

## 1 Frequency and Distribution of Corneal Astigmatism and Keratometry

## 2 Features: Methodology and Findings of the UK Biobank Study

3

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29

30 **Abstract**

31 **Purpose:**

32 To describe corneal astigmatism in the UK Biobank population, to look for associations with other  
33 biometric variables and socio-demographic factors, and to report the proportion with abnormal  
34 keratometry and irregular astigmatism suggestive of pathological corneal ectasias such as keratoconus.

35 **Methods:**

36 Cross-sectional data were obtained from UK Biobank ([www.ukbiobank.ac.uk/](http://www.ukbiobank.ac.uk/)). A subsample of 107,452  
37 participants from UK communities had undergone an enhanced ophthalmic examination including  
38 autorefractor keratometry (Tomey RC 5000, Tomey Corp., Nagoya, Japan). After quality control and  
39 applying relevant exclusions, data on corneal astigmatism on 83,751 participants was available for  
40 analysis. Potential associations were tested through univariable regression and significant parameters  
41 carried forward for multivariable analysis.

42 **Results:**

43 In a univariable analysis, the characteristics significantly protective against corneal astigmatism were  
44 gender (male), older age, darker skin colour and increased alcohol intake (all  $p < 0.001$ ). The parameters  
45 significantly associated with increased corneal astigmatism were older age at completion of full time  
46 education, use of UV protection and lower corrected visual acuity. After inclusion in the multivariable  
47 analysis, age, gender, age at completion of full time education, corrected visual acuity and skin colour  
48 remained significant (all  $p < 0.001$ ). Increased corneal astigmatism was also found to be significantly  
49 associated with amblyopia or strabismus. No individuals with abnormal keratometry or irregular  
50 astigmatism were reported.

51 **Conclusions:**

52 This analysis of associations with astigmatism in a large cohort of volunteers confirms previous  
53 associations including adverse associations with younger age and female gender, and identified novel  
54 associations including darker skin colour and frequency of alcohol intake. The highest risk group for  
55 corneal astigmatism were younger females of lighter skin colour, having completed full time education

56 later, with higher logMAR corrected visual acuity. We also confirmed that corneal astigmatism is a high  
57 risk factor for amblyopia and strabismus. Finally since no cases of keratoconus were identified, this  
58 would suggest that simple keratometry indices may not be sufficient for population screening of  
59 keratoconus.

## 60 Introduction

61 Uncorrected refractive error is the leading cause of moderate to severe visual impairment in all age  
62 groups globally (101.2 million individuals in 2010), and the second commonest cause of avoidable  
63 blindness in children after cataract (6.8 million individuals in 2010) [1][2]. Refractive error (ametropia), is  
64 a significant public health burden, frequently associated with worse visual acuity and higher risk of  
65 developing amblyopia (lazy-eye). Corneal astigmatism is a leading cause of refractive error in children  
66 and a significant increase in myopia as well as astigmatism has been reported in the Singaporean  
67 population[3] over the last 12 years. In a previous study, Cumberland et al [4] found that 54% of  
68 participants in the UK Biobank (UKBB) had a refractive error.

69 The two major components of refractive error in the eye are astigmatism, which is linked to the  
70 refractive properties of the cornea and the lens, and the spherical refractive error, which is additionally  
71 related to axial length of the eye. Spherical refractive error (myopia or hyperopia) can be corrected by a  
72 spherical spectacle lens. Astigmatism is caused by a corneal component and lenticular component and  
73 can in many cases be corrected by a cylindrical spectacle lens. Corneal astigmatism occurs when there  
74 are differences in the radius of curvature of the cornea in different meridians such that there is a  
75 different focal point for each meridian, with an area of intermediate focus between the two termed the  
76 conoid of Sturm[5]. In regular astigmatism the strong and weak meridians are normally at 90 degrees to  
77 each other. Regular astigmatism is usually defined according to the orientation (meridian) of the  
78 steepest radius of curvature of the cornea in relation to the horizontal axis of the cornea (0 to 180  
79 degrees). The axis of regular astigmatism is normally at 90 degrees to the steep meridian, and this angle  
80 also corresponds to the minimum radius of curvature of the cornea. Its axis defines the orientation of

81 the negative power cylindrical spectacle lens required to cancel the effect of the astigmatism. Irregular  
82 astigmatism occurs when the radius of curve of the central cornea in any one meridian varies, and the  
83 angle between the strong and weak meridians may not be 90 degrees. In irregular astigmatism, full  
84 correction with a spectacle lens is usually impossible, but a point focus can be achieved with a rigid  
85 contact lens. Irregular astigmatism can be indicative of higher-order aberrations such as keratoconus or  
86 corneal ectasia.

87 The magnitude of corneal astigmatism has been reported to increase with age[6,7] and there is a shift  
88 from the steepest corneal meridian from the vertical (with-the-rule) to the horizontal meridian (against-  
89 the-rule)[8–11]. Data on the prevalence and severity of corneal astigmatism is typically obtained from  
90 case series of patients undergoing cataract surgery[11–16], with limited data from population based  
91 cross-sectional studies or large cohort studies[17].

92 The UKBB study[18–20] recruited over 500,000 men and women aged 40 to 69 years between 2006–  
93 2010 from the general population. In 2009 the study protocol was updated to include measurement of  
94 ocular data including corneal keratometry, on a subset of these[20]. The aim of our analysis is to  
95 describe corneal astigmatism and derived variables in the UKBB population, to look for associations with  
96 other biometric variables, socio-demographic factors, and eye conditions.

97

## 98 Methodology

### 99 UKBB Participants

100 The UK Biobank participants have previously been described in detail[20]. In brief, all adults aged  
101 between 49 and 69 years old who were registered with the UK National Health Service and living within  
102 25 miles of one of the 22 participating study sites were invited to participate. From a total of 9.2 million  
103 postal invitations, 503,325 participants were recruited between 2006 and 2010 (response rate of 5.5%)  
104 and after accounting for withdrawals; data on 502,642 participants were available for analysis. All those  
105 recruited completed detailed questionnaires on their lifestyle, socioeconomic status, environment and

106 health, and had a number of physiological measures from urine, saliva and blood samples. Further  
107 information can be found on the UK Biobank online data showcase  
108 (<http://biobank.ctsu.ox.ac.uk/crystal/label.cgi>).

109

110 **Ethics**

111 All UK Biobank participants gave written, informed consent. The UK Biobank study was conducted under  
112 approval from the NHS National Research Ethics Service (Ref. 11/NW/ 0382), and anonymised data were  
113 provided from UK Biobank under application reference 10536.

114

115 **Eye measurements**

116 Six of the recruiting centres performed an ophthalmic assessment[4] that included LogMAR visual  
117 acuity, autorefraction and keratometry (Tomey RC 5000 auto-ref-keratometer Tomey Corp., Nagoya,  
118 Japan), intraocular pressure (IOP) (Goldmann-correlated and Corneal-compensated) and corneal  
119 biomechanics (both Ocular Response Analyzer, Reichert, Depew, NY, USA). In total 117,279 (23.3%) of  
120 those enrolled had an ophthalmic assessment.

121 The Tomey RC 5000 examination produced 38 autorefraction and keratometric measurements for each  
122 eye (category: <http://biobank.ctsu.ox.ac.uk/crystal/label.cgi?id=100014>). This category includes data on  
123 whether the measurement was made, and the test result for refractometry (sphere, cylinder, axis, pupil  
124 diameter) and keratometry (corneal refraction and astigmatism). Corneal astigmatism was defined as  
125 the 3mm strong meridian minus the 3mm weak meridian. The average of these two values was defined  
126 as the mean corneal power. Similarly to[4], we defined spherical equivalent as the spherical power plus  
127 half of the refractive cylindrical power.

128 The Reichert Ocular Response Analyser (Reichert Corp., Philadelphia, PA), which measures the  
129 biomechanical distortion of the cornea produced by a puff of air, yielded a further 9 types of  
130 measurements for each eye (category: <http://biobank.ctsu.ox.ac.uk/crystal/label.cgi?id=100015>). These  
131 included eye applanation, corneal hysteresis, corneal resistance factor, corneal-compensated

132 intraocular pressure, and an IOP graph for each eye. Participants who had eye surgery within the  
133 previous 4 weeks or those with possible eye infections did not have IOP measured.

134

### 135 **Self-reported eye conditions**

136 The UKBB touchscreen questionnaire allowed participants to report if they wore glasses or contact  
137 lenses, and if they had an eye disorders or eye diseases, any injury or trauma, which eye was affected  
138 and when it was diagnosed. Refractive eye conditions included astigmatism, myopia, hyperopia,  
139 presbyopia, strabismus and amblyopia. Eye diseases include diabetic retinopathy, glaucoma, cataract or  
140 age-related macular degeneration.

141

### 142 **Socio-economic status and ethnicity**

143 The Townsend deprivation index was determined using the participant's postcodes at recruitment. The  
144 Townsend deprivation index has a UK mean of zero, with negative being less deprived and positive being  
145 more deprived. Ethnicity choices included white (English/Irish or other white), Asian or British Asian  
146 (Indian/Pakistani/Bangladeshi or other Asian), black or black British (Caribbean, African, or other black),  
147 Chinese, mixed (white and black Caribbean or African, white and Asian, or other mixed ethnicity), or  
148 other ethnic group (not defined).

149

### 150 **Lifestyle and environment**

151 The UKBB touchscreen questionnaire also offered questions to participants about their lifestyle, health  
152 and environment. In particular, smoking status, alcohol intake frequency, use of sun/UV protection, skin  
153 colour without tanning, presence of diabetes. The possible questions/answers and their encoding are  
154 explained in more detail in the Table S1.

155

### 156 **Physical measures and disease**

157 Blood pressure and heart rate were measured using the HEM-70151T digital blood pressure monitor  
158 (Omron, Hoofddorp, The Netherlands). Weight was measured with the BV-418 MA body composition  
159 analyzer (Tanita, Arlington Heights, IL). Height was measured using a Seca 202 height measure (Seca,  
160 Birmingham, UK). Body mass index (BMI) was calculated as weight in kg divided by height in m<sup>2</sup>. Waist  
161 circumference at the level of the umbilicus was measured using a Wessex non-stretchable tape  
162 measure. The UKBB includes diagnoses extracted from records across all their episodes in hospital  
163 coded using the International Classification of Diseases version-10 (ICD10).

164

165 **Participant selection**

166 Of the 502642 participants in UK Biobank, 109,935 had 3mm strong or weak corneal meridian  
167 measurement values available for both eyes from which corneal astigmatism measurements could be  
168 derived. Participants were excluded if they had any of the following: previous laser refractive eye  
169 surgery (n=7440), previous eye surgery (for cataract, glaucoma or corneal graft) (n=8051), unreliable  
170 3mm asymmetry index (n=12,910) or an unreliable keratometry result (n=6916). This left a total of  
171 83,751 individuals for further analysis.

172

173 **Mean corneal power and axis of astigmatism**

174 We tested the association of mean corneal power and axis of astigmatism with age and gender for both  
175 eyes. The axis of astigmatism was defined as the angle of the strong meridian minus the angle of the  
176 weak meridian. The axis of astigmatism was either 90 or -90 degrees for all individuals; this implies that  
177 no irregular astigmatism was detected among our participants.

178

179 **Corneal astigmatism, irregular corneal astigmatism and keratoconus**

180 We explored the distribution of astigmatism and compared this to previously published studies. We  
181 then looked for patients with features suggestive of keratoconus such as mean corneal power exceeding  
182 48, 49 or 50 dioptres[21,22]. The Tomey RC 5000 auto-ref-keratometer also provided an index irregular

183 corneal astigmatism (normal, doubtful, high possibility of abnormality) and we therefore further refined  
184 our search for keratoconus using a steep corneal meridian of 48D or more, in the presence a “doubtful”  
185 or “high possibility of abnormality” 3mm index of irregular astigmatism.

186 **Statistical associations with corneal astigmatism, mean corneal power**

187 Univariable linear regression and multivariable regression analysis models were applied to investigate  
188 predictors of corneal astigmatism. Variables were re-coded according to Table S1. To account for  
189 multiple testing, a Bonferroni corrected P value threshold of  $< 0.001$  was applied to avoid false-positives  
190 due to the large number of tests carried out. Only parameters that showed significant association in the  
191 univariable analysis were included in the multivariable analysis. Since we found that corneal astigmatism  
192 measurements were asymmetric, with left eye having on average higher corneal astigmatism than right  
193 eye (Figure S1.a), we repeated statistical analysis in both eyes and only reported parameters which were  
194 consistently significantly associated in both eyes. We also repeated the statistical associations with a  
195 log-scaled corneal astigmatism variable since the p-value calculation in a linear regression assumes a  
196 normally distributed response variable (Figure S2.a.b). All analyses were performed using R statistical  
197 software version 3.2.3. The code is available at <https://github.com/pontikos/UKBB/>.

198 **Results**

199 **Participant selection and distribution of corneal astigmatism**

200 Of the 502,642 UKBB participants who had keratometry measures, after exclusions, 83,751 participants  
201 were selected for the purpose of this study. Of these, 36,490 (44%) were male. Ethnicity was 90% white,  
202 3.44% Asian, 3.01% black, 0.89% mixed and 0.41% Chinese (Table 1). In the right eye, 69%, 46%, 29%,  
203 11% and 5% had corneal astigmatism greater than or equal to 0.5, 0.75, 1.0, 1.5 and 2.0 dioptres  
204 respectively, and in the left eye, 69%, 46%, 30%, 11% and 5% (Figure S2.c). Anisometropia of less than 1  
205 dioptre was found in 95% of individuals and a difference of more than 2 dioptres was found in the 0.83%  
206 of eyes. After stratification of participants by age group (decade) and gender, corneal astigmatism was

207 found to decrease with age and to be on average higher in females than in males across age groups  
208 (Table 2).

209

210 **Association of mean corneal power, axis of astigmatism and anisometropia with age and**  
211 **gender**

212 Older age was significantly associated with increased mean corneal power in both eyes, with an average  
213 increase of 0.015 (0.014 to 0.016) dioptres per year (Figure S3.b). Axis of astigmatism changed with  
214 older age from with-the-rule (90 degrees) to against-the-rule (-90 degrees) (Figure S3.c). Anisometropia  
215 was slightly more prevalent in males than in females (0.98% vs 0.71%).

216

217 **Irregular corneal astigmatism and keratoconus**

218 The number of individuals with a strong 3mm corneal meridian greater than 48, 49 and 50 dioptres, in  
219 the presence of “doubtful” or “high possibility of abnormality” index of irregular corneal astigmatism in  
220 both eyes, were 132, 46 and 5 respectively (less than 0.16% of the cohort). However, none of these  
221 individuals had a keratoconus diagnosis (H18.6) in the UKBB. Of the 502,642 in the UKBB, only 9 had a  
222 keratoconus diagnosis, none of which were in our filtered list of 83,751 participants. Four of these  
223 individuals were filtered out because they previously had surgery, the other five were not included  
224 because they had no keratometry values.

225

226 **Univariable and multivariable analysis of corneal astigmatism**

227 By order of magnitude, the univariable analysis found that - decreased corrected visual acuity, Asian and  
228 black ethnicity, male gender, darker skin colour, decreased use of UV protection, increased alcohol  
229 intake, increased corneal corrected IOP, older age and younger age completed full-time education –  
230 were significantly associated with decreased corneal astigmatism (Table 3.1 and Table S2.1). After  
231 including these variables in the multivariable analysis (Table 3.2 and Table S2.2), the following  
232 parameters remained significantly associated with decreased corneal astigmatism: decreased corrected

233 visual acuity, male gender, darker skin colour, increased alcohol intake, older age and younger age  
234 completed full-time education.

## 235 Discussion

### 236 **Distribution of corneal astigmatism in the UKBB compared to other cohorts**

237 The distribution of astigmatism in the large population reported in this study supports evidence from  
238 previous smaller studies, both in the UK and worldwide, in pre-operative patients [X1] and from large  
239 consortiums such as CREAM (n=55,177)[17]. We found that 69%, 29%, 11% and 5% had corneal  
240 astigmatism  $\geq 0.5$ , 1.0, 1.5 and 2.0 dioptres respectively. These are slightly lower than values reported  
241 from a recent series of 110,468 cataract pre-operative eyes [23] where 78%, 42%, 21% and 11% having  
242 corneal astigmatism  $\geq 0.5$ , 1.0, 1.5 and 2.0 dioptres respectively. A study of 1,230 eyes undergoing  
243 cataract surgery in Wales found corneal astigmatism of  $>0.5$ D in 75% in Wales[15] (N=1,230 eyes).  
244 Corneal astigmatism  $\geq 1.0$ D was found in 36% of eyes with cataract in Germany[24] (N=15,448 eyes),  
245 47% in China (N=12,449)[25] and 35% in South Korea[26] (N=2,847 eyes). Recently, Curragh et al[27]  
246 reported that 41% of eyes undergoing cataract surgery (N=2,080) in Northern Ireland had  $>1.0$ D of  
247 corneal astigmatism. However cataract surgery is usually performed in an older age group than those of  
248 the participants in the UK Biobank and these pre-operative clinical groups are not necessarily  
249 comparable to UKBB participants. A recent CREAM study[28] reported the median corneal astigmatism  
250 and median age across 22 studies (8 Asian and 14 European). The median corneal astigmatism was  
251 reported in each study and this ranged from 0.539D in the Rotterdam-II European study (N=3964, mean  
252 age=64.8), to 1.21D in the Asian Singapore Cohort Study of the Risk Factors for Myopia (SCORM) study  
253 (N=1894, mean age=10.8). Comparable studies to the UKBB in terms of age and gender demographics  
254 of the participants are the Rotterdam-III Study (N=5850 eyes, mean age=57)[29], the Singapore Chinese  
255 Eye Study (SCES-610K) (N=1106 eyes, mean age=57.6)[30], the Gutenberg Health Study (GHS-1) study  
256 (N=4796 eyes, mean age=55.9)[31] which reported a median corneal astigmatism of 0.618D, 0.703D and  
257 0.65D respectively. This is comparable to the UKBB median corneal astigmatism of 0.71D.

258

259 **Modelling of corneal astigmatism**

260 In the multivariable analysis, parameters known to be strongly associated with gender, such as height  
261 and weight (Table 3.2), were no longer significantly associated with corneal astigmatism. The adjusted  
262 R-squared of the multivariable regression was remarkably low at 0.015 which highlights that there are  
263 many other unobserved variables which influence corneal astigmatism.

264

265 **Corneal astigmatism, amblyopia and strabismus**

266 The number of eyes affected by amblyopia and strabismus in the UKBB are 2483 and 1052 respectively.  
267 Corneal astigmatism is highest in eyes affected by amblyopia and strabismus (Figure S4.a). This confirms  
268 that, as previously reported by [32,33], uncorrected high corneal astigmatism is a significant risk factor  
269 for amblyopia (OR=1.98 (1.87 to 2.09), P<0.001) and strabismus (OR=1.73 (1.59 to 1.88), P<0.001)  
270 (Figure S4.b).

271

272 **Corneal astigmatism and IOP measurements**

273 Of interest, corneal hysteresis, which measures the cornea's ability to absorb and dissipate energy, was  
274 not found to be associated with corneal astigmatism in the univariable or multivariable  
275 analysis. However when corneal astigmatism was log-transformed, a small but positive significant  
276 association was detected for both eyes in the univariable analysis (Table S2.1) but not in the  
277 multivariable analysis (Table S2.2). These results suggest that the ability of the cornea to absorb and  
278 dissipate energy (corneal hysteresis) was not strongly significantly associated with corneal astigmatism.  
279 However, corneal hysteresis is significantly positively associated with mean corneal power in both eyes.  
280 In the univariable analysis (Table 3.1), we found a small but significant negative association between  
281 corneal corrected intraocular pressure and corneal astigmatism in both eyes, however in the  
282 multivariable analysis the association was no longer significant in both eyes (Table 3.2).

283

284 **Corneal astigmatism and gender**

285 Our study confirms as previously reported by[25], that corneal astigmatism is higher in females than in  
286 males even after adjusting for weight and height (Table 3.2). Males have on average 0.06D less corneal  
287 astigmatism in right eye than females and 0.08D less in left eye.

288

289 **Corneal astigmatism and age**

290 Corneal astigmatism decreases significantly with age by an average 0.06D in both eyes per decade even  
291 after controlling for weight and height (Table 3.2). This is contrary to what is reported by[34] namely  
292 that the level of corneal astigmatism is relatively constant across age. As reported by Shah et al in a  
293 previous UKBB analysis[34], we did confirm the stronger association between age and refractive  
294 (cylindrical) astigmatism in right eye ( $B=0.011$  (0.010 to 0.011),  $P<.001$ ) and left eye ( $B=0.010$  (0.09 to  
295 0.010),  $P<0.001$ ) (Figure S3.a). The fact that refractive astigmatism increases with age but that corneal  
296 astigmatism decreases with age suggest that lenticular astigmatism may be driving the increase in  
297 refractive astigmatism, possibly due to the onset of presbyopia. We also found that age is significantly  
298 positively associated with corneal power both in right ( $B=0.015$  (0.014 to 0.016),  $P<0.001$ ) and left eye  
299 ( $B=0.015$  (0.014 to 0.016),  $P<0.001$ ) (Figure S3.b). We also observed that the axis of astigmatism changes  
300 with age from with to against the rule (Figure S3.c) significantly in the right eye but not in the left eye.

301  
302 **Corneal astigmatism and age completed full-time education**

303 We discovered a significant positive association between age at which full-time education was  
304 completed and corneal astigmatism ( $B=0.006$  (0.004 to 0.008)). This result was consistent with  
305 participants with self-reported astigmatism finishing full-time education later than other participants  
306 (Figure S4.c). Interestingly, this relationship was not observed in individuals with myopia (Figure S4.c). In  
307 fact, recent evidence suggests that myopia is perhaps not linked as much to poor lighting conditions and  
308 near work[35], but rather to earlier life exposures [36].

309

310 **Corneal astigmatism, ethnicity and skin colour**

311 Asian and black ethnicities appear to be significantly protective for corneal astigmatism in both eyes  
312 according to the univariable analysis (Table 3.1 and S3.1), but are no longer significant in the  
313 multivariable analysis (Table 3.2 and S3.2) for log transformed corneal astigmatism. However skin colour  
314 remains significantly associated with darker skin being protective ( $B=-0.032$ ) (Table 3.2 and S3.2). This  
315 relationship can also be clearly seen in Figure S5. The link between corneal astigmatism and deficiency in  
316 melanin production has been previously reported for albinism[37] but we have now also reported this  
317 association in a healthy population via darkness of skin showing that darker skin and hence increased  
318 melanin production appears protective for corneal astigmatism.

319

320 **Corneal astigmatism and alcohol intake**

321 Alcohol intake is significantly protective for corneal astigmatism according to the univariable and  
322 multivariable analysis. In particular, the group that drink nearly every day has the lowest corneal  
323 astigmatism. This is surprising due to the negative consequences of alcohol abuse on eye  
324 conditions. However on closer inspection it appears that the group that drinks nearly every day in the  
325 UKBB consists primarily of men in the 65+ age group; 55% of men drink every day in this study vs 44% of  
326 women. It then follows that alcohol intake effect is difficult to decouple from gender due to the high  
327 correlation. In fact, the three-way interaction between alcohol-intake, age and gender is illustrated in  
328 Figure S6, with “never-drinkers” and “daily drinkers” showing a clear interaction.

329

330 **Corneal astigmatism and keratoconus**

331 We looked for participants with features suggestive of keratoconus such as mean corneal power  
332 exceeding 48, 49 or 50 dioptres[21,22] and also explored the Tomey RC 5000 auto-ref-keratometer  
333 specific parameter of irregular corneal astigmatism as a proxy for a keratoconus diagnosis. However  
334 none of the 83,751 participants had a prior diagnosis of keratoconus (H18.6). In the entire UKBB, only 9  
335 participants had a keratoconus diagnosis, none of these were in our included list of 83,751 participants

336 due to previous exclusion as detailed earlier. This number (1:10,000) is a factor of 10 less than  
337 population-based estimates from North Europe [38]. Based on these findings, identification of  
338 keratoconus in cross-sectional or population studies would appear to require corneal topography or  
339 corneal tomography map review rather than evaluation of simple keratometry indices.

340

341 **Strengths and limitations of our study**

342 The strength of this study is the large sample size of 83,751 participants and that participants were not  
343 pre-operative patients hence more representative of the general population. However due to the  
344 limited age range of the participants, between 40 and 69 years, and the voluntary nature of study  
345 participation, the age distribution is not representative of the UK and participants are likely to be a  
346 healthier more educated sample of the UK population. Regardless, a range of exposures and  
347 characteristics are likely to have been captured due to the sample size and so the results can still be  
348 applicable to other populations.

349

350 **Conclusion**

351 In conclusion, this analysis of associations with astigmatism in a large cohort confirms previous  
352 associations including age and gender, and identified novel associations including age completed full  
353 time education, skin colour and alcohol intake. The highest risk group for corneal astigmatism were  
354 younger females of lighter skin colour, having completed full time education later, with higher corrected  
355 visual acuity. It was also confirmed that uncorrected corneal astigmatism is a high-risk factor for  
356 amblyopia and strabismus.

357

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366

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369

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**Table 1: Distribution of participants in the UKBB across the different variables. Mean/sd or percentage of the 83,751 study participants in the UKBB by sex.**

variable	total	males	females	P value
Age, years	57.1 (8.1)	57.3 (8.2)	56.9 (8.0)	<.001
Ethnicity white	92.1	92.2	92	<.001
Ethnicity asian	3.5	4	3.1	
Ethnicity black	3.1	2.8	3.3	
Ethnicity mixed	0.9	0.7	1	
Ethnicity chinese	0.4	0.3	0.5	
Age completed full time education	16.9 (2.5)	16.9 (2.7)	16.8 (2.3)	<.001
Skin colour *	2.3 (0.9)	2.4 (0.9)	2.3 (0.9)	<.001
Use of UV protection	2.7 (0.9)	2.5 (0.9)	2.9 (0.9)	<.001
Alcohol intake **	3.0 (1.6)	3.3 (1.5)	2.8 (1.6)	<.001
Season of assessment spring	34.6	34.7	34.6	
Season of assessment autumn	23.7	23.5	23.8	
Season of assessment winter	22.1	22.4	21.9	
Season of assessment summer	19.6	19.5	19.7	
Corneal corrected IOP, mmHg	16.1 (4.2)	16.4 (4.2)	15.9 (4.3)	<.001
Corrected Visual acuity, logMAR	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)	<.001
Corneal resistance factor	10.7 (2.3)	10.6 (2.3)	10.9 (2.4)	<.001
Corneal hysteresis	10.6 (2.3)	10.4 (2.2)	10.8 (2.3)	<.001
Height, m	168.3 (9.2)	175.7 (6.8)	162.7 (6.3)	<.001
Weight, 10 kg	77.4 (15.8)	85.5 (14.2)	71.3 (14.0)	<.001
BMI, kg/m <sup>2</sup>	27.3 (4.8)	27.7 (4.2)	27.0 (5.1)	<.001
SBP, mmHg	139.7 (19.5)	142.3 (18.3)	137.6 (20.2)	<.001
DBP, mmHg	81.9 (10.6)	83.6 (10.4)	80.5 (10.5)	<.001
Townsend deprivation index	-1.0 (3.0)	-1.0 (3.0)	-1.0 (2.9)	
Smoker: true	90.1	87.9	91.8	<.001
Smoker: false	9.9	12.1	8.2	
Age Asthma Diagnosed, self reported	30.5 (18.5)	27.3 (19.1)	32.7 (17.7)	<.001
Diabetes, doctor diagnosed: true	94.8	93.1	96.1	<.001
Diabetes, doctor diagnosed: false	5.2	6.9	3.9	

D = dioptres; \* Skin colour is coded as: very fair=1, fair=2, light olive=3, dark olive=4, brown=5, black=6;

\*\* Alcohol intake is coded as: never=0, special occasions=1, one to three times a month=2, once twice a week=3, three four times a week=4, daily=5.

**Table 2: Mean, standard deviation, 25th and 75th percentile of right and left corneal astigmatism by age and gender of the 83,751 study participants in the UK BioBank. Corneal astigmatism decreases slightly with age and is slightly higher in females than in males. Left corneal astigmatism tends to be consistently higher than right corneal astigmatism (as illustrated in Figure S1.a).**

cohorts	right eye 3mm corneal astigmatism	left eye 3mm corneal astigmatism
Men 40-49	0.861 (0.683, 0.430-1.090)	0.864 (0.674, 0.440-1.100)
Men 50-59	0.810 (0.640, 0.400-1.030)	0.818 (0.646, 0.400-1.050)
Men 60-69	0.788 (0.619, 0.390-1.000)	0.792 (0.627, 0.400-1.000)
Women 40-49	0.923 (0.625, 0.510-1.190)	0.942 (0.638, 0.520-1.200)
Women 50-59	0.890 (0.611, 0.470-1.140)	0.915 (0.645, 0.490-1.170)
Women 60-69	0.850 (0.619, 0.440-1.090)	0.855 (0.619, 0.440-1.090)
Total 40-49	0.896 (0.652, 0.470-1.150)	0.908 (0.655, 0.480-1.160)
Total 50-59	0.857 (0.624, 0.440-1.100)	0.875 (0.647, 0.450-1.120)
Total 60-69	0.822 (0.620, 0.420-1.050)	0.827 (0.623, 0.420-1.050)
All	0.848 (0.627, 0.430-1.090)	0.857 (0.636, 0.440-1.100)
Difference (left-right)		-0.009 (-0.026 0.01), P=0.340730

**Table 3.1. Results of univariable regression in 83,751 study participant in the UKBB for right and left eye corneal astigmatism. Significant associations are highlighted in bold.**

Description	Right eye univariate beta (95% CI)	P value	Left eye univariate beta (95% CI)	P value
<b>Age, years</b>	<b>-0.004 (-0.004 to -0.003)</b>	<b>&lt;0.001</b>	<b>-0.004 (-0.005 to -0.004)</b>	<b>&lt;0.001</b>
<b>Sex (Ref = F)</b>	<b>-0.070 (-0.079 to -0.061)</b>	<b>&lt;0.001</b>	<b>-0.080 (-0.089 to -0.071)</b>	<b>&lt;0.001</b>
<b>Ethnicity (Ref=white)</b>				
asian	<b>-0.081 (-0.104 to -0.058)</b>	<b>&lt;0.001</b>	<b>-0.102 (-0.126 to -0.079)</b>	<b>&lt;0.001</b>
black	<b>-0.061 (-0.086 to -0.036)</b>	<b>&lt;0.001</b>	<b>-0.068 (-0.093 to -0.043)</b>	<b>&lt;0.001</b>
mixed	-0.017 (-0.063 to 0.028)	0.45	-0.018 (-0.064 to 0.028)	0.447
chinese	-0.022 (-0.089 to 0.044)	0.515	-0.040 (-0.108 to 0.027)	0.243
<b>Age completed full time education</b>	<b>0.004 (0.002 to 0.006)</b>	<b>0.001</b>	<b>0.005 (0.003 to 0.007)</b>	<b>&lt;0.001</b>
<b>Skin colour, lighter to darker*</b>	<b>-0.029 (-0.034 to -0.024)</b>	<b>&lt;0.001</b>	<b>-0.030 (-0.035 to -0.026)</b>	<b>&lt;0.001</b>
<b>Use of UV protection</b>	<b>0.017 (0.013 to 0.022)</b>	<b>&lt;0.001</b>	<b>0.016 (0.011 to 0.020)</b>	<b>&lt;0.001</b>
<b>Alcohol intake, never to daily**</b>	<b>-0.009 (-0.012 to -0.006)</b>	<b>&lt;0.001</b>	<b>-0.009 (-0.012 to -0.007)</b>	<b>&lt;0.001</b>
Season of assessment (baseline=spring)				
autumn	-0.005 (-0.016 to 0.006)	0.387	-0.011 (-0.023 to 0.000)	0.055
winter	-0.007 (-0.019 to 0.004)	0.212	-0.006 (-0.018 to 0.006)	0.324
summer	0.017 (0.005 to 0.029)	0.005	0.014 (0.002 to 0.026)	0.026
<b>Corneal corrected IOP, mmHg</b>	<b>-0.006 (-0.007 to -0.005)</b>	<b>&lt;0.001</b>	<b>-0.007 (-0.008 to -0.006)</b>	<b>&lt;0.001</b>
<b>Corrected Visual acuity, logMAR</b>	<b>0.384 (0.362 to 0.405)</b>	<b>&lt;0.001</b>	<b>0.421 (0.400 to 0.442)</b>	<b>&lt;0.001</b>
Corneal resistance factor	-0.003 (-0.005 to -0.002)	<0.001	-0.001 (-0.003 to 0.001)	0.35
Corneal hysteresis	0.003 (0.001 to 0.005)	0.004	0.006 (0.004 to 0.007)	<0.001
<b>Height, m</b>	<b>-0.002 (-0.002 to -0.002)</b>	<b>&lt;0.001</b>	<b>-0.002 (-0.002 to -0.001)</b>	<b>&lt;0.001</b>
Weight, 10 kg	-0.000 (-0.001 to -0.000)	0.012	-0.000 (-0.001 to -0.000)	0.044
BMI, kg/m <sup>2</sup>	0.001 (0.000 to 0.002)	0.021	0.001 (0.000 to 0.002)	0.011
<b>SBP, mmHg</b>	<b>-0.001 (-0.001 to -0.001)</b>	<b>&lt;0.001</b>	<b>-0.001 (-0.001 to -0.001)</b>	<b>&lt;0.001</b>
DBP, mmHg	-0.001 (-0.001 to -0.000)	0.001	-0.001 (-0.001 to -0.000)	<0.001
<b>Townsend deprivation index</b>	<b>0.003 (0.001 to 0.004)</b>	<b>&lt;0.001</b>	<b>0.003 (0.002 to 0.005)</b>	<b>&lt;0.001</b>
Smoker (baseline = false)	-0.011 (-0.025 to 0.004)	0.144	-0.012 (-0.026 to 0.003)	0.112

Age Asthma Diagnosed, self reported	-0.001 (-0.002 to -0.000)	0.014	-0.001 (-0.002 to -0.000)	0.014
Diabetes, doctor diagnosed (baseline = false)	-0.023 (-0.042 to -0.004)	0.018	-0.006 (-0.025 to 0.014)	0.561

D = dioptres; \* Skin colour is coded as: very fair=1, fair=2, light olive=3, dark olive=4, brown=5, black=6;

\*\* Alcohol intake is coded as: never=0, special occasions=1, one to three times a month=2, once twice a week=3, three four times a week=4, daily=5.

**Table 3.2. Results of multivariable regression in 83751 study participant in the UKBB for right and left eye corneal astigmatism. Only parameters that were significant in the univariable regression were included in the multivariable regression. Significant associations are highlighted in bold.**

Description	Right eye multivariate beta (95% CI)	P value	Left eye multivariate beta (95% CI)	P value
<b>Age, years</b>	<b>-0.006 (-0.006 to -0.005)</b>	<b>&lt;0.001</b>	<b>-0.006 (-0.006 to -0.005)</b>	<b>&lt;0.001</b>
<b>Sex (Ref = F)</b>	<b>-0.058 (-0.075 to -0.042)</b>	<b>&lt;0.001</b>	<b>-0.082 (-0.099 to -0.066)</b>	<b>&lt;0.001</b>
Ethnicity (Ref=white) asian	-0.043 (-0.083 to -0.003)	0.034	-0.083 (-0.124 to -0.043)	<0.001
black	0.003 (-0.043 to 0.049)	0.896	-0.033 (-0.079 to 0.014)	0.165
mixed	-0.071 (-0.133 to -0.009)	0.025	-0.030 (-0.092 to 0.033)	0.356
chinese	-0.100 (-0.201 to 0.002)	0.054	-0.085 (-0.186 to 0.017)	0.102
<b>Age completed full time education</b>	<b>0.006 (0.004 to 0.008)</b>	<b>&lt;0.001</b>	<b>0.007 (0.005 to 0.009)</b>	<b>&lt;0.001</b>
<b>Skin colour, lighter to darker*</b>	<b>-0.032 (-0.041 to -0.023)</b>	<b>&lt;0.001</b>	<b>-0.027 (-0.036 to -0.018)</b>	<b>&lt;0.001</b>
Use of UV protection	0.010 (0.003 to 0.016)	0.003	0.003 (-0.004 to 0.009)	0.379
<b>Alcohol intake, never to daily**</b>	<b>-0.007 (-0.010 to -0.003)</b>	<b>&lt;0.001</b>	<b>-0.007 (-0.011 to -0.003)</b>	<b>&lt;0.001</b>
Corneal corrected IOP, mmHg	-0.004 (-0.007 to -0.001)	0.009	<b>-0.006 (-0.007 to -0.004)</b>	<b>&lt;0.001</b>
<b>Corrected Visual acuity, logMAR</b>	<b>0.441 (0.413 to 0.469)</b>	<b>&lt;0.001</b>	<b>0.476 (0.449 to 0.504)</b>	<b>&lt;0.001</b>
Corneal resistance factor	-0.009 (-0.019 to 0.002)	0.096		
Corneal hysteresis	0.003 (-0.009 to 0.015)	0.621	-0.003 (-0.006 to -0.001)	0.019
Height, m	-0.000 (-0.001 to 0.001)	0.65	0.001 (-0.000 to 0.001)	0.203
SBP, mmHg	-0.000 (-0.000 to 0.000)	0.773	-0.000 (-0.001 to 0.000)	0.12
DBP, mmHg	0.001 (0.000 to 0.002)	0.022	0.001 (0.000 to 0.002)	0.024
Townsend deprivation index	0.002 (0.000 to 0.004)	0.018	0.002 (0.000 to 0.004)	0.02

D = dioptres; \* Skin colour is coded as: very fair=1, fair=2, light olive=3, dark olive=4, brown=5, black=6;

\*\* Alcohol intake is coded as: never=0, special occasions=1, one to three times a month=2, once twice a week=3, three four times a week=4, daily=5.

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