Unadjusted versus adjusted intraocular pressure for central corneal thickness in healthy Congolese subjects

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Abstract

Background: Central corneal thickness (CCT) affects intraocular pressure (IOP) measurement. Available formulas for adjusting IOP for CCT are derived from Caucasian populations. It remains unknown whether these formulas are readily applicable to populations with thin corneas such as people from sub-Saharan Africa (SSA).

Purpose: To compare uncorrected and corrected IOP using existing reference CCT values and Congolese reference CCT value and to assess the relationship of CCT with uncorrected and corrected IOP.

Methods: IOP and CCT were measured in 556 healthy eyes (278 subjects). IOP was corrected with original Kohlhaas', Ehlers', Shah's, and Dresden's formulas and after substituting the reference CCT with the Congolese reference CCT value. Comparisons were made between uncorrected and corrected IOPs and between corrected IOPs under the two paradigms. IOP-CCT relationship was assessed with simple linear regression.

Results: Uncorrected IOP was significantly lower than corrected IOPs obtained with the four original formulas (all $P<0.001$) but did not differ from corrected IOPs obtained using the Congolese reference CCT value ($P = 0.07$-0.69). The proportions of eyes with significant IOP change after correction with the original vs. the Congolese versions of the formulas were 0/10 vs. 0/10 (Kohlhaas), 6/10 vs. 2/10 (Ehlers, $P<0.001$), 4/10 vs. 1/10 (Shah, $P<0.001$), and 2/10 vs 0/10 (Dresden, $P<0.001$). Uncorrected IOP increased non-significantly by 0.27 mmHg per 100 µm thickening of central cornea ($P = 0.48$).

Conclusions: The lack of difference between uncorrected and corrected IOPs after substituting the standards with the Congolese reference CCT and the small proportion of eyes with significant IOP change after correction suggest the IOP adjustment is not necessary.

Keywords: Adjusted intraocular pressure, central corneal thickness, sub-Saharan Africa.

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Introduction

Central corneal thickness (CCT) is an important clinical information that assists the clinician in the stratification of risks and the diagnosis, treatment, and management of several ocular conditions. CCT affects Goldmann applanation tonometry (GAT) by yielding erroneously lower intraocular pressure (IOP) values on thinner and higher IOP values on thicker central corneas.[1,2] Thin central cornea is a known risk factor for glaucoma development and may influence the decision to initiate treatment when other risk factors are present.[3-7] CCT is equally valuable as an indicator of overall corneal health. It may help diagnose and monitor keratoconus and predict the outcome of refractive surgical procedures. Refractive procedures, including laser in situ keratomileusis, photorefractive keratotomy, and small incision lenticule extraction, are known to yield lower postoperative IOP readings than they are, meaning they lead to IOP underestimation because of change both in the corneal structure, thickness, and biomechanics.[8-10]

IOP underestimation in these circumstances had prompted researchers to develop various formulas to adjust IOP readings for CCT to approximate correct IOP values. While there is a general agreement that GAT IOP readings are affected by CCT, the clinical usefulness and applicability of IOP correction in real world have long been controversial, particularly in glaucoma.[11-13] Among the reasons for opposing the correction are (1) the fact that the corrected IOP is still an estimate rather than the true IOP value because in addition to CCT, true IOP is dependent on other corneoscleral factors, and (2) it remains unclear which of the numerous formulas is best.[14] It is important to note that available formulas use various reference CCT values ranging between 520 and 550 µm derived from populations with thick corneas.[15-17] Because of interracial and interethnic differences in CCT, it is not clear if correction factors derived from these formulas are readily applicable to populations with thin corneas such as people from sub-Saharan Africa (SSA). In fact, Doughty and Zaman[18] wondered whether the correction they proposed in their meta-analysis (2-3 mmHg per 50 µm change in CCT, with 535 µm as reference value) is applicable in non-White subjects. Recently, Sharma *et al.*[12] used the South Indian reference CCT and found a significant difference between correction factors obtained with the 'White' and South Indian reference CCTs. They suggested that ethnicity-specific reference CCT should be used for IOP correction. Additionally, it is not known if IOP correction is necessary in these eyes with thin CCT. The purpose of this study was twofold: (1) to compare uncorrected and corrected GAT IOP for CCT using existing reference CCT values and Congolese reference CCT value and (2) to assess the relationship of CCT with both uncorrected IOP.

Methods

Subjects

Participants were recruited among consecutive outpatients attending the eye clinic, medical personnel, and administrative staff of the University Hospital of Kinshasa. All subjects included were 10 years or older, had a normal cornea on biomicroscopic examination, and a refraction between -5 and +3 spherical diopters and less than 3 cylindric diopters. Exclusion criteria were current or past corneal pathology or surgery, contact lens wear or any type of glaucoma. In addition, those with a history of systemic or ocular conditions and any treatment that may affect the cornea were also excluded.

Central corneal thickness and intraocular pressure measurements

CCT was measured in both eyes with a non-contact specular microscope (Topcon Corporation, Tokyo, Japan). The value used was the average of three consecutive measurements. Two IOP measurements IOP was measured quantified with a Goldmann applanation tonometer. Corrected IOP for CCT was obtained for each eye using the following four correction formulas:

1. Kohlhaas:[8] Corrected IOP = measured GAT IOP+(540-measured CCT)/71)+(43 -K)/2.7)+0.75.
   Because keratometry was not performed in the present study, we used 43.3 D as a mean value of keratometry readings found in Nigeria[19] and South Africa.[20]
2. Ehlers:[15] Corrected IOP = measured GAT IOP+[5 mmHg*(545-measured CCT)/70)]
3. Shah:[17] Corrected IOP = measured GAT IOP+0.05*(550- measured CCT)
4. Dresden:[16] Corrected IOP = measured GAT IOP+0.04*(550-measured CCT)

For comparison purposes, corrected IOP was also computed with these formulas using 504.2 µm as the reference mean CCT for this same population, based on our previous report.[21] Eyes were stratified using what is labeled in this study as 'international into those with thin (<449 µm), normal (449-556 µm) and thick (≥557 µm).[21]

Statistical analysis

Statistical analyses were run using SPSS version 27.0. Uncorrected and corrected mean IOPs were compared with paired Student t-test in the whole group of eyes and after stratifying eyes into those with thin, average, and thick central corneas using the two classifications described above. Although there is no consensus on the minimum cutoff of absolute IOP change considered significant after correction, values from 1.5 to 3 mmHg and 20% or higher of uncorrected IOP have been suggested.[22] For this study we arbitrarily chose 2.5 mmHg as the cutoff for significant change, regardless of the direction of the change. The proportions of eyes with significant IOP change derived from the two versions of each formula were compared with Pearson chi-squared test. Simple linear regression was performed to determine the relationship between CCT and uncorrected as well as corrected IOP. For all statistical analyses, the level of significance was set at $P<0.05$.

Ethical considerations

Ethical clearance to conduct this study was granted by the Ethics Committee of the Institutional Review Board at the School of Public Health of the University of Kinshasa. The study execution abided to the tenets of the Declaration of Helsinki and all participants provided written informed consent after the study protocol had been explained to them.

Results

Subjects' demographic and clinical attributes

Two hundred and seventy-eight subjects (556 eyes) were studied. The demographic and clinical features have been described previously.[21] Briefly, age ranged from 10.9 to 80.7 years with a mean of 38.9 ± 17.2 years. Thirty-one subjects (11.5%) were younger than 18 years old. Males (43.9%) and females (56.1%) were comparable in age, IOP, spherical equivalent refraction, cup-to disc ratio, ocular prefusion pressure, weight, systolic blood pressure, and diastolic blood pressure ($P > 0.05$ for all), but the former were significantly taller and gad a lower body mass index than the latter ($p < 0.001$ for all).

Uncorrected vs. corrected IOP and proportion of eyes with significant IOP change

Data in *Table I* show that corrected mean

Table I: Comparison between uncorrected* and corrected IOP for central corneal thickness

Correction formula	$cIOP_1$	P_1	$cIOP_2$	P_2
Overall				
Kohlhaas	15.4 ± 2.8	<0.001	14.6 ± 2.8	0.07
Ehlers	17.2 ± 3.4	<0.001	14.3 ± 3.4	0.69
Shah	16.6 ± 3.0	<0.001	14.3 ± 3.1	0.68
Dresden	16.0 ± 2.9	<0.001	14.3 ± 3.0	0.67

*Uncorrected IOP = 14.3 ± 2.8 mmHg; IOP: intraocular pressure; cIOP: corrected intraocular pressure; $cIOP_1$: corrected intraocular pressure for CCT using original CCT reference values; $cIOP_2$: corrected intraocular pressure for CCT using Congolese reference value; P_1: significance level of the difference between $cIOP_1$ and cIOP; P_2: significance level of the difference between $cIOP_2$ and cIOP

Table II: Proportion of eyes with significant change after IOP correction with various formulas using original and Congolese reference CCT values.

Correction formula	Cutoff of significant IOP change			
	≥1.5 mmHg	≥2 mmHg	≥2.5 mmHg	≥3 mmHg
Kohlhaas				
Original	98 (17.6%)	8 (1.4%)	4 (0.7%)	0 (0%)
Congolese	8 (1.4%)	4 (0.7%)	0 (0%)	0 (0%)
P	<0.0001	0.25	N/A	N/A
Ehlers				
Original	445 (80.0%)	395 (71.9%)	339 (61.0%)	276 (49.6%)
Congolese	243 (43.7%)	170 (30.6%)	124 (22.3%)	79 (14.2%)
P	<0.0001	<0.0001	<0.0001	<0.0001
Shah				
Original	413 (74.3%)	330 (59.4%)	241 (43.3%)	162 (29.1%)
Congolese	157 (28.2%)	92 (16.6%)	56 (10.1%)	27 (4.9%)
P	<0.0001	<0.001	<0.0001	<0.0001
Dresden				
Original	352 (63.3%)	241 (43.4%)	139 (25.0%)	79 (14.2%)
Congolese	107 (19.2%)	56 (10.1%)	22 (4.0%)	15 (2.7%)
P	<0.0001	<0.0001	<0.0001	<0.0001

IOP: intraocular pressure; CCT: central corneal thickness

IOP values obtained with all four formulas using the original reference mean CCT values were significantly higher than the uncorrected mean IOP (P < 0.001 for all). On the contrary, corrected mean IOPs computed using the Congolese mean reference CCT were all comparable to the uncorrected mean IOP (P > 0.05 for all).

The proportions of eyes with significant IOP change after correction with each formula using the original and the Congolese mean reference CCT values are given in *Table II*. Using Ehlers', Shah's, and Dresden's correction formulas with the Congolese mean reference CCT, the proportions of eyes with significant IOP change (≥2.5 mmHg) were 0%, 22.3%, 10.1%, and 4%, respectively. No eyes showed significant IOP change with both versions of Kohlhaas' formula. These proportions were significantly lower than 61%, 43.3%, and 25.0%, respectively, yielded by the same formulas using the original mean reference CCT values (P < 0.0001 for all). Similar observations were made with these four adjustment formulas when the cutoff for significant IOP change after correction was ≥1.5, ≥2, and ≥3 mmHg.

Magnitude of IOP change after correction

The trend and magnitude of the true change in IOP (negative or positive) after correction with each formula is depicted in *Figure 1*. Application of the Kohlhaas' adjustment formula with the original reference CCT value resulted in IOP change ranging between -0.07 and 2.85 mmHg (n = 552 with positive and four with negative change). The IOP change range shifted down (-0.58 to 2.35 mmHg) and

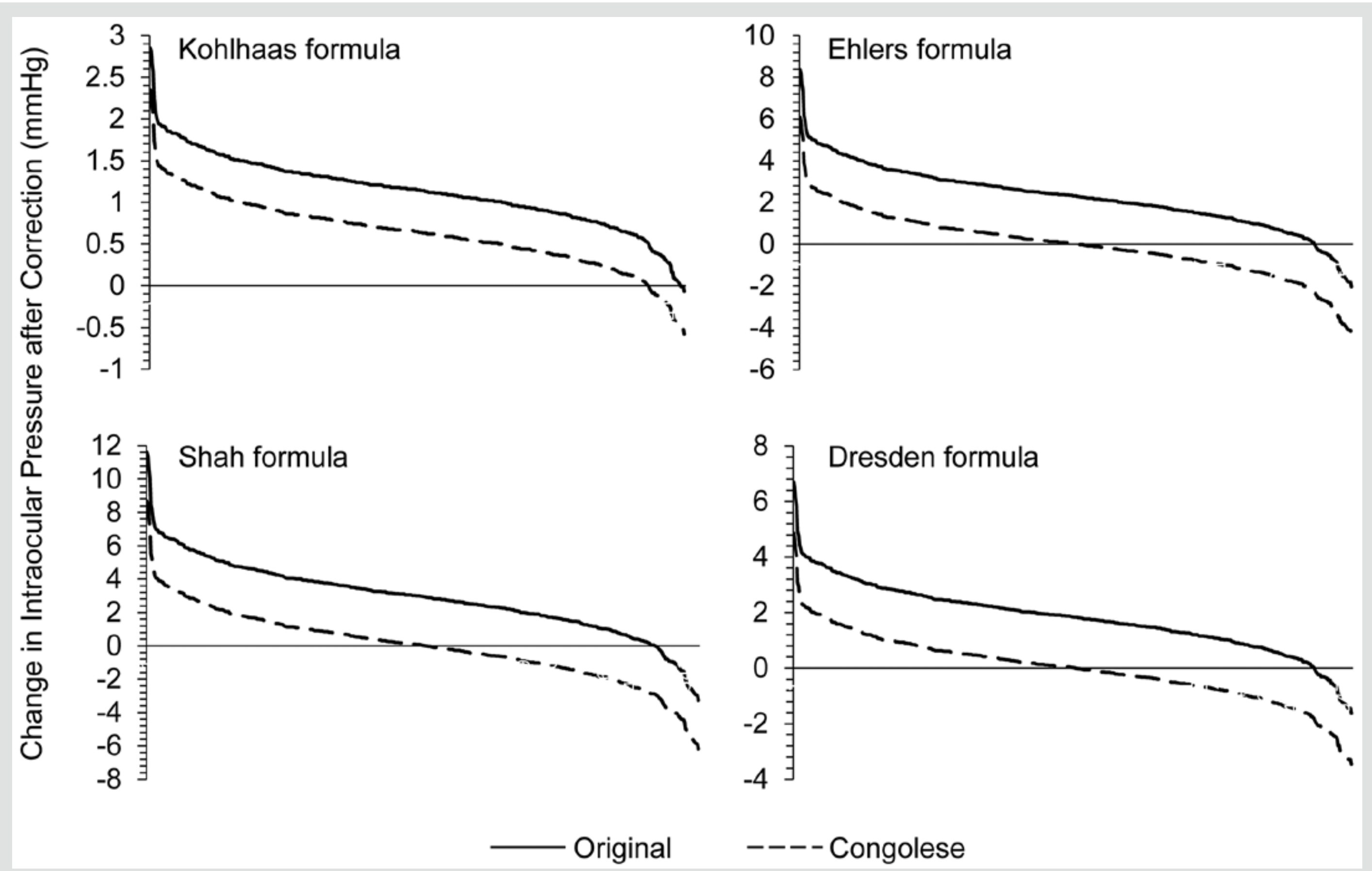

Figure 1. Trend and magnitude of the change in IOP after adjustment with original and Congolese version of Kohlhaas', Ehlers, Shah's and Dresden's formulas.

was associated with a slight decrease in the number of eyes with positive change in IOP (n = 518) and an increase in those with negative change (n = 38) when the Congolese reference CCT value was used. Ehlers' original formula yielded the widest IOP change range (-3.26 to 11.6 mmHg), with 512 eyes registering positive change, 43 eyes negative change and one eye no change. These numbers were -6.18 to 8.68 mmHg, 281 eyes with positive and 275 eyes with negative IOP change after using the Congolese reference CCT value. Original versions of Shah's and Dresden's adjustment formulas produced similar numbers of eyes with positive (n = 518), negative (n = 37) and no change (n = 1) in IOP. They also yielded the same number of eyes with positive (n = 281) and negative change (n = 275) in IOP when the Congolese versions were used. The change in IOP that resulted from the original and the Congolese versions of Shah's and Dresden's formulas ranged from -2.03 to 8.37 mmHg and -4.32 to 6.08 mmHg, and from -1.63 to -6.69 mmHg and -3.46 to 4.86 mmHg, respectively.

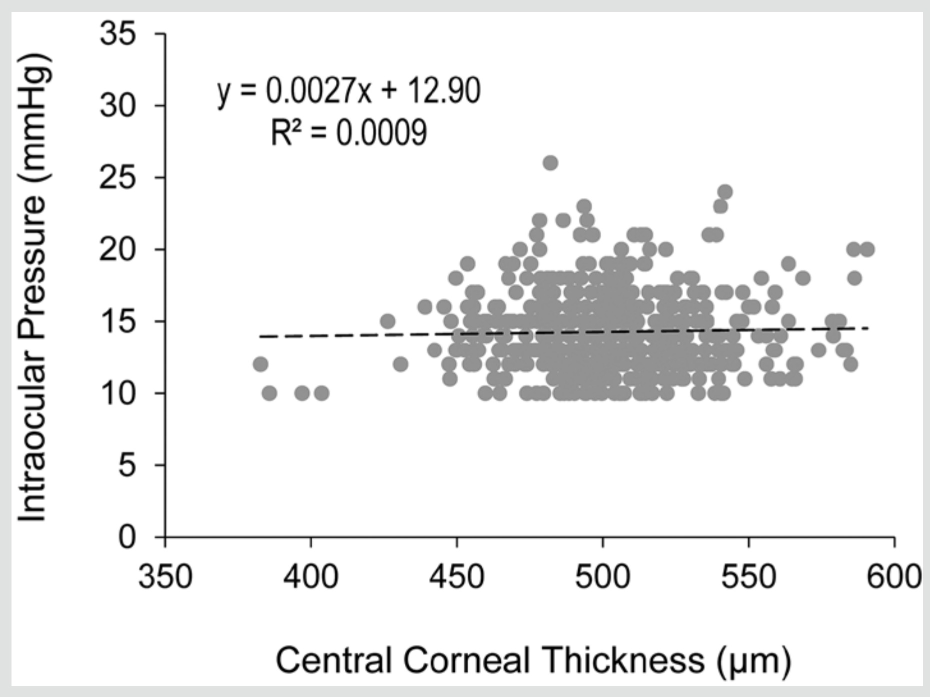

Figure 2. Simple linear regression plots of the relationship between CCT and uncorrected IOP.

IOP correction in thin, normal and thick corneas

Corrected IOP values computed with the original and the Congolese version of the four formulas were also compared after stratifying eyes into those with thin, average, and thick central cornea *(Table III)*. There were no significant differences between mean IOP values obtained with the two versions of all four formulas in eyes with thin, average and thick central cornea (P > 0.05 for all), except that both Ehlers' and Shah's formulas generated significantly higher corrected IOPs (all P ≤ 0.0001) with the original (12.6 ± 2.6 and 13.5 ± 2.7 mmHg, respectively) than the Congolese version (9.5 ± 2.5 and 10.9 ± 2.6 mmHg, respectively).

Table III: Corrected intraocular pressure using international vs. Congolese reference central corneal thickness values stratified into thin, average and thick

Correction formula	$cIOP_1$	$cIOP_2$	P
Thin CCT			
Kohlhaas	15.6 ± 2.7	14.4 ± 2.1	0.15
Ehlers	17.8 ± 3.1	18.3 ± 1.9	0.52
Shah	16.9 ± 2.9	16.6 ± 1.9	0.69
Dresden	16.4 ± 2.8	15.9 ± 1.8	0.47
Normal CCT			
Kohlhaas	14.4 ± 3.1	15.0 ± 2.8	0.19
Ehlers	13.9 ± 3.2	14.4 ± 3.3	0.23
Shah	14.2 ± 3.1	14.4 ± 3.0	0.55
Dresden	14.1 ± 3.1	14.4 ± 2.9	0.49
Thick CCT			
Kohlhaas	14.9 ± 2.8	14.0 ± 2.7	0.20
Ehlers	12.6 ± 2.6	9.5 ± 2.5	<0.001
Shah	13.5 ± 2.7	10.9 ± 2.6	0.001
Dresden	13.8 ± 2.7	12.3 ± 2.6	0.058

IOP: intraocular pressure; $cIOP_1$: corrected intraocular pressure using original central corneal thickness reference values; $cIOP_2$: corrected intraocular pressure using Congolese reference value; CCT: central corneal thickness

Relationship between CCT and IOP

Regression analysis indicated that uncorrected IOP increased in a nonsignificant manner by 0.27 mmHg on average per 100 µm increase in CCT (P = 0.48) *(Figure 2)*.

Discussion

GAT provides an indirect estimate of IOP and requires corneal contact. Therefore, it can be influenced by CCT and other corneal biomechanical attributes. Consequently, various nomograms have been proposed for GAT reading adjustment. However, the usefulness of IOP adjustment for CCT has been controversial. Doughty and Zaman[18] performed a meta-analysis and confirmed that GAT readings are low in eyes with thin and high in those with thick central corneas. Interestingly, they wondered whether the correction factor they proposed (2-3 mmHg for each 50 µm change in CCT with a reference of 535 µm) would be applicable in non-Caucasian subjects. Nearly a quarter century later, this important question has remained unexplored. In the present study, we compared uncorrected and corrected IOP for CCT and assessed the relationship between IOP and CCT. Unlike previous studies, the uniqueness of the present investigation is to have been conducted exclusively in black Africans, in whom CCT is known to be thinner than in people of European and Asian descents.

Use of the formulas with the proposed reference CCT values generated significantly higher IOPs than the uncorrected mean IOP. This finding is understandable since most eyes in the present study had thinner corneas than standard references used in those formulas, and therefore, IOP required upward adjustment. Correcting IOP this way in this population would suggest that the proposed formulas should be used universally. However, it is worth noting that CCT is genetically inherited[23-25] and varies across races and even across ethnic groups within a given population.[26-32] Although the true prevalence of glaucoma in the DRC in unknown due to the lack of population-based studies, kit is only assumed that it is higher than reported in Caucasians. Thus, since the correction resulted in higher IOP values, the possibility of an association between these values and a high prevalence of glaucoma in this population cannot be ruled out. Per our observations, a CCT value that falls within normal range in a healthy Congolese subject may be lower than normal if compared to Caucasians reference values. For this reason, reference CCT values proposed in the original formulas should be adapted if needed. As proof of concept, use of the same formulas with the Congolese reference CCT value revealed no difference between uncorrected and corrected mean IOPs, suggesting no need for correction. This was also corroborated by the lack of significant difference between mean corrected IOPs computed using the original and the Congolese reference CCT values. Sharma *et al.*[12] studied IOP correction for CCT in 200 eyes of 100 glaucoma suspects. They compared corrected mean IOP obtained with 520 µm as the South Indian population reference CCT value[33] and 545 µm derived from the meta-analysis of 80 studies conducted by Doughty and Zaman.[18] Contrary to our findings, the mean IOP corrected for South Indian reference CCT was significantly lower than the mean IOP corrected for Doughty and Zaman's reference CCT. Compared to their study, ours is unique in that it tested four different formulas rather than only one. Because there is no true CCT value to use as reference point universally, it is challenging to assess the accuracy of any of the formulas and all the measurements derived from their use.

It was interesting to note that, apart from Ehlers' and Shah's formulas in thick corneas, mean IOPs corrected using the original reference CCT and the Congolese reference using Kohlhaas and Dresden formulas did not differ regardless of whether the cornea was classified as thin, normal, or thick based on Congolese normative values. This further confirmed that IOP adjustment for CCT is not necessary.

Uncorrected GAT IOP increased non-significantly by 0.27 mmHg per 100 µm increase in CCT in the present study, which approximates the rate of 0.4 mmHg per 100 µm reported in a Nigerian population,[34] but is far lower than rates ranging between 1.6 and 6.1 mmHg per 100 µm reported in clinical-based studies outside SSA.[15,16,31,35-41] It is also lower than 1.3 to 2.4 mmHg per 100 µm found in population-based studies.[42-44]

After IOP correction, the four standard formulas yielded higher proportions of eyes with significant IOP change after substituting the standard CCT with the Congolese reference CCT. In essence, these findings as shown in *Table II* reflect 1) the inconsistency between results yielded by the four formulas, 2) the impact of the CCT value used as reference on the proportion of eyes with significant IOP change, and 3) the continuous difficulty of deciding which formula is accurate. Ultimately, because the present study was conducted in healthy eyes, there is no ground to believe that IOP correction is needed within the Congolese context. For example, out of 10 eyes, the number of eyes that fell outside our cutoff of significant IOP change after correction was 0 with Kohlhaas', 2 with Ehlers', 1 with Shah's, and 0 with Dresden's formula. The smaller proportion of eyes with significant IOP change after substituting the standard with the Congolese reference CCT is in line with the suggestion that the effect of CCT on IOP is small and likely insignificant in most patients.[40]

This study has shortcomings. The findings cannot be applied to eyes with pathologies like glaucoma because only healthy eyes were studied. Thus, the clinical relevance of the effect of the CCT on IOP in glaucomatous eyes in this population will need to be assessed. Our findings may also not be generalisable because CCT distribution in the clinical setting may differ from that in the general population. We also acknowledge that other corneal factors that may influence IOP (i.e. hysteresis, corneal curvature) were not studied. However, the findings provide a foundation to inspire more studies of this nature in eyes with constitutional thin corneas. Lastly, while one may argue that our findings may not be compared to those on IOP correction that used ultrasonic pachymetry, it is important to note that the key factor for applying these formulas is to use IOP measured with Goldmann aplanation tonometry rather than the method used to measure CCT.

In conclusion, our findings shed light on the relationship between CCT and IOP in normal eyes of Congolese with thin corneas. Even though GAT IOP was affected by change in CCT, the magnitude of the change did not differ between uncorrected and corrected IOP using the Congolese CCT reference value. Additionally, the proportion of eyes with significant IOP change after correction was small. For these reasons, our findings suggest that adjusting IOP readings based on individual CCT is not necessary in this population.

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