EVALUATION OF THE ACCURACY OF INTRAOCULAR LENS FORMULAE IN THE DIFFERENT ETHNIC GROUPS IN SINGAPORE

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Thesis Summary

The formation of cataract is a natural aging process of the crystalline lens where it is replaced by an artificial intraocular lens (IOL) during the cataract operation. New IOL formulae have been developed over the years with the purpose of meeting the patient's expectation of a clear vision with minimal residual refractive error after the cataract operation.

This retrospective database study sets out to evaluate the accuracy of the various IOL formulae in the different ethnic groups in Singapore, involving the Chinese, Malay and Indian ethnic groups over a period of 2 years with axial lengths of 22.00 to 25.99 mm (medium axial lengths).

Different generation of IOL formulae were compared in this study with the 3rd generation IOL formulae comprising of SRK/T, Hoffer Q and Holladay 1. The 4th generation IOL formula comprised of Haigis and the 5th generation formulae comprised of both Barrett Universal II and Emmetropia Verifying Optical (EVO).

In this study, the participants were divided into 2 groups, namely Chinese group and Non-Chinese group (Malay and Indian ethnic groups). It was found that SRK/T has the smallest mean absolute error (MAE) when compared to other IOL formulae, followed by Barrett Universal II and EVO in the Chinese group. In the Non-Chinese group, it was found that Barrett Universal II has the lowest MAE, followed by EVO and SRK/T. However, SRK/T, Barrett Universal II and EVO could be used interchangeably when generating the IOL powers in both the Chinese and Non-Chinese groups.

In conclusion, this study showed that SRK/T, Barrett Universal II and EVO could be used interchangeably to generate IOL powers for medium axial lengths in the different ethnic groups in Singapore. Despite the emergence of newer generation IOL formulae, SRK/T formula is proven to be just as accurate as its newer counterparts.

Keywords: IOL formulae, axial length, cataract operation, post-operative subjective refraction, Chinese ethnic group, Malay ethnic group, Indian ethnic group

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LIST OF ABBREVIATIONS

AAO	American Academy of Ophthalmology
ACD	Anterior Chamber Depth
AI	Artificial Intelligence
AL	Axial Length
AME	Arithmetic Mean Error
BU II	Barrett Universal II
ELP	Estimated Lens Plane
EVO	Emmetropia Verifying Optical
IOL	Intraocular Lens
K	Keratometry / Corneal Curvature / Corneal Power
MAE	Mean Absolute Error
ME	Mean Error
MedAE	Median Absolute Error
MPE	Mean Prediction Error
PCI	Partial Coherence Laser Interferometer
RBF	Radial Basis Function
RCOphth	Royal College of Ophthalmologists
RMSAE	Root Mean Square Absolute Error
SD	Standard Deviation
SF	Surgeon Factor
SRK	Sanders-Retzlaff-Kraff
SRK/T	Sanders-Retzlaff-Kraff/Theoretical
VCD	Vitreous Chamber Depth
WHO	World Health Organisation
WTW	White-To-White

CHAPTER 1 LITERATURE REVIEW

Cataract surgery is the most common ophthalmic surgery performed worldwide (Kaswin et al., 2014, as cited in Karabela et al., 2016) (Ozcura et al., 2015). Intraocular lens (IOL) power selection is a critical factor that affects the visual outcome in all eyes undergoing cataract operation. However, the IOL power is derived from the formula that is developed to achieve a precise IOL power and the predicted residual refractive error. The surgeon will then choose the most appropriate formulae among the various biometric formulae that can achieve a post-operative refractive error, which in most cases, closest to emmetropia.

The World Health Organisation (WHO) defines a cataract as any opacity in the crystalline lens. Cataract development is a natural ageing process of the transparent crystalline lens, where it becomes opaque with age. Cataract can also happen due to other causes known as secondary cataract such as traumatic or related to systemic medication. Cataract extraction is necessary when a person’s vision is affected to the point that they are unable to perform their daily tasks. Modern cataract surgery includes installation of a replacement lens, known as an intraocular lens, to counter the refractive power of the crystalline lens.

The refractive power of the human eye relies on the power of the cornea, lens, axial length (AL) of the eye and the axial position of the lens (Shrivastava et al., 2018). Cornea power accounts for about two-thirds of the total dioptric power of the eye and the crystalline lens accounts for the remaining one-third. The crystalline lens accounts approximately 20D of the eye’s refractive status, so an intraocular implant (IOL) with dioptric power is necessary to replace dioptric power of the crystalline lens. It is expected that the IOL will be placed exactly where the crystalline lens is positioned. The lens capsule is not removed during cataract extraction, and this becomes the cradle to hold the IOL. Hence, in order to calculate the dioptric power of the IOL, various IOL formulae have been formulated in an attempt. In a nutshell, the dioptric power of the IOL is calculated with the anterior corneal curvature measurements and the axial length of the eyeball.

Intraocular lens (IOL) power calculation is an important factor that affects the visual outcome in eyes undergoing cataract surgery. The power of the intraocular lens (IOL) is derived from the biometric formula that is developed to achieve a precise IOL power and the predicted residual refractive error. The surgeon will then choose the most appropriate formulae from the biometric formulae that can achieve a post-operative refractive error closest to emmetropia. There are various IOL formulae that have been developed in an attempt to achieve the best visual outcome. With the advancement of technology and improvement in surgical techniques, coupled with increasing patients’ demands of clear vision postoperatively, newer generations of biometric formulae have been developed to achieve optimum visual outcomes for the patients (Kaswin et al., 2014, as cited in Karabela et al., 2016) (Ozcura et al., 2015) (Davis, 2016) (Zhang et al., 2020).

1.1 IOL FORMULAE

1.1.1 1st Generation IOL formula

The history of IOL power calculation started in 1949 when Harold Ridley implanted the first IOL in a blind eye but ended with a postoperative refraction error of -20D (Olsen, 2007).

Since then, researchers attempted to develop IOL formulae with hopes to improve postoperative outcome. The theoretical formula was first described by Fedorov et al. (1967) with the notion of determining the vergence power of a lens at the pupillary space that will bring rays to a focus on the retina.

The formula was based on the following 3 clinically measurable quantities, namely, measurements of the axial length of the eye, the refracting power of the cornea and an estimate of anterior chamber depth (ACD) with the implant in place. All theoretical formulas are based on the same fundamental equation (Olsen, 2007):

$$P = nlACD - AL - n^*Kln - K^*AL$$

P = IOL power for emmetropia, n = refractive indices of aqueous and vitreous, ACD = estimated postoperative anterior chamber depth, AL = axial length and K = corneal curvature

Since then, other ophthalmologists (i.e. Blinkhorst, Holladay, Hoffer, and Shammas) have refined the existing theoretical formulas.

The 1st generation IOL formula was of regression-based which relied on a single, fixed constant for ACD based on the IOL. One of the 1st generation IOL formulae was the Sanders-Retzlaff-Kraff (SRK) formula. The Sanders-Retzlaff-Kraff (SRK) formula used the regression approach to generate the IOL powers. The SRK formula used a simple linear regression equation (Olsen, 2007):

$$P_o = A - 0.9 * K - 2.5 * Ax$$

where P_o = power of implant for emmetropia, K = dioptric keratometry reading (using index 1.3375), Ax = axial length of the eye as measured by ultrasound and A = the A-constant according to the type of IOL and the mean values of the K-readings and axial length readings

The SRK formula used a fixed A-constant of the individual IOL, together with corneal power and axial length to estimate the power of the IOL implant that was needed to replace the cataract.

The regression formula generates a mean value and incorporates a correction (through regression coefficients) to deviations from means values. However, there were some drawbacks. The SRK formula did not include anterior chamber depth (ACD) and was less accurate in eyes with extreme axial lengths (ALs). It only worked works for the dataset from which it is derived and it is sensitive to the surgical as well as the measurement techniques (Olsen, 2007).

Thus, it was suggested that the SRK formula to be personalized and that the A-constant in a representative number of cases is back-solved in order to make it accurate in order to overcome problems regarding measurement differences and surgical techniques (Olsen, 2007).

1.1.2 2nd Generation IOL formula

With the advancement of medical technology, the position of IOL implant has changed from the anterior chamber to the posterior chamber of the eye. The 1st generation theoretical formula had assumed that the position of the IOL, resulting in the usage of a fixed A-constant in their formulae. However, when the position of the IOL has changed to the posterior chamber, the usage of a fixed A-constant was deemed as not suitable anymore. As such, the 2nd generation formulae such as SRK II formula was designed by combining linear regression analysis with stepwise adjustments for long and short eyes. The SRK II formula had changes to the ACD constant as a function of axial length (AL) as the fixed-ACD model predicted ACDs that were too short in long eyes and too deep in short eyes. This resulted in a myopic error in a short eye and a hyperopic error in the long eye (Olsen, 2007) (Xia et al., 2020). The new SRK II formula was more accurate after the modifications of A-constants as compared to the original SRK formula (Dang and Raj, 1989) (Tsang et al., 2003). However, many ophthalmologists were not comfortable with this formula based on an artificial linear model (Tsang et al., 2003) and this led to the development of the 3rd generation IOL formulae.

1.1.3 3rd Generation IOL formula

The third generation theoretical formulae were different from the previous generations. They were based on thin lens optical principles (Hoffer,1993).

The third generation IOL formulae require the axial length (AL) and corneal curvature (K) to predict the estimated lens plane (ELP) without the ACD measurement. Instead, various methods such as Fyodorov's corneal height method were developed by using a-constant to predict the ACD measurements (Hoffer, 1993) (Bang et al.,2011).

In order to estimate the position where the IOL is placed postoperatively, ELP has been formulated to replace A-constant as one of the drawbacks of A-constant was that A-constant is greatly affected by the manufacturer as well as the surgeon's personal surgical technique. The ELP is defined as the estimated postoperative distance between the anterior corneal surface and the principal plane of a thin IOL (as if the lens was of infinite thickness). A principle determinant of IOL power estimation error is the inaccurate prediction of the ELP (Olsen, 2007) (Chen et al., 2015) (Amro et al., 2018). However, ELP is difficult to predict because an IOL is thinner than crystalline lens or cataract and thus, the ACD after cataract surgery for a pseudophakic eye would be longer than a phakic eye. Despite A-constant was not computed into the formula directly, A-constant was used when calculating the Fyodorov's corneal height to predict postoperative ACD in Holladay 1 and SRK/T formulae whereas the Hoffer Q formula uses an independently developed formula in which the tangent of corneal power is used (Aristodemou et al., 2011).

Some of the 3rd generation IOL formulae included SRK/T, Holladay 1 and Hoffer Q formulae.

SRK/T

SRK/T formula is a customized formula used to calculate ACD based on AL and corneal curvature. It represented a combination of linear regression method with a theoretical eye model (Retzlaff, 1990).

SRK/T formula can be calculated using the same A constants used with the original SRK formula or with ACD estimates. It optimizes the prediction of postoperative ACD, retinal thickness AL correction, and corneal refractive index.

A constant is adjustable and depends on multiple variables including IOL manufacturer, style and placement within the eye. Different model of IOL has different A-constant.

SRK/T formula uses the A-constant to produce an offset factor, or value, to add to the corneal height of Fyodorov to produce an ACD (Hoffer,1993).

The SRK/T formula is not a regression formula but rather, a modified Binkhorst formula with modified ACD-prediction algorithms (Olsen, 2007).

Holladay 1

Holladay 1 was developed by Jack Holladay in 1988. He combined a personalized ACD factor with the Fyodorov method of using axial length and K-reading to predict the corneal height, the thickness of the cornea (0.56mm), and the distance from the iris plane to the IOL optic plane which is also known as the surgeon factor (SF). As the SF could not be known before surgery, it was necessary to calculate it from a series of postoperative eyes of one IOL style using Holladay's formula and the average for that lens style (Hoffer, 1993).

Hoffer Q

Hoffer Q was developed by Dr Kenneth Hoffer in 1993. Hoffer Q was developed to predict the pseudophakic ACD for theoretic IOL power formulae. He attempted to predict the pseudophakic ACD by personalizing the ACD. The Hoffer Q formula used the personalized ACD for any lens style, axial length and corneal curvature to calculate the IOL dioptric power without using Fyodorov's corneal height formula (Hoffer, 1993).

1.1.4 4th Generation IOL formula

Fourth generation theoretical formulae have been developed and they included Haigis and Holladay 2. Fourth generation formulae took into the consideration of the preoperative ACD for better prediction of the ELP, and any change in ACD measurement after posterior IOL implantation can influence IOL power calculation (Moschos et al., 2014) (Chen et al., 2015) (Amro et al., 2018).

Some of the 4th Generation IOL formulae included Haigis and Holladay 2 formulae.

Haigis Formula

The Haigis formula assumes the postoperative position of the theoretical thin lens as a function of 3 constants that are tied to the preoperative measurements of AL and anterior chamber depth (ACD). Haigis formula does not use A-constant to predict the effective lens position (ELP). Instead, it used the measured anterior chamber depth (ACD) as a predictor of the ELP (Ladas et al., 2021).

$$D = A_o + (A_1 \times ACD) + (A_2 \times AL)$$

D = Effective lens position

ACD = Measured anterior chamber depth of the eye (corneal vertex to the anterior lens capsule)

AL = axial length of the eye (the distance from the cornea vertex to the vitreoretinal interface)

A_o = moves the power prediction curve up/down

A_1 = measured anterior chamber depth

A_2 = measured axial length

1.1.5 5th Generation IOL formula

The fifth generation formulae or the latest generation formulae include Barrett Universal II and Olsen where incorporation of the principle plane or ray tracings techniques are used to derive the IOL power (Gokce et al., 2017) (Xia et al., 2020).

Barrett Universal II

The Barrett Universal II formula is based on a combination of a theoretical and regression model; the theoretical model is conceived as the intersection of two spheres, a corneal sphere and a global sphere at whose junction the iris root is located. The point of intersection is determined by the axial length, the peripheral radius of curvature of the posterior cornea, and the radius of the globe. The regression model predicts the distance from the iris root to the second principal plane of the lens denoted by an individualized lens constant known as the lens factor (Khatib et al., 2021).

The Barrett Universal II formula is based on paraxial ray tracing (Gaussian/thick lens), considers the effective lens position to be a result of the ACD and a lens factor associated with the physical position and locations of the principal planes of the IOL. It also takes into account the change in the principle planes encountered with different powered IOLs. It has the option to use up to 5 variables consisting of AL, K, ACD, lens thickness, and white-to-white (WTW) (Reitblat et al., 2017) (Rong et al., 2019).

Emmetropia Verifying Optical

The Emmetropia Verifying Optical (EVO) formula (unpublished) developed by Dr Tun Kuan Yeo, is based on the theory of emmetropization of the eye. This formula generates an “emmetropia factor” for each eye and takes into account of the optical dimensions of the eye for different IOL geometry and powers (Khatib et al., 2021).

New IOL formulae have been developed after 5th generation IOL formulae with newer calculation methods such as the use of ray tracing, artificial intelligence etc.

1.1.6 Ray Tracing

Olsen

The Olsen formula was developed by Thomas Olsen in 2006. The aim was to develop a thick-lens formula based on paraxial ray tracing. The Olsen formula uses both exact and paraxial ray tracings of optical light through the refractive media in the eye, including the specifics optics of a particular IOL, to derive the postoperative position of that lens. The Olsen formula precisely estimates the physical position of the IOL using a newly developed concept, the C-constant (a ratio by which the empty capsular bag will encapsulate and fixate an IOL following in the-bag implantation). This unique approach considers the IOL position as a function of preoperative ACD and LT; therefore, traditional factors such as AL, K, WTW, IOL power, age, and gender are unnecessary (Xia et al., 2020) (Stopyra et al., 2023) (Olsen, 2024).

1.1.7 Artificial intelligence

Artificial intelligence (AI), as a term, was coined by McCarthy et al. in 1955. AI refers to techniques for machines that mimic human behaviour; machine learning is a subset of AI whereby machines can improve without explicit programming, and deep learning is a subset of machine learning whereby machines can self-train to perform tasks using extensive data sets fed into multi-layered neural networks (Stopyra et al., 2024). In short, AI is reliant on large database to improve on its accuracy. The Hill-radial basis function (RBF) formula, Kane formula, Hoffer QST formula and Ladas formula are examples of AI (Xia et al., 2020) (Carmona-González and Palomino-Bautista, 2021) (Yoon and Whang, 2023).

Hill-Radial Basis Function (RBF)

The Hill-RBF was introduced in 2016 by Warren E.Hill, MD, and was based on RBF, which is similar to a neural network. The Hill-RBF uses AI and regression analysis of a very large database of actual postsurgical refractive outcomes to predict the IOL power. The Hill-RBF formula is a pure data-driven IOL power calculation method and therefore is free of the restriction and benefit of a lens-position assessment. It uses pattern recognition developed by Matlab and a refined form of data interpolation. As it uses the method of pattern recognition, the algorithm may be able to account for undefined factors in IOL power calculation that cannot be modelled with vergence or ray-tracing equations (Xia et al., 2020) (Stopyra et al., 2024).

Kane

The Kane formula was developed utilizing several large data sets from chosen eye surgeons. It combines features of thin lens formulas, theoretical optics, and ‘big data’ techniques to make its predictions. Cloud-based computing was used to develop the formula. As a hybrid method, it is based on theoretical optics and incorporates both regression and AI components for IOL power prediction. The required parameters are axial length (AL), corneal power (K), anterior chamber depth (ACD), biological sex and an A-constant. Lens thickness (LT) and central corneal thickness (CCT) are optional parameters but can increase the formula accuracy further (Xia et al., 2020) (Stopyra et al., 2024)

Ladas

In 2015, John G. Ladas, Albert Jun, Aazim Siddiqui, and Uday Devgan introduced the idea of an IOL ‘super formula’, which incorporated the qualities of 3rd generation formulas (Holladay 1, Hoffer Q, Holladay 1 with Koch adjustment, SRK/T) and a 4th generation formula (Haigis). They achieved this by developing a novel way of depicting these formulae which were thought of as two-dimensional algebraic equations and rendered them in three dimensions. In this way they provided a framework to analyze these formulas in three dimensions and observe areas of differentiation. Using this observation and peer-reviewed literature, the Ladas formula selects the optimal formula among the various IOL formulae (SRK/T, Hoffer Q, Holladay 1, Holladay with WK adjustment, and Haigis) that are incorporated into it to calculate the IOL power. The Ladas formula has evolved to be a more accurate with the help of complex deep learning techniques and AI (Xia et al., 2020) (Stopyra et al., 2024).

1.2 AXIAL LENGTHS

With the introduction of newer formulae, researchers have started to compare the 4th and 5th generation formulae against 3rd generation formulae with regards to the different axial lengths.

There had been various studies that looked into the relationship between different formulas and axial lengths (AL). Evaluating the accuracy of the newer generation formula is important. Researchers have also compared the older generation IOL formulae especially the 3rd generation IOL formulae such as SRK/T, Hoffer Q, Holladay 1 with the newer generation formulae such as Haigis, Holladay 2 (4th generation) and Barrett Universal II, Kane, EVO 2.0 (5th generation) to determine accuracy as well as the differences between them.

In order to evaluate the accuracy of IOL formulae, researchers have categorized the axial lengths into different axial length groups, namely short, medium and long. As such, some studies classified the short axial length group as axial lengths shorter or equal than 22.00 mm (Gavin et al., 2008) (Aristodemou et al., 2011) (Kane et al., 2016) (Doshi et al., 2017). The medium axial length group comprised of axial lengths between 22.00 mm and 26.00 mm (Aristodemou et al., 2011) (Kane et al., 2016) (Doshi et al., 2017) (Hipólito-Fernandes et al., 2020). The long axial length group comprised of axial lengths 26.00 mm or longer (Aristodemou et al., 2011) (Bang et al, 2011) Chen et al. (2015) (Kane et al., 2016) (Zhang et al., 2016). The 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines suggested that the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm.

1.2.1 Short Axial Length

The short axial length group usually comprised of axial lengths shorter or equal than 22.00 mm.

<u>3rd Generation</u>

Among the 3rd generation formulae, Hoffer Q was found to be the most accurate and reliable among Holladay 1 and SRK/T (Gavin et al., 2008) (Aristodemou et al., 2011).

Gavin et al. (2008) compared the accuracy of the Hoffer Q and SRK-T formulae in 41 eyes below 22.00 mm in axial length, using biometry measured with partial coherence interferometry (PCI), without a customised ACD constant and found that Hoffer Q was significantly more accurate than the SRK-T.

Aristodemou et al. (2011) also found that Hoffer Q formula had performed best for ALs from 20.00 mm to 20.99 mm when compared to Holladay 1 and SRK/T. However, when ALs from 21.00 to 21.49 mm were being analysed, Holladay 1 was found to be as accurate as Hoffer Q as compared to SRK/T. There were no statistically significant difference in mean absolute errors (MAE) for ALs from 21.50 to 21.99 mm (106 eyes) with SRK/T, Hoffer Q and Holladay 1 formulae (Aristodemou et al., 2011). This result was later duplicated by Doshi et al. (2017).

With the development of the 4th generation formulae (e.g. Haigis, Holladay 2) and 5th generation formulae (e.g. Barrett Universal II), researchers had been comparing the accuracy of the 4th generation formulae to the 3rd generation formulae. One would expect that the accuracy of the IOL formulae would increase with newer generations, but there were conflicting findings from the researchers.

3rd Generation vs 4th Generation

In a study conducted by Doshi et al. (2017), they found that the 3rd generation IOL formulae (Hoffer Q, Holladay 1 and SRK/T) were more accurate than the 4th generation IOL formula (Haigis). Doshi et al. (2017) found that Hoffer Q, Holladay 1 and SRK/T formulae were equally accurate in predicting the postoperative refraction after cataract surgery in eyes with AL less than 22.0 mm and accuracy of these three formulae was significantly higher than Haigis formula in 40 eyes.

3rd Generation vs 4th Generation vs 5th Generation

Kane et al. (2016) assessed the accuracy of 7 intraocular lens (IOL) power formulae using 3rd generation IOL formulae (Hoffer Q, Holladay 1, SRK/T), 4th generation IOL formulae (Haigis, Holladay 2) and 5th generation IOL formulae (Barrett Universal II, T2) in 156 eyes with a short axial length. Surprisingly, despite the advancement of the newer IOL formulae, they concluded that there was no statistically significant difference in the absolute error between the 7 IOL power formulas in eyes with a short AL (< 22.0 mm). Due to the lack of a statistically significant result, post hoc analysis was not performed.

In summary, the 3rd generation IOL formula, Hoffer Q, was found to be the most accurate among 3rd and 4th generation IOL formulae in determining the IOL power in short axial length. Hoffer Q can be an alternative even if 5th generation IOL formulae are available as it is as equally accurate as the 5th generation formulae.

1.2.2 Medium Axial Length

The medium axial length group comprised of axial lengths between 22.00 mm and 26.00 mm.

3rd Generation

Among the 3rd generation IOL formulae used in the evaluation of the accuracy in the medium axial length groups, there was a difference among the formulae depending on the axial lengths as well. In a study conducted by Aristodemou et al. (2011), they found that there were no statistically significant differences in MAE for any IOL formula (SRK/T, Hoffer Q and Holladay 1) for ALs from 22.00 to 23.49 mm. However, for ALs from 23.50 to 25.99 mm, Holladay 1 might perform marginally better, although the 3 formulae (SRK/T, Hoffer Q and Holladay 1) gave comparable refractive outcomes. In short, for ALs from 22.00 to 25.99 mm, SRK/T, Hoffer Q and Holladay 1 could be used interchangeably to determine the IOL power (Aristodemou et al., 2011).

3rd Generation vs 4th Generation

With the development of 4th generation IOL formulae, Doshi et al. (2017) found that the accuracy of the 4th generation IOL formula, Haigis, did not differ much from its 3rd generation IOL formulae counterparts such as Hoffer Q, Holladay 1, SRK/T. They found that Hoffer Q, Holladay 1, SRK/T and Haigis formulae were equally accurate in predicting the postoperative refraction after cataract surgery in eyes with AL of more than 24.5 mm (Doshi et al., 2017).

Zhao et al. (2018) evaluated the accuracy of third and fourth generation IOL power formulae (Holladay I, Hoffer Q, SRK/T, Holladay II and Haigis) in 3258 Chinese eyes where they were divided into short (AL < 23.0 mm), medium (23.0 mm ≤ AL < 27.0 mm) and long eyes (AL ≥ 27.0 mm). They found that there was no difference between Holladay I, Hoffer Q, SRK/T, and Haigis formulae in medium eyes.

Delfi et al. (2021) evaluated and compared the changes in visual acuity in 84 post-phacoemulsification patients using the SRK/T and Haigis formulae. The patients from Medan Baru Eye Hospital, Indonesia, were divided into 3 groups which were short eyes (AL < 23.0 mm), medium eyes (AL 23 – 24.0 mm) and long eyes (AL > 24.0 mm). They found that there was no significant difference between the SRK/T and Haigis formulae in predicting the accuracy of the mean error (ME).

3rd Generation vs 4th Generation vs 5th Generation

Kane et al. (2016) assessed the accuracy of 3rd, 4th and 5th generation IOL formulae using IOLMaster biometry and optimized lens constants in medium AL from 22.01 to 25.99 mm. The 7 intraocular lens (IOL) power formulae included Hoffer Q, Holladay 1 and SRK/T, Haigis and

Holladay 2, Barrett Universal II and T2 respectively. They found that the Barrett Universal II formula had a lower absolute error than the other 6 formulas in the medium AL group (2638 eyes). However, if only 3rd generation IOL formulae were taken into consideration, their results for the 3rd generation formulae (Holladay 1, SRT/T and Hoffer Q) agreed with Aristodemou et al. (2011)'s findings for medium AL (22.01 to 24.49 mm) as well as medium long AL (24.50 to 25.99 mm).

Hipólito-Fernandes et al. (2020) compared the accuracy of a newly developed intraocular lens (IOL) power formula (VRF-G) with twelve existing formulas (Barret Universal II, EVO 2.0, Haigis, Hill-RBF 2.0, Hoffer Q, Holladay 1, Kane, Næeser 2, PEARL-DGS, SRK/T, T2 and VRF) in 695 Caucasian eyes of medium AL between 22.0 and 26.0 mm. They found that Kane, EVO 2.0 and VRF-G formulae had the most accurate performances (lowest MAE).

Kuthirummal et al. (2020) evaluated the accuracy of Barrett Universal II, modified SRK-II, SRK/T, and Olsen formulae in predicting the IOL power for cataract surgery in Asian Indian population with normal axial lengths (AL 22.0 – 24.5 mm). They found that Barrett Universal II gave the lowest mean prediction error in postoperative refraction and median absolute error. There was a statistically significant difference between Barrett Universal II and modified SRK II or SRK/T. However, there was no statistically significant difference between Barrett Universal II and Olsen.

Delfi et al. (2021) evaluated and compared the changes in visual acuity in 84 post-phacoemulsification patients using the SRK/T and Haigis formulae. The patients were divided into 3 groups which were short eyes (AL < 23.0 mm), medium eyes (AL 23 – 24.0 mm) and long eyes (AL > 24.0 mm). They found that there was no statistically significant difference between the SRK/T and Haigis formulas in predicting the accuracy result of the ME.

Pereira et al. (2021) evaluated the accuracy of 12 intraocular lens (IOL) power calculations: Barrett Universal II, EVO, Haigis, Hill-RBF version 2.0, Hoffer Q, Holladay 1, Holladay 2, Kane, Olsen, SRK/T, Super Formula and T2. They found that the Kane formula was the most accurate formula for medium axial length between 22.5 mm and 25.5 mm among 595 eyes with medium axial lengths.

Amita et al. (2022) evaluated the accuracy of SRK-II and Barrett Universal IOL formulae in 35 patients with AL ranging from 22.0 to 24.5 mm, who had their cataract operations in North Jakarta, Indonesia. They found that there is no statistically significant difference in refraction prediction error (RPE) value between the two IOL formulae.

Jiang et al. (2022) compared the accuracy of various intraocular lens power formulas (Barrett Universal II, Haigis, Hoffer Q, Holladay 2, and SRK/T) for two monofocal hydrophobic foldable lenses, the AcrySof SN60WF and the Tecnis ZCB00 in short eyes (< 22.5 mm), medium eyes (22.5 – 25.5 mm), and long eyes (> 25.5 mm). They found that there were no significant differences in the mean absolute error (MAE) and the percentage of eyes within ±0.5 D (%±0.5 D) between both IOLs in patients with medium eyes (22.5 – 25.5 mm).

Voytsekhivskyy (2023) compared the VRF and VRF-G formulas with seven 3rd and 4th generation thin and thick-lens formulas: Haigis, Hoffer Q, Holladay 1, Holladay 2, SRK/T, T2, and Barrett Universal II in 295 Caucasian eyes. He categorised medium eyes with AL of between 22.00 – 26.00 mm. In this study, the participants were divided into 3 groups: short AL $\leqslant$ 22.00 mm, medium AL between 22.00 – 26.00 mm, long AL $\geqslant$ 26.00 mm. The best median absolute error values (MedAE) in medium AL were found for Haigis (0.271 D) and VRF (0.272 D) and the worst result was produced by the SRK/T formula (0.327 D). VRF, VRF-G, Haigis and Barrett Universal II formulae had the lowest standard deviation (SD), MedAE and MAE and percentage of eyes within ±0.50D predicted refraction values and may therefore be the most accurate. The fourth-generation Haigis and Holladay 2 formulas demonstrated acceptable accuracy and outperformed 3rd generation formulas in medium eyes.

Solomon et al. (2022) evaluated and compared the accuracy of the Barrett Universal II formula for all ALs versus the third-generation formula: SRK/T for long eyes (AL > 24.0 mm), Holladay 1 for medium eyes (AL = 22.00 – 23.99 mm), and Hoffer Q for short eyes (AL $\leqslant$ 21.99 mm) in predicting refractive outcome for standard cataract surgery in 981 Indian eyes. They found that there were no significant differences in the median absolute error predicted by Barrett and the third-generation formulae across all axial lengths and that Barrett Universal II formula had the lowest predictive refraction error and mean absolute error.

In summary, for 3rd generation IOL formulae, either SRK/T, Hoffer Q and Holladay 1 is the IOL formula choice for medium axial length. If both 3rd and 4th generation IOL formulae are available, Haigis formula is the 1st IOL formula choice, followed by either Hoffer Q, Holladay 1, or SRK/T formulae. However, if Barrett Universal II or EVO or Kane was available among other IOL formulae (Hoffer Q, Holladay 1, SRK/T, Haigis, Holladay 2, Barrett Universal II, T2, EVO, Kane), either one could be used to generate the IOL power.

1.2.3 Long Axial Length

Axial length of 26.00 mm or longer is usually categorised as long axial length.

3rd Generation

Among the 3rd generation IOL formulae (SRK/T, Hoffer Q and Holladay 1), SRK/T would perform the best for AL 26.00 mm or longer (eyes), with statistically significant differences for ALs of 27.00 mm or longer when compared to Hoffer Q and Holladay 1 (Aristodemou et al., 2011).

3rd Generation vs 4th Generation

However, when 4th generation IOL formula was available in calculating the IOL power besides the 3rd generation formulae, the results varied according to the long axial lengths as concluded by Bang et al. (2011). Haigis formula was found to be the most accurate in predicting postoperative refractive error in long eyes (AL > 27.0 mm). The SRK/T formula was the second most accurate, followed by Holladay 2, Holladay 1, and lastly, the Hoffer Q formulae. These results suggested using the Haigis, SRK/T, or Holladay 2 formulas for very long eyes. However, if the long axial lengths were further divided into groups based on the length, SRK/T formula, which is a 3rd generation formula, was the most accurate at predicting postoperative refractions in eyes with axial lengths from 27 to less than 29.07 mm (group A). Haigis formula was the most accurate at predicting postoperative refractions in groups B (18 eyes, AL of 29.07 to 30.62 mm) and C (17 eyes, AL > 30.62 mm).

Chen et al. (2015) also had similar results to Bang et al. (2011). They found that, overall, the Haigis formula resulted in the lowest median absolute error (MedAE) (1.025D) in high and extremely high myopic Chinese eyes with an AL of > 26.0 mm (mean AL = 29.02 mm) among Hoffer Q, Holladay 1 and SRK/T. The SRK/T formula generated the second most accurate results (1.040D), whereas the Hoffer Q was the least accurate in all subgroups.

3rd Generation vs 4th Generation vs 5th Generation

With the addition of 5th generation IOL formulae, it seemed that 5th generation IOL formulae provided the most accuracy against 3rd and 4th generation formulae and this result was proven by both Zhang et al. (2016) and Kane et al. (2016).

Zhang et al. (2016) evaluated and compared the accuracy of different intraocular lens (IOL) power calculation formulae (SRK/T, Haigis, Holladay, Hoffer Q, and Barrett Universal II) for 171 eyes with an axial length (AL) greater than 26.00 mm. The results of this study suggested that, for high myopic eyes, the Barrett Universal II formula provided the most predictable outcomes. The SRK/T and Haigis formulae, employing ULIB constants, performed similarly but better than the Holladay and Hoffer Q formulae.

Kane et al. (2016) assessed the accuracy of 7 intraocular lens (IOL) power formulae (Barrett Universal II, Haigis, Hoffer Q, Holladay 1, Holladay 2, SRK/T, and T2) using IOLMaster biometry and optimized lens constants. They found that the Barrett Universal II had the lowest MAE of all formulae assessed for 77 long eyes (26.00 mm or above), and the difference was statistically significant compared with the Haigis, Hoffer Q, Holladay 1, Holladay 2, SRK/T formulae. The SRK/T formula had lower absolute errors than the T2 formula and all other formulae except the Barrett Universal II.

In summary, SRK/T formula has proven to be the most accurate among the 3rd generation IOL formulae in predicting the IOL power for long axial lengths. Haigis formula (4th generation) is the first choice among 3rd and 4th generation IOL formulae. However, if Haigis formula is not available, SRK/T is the next best choice for IOL power calculation among 3rd and 4th generation IOL formulae. In the event that Barrett Universal II, a 5th generation IOL formula, is available, it would be the 1st choice among other IOL formulae.

Limitations of the studies

The previous studies have evaluated and compared the accuracy of the various IOL formulae but they were not without limitations.

Gavin et al. (2008) compared the accuracy of the Hoffer Q and SRK-T formulae in 41 eyes below 22.00 mm in axial length, using biometry measured with partial coherence interferometry (PCI), without a customised ACD constant and found that Hoffer Q was significantly more accurate than the SRK-T. The small sample size of 41 eyes might undermine the internal and external validity of a study (Faber et al., 2014). The postoperative spherical equivalent was measured using an autorefractor instead of manifest subjective refraction. Due to the use of an autorefractor, best corrected visual acuity (BCVA) was not performed to determine the visual status of the operated eye. This might contribute bias during the analysis despite there were studies that found no significant differences in the accuracy of the autorefractor and subjective refraction in assessment of the final achieved refractive outcome for between Lasik and cataract surgeries (Faber et al., 2014) (Pesudovs, 2004, as cited in Gavin et al., 2008) (Gavin, 1992, as cited in Gavin et al., 2008). The ethnicity of the patients was not revealed. However, as this study was conducted in the West Kent Eye Centre UK, there was a high likelihood that the patients were Caucasians.

Aristodemou et al. (2011) evaluated the accuracy of 3rd generation IOL formulae (SRK/T, Hoffer Q and Holladay 1) and used an appropriate optimized formula constant for the IOL formulae as opposed to Gavin et al. (2008). They included post-operative patients with best corrected visual acuity (BCVA) of 20/40 (6/12) or better. However, the rationale to use a postoperative BCVA of 20/40 (6/12) or better instead of 20/25 (6/7.5) was not explained. Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but they did not have a vision that is worse than 20/25 (6/7.5). Hence, for people with healthy eyes and had cataract surgery done, one would expect to have a BCVA of 20/25 (6/7.5) or better. If a person had BCVA of 20/40 (6/12) and yet, the eye was healthy, what could be the cause of the reduced vision, and would that affect the accuracy of the IOL formulae? The ethnicity of the patients was not revealed. However, as this study was conducted in the West Kent Eye Centre UK, there was a high likelihood that the patients were Caucasians.

Doshi et al. (2017) found that Hoffer Q, Holladay 1 and SRK/T formulae were equally accurate in predicting the postoperative refraction after cataract surgery and the accuracy of these 3 formulae was significantly higher than Haigis formula in small eyes (AL < 22.0 mm). However, the small sample size of 40 might undermine the internal and external validity of a study (Faber et al., 2014). The post-operative BCVA of 6/12 (20/40) or better was chosen as inclusion criteria. However, the rationale to use a postoperative BCVA of 20/40 (6/12) or better instead of 20/25 (6/7.5) was not explained. For a person with healthy eyes and had cataract surgery done, one would expect to have a BCVA of 20/25 (6/7.5) or better (Radner et al., 2019). If a person had BCVA of 20/40 and yet, the eye was healthy, what could be the cause of the reduced vision, and would that affect the accuracy of the IOL formulae? Similar to Aristodemou et al. (2011) study, in Doshi et al. (2017) study, IOL power calculation in each group was done with the Haigis, Hoffer Q, Holladay I and SRK/T formulae using the software of ECHORULE 2 with optimization of A-constant. The ethnicity of the participants was not revealed. However, as this study was conducted in the Government Medical College and Sir T. Hospital, India, there was a high likelihood that the patients were Indians.

Kane et al. (2016) assessed the accuracy of 7 intraocular lens (IOL) power formulae using 3rd generation IOL formulae (Hoffer Q, Holladay 1, SRK/T), 4th generation IOL formulae (Haigis, Holladay 2) and 5th generation IOL formulae (Barrett Universal II, T2) in 156 eyes with a short axial length (< 22.0 mm) and found that all the 7 IOL formulae were similar. In this study, only 6 IOL formulae (Hoffer Q, Holladay 1, SRK/T, Holladay 2, T2, Haigis) were optimized and Barrett Universal II was not optimized. Instead, the recommended lens constant for Barrett Universal II formula was used because there was no method to optimize the lens constant using the online calculator as stated by Kane et al. (2016). Kane et al. (2016) used Holladay 1 surgeon factor of 1.686, SRK/T A-constant of 118.824, Hoffer Q personalised ACD of 5.462 and Holladay 2 constant of 5.630. Haigis a0, a1 and a2 constants were 0.996, 0.279, 0.129, and the recommended constant for Barrett Universal II was 118.99. This might introduce a bias to the result as the comparison might not be fair as 6 IOL formulae were optimized and 1 was not. The post-operative BCVA of 20/40 (6/12) or better was chosen as inclusion criteria and there was no explanation why a BCVA of 20/40 (6/12) was chosen instead of 20/25 (6/7.5) as one would expect to have a BCVA of 20/25 (6/7.5) if the eye is healthy (Radner et al., 2019). Subjective refraction was performed after 14 days postoperatively by orthoptic staff or optometrist. However, the 2018 UK Royal College of Ophthalmologists Guidelines recommends that new glasses should only be provided 4–6 weeks after surgery despite Charlesworth et al. (2020) conducted a meta-analysis of five studies (301 eyes) and found that there was no statistical difference between spherical, spherical equivalent and cylindrical refraction between 1-week and the current standard of 4-weeks and was shown to have high statistical power. However, Charlesworth et al. (2020) also suggested to surgeons that there might be a relatively small number of patients who may take longer to stabilize and should obtain a spectacle prescription later. The stabilization of the refractive error plays an important part in the evaluation of the accuracy of the IOL formulae as they provide the spherical equivalent of the refractive error postoperatively to analyze the data. If the refractive error is not stabilized and inaccurate, it would affect the result of the analysis of the various IOL formulae. The ethnicity of the participants was not revealed but this study was conducted in the Alfred Health Hospital and there is a likelihood that the patients were Caucasians.

Zhao et al. (2018) evaluated the accuracy of third and fourth generation IOL power formulae (Holladay I, Hoffer Q, SRK/T, Holladay II and Haigis) in 3258 Chinese eyes where they were divided into short (AL < 23.0 mm), medium (23.0 mm ⩽ AL < 27.0 mm) and long eyes (AL ⩾ 27.0 mm). They found that there was no difference between Holladay I, Hoffer Q, SRK/T, and Haigis formulae in medium eyes. However, their categorization of the short, medium and long eyes were different from the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. The different in categorization might cause confusion when surgeons are choosing the most appropriate IOL formula for their patients based on the recommendations made by different studies. Despite the authors attempted to include Holladay II in their evaluation, it was not possible due to the limitation of the IOLMaster as the IOLMaster was unable to capture the lens thickness (LT) as the component was not integrated into the IOLMaster. The predictive IOL powers were estimated by each IOL formulae (SRK/T, Hoffer Q, Holladay I, Holladay II and Haigis) with ULIB optimized constants. An optimized AL was recalculated in the present study based on measured AL by IOLMaster.

Hipólito-Fernandes et al. (2020) compared the accuracy of a newly developed intraocular lens (IOL) power formula (VRF-G) with 12 existing formulas (Barret Universal II, EVO 2.0, Haigis, Hill-RBF 2.0, Hoffer Q, Holladay 1, Kane, Næeser 2, PEARL-DGS, SRK/T, T2 and VRF) in 695 Caucasian eyes of medium AL between 22.0 and 26.0 mm. They found that Kane, EVO 2.0 and VRF-G formulae had the most accurate performances (lowest MAE). The post-operative BCVA of 20/40 (6/12) or better was chosen as inclusion criteria and the decision to use BCVA of 20/40 (6/12) or better was not revealed. Postoperative manifest refraction was assessed 4 weeks after surgery by an ophthalmologist. All the IOL formulae (Barret Universal II, EVO 2.0, Haigis, Hill-RBF 2.0, Hoffer

Q, Holladay 1, Kane, Næeser 2, PEARL-DGS, SRK/T, T2 and VRF) were optimized by either the study's author or the formula's author. Inclusion of data from different surgeons or formula's authors as well as the manifest refraction performed by an ophthalmologist might introduce biases to the study.

Kuthirummal et al. (2020) evaluated the accuracy of Barrett Universal II, modified SRK-II, SRK/T, and Olsen formulae in predicting the IOL power for cataract surgery in Asian Indian population with normal axial lengths (AL 22.0 – 24.5 mm) where the AL for medium eyes were classified differently when compared to the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines. The inclusion criteria of postoperative BCVA was not stated in the study and the postoperative refractive error was documented using auto-refractometer. This might contribute to a bias in the analysis of the data despite there were studies that found no significant differences in the accuracy of the autorefractor and subjective refraction in assessment of the final achieved refractive outcome for between Lasik and cataract surgeries (Faber et al., 2014) (Pesudovs, 2004, as cited in Gavin et al., 2008) (Gavin, 1992, as cited in Gavin et al., 2008). A non-parametric test (Friedman test) was used as the data does not follow a normal distribution and MAE was used during the analysis of the data. There was also no mentioning if the IOL constants used in the study were optimized.

Delfi et al. (2021) evaluated and compared the changes in visual acuity in 84 post-phacoemulsification patients using the SRK/T and Haigis formulae. The patients were divided into 3 groups which were short eyes (AL < 23.0 mm), medium eyes (AL 23 – 24.0 mm) and long eyes (AL > 24.0 mm). However, their categorization of the short, medium and long eyes were different from the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. The inclusion criteria of postoperative BCVA was not stated in the study. There was also no mentioning regarding the optimization of the lens constant used for both IOL formulae. The normality of the data distribution was not stated and ME was used to analyze the data. These factors might undermine the validity of the study. The ethnicity of the patients was not revealed but this study was conducted in Medan Baru Eye Hospital, Indonesia.

Pereira et al. (2021) evaluated the accuracy of 12 intraocular lens (IOL) power calculations: Barrett Universal II, EVO, Haigis, Hill-RBF version 2.0, Hoffer Q, Holladay 1, Holladay 2, Kane, Olsen, SRK/T, Super Formula and T2. They found that the Kane formula was the most accurate formula for medium axial length between 22.5 mm and 25.5 mm among 595 eyes where the AL for medium eyes were classified differently when compared to the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines. The inclusion criteria of postoperative BCVA 20/40 (6/12) or better was used instead of 20/25 (6/7.5) where healthy eyes should have (Radner et al., 2019). The ethnicity of the patients was not revealed but the data was collected in 2 cataract centres in

Toronto, Canada. In this study, lens constant optimization was performed for Haigis, Hoffer Q, Holladay 1, SRK/T and Holladay 2 as they had associated open-source software available for lens constant optimization whereas Barrett Universal II, EVO, Hill-RBF version 2.0, Kane, Olsen, Super Formula and T2 were not optimized. This might result in a bias when analyzing the data.

Amita et al. (2022) evaluated the accuracy of SRK-II and Barrett Universal IOL formulae in 35 patients with normal AL ranging from 22.0 to 24.5 mm, who had their cataract operations in Atma Jaya Hospital, North Jakarta, Indonesia. They found that there was no statistically significant difference in refraction prediction error (RPE) value between the two IOL formulae. The RPE is known as the difference between presurgical refraction of patients subjectively in the Snellen chart and postsurgical refraction or the prediction of refractive value post-surgically from each formula and they used the smallest RPE value for statistical analysis. The usage of RPE in the analysis was uncommon as most studies would either use the MAE or MedAE where the difference between the postsurgical refractive spherical equivalent and estimated residual spherical equivalent would be used to analyse the data. The inclusion criteria of postoperative BCVA of 5/7.5 (20/30) (6/9) was used instead of 6/7.5 as one would expect to have a BCVA of 6/7.5 if the eye is healthy (Radner et al., 2019). In this study, patients with AL ranging from 22.0 to 24.5 mm were analysed where this range fell into the medium eyes as suggested by the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the medium AL is between 22.00 and 26.00 mm. In this study, the measurement of the Al was performed using applanation technique with SonomedPac 300A-scan. However, there are disadvantages when using applanation biometry such as corneal indentation, risk of corneal abrasions and infection, and off-axis measurements (Olsen, 2007).

Jiang et al. (2022) compared the accuracy of various intraocular lens power formulas (Barrett Universal II, Haigis, Hoffer-Q, Holladay 2, and SRK/T) for two monofocal hydrophobic foldable lenses, the AcrySof SN60WF and the Tecnis ZCB00 in short eyes (< 22.5 mm), medium eyes (22.5 – 25.5 mm), and long eyes (> 25.5 mm) where the AL for medium eyes were classified differently when compared to the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines. The inclusion criteria for postoperative BCVA was not stated in the study and this might affect the validity of the study despite all the IOL formulae were optimized.

Solomon et al. (2022) evaluated and compared the accuracy of the Barrett Universal II formula for all ALs versus the third-generation formula: SRK/T for long eyes (AL > 24.0 mm), Holladay 1 for medium eyes (AL = 22.00 – 23.99 mm), and Hoffer Q for short eyes (AL ⩽ 21.99 mm) in predicting refractive outcome for standard cataract surgery in 981 Indian eyes. They found that there were no significant differences in the median absolute error predicted by Barrett Universal II and the third-generation formulae across all axial lengths and that Barrett Universal II formula had the lowest predictive refraction error and mean absolute error. In their study, their categorization of the short, medium and long eyes were different from the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. The inclusion criteria of postoperative BCVA 20/40 (6/12) or better was used instead of 20/25 (6/7.5) where healthy eyes should have (Radner et al., 2019). In their study, it was uncertain if the A-constants were optimized for data analysis. The authors also did not explain the reason to compare Barrett Universal II with Hoffer Q in short eyes, Barrett Universal II with Holladay 1 in medium eyes nor Barrett Universal II with SRK/T in long eyes.

Voytsekhivskyy (2023) compared the VRF and VRF-G formulas with seven 3rd and 4th generation thin and thick-lens formulas: Haigis, Hoffer Q, Holladay 1, Holladay 2, SRK/T, T2, and Barrett Universal II in 295 Caucasian eyes where all the lens constant was optimized for the IOL formulae. In this study, patients with postoperative BCVA of 20/30 (6/9) or better were included where a postoperative BCVA of 20/25 (6/7.5) might be a better choice if the eyes are healthy (Radner et al., 2019).

Bang et al. (2011) evaluated the relationship between eyes with long AL and postoperative refractive errors as predicted by various commonly used IOL formulae. This study included 53 eyes where group A (AL 27.00 to < 29.07 mm) consists of 18 eyes, group B (AL 29.07 – 30.62 mm) consists of 18 eyes and group C (AL > 30.62 mm). However, the small sample size might undermine the internal and external validity of a study (Faber et al., 2014). The post-operative BCVA of 20/40 (6/12) or better was chosen as inclusion criteria and there was no explanation why a BCVA of 20/40 (6/12) was chosen instead of 20/25 (6/7.5) as one would expect to have a BCVA of 20/25 (6/7.5) if the eye is healthy (Radner et al., 2019). MAE was used to analyze the data despite the normality of the data was not specified in the study. The ethnicity of the patients was not revealed but this study was conducted in John Hopkins hospital, United States of America (USA).

Chen et al. (2015) compared the accuracy of IOL power calculation formulae in 148 Chinese eyes with long AL where group A (AL = 26.01 – 28.00 mm) consisted of 57 eyes, group B (AL = 28.01 – 30.00 mm) consisted of 48 eyes, group C (AL = 30.01 – 33.00 mm) consisted of 37 eyes, and group D (AL = 33.01 – 36.00 mm) consisted of 6 eyes. However, the small sample size might undermine the internal and external validity of a study (Faber et al., 2014). The inclusion criteria for postoperative BCVA was not stated in the study and this might affect the validity of the study.

Zhang et al. (2016) evaluated and compared the accuracy of different intraocular lens (IOL) power calculation formulae (SRK/T, Haigis, Holladay, Hoffer Q, and Barrett Universal II) for 171 eyes with an axial length (AL) greater than 26.00mm. During the analysis of the data, MAE was used to evaluate and compare the accuracy of the various IOL formulae but the normality of the data distribution was not specified. The inclusion criteria for postoperative BCVA was not stated in the study and this might affect the validity of the study. The ethnicity of the patients were not mentioned in the study but as the cataract extraction with IOL implantation was performed at C-MER (Shenzhen) Dennis Lam Eye Hospital (Shenzhen, China) or Dennis Lam & Partners Eye Center (Hong Kong, China), the patients might be of Chinese ethnicity.

This thesis will consist of 3 studies where the main study will evaluate and compare the accuracy of the various IOL formulae of the different ethnic groups in Singapore. The sub-study 1 will evaluate and compare the accuracy of the various IOL formulae using applanation biometry in the Chinese population in Singapore. The sub-study 2 will evaluate and compare the accuracy of the IOL formulae (Barrett Universal II and Emmetropia Verifying Optical) with the inclusion and exclusion of anterior chamber depth (ACD) measurements.

MAIN STUDY

CHAPTER 2 EVALUATION OF THE ACCURACY OF INTRAOCULAR LENS FORMULAE IN DIFFERENT ETHIC GROUPS IN SINGAPORE

2.1 INTRODUCTION

Cataract surgery is the most common ophthalmic surgery performed worldwide (Kaswin et al., 2014, as cited in Karabela et al., 2016) (Ozcura et al., 2015).

The World Health Organisation (WHO) defines a cataract as any opacity in the crystalline lens. Cataract development is a natural ageing process of the transparent crystalline lens, where it becomes opaque with age. Cataract can also happen due to other causes known as secondary cataract such as traumatic or related to systemic medication. Cataract extraction is necessary when a person’s vision is affected to the point that they are unable to perform their daily tasks. Modern cataract surgery includes installation of a replacement lens, known as an intraocular lens, to counter the refractive power of the crystalline lens.

The refractive power of the human eye relies on the power of the cornea, lens, axial length (AL) of the eye and the axial position of the lens (Shrivastava et al., 2018). Cornea power accounts for about two-thirds of the total dioptric power of the eye and the crystalline lens accounts for the remaining one-third. The crystalline lens accounts approximately 20D of the eye’s refractive status, so an intraocular implant (IOL) with dioptric power is necessary to replace dioptric power of the crystalline lens. It is expected that the IOL will be placed exactly where the crystalline lens is positioned. The lens capsule is not removed during cataract extraction, and this becomes the cradle to hold the IOL. Hence, in order to calculate the dioptric power of the IOL, various IOL formulae have been formulated in an attempt. In a nutshell, the dioptric power of the IOL is calculated with the anterior corneal curvature measurements and the axial length of the eyeball.

Intraocular lens (IOL) power calculation is an important factor that affects the visual outcome in eyes undergoing cataract surgery. The power of the intraocular lens (IOL) is derived from the biometric formula that is developed to achieve a precise IOL power and the predicted residual refractive error. The surgeon will then choose the most appropriate formulae from the biometric formulae that can achieve a post-operative refractive error closest to emmetropia. There are various IOL formulae that have been developed in an attempt to achieve the best visual outcome. With the advancement of technology and improvement in surgical techniques, coupled with increasing patients’ demands of clear vision postoperatively, newer generations of biometric formulae have been developed to achieve optimum visual outcomes for the patients (Kaswin et al., 2014, as cited in Karabela et al., 2016) (Ozcura et al., 2015) (Davis, 2016) (Zhang et al., 2020).

There are various formulas that have been developed in an attempt to achieve the best visual outcome in different types of eyes. These include hyperopic eyes, emmetropic eyes, myopic eyes, eyes with previous Lasik surgeries etc. For patients who have not undergone any Lasik surgery previously, various IOL formulae such as SRK/T, Haigis, Barrett Universal II have been developed over the years in an attempt to achieve the best optimal vision postoperatively. For patients who had previous refractive surgery and are planning to undergo cataract surgery, Hagis-L IOL formula is recommended as one of the IOL formulae according to the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines. Surgeons could also assess the IOLCalc website (https://iolcalc.ascrs.org) to select an appropriate IOL for the patients. Alternatively, surgeons could also consider Barrett True-KT formula for patients with previous LASIK/PRK surgeries. Zheng et al. (2024) has found that the Barrett True-KT formula exhibited the highest prediction accuracy in eyes after myopic LASIK/PRK (Zheng et al, 2024).

As this study focuses on pre-operative eyes without Lasik interventions or refractive surgeries, various IOL formulae that have been developed over the years to improve the best optimal vision postoperatively will be discussed here.

There had been various studies that looked into the relationship between different formulas and axial lengths (AL). Evaluating the accuracy of the newer generation formula is important. Researchers have also compared the older generation IOL formulae especially the 3rd generation IOL formulae such as SRK/T, Hoffer Q, Holladay 1 with the newer generation formulae such as Haigis, Holladay 2 (4th generation) and Barrett Universal II, Kane, EVO 2.0 (5th generation) to determine accuracy as well as the differences between them.

In order to evaluate the accuracy of IOL formulae, researchers have categorized the axial lengths into different axial length groups, namely short, medium and long. As such, some studies classified the short axial length group as axial lengths shorter or equal than 22.00 mm (Gavin et al., 2008) (Aristodemou et al., 2011) (Kane et al., 2016) (Doshi et al., 2017). The medium axial length group comprised of axial lengths between 22.00 mm and 26.00 mm (Aristodemou et al., 2011) (Kane et al., 2016) (Doshi et al., 2017) (Hipólito-Fernandes et al., 2020). The long axial length group comprised of axial lengths 26.00 mm or longer (Aristodemou et al., 2011) (Bang et al, 2011) Chen et al. (2015) (Kane et al., 2016) (Zhang et al., 2016). The 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines suggested that the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm.

Aim of this study

There are a lot of studies that examined the accuracy of IOL formulae in their population. Most of the IOL formulae studies that were conducted, were using a Western population (Gavin et al., 2008) (Aristodemou et al., 2011) (Bang et al., 2011) (Kane et al., 2016) (Hipólito-Fernandes et al., 2020) (Pereira et al., 2021) (Jiang et al., 2022) (Voytsekhivskyy, 2023). As such, would there be a difference in the choice of the IOL formulae in the Asian population? Would ethnicity influence the choice of IOL formulae for different axial lengths?

There are different ethnic groups in Singapore, namely Chinese ethnic group, Malay ethnic group and Indian ethnic group. The accuracy of IOL formulae in the Chinese ethnic group (Chen et al., 2015) (Zhang et al., 2016) (Zhao et al., 2018), Malay ethnic group (Delfi et al., 2021) (Amita et al., 2022) and Indian ethnic group (Doshi et al., 2017) (Kuthirummal et al., 2020) (Solomon et al., 2022) had been studied by various researchers. However, there has been limited information regarding the accuracy of IOL formulae in the Chinese, Malay and Indian ethnic groups with medium axial lengths.

The purpose of this study was to examine the accuracy of 6 IOL formulae (SRK/T, Hoffer Q, Haigis, Holladay 1, Barrett Universal II and EVO) in medium axial lengths (22.00 to 25.99 mm) with regards to the diverse population (Chinese, Malay and Indian ethnic groups) in Singapore. The primary outcome measure was the mean absolute error (MAE) of each IOL formula. The secondary outcome measure was the percentage of eyes within ±0.50D.

2.2 METHODOLOGY

Study Design and Participant Recruitment

This study was reviewed and approved by the JurongHealth Campus Research Ethics Committee and the NHG DOMAIN SPECIFIC REVIEW BOARD (DSRB) (Appendix 1). The research protocol of this study adhered to the tenets of the Declaration of Helsinki. Aston University Ethics Committee gave a waiver because local ethics was in place. JurongHealth Campus Research Ethics Committee and the NHG DOMAIN SPECIFIC REVIEW BOARD reviewed this study and confirmed that informed consent is not needed from the participants as this is a database retrospective study. As such, the data was retrieved according to the criteria and were anonymised before data analysis by the researcher.

This is the first database retrospective study that examined the accuracy of various IOL formulae in different axial length groups of various ethnic groups in Singapore. As this is a database retrospective study, informed consent was not obtained from the participants.

As per the Ophthalmology Department's protocol in Jurong Medical Centre, all patients consented to cataract operations are required to undergo a series of test procedures which include pre-operative biometry measurements.

All preoperative biometric measurements were measured using either partial coherence interferometry with the IOLMaster 500 V.7.7. (Carl Zeiss-Meditec, Jena, Germany). The IOLMaster 500 is calibrated every day as part of the routine checks when the equipment is switched on. The keratometry readings and anterior chamber depth (ACD) are captured using the IOLMaster 500. As the IOLMaster 500 does not provide lens thickness (LT) or corneal thickness information, these parameters were not included as preoperative parameters. The Hoffer Q, SRK-T, Haigis and Holladay 1 formulae were calculated using the IOL Master 500 biometer. Other IOL formulae such as Barrett Universal II, EVO 2.0etc, were accessed online from their respective websites.

As part of the pre-operative assessment, besides the biometry measurements, endothelial cell count (ECC) measurement was also performed for all patients. If the ECC was less than 1,500, patients were not allowed to have their cataract operations conducted in the medical centre. Instead, they would have their cataract operations performed in other institutions.

Phacoemulsification is performed by the surgeons and different IOL models such as AR40, AABOO, SA60AT, MX60, SN60WF, and ZCB00 were used. The choice of IOL model is based on individual surgeon's preferences.

Subjective manifest refraction was performed for all patients undergoing cataract operations 1 month postoperatively as part of the routine protocol for patients undergoing cataract operations.

Subjective manifest refraction was performed by qualified optometrists who underwent competency checks annually as mandated by the institution.

Recruitment, Criteria and Eligibility

This research will involve all patients undergoing cataract operation in Jurong Medical Centre from January 2018 to December 2019. The starting date for the study was chosen due to the purchase of IOLMaster 500 in the centre and all patients underwent biometry measurements using IOLMaster 500 since January 2018. Due to the outbreak of COVID in early 2020, all elective surgeries including cataract operations in the centre were put on hold since March 2020. Hence, all patients who underwent cataract operation in the centre from January 2018 to December 2019 had their records retrieved for analysis.

The patient will be included if they meet the inclusion criteria of 1) underwent cataract operation in Jurong Medical Centre from 01 January 2018 to 31 December 2019, 2) no other eye abnormalities except cataract, 3) post-operative subjective refraction best corrected visual acuity (BCVA) of 20/25 (6/7.5) or better, 4) monofocal IOL was implanted, and 5) 1 month post operation details such as subjective refraction was available.

The patient will be excluded if 1) post cataract operation adverse events such as Irvine Gass Syndrome occurred, 2) patient’s case records were incomplete such as no postoperative subjective refraction was recorded, 3) best corrected visual acuity (BCVA) of 20/30 (6/9) or worse postoperatively, 4) toric, multifocal or accommodative IOL was implanted, 5) other eye surgeries such as epi-retinal membrane surgery was conducted together with the cataract operation, 6) previous refractive surgery.

Data Analysis

A minimum sample size of 94 eyes was calculated with G*Power (version 3.1.9.7, Franz Faul, Universität Kiel, Germany) with a significance level of $\alpha = 0.05$, power of 0.80, and an effect size of 0.30. The mean prediction error (MPE) and the mean absolute error (MAE) were calculated to evaluate the accuracy of each IOL formula. The differences in absolute error between formulae were assessed using the Friedman test. In the event of a significant result, post-hoc analysis was undertaken using the Wilcoxon signed-ranks test with Bonferroni correction for multiple comparisons of the IOL formulae. A p value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS Statistics 29.0 (IBM, Armonk, North Castle, New York, United States).

Due to the stringent inclusion criteria, a total of 541 participants' data were retrieved and analysed (Table 1).

Table 1. Characteristics of the 541 participants

	Chinese	Malay	Indian
Short AL (< 22.0 mm)	11	1	1
Medium AL (22.0 to 25.99 mm)	383	43	42
Long AL (≥ 26.0 mm)	53	5	2
Total	447	49	45

Due to the small sample size retrieved for short and long axial length groups, this study will focus on analysing the data with participants whose axial lengths were between 22.00 and 25.99 mm. This was in reference to 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm and other studies (Aristodemou et al., 2011) (Kane et al., 2016).

The participants were divided into 2 groups, namely the Chinese group and Non-Chinese group. The Chinese group include all participants of Chinese ethnicity (N = 383). The Non-Chinese group will include participants of Malay ethnic group and Indian ethnic group as the retrieved data for both the Malay and Indian ethnic groups was small with only 85 participants.

2.3 RESULTS

Four hundred and sixty-eight eyes were included in the study. The demographic details and biometric data of the study eyes are listed in Table 2. The demographic details and biometric data of the Chinese and Non-Chinese groups are listed in Table 3.

Table 2 Preoperative biometry data of the 468 study subjects (Chinese, Malay and Indian ethnic groups)

Statistical Parameters	Age	Axial Length (mm)	Anterior Chamber Depth (ACD)	Average Keratometry (dioptre)
Chinese				
Mean ± SD	68.35 ± 6.63	23.84 ± 0.95	3.08 ± 0.39	44.22 ± 1.51
Range	44.27	3.95	1.87	9.22
Malay				
Mean ± SD	66.41 ± 7.61	23.86 ± 0.83	3.16 ± 0.37	44.18 ± 1.61
Range	29.36	3.36	1.41	7.36
Indian				
Mean ± SD	65.98 ± 6.44	24.00 ± 0.89	3.26 ± 0.29	44.08 ± 1.45
Range	30.54	3.17	1.27	5.93

Table 3 Preoperative biometry data of the Chinese and Non-Chinese groups

Statistical Parameters	Age	Axial Length (mm)	Anterior Chamber Depth (ACD)	Average Keratometry (dioptre)
Chinese				
Mean (± SD)	68.35 ± 6.63	23.84 ± 0.95	3.08 ± 0.39	44.22 ± 1.51
Range	44.27	3.95	1.87	9.22
Non-Chinese				
Mean (± SD)	66.19 ± 7.02	23.93 ± 0.86	3.21 ± 0.34	44.13 ± 1.53
Range	30.54	3.54	1.48	5.93

In order to evaluate the accuracy of each IOL formula, we calculated the mean prediction error (MPE) and the mean absolute error (MAE). The MPE was defined as the average of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula. The MAE was defined as the average of the absolute values of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula.

In the medium axial length group, it was found that SRK/T had the lowest mean absolute error (MAE) of 0.3351D, followed by Barrett Universal II, EVO 2.0, Holladay 1, Hoffer Q and Haigis of 0.3368D, 0.3381D, 0.5078D, 0.5719D and 0.6535D respectively (Table 4).

Table 4 Mean prediction error (MPE) and mean absolute error (MAE) for IOL formulae in medium axial length group

	MPE (D) Mean ± SD	MAE (D) Mean ± SD
SRK/T	-0.07 ± 0.46	0.34 ± 0.32
Barrett Universal II	-0.02 ± 0.45	0.34 ± 0.30
EVO 2.0	0.03 ± 0.45	0.34 ± 0.30
Haigis	0.59 ± 0.49	0.65 ± 0.41
Holladay 1	0.41 ± 0.45	0.51 ± 0.34
Hoffer Q	0.49 ± 0.47	0.57 ± 0.38

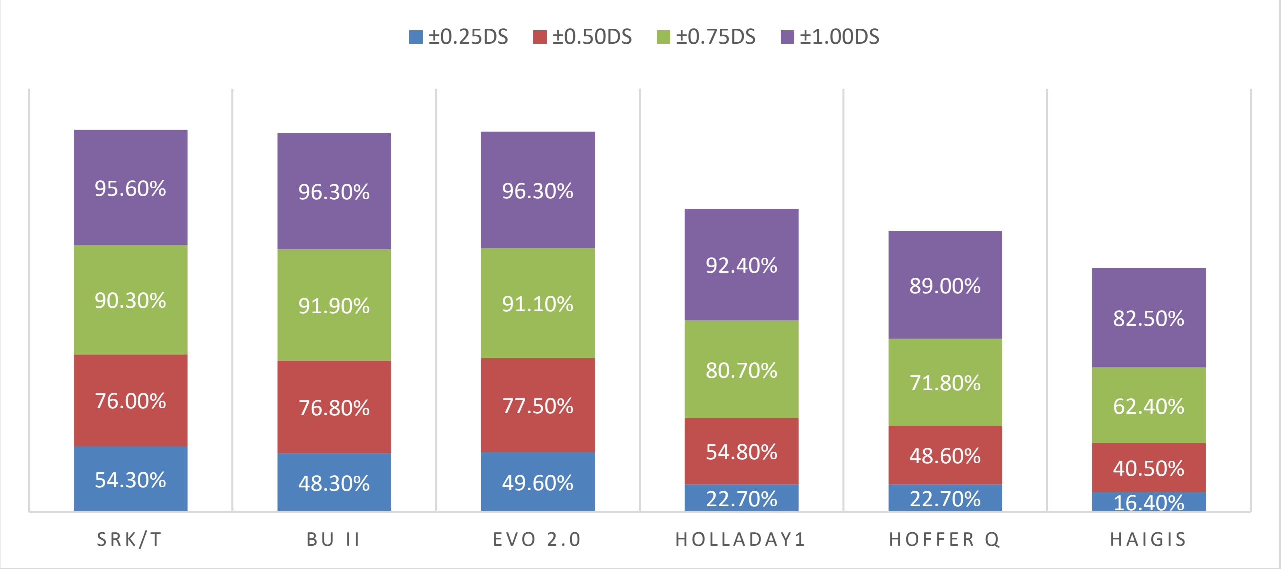
However, when the study participants were grouped according to their respective groups (Chinese and Non-Chinese groups), SRK/T was found to have the smallest MAE in the Chinese group and Barrett Universal II was found to have the smallest MAE in the Non-Chinese group (Table 5).

Table 5 Mean prediction error (MPE) and mean absolute error (MAE) for IOL formulae in medium axial length group and ethnic groups

	Chinese (N = 383)		Non-Chinese (N = 85)	
Formula	MPE (D) Mean ± SD	MAE (D) Mean ± SD	MPE (D) Mean ± SD	MAE (D) Mean ± SD
SRK/T	-0.08 ± 0.45	0.33 ± 0.32	-0.02 ± 0.47	0.35 ± 0.31
Barrett Universal II	-0.02 ± 0.45	0.33 ± 0.31	-0.00 ± 0.45	0.34 ± 0.29
EVO 2.0	0.02 ± 0.45	0.34 ± 0.30	0.04 ± 0.44	0.34 ± 0.27
Haigis	0.59 ± 0.49	0.66 ± 0.41	0.57 ± 0.50	0.63 ± 0.41
Holladay 1	0.40 ± 0.45	0.51 ± 0.33	0.45 ± 0.45	0.52 ± 0.36
Hoffer Q	0.48 ± 0.48	0.57 ± 0.37	0.54 ± 0.47	0.59 ± 0.40

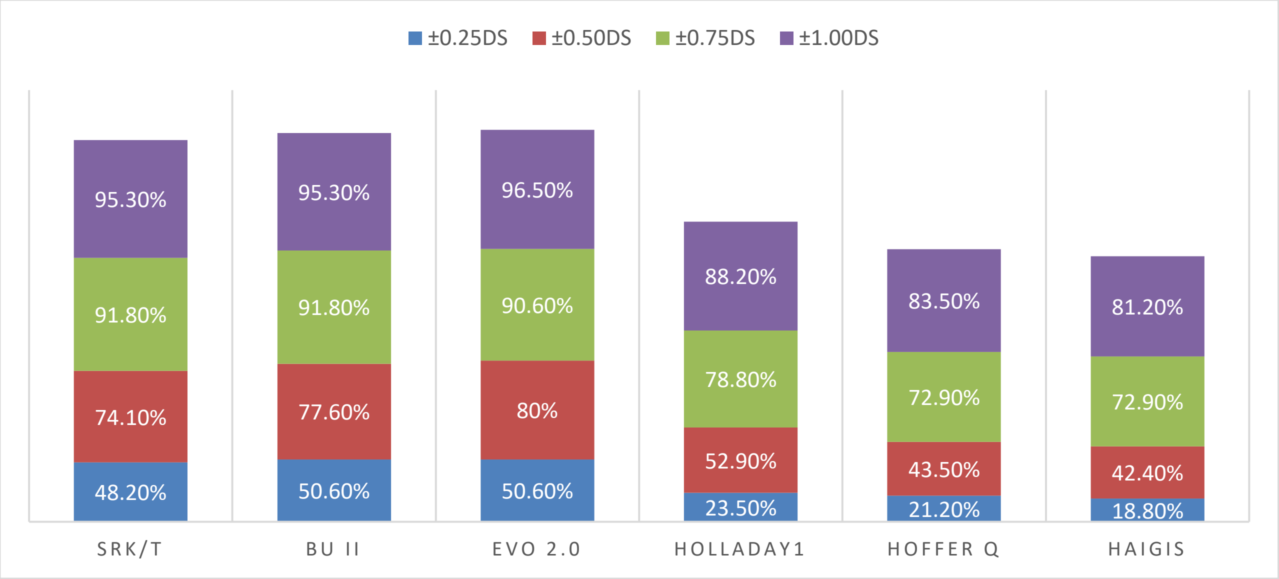
In the Chinese group, SRK/T has the smallest MAE of 0.331D, followed by Barrett Universal II, EVO 2.0, Holladay 1, Hoffer Q and Haigis of 0.336D, 0.338D, 0.505D, 0.567D and 0.658D respectively (Table 4). At least 76% of the participants had ±0.50DS residual refractive errors when using the SRK/T, Barrett Universal II and EVO 2.0 formulae with SRK/T formula had a residual refractive error within ±0.25DS in 54.3% of the participants (Figure 1).

Figure 1 Percentage of eyes with prediction error (PE) within ±0.25DS, ±0.50DS, ±0.75DS, ±1.00DS in Chinese group



In the Non-Chinese group, Barrett Universal II has the smallest MAE of 0.3391D, followed by EVO 2.0, SRK/T, Holladay 1, Hoffer Q and Haigis of 0.3401D, 0.3532D, 0.5212D, 0.5924D and 0.6348D respectively (Table 5). At least 74.1% of the participants had ±0.50DS residual refractive errors when using the SRK/T, Barrett Universal II and EVO 2.0 formulae with Barrett Universal II formula had a residual refractive error within ±0.25DS in 50.6% of the participants (Figure 2).

Figure 2 Percentage of eyes with prediction error (PE) within ±0.25DS, ±0.50DS, ±0.75DS, ±1.00DS in Non-Chinese group



Shapiro-Wilks Normality Test is used to determine the distribution of the data. The test rejects the hypothesis of normality when the *p*-value is less than or equal to 0.05.

The Shapiro-Wilks test is used to determine the distribution of the MPE of the IOL formulae (SRK/T, Hoffer Q, Holladay 1, Haigis, Barrett Universal II and EVO 2.0) in both the Chinese and Non-Chinese groups (Table 6).

Table 6 Shapiro-Wilks normality test in Chinese and Non-Chinese groups

	Chinese			Non-Chinese		
	Statistic	df	Sig	Statistic	df	Sig
SRK/T	0.967	383	<.001	0.986	85	0.503
EVO 2.0	0.969	383	<.001	0.987	85	0.545
Barrett Universal II	0.969	383	<.001	0.984	85	0.394
Haigis	0.976	383	<.001	0.981	85	0.244
Holladay 1	0.971	383	<.001	0.985	85	0.405
Hoffer Q	0.984	383	<.001	0.987	85	0.530

In this study, it was found that there was a statistically significant difference between the 6 IOL formulae, with X^2 (5) = 403.794, p<.001 in the Chinese group with Friedman Test. As such, Wilcoxon signed-ranks test with Bonferroni correction was conducted to examine the relationships between the different IOL formulae (Table 7).

Table 7 Comparison between IOL formulae in Chinese group

Comparison between formulae		*p* value	Comparison between formulae		*p* value
SRK/T	EVO	0.37	Haigis	SRK/T	<.001*
	BU II	0.31		EVO	<.001*
	Haigis	<.001*		BU II	<.001*
	Holladay 1	<.001*		Holladay 1	<.001*
	Hoffer Q	<.001*		Hoffer Q	<.001*
EVO	SRK/T	0.37	Holladay 1	SRK/T	<.001*
	BU II	0.556		EVO	<.001*
	Haigis	<.001*		BU II	<.001*
	Holladay 1	<.001*		Haigis	<.001*
	Hoffer Q	<.001*		Hoffer Q	<.001*
BU II	SRK/T	0.31	Hoffer Q	SRK/T	<.001*
	EVO	0.556		EVO	<.001*
	Haigis	<.001*		BU II	<.001*
	Holladay 1	<.001*		Haigis	<.001*
	Hoffer Q	<.001*		Holladay 1	<.001*

Friedman test and Wilcoxon signed-rank test with Bonferroni correction for post hoc analysis, $p<0.05$
*statistically significant

There was no statistically significant difference between SRK/T, Barrett Universal II and EVO 2.0 formulae in the Chinese group (Table 7). However, there was a statistically significant difference when SRK/T was compared to either Holladay 1 or Hoffer Q or Haigis. Either Barrett Universal II or EVO 2.0 formulae were also found to have a statistically significant difference when compared to Holladay 1 or Hoffer Q or Haigis. Holladay 1 or Hoffer Q or Haigis were found to have a statistically significant difference with all the other IOL formulae. As such, SRK/T, Barrett Universal II and EVO 2.0 formulae can be used interchangeably as they provide similar results when generating the IOL powers.

Friedman Test was conducted in the Non-Chinese group and it was found that there was a statistically significant difference in the 6 IOL formulae with X^2 (5) = 78.709, p<.001. As such, Wilcoxon signed-ranks test with Bonferroni correction was conducted to examine the relationships between the different IOL formulae (Table 8).

Table 8 Comparison between IOL formulae in Non-Chinese group

Comparison between formulae		*p* value	Comparison between formulae		*p* value
BU II	EVO	0.82	Holladay 1	BU II	<.001*
	SRK/T	0.591		EVO	<.001*
	Holladay 1	<.001*		SRK/T	<.001*
	Hoffer Q	<.001*		Hoffer Q	<.001*
	Haigis	<.001*		Haigis	<.001*
EVO	BU II	0.82	Hoffer Q	BU II	<.001*
	SRK/T	0.309		EVO	<.001*
	Holladay 1	<.001*		SRK/T	<.001*
	Hoffer Q	<.001*		Holladay 1	<.001*
	Haigis	<.001*		Haigis	0.093
SRK/T	BU II	0.591	Haigis	BU II	<.001*
	EVO	0.309		EVO	<.001*
	Holladay 1	<.001*		SRK/T	<.001*
	Hoffer Q	<.001*		Holladay 1	<.001*
	Haigis	<.001*		Hoffer Q	0.093

Friedman test and Wilcoxon signed-rank test with Bonferroni correction for post hoc analysis, $p<0.05$

*statistically significant

In the Non-Chinese group, it was found that there was no statistically significant difference between SRK/T, Barrett Universal II and EVO 2.0 formulae (Table 8). However, there was a statistically significant difference when Barrett Universal II was compared to either Holladay 1 or Hoffer Q or Haigis. Either EVO 2.0 or SRK/T formulae were also found to have a statistically significant difference when compared to Holladay 1 or Hoffer Q or Haigis. There was a statistically significant difference when Holladay 1 was compared to all other IOL formulae but there was no statistically significant difference between Hoffer Q and Haigis formulae.

2.4 DISCUSSION

Singapore has at least 4 different ethnic groups with Chinese, Malay and Indian ethnicities making up the majority of the ethnic groups. Ethnicity studies in Singapore have examined the eye structures of different ethnicities and found that Chinese has the longest mean axial length (AL), anterior chamber depth (ACD) and steepest corneal curvature (K) as compared to Malays and Indians (Sng et al., 2012) (Lim et al., 2010) (Pan et al., 2011). Chinese were found to have a mean AL of 24.00 mm, K of 6.47 mm and ACD of 3.24 mm in 1063 participants from the age of 44 to 84 years old (Sng et al., 2012). Malays were found to have a mean AL of 23.55 mm, K of 7.65 mm and ACD of 3.10 mm in 2788 participants from the age of 40 to 80 years old (Lim et al., 2010). Indians were found to have a mean AL of 23.45 mm, K of 7.61 mm and ACD of 3.15 mm in 2785 participants from the age of 40 to 83 years old (Pan et al., 2011).

In this study, 541 participants' data was retrieved and the mean age of the participants was 67.57 years old. The mean AL of the participants in this study was 24.19 mm, with mean ACD of 3.13 mm and mean K of 44.22D (Table 9).

Table 9 Preoperative biometry data of 541 participants

Statistical Parameters	Age	Axial Length (mm)	Anterior Chamber Depth (ACD)	Average Keratometry (dioptre)
Mean (± SD)	67.57 ± 6.94	24.19 ± 1.49	3.13 ± 0.4	44.22 ± 1.55
Range	47.67	9.19	1.96	9.62

When the results were further analysed by ethnicity, there were some differences between this study and the previous ethnicity studies as mentioned earlier (Sng et al., 2012) (Lim et al., 2010) (Pan et al., 2011).

Among the 3 ethnicity groups, Chinese and Indians had the longest mean AL of 24.19 mm with Malays having the shortest mean AL of 24.16 mm. ACD was found to be longest in Indians, followed by Malays and Chinese of 3.24 mm, 3.18 mm and 3.11 mm respectively. In this study, it was found that Chinese ethnic group has the steepest K followed by Malays and then Indians with 44.24D, 44.17D and 44.15D respectively.

Table 10 Preoperative biometry data of 541 participants in different ethnic groups

Statistical Parameters	Age	Axial Length (mm)	Anterior Chamber Depth (ACD)	Average Keratometry (dioptre)
Chinese (N = 447)				
Mean (± SD)	67.83 ± 6.88	24.19 ± 1.52	3.11 ± 0.4	44.24 ± 1.56
Range	44.27	9.19	1.96	9.62
Malay (N = 49)				
Mean (± SD)	66.68 ± 7.95	24.16 ± 1.33	3.18 ± 0.4	44.17 ± 1.58
Range	35.92	6.13	1.49	7.36
Indian (N = 45)				
Mean (± SD)	65.89 ± 6.24	24.19 ± 1.43	3.24 ± 0.33	44.15 ± 1.43
Range	30.54	7.4	1.57	5.93

Axial length and corneal curvature are the 2 most basic measurements required to generate IOL power using various IOL formulae. However, as the AL, K, and ACD measurements could differ in different ethnic groups, this might be one of the reasons why different authors recommended different IOL formulae in the calculation of IOP power based on their studies' findings.

In this study, it was found that SRK/T, Barrett Universal II and EVO 2.0 formulae could be used interchangeably when predicting the IOL powers for medium axial length group in Chinese, Malay and Indian ethnic groups.

On calculating the percentage of prediction error within the acceptable range of error in Chinese group, SRK/T, Barrett Universal II and EVO 2.0 formulae gave the best results with 76.0%, 76.8% and 77.5% within ±0.5D respectively and 95.6%, 96.3% and 96.3% within ±1.0D. This is well within the benchmark standard determined for National Health Services, United Kingdom (55% of prediction error within ±0.5D and 85% of prediction error within ±1.0D) (Kithirummal et al., 2020). As for the Non-Chinese group, on calculating the percentage of prediction error within the acceptable range of error, EVO 2.0, Barrett Universal II and SRK/T formulae gave the best results with 80.0%, 77.6% and 74.1% within ±0.5D respectively and 96.5%, 95.3% and 95.3% within ±1.0D. This is well within the benchmark standard determined for National Health Services, United Kingdom (55% of prediction error within ±0.5D and 85% of prediction error within ±1.0D) (Kithirummal et al., 2020).

Limitations of the study

There are however, some limitations in this study. The limitations include the range of axial lengths used for medium eyes, the optimization of A-constant and the utilization of MAE to evaluate the accuracy of each IOL formula in a non-Gaussian distribution.

Medium Axial Length Group (22.00 to 25.99 mm)

The medium axial length group for this study was defined as axial lengths from 22.00 to 25.99 mm. The 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines suggested the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. The American Academy of Ophthalmology (AAO) defined high myopia as eyes with a measured AL of at least 26 mm (Ang et al., 2021). Besides these recommendations by RCOphth and AAO, there were also several studies that defined medium axial lengths as between 22.00 mm and 25.99 mm (Aristodemou et al., 2011) (Kane et al., 2016). As such, the decision to define medium eyes with axial lengths from 22.00 to 25.99 mm was made.

Medium-Long Eyes

Recently, there had been studies that evaluated the accuracy of IOL formulae in medium-long eyes (Aristodemou et al., 2011) (Kane et al., 2016) (Stopyra et al., 2024). However, there was a disagreement on the axial lengths pertaining to medium-long eyes with Aristodemou et al. (2011) suggested 23.50 to 25.99 mm and some authors (Kane et al., 2017) (Stopyra et al., 2024) disputed it as between 24.5 to 25.99 mm. Aristodemou et al. (2011) evaluated the accuracy of SRK/T, Hoffer Q and Holladay 1 formulae and found that there was no statistically significant differences between SRK/T, Hoffer Q and Holladay 1 in medium eyes (22.00 to 23.49 mm) and medium-long eyes (23.5 to 25.99 mm) despite Holladay 1 may perform marginally better than SRK/T and Hoffer Q in medium-long eyes. Kane et al. (2016) found that the Barrett Universal II formula was more accurate than SRK/T, Holladay 1, Holladay 2, Haigis, Hoffer Q and T2 formulae in medium eyes (AL 22.01 to 24.49 mm). They also found that Barrett Universal II, Holladay 1 and T2 formulae were more accurate than SRK/T, Holladay 2, Haigis, and Hoffer Q formulae in medium-long eyes (AL 24.5 to 25.99 mm). Stopyra et al. (2024) compared the accuracy of 20 IOL formulae (Holladay1, SRK/T, Hoffer Q, Holladay 2, Haigis, Barrett Universal II, Kane, K6, Olsen (OLCR), Olsen (standalone), PEARL-DGS, Ladas Super Formula AI (LSF AI), T2, EVO, VRF, Hoffer QST, Castrop, VRF-G, Karmona, and Naeser 2 in medium long eyes (24.50 – 25.99 mm). They concluded that SRK/T and Holladay 1 (3rd generation) formulae provided highly accurate outcomes in medium-long eyes with SRK/T yielding the lowest root mean square absolute error (RMSAE) and median absolute error (MedAE). Both Aristodemou et al. (2011) and Kane et al. (2016) compared the accuracy of IOL formulae in medium and medium-long eyes and found that the IOL formula with the best accuracy could be used in both medium and medium-long eyes. Nevertheless, future studies could compare the accuracy of the IOL formulae in both medium and medium-long eyes to determine the best IOL formula. However, the range of axial lengths for medium-long eyes would need to be explored further as different studies used different axial lengths for medium-long eyes.

Sample Size

This study aimed to evaluate the accuracy of IOL formulae in the 3 different ethnic groups (Chinese, Malay and Indian) in Singapore. A minimum sample size of 94 eyes was calculated with G*Power (version 3.1.9.7, Franz Faul, Universität Kiel, Germany) with a significance level of $\alpha = 0.05$, power of 0.80, and an effect size of 0.30. However, due to the small sample size of the Malay and Indian ethnic groups, participants from the Malay and Indian ethnic groups were grouped together to form the non-Chinese group (Table 1).

The small sample size collected might be due to the stringent criteria of the post-operated best corrected visual acuity of 20/25 (6/7.5) whereas other studies (Aristodemou et al., 2011) (Kane et al., 2016) used post-operated BCVA of 20/40 (6/12) as their inclusion criteria. However, Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but yet, they did not have a vision that is worse than 20/25 (6/7.5). Hence, the exclusion criteria of BCVA of 20/25 (6/7.5) after cataract operation, might give a better indication on the evaluation and accuracy of various IOL formulae in the study population.

Ethnic Groups

Chinese Group

In this study, SRK/T had the smallest MAE and SRK/T, Barrett Universal II and EVO 2.0 were found to have similar results in the Chinese group. Hence, it is recommended to use SRK/T, Barrett Universal II and EVO formulae for IOL power calculation. However, this result was different from Zhao et al. (2018) where they evaluated the accuracy of third and fourth generation IOL power formulae (Holladay I, Hoffer Q, SRK/T, Holladay II and Haigis) in 3258 Chinese eyes where they were divided into short (AL < 23.0 mm), medium (23.0 mm ⩽ AL < 27.0 mm) and long eyes

(AL ⩾ 27.0 mm). They found that there was no statistically significant difference between Holladay I, Hoffer Q, SRK/T, and Haigis formulae in medium eyes. In both Zhao et al. (2018) and this study, SRK/T formula was the best choice among all other formulae to use in Chinese medium eyes. However, the medium axial length (23.0 mm ⩽ AL < 27.0 mm) used in Zhao et al. (2018) was different from this study's medium axial length (22.00mm ≥ AL ≤ 25.99mm).

Non-Chinese Group

As for the Non-Chinese group (Malay and Indian ethnic groups) in this study, it was found that SRK/T, Barrett Universal II and EVO 2.0 formulae were similar (Table 8) with Barrett Universal II having the smallest MAE. However, there was a statistically significant difference when Barrett Universal II or SRK/T or EVO 2.0 was compared to either Holladay 1 or Hoffer Q or Haigis. As the Non-Chinese group comprised of Malay and Indian ethnic groups, the studies involving Malay and Indian ethnic groups also showed similar results with Barrett Universal II as the 1st IOL formula choice, followed by SRK/T formula and both the Malay and Indian ethnic studies did not include EVO 2.0 formula during their evaluation (Delfi et al., 2021) (Amita et al., 2022) (Doshi et al., 2017) (Kuthirummal et al., 2020) (Solomon et al., 2022).

Singapore is made up of diverse ethnic groups, namely Chinese, Malay and Indian. 75.70% of the population in Singapore are Chinese, 15.15% are Malays, 8.0% are Indians and the rest 1.15% are of other ethnic groups (Department of Statistics Singapore, 2022). This imbalance of the ethnic groups might result a bias in the analysis as the data collected for Malay and Indian ethnic groups were smaller than the Chinese ethnic group. Further research is required to examine the accuracy of the IOL formulae in these 3 ethnic groups as there are limited studies (Zhao et al., 2018) (Delfi et al., 2021) (Amita et al., 2022) (Doshi et al., 2017) (Kuthirummal et al., 2020) (Solomon et al., 2022) that evaluate the accuracy of IOL formulae in medium axial lengths (22.00 to 25.99 mm).

IOL Models

In this study, different types of IOL were used such as AR40, AABOO, SA60AT, MX60, SN60WF, and ZCB00. The influence of the different models of IOL affecting the accuracy of the various IOL formulae is not evaluated due to the small number of some IOL models implanted in this study. However, Jiang et al. (2022) compared the accuracy of various IOL formulae for two monofocal hydrophobic foldable lenses, the AcrySof SN60WF and the Tecnis ZCB00 and found that there were no significant differences in the formula accuracy between these two lenses in medium eyes for all formulae namely, Barrett Universal II, Haigis, Hoffer Q, Holladay 2 and SRK/T. However, they found that the accuracy decreased in short eyes for some formulae and decreased significantly in long eyes for ZCB00 compared to SN60WF. With newer IOL models emerging in the market, it might be worthwhile to evaluate the accuracy of the various IOL formulae for the different IOL models.

Utilization of Mean Absolute Error (MAE) in a non-Gaussian Distribution

In this study, the mean absolute error (MAE) was used instead of mean prediction error (MPE) during statistical analysis as the latter can lead to erroneous results due to cancellation during summation (Kuthirummal et al., 2020). Hoffer et al. (2021) recommended to utilize MedAE as a primary outcome instead of MAE due to the not-normal distribution of absolute refractive prediction error.

Despite the recommendation made by Hoffer et al. (2021), there were many studies that utilize MAE as a primary outcome instead of MAE (Zhao et al., 2018) (Hipólito-Fernandes et al., 2020) (Kuthirummal et al., 2020) (Jiang et al., 2022). Future studies could evaluate and compare the accuracy of IOL formulae using MAE and MedAE to determine if there is any difference in the accuracy of IOL formulae in their study population.

Optimization of A-Constant

In this study, the recommended A-constant provided by the Manufacturer for Hoffer Q, SRK-T, Haigis, Holladay 1, Barrett Universal II formulae were used. Moshirfar et al. (2023) had commented that optimization is critical to studies that compare IOL formulae as the optimized constants involved adjusting each formula’s arithmetic mean error (AME) as close to zero as possible to eliminate existing systematic errors prior to statistical analysis. Moshirfar et al. (2023) also commented that optimizing the A-constant for each formula to make AME for formulae equal to zero might not be possible if the IOL formula is not publicly available for individualized lens constant optimization method and that some IOL formulae might require advanced computer programming software, to which the surgeon might not have the access and time to optimize the constant to each IOL formula for each patient before the cataract surgery.

Due to the possibility of the unavailability of the A-constant, there were some studies (Kane et al., 2016) (Pereira et al., 2021) (Moshirfar et al., 2023) that evaluated and compared the accuracy of IOL formulae where some of the A-constant in the IOL formulae were optimized and some were not optimized. This approach might introduce bias to the study during the analysis as this will not be a fair comparison and evaluation of the accuracy of the IOL formulae.

2.5 CONCLUSION

The purpose of this study was to examine the accuracy of 6 IOL formulae (SRK/T, Hoffer Q, Haigis, Holladay 1, Barrett Universal II and EVO 2.0) in medium axial lengths (22.00 to 25.99 mm) with regards to the diverse population (Chinese, Malay and Indian ethnic groups) in Singapore. In this study, it was found SRK/T, Barrett Universal II and EVO 2.0formulae could be used interchangeably when predicting the IOL powers for medium axial length group in Chinese, Malay and Indian ethnic groups. In the event that only 3rd generation IOL formulae are available, SRK/T would be the best choice among the 3rd generation IOL formulae such as Hoffer Q and Holladay 1, to generate the IOL power.

This study showed that good refractive outcomes can be achieved with SRK/T, Barrett Universal II and EVO 2.0 formulae. These 3 IOL formulae had a prediction error of ±0.50DS or less in at least 74.1% of the Chinese, Malay and Indian eyes, and a prediction error of ±1.0DS or less in at least 95.3% of the Chinese, Malay and Indian eyes in this study. This is well within the benchmark standard determined for National Health Services, United Kingdom (55% of prediction error within ±0.5D and 85% of prediction error within ±1.0D) (Kithirummal et al., 2020).

SUB-STUDY 1

CHAPTER 3 EVALUATION OF THE ACCURACY OF IOL FORMULAE IN APPLANATION BIOMETRY

3.1 INTRODUCTION

Axial length (AL) measurement is the most important factor in IOL formulae calculation. A 1-mm error in AL measurement can result in a refractive error of approximately 2.5 D in an average eye. AL can be measured by ultrasound methods (applanation biometry) or infrared laser methods (Optical biometry). Before the invention of noncontact partial coherence laser interferometer, AL measurements were obtained using applanation biometry (Lee et al., 2008).

Applanation biometry uses the ultrasound beam by emitting a parallel sound beam from the probe tip at approximately 10 MHz, which echoes back into the probe tip as the sound beam strikes each interface. The echoes received back into the probe from each of these interfaces are converted by the biometer to spikes arising from the baseline. These echoes allow us to calculate the distance between the probe and various structures of the eye. The axial length is measured as the product of the time taken by the sound to travel from one interface to another at a given velocity. The other measurements obtained are the anterior chamber depth (ACD), lens thickness (LT), and vitreous chamber depth (VCD) (Lee et al., 2008) (Kasturi et al., 2022). However, there are also disadvantages when using applanation biometry. Due to the positioning of the ultrasound probe on the cornea during the measurement of AL, it can cause corneal indentation as well as risk of corneal abrasions and infection, and off-axis measurements (Olsen, 2007).

Introduction to Optical Biometry (Partial Coherence Laser Interferometer)

In 1999, Carl Zeiss introduced a noncontact partial coherence laser interferometer (IOL Master; Carl Zeiss Meditec, Jena, Germany) as an alternative technique to measure the axial length of the eye. The IOL Master uses an infrared laser-based measurement technique by emitting a 780-nm wavelength to measure the delay and intensity of infrared light reflected back from media interfaces in order to determine the distance from the cornea to the retinal pigment epithelium. The IOL Master has an inherent advantage over a sound-based system with a frequency of 10MHz and a resolution of 200μm (Kasturi and Chakrabarti, 2022). However, IOL Master does have its pitfalls. Accurate measurements require that the infrared laser be able to pass through the eye and return to the interferometer. Therefore, opacities along the visual axis can block the infrared laser. They include tear film abnormalities, corneal pathology, mature and posterior subcapsular cataracts, vitreous opacities, maculopathy or retinal detachment. In addition, the patient must be able to maintain fixation. All these can affect the accurate measurements of AL. Lee et al. (2008) had reviewed various studies in their study and reported that 8-20% of patients cannot be measured with optical biometry due to poor fixation, dense cataract or corneal pathology.

Optical Biometry versus Applanation Biometry

The axial length measurements by optical biometry and applanation biometry differed by the way that they are measured even if there is no corneal indentation by the applanation method. Ultrasound biometry measures the distance from the anterior corneal to the inner limiting membrane, while optical biometry measures from the cornea to the retinal pigment epithelium. Thus, the measured axial length obtained from ultrasound and optical biometry cannot be expected to yield the same values. Hitzenberger et al. (1993) found that the axial lengths measured by the optical biometry were 0.47mm longer than those measured by the applanation technique (as cited in Lee et al., 2008). This was further proven by Rose et al. (2003) and Gaballa et al. (2017).

Rose et al. (2003) compared axial length estimates using applanation A-scan ultrasound and IOL Master and the accuracy in predicting postoperative refraction determined by each method using the SRK/T formula in 51 eyes with axial lengths from 20.00 to 27.00 mm. They found that the axial lengths measured by the IOL Master were longer by 0.15 mm as compared to ultrasound biometry and that using the IOL Master over applanation ultrasound biometry significantly improved the postoperative refractive outcome from 0.65D to 0.42D. Hence, they concluded that the IOL Master provided an accurate axial length measurement and resulted in accurate intraocular lens power calculation based on the SRK/T formula.

Gaballa et al. (2017) evaluated the differences between IOLMaster and A-scan regarding axial length (AL) and predicted IOL power in high myopic patients with spherical equivalent or greater than -6.00D and or AL 26.00 mm or longer (15 eyes), 10 silicone oil-filled eyes and 15 eyes with nuclear cataracts (I and II). They reported that there was no difference between both methods in different types of cataract regarding AL measurement and IOL power calculation except for estimating AL in nuclear cataracts, where the AL is significantly longer with the IOL master. However, they found that there was a statistically significant difference between both methods when comparing the predicted IOL power to the postoperative spherical equivalent. The AL measured using the IOL master was significantly longer by 0.2 mm than the AL measured by A-scan.

Despite the popularity and accuracy of the optical biometers, applanation biometry is still needed to capture the AL measurement in the event that optical biometers are unable to do so. As such, there were some studies that evaluated the accuracy of the IOL formulae using applanation biometry (Ozcura et al., 2015) (Amita et al., 2022).

Ozcura et al. (2015) conducted a study to compare the accuracy of various biometric formulae such as SRK-II, SRK-T, Holladay I, Hoffer Q and Binkhorst II, for predicting postoperative refraction determined using applanation A-scan ultrasound in 485 eyes where they were divided into short AL group (< 22.0 mm) with 32 eyes, average AL group (22.0 – 25.0 mm) with 422 eyes and long AL group (≥ 25.0 mm) with 31 eyes. They found that there was no statistical difference among SRK-II, SRK-T, Holladay I, Hoffer Q formulae except Binkhorst II formula in the average AL (22.0 – 25.0 mm). However, in their study, the inclusion criteria for postoperative BCVA was 20/40 (6/12) or better and the rationale to use a postoperative BCVA of 20/40 (6/12) or better instead of 20/25 (6/7.5) was not explained. Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but they did not have a vision that is worse than 20/25 (6/7.5). Hence, for people with healthy eyes and had cataract surgery done, one would expect to have a BCVA of 20/25 (6/7.5) or better. If a person had BCVA of 20/40 (6/12) and yet, the eye was healthy, what could be the cause of the reduced vision, and would that affect the accuracy of the IOL formulae? All eyes were also divided into three groups according to AL: short (≤ 22.0 mm), average (22.0 – 25.0 mm), and long (≥ 25.0 mm) eyes. However, their categorization of the short, medium and long eyes were different from the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. In this study, it was unsure if the A-constants were optimized. The normality of the continuous variables was evaluated with the Shapiro–Wilk test and MAE was used in the analysis but the normality of the data distribution was not mentioned.

Amita et al. (2022) evaluated the accuracy of SRK-II and Barrett Universal IOL formulae in 35 patients with normal AL ranging from 22.0 to 24.5 mm, who had their cataract operations in Atma Jaya Hospital, North Jakarta, Indonesia. They found that there was no statistically significant difference in refraction prediction error (RPE) value between the two IOL formulae. The authors defined RPE as the difference between presurgical refraction of patients subjectively in the Snellen chart and postsurgical refraction or the prediction of refractive value post-surgically from each formula and they used the smallest RPE value for statistical analysis. The usage of RPE in the analysis was uncommon as most studies would either use the MAE or MedAE where the difference between the postsurgical refractive spherical equivalent and estimated residual spherical equivalent would be used to analyse the data. The inclusion criteria of postoperative BCVA of 5/7.5 (20/30) (6/9) was used instead of 20/25 (6/7.5) as one would expect to have a BCVA of 20/25 (6/7.5) if the eye is healthy (Radner et al., 2019). In this study, patients with AL ranging from 22.0 to 24.5 mm were analysed where this range fell into the medium eyes as suggested by the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the medium AL is between 22.00 and 26.00 mm. It was unknown if the A-constants were optimized and the normality of the continuous variables was evaluated in this study.

Aim of this sub-study

Due to the popularity and accuracy of optical biometers, there has been reduced interest in the accuracy of newer generation of IOL formulae when using applanation biometry. Despite IOLMaster is more preferred than applanation biometry in determining the axial length and IOL formulae, there are times whereby applanation biometry is needed when IOLMaster is unable to determine the axial length. IOLMaster is limited by its inability to measure axial length in dense ocular media such as a mature or brunescent lens, dense posterior subcapsular cataracts in which ultrasound biometry can be used. Ultrasound biometry is also useful in situations where patients are unable to place their chins on the chin-rest of the IOLMaster or mobility issues or unable to maintain optimal fixation (Gaballa et al., 2017). In these circumstances, applanation biometry is needed to measure the AL of these individuals. Hence, it would be worthwhile to examine and evaluate the accuracy of the newer generation IOL formulae and its postoperative results with regards to applanation biometry.

The purpose of this study was to examine the accuracy of 6 IOL formulae (SRK/T, Hoffer Q, Haigis, Holladay 1, Barrett Universal II and EVO 2.0) in Chinese eyes with medium axial lengths (22.00 to 25.99 mm) where the AL was measured using applanation biometry. The primary outcome measure was the mean absolute error (MAE) of each IOL formula. The secondary outcome measure was the percentage of eyes within ±0.50D.

Despite the accuracy of IOLMaster 500 to measure the axial lengths, there will be times where applanation biometry is needed to measure the axial length of the eyes with dense cataract or other issues that prevent the measurement of AL by IOLMaster. With the limited studies on newer IOL formulae with AL measured using applanation biometry, this study would help in assisting the surgeons to choose the most accurate IOL formula when the axial length measurement is obtained via applanation biometry.

3.2 METHODLOGY

Study Design and Participant Recruitment

This study was reviewed and approved by the JurongHealth Campus Research Ethics Committee and the NHG DOMAIN SPECIFIC REVIEW BOARD (DSRB) (Appendix 1). The research protocol of this study adhered to the tenets of the Declaration of Helsinki. Aston University Ethics Committee gave a waiver because local ethics was in place.

This is the first database retrospective study that examined the accuracy of various IOL formulae in different axial length groups of various ethnic groups in Singapore. As this is a database retrospective study, informed consent was not obtained from the participants.

As per the Ophthalmology Department's protocol in Jurong Medical Centre, all patients consented to cataract operations are required to undergo a series of test procedures which include pre-operative biometry measurements.

In this sub-study, the measurement of the axial lengths by applanation biometry is captured using Alcon Ocuscan RxP (Alcon Laboratories, Texas, U.S.A.). The keratometry (K) readings and anterior chamber depth (ACD) are captured using the IOLMaster 500 V.7.7. (Carl Zeiss-Meditec, Jena, Germany).

As such, both the IOLMaster 500 and Alcon Ocuscan RxP are calibrated every day as part of the routine checks when the equipment is switched on. The Hoffer Q, SRK-T, Haigis and Holladay 1 formulae were calculated using the IOL Master 500 biometer. Other IOL formulae such as Barrett Universal II and EVO 2.0, were accessed online from their respective websites.

As part of the pre-operative assessment, besides the biometry measurements, endothelial cell count (ECC) measurement was also performed for all patients. If the ECC was less than 1,500, patients were not allowed to have their cataract operations conducted in the medical centre. Instead, they would have their cataract operations performed in other institutions.

Phacoemulsification is performed by the surgeons and different IOL models such as AR40, AABOO, SA60AT and MI60 were used. IOL model was chosen based on the surgeon's preference.

Subjective manifest refraction was performed for all patients undergoing cataract operations 1 month postoperatively as part of the routine protocol for patients undergoing cataract operations. Subjective manifest refraction was performed by qualified optometrists who underwent competency checks annually as mandated by the institution.

The participants that were analysed in this study were of Chinese ethnicity due to the small number of data retrieved from the database. In this study, medium axial length (22.00 to 25.99 mm) was analysed as the data retrieved for other axial lengths was small.

Recruitment, Criteria and Eligibility

This research will involve all patients undergoing cataract operation in Jurong Medical Centre from January 2018 to December 2019. The starting date for the study was chosen due to the purchase of IOL Master 500 in the centre and all patients underwent biometry measurements using IOL Master 500 since January 2018. Due to the outbreak of COVID in early 2020, all elective surgeries including cataract operations in the centre were put on hold since March 2020. Hence, all patients who underwent cataract operation in the centre from January 2018 to December 2019 had their records retrieved for analysis. As this chapter is a sub-study from the main chapter, applanation biometry data was also retrieved together with the optical biometry measurements.

The patient will be included if they meet the inclusion criteria of 1) underwent cataract operation in Jurong Medical Centre from 01 January 2018 to 31 December 2019, 2) no other eye abnormalities except cataract, 3) post-operative subjective refraction best corrected visual acuity (BCVA) of 20/25 (6/7.5) or better, 4) monofocal IOL was implanted, and 5) 1 month post operation details such as subjective refraction was available.

The patient will be excluded if 1) post cataract operation adverse events such as Irvine Gass Syndrome occurred, 2) patient’s case records were incomplete such as no postoperative subjective refraction was recorded, 3) best corrected visual acuity (BCVA) of 20/30 (6/9) or worse postoperatively, 4) toric, multifocal or accommodative IOL was implanted, 5) other eye surgeries such as epi-retinal membrane surgery was conducted together with the cataract operation, 6) previous refractive surgery.

Data Analysis

A minimum sample size of 94 eyes was calculated with G*Power (version 3.1.9.7, Franz Faul, Universität Kiel, Germany) with a significance level of α = 0.05, power of 0.80, and an effect size of 0.30. The mean prediction error (MPE) and the mean absolute error (MAE) were calculated to evaluate the accuracy of each IOL formula. The differences in absolute error between formulae were assessed using the Friedman test. In the event of a significant result, posthoc analysis was undertaken using the Wilcoxon signed-ranks test with Bonferroni correction for multiple comparisons of the IOL formulae. A p value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS Statistics 29.0 (IBM, Armonk, North Castle, New York, United States).

Due to the stringent inclusion criteria, a total of 133 participants’ data were retrieved and analysed. This study will focus on analysing the data with participants whose axial lengths were between 22.00 and 25.99 mm due to the small sample size retrieved for short and long axial length group. As the number of participants of Malay ethnic group and Indian ethnic group was small, only participants of Chinese ethnicity were selected for analysis.

3.3 RESULT

One hundred and thirty-three eyes were included in the study. The demographic details and biometric data of the study eyes are listed in Table 11.

Biometry measurements of medium axial length in Chinese patients

The mean axial length in this study was 23.62 ± 0.88 mm and mean anterior chamber depth was 3.16 ± 0.36 mm.

Table 11 Preoperative biometry data of the Chinese participants

Statistical Parameters	Age	Axial Length (mm)	Anterior Chamber Depth (ACD)	Average Keratometry (dioptre)
Mean (± SD)	69.26 ± 7.38	23.62 ± 0.88	3.16 ± 0.36	44.27 ± 1.55
Range	39.59	3.94	2.08	7.65

In order to evaluate the accuracy of each IOL formula, we calculated the mean prediction error (MPE) and the mean absolute error (MAE). The MPE was defined as the average of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula. The MAE was defined as the average of the absolute values of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula.

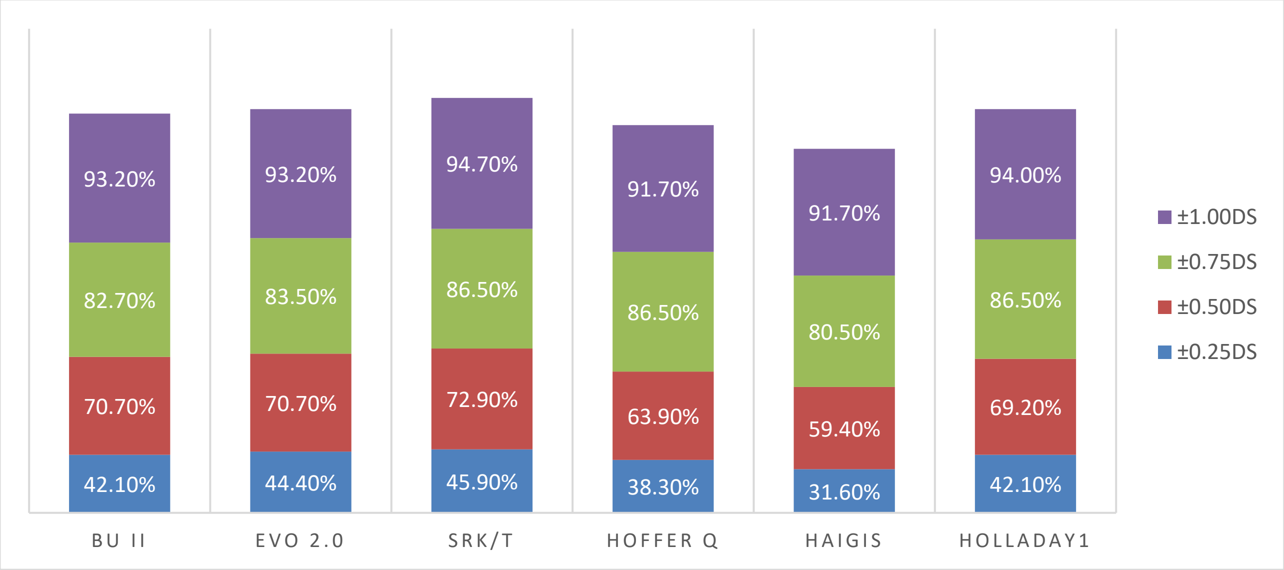
In this study, it was found that SRK/T has the smallest MAE of 0.3766D, followed by Barrett Universal II, EVO 2.0, Holladay 1, Hoffer Q and Haigis of 0.4054D, 0.4070D, 0.4075D, 0.4527D and 0.4876D respectively (Table 12).

Table 12 Mean prediction error (MPE) and mean absolute error (MAE) in medium axial length group.

	MPE (D) Mean ± SD	MAE (D) Mean ± SD
SRK/T	-0.05 ± 0.48	0.38 ± 0.31
Barrett Universal II	-0.09 ± 0.53	0.41 ± 0.35
EVO 2.0	-0.00 ± 0.54	0.41 ± 0.35
Haigis	0.22 ± 0.60	0.49 ± 0.41
Holladay 1	0.13 ± 0.51	0.41 ± 0.33
Hoffer Q	0.18 ± 0.57	0.45 ± 0.39

At least 70.7% of the participants had ±0.50DS residual refractive errors when using the SRK/T, Barrett Universal II and EVO 2.0 formulae with SRK/T formula had a residual refractive error within ±0.25DS in 45.9% of the participants (Figure 3).

Figure 3 Percentage of eyes with prediction error (PE) within ±0.25DS, ±0.50DS, ±0.75DS, ±1.00DS in Chinese group.



Shapiro-Wilks Normality Test is used to determine the distribution of the data. The test rejects the hypothesis of normality when the *p*-value is less than or equal to 0.05.

The Shapiro-Wilks test is used to determine the distribution of the MPE of the IOL formulae (SRK/T, Hoffer Q, Holladay 1, Haigis, Barrett Universal II and EVO 2.0) (Table 13).

Table 13 Shapiro-Wilks normality test

	Statistic	df	Sig.
SRK/T	0.990	133	0.419
Barrett Universal II	0.983	133	0.097
EVO 2.0	0.985	133	0.156
Haigis	0.979	133	0.042*
Holladay 1	0.987	133	0.269
HofferQ	0.979	133	0.041*

In this study, it was found that there was a statistically significant difference between the 6 IOL formulae, with X^2 (5) = 26.832, p<.001 in the Chinese group with Friedman Test. As such, Wilcoxon signed-ranks test with Bonferroni correction was conducted to examine the relationships between the different IOL formulae (Table 14).

Table 14 Comparison between IOL formulae using applanation biometry

Comparison between formulae		*p* value	Comparison between formulae		*p* value
SRK/T	BU II	0.065	Holladay 1	SRK/T	0.120
	EVO	0.159		BU II	0.824
	Holladay 1	0.120		EVO	0.846
	Hoffer Q	.005*		Hoffer Q	<.001*
	Haigis	<.001*		Haigis	<.001*
BU II	SRK/T	0.065	Hoffer Q	SRK/T	.005*
	EVO	0.909		BU II	0.074
	Holladay 1	0.824		EVO	.024*
	Hoffer Q	0.074		Holladay 1	<.001*
	Haigis	.002*		Haigis	.034*
EVO	SRK/T	0.159	Haigis	SRK/T	<.001*
	BU II	0.909		BU II	.002*
	Holladay 1	0.846		EVO	<.001*
	Hoffer Q	.024*		Holladay 1	<.001*
	Haigis	<.001*		Hoffer Q	.034*

Friedman test and Wilcoxon signed-rank test with Bonferroni correction for post hoc analysis, $p<0.05$
*statistically significant

There was no statistically significant difference between SRK/T, Barrett Universal II, EVO 2.0 and Holladay 1 formulae. There was a statistically significant difference between SRK/T formula with Hoffer Q and Haigis. There was also no statistically significant difference between Barrett Universal II and Hoffer Q. However, there was a statistically significant difference between Barrett Universal II and Haigis formulae. There was a statistically significant difference in EVO 2.0 formula with Hoffer Q and Haigis. There was a statistically significant difference between Holladay 1, Haigis and Hoffer Q formulae.

3.4 DISCUSSION

In this study, it was found that SRK/T has the smallest MAE, followed by Barrett Universal II, EVO 2.0, Holladay 1, Hoffer Q and Haigis. SRK/T, Barrett Universal II, EVO and Holladay 1 formulae can be used interchangeably when generating the predicted residual errors of the various IOL formulae in Chinese patients with axial lengths between 22.00 and 25.99 mm. This result was further supported by Ozcura et al. (2015) and Amita et al. (2022) where SRK-T, Holladay I, Hoffer Q and SRK II were the IOL formulae choice in the event that Barrett Universal II was not available. However, the range of axial lengths used in medium eyes was different between this study and Ozcura et al. (2015) and Amita et al. (2022). Ozcura et al. (2015) used AL from 22.0 to 25.0 mm and Amita et al. (2022) used AL ranging from 22.0 to 24.5 mm for the average eyes. Hence, the comparison between these studies with regards to the IOL formula choice for medium eyes might not be ideal.

In this study and Ozcura et al. (2015), MAE was used to evaluate the accuracy of the IOL formulae whereas Amita et al. (2022) used RPE where they defined RPE as the difference between presurgical refraction of patients subjectively in the Snellen chart and postsurgical refraction or the prediction of refractive value post-surgically from each formula and they used the smallest RPE value for statistical analysis.

Both this study and Ozcura et al. (2015), agreed that SRK-T, Holladay I, Hoffer Q formulae were the choice for IOL formulae to be used if only 3rd generation IOL formulae were available. However, if Barrett Universal II was available, both this study and Amita et al. (2022) agreed that Barrett Universal II could be used to calculate the IOL power.

Limitations of the study

There are however, some limitations in this study. The limitations include the range of axial lengths used for medium eyes, the optimization of A-constants and the utilization of MAE to evaluate the accuracy of each IOL formula in a non-Gaussian distribution.

Medium Axial Length Group (22.00 to 25.99 mm)

The medium axial length group for this study was defined as axial lengths between 22.00 to 25.99 mm. The 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines where the short AL to be < 22.00 mm, medium AL to be between 22.00 and 26.00 mm and long AL to be > 26.00 mm. The American Academy of Ophthalmology defines high myopia as eyes with a measured AL of at least 26 mm (Ang et al., 2021). As such, there are several studies that defined medium axial lengths as between 22.00 mm and 25.99 mm (Aristodemou et al, 2011) (Kane et al, 2016) (Hipólito-Fernandes et al, 2020) (Ghaffari et al, 2022) (Voytsekhivskyy, 2023). Hence, the decision to define axial lengths of between 22.00 to 25.99 mm as medium axial lengths was made based on the 2018 Royal College of Ophthalmologists (RCOphth) Cataract Surgery Guidelines as well as the previous studies.

Medium-Long Eyes

Recently, there had been studies that evaluated the accuracy of IOL formulae in medium-long eyes (Aristodemou et al., 2011) (Kane et al., 2016) (Stopyra et al., 2024). However, there was a disagreement on the axial lengths pertaining to medium-long eyes with Aristodemou et al. (2011) suggested 23.50 to 25.99 mm and some authors (Kane et al., 2017) (Stopyra et al., 2024) disputed it as between 24.5 to 25.99 mm. Aristodemou et al. (2011) evaluated the accuracy of SRK/T, Hoffer Q and Holladay 1 formulae and found that there was no statistically significant differences between SRK/T, Hoffer Q and Holladay 1 in medium eyes (22.00 to 23.49 mm) and medium-long eyes (23.5 to 25.99 mm) despite Holladay 1 may perform marginally better than SRK/T and Hoffer Q in medium-long eyes. Kane et al. (2016) found that the Barrett Universal II formula was more accurate than SRK/T, Holladay 1, Holladay 2, Haigis, Hoffer Q and T2 formulae in medium eyes (AL 22.01 to 24.49 mm). They also found that Barrett Universal II, Holladay 1 and T2 formulae were more accurate than SRK/T, Holladay 2, Haigis, and Hoffer Q formulae in medium-long eyes (AL 24.5 to 25.99 mm). Stopyra et al. (2024) compared the accuracy of 20 IOL formulae (Holladay1, SRK/T, Hoffer Q, Holladay 2, Haigis, Barrett Universal II, Kane, K6, Olsen (OLCR), Olsen (standalone), PEARL-DGS, Ladas Super Formula AI (LSF AI), T2, EVO, VRF, Hoffer QST, Castrop, VRF-G, Karmona, and Naeser 2 in medium long eyes (24.50 – 25.99 mm). They concluded that SRK/T and Holladay 1 (3rd generation) formulae provided highly accurate outcomes in medium-long eyes with SRK/T yielding the lowest root mean square absolute error (RMSAE) and median absolute error (MedAE). Both Aristodemou et al. (2011) and Kane et al. (2016) compared the accuracy of IOL formulae in medium and medium-long eyes and found that the IOL formula with the best accuracy could be used in both medium and medium-long eyes. Nevertheless, future studies could compare the accuracy of the IOL formulae in both medium and medium-long eyes to determine the best IOL formula. However, the range of axial lengths for medium-long eyes would need to be explored further as different studies used different axial lengths for medium-long eyes.

As Singapore is comprised of different ethnic groups with Chinese, Malay and Indian ethnicities making up of the majority of the population, this study aimed to evaluate the accuracy of IOL formulae in the 3 different ethnic groups using applanation biometry. However, due to the small sample size of the Malay and Indian ethnic groups, this study only analysed the data retrieved from the Chinese ethnic group. The small sample size collected might be due to the stringent criteria of the post-operated best corrected visual acuity of 20/25 (6/7.5) whereas Ozcura et al. (2015) used post-operated BCVA of 20/40 (6/12) as their inclusion criteria and Amita et al. (2022) used post-operated BCVA of 5/7.5 (20/30) (6/9) as their inclusion criteria. However, Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but yet, they did not have a vision that is worse than 20/25 (6/7.5).

IOL Models

In this study, different types of IOL were used such as AR40, AABOO, SA60AT, MX60, SN60WF, and ZCB00. The influence of the different models of IOL affecting the accuracy of the various IOL formulae is not evaluated due to the small number of some IOL models implanted in this study. However, Jiang et al. (2022) compared the accuracy of various IOL formulae for two monofocal hydrophobic foldable lenses, the AcrySof SN60WF and the Tecnis ZCB00 and found that there were no significant differences in the formula accuracy between these two lenses in medium eyes for all formulae namely, Barrett Universal II, Haigis, Hoffer Q, Holladay 2 and SRK/T. However, they found that the accuracy decreased in short eyes for some formulae and decreased significantly in long eyes for ZCB00 compared to SN60WF. With newer IOL models emerging in the market, it might be worthwhile to evaluate the accuracy of the various IOL formulae for the different IOL models.

Utilization of Mean Absolute Error (MAE) in a non-Gaussian Distribution

In this study, the mean absolute error (MAE) was used instead of mean prediction error (MPE) during statistical analysis as the latter can lead to erroneous results due to cancellation during summation (Kuthirummal et al., 2020). Hoffer et al. (2021) recommended to utilize MedAE as a primary outcome instead of MAE due to the not-normal distribution of absolute refractive prediction error.

Despite the recommendation made by Hoffer et al. (2021), there were many studies that utilize MAE as a primary outcome instead of MAE (Zhao et al., 2018) (Hipólito-Fernandes et al., 2020)

(Kuthirummal et al., 2020) (Jiang et al., 2022). Future studies could evaluate and compare the accuracy of IOL formulae using MAE and MedAE to determine if there is any difference in the accuracy of IOL formulae in their study population.

Optimization of A-Constant

In this study, the recommended A-constant provided by the Manufacturer for Hoffer Q, SRK-T, Haigis, Holladay 1, Barrett Universal II formulae were used. Moshirfar et al. (2023) had commented that optimization is critical to studies that compare IOL formulae as the optimized constants involved adjusting each formula's arithmetic mean error (AME) as close to zero as possible to eliminate existing systematic errors prior to statistical analysis. Moshirfar et al. (2023) also commented that optimizing the A-constant for each formula to make AME for formulae equal to zero might not be possible if the IOL formula is not publicly available for individualized lens constant optimization method and that some IOL formulae might require advanced computer programming software, to which the surgeon might not have the access and time to optimize the constant to each IOL formula for each patient before the cataract surgery.

Due to the possibility of the unavailability of the A-constant, there were some studies (Kane et al., 2016) (Pereira et al., 2021) (Moshirfar et al., 2023) that evaluated and compared the accuracy of IOL formulae where some of the A-constant in the IOL formulae were optimized and some were not optimized. This approach might introduce bias to the study during the analysis as this will not be a fair comparison and evaluation of the accuracy of the IOL formulae. Future studies should aim to optimize the A-constants in all the IOL formulae in order to have a fairer comparison between them.

Anterior Chamber Depth measurements

The ACD measurements used in this study was captured using IOLMAster 500 V.7.7. (Carl Zeiss-Meditec, Jena, Germany) instead of Alcon Ocuscan RxP (Alcon Laboratories, Texas, U.S.A.). Hence, the IOL power was calculated using the ACD measurements captured by the optical biometer (IOLMaster 500) instead of the applanation biometer (Alcon Ocuscan RxP). The positioning of the ultrasound probe on the cornea during the measurement of AL, could cause corneal indentation (Olsen, 2007). However, would this affect the ACD measurement?

Previous studies have reported that every 1 mm erroneous measurement of anterior chamber depth (ACD) can result in 1.5 D of refractive error which contributed to 42% of error when compared to AL and corneal power (K) (Olsen, 2007). Eom et al. (2014) and Jeong et al. (2017)

concluded that the preoperative ACD was the key factor in the accuracy of various formulas, even in eyes with the same K and AL.

As such, Dong et al. (2018) compared the axial length (AL), anterior chamber depth (ACD) and IOL power of IOLMaster and Ultrasound in normal, long and short eyes. In their studies, they found that the ACD measurements of the IOLMaster were higher than Ultrasound in each group, and a statistically significant differences were found in the normal and short eye group. Hashemi et al. (2005) also found that Ultrasound measured a significantly lower ACD compared to IOLMaster. However, Elbaz et al. (2007) found that the Ultrasound measured a higher significantly higher ACD compared to IOLMaster. Hence, future studies could investigate the influence of ACD measurement captured by both optical biometer and applanation biometer on the accuracy of the various IOL formulae.

3.5 CONCLUSION

The purpose of this study was to examine the accuracy of 6 IOL formulae (SRK/T, Hoffer Q, Haigis, Holladay 1, Barrett Universal II and EVO 2.0) in Chinese eyes with medium axial lengths (22.00 to 25.99 mm) where the AL was measured using applanation biometry. In this study, it was found that SRK/T has the smallest MAE, followed by Barrett Universal II, EVO 2.0, Holladay 1, Hoffer Q and Haigis and that SRK/T, Barrett Universal II, EVO 2.0 and Holladay 1 formulae can be used interchangeably when generating the predicted residual errors of the various IOL formulae in Chinese patients with axial lengths between 22.00 and 25.99 mm.

This study showed that good refractive outcomes can be achieved with SRK/T, Barrett Universal II and EVO 2.0 formulae. These 3 IOL formulae had a prediction error of ±0.50DS or less in at least 70.7% of the Chinese eyes, and a prediction error of ±1.0DS or less in at least 93.2% of the Chinese eyes in this study. This is well within the benchmark standard determined for National Health Services, United Kingdom (55% of prediction error within ±0.5D and 85% of prediction error within ±1.0D) (Kithirummal et al., 2020).

This study showed that good refractive outcomes can be achieved with SRK/T, Barrett Universal II, EVO 2.0 and Holladay 1 formulae. These 4 IOL formulae had a prediction error of ±0.50DS or less in at least 69.2% of the Chinese, Malay and Indian eyes, and a prediction error of ±1.0DS or less in at least 93.2% of the Chinese, Malay and Indian eyes in this study. Surprisingly, all the 6 IOL formulae (SRK/T, Barrett Universal II, EVO 2.0, Holladay 1, Hofer Q and Haigis) had a prediction error of ±0.50DS or less in at least 59.4% of the Chinese, Malay and Indian eyes, and a prediction error of ±1.0DS or less in at least 91.7% of the Chinese, Malay and Indian eyes in this study. This is well within the benchmark standard determined for National Health Services, United Kingdom (55% of prediction error within ±0.5D and 85% of prediction error within ±1.0D) (Kithirummal et al., 2020).

SUB-STUDY 2

CHAPTER 4 EVALUATION OF THE ACCURACY OF IOL FORMULAE WITH THE INCLUSION AND EXCLUSION OF ANTERIOR CHAMBER DEPTH MEASUREMENTS

4.1 INTRODUCTION

Intraocular lens formulae have evolved over the years where the 1st generation theoretical formula had assumed that the position of the IOL is fixed, resulting in the usage of a fixed A-constant in their formulae. Since then, the position of IOL implant has changed from the anterior chamber to the posterior chamber of the eye and the evolvement of the 2nd generation formula was necessary to account for the IOL implant position. Since the position of the IOL has changed to the posterior chamber, the usage of a fixed A-constant was deemed as not suitable anymore. As such, the 2nd generation formulae were designed by combining linear regression analysis with stepwise adjustments for long and short eyes. Modifications of A-constants to the 2nd generation formulae was deemed necessary as the fixed-ACD model had predicted ACDs that were too short in long eyes and too deep in short eyes. This resulted in a myopic error in a short eye and a hyperopic error in the long eye (Olsen, 2007) (Xia et al., 2020). However, one of the drawbacks of A-constant was that A-constant is greatly affected by the manufacturer as well as the surgeon's personal surgical technique ELP (Olsen, 2007) (Chen et al., 2015) (Amro et al., 2018). Hence, this led to the evolvement of the third generation formula.

The third generation theoretical formulae were different from the previous generations as they were based on thin lens optical principles (Hoffer, 1993). The third generation IOL formulae require the axial length (AL) and corneal curvature (K) to predict the estimated lens plane (ELP) without the ACD measurement. In order to estimate the position where the IOL is placed postoperatively, ELP has been formulated to replace A-constant. The ELP is defined as the estimated postoperative distance between the anterior corneal surface and the principal plane of a thin IOL (as if the lens was of infinite thickness). A principle determinant of IOL power estimation error is the inaccurate prediction of the ELP (Olsen, 2007) (Chen et al., 2015) (Amro et al., 2018).

Fourth generation formulae took into the consideration of the preoperative ACD for better prediction of the ELP, and any change in ACD measurement after posterior IOL implantation can influence IOL power calculation (Moschos et al., 2014) (Chen et al., 2015) (Amro et al., 2018).

The fifth generation formulae or the latest generation formulae include Barrett Universal II where incorporation of the principle plane or ray tracings techniques are used to derive the IOL power (Gokce et al., 2017) (Xia et al., 2020).

Barrett Universal II

The Barrett Universal II formula is based on a combination of a theoretical and regression model; the theoretical model is conceived as the intersection of two spheres, a corneal sphere and a global sphere at whose junction the iris root is located. The point of intersection is determined by the axial length, the peripheral radius of curvature of the posterior cornea, and the radius of the globe. The regression model predicts the distance from the iris root to the second principal plane of the lens denoted by an individualized lens constant known as the lens factor (Khatib et al., 2021).

The Barrett Universal II formula is based on paraxial ray tracing (Gaussian/thick lens), considers the effective lens position to be a result of the ACD and a lens factor associated with the physical position and locations of the principal planes of the IOL. It also takes into account the change in the principle planes encountered with different powered IOLs. It has the option to use up to 5 variables consisting of axial length (AL), keratometry (K), anterior chamber depth (ACD), lens thickness (LT), and White-To-White (WTW). However, AL, K and ACD (measured from epithelium to lens) are sufficient to generate the IOL powers from the Barrett Universal II formula (Reitblat et al., 2017) (Rong et al., 2019) (Sanchez-Linan et al., 2023).

Emmetropia Verifying Optical 2.0

The emmetropia verifying optical (EVO) 2.0 formula (unpublished) developed by Dr Tun Kuan Yeo, is based on the theory of emmetropization of the eye. This formula generates an “emmetropia factor” for each eye and takes into account of the optical dimensions of the eye for different IOL geometry and powers (Khatib et al., 2021).

Previous studies have reported that every 1 mm erroneous measurement of anterior chamber depth (ACD) can result in 1.5 D of refractive error which contributed to 42% of error when compared to AL and corneal power (K) (Olsen, 2007). Eom et al. (2014) and Jeong et al. (2017) concluded that the preoperative ACD was the key factor in the accuracy of various formulas, even in eyes with the same K and AL. Eom et al. (2014) suggested that in eyes with short AL and shallow ACD, the accuracy of predicted refractions based on ACD was higher than without considering ACD in eyes.

Accurate prediction of the postoperative effective lens position (ELP) deriving from axial length, keratometry and anterior chamber depth might be the key to achieving a good visual outcome with the least residual refractive error postoperatively. Traditional vergence formulae performed poorly in estimating ELP whereas 5th generation IOL formulae such as Barrett Universal II and EVO 2.0 had shown good results (Chang et al., 2023).

In order for an accurate prediction of the postoperative refractive error, newer generation IOL formulae deemed the computation of anterior chamber depth measurement to be necessary. Traditional vergence formulae performed poorly in estimating ELP, resulting in a less satisfactory outcome whereas 5th generation IOL formulae such as Barrett Universal II and EVO 2.0 had shown good results (Chang et al., 2023).

As the 5th generation IOL formulae such as Barrett Universal II and EVO 2.0 were more advanced, some authors began to question the need of ACD measurement in the 5th generation IOL formulae (Savini et al., 2021).

Savini et al. (2021) compared the accuracy of 13 formulae (Barrett Universal II, Emmetropia Verifying Optical 2.0, Haigis, Hoffer Q, Holladay 1, Holladay 2AL, Kane, Næser 2, Pearl- DGS, RBF 2.0, SRK/T, T2 and VRF) for IOL power calculation in 200 eyes. However, they also included Barrett Universal II without anterior chamber depth (ACD) as a predictor as well as EVO 2.0 without ACD as a predictor. In their study, they found that the MedAE for both Barrett Universal II with the inclusion and exclusion of ACD was the same and the exclusion of ACD for Barrett Universal II achieved a smaller MAE than with the inclusion of ACD. They also found that exclusion of ACD in EVO 2.0 had achieved a smaller MedAE as well as MAE than with the inclusion of ACD in EVO 2.0. The authors concluded that all the investigated formulae (Barrett Universal II, Emmetropia Verifying Optical 2.0, Haigis, Hoffer Q, Holladay 1, Holladay 2AL, Kane, Næser 2, Pearl- DGS, RBF 2.0, SRK/T, T2 and VRF) achieved good results and there was a tendency towards better outcomes with newer formulas. The exclusion of ACD in both Barrett Universal II and EVO 2.0 led to better results than with the inclusion of ACD in both Barrett Universal II and EVO 2.0. However, this study was not without limitations. The optimization of the A-constant was not carried out for all the IOL formulae. Some of the lens constant for the IOL formulae used in the study was optimized and some were not optimized. This approach might introduce bias to the study during the analysis as this will not be a fair comparison and evaluation of the accuracy of the IOL formulae. The biometry measurements were captured using Nidek AL-Scan (software V.1.03) in this study. Hoffer et al. (2016) conducted a study to investigate the agreement between the ocular biometry measurements captured by AL-Scan (Nidek Co, Ltd., Gamagori, Japan) and IOLMaster 500 (Carl Zeiss Meditec, Jena Germany). They found that the AL-Scan measured a deeper ACD by 0.13 mm, which was statistically significant ($p < .001$).

Previous studies have reported that every 1 mm erroneous measurement of anterior chamber depth (ACD) can result in 1.5 D of refractive error which contributed to 42% of error when compared to AL and corneal power (K) (Olsen, 2007). Eom et al. (2014) and Jeong et al. (2017) concluded that the preoperative ACD was the key factor in the accuracy of various formulas, even in eyes with the same K and AL. Eom et al. (2014) suggested that in eyes with short AL and shallow ACD, the accuracy of predicted refractions based on ACD was higher than without considering ACD in eyes. Jeong et al. (2017) showed that the preoperative ACD demonstrated the greatest influence on the IOL calculation formulas. Ning et al. (2019) assessed the ACD changes and their relationship with the refractive errors (REs) after phacoemulsification and intraocular lens (IOL) implantation in patients with age-related cataracts and suggested that the ACD played an important role in predicting postoperative RE after cataract surgery. Hence, the biometry measurements captured using the AL-Scan might contribute to the difference in results when compared to other studies.

Aim of this sub-study

The importance of ACD measurements have been emphasized by Olsen (2007), Eom et al. (2014) and Jeong et al. (2017). However, there might be occasions where the ACD measurements are unable to capture using partial coherence interferometry (PCI) such as IOLMaster 500 V.7.7. (Carl Zeiss-Meditec, Jena, Germany) and this might affect the accuracy of the IOL formulae.

As such, this chapter aims to evaluate and compare the accuracy of the 5th generation IOL formulae in the event that ACD measurements are impossible to obtain. In this chapter, the accuracy of the Barrett Universal II formula with the inclusion of ACD and without ACD measurements would be determined. The accuracy of the EVO formula with the inclusion of ACD and without ACD measurements would also be determined in this chapter.

4.2 METHODOLOGY

Study Design and Participant Recruitment

This study was reviewed and approved by the JurongHealth Campus Research Ethics Committee and the NHG DOMAIN SPECIFIC REVIEW BOARD (DSRB) (Appendix 1). The research protocol of this study adhered to the tenets of the Declaration of Helsinki. Aston University Ethics Committee gave a waiver because local ethics was in place.

This is the first database retrospective study that examined the accuracy of various IOL formulae in different axial length groups of various ethnic groups in Singapore. As this is a database retrospective study, informed consent was not obtained from the participants.

As per the Ophthalmology Department's protocol in Jurong Medical Centre, all patients consented to cataract operations are required to undergo a series of test procedures which include pre-operative biometry measurements.

All preoperative biometric measurements were measured using partial coherence interferometry (PCI). PCI device software (IOLMaster 500, version 7.7.; Carl Zeiss Meditec, Jena, Germany) was used for measurement of AL, ACD (distance from corneal epithelium to anterior lens surface), average K, and horizontal corneal diameter. The IOLMaster 500 is calibrated every day as part of the routine checks when the equipment is switched on. Calculation for Barrett Universal II and EVO formulae were accessed online from their respective websites.

As part of the pre-operative assessment, besides the biometry measurements, endothelial cell count (ECC) measurement was also performed for all patients. If the ECC was less than 1,500, patients were not allowed to have their cataract operations conducted in the medical centre. Instead, they would have their cataract operations performed in other institutions.

Phacoemulsification is performed by the surgeons and different IOL models such as AR40, AABOO, SA60AT, MX60, SN60WF, and ZCB00.

Subjective manifest refraction was performed for all patients undergoing cataract operations 1 month postoperatively as part of the routine protocol for patients undergoing cataract operations. Subjective manifest refraction was performed by qualified optometrists who underwent competency checks annually as mandated by the institution.

Recruitment, Criteria and Eligibility

This research will involve all patients undergoing cataract operation in Jurong Medical Centre from January 2018 to December 2019. The starting date for the study was chosen due to the purchase of IOL Master 500 in the centre and all patients underwent biometry measurements using IOL Master 500 since January 2018. Due to the outbreak of COVID in early 2020, all elective surgeries including cataract operations in the centre were put on hold since March 2020. Hence, all patients who underwent cataract operation in the centre from January 2018 to December 2019 had their records retrieved for analysis.

The patient will be included if they meet the inclusion criteria of 1) underwent cataract operation in Jurong Medical Centre from 01 January 2018 to 31 December 2019, 2) no other eye abnormalities except cataract, 3) post-operative subjective refraction best corrected visual acuity of 6/7.5 or better, and 4) monofocal IOL was implanted, 5) 1 month post operation details such as subjective refraction was available.

The patient will be excluded if 1) post cataract operation adverse events such as Irvine Gass Syndrome occurred, 2) patient’s case records were incomplete such as no postoperative subjective refraction was recorded, 3) best corrected visual acuity (BCVA) of 20/30 (6/9) or worse postoperatively, 4) toric, multifocal or accommodative IOL was implanted, 5) other eye surgeries such as epi-retinal membrane surgery was conducted together with the cataract operation, 6) previous refractive surgery.

Data Analysis

A minimum sample size of 94 eyes was calculated with G*Power (version 3.1.9.7, Franz Faul, Universität Kiel, Germany) with a significance level of $\alpha = 0.05$, power of 0.80, and an effect size of 0.30. The mean prediction error (MPE) and the mean absolute error (MAE) were calculated to evaluate the accuracy of each IOL formula. The differences in absolute error between formulae were assessed using the Friedman test. In the event of a significant result, post-hoc analysis was undertaken using the Wilcoxon signed-ranks test with Bonferroni correction for multiple comparisons of the IOL formulae. A p value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS Statistics 29.0 (IBM, Armonk, North Castle, New York, United States).

4.3 RESULTS

Five hundred and fifty eyes were included in the study. The demographic details and biometric data of the study eyes are listed in Table 15.

Table 15 Preoperative biometry data of the 550 study subjects

Demographics	Mean (± SD)	Range
Age	67.60 ± 6.87	47.67
Axial length (mm)	24.17 ± 1.48	9.19
Anterior Chamber Depth (ACD)	3.13 ± 0.4	1.96
Average Keratometry (dioptre)	44.21 ± 1.55	9.64

In order to evaluate the accuracy of each IOL formula, we calculated the mean prediction error (MPE) and the mean absolute error (MAE). The MPE was defined as the average of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula. The MAE was defined as the average of the absolute values of the difference between the actual postoperative refractive error and the estimated refractive error by each IOL formula.

Barrett Universal II

For the Barrett Universal II formula, it was found that the MAE was smaller in Barrett Universal II without ACD measurements than with ACD measurements of 0.3303D and 0.3351D respectively (Table 16).

Table 16 Mean prediction error (MPE) and mean absolute error (MAE) for Barrett Universal II formula with inclusion and exclusion of ACD measurement.

	MPE (D) Mean ± SD	MAE (D) Mean ± SD
Barrett Universal II with ACD measurements	-0.0267 ± 0.4471	0.3351 ± 0.2969
Barrett Universal II without ACD measurements	-0.0546 ± 0.4429	0.3303 ± 0.2998

Shapiro-Wilks Normality Test is used to determine the distribution of the data. The test rejects the hypothesis of normality when the *p*-value is less than or equal to 0.05.

The Shapiro-Wilks test is used to determine the distribution of the MPE of the Barrett Universal II IOL formula (Table 17) where it revealed a non-Gaussian distribution.

Table 17 Shapiro-Wilks normality test in Barrett Universal II formula

	Statistic	df	Sig.
Barrett Universal II with ACD measurements	0.977	550	<.001*
Barrett Universal II without ACD measurements	0.977	550	<.001*

In this study, Friedman's test did not reveal a statistically significant difference result for Barrett Universal II formula with the inclusion and exclusion of ACD measurements (p = 0.792). A nonparametric Wilcoxon Signed-Ranks Test was also used to further determine the accuracy of Barrett Universal II formula with and without ACD measurements. It was found that there was no statistically significant difference (p = 0.293) between the accuracy of Barrett Universal II formula with the inclusion and exclusion of ACD measurements in the calculation for the prediction of residual refractive errors.

Emmetropia Verifying Optical 2.0

For Emmetropia Verifying Optical (EVO) 2.0 formula, it was found that the MAE was smaller in EVO 2.0 without ACD measurements than with ACD measurements of 0.3303D and 0.3351D respectively (Table 18).

Table 18 Mean absolute error (MAE) for EVO 2.0 formula with inclusion and exclusion of ACD measurement.

	MPE (D) Mean ± SD	MAE (D) Mean ± SD
EVO 2.0 with ACD measurements	0.0155 ± 0.4425	0.3331 ± 0.2913
EVO 2.0 without ACD measurements	0.0154 ± 0.4388	0.3296 ± 0.2898

Shapiro-Wilks Normality Test is used to determine the distribution of the data. The test rejects the hypothesis of normality when the *p*-value is less than or equal to 0.05.

The Shapiro-Wilks test is used to determine the distribution of the MPE of the EVO 2.0 formula (Table 19) where it revealed a non-Gaussian distribution.

Table 19 Shapiro-Wilks normality test in Emmetropia Verifying Optical 2.0 formula

	Statistic	df	Sig.
EVO 2.0 with ACD measurements	0.975	550	<.001*
EVO 2.0 without ACD measurements	0.978	550	<.001*

In this study, Friedman’s test did not reveal a statistically significant difference result for Emmetropia Verifying Optical 2.0 formula with the inclusion and exclusion of ACD measurements (p = 0.792). A nonparametric Wilcoxon Signed-Ranks Test was also used to further determine the accuracy of Emmetropia Verifying Optical 2.0 with and without ACD measurements. It was also found that there was no statistically significant difference (p = 0.332) between the accuracy of Emmetropia Verifying Optical 2.0 formula with the inclusion and exclusion of ACD measurements in the calculation for the prediction of residual refractive errors.

4.4 DISCUSSION

In this chapter, it was found that both the 5th generation IOL formulae, Barrett Universal II and EVO 2.0 showed comparable results with the inclusion and exclusion of ACD measurements in the IOL calculation. This result supported the findings of Savini et al. (2021). Savini et al. (2021) postulated that the AL-Scan might be the reason that both the Barrett Universal II and EVO 2.0 formulae with the exclusion of the ACD showed better results in their studies, possibly due to a different technology used to measure this parameter as Hoffer et al. (2016) had found that the AL-Scan measured a deeper ACD than IOLMaster 500 by 0.13 mm, which was statistically significant ($P < .001$). However, this sub-study used IOLMaster 500 to capture the biometry data of the participants. And this sub-study found that the exclusion of ACD measurements in both Barrett Universal II and EVO 2.0 showed better results than with the inclusion of ACD measurements, which coincided with Savini et al. (2021).

Savini et al. (2021) found that the 3rd and 4th generation IOL formulae were as accurate as the newer generation IOL formulae. Their findings were similar to this main study's results where SRK/T, Barrett Universal II and EVO 2.0 could be used interchangeably to calculate the IOL power for medium eyes. The inclusion criteria of post-operative BCVA 20/25 (6/7.5) might be one of the contributing factors for this result. Most studies included post-operative BCVA 20/40 (6/12) as one of the inclusion criteria. However, a post-operative BCVA of 20/25 (6/7.5) might be a more reasonable choice as Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but they did not have a vision that is worse than 20/25 (6/7.5). Hence, future studies could compare the accuracy of the IOL formulae for post-operative BCVA of 20/25 (6/7.5) with 20/40 (6/12).

Further research is needed in order to establish the importance of ACD in the calculation of the IOL formulae especially in newer generation IOL formulae.

Limitations of the study

There are however, some limitations in this study. They include the optimization of A-constants and the utilization of MAE to evaluate the accuracy of each IOL formula in a non-Gaussian distribution.

Utilization of Mean Absolute Error (MAE) in a non-Gaussian Distribution

In this study, the mean absolute error (MAE) was used instead of mean prediction error (MPE) during statistical analysis as the latter can lead to erroneous results due to cancellation during summation (Kuthirummal et al., 2020). Hoffer et al. (2021) recommended to utilize MedAE as a primary outcome instead of MAE due to the non-Gaussian distribution of absolute refractive prediction error.

Despite the recommendation made by Hoffer et al. (2021), there were many studies that utilize MAE as a primary outcome instead of MAE (Zhao et al., 2018) (Hipólito-Fernandes et al., 2020) (Kuthirummal et al., 2020) (Jiang et al., 2022). Future studies could evaluate and compare the accuracy of IOL formulae using MAE and MedAE to determine if there is any difference in the accuracy of IOL formulae in their study population.

Optimization of A-Constant

In this study, the recommended A-constant provided by the Manufacturer for Hoffer Q, SRK-T, Haigis, Holladay 1, Barrett Universal II formulae were used. Moshirfar et al. (2023) had commented that optimization is critical to studies that compare IOL formulae as the optimized constants involved adjusting each formula’s arithmetic mean error (AME) as close to zero as possible to eliminate existing systematic errors prior to statistical analysis. Moshirfar et al. (2023) also commented that optimizing the A-constant for each formula to make AME for formulae equal to zero might not be possible if the IOL formula is not publicly available for individualized lens constant optimization method and that some IOL formulae might require advanced computer programming software, to which the surgeon might not have the access and time to optimize the constant to each IOL formula for each patient before the cataract surgery.

Due to the possibility of the unavailability of the A-constant, there were some studies (Kane et al., 2016) (Pereira et al., 2021) (Moshirfar et al., 2023) that evaluated and compared the accuracy of IOL formulae where some of the A-constant in the IOL formulae were optimized and some were not optimized. This approach might introduce bias to the study during the analysis as this will not be a fair comparison and evaluation of the accuracy of the IOL formulae. Future studies should aim to optimize the A-constants in all the IOL formulae in order to have a fairer comparison between them.

4.5 CONCLUSION

This sub-study found that the predicted refractive errors with the inclusion or exclusion of ACD measurements in either the Barrett Universal II or EVO 2.0 formulae did not prove to be of a difference. In fact, the exclusion of ACD measurements in both the Barrett Universal II and EVO 2.0 gave a better result than with the inclusion of ACD measurements. This finding might assure the surgeons that in the event of the absence of ACD measurements in the IOL formulae calculation in Barrett Universal II and EVO 2.0, the predicted residual errors would be similar to one where ACD measurements are available.

CHAPTER 5 GENERAL DISCUSSION

The research objective in this thesis was to evaluate and compare the accuracy of 6 IOL formulae (SRK/T, Hoffer Q, Haigis, Holladay 1, Barrett Universal II and EVO) in medium axial lengths (22.00 to 25.99 mm) with regards to the diverse population (Chinese, Malay and Indian ethnic groups) in Singapore.

There are a lot of studies that examined the accuracy of IOL formulae in the Western population. However, as Singapore is made up of various ethnic groups, one may wonder if there would be a difference in the choice of the IOL formulae in the Asian population? Would ethnicity influence the choice of IOL formulae for different axial lengths?

There are different ethnic groups in Singapore, with Chinese, Malay and Indian being the majority. The accuracy of IOL formulae in the Chinese, Malay and Indian ethnic group had been studied by various researchers. However, there has been limited information regarding the accuracy of IOL formulae in these 3 ethnic groups, especially for the medium axial length (22.0 to 25.99 mm). As such, this study examined the accuracy of IOL formulae in medium axial length with regards to the diverse population in Singapore.

In this study, it was found that SRK/T, Barrett Universal II and EVO 2.0 formulae could be used interchangeably when predicting the IOL powers for all ethnic groups in Singapore such as Chinese, Malay and Indian if their axial lengths are within the medium axial length range (22.00 to 25.99 mm). This study supported Savini et al. (2021) whom found that the older generation IOL formulae (Haigis, Hoffer Q, Holladay 1, Holladay 2AL and SRK/T) were as accurate as the newer generation IOL formulae (Barrett Universal II, Emmetropia Verifying Optical 2.0, Kane, Næser 2, Pearl- DGS, RBF 2.0, T2 and VRF). However, these findings differed to that of Kane et al. (2016) whom found that Barrett Universal II formula had a lower absolute error than the other 6 formulae (Hoffer Q, Holladay 1, SRK/T, Haigis, Holladay 2, and T2) in the medium AL group which comprised of 2638 eyes and statistically significant when compared to SRK/T. This discrepancy could be due to the inclusion criteria for post-operated BCVA of 20/25 (6/7.5) which is a stringent criteria when compared to most studies which also evaluated the accuracy of the IOL formulae. In this study and Savini et al. (2021), a post-operated BCVA of 20/25 (6/7.5) was included as the inclusion criteria where Radner et al. (2019) found that individuals with healthy eyes may be expected to have better than 20/20 (6/6) vision until 64 years old and for the individuals aged 65 to 74 years old, their vision might be worse than those from 25 to 64 years old but they did not have a vision that is worse than 20/25 (6/7.5). This study found that SRK/T was as accurate as Barrett Universal II and EVO 2.0 formulae in the calculation of the IOL power. This result was similar to Savini et al. (2021) where they also found that the 3rd and 4th generation IOL formulae were as accurate as the newer generation IOL formulae. The inclusion criteria of post-operative BCVA

20/25 (6/7.5) might be one of the contributing factors for this result. Most studies included post-operative BCVA 20/25 (6/7.5) as one of the inclusion criteria. Future studies could compare the accuracy of the IOL formulae for BCVA 20/25 (6/7.5) and 20/40 (6/12).

The popularity and accuracy of the partial coherence interferometer such as IOLMaster had gained traction in axial length measurements. However, IOLMaster does have its pitfalls. Accurate measurements require that the infrared laser be able to pass through the eye and return to the interferometer. Lee et al. (2008) had reviewed various studies in their study and reported that 8-20% of patients cannot be measured with optical biometry due to poor fixation, dense cataract or corneal pathology. With the emergence of newer generation IOL formulae, one would wonder which IOL formula would achieve the best visual outcome with the least residual post-operative refractive errors. However, due to the popularity of partial coherence interferometers, the reviewed applanation biometry studies had limited IOL formulae being studied with the focus on the 3rd generation formulae. Hence, it is necessary to evaluate and compare the accuracy of the various newer generation IOL formulae with the older generation IOL formulae with the use of applanation biometry.

In this sub-study, it was found that SRK/T has the smallest MAE, and that SRK/T, Barrett Universal II, EVO 2.0 and Holladay 1 formulae can be used interchangeably when generating the predicted residual errors of the various IOL formulae. Due to the limited reviewed applanation biometry studies focussing on the 3rd generation IOL formulae, this sub-study showed that SRK/T formula was as accurate as the 4th and 5th generation IOL formulae in generating IOL powers. However, due to the limited data retrieved, only participants in the Chinese ethnic group were being analysed. Further studies could examine the accuracy of the newer generation formulae with the use of applanation biometry.

With the emergence of 5th generation IOL formulae that did not use traditional vergence formula in the calculation and generation of IOL powers, one would wonder if the exclusion of the anterior chamber depth would affect the accuracy of the IOL formulae as the inclusion of ACD was deemed as one of the crucial parameters. As such, a sub-study that evaluated the accuracy of the IOL formulae with the inclusion and exclusion of ACD measurements was carried out. Surprisingly, in this sub-study, it was found that the predicted refractive errors with the inclusion or exclusion of ACD measurements in either the Barrett Universal II or EVO 2.0 formulae did not prove to be of a difference. This finding could act as an assurance to the surgeons that in the event of the absence of ACD measurements in the IOL formulae calculation, the predicted residual errors would be similar to one where ACD measurements are available. In fact, this sub-study found that the exclusion of ACD in Barrett Universal II and EVO 2.0 gave better results when compared to the inclusion of ACD in both IOL formulae. This study coincided with the findings of Savini et al. (2021). Future studies could examine the influence of ACD measurements in newer generation IOL formulae. Possibly, the exclusion of ACD measurements could generate a better result in the accuracy of the newer generation IOL formulae.

CHAPTER 6 CONCLUSION

The research objective in this thesis was to evaluate and compare the accuracy of the various generations such as 3rd, 4th and 5th generation IOL formulae in the Singapore population which comprises of different ethnic groups mainly Chinese ethnic group, Malay ethnic group and Indian ethnic group with different modes of measurement such as partial coherence interferometry (PCI) as well as applanation biometry. It also aims to evaluate the importance of the anterior chamber depth in 5th generation IOL biometry.

With the emergence of newer equipment such as IOLMaster 700 and immersion biometry, not all institutions have the luxury to trade their equipment to the latest models of biometers. Hence, this study attempted to evaluate and compare the accuracy of IOL formulae using the “outdated” equipment.

In this thesis, it was found that SRK/T, Barrett Universal II and EVO 2.0 formulae can be used interchangeable in the calculation of IOL powers in the medium axial length group in the different ethnic groups in Singapore.

However, there are some limitations in the study.

One, the small sample size retrieved from the various ethnic groups might contribute to a bias in the study. Due to the small sample size retrieved for the Malay and Indian ethnic groups, both ethnic groups were grouped together and analysed under “Non-Chinese” group. Due to the small sample size retrieved, the comparison of the accuracy of the IOL formulae could not be carried out for short axial length group and long axial length groups. Hence, the increase in sample size might help to reduce the sample bias in future studies.

Second, participants could be recruited to have their axial length measured using both PCI and applanation biometry. A comparison between 2 different modes of biometers might enrich our knowledge in the evaluation and comparison of the different IOL formulae especially in the newer generation IOL formulae.

Third, with the emergence of newer IOL formulae, it might be worthwhile to study the various ocular parameters that are necessary in the calculation of the IOL powers. The exclusion of the ACD measurements in 5th generation IOL formulae (Barrett Universal II and EVO 2.0) did not affect the accuracy of the IOL formulae in predicting the residual post-operative refractive errors. In fact, the exclusion of the ACD measurements gave a better result in the accuracy of the IOL formulae in predicting the residual post-operative refractive errors. However, this could be also due to the newer calculation methods of the IOL formulae that resulted in this study. Hence, this could be of interest to surgeons in determining the crucial ocular parameters that are necessary to provide the best visual outcome after cataract operation.

In conclusion, the present study shows that SRK/T, Barrett Universal II and EVO 2.0 formulae could be used interchangeably in determining the IOL powers in the population studied. These 3 formulae could be used to generate IOL formulae either by partial coherence interferometer or applanation biometer. The inclusion or exclusion of anterior chamber depth measurements in both Barrett Universal II and EVO 2.0 formulae did not seem to be crucial when generating the IOL powers.

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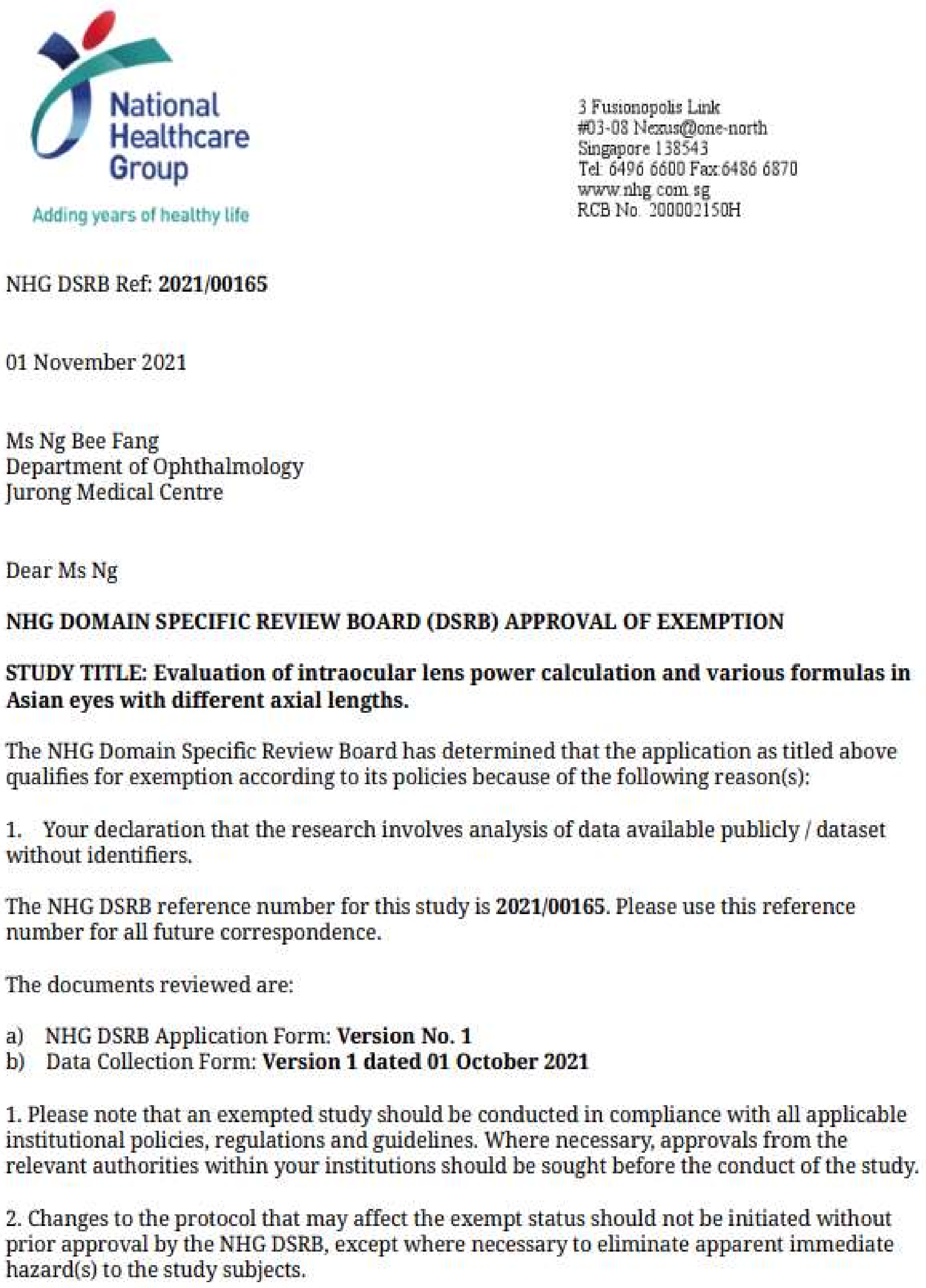
APPENDIX

Appendix 1: Ethics Approval



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NHG DSRB Ref: **2021/00165**

01 November 2021

Ms Ng Bee Fang
Department of Ophthalmology
Jurong Medical Centre

Dear Ms Ng

NHG DOMAIN SPECIFIC REVIEW BOARD (DSRB) APPROVAL OF EXEMPTION

STUDY TITLE: Evaluation of intraocular lens power calculation and various formulas in Asian eyes with different axial lengths.

The NHG Domain Specific Review Board has determined that the application as titled above qualifies for exemption according to its policies because of the following reason(s):

1. Your declaration that the research involves analysis of data available publicly / dataset without identifiers.

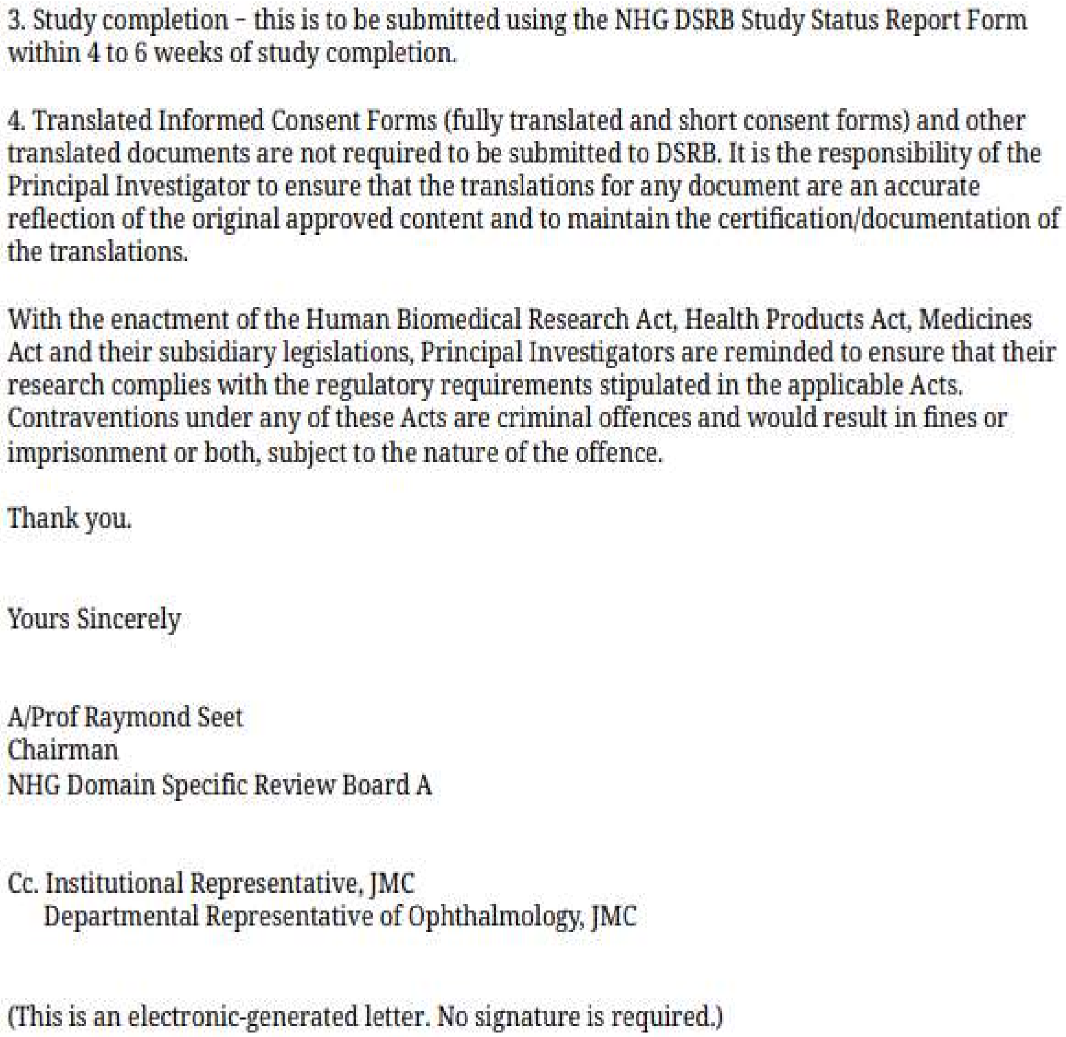
The NHG DSRB reference number for this study is **2021/00165**. Please use this reference number for all future correspondence.

The documents reviewed are:

a) NHG DSRB Application Form: **Version No. 1**
b) Data Collection Form: **Version 1 dated 01 October 2021**

1. Please note that an exempted study should be conducted in compliance with all applicable institutional policies, regulations and guidelines. Where necessary, approvals from the relevant authorities within your institutions should be sought before the conduct of the study.

2. Changes to the protocol that may affect the exempt status should not be initiated without prior approval by the NHG DSRB, except where necessary to eliminate apparent immediate hazard(s) to the study subjects.



3. Study completion – this is to be submitted using the NHG DSRB Study Status Report Form within 4 to 6 weeks of study completion.

4. Translated Informed Consent Forms (fully translated and short consent forms) and other translated documents are not required to be submitted to DSRB. It is the responsibility of the Principal Investigator to ensure that the translations for any document are an accurate reflection of the original approved content and to maintain the certification/documentation of the translations.

With the enactment of the Human Biomedical Research Act, Health Products Act, Medicines Act and their subsidiary legislations, Principal Investigators are reminded to ensure that their research complies with the regulatory requirements stipulated in the applicable Acts. Contraventions under any of these Acts are criminal offences and would result in fines or imprisonment or both, subject to the nature of the offence.

Thank you.

Yours Sincerely

A/Prof Raymond Seet
Chairman
NHG Domain Specific Review Board A

Cc. Institutional Representative, JMC
Departmental Representative of Ophthalmology, JMC

(This is an electronic-generated letter. No signature is required.)