findings. Highly significant differences between sexes in ocular biometry were found; this supports the idea that including sex as a parameter in IOL calculation should be explored and may improve results. Additionally, the distribution of IOL powers was provided, which may be useful for manufacturers and hospital stock planning. |
| **Keywords:** | cataract; Ocular biometry; intraocular lens; cataract surgery; pseudophakia |

*Department of Ophthalmology*
*Miguel Servet University Hospital*
*Pº Isabel la Católica 1–3*
*50009 Zaragoza (Spain)*

**William J. Dupps Jr, MD, PhD Thomas Kohnen, MD, PhD**

Zaragoza, 14th November 2023

Dear Editor-in-Chief,

Please find enclosed a copy of our manuscript entitled '*Biometric description of 34589 eyes undergoing cataract surgery: sex differences'* by Jiménez-García et al. to be considered for publication in *Journal of Cataract and Refractive Surgery*.

Cataract surgery has evolved from a vision restoration procedure to an actual refractive surgery, with patients increasingly expecting optimal post-surgical outcomes and spectacle independence. This achievement may be partly attributed to the increased reliability of ocular biometry and modern intraocular lens (IOL) calculation formulas. However, experts agree that IOL formula's precision is reaching its limit. On the other hand, preoperative biometry varies according to age, sex, and ethnicity, and is likely to change in the following years owing to a global myopisation trend or to the growing popularity of refractive procedures. In this context, large sample size descriptive studies — with higher statistical power, smaller error, and controlled risk of reporting false findings — are instrumental in refining normative databases and in future modelling of the cataractous eye. Here, highly significant differences in ocular biometry between sexes were found, and the distribution of IOL powers provided.

Our findings support the idea that including sex in IOL formulas should be explored, since artificial intelligence may find currently unknown patterns in data. Moreover, adding certainty to the IOL power distribution — where 50% of this sample required an IOL 20–23D —, intends to push the manufacturing industry, and thus represents a step forward in reducing the IOL labelling step from 0.50D to 0.25D, giving cataract surgeons more control. We believe these findings can be appropriate for publication as a Full Length Article in *Journal of Cataract and Refractive Surgery*.

*Department of Ophthalmology*
*Miguel Servet University Hospital*
*Pº Isabel la Católica 1–3*
*50009 Zaragoza (Spain)*

The collaborators agreed to be included as such in the acknowledgements section and do not have conflicts of interest. All the authors have approved the document and agree with its submission to *Journal of Cataract and Refractive Surgery*. We have no conflicts of interest to disclose, and we confirm that this manuscript is original, has not been published elsewhere and is not under consideration by another journal. As the corresponding author (MJG), I had full access to all the data in the study and I take responsibility for the integrity of the data, the accuracy of the data analysis and the decision to submit for publication.

Looking forward to hearing from you at your earliest convenience.

Sincerely,

Marta Jiménez-García, PhD

## Synopsis

Including sex in IOL formulas may reveal new data patterns using artificial intelligence. Additionally, the presented IOLs distribution is a significant advancement to reduce the labeling step to 0.25D.

# Biometric description of 34 589 eyes undergoing cataract surgery: sex differences.

**Marta Jiménez-García, PhD**[*][a, b, c] (https://orcid.org/0000-0002-2839-9696)

**Francisco J. Segura-Calvo, PhD** [a, b, c, d] (https://orcid.org/0000-0002-9250-9060)

**Martín Puzo, MD** [a, b, c, e] (https://orcid.org/0000-0002-5048-4846)

**Francisco J. Castro-Alonso, MD, PhD** [a, b, c, e] (https://orcid.org/0000-0002-4682-8706)

**on behalf of the UFR-ARCCA Group Zaragoza**

a. *GIMSO, Institute for Health Research Aragón, Hospital Universitario Miguel Servet, Zaragoza, Spain*
b. *UFR, Department of Ophthalmology, University Hospital Miguel Servet, Zaragoza, Spain*
c. *ARCCA, Department of Ophthalmology, Hospital Nuestra Señora de Gracia, Zaragoza, Spain*
d. *Surgery Department, Ophthalmology Area, University of Zaragoza, Zaragoza, Spain*
e. *Department of Ophthalmology, Alcañiz Hospital, Alcañiz (Teruel), Spain*

**** Marta Jiménez-García***

*Institute for Health Research Aragón - Hospital Universitario Miguel Servet*

*Pº de Isabel la Católica, 1-3*

*50009 Zaragoza SPAIN*

*Mail to: marta.jimenez.garcia@outlook.com*

*Phone Number: +34 976765500*

**Running title:** Biometric description of cataract patients

**Keywords:** Cataract; ocular biometry; intraocular lens; cataract surgery; pseudophakia

**Word count:** 2706 words

**Conflicts of interests and source of funding:** There was no specific financial support for this study. The authors declare no conflicts of interest.

**Meeting:** Presented at Sociedad Española de Cirugía Ocular Implanto-Refractiva Congress (SECOIR 2023)

Manuscript

# Biometric description of 34 589 eyes undergoing cataract surgery: sex differences.


## ABSTRACT

### Purpose

To describe gender differences in the biometric parameters of a large sample of cataract patients. Cataract surgery has evolved from a vision restoration to a refractive procedure, and population-based studies are vital to optimise normative databases and post-surgical outcomes.

### Setting

Miguel Servet University Hospital, Zaragoza, Spain.

### Design

Retrospective single-centre observational study.

### Methods

The study included 34589 eyes (20004 cataract patients). Biometric data was obtained from IOL Master 700 and Pentacam HR. Linear mixed models were used to account for inter-eye correlation. HofferQST formula was used to calculate the hypothetical distribution of IOL power (arbitrary lens; A=119.2).

### Results

Most biometric variables showed significant differences between sexes ($p<0.0001$), such as 0.53mm shorter eyes found in females, of which 0.16mm are explained by shorter aqueous depth. Steeper anterior keratometries (~0.75D) were found in females, to end up in no difference on anterior astigmatism magnitude, but different orientation ($p<0.0001$). The distribution of IOL power differed between sexes ($p<0.001$), with the interquartile range shifting one dioptre towards more powerful lenses in females and odds ratio (power>26D) = 2.26, $p<0.0001$ (Fisher's).

## Conclusions

Large sample size studies provide smaller margin of error, higher power, and controlled risk of reporting false (negative or positive) findings. Highly significant differences between sexes in ocular biometry were found; this supports the idea that including sex as a parameter in IOL calculation should be explored and may improve results. Additionally, the distribution of IOL powers was provided, which may be useful for manufacturers and hospital stock planning.

# INTRODUCTION

According to the latest projections of the World Health Organization, the global demand for eye care is likely to surge in the coming years due to population growth, ageing, and lifestyle changes. Fortunately, efficacious preventive interventions, treatments, and management options for the most prevalent eye conditions, such as cataract, are already available. Cataract surgery is highly cost-effective,[1] and post-surgical quality-of-life improvement has been extensively documented.[2] However, cataract surgery success is highly dependent on the prediction of the intraocular lens (IOL) power, which, in turn, relies on the accurate acquisition of pre-operative biometric data and the selection of an appropriate calculation formula.[3] The first optical biometer was introduced in 1999, soon becoming the gold standard for IOL calculations. Nowadays, biometers based on different techniques, such as partial coherence interferometers, optical low-coherence reflectometers or swept-source optical coherence tomographers (SS-OCT), provide precise and highly repeatable biometry measurements.[4]

Cataract surgery itself has evolved from a vision restoration procedure[5] to an actual refractive surgery, with patients increasingly expecting an optimal post-surgical outcome and spectacle independence.[6,7] Concurrently, delayed retirement and extension of working lives are becoming a reality in Europe, where policy-makers have already implemented some reforms, and cataract surgery will become a more and more common intervention among the workforce. Guaranteeing closer-to-emmetropia results or adjusting the periods for post-surgical stabilization will be some of the challenges for the near future.[8]

Ocular biometric parameters are known to vary with age, sex and ethnicity;[9–11] therefore, population-based studies are instrumental in refining normative databases and optimizing post-surgical outcomes. This study aimed to describe the ocular biometry of a large sample undergoing cataract surgery, verify the magnitude of previously reported associations, and calculate the distribution of predicted IOL powers.

Pre-operative biometry is likely to drastically change in the following years owing to a global myopization trend[12] and to the growing popularity of refractive procedures. The comprehensive statistical description of large not surgically-treated samples, as the one presented here, may be of use in eye modelling, to hospitals, manufacturers, or future clinical trials design not only today but in the future.

## SUBJECTS AND METHODS

### Data collection

This was a retrospective single-center observational study in a purpose-built cataract unit (ARCCA), that provides surgical treatment to cataract patients from three major public hospitals in Spain (Hospital Miguel Servet, Hospital Royo Villanova, Hospital Nuestra Señora de Gracia, in Zaragoza). This study leveraged pre-existing clinical data from routine preoperative visits for secondary use in the research domain. All the studied variables are described on **Supplementary material A**. This study was designed and carried out in compliance with the tenets of the Declaration of Helsinki, and ethical approval was granted from the Research Ethics Committee of Aragon region (CEICA C.I. PI22/488), that waived the requirement to obtain informed consent due to the retrospective nature of the study. Cataract patients were examined March 2016–June 2022. In general, patients are added to the cataract surgery waiting list when decimal best spectacle-corrected visual acuity (BSCVA) ≤0.4 nevertheless, the final decision is made on a case-by-case basis. All patients underwent a comprehensive preoperative examination, which included optical biometry (IOL Master 700; Carl Zeiss Meditec, Jena, Germany). Corneal tomography (Pentacam HR, Oculus Optikgeräte GmbH, Germany) was also available for those patients eligible for arcuate incisions, toric or multifocal IOL implantation. Patients with previous corneal or refractive surgery or corneal ectasia, verified by a cornea specialist, were excluded. Pentacam HR and IOL Master 700 databases were linked using patient ID before anonymization.

## Data pre-processing and curation

Secondary use of clinical data for research is challenging, and data normally requires pre-processing and curation. For each biometry, the relevant error was calculated as the sum of warnings in axial length (AL), keratometry, anterior chamber depth (ACD) and lens thickness (LT). Those variables frequently figure in IOL calculation formulas, and have an enormous influence on the IOL power estimation.[3] If relevant error >3, the biometry was excluded. When multiple measurements on the same date were available for the same eye, we selected the one with minimal error. When two biometries on different dates were available, we kept the latest, provided it had at least the same quality. Moreover, the analysis included derived variables, such as anterior segment (AS = ACD + LT) and posterior segment (PS = AL - AS). Corneal tomographies were used to analyze the astigmatism of the back corneal surface. For both corneal surfaces, astigmatism was calculated as (K2-K1) x Steep Axis, where K2 is the simulated steep keratometry and K1 the flat keratometry. Astigmatism was subsequently transformed into power vectors (J0, J45).[13]

Finally, Hoffer QST formula was used to calculate the distribution of the IOL powers for an arbitrary IOL (lens constant A=119.2, personalized ACD pACD=5.68) and target refraction +0.00D. The IOL (in 0.50D steps) with a closer to emmetropia residual was selected. To avoid distortion of the distribution, a random eye for each patient, obtained by means of a computerized method, was considered in this graphical analysis.

## Statistical analysis

Matlab R-2021b (The MathWorks Inc., Natick, MA) was used for data curation, pre-processing, and visualization; JMP Pro 16 (SAS Institute Inc., Cary, NC, USA) for statistical analysis, where 0.05 was considered the cut-off for significance.

Mixed models, that can analyze grouped data and account for inter-eye correlation, were used to investigate the biometric differences in male and female candidates. Moreover, mixed models can deal with missing data. An unstructured covariance model was assumed:

$$\begin{pmatrix} \sigma_1^2 & \sigma_{12} \\ \sigma_{12} & \sigma_2^2 \end{pmatrix}$$

where the variance in one eye ($\sigma_1^2$) and the contralateral eye ($\sigma_2^2$) may differ, and $\sigma_{12}$ is their covariance.

Normality was assessed with Anderson-Darling test, however, rejection of normality is habitual in large sample sizes.[14] Visual inspection of Q-Q plots and skewness/kurtosis analysis are recommended for N>300, and skewness>2 or kurtosis>7 are the reference limits for substantially non-normal distributions.[14] In any case, mixed models have proved to be robust even with very skewed distributions that violate the distributional assumption of normality.[15]

## RESULTS

Data belonged to 20 004 patients, of whom 11 572 were female (20 171 eyes) and 8 432 male (14 418 eyes). Age at 1st eye surgery was 74.1±9.5 for males and 75.6±8.9 for female patients.

### Overall ocular biometry

The biometric parameters for the overall population are presented in **Table 1** and graphically represented with violin plots (**Supplementary material B**). When normality was assessed (overall and within the groups), none of the study variables presented a normal distribution (Anderson-Darling p<0.05), but visual inspection of Q-Q plots, and analysis of skewness and kurtosis (**Table 1** ) yielded different results. AL, kappa (Chang Waring Chord), alpha angle and PS were the only variables that presented either skewness>2 or kurtosis>7.[14] Only White to White (W2W), alpha and kappa angles presented missing values. Data from the corneal posterior surface was available for 1960 eyes, and all the variables presented some missing values (<1%).

### Differences between sexes in ocular biometry

When analyzing the ocular biometry data, anatomical differences between male and female patients became apparent (most of them p<0.0001, **Table 2**, **Figure 1**). Some of them were clinically significant, such as 0.53mm shorter eyes found in women, of which 0.16mm are explained by shallower ACDs. The difference in LT, although statistically significant (p<0.0002), was negligible (0.02mm shorter crystalline lenses found in females), and central corneal thickness (CCT) differed barely by 5µm. Differences in the posterior segment (0.39mm larger in male patients) explained most of the difference in AL.

When analyzing the probability distribution of the steep meridian axis by sex (**Figure 2**), clearly identifiable differences were found. The distribution of the calculated IOL power (overall and within the groups) is shown on **Figure 3**. Significant differences were found in this distribution, where female patients required higher IOL power to achieve emmetropia (0.83D, p>0.0001). While the probability to require an IOL power<14.50D (corresponding with the overall 5$^{th}$ percentile) was not different across sex, the probability to require an IOL>26D (95$^{th}$ overall percentile) was lower for male patients (p<0.0001, Fisher's Exact Test) with odds ratio 0.44 [0.38–0.51].

## DISCUSSION

This study analyzed biometric data from 20 004 patients (34 589 eyes) awaiting cataract surgery, all of them measured with IOL Master 700, whose high precision and repeatability has been formerly described in cataract patients.[4] To the best of our knowledge, this is the most comprehensive study on cataract patients' ocular biometry in Europe.

Knowledge of the ocular biometry normal ranges is instrumental in adequately establishing the eyes prone to an IOL power calculation error; and its segmentation, an opportunity to define the method that optimizes the calculations on each subgroup.

The sample analyzed here included more female than male patients (57.8% vs 42.2%), rates similar to those previously reported.[16,17] Female patients received surgery slightly later, a finding previously reported in the US and China.[18,19] Both findings agree with the higher life expectancy for women in Europe published by Eurostat.

The overall AL (23.47±1.70mm) was shorter than those reported in Asian populations,[17,19–21] Portugal,[16] and Israel.[11] Nonetheless, previous populational studies in Europe,[22,23] USA,[10,18] Australia,[24] and (surprisingly) Singapore[25] reported similar AL values. The difference in AL between sexes was 0.53mm, but differences over 0.80mm have been reported previously.[11,20]

The overall ACD found in our study (3.04±0.51mm) is one of the shallowest reported along with Jivrajka's and Lei's.[18,19] ACD was significantly ($p<0.0001$) higher in men than in women (3.14mm vs 2.97mm), a difference consistent with previous research.[11,16] However, smaller differences on the range of 0.1mm have also been reported in Caucasians.[10,23,24]

The difference on LT was statistically significant between sexes ($p<0.0002$) but clinically irrelevant. Previous reports have documented comparable results,[11,16,22] but inconsistencies on the sign of the difference seem to indicate no real difference in this parameter. We obtained an overall LT of 4.56±0.57mm, akin to previously reported LTs.[11,17,22] Our LT was lower than Jivrajka's (4.93mm), but the ACDs were comparable. This finding is surprising considering that a multivariate regression analysis found that LT has the major impact on ACD, followed by AL.[19] Our lenses were thicker than the ones described by Ferreira (4.32mm),[16] but their patients were 6 years younger and their eyes longer —LT increases with age and longer eyes have slightly thinner lenses.[26]

Median AS and PS in our population were 7.62mm, and 15.70mm respectively, and the median ratio PS/AS=2.06. Whilst AS was very similar to the one reported in a recent study in China, our PS was significantly smaller.[21] PS is highly correlated with AL,[26] and makes up a greater proportion of AL in longer eyes.[27] The use of PS becomes relevant when different refractive indices are used for IOL power calculation, since sum-of-segments AL may provide better IOL predictions, at least in some cases, than traditional measures of AL.[28]

W2W is used by some modern calculation formulas, such as Barrett Universal Formula, K6 or VRF-G, and may play a role in post-operative corneal astigmatism.[29] Average W2W in this sample was 11.98±0.53mm, being larger in men than in women (0.19mm, $p<0.0001$). This difference has shown high variability among studies, from 0.05mm in Portugal, to 0.24mm in China, yet W2W was always smaller in women.[16,19] A study on *ex-vivo* eyes revealed some correlation between corneal and lens diameters, a quite unknown variable as of today.[30] These relationships among anatomical descriptors may provide invaluable insights into the dimensions of the anterior segment, some of them barely described, theoretically allowing to make improved IOL platform choices, especially in multifocal or toric IOLs.

Both flat and steep meridian of the anterior corneal surface (K1, K2) were about 0.75D more powerful in women —accompanied by steeper corneal radii, with 0.13 and 0.12mm difference in RfF and RsF, respectively— while the anterior astigmatism magnitude (K2-K1) presented no significant difference between sexes ($p=0.4933$).

Regarding the axis, while the distribution for male patients presented a main lobe oriented horizontally —covering approximately 0º±15º and corresponding with against the rule (ATR) astigmatism—, the distribution for female patients was more uniform, with similar values for ATR and with the rule astigmatism (WTR, 90º±15º) and lower values for oblique astigmatism (**Figure 2**). Both the 0º and 45º Jackson cross-cylinder of the front surface (J0F, J45F) were significantly different ($p<0.0001$) between sexes.

Women presented significantly steeper posterior radii as well (0.10 and 0.14mm difference in the steep and flat radii respectively). The 45º Jackson cross-cylinder of the back surface (J45B) was not significantly different between groups ($p>0.05$) whereas the disparity in J0B was significant ($p<0.001$).

Preoperative alpha and kappa angles may have potential in predicting adverse photic phenomena subsequent to the implantation of multifocal IOLs.[31] A preoperative kappa >0.4mm has been associated with postoperative halos and glare following trifocal diffractive IOL implantation.[32] The magnitude of angle kappa and alpha angles were 0.35±0.22mm and 0.51±0.22mm respectively, very similar to the results of previous studies (0.34±0.17mm and 0.49±0.17mm).[11] In the present study, 42.1% of patients presented an angle kappa >0.4mm in at least one eye, and may not be ideal candidates for multifocal IOL implantation, but further studies are required to evaluate the real clinical impact of these variables.

Female patients required higher IOL power to achieve emmetropia (0.83D, p>0.0001), calculated using Hoffer QST formula.[33] The median IOL for female patients was +22.00D, 1D higher than IOL power in male patients. Furthermore, 5 and 95 percentiles were 14.00D and 26.50D (vs 14.50D and 24.00D in male), indicating that extremely long and extremely short eyes were more commonly found in female patients. However, while the probability to require an IOL power<14.50D (corresponding with the overall 5$^{th}$ percentile) was not different across sex, the probability to require an IOL>26D (95$^{th}$ overall percentile) was lower for male patients (p<0.0001) with odds ratio 0.44.

The cross-sectional nature of this study, which precludes the assessment of changes that may occur over time, is one of its limitations. Moreover, the single-center design prevents generalization to the entire population, and the findings may exclusively apply to this particular region.

Normally, both eyes are measured in our clinical setting even if only one has cataract. Unfortunately, with this volume of data, verifying if both eyes did have cataract at the acquisition time was not possible. In any case, unilateral cataract is rare.

Posterior corneal surface data, obtained from Pentacam, was only available for candidates undergoing arcuate incisions, or being implanted with special IOLs (toric, EDOF, multifocal). However, most of the formulas do not consider the posterior surface, and obtaining a Pentacam for every patient may be deemed, at present, a nonessential intervention. Furthermore, since patients in those subgroups present different levels of pre-operative corneal astigmatism, the results presented for the posterior corneal surface are likely unbiased.

This study is presumably the biggest in Europe analyzing ocular biometry. A single, state-of-the-art optical biometer was used. Large sample size studies provide smaller margin of error, higher power, and controlled risk of reporting false negative or false positive findings. Most of the variables showed significant differences between sexes, but the lack of significance in front astigmatism magnitude is also relevant. As of today, some formulas based on artificial intelligence, such as Kane or Hill RBF3, contemplate the sex of the patient, and, in fact, some studies have proven that Kane formula might be one of the most accurate.[34,35] Exploring if the refractive residuals may improve when including sex may be of interest, since artificial intelligence may find currently unknown patterns in data. We presented the (overall and per sex) hypothetical distribution of IOL powers, which may be practical for manufacturers, or in hospital stock planning. Adding certainty to the IOL power distribution represents a step forward in reducing the labelling step from 0.50D to 0.25D —e.g., within the 3 diopters interquartile range— by manufacturers or ANSI Z80.7 subcommittee in the near future. In the scenario of increasingly precise formulas, the contribution of IOL tolerance and mislabeling to the final refractive error is increasingly big. Considering that the tolerance for IOL within the range 15–25D is 0.40D, with overlapping intervals, manufacturers may as well label the manufactured lenses in 0.25D steps; that would contribute to the minimization of post-surgical error and to closer-to-emmetropia results, giving the surgeon higher control.

This study provided reference values for the ocular biometric parameters obtained by means of an IOL Master 700 for adult cataract patients in Spain. Overall, the results of this study may help identify potential biometric refinements in calculation of IOL power and also identify those eyes with an increased risk of post-surgical refractive surprise due to extreme parameters.

## ACKNOWLEDGEMENTS

Daniel BORDONABA BOSQUE, statistician at Instituto Aragonés de Ciencias de la Salud (IACS), that helped us with the statistical analysis.

UFR-ARCCA Group Zaragoza, from Hospital Universitario Miguel Servet helped with data contribution. (José Manuel LARROSA POVÉS, Galadriel GIMENEZ CALVO, Rubén HERNÁNDEZ VIÁN, Álvaro FANLO ZARAZAGA, Sara MARQUINA MARTÍN)

## What Was Known

- Experts agree that intraocular lens formula's precision is reaching its limit.
- Ocular biometric parameters vary with age, sex and ethnicity. Population-based studies analysing the magnitude of these differences are instrumental in refining normative databases and in future modelling of the cataractous eye.
- Large sample size studies, such as the one presented here, provide smaller margin of error and higher statistical power.

## What This Paper Adds

- Not only traditional but calculated variables —including intraocular lens power— were analysed.
- Our findings support the idea that including sex in IOL formulas should be explored, since artificial intelligence may find currently unknown patterns in data.
- Adding certainty to the IOL power distribution represents a step forward in reducing the IOL labelling step from 0.50D to 0.25D —e.g. within the interquartile range— by manufacturers or ANSI Z80.7 subcommittee in the near future.

## FINANCIAL DISCLOSURE

- **Funding/Support**

There was no specific financial support for this study.

- **Financial Disclosures**

The authors declare no conflicts of interest. The contributors listed under acknowledgements have no conflicts of interest to disclose either.

## DATA AVAILABILITY

Data and codes may be accessible upon reasonable request to the corresponding author.

## REFERENCES


1. *Marques AP, Ramke J, Cairns J, et al. The economics of vision impairment and its leading causes: A systematic review. eClinicalMedicine. 2022;46:101354. doi:10.1016/j.eclinm.2022.101354*
2. *Lamoureux EL, Fenwick E, Pesudovs K, Tan D. The impact of cataract surgery on quality of life. Curr Opin Ophthalmol. 2011;22(1):19-27. doi:10.1097/ICU.0b013e3283414284*
3. *Norrby S. Sources of error in intraocular lens power calculation. J Cataract Refract Surg. 2008;34(3):368-376. doi:10.1016/j.jcrs.2007.10.031*
4. *Kurian M, Negalur N, Das S, et al. Biometry with a new swept-source optical coherence tomography biometer: Repeatability and agreement with an optical low-coherence reflectometry device. J Cataract Refract Surg. 2016;42(4):577-581. doi:10.1016/j.jcrs.2016.01.038*
5. *Lundström M, Barry P, Henry Y, Rosen P, Stenevi U. Visual outcome of cataract surgery; Study from the European Registry of Quality Outcomes for Cataract and Refractive Surgery. J Cataract Refract Surg. 2013;39(5):673-679. doi:10.1016/j.jcrs.2012.11.026*
6. *Donaldson K, Fernández-Vega-Cueto L, Davidson R, et al. Perioperative assessment for refractive cataract surgery. J Cataract Refract Surg. 2018;44(5):642-653. doi:10.1016/j.jcrs.2018.02.022*
7. *Lundström M, Dickman M, Henry Y, et al. Changing practice patterns in European cataract surgery as reflected in the European Registry of Quality Outcomes for*

*Cataract and Refractive Surgery 2008 to 2017. J Cataract Refract Surg. 2021;47(3):373-378. doi:10.1097/j.jcrs.0000000000000457*

8. *Caglar C, Batur M, Eser E, Demir H, Yaşar T. The Stabilization Time of Ocular Measurements after Cataract Surgery. Semin Ophthalmol. 2017;32(4):412-417. doi:10.3109/08820538.2015.1115089*

9. *Yoon JJ, Misra SL, McGhee CN, Patel D V. Demographics and ocular biometric characteristics of patients undergoing cataract surgery in Auckland, New Zealand. Clin Experiment Ophthalmol. 2016;44(2):106-113. doi:10.1111/ceo.12634*

10. *Lee KE. Association of Age, Stature, and Education With Ocular Dimensions in an Older White Population. Arch Ophthalmol. 2009;127(1):88. doi:10.1001/archophthalmol.2008.521*

11. *Wasser LM, Tsessler M, Weill Y, Zadok D, Abulafia A. Ocular Biometric Characteristics Measured by Swept-Source Optical Coherence Tomography in Individuals Undergoing Cataract Surgery. Am J Ophthalmol. 2022;233:38-47. doi:10.1016/j.ajo.2021.06.032*

12. *Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-1042. doi:10.1016/j.ophtha.2016.01.006*

13. *Thibos LN, Wheeler W, Horner D. Power vectors: An application of fourier analysis to the description and statistical analysis of refractive error. Optom Vis Sci. 1997;74(6):367-375. doi:10.1097/00006324-199706000-00019*

14. *Kim HY. Statistical notes for clinical researchers: assessing normal distribution (2) using skewness and kurtosis. Restor Dent Endod. 2013;38(1):52. doi:10.5395/rde.2013.38.1.52*

15. *Schielzeth H, Dingemanse NJ, Nakagawa S, et al. Robustness of linear mixed-effects*

*models to violations of distributional assumptions. Methods Ecol Evol. 2020;11(9):1141-1152. doi:10.1111/2041-210X.13434*

16. *Ferreira TB, Hoffer KJ, Ribeiro F, Ribeiro P, O'Neill JG. Ocular biometric measurements in cataract surgery candidates in Portugal. Vavvas DG, ed. PLoS One. 2017;12(10):e0184837. doi:10.1371/journal.pone.0184837*
17. *Kamiya K, Hayashi K, Tanabe M, et al. Nationwide multicentre comparison of preoperative biometry and predictability of cataract surgery in Japan. Br J Ophthalmol. 2022;106(9):1227-1234. doi:10.1136/bjophthalmol-2021-318825*
18. *Jivrajka R, Shammas MC, Boenzi T, Swearingen M, Shammas JH. Variability of axial length, anterior chamber depth, and lens thickness in the cataractous eye. J Cataract Refract Surg. 2008;34(2):289-294. doi:10.1016/j.jcrs.2007.10.015*
19. *Lei Q, Tu H, Feng X, Ortega-Usobiaga J, Cao D, Wang Y. Distribution of ocular biometric parameters and optimal model of anterior chamber depth regression in 28,709 adult cataract patients in China using swept- source optical biometry. BMC Ophthalmol. 2021;21(1):178. doi:10.1186/s12886-021-01932-4*
20. *Huang Q, Huang Y, Luo Q, Fan W. Ocular biometric characteristics of cataract patients in western China. BMC Ophthalmol. 2018;18(1):99. doi:10.1186/s12886-018-0770-x*
21. *Qi J, He W, Meng J, et al. Distribution of Ocular Anterior and Posterior Segment Lengths Among a Cataract Surgical Population in Shanghai. Front Med. 2021;8. doi:10.3389/fmed.2021.688805*
22. *Arriola-Villalobos P, Burgos-Blasco B, Fernández-Vigo JI, et al. Biometry data and prevalence of corneal astigmatism in caucasian spanish candidates for cataract surgery. J Fr Ophtalmol. 2021;44(1):76-83. doi:10.1016/j.jfo.2020.03.025*
23. *Hoffmann PC, Hütz WW. Analysis of biometry and prevalence data for corneal*

*astigmatism in 23 239 eyes. J Cataract Refract Surg. 2010;36(9):1479-1485. doi:10.1016/j.jcrs.2010.02.025*

24. *Fotedar R, Wang JJ, Burlutsky G, et al. Distribution of Axial Length and Ocular Biometry Measured Using Partial Coherence Laser Interferometry (IOL Master) in an Older White Population. Ophthalmology. 2010;117(3):417-423. doi:10.1016/j.ophtha.2009.07.028*

25. *Lim LS, Saw SM, Jeganathan VSE, et al. Distribution and Determinants of Ocular Biometric Parameters in an Asian Population: The Singapore Malay Eye Study. Investig Opthalmology Vis Sci. 2010;51(1):103. doi:10.1167/iovs.09-3553*

26. *Feng X, Wang Y, Liang J, Xu Y, Ortega-Usobiaga J, Cao D. Analysis of Lens Thickness Distribution Based on Swept-Source Optical Coherence Tomography (SS-OCT). J Ophthalmol. 2021;2021. doi:10.1155/2021/4717996*

27. *Takkar B, Gaur N, Saluja G, et al. Evaluation of the vitreous chamber depth: An assessment of correlation with ocular biometrics. Indian J Ophthalmol. 2019;67(10):1645. doi:10.4103/ijo.IJO_56_19*

28. *Cooke DL, Cooke TL. Approximating sum-of-segments axial length from a traditional optical low-coherence reflectometry measurement. J Cataract Refract Surg. 2019;45(3):351-354. doi:10.1016/j.jcrs.2018.12.026*

29. *Theodoulidou S, Asproudis I, Kalogeropoulos C, Athanasiadis A, Aspiotis M. Corneal Diameter as a Factor Influencing Corneal Astigmatism After Cataract Surgery. Cornea. 2016;35(1):132-136. doi:10.1097/ICO.0000000000000668*

30. *Khng C, Osher RH. Evaluation of the relationship between corneal diameter and lens diameter. J Cataract Refract Surg. 2008;34(3):475-479. doi:10.1016/j.jcrs.2007.10.043*

31. *Prakash G, Prakash DR, Agarwal A, Kumar DA, Agarwal A, Jacob S. Predictive*

*factor and kappa angle analysis for visual satisfactions in patients with multifocal IOL implantation. Eye. 2011;25(9):1187-1193. doi:10.1038/eye.2011.150*

32. *Qi Y, Lin J, Leng L, et al. Role of angle κ in visual quality in patients with a trifocal diffractive intraocular lens. J Cataract Refract Surg. 2018;44(8):949-954. doi:10.1016/j.jcrs.2018.05.026*

33. *Taroni L, Hoffer KJ, Pellegrini M, Lupardi E, Savini G. Comparison of the new Hoffer QST with 4 modern accurate formulas. J Cataract Refract Surg. 2023;49(4):378-384. doi:10.1097/j.jcrs.0000000000001126*

34. *Melles RB, Kane JX, Olsen T, Chang WJ. Update on Intraocular Lens Calculation Formulas. Ophthalmology. 2019;126(9):1334-1335. doi:10.1016/j.ophtha.2019.04.011*

35. *Darcy K, Gunn D, Tavassoli S, Sparrow J, Kane JX. Assessment of the accuracy of new and updated intraocular lens power calculation formulas in 10 930 eyes from the UK National Health Service. J Cataract Refract Surg. 2020;46(1):2-7. doi:10.1016/j.jcrs.2019.08.014*

## FIGURE LEGENDS

**Figure 1.** Violin plots showing the difference between sexes in diverse biometric variables and age at first eye surgery. One random eye per patient was plotted to avoid data distortion (N=20 004). W2W: white to white (mm), AL: axial length (mm), CCT: central corneal thickness (μm), AQD: aqueous depth (mm), ACD: anterior chamber depth (mm), LT: lens thickness (mm), RfF: flat corneal radius front (mm), RsF: steep corneal radius front (mm), KfF: flat corneal keratometry front (D), KsF: steep keratometry front (D), CW Chord: Chang Waring Chord (angle kappa module, mm).

**Figure 2.** Double angle plots showing the difference between sexes in front astigmatism orientation (Steep Keratometry Axis). One random eye per patient was plotted to avoid data distortion (N=20 004). **A.** A peak can be observed at 90º, that accounts for patients with spherical anterior surface. **B.** Eyes with anterior astigmatism >0 only. While male patients' distribution presents a clearly defined lobe in 0º±15º (predominance of against the rule astigmatism), the distribution in females is  more uniform between with the rule and against the rule astigmatism. Oblique astigmatism was less prevalent than with/against the rule in both sexes.

**Figure 3.** Intraocular lens (IOL) power distribution for an arbitrary IOL (A=119.2), calculated with Hoffer QST formula. One random eye per patient was plotted to avoid data distortion (N=20 004). Median, interquartile range(IQR), $5^{th}$ and $95^{th}$-percentiles are shown. **A.** Male distribution **B.** Female distribution **C.** Male vs female distribution **D.** Overall distribution

Figure 1



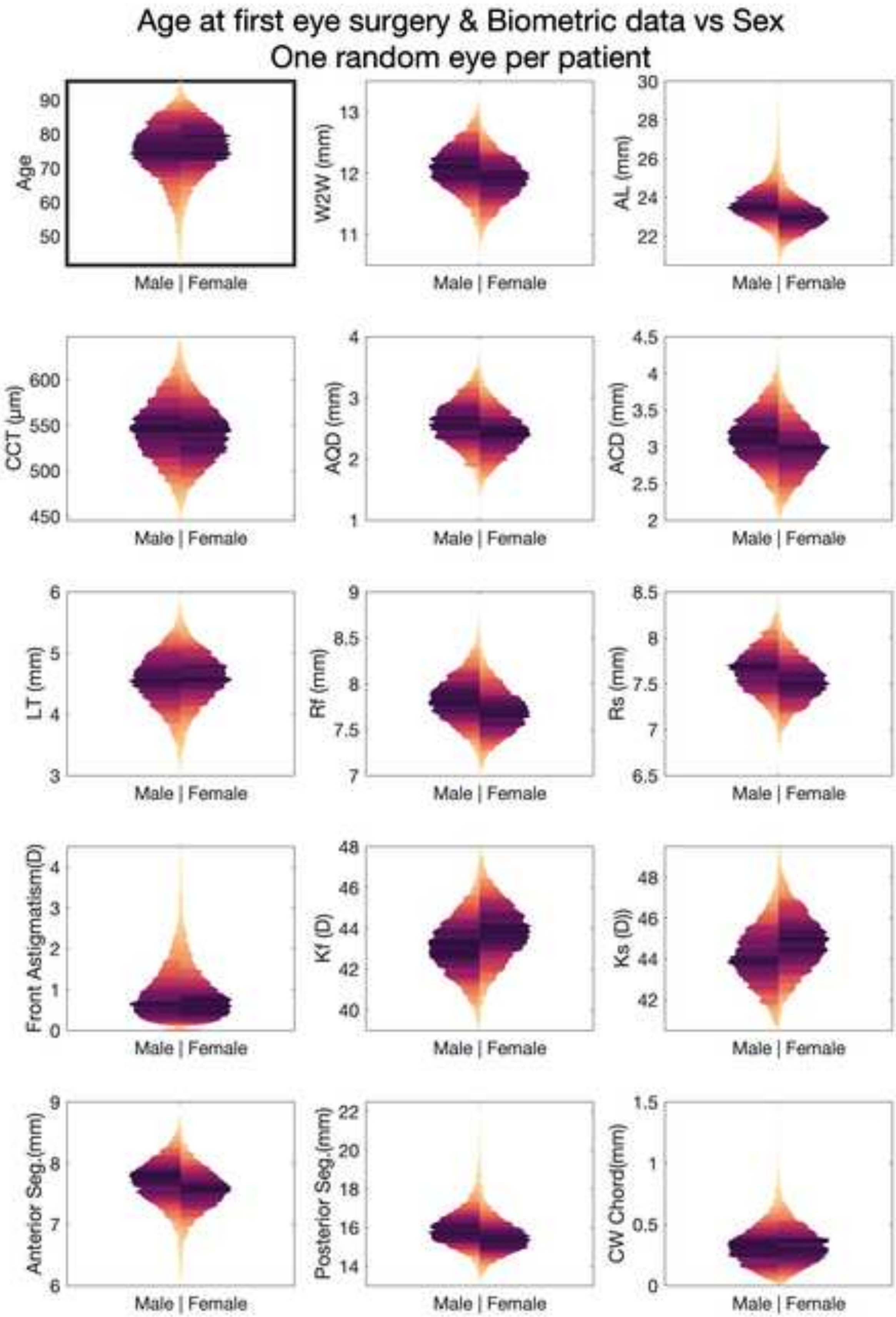
Age at first eye surgery & Biometric data vs Sex
One random eye per patient
Age
W2W (mm)
AL (mm)
CCT (µm)
AQD (mm)
ACD (mm)
LT (mm)
Rf (mm)
Rs (mm)
Front Astigmatism(D)
Kf (D)
Ks (D)
Anterior Seg.(mm)
Posterior Seg.(mm)
CW Chord(mm)
Male | Female

Figure 2

Click here to access/download;Figure;FIGURE 2_DoubleAlphaPlot_RandomEye (1).tif

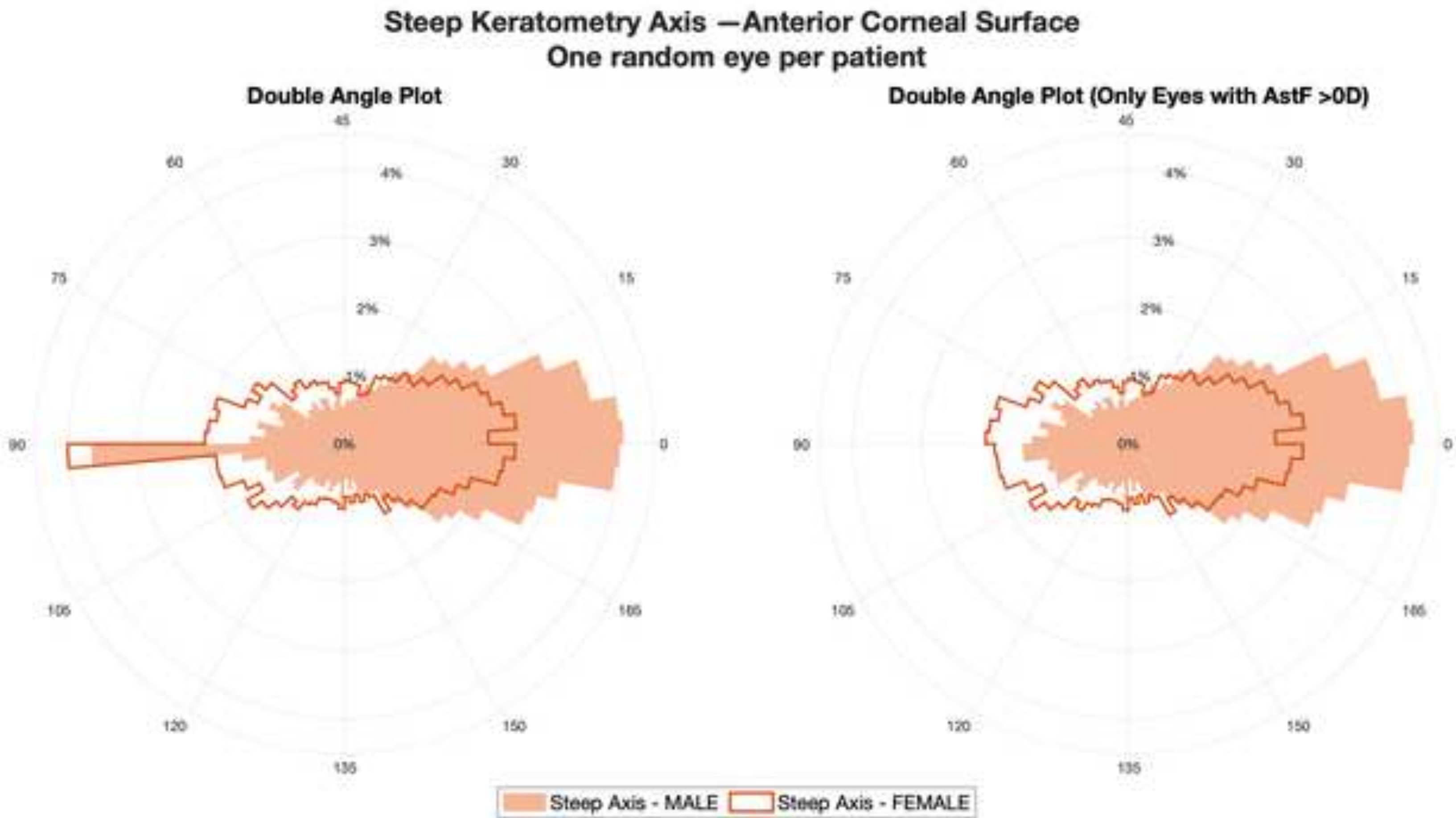

Figure 3

Click here to access/download;Figure;FIGURE 3_IOL_power_RandomEye (1).tif

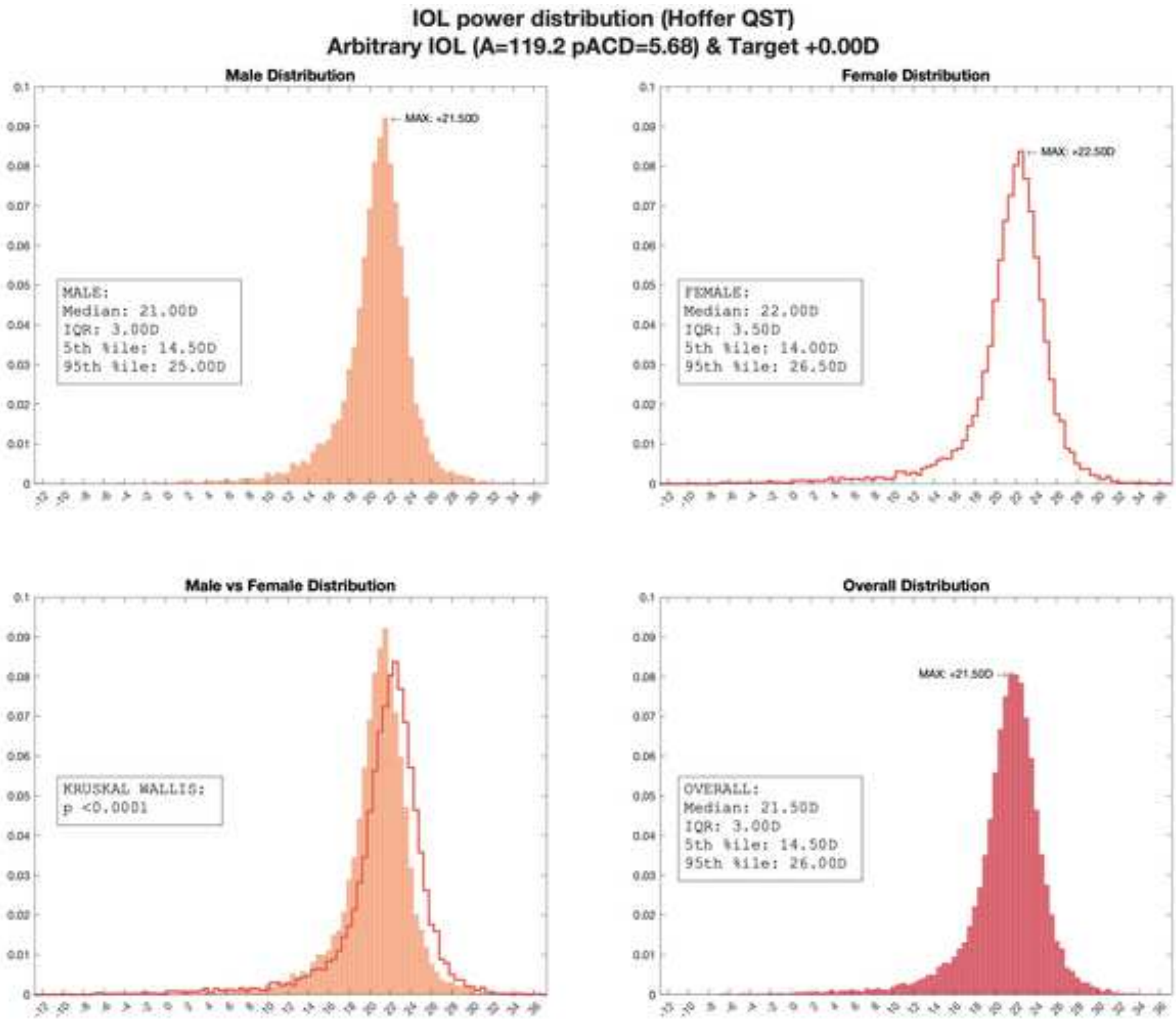

Table 1

Table 1. Ocular biometry overall population

| | N | Mean | Std Dev* | Skewness | Kurtosis | Median | IQR |
|---|---|---|---|---|---|---|---|
| DEVICE: IOL MASTER 700 (N=34589 eyes) | | | | | | | |
| W2W | 34135 | 11,98 | 0,53 | -0,08 | 2,14 | 11,98 | 0,54 |
| AL | 34589 | 23,47 | 1,7 | 1,95 | 8,56 | 23,3 | 1,3 |
| CCT | 34589 | 0,54 | 0,04 | 0,09 | 0,46 | 0,54 | 0,05 |
| AQD | 34589 | 2,49 | 0,51 | 0,03 | -0,02 | 2,49 | 0,53 |
| ACD | 34589 | 3,04 | 0,51 | 0,04 | -0,01 | 3,03 | 0,53 |
| LT | 34589 | 4,56 | 0,57 | -0,32 | 0,3 | 4,58 | 0,6 |
| RfF | 34589 | 7,76 | 0,36 | 0,21 | 0,24 | 7,75 | 0,37 |
| K1F | 34589 | 43,54 | 2,03 | 0,03 | 0,19 | 43,54 | 2,09 |
| RsF | 34589 | 7,58 | 0,35 | 0,03 | 0,25 | 7,58 | 0,36 |
| K2F | 34589 | 44,58 | 2,22 | 0,21 | 0,41 | 44,53 | 2,11 |
| AST. FRONT | 34589 | 1,04 | 0,96 | 1,95 | 6,3 | 0,84 | 0,85 |
| J0F | 34589 | -0,08 | 0,68 | 0,32 | 2,61 | -0,09 | 0,61 |
| J45F | 34589 | -0,004 | 0,26 | 0,25 | 6,44 | -0,001 | 0,35 |
| CW CHORD | 34134 | 0,35 | 0,22 | 1,79 | 8,99 | 0,33 | 0,22 |
| ALPHA | 34133 | 0,51 | 0,22 | 1,96 | 9,63 | 0,48 | 0,19 |
| ANT. SEG. | 34589 | 7,6 | 0,51 | -0,46 | 1,14 | 7,62 | 0,5 |
| POST. SEG. | 34589 | 15,87 | 1,65 | 1,97 | 8,68 | 15,7 | 1,3 |
| DEVICE: PENTACAM (N=1960 eyes) | | | | | | | |
| RfB | 1948 | 6,49 | 0,43 | 0,85 | 5,09 | 6,47 | 0,41 |
| K1B | 1948 | -6,17 | 0,4 | 0,06 | 2,26 | -6,2 | 0,4 |
| RsB | 1948 | 6,11 | 0,39 | -0,02 | 2,17 | 6,13 | 0,38 |
| K2B | 1948 | -6,55 | 0,42 | -0,6 | 2,25 | -6,5 | 0,5 |
| AST. BACK | 1948 | -0,37 | 0,33 | -1,45 | 3,71 | -0,3 | 0,3 |
| J0B | 1948 | -0,11 | 0,2 | -0,11 | 1,51 | -0,1 | 0,18 |
| J45B | 1948 | -0,003 | 0,09 | -0,62 | 6,45 | 0 | 0,12 |

*W2W: white to white (mm), AL: axial length (mm), CCT: central corneal thickness (mm), ACD: anterior chamber depth (mm), RfF: flat corneal radius front (mm), RsF: steep corneal radius front (mm), K1F: flat corneal keratometry front, K2F: steep keratometry front, IQR: inter quartile range*

**Standard deviation corrected for intra-subject correlation*

Table 2. Gender difference estimates in biometric parameters. ΔFemale estimate (including its sign) is to be added to the estimate for male in order to calculate female group values.

| | Gender | Estimate | Std Error | p-value | Lower 95% | Upper 95% |
|---|---|---|---|---|---|---|
| **DEVICE: IOL MASTER 700 (N=34589 eyes)** | | | | | | |
| **W2W** | Male | 12,087165 | 0,004312 | <.0001* | 12,078714 | 12,095616 |
| | ΔFemale | -0,192241 | 0,005666 | <.0001* | -0,203347 | -0,181134 |
| **AL** | Male | 23,783898 | 0,01381 | <.0001* | 23,756829 | 23,810966 |
| | ΔFemale | -0,533643 | 0,018148 | <.0001* | -0,569214 | -0,498072 |
| **CCT** | Male | 545,99563 | 0,388204 | <.0001* | 545,23472 | 546,75654 |
| | ΔFemale | -4,70853 | 0,510088 | <.0001* | -5,708343 | -3,708716 |
| **AQD** | Male | 2,5899906 | 0,004165 | <.0001* | 2,5818272 | 2,5981541 |
| | ΔFemale | -0,161998 | 0,005473 | <.0001* | -0,172726 | -0,151271 |
| **ACD** | Male | 3,1359684 | 0,004159 | <.0001* | 3,1278155 | 3,1441213 |
| | ΔFemale | -0,166728 | 0,005466 | <.0001* | -0,177441 | -0,156014 |
| **LT** | Male | 4,5485255 | 0,004741 | <.0001* | 4,5392331 | 4,5578179 |
| | ΔFemale | 0,0231093 | 0,006227 | 0.0002* | 0,0109043 | 0,0353144 |
| **RfF** | Male | 7,838002 | 0,002925 | <.0001* | 7,8322693 | 7,8437346 |
| | ΔFemale | -0,132621 | 0,003843 | <.0001* | -0,140155 | -0,125088 |
| **K1F** | Male | 43,111767 | 0,016352 | <.0001* | 43,079717 | 43,143818 |
| | ΔFemale | 0,7421335 | 0,021488 | <.0001* | 0,700015 | 0,784252 |
| **RsF** | Male | 7,6529753 | 0,002847 | <.0001* | 7,647395 | 7,6585557 |
| | ΔFemale | -0,124841 | 0,003741 | <.0001* | -0,132175 | -0,117508 |
| **K2F** | Male | 44,154702 | 0,016787 | <.0001* | 44,121798 | 44,187605 |
| | ΔFemale | 0,7320031 | 0,02206 | <.0001* | 0,6887646 | 0,7752416 |
| **ASTIG. FRONT** | Male | 1,0420058 | 0,007929 | <.0001* | 1,0264639 | 1,0575477 |
| | ΔFemale | -0,007132 | 0,01041 | 0,4933 | -0,027536 | 0,0132716 |
| **J0F** | Male | -0,188466 | 0,005556 | <.0001* | -0,199355 | -0,177577 |
| | ΔFemale | 0,1727531 | 0,007296 | <.0001* | 0,1584514 | 0,1870548 |
| **J45F** | Male | -0,009298 | 0,002177 | <.0001* | -0,013564 | -0,005032 |
| | ΔFemale | 0,0095245 | 0,002844 | 0.0008* | 0,0039509 | 0,0150981 |
| **CW CHORD** | Male | 0,3428103 | 0,001824 | <.0001* | 0,3392349 | 0,3463857 |
| | ΔFemale | 0,0098749 | 0,002395 | <.0001* | 0,0051807 | 0,0145691 |
| **ALPHA ANGLE** | Male | 0,491484 | 0,001801 | <.0001* | 0,487918 | 0,4949788 |
| | ΔFemale | 0,0303035 | 0,002364 | <.0001* | 0,0256695 | 0,0349374 |
| **ANT. SEG** | Male | 7,6846469 | 0,004155 | <.0001* | 7,6765025 | 7,6927914 |
| | ΔFemale | -0,143914 | 0,005458 | <.0001* | -0,154612 | -0,133216 |
| **POST. SEG** | Male | 16,099288 | 0,013518 | <.0001* | 16,072792 | 16,125785 |
| | ΔFemale | -0,389857 | 0,017763 | <.0001* | -0,424674 | -0,355039 |
| **IOL (TARGET 0)** | Male | 20.600.733 | 0,041205 | <,0001* | 20.519.967 | 20.681.498 |
| | ΔFemale | 0,8355862 | 0,054146 | <,0001* | 0,7294552 | 0,9417172 |
| **DEVICE: PENTACAM (N=1960 eyes)** | | | | | | |
| **RfB** | Male | 6,5458952 | 0,014916 | <.0001* | 6,5166278 | 6,5751625 |
| | ΔFemale | -0,098861 | 0,019375 | <.0001* | -0,136877 | -0,060845 |
| **K1B** | Male | -6,124321 | 0,013926 | <.0001* | -6,151645 | -6,096998 |
| | ΔFemale | -0,094898 | 0,018088 | <.0001* | -0,130388 | -0,059407 |
| **RsB** | Male | 6,1938925 | 0,013303 | <.0001* | 6,1677919 | 6,2199931 |
| | ΔFemale | -0,138329 | 0,017278 | <.0001* | -0,17223 | -0,104427 |
| **K2B** | Male | -6,475388 | 0,014528 | <.0001* | -6,503892 | -6,446884 |
| | ΔFemale | -0,144651 | 0,018869 | <.0001* | -0,181674 | -0,107629 |
| **ASTIG. BACK** | Male | -0,349662 | 0,011238 | <.0001* | -0,371713 | -0,327611 |
| | ΔFemale | -0,048824 | 0,014594 | 0.0008* | -0,077459 | -0,02019 |
| **J0B** | Male | -0,083297 | 0,006846 | <.0001* | -0,096728 | -0,069865 |
| | ΔFemale | -0,043585 | 0,00889 | <.0001* | -0,061027 | -0,026143 |
| **J45B** | Male | -0,002115 | 0,003186 | 0,5069 | -0,008368 | 0,0041377 |
| | ΔFemale | -0,000238 | 0,004134 | 0,9541 | -0,008352 | 0,0078758 |

*W2W: white to white (mm), AL: axial length (mm), CCT: central corneal thickness (µm), AQD: aqueous depth (mm), ACD: anterior chamber depth (mm), RfF/B: flat corneal radius front/back (mm), RsF/B: steep corneal radius front/back (mm), K1F/B: flat corneal keratometry front/back, K2F/B: steep keratometry front/back*