1 Association between ocular biometrical parameters and diabetic retinopathy in
2 Chinese adults with type 2 diabetes mellitus

3

4 **Running title:** Ocular biometry parameters and DR

5

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31 Abstract

32 **Purpose:** To investigate the association between ocular biometrical parameters and
33 diabetic retinopathy (DR) in ocular treatment naive patients with diabetes.

34 **Methods:** This cross-sectional study recruited type 2 diabetes mellitus patients with
35 no history of ocular treatment in Guangzhou, China. The ocular biometrical
36 parameters were obtained by Lenstar, including corneal diameter, central corneal
37 thickness (CCT), corneal curvature (CC), anterior chamber depth (ACD), lens
38 thickness (LT), and axial length (AL). The lens power and axial length-to-cornea
39 radius ratio (AL/CR ratio) were calculated. Spherical equivalent (SE) was determined
40 by auto-refraction after pupil dilation. Multivariate logistic regression analyses were
41 performed to explore the associations of ocular biometry with any DR and vision
42 threatening DR (VTDR).

43 **Results:** A total of 1838 patients were included in the final analysis, involving 145
44 5(79.2%) patients without DR and 383(20.8%) patients with DR. After adjusting
45 confounding factors, any DR was independently associated with AL (OR = 0.84 per 1
46 mm increase, 95%CI: 0.74, 0.94), lens power (OR = 0.9951 per 1 D increase, 95%CI:
47 0.9904, 0.9998), and AL/CR ratio (OR = 0.26 per 1 increase, 95%CI: 0.10-0.70).
48 Similarly, the presence of VTDR was independently related to AL (OR = 0.67 per 1
49 mm increase, 95%CI: 0.54-0.85), lens power (OR = 0.99 per 1 D increase, 95%CI:
50 0.98, 0.997), and AL/CR ratio (OR = 0.04 per 1 increase, 95%CI: 0.01, 0.25). The CC,
51 corneal diameter, and refractive status were not significantly correlated with presence
52 of DR or VTDR.

53 **Conclusion:** Longer AL, deeper ACD, higher lens power, and higher AL/CR ratio
54 may be protective factors against DR. Considering the high prevalence of myopia in
55 the Chinese juvenile population, it is worth paying attention to how the incidence of
56 DR in this generation may change over time.

57

58 **Keywords:** diabetic retinopathy; myopia; axial length; AL/CR ratio; ocular biometry

59

60

61 **Introduction**

62 Diabetic retinopathy (DR) is a common cause of visual impairment in the
63 working-age population.¹ However, the pathogenesis of DR still remains unclear.
64 Systemic risk factors for DR (e.g. course of diabetes, blood glucose and blood
65 pressure) have broadly drawn the attention of investigators; however, few studies
66 have focused on ocular risk factors.² Prevalence of myopia increased significantly in
67 the last decades globally, especially become epidemic in some Asian regions.³ It was
68 found however in clinical practice that diabetic patients with myopia are less likely to
69 suffer from severe DR.⁴ A small number of clinical studies and epidemiological
70 studies have suggested that myopia could be a protective factor against DR; however,
71 this conclusion remains controversial.⁴⁻⁷

72
73 Whether the ocular structure or the refracting media, or both, contribute to the
74 protective relationship is still under debate. Several studies have evaluated the
75 association of axial length (AL), myopia and refracting media in cases of DR.⁶⁻¹⁰
76 However, the investigators have not yet reached a consensus on the implications of
77 these results. Similarly, the association of the anterior chamber depth (ACD), lens,
78 cornea curvature (CC) and AL/CR ratio with the risk of DR was elusive.^{9, 11}
79 Furthermore, the majority of previous studies were conducted no further subdivision
80 to exclude the influence of potential confounding factors including age, sex,
81 glycaemic level, and history of cataract surgery, which may bias the results.¹² Thus,
82 the which component of the ocular biometrical parameter contribute to the association
83 between myopia and DR remains unclear.

84
85 The influence of myopia and ocular biometry parameters on the occurrence and
86 progression of DR needs further clarification; therefore, the objective of this study
87 was to investigate the association between ocular biometrical parameters and DR
88 assessed in a large sample size of patients with type 2 diabetes mellitus (T2DM).

90 **Methods**

91 **Subjects**

92 This cross-sectional study was performed at Zhongshan Ophthalmic Centre (ZOC),
 93 Sun Yat-sen University, China. The protocol of the study was approved by the
 94 Institute Ethics Committee of ZOC and the study was performed according to the
 95 guidelines of the Helsinki Declaration. All subjects gave their informed written
 96 consent prior to enrolling in the study. Individuals aged 30 to 85 who were diagnosed
 97 with T2DM without ocular treatment history were recruited from the local
 98 government diabetes registry system. Exclusion criteria were as follows: (1) history of
 99 serious systemic diseases except for diabetes, such as serious cardiovascular and
 100 cerebrovascular diseases, malignant tumour, renal diseases; (2) history of systemic
 101 surgery such as coronary artery bypass graft, thrombolytic therapy and renal
 102 transplant; (3) presence of cognitive impairment, mental disorders, or inability to
 103 complete the questionnaire and examination; (4) history of ocular surgical
 104 interventions, such as retinal laser, intraocular injection, glaucoma surgery, cataract
 105 surgery, or laser myopia surgery; and (5) abnormal refractive media (severe cataract,
 106 corneal ulcer, pterygium, or corneal turbidity), poor fixation and other conditions
 107 resulting in poor quality of the fundus images.

109 **Procedures and definitions**

110 A detailed questionnaire was used to collect the subjects' demographic data, lifestyle
 111 risk factors, medical history and medication history. Outpatient medical records were
 112 reviewed to confirm details of medical history. All subjects underwent complete
 113 ocular examinations, including visual acuity, intraocular pressure (IOP), slit lamp
 114 examination, fundus examination, auto refraction, ocular biometric measurement,
 115 fundus photography, OCT and OCTA. The right eye was examined first in all eye
 116 examinations. Best corrected vision acuity (BCVA) were measured using ETDRS
 117 LogMAR E charts (Precision Vision, Villa Park, Illinois, USA) at a distance of 4 m.
 118 The IOP was measured with a noncontact tonometer (CT-1 Computerized Tonometer,
 119 Topcon Ltd., Topcon). The anterior and posterior segments were examined with a slit
 120 lamp bio-microscope (BQ-900, Haag-Streit, Switzerland) and a 90 D indirect

ophthalmoscope.

Refraction errors were measured with an auto refractometer (KR-8800; Topcon, Japan), and spherical equivalent (SE) was calculated by adding half of the cylindrical power to the spherical power. Emmetropia was defined as SE between -0.5 and 0.5 D. Myopia, mild myopia, moderate myopia, and high myopia were defined as SE < -0.5 D, -0.5 to -3 D, -3 to -6 D, and < -6 D, respectively. Hyperopia was defined as SE > 0.5 D.¹³

Ocular biometric parameters were measured using Lenstar LS900 (Haag-Streit AG, Koeniz, Switzerland), including central corneal thickness (CCT), corneal diameter, corneal curvature (CC), anterior chamber depth (ACD), lens thickness (LT), axial length (AL). The axial length-to-corneal radius ratio (AL/CR ratio) was defined as the AL divided by the mean radius of the corneal curvature. The lens power was calculated according to the modified Bennette-Rabbetts formula.¹⁴

Pupil dilation was performed with instillation of 0.5% tropicamide plus 0.5% phenylephrine eye drops. Once the pupils were fully dilated, standardised 7-field colour retinal photographs were taken, according to criteria from the Early Treatment Diabetic Retinopathy Study (ETDRS), using a digital fundus camera (Canon CR-2, Tokyo, Japan). Diabetic retinopathy (DR) was graded according to the American Academy of Ophthalmology (AAO) International Clinical Diabetic Retinopathy Disease Severity Scale by 2 ophthalmologists.¹⁵ Any DR was defined as presence of non-proliferative DR (NPDR), proliferative DR (PDR), diabetic macular oedema (DME), or any combination; and vision threatened DR (VTDR) was defined as presence of PDR and / or DME.¹⁶

Systolic and diastolic blood pressure were measured using a blood pressure monitor (HBP-9020; OMRON, Osaka, Japan). Weight and height were measured using an automatic weight and height scale (HNN-318; OMRON), with subjects standing on

151 the scale with light clothes and no shoes on. All examinations were performed in
152 compliance with the standardisation of procedures by an experienced nurse. Body
153 mass index (BMI) was calculated as the weight (kg) divided by the square of height
154 (m). Fasting (8 hours) venous blood samples were collected and sent for analysis of
155 serum creatinine (Scr), glycosylated haemoglobin (HbA1c), total cholesterol (TC),
156 high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol
157 (LDL-c), triglyceride (TG), serum uric acid, and urine microalbuminuria (MAU) in
158 accordance with standardised procedures from a certified laboratory in China.

159

160 **Statistical analyses**

161 Only the data of worse eyes were incorporated into the analyses. The
162 Kolmogorov-Smirnov test was conducted to verify normal distribution. When
163 normality was confirmed, a t-test was carried out to evaluate the differences in
164 demographic, systemic and ocular parameters between patients with and without DR.
165 Next, Pearson's correlation analyses were conducted to assess the associations
166 between ocular components and HbA1c. Univariate and multivariate logistic
167 regression analyses were used to explore the correlations of ocular biometry and
168 diabetic retinopathy in patients with any DR or with (VTDR). Potential confounding
169 factors were first adjusted for age and sex, and then adjusted for age, sex, course of
170 T2DM, HbA1c, TC, serum Scr, serum uric acid, BMI and mean blood pressure. We
171 next investigated the dose-response relationship between AL as a continuous variable
172 and presence of DR or VTDR. We used restricted cubic splines with 5 knots located at
173 5%, 27.5%, 50%, 72.55 and 95% of the distribution of AL. All analyses were
174 performed using Stata Version 14.0 (Stata Corporation, College Station, TX, USA). P
175 value of < 0.05 was considered statistically significant.

176

177 **Results**

178 **Demographic and clinical characteristics**

179 A total of 1838 individuals were included in the final statistical analyses, involving
180 1455 (79.2%) patients without DR and 383 (20.8%) patients with DR. Table 1 shows

the demographic and clinical characteristics of the subjects. The mean age of the subjects was 64.5 ± 7.9 years, 42.7% of them were male, and the duration of diabetes was 9.0 ± 7.9 years. Of the 1455 patients without DR, 591(40.6%) were male, the average age was 64.6 ± 8.0 years, and the average course of diabetes was 8.3 ± 6.7 years. Of the 383 patients with DR, 193(50.4%) were male, the average age was 64.1 ± 7.9 years and the duration of diabetes was 11.7 ± 7.5 years. Demographically, individuals with DR had a longer course of diabetes ($P < 0.001$). In terms of systemic and ocular parameters, subjects with DR also had higher levels of HbA1c, higher mean blood pressure, higher serum creatinine level, shorter AL, smaller lens power, and smaller AL/CR ratio (all, $P < 0.05$). There were no differences in age, BMI, total cholesterol, TG, serum uric acid, CCT, CC, corneal diameter, CCT, ACD and LT (all, $P > 0.05$) between individuals with and without DR.

193

194 **Ocular biometrical components and HbA1c**

Table 2 shows the correlation between different ocular biometrical components and HbA1c levels. Both CCT and lens power were correlated with HbA1c ($r = 0.0839$, $P = 0.0014$ for CCT, $r = -0.0669$, $P = 0.0051$ for lens power), respectively. Other ocular parameters showed no correlation with HbA1c, including SE, corneal diameter, CC, AL, ACD, LT, and AL/CR ratio (all, $P > 0.05$). AL was correlated with all other ocular biometrical parameters (all, $P < 0.05$).

201

202 **Ocular biometry parameters and DR presence**

Table 3 presents the association between ocular biometry and DR after adjusting for age and sex. The results revealed that AL, LT, lens power, AL/CR ratio, and corneal diameter were all significantly correlated with DR (all, $P < 0.05$). These correlations remained statistically significant when considering VTDR as a dependent variable, with the exception for corneal diameter. However, CC, SE, CCT, and refractive status persistently showed no correlation (all, $P > 0.05$).

209

Table 4 shows the results of further adjusting for other potential confounding factors. Any DR was independently associated with AL (OR = 0.84 per 1 mm increase, 95%CI: 0.74, 0.94), lens power (OR = 0.9951 per 1 D increase, 95%CI: 0.9904, 0.9998), and AL/CR ratio (OR = 0.26 per 1 increase, 95%CI: 0.10-0.70). The ACD only showed a negative correlation with DR when taking it as a quantile. The CC, corneal diameter, and SE were not significantly correlated with presence of DR. Similarly, the presence of VTDR was significantly related to AL (OR = 0.67 per 1 mm increase, 95%CI: 0.54-0.85), lens power (OR = 0.99 per 1 D increase, 95%CI: 0.98, 0.997), and AL/CR ratio (OR = 0.04 per 1 increase, 95%CI: 0.01, 0.25) after adjusting for potential confounding factors. The ACD only showed a negative correlation with VTDR when taking it as a quantile. The CC, corneal diameter, and refractive status were not significantly correlated with presence of VTDR. Figure 1 shows the results of restrictive cubic spline regression analysis evaluating the association between AL and DR. As expect, the odds ratio for any DR and VTDR all tended to decrease as the AL lengthened.

Discussion

The DR and myopia have been increasing in prevalence in recent decades, and both contribute greatly to visual impairment. Diabetes has been linked to changes in refractive errors under hyperglycaemic conditions. It was reported that high myopia may decrease the progression of DR, even though it is associated with serious ocular complications, such as an increased risk of glaucoma, cataract, and retinal detachment.¹⁷ Myopia was highly related to the changes of ocular structure, however, which component of the ocular biometry play the major role in this relationship remains unclear. This study demonstrated that longer AL, deeper ACD, higher lens power, and higher AL/CR ratio may all be protective factors against DR and VTDR, independent of age, sex and other potentially confounding factors. However, the CC, corneal diameter, LT, refractive status or SE were not associated with DR. To the best of our knowledge, this is the first study to investigate the ocular components and DR risk in ocular treatment naïve patients with T2DM in the Chinese population.

240

241 This study found that refractive status was not associated with presence of DR.
 242 Although several small sample clinical and epidemiological studies have suggested
 243 that myopia could be a protective factor against DR, this conclusion remains
 244 controversial. Moss et al. (1994) conducted a cohort study in 1210 young diabetic
 245 patients but reported no correlation of myopia with DR and PDR in univariate
 246 analysis, while it was found that myopia may delay the progression from DR to PDR
 247 after controlling for confounding factors.¹⁸ Furthermore, Dogru et al. (1998) reported
 248 that high myopia may be a protective factor against PDR in a small sample size
 249 retrospective study.¹⁹ Bazzazi et al. (2017) compared two eyes in anisometropia and
 250 verified that high myopia could decrease the incidence of DR, and higher myopia and
 251 longer AL provided a greater protective effect.²⁰ Several studies based on the Chinese,
 252 Korean, and Singaporean population suggest that myopia is protective against PDR,
 253 but how different myopia status could influence DR was not mentioned in these
 254 studies.^{10, 21, 22} A recent longitudinal cohort study demonstrated that refractive status
 255 did not influence the incidence and progression of DR. Consistent with this cohort
 256 study, the present study indicate that different myopia status may not influence DR
 257 risk.

258

259 Longer AL was associated with lower risk for both DR and VTDR, which was
 260 consistent with previous studies. Several population-based studies suggested that AL
 261 played a different role in DR genesis and development in different ethnicities,
 262 although some contradictory results existed in literature.⁷⁻⁹ A recent cohort study of
 263 Singaporean population demonstrated that the any DR risk decreased by 42% for each
 264 1 mm increase. However, the aforementioned study reported no correlation of AL
 265 with the risk of VTDR.⁶ Considering the high prevalence of myopia in the juvenile
 266 population, it is worth keeping a watchful eye on how the incidence of DR in this
 267 generation changes over time. Further longitudinal studies with large sample size are
 268 needed.

269

270 The mechanism of the protective effect of longer AL against DR remains unclear.
 271 Several factors may play a role in this protective phenomenon. First, it was might
 272 related to the pathological alteration caused by AL that increases with the progression
 273 of myopia. This may result in a thinner retina and choroid as well as reduced blood
 274 flow in the retina.^{23, 24} The low perfusion status relatively decreases the structural
 275 damage of the retinal vessel wall, and also prevents biochemical damage caused by
 276 high glycogen accumulation. Second, oxygen demand is also decreased as the retina
 277 becomes thinner, which alleviates the retina's hypoxic status in diabetic patients.²⁵
 278 Third, posterior vitreous detachment (PVD) and synchysis may occur as myopia
 279 progresses, which enables the retina to gain oxygen from the liquefied vitreous body,
 280 resulting in a decreased rate of angiogenesis.²⁶ Fourth, alterations in cytokines could
 281 also be a potential mechanism, such as vascular endothelial growth factor, pigment
 282 epithelium-derived factor, tumor necrosis factor, erythropoietin, and TGF- β .²⁷ Further
 283 basic studies are warranted to elaborate the underling mechanism.

284

285 Both AL and corneal radius are closely related to the refractive status, with the finding
 286 that AL/CR is linearly dependent on the diopter in populations aged 40 to 64. It was
 287 also reported that AL/CR had a stronger relationship with myopia compared to other
 288 ocular biometry parameters such as AL, ACD and CC. Previous only 1 study have
 289 evaluated the influence of AL/CR ratio and lens power on risk of DR and reported
 290 that both AL/CR and lens power were related to DR, which is consistent with our
 291 results. These findings indicated that lens power and corneal refractive components
 292 also play a role in protective effects of ocular elongation against DR.

293

294 Few studies have investigated the relationship between DR and other biometrical
 295 parameters including CC, ACD, and LT. Pierro et al.²⁸ found that the LT increased in
 296 patients with insulin-dependent diabetes and the thicker LT was associated with lower
 297 risk for PDR. Another hospital-based study did not observed any correlation between
 298 LT and DR after adjusting confounding factors.²⁹ The population-based Beijing Eye
 299 Study reported that ACD was not related to presence of DR.¹¹ We found that the

300 deeper ACD was associated with lower risk of DR in when taking it as a quantile.
 301 Thus, further studies are required to verify our finding that a correlation may exist
 302 between ACD and lens thickness and DR or VTDR.

303

304 The strengths of our study include the enrolment of only ocular treatment naïve
 305 patients with T2DM, a relatively large sample size based on the community
 306 population, and fully adjusting for confounding factors. This study also has several
 307 limitations. First, the causal relationship between biometry parameters and DR could
 308 not be determined due to the inherent features of a cross-sectional study, which need
 309 to be verified in a longitudinal study. Second, the subjects in this study were all type 2
 310 diabetic patients, and the conclusion of this study needs to be confirmed in further
 311 studies with type 1 diabetic patients. Finally, the subjects were all recruited from
 312 communities in south China. Considering myopia has an ethnic heterogeneity, the
 313 generalisation of the conclusions is limited. Multi-ethnic and multi-centre studies are
 314 warranted to verify our findings.

315

316 **Conclusions**

317 This study demonstrated that longer AL, deeper ACD, higher lens power, and higher
 318 AL/CR ratio may be protective factors against DR, independent of age, sex and other
 319 potentially confounding factors. Further studies are warranted to elaborate the
 320 potential mechanisms of how the ocular biometry alterations influence DR.
 321 Considering the high prevalence of myopia in the juvenile population, it may prove
 322 beneficial to pay attention to how the incidence of DR in this generation changes over
 323 time.

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325

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332

333 **Author Contributions:** WW and WH had full access to all the data in the study and
334 take responsibility for the integrity of the data and the accuracy of the data analysis.
335 Study concept and design: WW, WL, MH, WH. Acquisition, analysis, or
336 interpretation of data: LS, YL, XG, XK, WL. Drafting of the manuscript: LS, WW.
337 Critical revision of the manuscript for important intellectual content: All authors.
338 Statistical analysis: WW. Obtained funding: WH. Administrative, technical, or
339 material support: MH, WW. Study supervision: MH.

340

341 **Conflict of Interest Disclosures:** All authors declare no conflicts of interest related to
342 this study.

343

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- 419
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- 421

422 Table legends

423 **Table 1.** Demographic and clinical features of the included patients with type 2 diabetes mellitus.

	Overall	Non-DR	Any-DR	P-value
No. of subjects	1838	1455(79.2%)	383(20.8%)	-
Gender				0.001
Male	784(57.3%)	591(40.6%)	193(50.4%)	
Female	1054(42.7%)	864(59.4%)	190(49.6%)	
Mean age, year	64.5±7.9	64.6±8.0	64.1±7.9	0.239
Duration of diabetes, year	9.0±7.0	8.3±6.7	11.7±7.5	<0.001
HbA1c, %	7.0±1.4	6.8±1.3	7.7±1.7	<0.001
Body mass index, kg/m ²	24.7±3.3	24.7±3.3	24.5±3.2	0.306
Mean BP, mmHg	182.1±23.6	180.7±23.2	187.3±24.2	<0.001
Total cholesterol, mmol/L	4.8±1.0	4.8±1.0	4.8±1.1	0.548
Triglycerides, mmol/L	2.3±1.6	2.3±1.6	2.3±1.7	0.630
Serum creatinine, µmol/L	72.9±22.7	71.4±20.1	78.6±30.1	<0.001
Serum uric acid, µmol/L	367.4±97.6	367.6±96.4	366.7±102.2	0.866
Spherical equivalent, D	0.1±4.5	-0.04±2.7	0.1±2.4	0.247
CCT, µm	546.8±31.7	546.4±31.7	548.1±31.7	0.345
Corneal diameter, mm	11.6±0.4	11.6±0.4	11.6±0.4	0.269
Corneal curvature, D	44.2±1.5	44.2±1.5	44.2±1.5	0.733
Axial length, mm	23.6±1.2	23.6±1.2	23.4±1.2	0.006
ACD, mm	2.4±0.4	2.4±0.4	2.4±0.4	0.199
Len thickness, mm	4.7±0.3	4.7±0.3	4.7±0.4	0.112
Lens power, D	-144.3±30.9	-143.4±31.8	-147.9±26.7	0.014
AL/CR ratio	3.08±0.14	3.09±0.15	3.07±0.13	0.005

424 Data were presented as mean ± standard deviation (SD).

425 DR=diabetic retinopathy; BP=blood pressure; CCT=central corneal thickness; ACD=anterior

426 chamber depth; AL/CR ratio=axial length-to-corneal radius ratio.

427 Bold indicates statistical significance.

428 **Table 2.** Correlation coefficients between ocular components and HbA1c levels.

SE									
r=-0.0359 P=0.1305	CCT								
r=-0.0422 P=0.0758	r=-0.0011 P=0.9619	Corneal diameter							
r=-0.0276 P=0.2451	r=-0.1608* P<0.001	r=-0.4953* P<0.001	Corneal curvature						
r=-0.4493* P<0.001	r=0.0889* P<0.0012	r=0.3880* P<0.001	r=-0.4577* P<0.001	AL					
r=-0.1722* P<0.001	r=-0.0606* P=0.0098	r=0.3090* P<0.001	r=-0.0076 P=0.7477	r=0.3882* P<0.001	ACD				
r=0.1266* P<0.001	r=-0.0017 P=0.9417	r=-0.0396 P=0.0949	r=-0.0346 P=0.1443	r=-0.1752* P<0.001	r=-0.5890* P<0.001	Len thickness			
r=0.5889* P<0.001	r=-0.1205* P<0.001	r=0.1244* P<0.001	r=0.1183* P<0.001	r=0.0151 P=0.5264	r=0.4523* P<0.001	r=-0.1624* P<0.001	Lens power		
r=-0.5101* P<0.001	r=-0.0207 P=0.379	r=0.0648* P=0.0058	r=0.2204* P<0.001	r=0.7656* P<0.001	r=0.4199* P<0.001	r=-0.2167* P<0.001	r=0.1048* P<0.001	AL/CR ratio	
r=-0.021 P=0.3777	r=0.0839* P<0.0014	r=-0.0062 P=0.7925	r=-0.0022 P=0.9254	r=-0.0325 P=0.1676	r=0.0028 P=0.9053	r=-0.0249 P=0.2954	r=-0.0669* P=0.0051	r=-0.0366 P=0.1209	HbA1c

429 *Bold indicates statistical significance.

430 SE=spherical equivalent; CCT=central corneal thickness; AL=axial length; ACD=anterior chamber depth; AL/CR ratio=axial length to corneal
431 curvature ratio.

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Table 3. Associations of ocular biometry and diabetic retinopathy after adjusted for age and sex.

Age and sex adjusted	Any DR		VTDR	
	OR (95%CI)	P-value	OR (95%CI)	P-value
Axial length, mm	0.82 (0.73, 0.91)	<0.001	0.65 (0.52, 0.81)	<0.001
Corneal curvature, D	1.05 (0.97, 1.14)	0.238	1.04 (0.91, 1.19)	0.571
ACD, mm	0.73 (0.53, 1.00)	0.052	0.49 (0.26, 0.92)	0.027
Len thickness, mm	1.52 (1.06, 2.18)	0.024	2.42 (1.27, 4.63)	0.007
Lens power, D	0.99 (0.99, 1.00)	0.003	0.99 (0.98, 1.00)	0.001
AL/CR ratio	0.24 (0.10, 0.61)	0.003	0.03 (0.00, 0.20)	<0.001
Spherical equivalent, D	1.04 (0.99, 1.09)	0.160	1.09 (0.99, 1.21)	0.080
Corneal diameter, mm	0.75 (0.57, 0.99)	0.041	0.64 (0.39, 1.03)	0.068
CCT, μ m	1.00 (0.997, 1.00)	0.760	1.00 (0.996, 1.01)	0.388
Refractive status				
Emmetropia	Ref		Ref	
Hyperopia	1.01 (0.69, 1.47)	0.976	0.89 (0.46, 1.72)	0.736
Mild myopia	0.80 (0.45, 1.44)	0.456	0.46 (0.15, 1.44)	0.182
Moderate myopia	0.86 (0.42, 1.76)	0.676	0.49 (0.11, 2.21)	0.351
High myopia	1.07 (0.76, 1.51)	0.710	1.20 (0.66, 2.19)	0.542

DR=diabetic retinopathy; VTDR=vision threatened DR; OR=odds ratio; 95%CI=95%

confidential interval; ACD=anterior chamber depth; CCT=central corneal thickness;

AL/CR ratio=axial length to corneal curvature ratio.

Bold indicates statistical significance.

441 **Table 4.** Multivariable adjusted models to evaluate the associations of ocular
442 biometry and diabetic retinopathy.

Multivariable adjusted*	Any DR		VTDR	
	OR (95%CI)	P-value	OR (95%CI)	P-value
AL				
Quantile 1	1.00 (Ref)		1.00 (Ref)	
Quantile 2	0.84 (0.60, 1.18)	0.324	0.83 (0.47, 1.45)	0.513
Quantile 3	0.54 (0.38, 0.78)	0.001	0.73 (0.41, 1.30)	0.280
Quantile 4	0.49 (0.33, 0.70)	<0.001	0.35 (0.18, 0.68)	0.002
Per 1-mm increase	0.84 (0.74, 0.94)	0.003	0.67 (0.54, 0.85)	0.001
Corneal curvature				
Quantile 1	1.00 (Ref)		1.00 (Ref)	
Quantile 2	1.21 (0.85, 1.71)	0.293	0.91 (0.51, 1.61)	0.744
Quantile 3	1.32 (0.93, 1.88)	0.126	0.98 (0.55, 1.76)	0.943
Quantile 4	1.17 (0.81, 1.69)	0.393	0.96 (0.53, 1.74)	0.883
Per 1-D increase	1.03 (0.95, 1.12)	0.466	1.02 (0.89, 1.17)	0.783
ACD				
Quantile 1	1.00 (Ref)		1.00 (Ref)	
Quantile 2	0.58 (0.41, 0.82)	0.002	0.62 (0.35, 1.12)	0.112
Quantile 3	0.65 (0.46, 0.92)	0.016	0.74 (0.42, 1.31)	0.302
Quantile 4	0.58 (0.40, 0.83)	0.003	0.36 (0.18, 0.71)	0.003
Per 1-mm increase	0.79 (0.56, 1.10)	0.158	0.56 (0.29, 1.07)	0.080
Lens thickness				
Quantile 1	1.00 (Ref)			
Quantile 2	1.14 (0.79, 1.64)	0.483	2.03 (1.10, 3.75)	0.023
Quantile 3	0.92 (0.62, 1.35)	0.661	1.37 (0.68, 2.74)	0.378
Quantile 4	1.31 (0.90, 1.92)	0.161	1.81 (0.90, 3.62)	0.096
Per 1-mm increase	1.32 (0.89, 1.95)	0.168	2.03 (1.04, 3.97)	0.039
Lens power				
Quantile 1	1.00 (Ref)			
Quantile 2	0.87 (0.61, 1.23)	0.418	0.71 (0.41, 1.24)	0.230
Quantile 3	0.78 (0.55, 1.11)	0.174	0.53 (0.29, 0.97)	0.039
Quantile 4	0.66 (0.45, 0.96)	0.031	0.50 (0.26, 0.95)	0.033
Per 1-D increase	0.9951(0.9904, 0.9998)	0.042	0.99 (0.98, 0.997)	0.007
AL/CR ratio				
Quantile 1	1.00 (Ref)			
Quantile 2	0.84 (0.60, 1.18)	0.309	0.61 (0.35, 1.06)	0.079
Quantile 3	0.62 (0.44, 0.89)	0.009	0.59 (0.34, 1.04)	0.070
Quantile 4	0.65 (0.46, 0.92)	0.017	0.35 (0.19, 0.66)	0.001

Per 1 increase	0.26 (0.10, 0.70)	0.007	0.04 (0.01, 0.25)	0.001
Refractive status				
Emmetropia	1.00 (Ref)			
Hyperopia	1.13 (0.75, 1.71)	0.556	1.04 (0.52, 2.07)	0.913
Mild myopia	0.75 (0.40, 1.42)	0.379	0.48 (0.15, 1.54)	0.218
Moderate myopia	0.87 (0.40, 1.89)	0.730	0.48 (0.10, 2.27)	0.358
High myopia	1.14 (0.78, 1.66)	0.510	1.27 (0.67, 2.39)	0.462
Per 1-D increase	1.04 (0.99, 1.10)	0.133	1.10 (0.99, 1.23)	0.064
Corneal diameter				
Quantile 1	1.00 (Ref)			
Quantile 2	1.27 (0.90, 1.80)	0.175	0.79 (0.44, 1.42)	0.430
Quantile 3	1.00 (0.70, 1.44)	0.991	0.92 (0.52, 1.64)	0.778
Quantile 4	0.92 (0.64, 1.33)	0.670	0.68 (0.37, 1.24)	0.211
Per 1-mm increase	0.82 (0.60, 1.11)	0.205	0.72 (0.44, 1.20)	0.207

443 *Adjusted for age, sex, duration of diabetes mellitus, HbA1c, total cholesterol, serum
444 creatinine, serum uric acid, body mass index (BMI), and mean blood pressure.
445 DR=diabetic retinopathy; VTDR=vision threatened DR; OR=odds ratio; 95%CI=95%
446 confidential interval; ACD=anterior chamber depth; CCT=central corneal thickness;
447 AL/CR ratio=axial length to corneal curvature ratio.
448 Bold indicates statistical significance.
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Figure legend

Figure 1. Graph showing the odds ratios for any diabetic retinopathy (DR) and vision threatened DR (VTDR) according to axial length. Data were fitted using a Logistic regression model adjusting for age, sex, duration of diabetes mellitus, HbA1c, total cholesterol, serum creatinine, serum uric acid, BMI, and mean blood pressure. AL was modeled using restricted cubic splines (solid line is the point estimate and dashed lines are 95% confidence limits) with 5 knots at 5%, 27.5%, 50%, 72.55, and 95% percentiles of AL distribution. The reference value is 24.0 mm.